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# Professional Secrecy and Privileged Communication in Medical Practice

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**DOI:** *https://doi.org/10.51273/esc22.25183-editorial1*

***"To be trusted is a greater compliment than being loved."* - (George MacDonald)**

A man who is known to be good at keeping secrets is one who has greater esteem in the society. This ideal image of a noble man's relation to his society is the basic description of what a medical healthcare practitioner's association should be with each and every one of his patients.

Doctor-patient "interaction" falls under **"implied contract"** which starts when the patient agrees to receive treatment and medical practitioner agrees to provide it. The situation is governed under **"common law"**. When both parties mutually consented then both are bound for implied contractual obligations.

**Medical practitioners 's obligations are two, firstly to apply the skill with the competence of his own claim and to exercise reasonable carefulness towards his patient during professional work. Secondly, to maintain "professional secrecy".**

To that someone who believes medical person to be "**Messiah**", the least they deserve is utmost loyalty towards their cause which also includes respecting their confidentiality concerning any detail they'd like to keep private. Islam also teaches us to be always trustworthy and not the opposite. When someone confides in you, they are handing you over a sacred object and you have promised to fulfill their covenant by not losing it.

Allah, the Most Beneficent commands; ***"And fulfill (every) covenant. Verily, the covenant will be questioned about."*** **– Surah Al Isra' (17:34)**

So far we've solely taken an ethical approach to this discussion, but if laws concerning the profession are included as well; the term **"Professional Secrecy"** is what it ought to be called. The doctor being the **'professional'** by the book cannot unveil a client's information. (Whether it be personal or seemingly not). Any particulars about the patient should be safeguarded by the physician as a part of his humanitarian duty, even after his client has died. Not surprisingly, every doctor is under an ethical oath to withstand this standard as well.

It states, ***"What I may see or hear in the course of the treatment or even outside of the treatment in regard to the life of men, which on no account one must spread abroad, I will keep to myself, holding such things shameful to be spoken about."***

**– Hippocrates (460-370 B.C.)**

The same is also stated in the **Declaration of Geneva 1948;**

***"I shall respect the secrets confided in me, even after the patient has died."***

The **International Code of Medical Ethics** was amended in Venice in 1983, it resolved;

**"A physician shall preserve absolute confidentiality on all he knows about his patient even after the patient is dead."**

The **WHO** also put forward certain guidelines regarding Medical Confidentiality, i.e.

- **All information must be kept confidential.**
- **Information can only be disclosed if the patient gives explicit consent, or if the law specifically provides permission to disclose.**

Similar sentiments are expressed in the **"Code of Ethics"** formulated by the **Pakistan Medical & Dental Council (PMDC) now Pakistan Medical Commission**.

It is quite significant to note here its role in the formation of our beloved homeland Pakistan. During the era of **Quaid-e-Azam** (RA) emaciating to just skin & bones, he had a personal Parsi physician, **Dr. Patel** at Bombay. In the course of medical examination, he kept Quaid's illness in absolute secrecy–he used to get Quaid's chest X-rays done personally and destroy the films. Had **Lord Mount Batten** come to know the probable mortality of his illness at that time – he would have delayed the process of independence and Pakistan would not have come into existence. This example left us the ideal standards of morality, with an excellent

representation of the substantial consequences that may result if a patient's particulars are left to be invaded.

Professional Secrecy also includes the assurance of the fact that the hospital shall guarantee the safe keeping of his details, & **if not** the doctor's insurance would have to be sacrificed, as such negligence is a direct violation of the patient's right to the maintenance of professional secrecy. Which means the client can sue the target physician or any other healthcare worker & the practitioner can even get their license to practice medicine taken away forever. Such punishments signify the vitality of this legal & ethical code, since it relieves the patient of any reluctance he might have disclosing personal details which may affect his reputation, job, personal or social life. This also helps the physician in getting a complete history from his client which eases the diagnostic pathway to administering full treatment.

In Western countries, this important principle is practiced with great concern. For instance, the US has designed a **HIPAA** law solely to provide privacy standards to protect the patient's medical records & other health info provided to health plans. The law carries strict penalties & a risk of devastating law suits. The scenario in Pakistan is somewhat difference no necessary actions are taken to ensure the confidentiality in the first place. Doctors and paramedical staff discuss the patient's condition openly with their fellow doctors in clinics, cafeterias or elsewhere, forgetting the fact they are disclosing their patient's secret publically.

This practically highlights the amount of damage that may occur on the trust of a sick person who's had to face such violation which makes it clear that in spite of being one of the most traditional moral concepts in health care, secrecy is still one of the less respected principles. This is particularly worrying considering our times of intense exposition of privacy. Today's world of social networking has given a maximum invasive window to the world of secrets, as opposed to the key-hole apertures to information back in the days of photo albums and typewriters. Almost anyone can grab any required information, be it illegal to & more importantly transfer it to the rest of the world in the blink of an eye. Hundreds of people in each country have been violated in the same way; let it be an intentional act of criminal defamation or an accident, forever shattering their esteemed reputation in the community (in the worst case scenario) which can never be undone. Pakistan is facing the same tragedy with no one to stop these trouble mongers misusing their social media & ruining lives every day.

As much as we've emphasized on the importance of upholding professional secrecy, there are some circumstances in which disclosing that same private info is the ethically superior act and is also within the circle of law & order of the country. Such divulgence, which is specifically to the concerned authority, also makes them a confidant of the patient whose shoulders would carry the same burden of duty regarding preservation of the patient's data. This disclosure is known as **"privileged communication."**

Such a privilege can be claimed, disclosure of professional secrets justified, only if made in good faith & with caution; and is not a product of some other incentive or isn't driven by jealousy, revenge or maliciousness, and to ensure it is least embarrassing to the patient, as in the following circumstances:

**1. In The Interest of the Patient:**

- Referral to **health personnel** who assists in the clinical management.
- **Parents/guardian**, when there is a,
  - Patient who refuses to carry out treatment
  - Patient who has suicidal tendencies
  - Psychopath with violent anti-social tendencies.
  - Minor.
  - Insane person

**2. In The Interest of Public Welfare:**

Doctors have the ***qualified privilege*** to notify the proper authorities in situations where the interest of the community is superior to that of an individual & the "greater good" of the society is at risk. For instance,

a) Patients of **infectious diseases** like TB or typhoid are unfit to serve drinks to the public or be a hotel waiter.

b) **Hypertensiv**e or **brittle diabetes** patients being in charge of a public vehicle like school buses, is highly unsafe.

c) A pilot who is **colour blind** or **epileptic** is not fit for this job.

d) A person suffering from a **communicable disease** should be prohibited from entering swimming pools or contracting a marriage until cured.

e) Reporting of all suspected cases of **child**

**abuse** (physical, sexual or emotional) & protecting the child from further harm.

In all such state of affairs, it is a moral and legal duty of the physician to make known the confidential info to the people at threat or to the authorities that'll take necessary actions.

**3. Statutory Duty of the Physician:**

Doctors cannot withhold professional secrets in cases where he has a statutory duty to the public health authorities or the state. He must notify births, deaths or cases that pose a danger to the general public e.g. food poisoning from a restaurant or contamination of public drinking water. He must also notify the police cases of homicidal poisoning coming under his observation.

**4. Responsibility in Criminal Matters:**

If a practitioner is called to treat a patient with gunshot wounds or stab injuries, he may likely be lead to believe either his client is a **victim to** or **responsible of** a serious crime such as, murder, robbery, jail breaking etc. The doctor would be wrong in hiding such evidence and is duty bound to report it to the concerned authorities. **Criminal abortions** should also be documented. **Suicide** for us as Muslims is a religious offence, therefore a mere attempt to take one's own life shall be dealt with under section **325 PPC**, according to which it is a crime & punishment is simple imprisonment for a term which may extend to 1 year, or a fine, or both.

**5. In The Interest of the Patient's Family:**

· The partner of a person having a fatal STD (like AIDS) should be informed.

· Responsibility to warn only the parents or guardians, if they find in their patients a tendency to any violent act e.g. suicide or homicide.

**6. Courts of Law & the Parliament:**

Doctors have the ***absolute privilege*** to communicate to courts of law and the parliament when asked to do so. Refusal to comply may amount to contempt of court. In such a situation, it is made sure only those having absolute authority to know the information get handed it over & it is safe from others.

**7. Disclosure in Self Interest:**

Professional secrecy only lasts when the client hasn't sued his physician.e.g. if a patient sues his surgeon for a medical mistake, the surgeon can disclose the particulars of his procedure to defend himself in a court of law.

**8. Medical Teaching, Research & Audit:**

A doctor can report a case without revealing the patient's identity.

**9. Insurance Companies:**

· The medical examination for taking out an insurance policy is a **voluntary act** therefore consent is implied.

· Should not give information to any Insurance Company about a patient's past medical history, if the patient has consulted him before.

**10. Medical Records:**

· Medical records **belong to the hospital authority** and not to the doctor unless in the case of private patients.

If records are called for by Court the hospital authority must submit them confidentially

· Records **should not be given to lawyers** without prior consultation with the legal representatives of the hospital when legal action concerning negligence of medical or nursing staff in concerned.

· Records **should not be given to employers/insurance companies** without the **consent of the patient** or if dead/incapacitated without consent of next of kin.

Thus; **nobility, honesty, kindness** & **commitment to their duties** are the key morals that distinguish a person in a white coat from the rest of humanity. The burden lies on us to keep the sacred bond with our patients safe and polished, and be professionally alert in everything we say and do. Since trust and respect are both sides of the same coin, you can't have one without the other; safeguarding private info is a major concern that has to be looked into and paid more attention in Pakistan. Only then can we glue back the broken ties between our sick society and doctors, while simultaneously eradicating the paradigms that have lead to make our people believe that doctors are nothing more than 'butchers'. **PMDC** definitely needs to make more efforts for the implementation of this cause & any acts against it need to be condemned seriously.

# Hepatitis C treatment- Light at the End of the Tunnel

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Hepatitis C viral infection is one of the common communicable diseases in our country as well as in other developing world. It stands out as a top cause of chronic liver diseases, including chronic hepatitis, cirrhosis and hepatocellular carcinoma. In our local language, it is commonly called as "Black jaundice" or "Kaala Yarqan".

According to WHO, Globally an estimated 58 million people have chronic hepatitis C virus infection, with about 1.5 million new infections occurring per year. There are an estimated 3.2 million adolescents and children with chronic hepatitis C infection.[1] Approximately, 6% population of Pakistan is infected with HCV.[2]

WHO organizes the annual World Hepatitis Day campaign (as 1 of its 9 flagship annual health campaigns) to increase awareness and understanding of viral hepatitis. For World Hepatitis Day 2022, WHO focuses on the theme "Bringing hepatitis care closer to you" and calls for simplified service delivery of viral hepatitis services, bringing care closer to communities.

Acute hepatitis C is less common and usually is asymptomatic. A large proportion of infected people silently pass on to chronic hepatitis C disease with minimal generalized and non-specific symptoms, years before it is diagnosed. Diagnosis is incidentally during routine investigations or when investigated for one of the serious complications. People may get infected through a multitude of ways but the commonest being via infected syringes, instruments or transfusion of blood & its products. Barbers, quacks, tattooists, street healers and nose or ear piercing artists; may also be responsible through reuse of unsterilized razors and instruments etc. The diagnostic approach starts from screening tests, antibodies detection through ELISA, qualitative & quantitative Polymerase chain reaction (PCR) and Genotyping.

About two decades ago, when treatment was first made available, it was very much costly and accompanied with a lot of adverse effects and very low successfull cure rate. Relapses were also very common. The mainstay was a combination of Interferon injections and oral Ribavirin. There was a big fear of the adverse effects that mostly people were reluctant for this treatment option. Interferon injections which initially were given on alternate days changed into once weekly, but tolerability remained difficult. Patients either because of the cost or by the observation among other patients who had difficult time during treatment course were reluctant and in many cases used to accept this disease but not the treatment. Serious adverse effects of these regimens ranged from constitutional symptoms, depression, suicidal inclinations, hypothyroidism and serious haematological derangements.

In the recent times new medications called Direct-acting antiviral (DAA) like Sofosbuvir, Daclatasvir, Ledipasvir, Velpatasvir etc are available worldwide. Compared to the drugs used in the past like interferon and ribavirin, currently available DAAs are given for shorter duration and are tolerated in much better way due to negligible adverse effects. Over 95% of the patients treated with DAAs are cured, thereby reducing the risk of death from liver cancer and cirrhosis. The cost of these drugs is also decreasing gradually because of competitive environment among pharmaceuticals and is now in the range of most of the patients. Newer DAAs are effective

against all genotypes. Till date no vaccine is available for HCV, so the only effective strategy would be prevention of the spread of infection through awareness & education, early diagnosis and then early treatment. By this we can actually reduce the burden of this potentially deadly disease. The newer drugs are the only hope in the gloomy lives of Hepatitis C patients and the light at the end of the tunnel.

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# Effect of Probiotics on Rotavirus and Non-Rotavirus Diarrhea in Infants: Randomized Controlled Trial

**Fariha Ahmad Khan,[1] Zoobia Irum,[2] Muhammad Zeeshan Khan,[3] Neelofar Yousaf,[4] Mariyam Iftikhar Piracha,[5] Sarah Zaheer[6]**

**Abstract**

**Objective:** In this trial, we have observed efficacy of two different probiotics in Rotavirus and non-Rotavirus diarrhea in infants of 6 months to 12 months.

**Method:** The study was done to observe efficacy of two different probiotic strains in Rotavirus and non-Rotavirus diarrhea in infants. The study included the infants suffering from acute severe diarrhea. 105 infants were selected and they were divided randomly into three groups. There were 35 infants in one group. The samples of stool were sent to microbiology lab for Rotavirus testing. The treatment plan was standard treatment of diarrhea for infants in group A. The treatment plan for infants of group B and group C included same standard management of diarrhea, in addition they also received probiotics Enterococcus faecium SF68 and Saccharomyces boulardii respectively.

**Results:** There was reduction in stool output and improvement in consistency of stool in infants of group B and C as compared to infants of group A. There was decrease in stool frequency in non-Rotavirus diarrhea in infants of group B and C while there was no significant difference between groups regarding Rotavirus diarrhea.

**Conclusion:** Probiotics helped to decrease the stool output in non-Rotavirus diarrhea. There was not any significant difference in groups regarding Rotavirus diarrhea.

**Keywords:** Rotavirus, Non-Rotavirus, Saccharomyces boulardii, Enterococcus faecium Sf68

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## Introduction

Diarrhea is the major cause of death in children below five years of age worldwide. It is second important cause of death in infants in poor and developing nations. Infants and young children are mostly affected with childhood diarrhea which is responsible for 63% of the global burden of diarrhea. In developing continents like Asia and Africa, diarrhea is responsible for 1 in 8 deaths in infants annually.[1] Important pathogens responsible for diarrhea in infants include Shigella, Salmonella, Campylobacter, Rotavirus, Entamoeba histolytica and E coli. E coli and Rotavirus are the common causes of diarrhea in infants in developing nations.[2]

Dehydration due to diarrhea is the significant risk for the health of the child and it is the main reason for morbidity and mortality. Replacement of fluid to avoid dehydration is the main focus in the management of diarrhea. In mild and moderate dehydration oral route is preferred and for this purpose oral rehydrating salts are easily available all over the world. In severe dehy-

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dration or when children are unable to take orally, intravenous rehydration is recommended.[3] Antibiotic treatment is not mandatory in all children suffering from acute diarrhea except in some cases of infectious diarrhea. It should be given in severely ill children especially in those children who have risk factors.[4] Zinc supplementation has also an important role in decreasing the diarrheal duration as well as in improvement of consistency of stool in young children suffering from diarrhea.[5]

Probiotics help to decrease the diarrheal duration for the management of acute diarrhea in young children and infants. Probiotics increase efficacy of treatment and reduce days of hospital stay. Good quality RCTs are mandatory for verification of results of probiotics in severe diarrhea[6].

According to the trials, S. boulardii is proven to be effective for decreasing the severity and duration of diarrheal illness[7]. S. boulardii has shown an important role for the management of acute gastroenteritis in young children and infants[8]. E. faecium SF68 has shown efficacy for the management of acute gastroenteritis as well as for prevention of diarrhea associated with antibiotics. It has shown good safety profile.[9] Most of the studies suggested that S. boulardii is helpful for treatment of Rotavirus diarrhea as well as other types of diarrhea where etiology is not known.[10] Studies regarding use of probiotics in Rotavirus diarrhea are present but there are rare studies showing use of probiotics in non-Rotavirus diarrhea. The importance of this study is that effect of two different probiotics is observed in Rotavirus and Non-Rotavirus diarrhea in infants.

## Materials and Methods

It was an experimental, single blind, randomized controlled trial. It was conducted in the Paediatrics Department at Children Hospital Lahore from June 2016 to October 2016. The trial was approved by Ethical Committee of Children Hospital Lahore. Infants of age six months to one year with acute diarrhea were included in the trial. Dehydration was severe in the infants (more than 10%). Hydration status was assessed according to WHO guidelines.[10] Infants having malnutrition, suffering from chronic disease, already taking probiotics or who are passing bloody diarrhea are excluded from the trial. The sample size was taken in accordance with the previous study. It was estimated by taken into account mean±SD of frequency of stools in a day having standard management versus standard management plus probiotics.[11] The size of sample was 32, so we have taken 35 infants in each group. Non-probability purposive sampling was done to select the infants. Parents of the infants gave proper consent before the enrollment of infants in the trial. 105 infants were enrolled in the study and divided randomly into three groups. Infants in group A obtained standard management of diarrhea i.e. IV fluids, supplementation with zinc and ORS salts. Antibiotic treatment was only given if needed. Infants in group B obtained standard management of diarrhea plus E. faecium SF68 twice daily for five days. Infants in group C obtained standard treatment of diarrhea plus S. boulardii twice daily for five days. The sequence of randomization of infants into groups was maintained and generated by the person not involved in the trial directly. Allocation concealment was properly done with the help of serially numbered opaque sealed envelopes.

After admission, history and physical examination was done. Routine lab investigations were taken. Stool sample of the infants were sent to microbiology for detection of Rotavirus. All the infants obtained IV fluids as there was severe dehydration. ORS and zinc supplements were given to infants of all the groups as soon as the infants were able to take oral feed. Respective probiotics were also given to the infants of intervention groups when the infants were able to tolerate oral feed. Frequency of diarrhea or no. of stools per day was the parameter of our study which was monitored for five days. Infant was said to be recovered from illness when eight hours had passed after passing of normal stool[11].

The data was processed with the help of Statistical Package for Social Sciences. The data was checked for normal distribution by Shaprio Wilk test and it was normally distributed. Quantitative variables were presented in mean and SD. We have applied ANOVA for analyzing significance between three groups. Post hoc Tukey's test was applied to pairwise compare between three groups.

## Results

Total 105 sample of stool were sent to microbiology for detection Rotavirus antigen. 25 samples were positive for Rotavirus. 10 samples from group A (control group), 9 samples form group B (E. faecium SF68 group) and 6 samples of group C (S. boulardii grouop) were found to be positive for Rotavirus. The comparison of stool output per day in Rotavirus positive cases and non-Rotavirus cases was done.

Table 1 is showing mean ± SD of stool output per day

in infants having Rotavirus diarrhea. ANOVA showed no significant difference among three groups.

Table 2 is showing mean ± SD of stool output per day

**Table 1:** *Frequency of Stools in Infants of Rotavirus Diarrhea*

| Number of stool | Group | N | Mean | Std. Deviation | p-value |
|---|---|---|---|---|---|
| **Day1** | Group A | 10 | 10.40 | 2.41 | 0.284 |
| | Group B | 9 | 10.11 | 3.52 | |
| | Group C | 6 | 12.33 | 1.63 | |
| **Day2** | Group A | 10 | 9.00 | 1.89 | 0.150 |
| | Group B | 9 | 6.67 | 3.91 | |
| | Group C | 6 | 9.50 | 3.02 | |
| **Day3** | Group A | 10 | 7.70 | 3.23 | 0.173 |
| | Group B | 9 | 5.11 | 3.76 | |
| | Group C | 6 | 8.33 | 3.67 | |
| **Day4** | Group A | 10 | 6.00 | 2.94 | 0.354 |
| | Group B | 9 | 3.78 | 4.18 | |
| | Group C | 6 | 5.83 | 3.31 | |
| **Day5** | Group A | 10 | 3.90 | 2.18 | 0.857 |
| | Group B | 9 | 3.33 | 3.64 | |
| | Group C | 6 | 3.17 | 2.40 | |
| | Total | 25 | 3.52 | 2.74 | |

*Group A (control)* *Group B (SF68)* *Group C (S.boulardii)*

in infants having non-Rotavirus diarrhea. When means were compared by applying ANOVA, significant difference among three groups was shown. Table 3 is showing

**Table 2:** *Frequency of Stools in Infants in Non-Rotavirus Diarrhea*

| Number of stool | Group | N | Mean | Std. Deviation | p-value |
|---|---|---|---|---|---|
| **Day1** | Group A | 25 | 11.08 | 3.15 | <0.001 |
| | Group B | 26 | 7.23 | 2.64 | |
| | Group C | 29 | 8.86 | 3.02 | |
| **Day2** | Group A | 25 | 9.24 | 3.28 | <0.001 |
| | Group B | 26 | 4.46 | 2.60 | |
| | Group C | 29 | 6.14 | 2.95 | |
| **Day3** | Group A | 25 | 7.36 | 3.19 | <0.001 |
| | Group B | 26 | 3.15 | 2.01 | |
| | Group C | 29 | 4.00 | 2.20 | |
| **Day4** | Group A | 25 | 6.36 | 3.08 | <0.001 |
| | Group B | 26 | 2.54 | 1.65 | |
| | Group C | 29 | 3.34 | 2.32 | |
| **Day5** | Group A | 25 | 4.92 | 2.60 | <0.001 |
| | Group B | 26 | 1.88 | 1.63 | |
| | Group C | 29 | 2.52 | 1.90 | |

*Group A (control)* *Group B (SF68)* *Group C (S.boulardii)*

post hoc Tukey's test for analyzing difference among group means in non-Rotavirus infants. Mean difference among group A and group B was significant from day 1 to day 5 having p value less than 0.001. There was also significant difference among group A and group C having p value 0.02 on day 1, 0.001 on day 2 and less than 0.001 from day 3 to day 5. No significant difference was shown among group B and group C.

**Table 3:** *Multiple Comparison of Frequency of Stools in Infants in Non-Rotavirus Diarrhea*

| Stool for non-*Rotavirus* | Number of stool | I groups | J groups | Mean difference (I-J) | p-value |
|---|---|---|---|---|---|
| **Infants** | Day1 | Group A | Group B | 3.84923 | <0.001 |
| | | | Group C | 2.21793 | 0.020 |
| | | Group B | Group C | -1.63 | 0.107 |
| | Day2 | Group A | Group B | 4.77846 | <0.001 |
| | | | Group C | 3.10207 | 0.001 |
| | | Group B | Group C | -1.68 | 0.096 |
| | Day3 | Group A | Group B | 4.20615 | <0.001 |
| | | | Group C | 3.36000 | <0.001 |
| | | Group B | Group C | -0.85 | 0.426 |
| | Day4 | Group A | Group B | 3.82154 | <0.001 |
| | | | Group C | 3.01517 | <0.001 |
| | | Group B | Group C | -0.81 | 0.434 |
| | Day5 | Group A | Group B | 3.03538 | <0.001 |
| | | | Group C | 2.40276 | <0.001 |
| | | Group B | Group C | -0.63 | 0.498 |

*Group A (control)* *Group B (SF68)* *Group C (S.boulardii)*

## Discussion

It was an experimental study, randomized controlled trial conducted at Paediatric Medicine Department of Children Hospital Lahore. The trial was conducted to observe the effect of two different strains of probiotics on acute Rotavirus and non-Rotavirus gastroenteritis.

Childhood diarrhea is the major health challenges in the developing nations. Effective interventions should be done to reduce the child mortality due to diarrhea[12]. In this study we have selected the infants among 6 months to 12 months of age. Infants and young children are more affected by diarrhea due to risk of dehydration.[13] There are several studies which proved efficacy of probiotics for mild and moderate gastroenteritis. On the other hand, a lack of trials is observed showing efficacy of probiotics in infants and children having severe diarrhea. Some studies showed lack of effective role of probiotics in severe diarrhea.[14] So in this trial, we

observed the effect of probiotics in severe gastroenteritis in infants. All the infants enrolled in the study were suffering from severe diarrhea having more than 10 stools per day. Infants in all the three groups had severe dehydration and they obtained IV fluids.

The most common pathogens causing gastroenteritis in young children infants were Rotavirus and Norovirus.[15] Studies suggested the use of probiotic S. boulardii in acute Rotavirus gastroenteritis.[10] S. boulardii is the probiotic obtained from yeast and it is used for management of disorders of gastrointestinal tract. Several pathways accounted for its probiotic activity including immune modulation, release of anti-microbial substances and improvement in the barrier function of gut.[16] S. boulardii reported good results in reducing severity of gastroenteritis in children where etiology is not known.[17] E. faecium has got special role because of its beneficial strain marketed as probiotics and it also play an important role in traditional fermented foods like cheese. E. faecium SF68 is a pharmaceutical probiotic having history of safe use.[18]

In this trial we have observed the effect of S. boulardii and E. faecium SF68 in infants suffering from acute Rotavirus and non-Rotavirus diarrhea. In non-Rotavirus diarrhea, etiology of gastroenteritis was not known. The infants were randomly divided among three groups. Infants of group A got standard treatment of diarrhea including IV fluids, ORS salts and Zinc syrup. Infants in group B and C also got standard management of diarrhea plus E. faecium SF68 and S. boluardii respectively. In group A, 10 cases were Rotavirus positive, 9 cases were Rotavirus positive in group B and 6 cases were Rotavirus positive in group C. No significant difference was shown among groups in this trial in case of Rotavirus diarrhea. Probiotics did not reduce the frequency of diarrhea in Rotavirus positive cases. On the other hand, there was significant difference among groups in non-Rotavirus diarrhea. Both probiotics helped to reduce the frequency of stool in non-Rotavirus diarrhea. The result of this trial in case of Rotavirus positive cases showed contradictory results to the previous studies because previous studies showed beneficial effect of S. boulardii in Rotavirus positive cases.[10,19,20] E. faecium SF68 even showed better results in improving severity of diarrhea than S. boulardii in non-Rotavirus cases although no significant difference was shown among both probiotic groups in this regard. There are not much studies regarding the effect of E. faecium SF68 in gastroenteritis in children. One animal study suggested beneficial effect of SF68 on the gastrointestinal tract.[21] It is the strength of our study that we evaluate the efficacy of E. faecium SF68 in Rotavirus and non-Rotavirus diarrhea in infants.

## Importance of Study

The importance of this study is that it is the first study which shows comparison of two probiotics in Rotavirus and Non-Rotavirus diarrhea in infants.

## Conclusion

S. boulardii and E. faecium SF68 helped to decrease the frequency of stools in non-Rotavirus diarrhea.

**Conflict of Interest:** *None*

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## Authors Contribution

**FAK:** Conceptualization of Project
**ZI:** Data Collection
**MZK:** Literature Search
**NY:** Statistical Analysis
**MIP:** Drafting, Revision
**SZ:** Writing of Manuscript

# Effects of Small Sized Versus Medium Sized Bougies on Excess Weight Loss & Complication Rate for Laparoscopic Sleeve Gastrectomy

**Junaid Khan Lodhi,[1] Asim Malik,[2] Saba Tahir Bukhari,[3] Saima Amjad,[4] Tasadduq Hussain[5]**

**Abstract**

**Objective:** To assess excess weight loss results and complication rate with medium sized (36 Fr) & small sized (32 Fr) bougie.

**Method:** This study was conducted at Fatima Memorial hospital from Dec 2012 to Dec 2017. A total of 50 patients were segregated into two groups of 25 each. Group 1 had LSG using 36 Fr. sized bougie while group 2 had 32 Fr. bougie for neogastric sleeve formation. Patients were followed up for excess weight loss and BMI at 6months, 1 year, 2 years, 3 years and 4-year interval.

**Results:** EWL in group 1 & 2 was 39.2± 6.77kg & 41.9± 4.35kg at 6 months, 73.64± 6.49kg & 71.06± 7.77kg at 1 year, 65.52± 5.53kg & 63.92± 7.07kg at 2 years, 58.16± 4.97kg & 57.28± 5.75kg at 3 years and 55.48± 3.39kg & 55.36± 3.72kg for 4 years, not significant statistically. BMI in group 1 & 2 were 39.47± 5.11 & 35.88± 4.40 at 6 months, 29.22± 2.68 & 29.12± 2.00 at 1 year, 25.44± 1.96 & 24.73± 2.86 at 2 years, 22.84± 1.79 & 22.40±2.20 at 3 years and 21.66± 1.32, 21.67± 1.62 at 4 years and found statistically insignificant.

**Conclusion:** With regards to extra weight loss, medium and small sized bougies have identical effects but the former has lowest complication. Medium sized bougies are best choice to ensure safety in LSG.

**Key words:** Morbid obesity, laparoscopic sleeve gastrectomy, bougie size, suture line leak

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## Introduction

Morbid obesity is a serious health condition. An individual is considered morbidly obese if he or she is 20 % over his /her idea body weight, has a BMI of 40 or more, or 35 or more experiencing obesity related health conditions such as high BP, Diabetes or joint problems.[1] Laparoscopic sleeve gastrectomy (LSG) was done initially as a first stage of two staged bariatric surgeries for morbid obese patients.[2,3] It is a restrictive procedure in which about 70% stomach is cut along its vertical axis and stomach is converted in a tube preserving vagi and pylorus.[4] Outcomes for nutritional deficiency and morbidity/mortality are almost negligible for this simple procedure.[5] The data available in Pakistan is scanty. Multiple techniques have been described internationally with choice of size of bougies. Yet the standard size of bougie for LSG is not established. While most surgeons use 36 Fr bougie size, some surgeons prefer 32 Fr or smaller bougie size to form a neogastric sleeve. However, no consensus has been made yet.[6]

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## Material & Methods

This is a retrospective study carried out at surgical unit 1 of Fatima Memorial Hospital from Dec 2012 to Dec 2017. All the patients with morbid obesity aged 20 to 60years old who has undergone LSG were included in the study. An individual was considered morbidly obese if he or she was 20 % over his /her idea body weight, had a BMI of 40 or more, or 35 or more experiencing

obesity related health conditions such as high BP, Diabetes or joint problems. Patients under 20 years of age with some other abdominal pathology, who have alcohol or antidepressant addiction and with psychiatric illness were excluded from the study. Patients were segregated in two groups; Group 1 had neogastric tube creation using 36 Fr. calibration tube while in Group2, 32 Fr. calibration tube was used for this purpose. ERAS protocol was followed in postoperative recovery phase. Staple line leakage and bleeding was checked for 24 to 36 hrs by monitoring drain output & checking its contents and then oral intake was started. Patients were discharged when they feel fit and have resumed liquid intake without any problem. The follow up visits were planned after 6 months for the 1st year and yearly thereafter. At each visit excess weight loss (EWL) and BMI was calculated and all the data was gathered into a purposefully developed sheets for statistical calculation. We used SPSS version 21 for data analysis in our study. Descriptive statistics were computed and described as mean ± SD. Categorical variables were stated using frequency distribution. Paired samples were subjected to t test. P value of less than 0.001 was taken as significant.

**Table 1:** *Showing demographic data*

| Variables | Group 1 (N = 25) | Group 2 (N=25) | P value |
|---|---|---|---|
| Age (years) | 42.96 ± 8.82 | 41.64 ±8.2 | 0.588 |
| Sex (men: women) | 1:4 | 1:1 | 1.000 |
| Preoperative weight (kg) | 144.84 ± 13.24 | 142.16± 15.5 | 0.515 |
| Preoperative BMI (kg/m) | 48.9 ± 4.18 | 47.6 ± 4.7 | 0.315 |
| Operative time(minutes) | 113.40 ± 19.6 | 101.80 ± 12.4 | 0.016 |
| Oral intake (days) | 1.40 ± 0.57 | 1.17 ± 0.35 | 0.038 |
| Hospital stay (days) | 2.75 ± 0.92 | 2.24 ±0.66 | 0.027 |

**Table 2:** *Weight loss and BMI on each visit in both groups and their statistical significance*

| Follow up time | Group | Excess Weight loss (kg) | p value | BMI (kg/m²) | p value |
|---|---|---|---|---|---|
| **6months** | 1 | 39.2± 6.77 | 0.092 | 39.47± 5.11 | 0.011 |
| | 2 | 41.9± 4.35 | | 35.88± 4.40 | |
| **1 year** | 1 | 73.64± 6.49 | 0.209 | 29.22± 2.68 | 0.887 |
| | 2 | 71.06± 7.77 | | 29.12± 2.00 | |
| **2 years** | 1 | 65.52± 5.53 | 0.378 | 25.44± 1.96 | 0.378 |
| | 2 | 63.92± 7.07 | | 24.73± 2.86 | |
| **3 years** | 1 | 58.16± 4.97 | 0.566 | 22.84± 1.79 | 0.443 |
| | 2 | 57.28± 5.75 | | 22.40±2.20 | |
| **4 years** | 1 | 55.48± 3.39 | 0.906 | 21.66± 1.32 | 0.992 |
| | 2 | 55.36± 3.72 | | 21.67± 1.62 | |

## Results

A total of 50 patients were included in the study and categorized in two groups with 25 patients in each group. The demographic data of the patients included in the series along with their statistical significance is summarized in table 1.

Post-operative BMI and excess weight loss in each group after LSG measured in each follow up visit and its statistical significance is summarised in table 2.

Complications encountered in LSG peroperatively and postoperatively in both groups are summarised in table 3.

**Table 3:** *Showing complications encountered during LSG in both groups*

| | | | |
|---|---|---|---|
| **Intraoperative complications (N=50)** | **Splenic injury** | **Group1** | **0** |
| | | Group 2 | 0 |
| | Bleeding from short gastric vessels | Group 1 | 2 (4%) |
| | | Group 2 | 10 (20%) |
| | Staple line bleeding | Group 1 | 0 |
| | | Group 2 | 10 (20%) |
| | Staple line leakage | Group 1 | 0 |
| | | Group 2 | 0 |
| **Postoperative complications (N=50)** | Staple line leakage | Group 1 | 0 |
| | | Group 2 | 2 (4%) |
| | Staple line bleeding | Group 1 | 0 |
| | | Group 2 | 2 (4%) |
| | GERD | Group 1 | 3 (5 %) |
| | | Group 2 | 15 (30%) |
| | Pulmonary embolism | Group 1 | 0 |
| | | Group 2 | 0 |
| | Port site infection | Group 1 | 0 |
| | | Group 2 | 0 |
| | Port site hernia | Group 1 | 0 |
| | | Group 2 | 0 |
| | Death | Group 1 | 0 |
| | | Group 2 | 2 (4%) |

Based on data shown above, small & medium sized bougies both have equal EWL while lowest complication incidence is seen with latter group suggesting that medium sized bougies are favoured as the best choice to ensure effectiveness of LSG.

## Discussion

LSG is a restrictive bariatric surgical operation which not only affects GI motility but also has impact on gut microbiota and hormonal regulations.[7,8,9] Therefore, LSG is not only efficient in weight loss but also has impact

in improving morbidity associated comorbidities like diabetes mellitus type 2, hyperlipidaemia, obstructive sleep apnoea & hypertension.[8,9,10] It is imperative to note that for neogastric tube formation, role of proper sized bougie is pivotal to achieve best weight loss results while avoiding complications. The best decision about bougie calibration is done intraoperatively by availability of different bougie sizes so as to aid bariatric surgeons in determining expected neogastric tube. Although much emphasis has been put on pivotal role of bougie size in formation of ideal gastric sleeve, ideal bougie size has not been decided yet. Yuval et al in 2013 reported that large sized bougies not only have similar effects on EWL as the small sized bougie but also has decreased incidence of staple line leak.[11] Many studies have been done in recent decades to compare bigger & thinner bougie calibration.[4,12,13,14,15] Wang et al in 2013 reported more effective role of small sized bougie for weight loss with fewer complications.[16] However, our results in this study favour the weight loss results but not in agreement with safety in view of complications that are demonstrated more with small sized bougie.

Some named complications associated with LSG are bleeding, SLL, nausea, wound infection and dyspepsia. The controversy still exists about merits and demerits of LSG for GERD. Some patients with mild GERD are reported to be benefited by LSG but morbidly obese patients after LSG experience severe reflux esophagitis leading to problem of persistent GERD.[17] Some of the earlier studies have suggested that SLL risk can be decreased by use of large sized bougie.[11,18] Surgeon`s personal experience matter a lot in preventing this complication. In 2018, Demeusy et al postulated that it's the staple line reinforcement required intraoperatively to prevent SLL and bougie size has nothing to do with this complication.[19] Our findings are not in agreement with this study as we found out that SLL risk is greater in small sized bougie as compared to medium sized bougie with nil complication rate at all.

## Conclusion

With regards to extra weight loss, medium and small sized bougies have identical effects but the former has lowest complication incidence including SLL. Hence, use of medium sized bougie for intraoperative calibration is quintessential choice to ensure safety of LSG for morbidly obese patients.

**Conflict of interest** *None*

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## Authors Contribution

**AM:** Conceptualization of Project
**TH:** Data Collection
**STB:** Literature Search
**JKL:** Statistical Analysis
**SA:** Drafting, Revision
**JKL:** Writing of Manuscript

# Role of C-Reactive Protein (CRP) in Establishing the Diagnosis of Sepsis in Neonates

**Sonia Saleem,[1] Muhammad Affan Arif Butt,[2] Muhammad Irfan,[3] Bint ul Huda,[4] Muhammad Maaz Arif,[5] Shahid Mahmood[6]**

**Abstract**

**Objective:** To determine the accuracy of CRP in diagnosing neonatal sepsis when compared with blood culture as a reference.

**Method:** This cross-sectional study was conducted at the Neonatal Unit of Fatima Memorial Hospital, Lahore for 6 months. 300 Neonates presenting with complaints and clinical examination favouring sepsis were taken in this study through non-probability, purposive sampling. Informed consent and demographic information were obtained and a 2cc venous blood sample for blood culture and CRP were taken. CRP was measured quantitatively using the ELIZA method. All the information was recorded in a predesigned proforma and collected information was entered and analysed using SPSS version 17.0.

**Results:** The mean age of neonates was 10.68±7.45 days. There were 144(48%), neonates who were 1 week old, 75(25%) were 2 weeks old, 36(12%) were 3 weeks old and 45(15%) were 4 weeks old. There were 204(68%) male neonates and 96(32%) female neonates. The mean gestational age of neonates at the time of their birth was 35.88±3.64 weeks. There were 218(73%) neonates who were born at full term while 82(27%) were born preterm. The mean weight of all neonates was calculated as 2.42±0.62 kg. The calculated sensitivity, specificity, positive and negative predictive values were calculated as 93.18%, 71.43%, 71.93% and 93.02% respectively. The overall diagnostic accuracy of CRP was calculated as 81.0%.

**Conclusion:** This study depicts that we can rely on the results of CRP for confirmation of neonatal sepsis. The accuracy of CRP was sensitive enough based on haematological marker for early detection or confirmation of neonatal sepsis.

**Keywords:** Neonatal Sepsis, Prolonged rupture of membranes, Lethargy, Temperature instability, C-reactive protein

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## Introduction

Sepsis in the neonatal age group is defined as the activation of the systemic inflammatory response syndrome to any infection in the first 28 days of life. Sepsis in this age group can lead to severe neonatal complications including death. Though great advances have been made in recent times but still the incidence of sepsis has been recorded to be from 1-4/1000 births in developed countries and the number for developing countries is around 5.5/1000 births (blood culture-confirmed) but gets as high as 170/1000 live births (clinically detected).[1,2,3]

Sepsis is categorized into early onset, occurring within 3 days of life, and late-onset that takes place after 3 days.[4] Early-onset sepsis results because of acquiring the offending organism vertically from the womb or mother's birth canal while the late-onset infection is the one that

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happens because of horizontal transmission from the environment or the Hospital settings.

It is difficult to describe sepsis in the early days of life as neonates don't manifest typical signs and symptoms that are usually associated with sepsis. Thus, the clinicians tend to keep a low threshold for starting antibiotics when it comes to managing babies suspected to have sepsis.[5]

Neonatal sepsis can have a wide spectrum of presentations as well as clinical pictures. Neonates harbouring sepsis may either have subtle signs and symptoms or obvious signs of infection including refusal to feed, temperature instability, lethargy, mottled skin, apnoea, grunting, cyanosis, jaundice, poor perfusion, pallor, tachycardia or bradycardia, shock, seizures, petechiae, purpura and bleeding.[2]

Isolation of microorganisms from blood culture growth is considered the best available standard for diagnosing sepsis but with a sensitivity of only 32% and it usually takes 72 hours at least or more to give a result.[6] White cell count and differential leukocyte count, neutrophilia, band cells, platelet count, C-reactive protein, Chest x-ray and inflammatory markers (IL-6, 1L-8, TNF-a and procalcitonin) are taken as reliable septic screening tools.[7]

C-reactive protein is an inflammatory marker, produced by the liver, that takes around four to six hours to increase after an infectious/inflammatory trigger and reaches a peak level at around 48 hours. In new-borns, where an infectious etiology is suspected, serial C-reactive protein measurements are taken one to two days apart and values of <10mg/dl are useful in excluding sepsis.[8] Kumar et al, showed that serum C-reactive protein is a reliable marker for sepsis. Previous studies enlighten us that sensitivity of 95%, specificity of 85%, PPV of 80% and NPV of 96 % are offered by this useful septic marker. A single level of C-reactive protein is not that accurate in establishing sepsis even a few studies have concluded C-reactive protein to be not a good investigation for neonatal sepsis.[9] The current study aims to establish the role of CRP in the diagnosis of sepsis in neonates.

## Material and Methods

It was a cross-sectional study that took place at the Neonatal Unit of Fatima Memorial Hospital, Lahore, Pakistan. The duration of the study was about 6 months after the approval of the synopsis. The calculated sample size was 300 cases, with a 13% margin of error, 95% confidence level and taking 17% as an expected percentage of neonatal sepsis with sensitivity as 67.8% and specificity as 97% of C-reactive protein by taking blood culture as the gold standard in the diagnosis of neonatal sepsis. The sampling technique used was non-probability, purposive sampling.

Neonates of either genders. Gestational age 28-42 weeks. Birth weight of >1000g. Clinical signs and symptoms of neonatal sepsis i.e., babies of age <28 days presenting with one or more of the following symptoms: refusal to feed, temperature instability, lethargy, mottled skin, apnoea, grunting, jaundice, poor perfusion, pallor, cyanosis, tachycardia or bradycardia, hock and bleeding diathesis. Patients already on antibiotics. Babies having congenital alformations as following. Specific laboratory evidence of inborn error of metabolism. The asphyxia insult at the time of birth. Meconium aspiration syndrome (on clinical evaluation).

Three hundred cases with neonatal sepsis admitted to the neonatology unit of Fatima Memorial Hospital, Lahore (both inborn and outborn) were included for study purposes. Demographic information including name, age, sex and weight were recorded and informed consent was taken from their parents. There was no risk involved to the babies. Detailed history and physical examination were done. 2cc venous blood samples for blood culture were taken in a blood culture bottle under aseptic measures before starting antibiotics. 2cc clotted, venous blood samples for C-reactive protein were taken. C-reactive protein was collected under aseptic measures in a vacutainer at 24 hours of the onset of symptoms. C-reactive protein was measured quantitatively using ELIZA Method (Selective-E Autochemistry Analyzer). All the information was recorded in predesigned proforma to determine C-reactive protein level as raised / normal against blood culture report (positive/ negative)

The data gathered was entered and analysed by using SPSS version 17.0. The quantitative variables like age, gestational age, weight and height were presented by calculating mean and standard deviation. The qualitative variables like gender and positive cases of raised C-reactive protein were demonstrated as frequency and percentage. A 2×2 contingency table was generated to calculate specificity, sensitivity, PPV, NPV and accuracy of CRP in the diagnosis of neonatal sepsis by taking blood culture as the gold standard.

## Results

A total of 300 neonates of both genders with clinical signs of sepsis were enrolled in the study with a mean age of 10.68±7.45 days. The minimum age was 2 days while the maximum age was 28 days (Table 1). There were 144 (48%), neonates who were 1 week old, 75 (25%) were 2 weeks old, 36 (12%) were 3 weeks old and 45 (15%) were 4 weeks old (Table 2).

**Table 1:** *Descriptive statistics of gestational age, age and weight of neonates*

| Variable | Min. | Max. | Frequency [n] | Mean | Standard Deviation (SD) |
|---|---|---|---|---|---|
| **Gestational Age** | 28 days | 41 days | 300 | 35.88 | 3.64 |
| **Age** | 2 days | 28 days | 300 | 10.68 | 7.45 |
| **Weight** | 1.2 kg | 4.0 kg | 300 | 2.42 | 0.62 |

**Table 2:** *Distribution of neonates by age*

| No. | Age Groups | Frequency (n) | Percentage (%) |
|---|---|---|---|
| **1.** | 1st Week (1-7 days) | 144 | 48.0 % |
| **2.** | 2nd Week (8-14 days) | 75 | 25.0 % |
| **3.** | 3rd Week (15-21 days) | 36 | 12.0 % |
| **4.** | 4th Week (22-28 days) | 45 | 15.0 % |
| **Total** | | **300** | **100.0 %** |

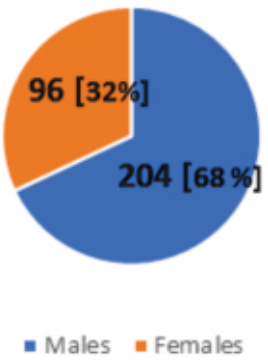


**Figure 1:** *Distribution of Gender of Neonates*

In this study, there were 204 (68%) male neonates and 96 (32%) female neonates. The male-to-female ratio was 2.1:1 (Figure 1). The mean gestational age of neonates at the time of their birth was 35.88±3.64 weeks. The minimum gestational age was recorded to be 28 weeks while the maximum duration of gestation was 41 weeks (Table 1). There were 218 (73%) neonates who were born at full term while 82 (27%) were born preterm (Figure 2). The mean weight of all neonates was calculated as 2.42+0.62 Kg. the minimum and maximum weights of neonates were 1.20 and 4.00 Kg respectively (Table 1). The calculated Sensitivity, Specificity, PPV and NPV of CRP were calculated as 93.18%, 71.43%, 71.93% and 93.02% respectively. The overall diagnostic accuracy of CRP was calculated as 81.0% (Table 3).

**Table 3:** *Diagnostic accuracy of C-reactive protein taking blood culture as the gold standard*

| CRP | Blood Culture | | Total |
|---|---|---|---|
| | Positive | Negative | |
| **< 4.5 gm/dl** | 123 | 48 | 171 |
| **> 4.5 gm/dl** | 9 | 120 | 129 |
| **Total** | 132 | 168 | 300 |

*Sensitivity = 93.18%; Specificity = 71.43%; PPV = 71.93%; NPV = 93.02%; Diagnostic accuracy = 81.0%*

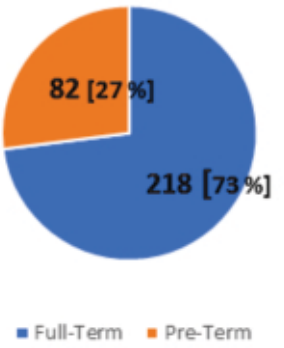


**Figure 2:** *Distribution of Neonates by Gestational Age*

## Discussion

Sepsis in the neonatal period has serious implications in the life to come. World over, nearly 1.6 million neonatal deaths are caused by neonatal infections.[10] In developing Asian countries like India, the cases of neonatal sepsis reach as high as 30 per 1000 live births.[11] As neonatal sepsis has a wide spectrum of presentations ranging from subtle signs to robust critical presentation, it is quite difficult and challenging to diagnose it in the early stages.[12] Early start of antibiotic therapy is life-saving for new-borns in septic conditions. Though blood culture is the investigation of choice to establish the diagnosis of sepsis, it is time-consuming and at times can give false-positive results.[13] A few studies have been done that showed individual parameters to be unreliable and the sensitivity of diagnosing sepsis increases when different parameters are combined.[14,15]

Hence, the researcher used simple laboratory tests i.e., C-reactive protein (CRP) for early detection of neonatal septicaemia. Thus, it was included a total of 300 neonates with clinical signs of sepsis with a mean age of 10.68± 7.45 Almost 48% of neonates were 1 week old, 25% were 2 weeks old, 12% were 3 weeks old and only 15% were 4 weeks old. Thus 48% of neonates presented with early neonatal sepsis while 52% presented with late neonatal sepsis. The ratio of early-to-late neonatal sepsis 1:1.1 is slightly higher than early sepsis in our study. One study also reported that the frequency of early neonatal sepsis (54.53%) was higher than late neonatal sepsis (45.57%) but this deference has no statistical significance.[16] One study reported that 67% of cases develop septicaemia in less than seven days.[17]

There were 68% male and 32% female. The male-to-female ratio was almost 2.13:1. This showed that males are at two times more risk of developing sepsis as compared to females. These results match with another study which reported the incidence of neonatal sepsis was higher in males (60%) than female neonates.[17] But one study reported that the risk of developing neonatal sepsis is equal in both genders and reported the frequency of sepsis in 57% male and 43% female neonates. In this study; no statistical difference was found in the frequency of proven bacterial sepsis between males and females.[16] Gender predisposition to sepsis, remains controversial, while a study carried out in Winthrop hospital showed no significant gender difference in terms of increased susceptibility to bacterial sepsis; multiple other studies show male gender to be a risk factor for severe sepsis.[18]

The researcher also obtained the history of gestational age of neo-nates at the time of birth either from the mothers or the medical records available and the mean gestational age was observed as 35.88±3.64 weeks. Premature infants have an increased incidence of sepsis.[19] In preterm babies, inflammatory markers produced due to sepsis may contribute to poor neurodevelopmental outcomes. In the present study, it was noticed that 27% of neonates were pre-term i.e., born before 36 weeks of gestation while 73% were term babies.[20] But one study reported prematurity to be a great risk factor for neonatal sepsis with a frequency of almost 88.3%.[17] In the present study, the mean weight of all neonates was 2.42±0.62 kg. The Sensitivity, Specificity, PPV and NPV of CRP at cut-off >4.5gm/dl were 93.18%, 71.43%, 71.93% and 93.02% respectively. The overall diagnostic accuracy of CRP was calculated as 81.0%. One study reported the Sensitivity and Specificity of CRP were 84% and 65% respectively.[21]

Another study reported that the sensitivity, specificity and PPV and NPV of CRP for proven sepsis were 100%, 94%, 91.6% and 100% respectively. The researchers concluded that the Sensitivity of CRP could be improved by serial rather than a single reading. Serial CRP values showed better predictive values for confirming neonatal sepsis than leukocyte indices in CBC.[22]

At different cut-off values, different pattern in sensitivity, specificity was observed from the literature. A study reported at cut-off >8mg/L, the corresponding sensitivity, specificity, PPV and NPV values at 24 hours of the onset of sepsis were 70%, 72.3%, 28% and 94% respectively.[7] The sensitivity of CRP is lowest during the initial stages of infection with the sensitivity and specificity ranging from 22% to 69% and from 90% to 96%, respectively. Benitz et al. found that the Sensitivity of CRP done after two days improved when compared with that done on the first day.[23] In a large series of neonates, Pourcyrous et al. reported that CRP being done twelve hours after the initial septic profile was having a higher sensitivity (54% vs. 74%).[24] Generally speaking, the Sensitivity improved dramatically when serial values are determined 24-48 hours after the onset of symptoms.[23,25]

## Conclusion

Through this study, it was proved that one can rely on the results of CRP for confirmation of neonatal sepsis. The accuracy of CRP was sensitive enough that one can rely on this haematological marker for early detection or confirmation of neonatal sepsis. So, in the future, neonates who will present with suspicion of neonatal sepsis will be diagnosed on basis of CRP values instead of waiting for blood culture, so that early medical interventions can be started and neonates can be prevented from hazardous events.

**Conflicts of interest** *None*
**Funding Source** *None*

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## Authors Contribution

**SS:** Conceptualization of Project
**MAAB:** Data Collection
**BH:** Literature Search
**MMA:** Statistical Analysis
**SM:** Drafting, Revision
**MI:** Writing of Manuscript

# Randomized Comparison of Compression Bandage and TR band for Radial artery Hemostasis in Patients Undergoing Transradial Coronary Interventions

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**Abstract**

**Objective:** To compare two different methods (TR band and compression bandage) for radial artery hemostasis in patients undergoing transradial coronary interventions.

**Method:** This was a randomized control trial carried out at Punjab Institute of Cardiology Lahore for six months. Total 200 indoor patients undergoing elective percutaneous Trans radial interventions were included in the study. Clinical features and investigations were noted in a predesigned proforma after informed consent. Patients were then randomized into TR band or conventional compression in blocks of 4. A resident was dedicated in the ward to remove the sheath immediately after randomization. All puncture sites were independently reviewed and measurements were recorded 24hrs after the procedure.

**Results:** Frequency of major bleeding was markedly higher in TR group (10) as compared to compression group (02) (p-value=0.017). Frequency of minor bleeding was markedly higher in TR group (23) as compared to compression group (09) i.e. p-value=0.007. In TR group significantly higher number of patients felt discomfort as compared to compression group i.e. TR: 49 vs. Compression: 35, p-value=0.045.

**Conclusion:** Compression band is more effective than TR band in terms of minimal vascular complications and less patient discomfort.

**Keywords:** TR band, Compression bandage, Hemostasis, Local vascular complications, Patient discomfort, Radial coronary intervention

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## Introduction

There are various arterial access lines and techniques for diagnostic coronary angiography (CAG) and percutaneous coronary intervention (PCI).[1,2] The most easily accessible arterial line is Radial artery and is widely used for trans radial intervention (TRI).[3,4] Percutaneous coronary intervention leads to number of vascular complications resulting in morbidity and mortality.[5]

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TRI may result in bleeding, hematoma formation, pseudo aneurysm, arteriovenous fistula, limb ischemia, or thromboembolism.[3]

In order to avoid complications, hemostasis of accessible site following percutaneous cardiac catheterization is a very important. Two compression techniques for achieving hemostasis post TRI common in clinical practice are manual compression with application of pressure bandage and the other is Trans Radial (TR) bandage. The most common technique for achieving local hemostasis is manual compression and pressure bandage application. But its painful and time taking with 35.7% patients reporting it as mild discomfort.[6,7] This may induce vasovagal reflexes with hypotension and tachycardia and also leads to fatigability of dresser. Local vascular complications are also associated with this

technique with major bleeding of 0.3% and minor bleeding reported in 2% in literature., i.e., 2-3% local vascular complication.[8]

TR band a newer hemostatic device on the other hand is a quicker, effective, and comfortable technique. It consists of 2 inflatable balloons and a transparent support plate. Among the two balloons, one provides pressure over hemostatic area and other keeps the first balloon in proper place. It is patient friendly and easy to handle with patient discomfort reported only in 16.6%.[8,9] Few previous studies have shown the hemostatic efficacy of the TR Band with minimal local vascular complications rate with no major bleeding incidence and minor bleed reported in only 2% of cases but Rathore et.al reported 20% minor bleed in TR Band.[9-12]

Head to head comparison of these two techniques is lacking and there is a need of more conclusive data regarding superiority of these newer devices over conventional methods in achieving hemostasis and tolerability of these techniques in patients. Studies must also be done at national level to validate the use of these newer techniques in our clinical practice for achieving hemostasis and tolerability of these techniques after Trans radial coronary intervention. As variation exist in literature.[9-12] This study was designed to help us in deciding the technique with little complications and better patient comfort.

## Material and Methods

This was a randomized control trial conducted at Angiography Department, Punjab Institute of Cardiology Lahore, Pakistan for a period of 6 months i.e. 1st August 2019 to 31st January 2020. A sample size of 200 (100 in each group) was calculated with 80% power of test, 5% significance level and taking expected percentage of local complications 18.2%[9] in TR band group vs 2.3%[11] in compression band group for achieving hemostasis. Non-probability consecutive sampling was done. Intended Trans radial coronary procedure (Angiography / Angioplasty) in patients with chest pain on exertion during last 1 month. Patient 18-70 years of age of both genders were included. Inability to demonstrate the presence of ulnar collateral circulation (by Allen's test), patients with chronic renal failure diagnosed on Serum Creatinine >2mg/dL or with A-V fistula or patients and previous ipsilateral trans radial procedure or absent Radial pulse were excluded. The clinical features especially Allen's test, anti-platelet therapy and anti-coagulant regime were noted on a predesigned proforma. All baselines including coagulation and lipid profile were sent before the procedure.[5] F arterial sheath was used for transradial coronary procedure; as a routine during the procedure 5000 units of Heparin was administered intra-arterially. Patients were shifted to indoor immediately 30 to 90 minutes after the procedure for removal of the sheath. Patients were assessed for systolic blood pressure. Patients with systolic BP of >160mmHg were given nitroglycerin to lower BP <160 mmHg. Patients were then randomized either to the TR band or conventional compression using computer-generated random digits in sealed envelopes in blocks of 4. Immediately after randomization sheaths were removed by a dedicated experienced resident at the indoor ward. All puncture sites were assessed after the procedure, and outcome measures of patient discomfort and local vascular complications was noted after 24 hours. All endpoints were examined by 2 independent examiners. Data was analyzed by SPSS version 17. The quantitative data like age was presented as Mean ± SD and qualitative data like vascular complication and Patient discomfort were given as frequencies and percentages (%). Chi-square test was applied to compare outcome in both groups. A p-value < 0.05 was taken as significant. Data units were stratified for age, gender and H/O Hypertension and Major & minor bleeding, BMI to combat effect modifiers. Chi-square test was used after stratification. P-value < 0.05 was taken as significant.

## Results

Mean age of patients in TR and compression band groups was 48.09±13.44 and 48.88±13.40 years respectively. In TR group there were 51 males and 49 females while in compression group there were 50 male and 50 female. In TR group there were 33 patients whose BMI was normal, 31 patients were obese and 36 were under weight. In compression Group 35 patients BMI was normal, 32 were obese and 33 were underweight. In TR group 58 and in compression group 44 patients were hypertensive. (Table-1)

In TR group 10 patients were observed with major bleeding and in compression group 2 patients were observed with major bleeding. In terms of p-value frequency of major bleeding was significantly higher in TR group as compared to that of compression group. i.e. p-value = 0.017(Table2)

In TR group 23 patients were observed with minor bleeding and in compression group 9 patients were

observed with minor bleeding. In terms of p-value frequency of minor bleeding was significantly higher in TR group as compared to that of compre-ssion group. i.e. p-value=0.007 (Table-3)

**Table 1:** *Discriptive Statistics Of Patients*

| | Banding | |
|---|---|---|
| | **TR** | **Compression** |
| **n** | **100** | **100** |
| Mean Age | 48.09 | 48.88 |
| SD | 13.44 | 13.40 |
| Minimum Age | 26 | 25 |
| Maximum Age | 70 | 70 |
| Normal BMI | 33(33%) | 35(35%) |
| Obese | 31(31%) | 32(32%) |
| Underweight | 36(36%) | 33(33%) |
| Hypertensive | 58(58%) | 44(44%) |
| Normotensive | 42(42%) | 56(56%) |

**Table 2:** *Frequency Distribution For Major Bleeding Disorder*

| Major Bleeding Disorder | Banding | | Total |
|---|---|---|---|
| | **TR** | **Compression** | |
| **Yes** | 10(10%) | 2(2%) | **12** |
| **No** | 90(90%) | 98(98%) | **188** |
| **Total** | **100** | **100** | **200** |
| ***Chi-Square Test = 5.67*** | ***p-value= 0.017*** | | |

**Table 3:** *Frequency Distribution For Minor Bleeding Disorder*

| Minor Bleeding Disorder | Banding | | Total |
|---|---|---|---|
| | **TR** | **Compression** | |
| **Yes** | 23(23%) | 9(9%) | **32** |
| **No** | 77(77%) | 91(91%) | **168** |
| **Total** | **100** | **100** | **200** |
| ***Chi-Square Test= 7.29*** | ***p-value= 0.007*** | | |

**Table 4:** *Patients Discomfort*

| Patients Discomfort | Banding | | Total |
|---|---|---|---|
| | **TR** | **Compression** | |
| **Yes** | 49(49%) | 35(35%) | **84** |
| **No** | 51(51%) | 65(65%) | **116** |
| **Total** | **100** | **100** | **200** |
| ***Chi-Square Test= 4.023*** | ***p-value= 0.045*** | | |

In TR group more patients felt discomfort as com-pared to the patients in compression group. i.e. TR: 49 vs. Compression: 35, p-value=0.045. (Table-4)

## Discussion

Radial artery as access site has shown lesser number of complications. Patient can be early mobilized and hence early discharge from the hospital thereby reducing staff workload and overall procedure cost.[13-21] Early hemostasis can be achieved by immediate removal of arterial sheath after the procedure with mechanical compression.[1,22,23] Among the commonly used compressive devices used to achieve hemostasis are the Radistop (RADI, Uppsala, Sweden), and the TR Band (Terumo, Japan). Both these devices are safe and effective and allow application of controlled pressure with sustained arterial flow and venous return.[10]

In this study it was seen that major bleeding in TR group and in compression group was seen in 10(10%) and 2(2%) patients only. However minor bleeding in TR and in compression group was seen in 23 and 9 patients respectively. Bleeding was markedly higher in TR compression banding group. (p - value = 0.017 & 0.007). Patients discomfort was also high in TR banding compression group. i.e. TR Banding: 49% vs. Compression banding: 35%., p-value= 0.045.

Major bleeding was not significantly associated in any of the age groups of patients. But frequency of major bleeding was high in TR banding compression group. Same trend was seen for minor bleeding but minor bleeding was markedly higher in patients in age group >55 years. Among female major as well as minor bleeding was also markedly higher in TR banding group however among male patients no statistically significant association was seen for major as well as for minor bleeding. Among hypertensive and non-hypertensive patients major and minor bleeding did not differ significantly except among non-hypertensive patients minor bleeding was markedly raised in TR banding group. Both major and minor bleeding was markedly higher in TR banding group among obese patients only. Chatelain and his collegues worked on the efficacy of Radistop in 159 patients and concluded that device was painful in 18% and vascular complications were seen in 19.4%.[22] Ochiai et al. in their study of 199 patients worked on the efficacy of Adapty (Medikit, Tokyo) compressive hemostatic device aad found it successful in 99.5% with no significant vascular problems.[1] Pancholy et al. evaluated hemostasis using conventional pressure by applying tourniquet with the TR band. None of 436 patients in this randomized study developed a bleeding complication.[24] Sudhir Rathore in his study compared the effects of Radistop and TR band. They studied

patient discomfort, time taken for hemostasis, and local vascular problems. In his findings they reported that there were large number of patients with no discomfort in the TR band(77%) as compared to the Radistop (61%) group (p-value= 0.0001). Radistop group reported more pain severity and three patients were shifted to TR band because of severe pain. Local vascular complications were similar in both groups. Minor vascular problems were seen in about 16% and major in 5.4%.[10]

Mai Miao in his study compared the effect of different hemostasis methods after the radial artery puncture and discuss its nursing methods and effect. In his results he reported that the proportion of patients without the swelling, pain and numbness in group B (the inflatable radial artery hemostasis device) was slightly lower than group A (compression elastic bandage) ($P<0.05$).[7] In order to reduce complications of TRA care should be taken in case selection. Those patients with absence of palmar collateralization TRA should be avoided. Vascular complications are more effectively reduced using TRA.[21] In patients with low BMI, use of lower profile access reduces the risk of most of the major complications.

Heparinization, makes the local environment less thrombotic and aids in recanalization after an occlusive hold. After the procedure, hemostasis is the most potent variable to lower the incidence of radial artery occlusion. Immediately after sheath removal it maintains patency, easy to use, and is not limited by other co-morbid. On the contrary this also does not cause systemic risks associated with anticoagulation and does not affect the overall procedure.[24]

Even with all these benefits there are certain complications associated with radial access, such as occlusion, perforation, local hematomas, spasm and pseudo-aneurysm. The risk factors for complications are prolonged occlusion,, repeated attempts, higher anticoagulation, diabetes mellitus, and low artery to sheath diameter ratio.[3] Many scholars concluded that degree of compression determines artery occlusion.[6,25]

## Conclusion

Compression band is more effective than TR band in terms of minimal vascular complications and less patient discomfort.

**Conflict of Interest** *None*

**Funding Source** *None*

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## Authors Contribution

**MNA, SI:** Conceptualization of Project
**SUM, :** Data Collection
**SUM:** Literature Search
**MNA, SI, SUM:** Statistical Analysis
**NHM:** Drafting, Revision
**SI, SUM, SH:** Writing of Manuscript

# Frequency of Dyslipidemia in Diabetic Anemic Patients with and without Nephropathy

**Mazhar Fareed,[1] Omar Razaq,[2] Laeeq-ur-Rehman,[3] Rehma Dar,[4] Sadaf Zahid,[5] Ali Raza[6]**


## Abstract

**Objective:** To compare frequency of dyslipidemia in anemic diabetics with and without nephropathy.

**Method:** The study design was comparative cross-sectional Hemotology Department. Eighty (n=80) patients who visited Diabetes management centre were included in the study. Sampling was done by using Non-probability, consecutive sampling technique. The participants were categorized in 2 groups. Group I consists of 40 anemic patients with diabetes and without nephropathy, group II includes 40 anemic diabetic nephropathy patients. Demo-graphic details were noted. Informed consent was obtained before taking blood sample. Analysis of samples for cholesterol level was done using ELISA technique. Reports were assessed and levels were noted. All the data was noted in specified proforma and analyzed through SPSS 22.0.

**Results:** During this study a total of 80 patients were inducted having mean ages of 49.2±7 years. There were 41.3% males and 58.3% female patients. Total iron binding capacity was 345±61.6mcg/dl, serum iron level was 24.24±5.54mmol/l. Mean serum cholesterol level in patients without diabetic nephropathy was 196.55 + 53.56mg/dl and in patients with diabetic nephropathy 221.11 + 41.11, p-value 0.04. Mean serum triglyceride levels were 170.35 + 35.94 in patients with diabetic nephropathy and 199.35 + 55.94, p-value 0.002. There were 37.5% patients having dyslipidemia without hephropathy and 70% in patients with hephropathy. p-value 0.001.

**Conclusion:** Study concluded that patients having any degree of diabetes associated nephropathy with concomitant anemia have increased frequency of dyslipidemia as compared to diabetics without nephropathy but having anemia.


**Keywords:** Diabetes, Anemia, Nephropathy, Dyslipidemia

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## Introduction

Diabetes Mellitus is a disease that affects almost every organ system of the body and results due to long standing and intricate overlap of an individual's lifestyle approaches, genetic makeup and environmental variables.[1] There has been a significant rise in the deaths and disabilities resulting from sedentary lifestyles, non-compliance to balanced diet and nicotine abuse. Type 2 DM has evolved into a serious concern threating the psycho-socio-economic and health provision status of a country.[2] Recent data from the International Diabetes Federation (IDF) suggest that globally 415 million people are suffering from diabetes and this number is predicted to float to 642 million till the year 2040 making every 11th person in the community affected by this disease. There has been a significant rise in the cases of type 2 DM especially in the developing countries.[3] IDF has allocated Pakistan in the Middle East Group which makes 9.7% of this total pool, of which 37 million

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people have developed diabetes.[4]

Diabetes disturbs the physiological processes of the body which has deleterious and wide ranging sequels accounting for the morbidity and complications. The long term hazards can further be categorized into micro and macro-vascular manifestations progressing from retinopathy to neuropathy and ultimately nephropathy in the former and coronary artery disease, cerebrovascular accident and limb ischemia in the later.[5] Renal involvement and insufficiency has the most lethal outcome of DM.[6] Apart from it cardiovascular health is subjected to a poor prognosis due to the altered lipid metabolism, endothelial injury and subsequent plaque formation (atherosclerosis).[7] Long standing diabetes alters the lipid metabolism and distribution leading to increased level of low density lipoproteins (LDL), trigycerides (TG) and Apo-lipoprotein B and sub-optimal levels of high density lipoproteins (HDL) threating intimal health and paving the way for micro and macro-vascular complications. Thus by managing lipid profile, the current study can modify risk and prevent cardiovascular complications.[7] Different studies have been done to determine frequency of dyslipidemia in diabetics and non-diabetics but no prospective study has been done to compare dyslipidemia in anemic diabetics with and without nephropathy.[5-8] The aim of the study was to ascertain the prevalence of dyslipidemia in diabetics with and without nephropathy having concomitant anemia.

## Material And Methods

This is a comparative cross sectional study conducted during 2018 to 2019 in which a total of 80 patients were enrolled via non-probability consecutive sampling technique. The study population was divided into 2 subgroups namely Group I Anemic individuals with diabetes and without nephropathy and Group II Anemic individuals with diabetes and diabetic nephropathy containing 40 patients each. The patients falling into to the predefined inclusion criteria i-e age 35-55years of either gender presenting with anemia having type 2 Diabetes Mellitus without diabetic nephropathy and patients with clinical and laboratory evidence of varying degree of diabetic nephropathy i-e stage 1, 2 and 3 (without dialysis). Similarly the patients with the history of or having type 1 diabetes, iron deficiency anemia, deranged Erythropoietin (EPO) level or taking EPO therapy, hemodialysis, uncontrolled hypertension, liver abnormalities, malignant, chronic inflammatory disorders and infectious diseases and those taking drugs such as ACE inhibitors, sex hormones and iron therapy were excluded from the study.

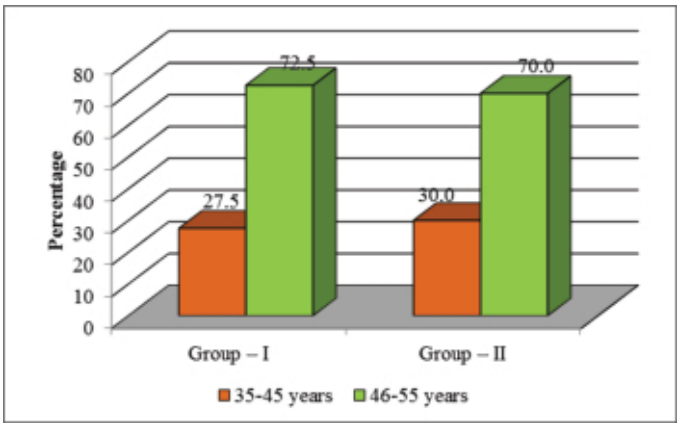
According to selection criteria 40 diabetic patients with anemia but without nephropathy were included in group I and another 40 diabetic patients with anemia and nephropathy were included in group II on the basis of medical record. Informed consent was obtained before taking blood sample. Demographic details including name, age, gender, smoking status and dyslipidemia were also recorded. Blood samples were obtained by using 5cc disposable syringe in tubes containing no additives. These specimens of the blood were sent to the pathology laboratory of the Services hospital for measurement of serum cholesterol level and serum triglyceride levels. All information was recorded on proforma.

Data was collected, organized, entered and analyzed through SPSS (Statistical Package for Social Sciences) 22.0. Mean ± SD, for quantitative variables. Percentage and frequency were calculated for qualitative variables. Chi- square test was applied for qualitative variables. ANOVA was applied for continuous variables. Any p-value less than or equal to 0.05 was considered significant.

The study was undertaken after approval from hospital ethical committee (IRB/2019/552/SIMS dated:25-05-2019). The official consent and permission was taken from concerned authority to conduct the study. Patients were included in the study after their informed consent was obtained. The samples were obtained as routine investigations under aseptic measures. Secrecy and privacy was maintained at all costs according to the principles laid down in Helsinki Declaration of Bioethics.

## Results

During this study a total of 80 patients were inducted having mean ages of 49.2±7 years. There were 41.3% males and 58.3% female patients. Total iron binding capacity was 345±61.6mcg/dl, serum iron level was 24.24±5.54mmol/l. Mean serum cholesterol level in patients without diabetic nephropathy was 196.55 + 53.56 mg/dl and in patients with diabetic nephropathy 221.11 + 41.11, p-value 0.04. Mean serum triglyceride levels were 170.35 + 35.94 in patients with diabetic nephropathy and 199.35+55.94, p-value 0.002. There were 37.5% patients having dyslipidemia without hephropathy and 70% in patients with nephropathy, p-value 0.001.




**Figure–1:** *Comparison of Age Between Both Groups*

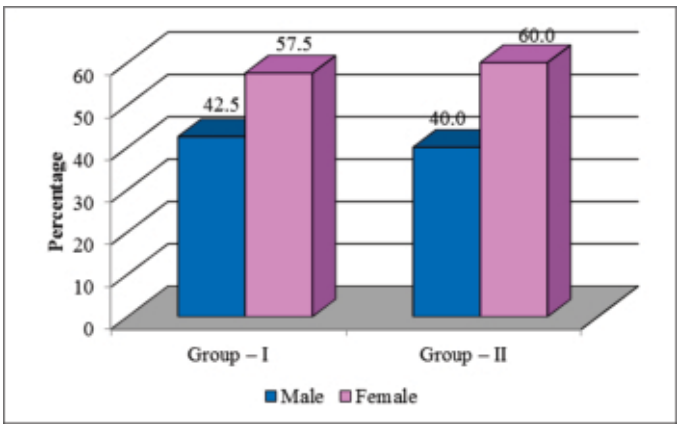



**Figure –2:** *Comparison of Sex Between Both Groups*

**Table 1:** *Comparison of Frequency of Dyslipidemia among Diabetic Anemics with and without Nephropathy*

| Variables | GROUP – I Diabetic Anemic without Nephropathy | GROUP – II Diabetic Anemic with Nephropathy | p-value |
|---|---|---|---|
| Age | 49.75 ± 8.536 | 48.78 ± 7.163 | 0.582 |
| HbA1c | 7.94 ± 1.20 | 7.69 ± 0.94 | 0.514 |
| Serum cholesterol | 196.55+53.56mg/dl | 221.11 + 41.11 | 0.04 |
| Serum triglyceride | 170.35 + 35.94 | 199.35 + 55.94 | |
| Dyslipidemia | 37.5% | 70% | 0.001 |

## Discussion

Renal involvement and insufficiency is one of the most lethal and notorious complication of DM exponentially increasing the risk of cardiovascular deaths from cardio-renal etiology particularly in the first-world countries where the incidence of DM related end-stage renal disease has been observed around 30%-50% in the past 20 years.[9-10] Diabetic nephropathy is characterized by the presence of micro-albuminuria which eventually leads to the renal shutdown.[11] The main trigger in the progression of diabetic nephropathy is the endothelial insult resulting from the raised glucose content of the blood apart from other subsidiary phenomenon such as subclinical inflammation, reactive oxygen species, accelerated atherosclerosis, caspases activation and smooth muscle proliferation.[12] Eventually elements of chronic inflammatory processes take over and turn the body into an arena of disrupted metabolism for the lipid, proteins and carbohydrates and further worsening the renal functions.[13]

The data on the dyslipidemia in this context is scarce therefore this prospective study under discussion was planned to compare dyslipidemia in diabetic patients with and without underlying nephropathy.

During the study 80 patients were inducted and found that there mean age was 49.26±7.84 years. The patients were divided into equal groups. In group-I diabetic anemic with nephropathy while in group-II diabetic anemic without nephropathy were included. Study revealed that in both groups most of the patients were more than 45 years old as 72.6% diabetic anemic without nephropathy and 70% diabetic anemic with nephropathy were 46-55 years old while remaining proportion in both groups was 35-45 years old. Study carried out by Nand L reported that 50% patients were upto 45 years old and 50% were more than 45 years.[14] A similar study was done by Shahwan MJ where subjects fulfilling the criteria were observed for and after formal informed consent were inducted. About 27 (8.4%) suffered from Type 1 DM and 293 (91.6%) had type 2 form of DM. 72 of the later had diabetes induced renal insufficiency (Diabetic Nephropathy). The overall prevalence of such variant remained 22.5%. Diabetic nephropathy developed at a mean age of 55±12 years versus 52±13 years in the group with no renal complication. The age group of 40-49 years experienced the highest incidence (37.5%) of renal compromise with a toll of 27 patients, followed by the age group 50-59% with incidence of 15 (20.8%). It was observed that there more female 51.4% sufferers versus males 48.6% group-I identical to 55.6% female versus 44.4% in group-II. The age and gender distribution in both the groups was not statistically significant (p=0.35).

It was found that the patients with diabetic nephropathy had their mean triglycerides levels 1.98 mmol/L higher than those without the nephropathy (p=0.004). Similarly the subjects had a total cholesterol of 5.05 mmol/L above mean versus 4.57 mmol/L in otherwise healthy adults (p = 0.04). Whereas the fractions of Low Density

Lipoprotein-C (LDL-C) and High Density Lipoprotein-C (HDL-C) in both the individuals remained unaffected. Renal compromised patients had an LDL-C of 3.28 mmol/L above their means as compared to 3.02 mmol/L in healthy adults (p = 0.33), likewise weightage of HDL-C existed 0.95 mmol/L for the renal involvement group and 0.86 mmol/L for the unaffected pool (p = 0.45). There existed a conspicuous evidence of altered lipid metabolism in all those diabetic patients with concomitant renal insufficiency. The fraction of total cholesterol and triglycerides showed an up steep pattern in the studied group (p=0.003). The distribution of LDL-C though found to be shifted towards the subjects (45.8%) versus the control (38.9%), but had not statistical relevance (p = 0.49). Similarly the HDL-C appeared to be optimum in the healthy individuals (69.4%) as compared to those with nephropathy (58.3%), yet the correlation remained non-significant (p = 0.26).[15,16]

The picture of the distribution of altered lipid fractions was also identical to the study conducted by Maurya NK, having an average rate of occurrence of this maladaptation of about 25-60% in individual with diabetes.[17] Evidence from the Sudanese population in north of Sudan have supported similar outcomes in terms of elevated cholesterol 43.5% and triglycerides 34.8% in the blood of type 2 diabetics.[18] The results of the present study were also found to be congruous to those of the Comparison of serum lipid profile in type 2 diabetes with and without adequate diabetes control, having abnormality index of triglycerides and total cholesterol to be around 25% and 50% respectively.[19]

## Conclusion

Diabetes is a leading life-threatening disease worldwide, if left untreated could cause several complications like diabetic ketoacidosis, cardiovascular disease, foot ulcers, kidney failure and retinopathy. Current study found that hyperlipidemia is more common in patient shaving diabetic nephropathy.

**Conflict of Interest:** *None*

**Funding Source** *None*

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## Authors Contribution

**MF:** Conceptualization of Project
**LR:** Data Collection
**RD:** Literature Search
**SZ:** Statistical Analysis
**AR:** Drafting, Revision
**UR:** Writing of Manuscript

# Gender Predisposition of Anemia in Children with Nutritional Rickets

**Sadaf Saeed Shami,[1] Farhan Saeed,[2] Qanita Mahmud,[3] Sara Aslam,[4] Jawariea Ali,[5] Tuba Tariq[6]**

**Abstract**

**Objective:** To find out association of gender with anemia in children with rickets.

**Methods:** This was a cross-sectional study, conducted in the Pediatrics Department, Allied Hospital, Faisalabad and spanned over 6 months ie. from January to June, 2017. A total of 80 children (40 patients of rickets with anemia and 40 controls) from pediatric outdoor, meeting the inclusion and exclusion criteria, were enrolled with written informed consent from the parents. Blood samples for evaluation of anemia and nutritional rickets with wrist X-rays were performed. Data was recorded on a proforma and entered in SPSS. Statistical tests were applied with p value ⩽ 0.05.

**Results:** In present study, 21 (52.5%) patients and 13 (32.5%) controls were male, whereas 19 (47.5%) patients and 27 (67.5%) controls were females. The mean hemoglobin level in cases was 9.4±1.53 while 11.08±1.89 in controls. In boys, 17 out of 21 cases had anemia, whereas in girls, 11 out of 19 cases had anemia. Similarly, in boys, 4 out of 13 controls had anemia, whereas in girls, 11 out of 27 controls had anemia.

**Conclusion:** The study concluded that the prevalence of anemia in children having nutritional rickets is significantly greater than in healthy age-matched children, with anemia more prevalent in boys as compared to girls.

**Keywords:** anemia, nutritional rickets, hemoglobin, vitamin D

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## Introduction

Anemia is decrease in concentration of hemoglobin (Hb) below reference level. It is also defined as a low Hb concentration or RBC volume, as compared to age-matched healthy individuals.[1] According to WHO, anemia is a Hb <13 gm/dL in adult males and <12 g/dL in adult females.[2] Clinical features of anemia generally manifest when Hb level decrease below 7-8 gm/dL.3 Furthermore, iron deficiency anemia is prevalent in our local population (both adults and children).[4] In a recent survey, 62.1% of children were found to be anemic and this observed frequency of anemia is significantly higher than in other populations.[5] Anemia is often observed in children during the periods of rapid growth. Anemia is more common in children with rickets than in children who do not have rickets.[6] The diagnosis of nutritional rickets is made by history and clinical features (physical examination, biochemical testing and x-ray findings). At the early stage, there is osteopenia; hypocalcaemia; hypophosphataemia; an increase in serum alkaline phosphatase; an increase in PTH levels; and a decrease in plasma 25-hydroxycholecalciferol.[6] As children of both genders are affected especially in developing countries, therefore various studies have been done to find the association of gender with anemia. The purpose of this study is to find gender predisposition of anemia among children having nutritional rickets.

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## Material and Methods

This study was aimed at finding out association of gender

with anemia in children having nutritional rickets. A child was labeled to have anemia if the estimated hemoglobin is <11 g/dL. The children of both genders coming to pediatric OPD, between the age of 2-12 years with clinical signs of rickets who met the inclusion and exclusion criteria, were recruited. This was a cross-sectional study, which was conducted in the Pediatrics department of Allied Hospital, Faisalabad. The study duration was 6 months after the approval of research synopsis ie. from January to June, 2017. Non-probability, convenient sampling was used. Sample size was calculated, using the formula: $n = z^2 . P (1 – P)/m^2$. Inclusion criteria was children of both genders, between ages 2-12 years who were having nutritional rickets, as per diagnostic criteria. Exclusion criteria was children who were receiving phenytoin for 4 weeks during last 6 months or children with disturbed liver/renal function tests. Forty cases of rickets along with 40 controls, were selected from OPD of Pediatrics Department Allied Hospital, Faisalabad. Written informed consent and detailed history was obtained from parents of each patient and control. A total of 5 mL of whole blood was taken for the evaluation of anemia. The diagnosis of anemia was made on Hb levels and other parameters (MCV, MCH, MCHC, Fe, TIBC). Blood samples were also used to evaluate serum calcium, phosphorus, 25-OH vitamin D and alkaline phosphatase. Also an X-ray wrist was performed for assessment of rickets. The whole data, recorded on proforma, was entered in SPSS-19. The numerical variables of age and hemoglobin were presented by mean ±SD, while the categorical variables of gender and anemia were presented by percentage and frequency. The whole data was stratified for gender and age and post-stratification odds ratio (OR) and chi square (2) test were applied. A p-value of ≤ 0.05 was taken as statistically significant.

## Results

In present study, 80 children (40 patients and 40 controls) were recruited. Study subjects were divided according to gender, which showed that 32.5% children (n=13) in controls and 52.5% children (n=21) in cases were male, while 67.5% children (n=27) in controls and 47.5% children (n=19) in cases were females (Table 1). The mean hemoglobin in controls was 11.08±1.8 gm/dL while that in cases was 9.4±1.5 gm/dL (p-value 0.0001). Also we compared for anemia in cases against controls. The comparison showed that 15 children in controls and 28 children in cases were having anemic, while 25 children in controls and 12 children in cases were having no anemia. In boys, 17 out of 21 cases had anemia, while in girls, 11 out of 19 cases had anemia. Similarly, in boys, 4 out of 13 controls had anemia, while in girls, 11 out of 27 controls had anemia. The results were significant for boys but did not show a significant difference for girls. The data was stratified for gender to address effect modifiers and odds ratio was calculated as 1.7, showing that boys had significantly greater chance of having anemia in both cases and control groups. These results were also evident with p value significant for boys (Table 2).

**Table 1:** *Gender distribution among cases and controls*

| | Cases | Controls | Total |
|---|---|---|---|
| **Boys** | 21 | 13 | 34 |
| **Girls** | 19 | 27 | 46 |
| **Total** | 40 | 40 | 80 |

**Table 2:** *Stratification for frequency of anemia with regards to gender*

| | Boys | | |
|---|---|---|---|
| | Anemia | | P value |
| | Yes | No | |
| **Cases (21)** | 17 | 4 | 0.003 |
| **Controls (13)** | 4 | 9 | |
| **Total (34)** | 21 | 13 | |
| | **Girls** | | |
| | Anemia | | P value |
| | Yes | No | |
| **Cases (19)** | 11 | 8 | 0.25 |
| **Controls (27)** | 11 | 16 | |
| **Total (46)** | 22 | 24 | |

## Discussion

Anemia poses a major health burden on community, and affects mainly poor or developing countries. Anemia also causes a negative impact on physical and social growth of children.[7,8] According to 2015 research by WHO, the greatest impact of anemia is seen in pediatric age group.[9] These consequences of anemia are worse in growing children as they limit not only the physical,[10] and mental growth,[11] but also social[12] and behavioral development.[13] Anemia can result from decreased consumption of both micronutrients and macronutrients eg. folic acid, iron and vitamin B12, which are necessary for the formation of RBCs.[14] Rickets is a disease that affects both children and adolescents in periods of rapid

growth. A significant association between nutritional rickets and anemia has been described worldwide. The results of our study were significant for boys but did not show a significant difference for girls. The data was stratified for gender to address effect modifiers and odds ratio was calculated as 1.7, showing that boys had significantly greater chance of having anemia in both cases and control groups. A study conducted in Ethiopia by Melku et al in 2018 is consistent with our results. Their results showed that the prevalence of anemia was higher among male children especially who were stunted or having deficiency disease like rickets. Hence they concluded that chances of anemia were higher among boys and malnourished individuals.[19] Another Some other studies have also shown the risk of anemia is more in pre-pubertal boys than girls.[20,21] Overall, malnutrition is a much prevalent among children, especially in Asian countries[22,23,24,25] that may result in nutritional deficiency anemia in growing male children. This study can be comparable to other international studies because of differences of methodology, study duration, and geographic location.

## Conclusion

The study concluded that the prevalence of anemia in children having nutritional rickets is significantly greater than in healthy age-matched children, with anemia more prevalent in boys as compared to girls. A prospective study with more sample size can be done to generalize the results.

**Conflict of Interest** *None*

**Funding Source** *None*

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## Authors Contribution

**SSS:** Conceptualization of Project
**FS:** Data Collection
**QM:** Literature Search
**QM:** Statistical Analysis
**JA:** Drafting, Revision
**SA:** Writing of Manuscript

# Comparative Study of Perception of Pharmacology Students about Power Point, White Board with Talk and Mixed Strategy as a Teaching Tool

**Sadia Maqsood,[1] Tayyaba Muzaffar,[2] Zia us salam Qazi,[3] Tehreem Zulfiqar,[4] Anila Irum,[5] Fatima Chaudhry[6]**

**Abstract**

**Objective:** To compare the general perception of students of pharmacology about three different teaching strategies (PPT, Whiteboard, mix strategy) for better teaching and learning.

**Method:** This study was conducted in Pharmacology department of Shaikh Khalifa Bin Zayed Al Nahyan Medical & Dental College (SKZMDC) Lahore. It was a Quantitative, questionnaire-based, cross-sectional study, conducted on 99 students of 3rd year, who were divided into three batches each of 33 students. Three different lectures were delivered via PPT, whiteboard and by mixed strategy. At the end of each lecture students filled a validated questionnaire, containing various questions about each method. Data collected was entered and analyzed by using SPSS version 20. Comparison among three strategies was done by using GLM-ANOVA. Post-hoc Tukey's test was used to make pair wise comparison among three strategies and type of lectures.

**Results:** The results of this study showed that students were most satisfied on whiteboard as compared to the teaching on PPT and with mixed strategy. Whiteboard was considered best for clarity and understandability, stimulation of interest, ability of taking notes, ability to copy diagrams, information received, solution of problems, flow of thoughts, proper summary, recalling of important points.

**Conclusion:** This study showed students' perception about various teaching tools. They considered whiteboard much better as compared to multimedia alone or with concomitant use of board and multimedia, for various aspects of teaching and learning. So, the total reliance on PPT is questionable.

**Keywords:** Pharmacology, teaching tools, PPT, Whiteboard, Mix strategy.

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## Introduction

Teaching and learning is an art that allows the students for better understanding. It is a continuous process by which the students not only gain the professional values but also the behavioral, clinical, social and psychomotor skills.[1] Proper and effectively made teaching skills can always improve these competencies among students. There are various methods used as learning and teaching tools. It includes lectures, small group discussions (SGD), large group discussions (LGD), tutorials, seminars, books, posters, handouts, audio-visual aids and information & communication technology.[2]

Lectures are the most common form of teaching and learning since the ancient times. Well organized lectures can be very effective tool to present integrated information from multiple sources.[3] There are various Pros and cons of every strategy; if we compare the Whiteboard or chalk & talk with that of the power point presentation

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(PPT), both have different advantages. Whiteboard is an inexpensive way whereby the students can always keep pace with the teacher. It is not dependent upon electricity.[4] Teacher can erase, redraw or even modify the material written on board according to understanding of students. But the disadvantage is that it is time consuming and it can be really troublesome for a large group of audience because it is difficult to have a continuous eye contact with the class. The other common problems are related mainly with training, support and practicalities. For examples, lack of trainings and inadequate IT supports can impede and frustrate teachers. Other issues addressed are: the position of whiteboard within a classroom, the day light reflection on board and shadow of the user on board can hinder and affect learning.[5]

PPT on the other hand is commonly used tool nowadays for delivering lectures. It has very many advantages as every student is well aware of modern technology. PowerPoint presentations are perceived as more fascinating than traditional lectures. Besides that, blending the lectures with PowerPoint presentations enhances students' self-efficacy.[6] Students feel that it is easier to understand the course material and to take notes when PPT is used. The enhanced self-efficacy of the students may be steered by their perception that the PPT lectures were better structured and accentuate the key points better than traditional lectures.

But it's not the fact that PPT always comes up with flying colors; if not properly used it can totally spoil the learning process. Most of the time, the students are passive listeners. Use of improper font size, dim light, crowded slides, too much of the information in order to pass the allotted time are the major flaws of PPT.[7] According to many critics PPT encourages simplistic thinking, with complex ideas being squashed into bulleted lists, and stories with beginning, middle, and end being turned into a collection of disparate, loosely disguised points. This may present a kind of image of objectivity and neutrality that people associate with science, technology, and "bullet points". Its outline format leads presenters to arrange material in an unnecessarily deep hierarchy, itself subverted by the need to restart the hierarchy on each slide.[8,9]

Keeping in mind all of the above mentioned studies and the feedback response from the students of given institute, we have decided to find statistical data from our students regarding subject of pharmacology. This study can guide us to find a better teaching tool which might be helpful and effective to improve the cognitive skill of students. We wanted to establish an evidence for our subject in pharmacology department, regarding which strategy is better than the other.

## Material & Method

It was a Quantitative, questionnaire-based, cross sectional study conducted in Pharmacology department of Shaikh Khalifa Bin Zayed Al Nahyan Medical & Dental College (SKZMDC) Lahore, after the IRB approval (UHS/Education/128-17/487). The class of 99 students was divided into three batches as A, B and C to look for the three teaching strategies.

The sample size of 33 in each group was estimated by using 95% confidence level. The sample size was estimated with error standard deviation of 1.40 and effect size of 0.3610 Power & precision 3.0 software was used. Purposive sampling. We wanted to compare the perception of students about the various teaching strategies for pharmacology so students of 3rd year MBBS were taken as purposive sampling. All the students of 3rd year MBBS class (both male and female), present in pharmacology lecture and willing to participate in this study, were included. While those who were absent and not interested, were excluded from this study. A validated questionnaire was used to determine their perception about various teaching strategies. Fifteen different aspects were included in the questionnaire regarding easiness, understandability, comfort, and interaction and response was taken on Likert scale and score were measured by summing up the scores for all fifteen items[11]. The class of 99 students was divided into three groups so as to expose every student to every topic and strategy. To minimize the confounding factors, groups were shuffled so as each group was taught by every instructor with all of the three strategies. A validated questionnaire was given to each student at the end of every lecture. Three lectures of pharmacology as lecture 1 (L1) on anti-hypertensive drugs, lecture 2 (L2) on anti anginal drugs and lecture 3 (L3) on drugs for congestive cardiac failure (CCF), were prepared by three different strategies as strategy 1(S1) i.e. by Power Point presentation/PPT, strategy 2(S2) by using white board only and strategy 3(S3) by the concomitant use of PPT and board and talk. All the 99 students were divided into 3 batches as A (n=33), batch B (n=33) and batch C (n=33) by random allocation. In first week, batch A was given L1 by Power Point, batch B was taught the same lecture L1 on whiteboard with talk and L1 was delivered to

batch C by mixed strategy i.e. PPT with concomitant use of whiteboard and talk. In second week batch A was taught the L2 by whiteboard, batch B got the same lecture i.e. L2 by mixed strategy and batch C was taught the same lecture by PPT. In third week of study L3 was given to batch A by mixed strategy, batch B got the L3 by PPT and batch C was taught the L3 on whiteboard. (Fig 1)

**WEEK 1**
Batch A → L1 → S1
Batch B → L1 → S2
Batch C → L1 → S3
**WEEK 2**
Batch A → L2 → S2
Batch B → L2 → S3
Batch C → L2 → S1
**WEEK 3**
Batch A → L3 → S3
Batch B → L3 → S1
Batch C → L3→ S2

**Fig-1:** *Methodology of Research Groups*

All the three lectures were prepared and conducted by 3 different instructors of equal qualification and experience, so as to minimize the instructor bias. All the instructors were properly guided and informed about the purpose and data collection technique, beforehand. The lecturers prepared their lectures by mutual discussion, so as to keep maximum uniformity in three types of strategies.

Data collected was entered and analyzed by using SPSS version 20. Data for response to each item in the questionnaire was described by using frequency and percentages. Mean ± SD (where data were normally distributed) and median (IQR) (where data distribution was skewed) were used to describe the scores for each strategy. Comparison of scores among three strategies and interaction with gender were made by using GLM-ANOVA. Post-hoc Tukey's test was used to make pair wise comparison among three strategies and type of lectures. Box plots were used to see the distribution of scores for each strategy. Association of three teaching strategies for total scores for each lecture and overall was measured by using likelihood ratio test. P value ≤ 0.05 was considered statistically significant.

## Results

When the response recorded against each strategy used for teaching, irrespective of the lecture, whiteboard was considered best for organization, clarity and understandability, stimulation of interest, ability of taking notes, ability to copy diagrams, information received,

**Table 1:** *Response of students for different aspects of three different strategies (N=number of students responded)*

| | | Strategy | | | | | |
|---|---|---|---|---|---|---|---|
| | | Multi-media | | White board | | Mix | |
| | | N | % | N | % | N | % |
| the lecture was more organized | strongly disagree | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| | Disagree | 8 | 8.1 | 1 | 1.0 | 2 | 2.0 |
| | Neutral | 8 | 8.1 | 11 | 11.1 | 19 | 19.2 |
| | Agree | 61 | 61.6 | 45 | 45.5 | 44 | 44.4 |
| | strongly agree | 22 | 22.2 | 42 | 42.4 | 34 | 34.3 |
| the lecture was clear & understandable | strongly disagree | 0 | 0.0 | 2 | 2.0 | 0 | 0.0 |
| | Disagree | 3 | 3.0 | 0 | 0.0 | 0 | 0.0 |
| | Neutral | 16 | 16.2 | 8 | 8.1 | 18 | 18.2 |
| | Agree | 54 | 54.5 | 41 | 41.4 | 42 | 42.4 |
| | strongly agree | 26 | 26.3 | 48 | 48.5 | 39 | 39.4 |
| stimulated the interest | strongly disagree | 3 | 3.0 | 3 | 3.0 | 3 | 3.0 |
| | Disagree | 20 | 20.2 | 2 | 2.0 | 14 | 14.1 |
| | Neutral | 24 | 24.2 | 20 | 20.2 | 21 | 21.2 |
| | Agree | 34 | 34.3 | 42 | 42.4 | 34 | 34.3 |
| | strongly agree | 18 | 18.2 | 32 | 32.3 | 27 | 27.3 |
| stressed the important points | strongly disagree | 0 | 0.0 | 2 | 2.0 | 0 | 0.0 |
| | Disagree | 5 | 5.1 | 0 | 0.0 | 6 | 6.1 |
| | Neutral | 18 | 18.2 | 7 | 7.1 | 17 | 17.2 |
| | Agree | 46 | 46.5 | 47 | 47.5 | 32 | 32.3 |
| | strongly agree | 30 | 30.3 | 43 | 43.4 | 44 | 44.4 |
| able to take notes | strongly disagree | 1 | 1.0 | 2 | 2.0 | 0 | 0.0 |
| | Disagree | 21 | 21.2 | 4 | 4.0 | 18 | 18.2 |
| | Neutral | 29 | 29.3 | 27 | 27.3 | 18 | 18.2 |
| | Agree | 34 | 34.3 | 34 | 34.3 | 40 | 40.4 |
| | strongly agree | 14 | 14.1 | 32 | 32.3 | 23 | 23.2 |
| able to copy the diagram/charts easily | strongly disagree | 2 | 2.0 | 0 | 0.0 | 0 | 0.0 |
| | Disagree | 26 | 26.3 | 13 | 13.1 | 22 | 22.2 |
| | Neutral | 25 | 25.3 | 37 | 37.4 | 32 | 32.3 |
| | Agree | 33 | 33.3 | 27 | 27.3 | 23 | 23.2 |
| | strongly agree | 13 | 13.1 | 22 | 22.2 | 22 | 22.2 |
| better understanding of subject | strongly disagree | 2 | 2.0 | 2 | 2.0 | 0 | 0.0 |
| | Disagree | 6 | 6.1 | 0 | 0.0 | 3 | 3.0 |
| | Neutral | 21 | 21.2 | 9 | 9.1 | 24 | 24.2 |
| | Agree | 49 | 49.5 | 37 | 37.4 | 39 | 39.4 |
| | strongly agree | 21 | 21.2 | 51 | 51.5 | 33 | 33.3 |
| well informative | strongly disagree | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| | Disagree | 6 | 6.1 | 2 | 2.0 | 3 | 3.0 |
| | Neutral | 17 | 17.2 | 7 | 7.1 | 13 | 13.1 |
| | Agree | 41 | 41.4 | 45 | 45.5 | 53 | 53.5 |
| | strongly agree | 35 | 35.4 | 45 | 45.5 | 30 | 30.3 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| problem solving | strongly disagree | 3 | 3.0 | 0 | 0.0 | 0 | 0.0 |
| | Disagree | 4 | 4.0 | 3 | 3.0 | 9 | 9.1 |
| | Neutral | 36 | 36.4 | 17 | 17.2 | 22 | 22.2 |
| | Agree | 39 | 39.4 | 47 | 47.5 | 43 | 43.4 |
| | strongly agree | 17 | 17.2 | 32 | 32.3 | 25 | 25.3 |
| flow of thought is better | strongly disagree | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| | Disagree | 14 | 14.1 | 1 | 1.0 | 9 | 9.1 |
| | Neutral | 19 | 19.2 | 13 | 13.1 | 17 | 17.2 |
| | Agree | 50 | 50.5 | 46 | 46.5 | 39 | 39.4 |
| | strongly agree | 16 | 16.2 | 39 | 39.4 | 34 | 34.3 |
| properly summarized | strongly disagree | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| | Disagree | 7 | 7.1 | 2 | 2.0 | 3 | 3.0 |
| | Neutral | 13 | 13.1 | 8 | 8.1 | 8 | 8.1 |
| | Agree | 51 | 51.5 | 37 | 37.4 | 42 | 42.4 |
| | strongly agree | 28 | 28.3 | 52 | 52.5 | 46 | 46.5 |
| best mode to recall important points | strongly disagree | 4 | 4.0 | 0 | 0.0 | 1 | 1.0 |
| | Disagree | 15 | 15.2 | 1 | 1.0 | 8 | 8.1 |
| | Neutral | 18 | 18.2 | 9 | 9.1 | 21 | 21.2 |
| | Agree | 30 | 30.3 | 31 | 31.3 | 33 | 33.3 |
| | strongly agree | 32 | 32.3 | 58 | 58.6 | 36 | 36.4 |
| covers more topics/lectures | strongly disagree | 1 | 1.0 | 1 | 1.0 | 2 | 2.0 |
| | Disagree | 8 | 8.1 | 11 | 11.1 | 3 | 3.0 |
| | Neutral | 16 | 16.2 | 17 | 17.2 | 20 | 20.2 |
| | Agree | 45 | 45.5 | 39 | 39.4 | 46 | 46.5 |
| | strongly agree | 29 | 29.3 | 31 | 31.3 | 28 | 28.3 |
| better demonstration of clinical conditions | strongly disagree | 0 | 0.0 | 0 | 0.0 | 2 | 2.0 |
| | Disagree | 11 | 11.1 | 7 | 7.1 | 12 | 12.1 |
| | Neutral | 24 | 24.2 | 20 | 20.2 | 14 | 14.1 |
| | Agree | 31 | 31.3 | 35 | 35.4 | 42 | 42.4 |
| | strongly agree | 33 | 33.3 | 37 | 37.4 | 29 | 29.3 |
| better student/teacher interaction | strongly disagree | 3 | 3.0 | 1 | 1.0 | 3 | 3.0 |
| | Disagree | 14 | 14.1 | 3 | 3.0 | 7 | 7.1 |
| | Neutral | 15 | 15.2 | 17 | 17.2 | 27 | 27.3 |
| | Agree | 29 | 29.3 | 32 | 32.3 | 28 | 28.3 |
| | strongly agree | 38 | 38.4 | 46 | 46.5 | 34 | 34.3 |

solution of problems, flow of thoughts, proper summary, recalling of important points, and better student teacher interaction with most of the students showing response of strongly agreed category. (Table.1)

The variation in distribution of score was recorded highest for anti-angina in all three strategies while smallest for anti-hypertension lecture. Generally, the scores for white board were higher for all anti-hypertension and CCF while mix for anti-angina. Also the man scores for CCF were relatively higher for all three categories. (Fig-2)

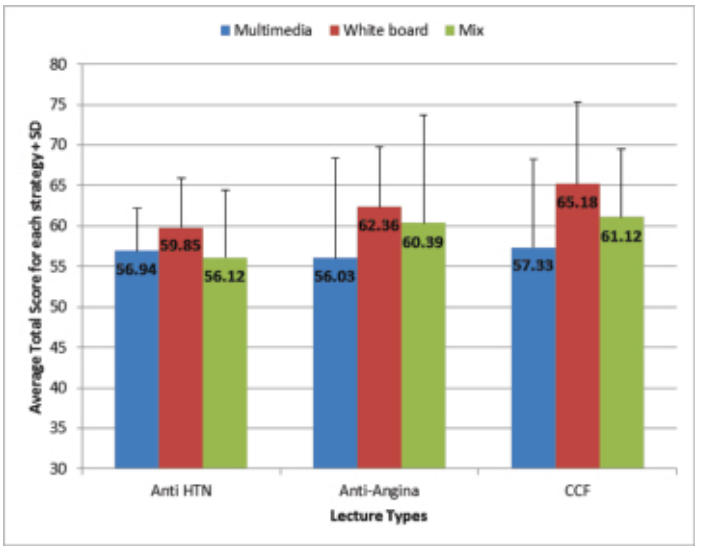


**Fig.2:** *Mean levels of total scores for three strategies by the lectures delivered.*

## Discussion

The results of this quantitative, cross-sectional study showed that students were most satisfied on whiteboard as compared to the teaching on PPT and with mixed strategy. Whiteboard was considered best for clarity and understandability, stimulation of interest, ability of taking notes, ability to copy diagrams, information received, solution of problems, flow of thoughts, proper summary, recalling of important points, and better student teacher interaction. In this regard most of the students showed response of strongly agreed category.

Several research studies found whiteboard to be superior mode of teaching, even in this android era. The results of given study were similar to those by Baruah & Patel (2014) which shows that 90% students found the traditional board & talk method to be more effective. According to their study, board method can be super added with PPT having less of written material and more of diagrams, animations, charts and videos. According to their students, time for interactive sessions is abolished in PPT use alone.[12,13,14]

Results of given study also showed that 48.5% of the students were in favor of the fact that lectures on whiteboard were clearer and more understandable. It is because; students can follow the instructor smoothly step by step during the lecture. Whiteboard was found to enhance the enjoyment and interest level of students as well. Almost all of the students in this study preferred to use white board either alone or as a part of mix strategy. According to some students, the whiteboard was easy to work with and that it helped to catch their attention.

46.3% of the participants said that it is easy to make notes via whiteboard. 51.5% students said that it was much feasible to understand the subject through whiteboard alone. In this study 45.5% students found the whiteboard lecture, well informative as compared to 35.5% and 30.3% for PPT and mix strategy respectively. 39% participants found the whiteboard method to be effective as flow of thoughts and concepts. According to them, lecture was properly and timely summarized with the help of white board. Also the ability to recall the important points after class is very high as compared to other two methods. The student teacher interaction was also found to be much better in case of white board teaching than PPT alone and mix strategy. This is in accordance with Mahalaxmi (2015), that whiteboard teaching still remains the most preferred teaching aid by students. According to her 60.43% of students preferred whiteboard lecture when compared to PPT teaching method (39.56%). According to her results, in whiteboard teaching, the students show active participation and are able to cope with the teaching speed.[15] This mode of teaching triggers an interest in students and enables to hold the attention in the class. In her study, majority of students disliked PPT as teaching method. The main reason quoted by students for this was dark room during the lecture. Due to this environment, students may get bored or feel sleepy. Students may also feel difficult to keep up to the speed of the teacher, making it difficult to copy diagrams or writing notes.[16,17]

In contrast to these findings there are other studies which are in favor of PPT.A survey including 62 students of MBBS in Jaipur India showed that 65% of students preferred PPT lecture over other methods. Our results are contradictory to the Study of Mishra et al (2015); which showed that PPT lecture was more attractive (56.66%) as compared to board & talk (43.19%).[2] But they have observed that most of the students (89.45%) were in favor of improving the class room lectures with concomitant use of PPT plus board and talk method. This might be due to the fact that students are more attentive when a diagram is drawn on board and explained on PPT. Animations and pictures with abundant written material on PPT may lead to poor understanding. Rani et al (2015) found that 66.9% were in favor of PPT followed by the traditional board & talk.[18] They have pointed out that in PPT; the ability to integrate pictures, text & images was of great advantage. The major reasons to dislike PPT are power failure, difficulty in notes taking and time spent in its setting. Student's concerns about the PPT were: teachers read the slides rapidly, do not prepare the slides, students felt themselves busy in writing down the notes. They also found that students could retain 15% less information when the lecture was conducted on PPT as compared to white board lectures. However as far as organization of the lecture was concerned; our results showed that 61.6% of the students agreed that it was more organized in PPT than whiteboard and mix technique. It was because of the fact that it was prepared and already written. Whereas, on whiteboard teacher can forget the proper sequence and organization of the topic.

According to some researchers students show greater positive response and efficaciousness in PPT lectures. It is claimed that lecture on PPT is more organized. This perception of organization influenced the student's self-efficacy beliefs. Understanding and organization via PPT is better for test preparation. Its entertaining potential is also considered to be more as compared to whiteboard.[19,20]

Question was asked about the stimulation produced by all the three technique; 32.2% students said that interest in lecture was more stimulated by whiteboard, followed by mix strategy (27.3%). Only 18% students found the PPT, innovative enough to stimulate the interest. The whiteboard and mix strategy were able to emphasize and stress the important points. Here the response of students was similar to each other. Only 30% students found the PPT to stress important points of all lectures. In our study, various suggestions and recommendations were given by the students like inclusion of interactive lectures by the teachers, proper training of clinical pharmacology and case scenarios.[21] These findings are consistent with the studies conducted by Manjunath et al (2015). Feedbacks from the students can definitely help the teachers to improve their PPT.[22]

Learning with audiovisual aids seems to have a great impact on the students. Generally, students liked the board and talk. Whiteboard can said to be more students centered, while PPT is more teacher centered. The main reasons for fondness of chalkboard could be that it enables the student to have enough time to write notes and it has more flexibility, spontaneity and non-linearity.

## Conclusions

This study showed students' perception about various teaching tools. They considered whiteboard much better as compared to multimedia alone or with concomitant use of board and multimedia, for various aspects of teaching and learning. So the total reliance on PPT is questionable.

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**Funding Source** *None*

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## Authors Contribution

**SM:** Conceptualization of Project
**TM:** Data Collection
**ZSQ:** Literature Search
**TZ:** Statistical Analysis
**AI:** Drafting, Revision
**FC:** Writing of Manuscript

# Comparison of Chondroprotective Efficacy of Hyaluronic Acid and Piroxicam in Murine Model of Osteoarthritis

**Noaman Ishaq,[1] Maryam Saqib,[2] Zari Salahuddin,[3] Shahzad Gul,[4] Nausheen Ata,[5] Zainab Rahman[6]**

**Abstract**

**Objective:** To evaluate and compare the chondroprotective efficacy of hyaluronic acid and piroxicam in murine model of osteoarthritis.

**Method:** Study was carried out at Pharmacology Department, Army Medical College (AMC), Rawalpindi. Duration of this study was from May to July 2019 Osteoarthritis was induced by medial meniscus and anterior cruciate ligament resection of right knee joints in twenty-four rats. They were divided in three groups. Group A, B and C were treated with intra articular saline, hyaluronic acid and piroxicam once weekly for four weeks respectively and then gait pattern was scored. Animals were sacrificed thereafter and samples were collected for histopathology.

**Results:** Comparison of gait score of A, B and C groups exhibited a p value of <0.01. while, comparison of gait of group A and B, group A and C and group B and C depicted p value of <0.001, <0.001and 0.771 respectively. Likewise, collective histopathological analysis of control, piroxicam and triamcinolone groups showed p value of <0.01. While Intergroup histopathological comparison of group A and B, group A and C and group B and C showed p value of <0.001, <0.001 and 0.239 respectively.

**Conclusion:** Intra articular administration of hyaluronic acid and piroxicam exhibited parallel chondroprotective efficacy in murine models.

**Keywords:** Chondroprotective efficacy, Hyaluronic acid, Piroxicam, Osteoarthritis

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## Introduction

Osteoarthrosis, a less common name of Osteoarthritis (OA) is a pandemic chronic joint ailment with 30 million patients worldwide. It is a complex joint disease in which old age and female gender are major risk factors having strong association with metabolic syndrome and obesity.[1] Interleukin-1β, tumor necrosis factor α and interleukin-6 are the molecular markers that contribute to expansion of bone deformity, joint space narrowing and development of osteophytes in OA.[2,3] It is one of unfortunate diseases whom complete cure is underdevelopment. However different non pharmacological (lifestyle and dietary habits modifications), pharmacological (Viscosupplements substances, Non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids) and surgical (osteotomy, arthroscopy, and joint replacement) techniques are available to manage this disease.[4,5]

Hyaluronic acid (HA), a viscosupplement, a ubiquitinous molecule consisting of long chain of D glucuronic acid and D acetyl glucosamine is major constituent of synovial fluid. Endogenous HA through its mechanical

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and viscoelastic properties provide joint lubrication and allow them to move a wide range of movement.[6] HA comes in the list of prevalent investigational substance in the drug management of OA. Nowadays it is common practice to use it through Intra articular (IA) route. Viscosupplementation of diseased joints with HA produces constructive outcome to relieve pain that ultimately plays role in improvement of joint function. Numerous researches illustrated chondroprotection offered by exogenous HA alongside with its positive clinical results. Several physiological responses of HA actually lead employs its clinical regenerative effects. These mechanisms include stimulation of endogenous proteoglycan and glycosaminoglycan synthesis, anti-inflammatory effect due to reduce synthesis of mediators and viscoelasticity maintenance. It also has a distinct effect on pro-inflammatory markers comprising cytokines, leukotrienes, prostaglandins and proteases. HA also exhibits antioxidant effects promoting articular chondrocytes protection against the harm induced by oxygen-derived free radicals.[7] Piroxicam (PIRO), belongs to oxicam group of NSAIDs, is non selective cyclooxygenase (COX) inhibitor. It is one of the NSAIDs used frequently in management of OA.[8] Repeated oral administrations have serious adverse profile including gastroduodenal bleeding and renal disorder.[9] To avoid untoward effects of oral route, targeted IA therapy of PIRO is common practice when expertise of IA drug administration are available. PIRO has advantageous consequences on cartilage destruction through its hindrance of prostaglandins E2 (PGE2) synthesis which eventually results in reduced proteoglycan component in cartilage.[10]

There is presently no definitive cure for OA. HA, PIRO, and a variety of other medications are experimental and are administered to alleviate symptoms and slow the progression of illness. The goal of this experiment is to assess the chondroprotection afforded by HA and PIRO in an OA murine model and determine the medicine with the best chondroprotective effectiveness. Results of this animal study can be beneficial clinically for OA patients as we have more knowledge about efficacy of chondroprotection between these two drugs.

## Material and Method

Laboratory based experimental study was the study design of this project. Center of the study was Pharmacology Department, Army Medical College (AMC), Rawalpindi. We got alliance from National Institute of Health (NIH), Islamabad for animal keeping. Ethical review committee "CREAM", AMC reviewed this project before releasing approval. Period of rat's intervention was two months from May to July 2019. Through non probability convenient sampling Twenty-four (24) adult Sprague Dawley rats, approximately of about ±500 grams were selected. Animals were separated in 03 groups with 08 in each one. Control group, HA group and PIRO group were the respective label of Group A, B and C. Standard laboratory conditions with optimum room temperature and 24 hours day/night cycle was maintained. Clean tap water for drinking and rodent chow ad libitum was provided to rats during the complete tenure of study. Right knee joint of all rats was selected for OA induction through surgical trauma. Mixture of 5% xylazine and 1% ketamine was intraperitoneally administered to anesthetize rats for surgery.[11] Joint skin was shaved and disinfected stalked by medial para patellar incision for full joint exposure. Dissections of cruciate ligament and menisci of medial side were performed following the standard protocol. Aseptic wound closure was done after the completion of procedure. Rats were conceded to move freely in their cages for a period of two weeks thereafter. Later on drugs through IA route were injected within OA induced knees of the rats. The rat model of control, HA and PIRO groups were administered with 100 microliter of 0.9% saline, 100 microliter of HA and 70 microliter PIRO once weekly for 04 weeks.[12,13] Gait score was analyzed one week after the drug administration.[14] After gait pattern scoring, rats were sacrificed by putting them in a desiccator full up of chloroform. Samples of distal femur were collected by availing angled bone cutter.[15] Histological slides was prepared by using standard technique and scored according to Modified Mankin score of histopathology.[16] By utilizing IBM SPSS version 23, statistical analysis of the results was carried out. Analysis of variance (ANOVA) and Post hoc tukey tests were used to compare the Gait score with the Modified Mankin score. Probability (p) value of $\leq 0.05$ was the cut off value to determine the significance of results.

## Results

One week post last dose; gait patterns of the rats were gauged by gross observations. A full length A2 (42×60cm) size blank white paper was placed on a smooth flat surface for each individual and the hind paws of each rat was heavily tainted with ink. To ensure their complete

walk progression from one border of the paper to another, a food treat was placed at the destination to allure them. This practice was aimed to compare the drug treated right leg and untreated control i.e. left leg. Amongst the eight rats of untreated control group, three rats scored 04, other four scored 03 and the last one scored 01. Their mean sums up to 3.25±0.707. On the contrary, amongst the eight rats of Hyaluronic acid (HA) group four rats notched 04, two rats scored 02, and two rats scored Zero. Their mean value came out to be 1.00± 0.756. In the interim the gait patterns of PIRO administrated group of one failed to notch up any score with a zero, four rats scored 01 and last three rats scored 02. Mean score of this group was 1.25±0.707. For evidential provision a detailed statistical scrutiny was done via ANOVA to carry out comparisons between the gait score of normal versus the drug treated groups. The p value between control and drug administered groups held a significant value as it turned out be <0.01, these results authenticates the chondroprotective efficacy of HA and PIRO. Further elaboration of inter drug group comparisons via Post Hoc Tuckey test was applied as detailed in Table 02.

X300 microscope lens were used to histopathological scoring of slides Modified Mankins scoring system was applied headed for the histopathological variations under both development and treatment of OA.

Under the aforementioned conditions, the control group's histology slide scores ranged from 10 to 13. Six of the eight slides had substantial irregularities in the perichondrium, whereas the other two had moderate irregularities. Similarly, six slides showed substantial cellular organisation irregularity, while two slides showed minor irregularity. On the other hand, perichondrium fibrosis was seen in one of the control slides, moderate in six, and mild in one. All slides in this group showed a significant rise in chondrocyte cellularity index, with five films showing a considerable increase in chondrocyte clusters with 10-20% chondrocyte necrosis, and the other three slides showing a modest increase in chondrocyte clusters. All slides include fibrous degeneration as a characteristic. The control group's mean score was 11.50 ±1.195.

In comparison to the other groups, the HA's score ranged between 04-07, the lowest possible. All slides showed modest to moderate perichondrium irregularity in comparison to the control group. Four slides showed perichondrium fibrosis, whereas the other half did not. All except one slide in the study exhibited mild to moderate perichondrium irregularity, while the other slides had moderate to noticeable irregularity. The cellularity of chondrocytes was somewhat increased on five slides, but not on the other nine. One picture indicated a significant increase in chondrocyte clusters in seven of the images. The chondrocyte necrosis on all of the slides was between 10 and 20 percent. All of the slides showed no signs of fibrinoid degeneration. The HA group had a mean score of 5.50±1.195.

By conducting procedure in similar manner the slides of group PIRO group scored an estimated range of 5-8. Slight perichondrial irregularity was homologous characteristic in all slides. Whereas, regarding perichondrial fibrosis in the eight slides one was devoid of any relevant findings, six had slight, whereas one had modest fibrosis of perichondrium. In addition mild and moderate to marked irregularity in cellular organization was the feature of one and seven slides respectively. Particularly regarding chondrocytes one slide exhibits none, four slides exhibit slight and three slides exhibit modest to mark increased in chondrocytes cellularity regardless of that all slide showed the feature of 10-20% chondrocyte necrosis. None of the slides exhibited fibrinoid degeneration. Summing up the findings the PIRO group displayed wide array of features like, modest unevenness in organization, hypercellularity and minor cellular necrosis. PIRO group's mean score was calculated to be 6.50±1.195.

Hence, a noticeable decrease of the variables including means of gait and Modified Mankins scores were seen in drug treated groups in competition to the disease

**Table 1:** *Mean± SD of Gait score and Modified Mankin scoring system*

| Groups | Mean ± SD of histopathology | Mean ± SD of histopathology | P value |
|---|---|---|---|
| Group A (control group) | 3.25± 0.707 | 11.50± 1.195 | |
| Group B (HA group) | 1.00± 0.756 | 5.50± 1.195 | <0.001* |
| Group C (piroxicam group) | 1.25± 0.707 | 6.50± 1.195 | |

P value was < 0.01 when ANOVA was applied

**Table 2:** *Tuckey test is applied when the results are significant*

| Groups | Gait analysis score | Histopathology score |
|---|---|---|
| **A and B** | <0.001 | <0.001 |
| **A and C** | <0.001 | <0.001 |
| **B and C** | 0.771 | 0.239 |

group with an all-rounder significant p value of <0.01, validating the regenerative properties of HA and PIRO. Amongst inter drug group comparison both drugs depicted their chondroprotective effects on parallel level.

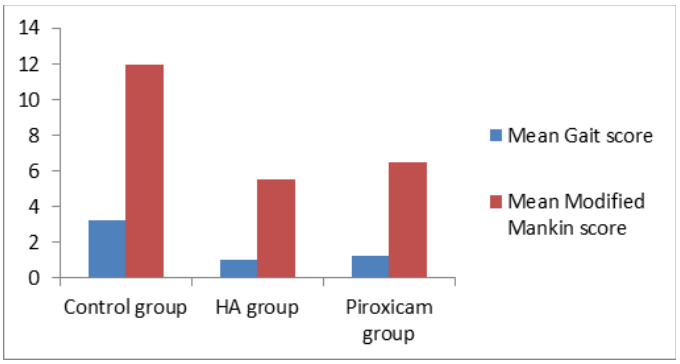


**Fig 1:** *Bar Chart of Mean Gait and mean Histopathology score*

## Discussion

Osteoarthritis (OA) is the most communal type of arthritis in the world, characterised by persistent joint pain and dysfunction. Increased average life expectancy and the obesity epidemic explain the majority of the global rise in OA. OA has significant macroeconomic consequences in addition to its personal costs; as a result, OA will be a growing public health challenge in the future decades.[17] The definitive therapy for OA has yet to be established. Many medication categories are still under study and are availed to treat traits and lessens the course of illness These are viscosupplement compounds, nonsteroidal anti-inflammatory drugs (NSAIDs), and glucocorticoids.[18] Many investigations on the chondroprotective effectiveness of different viscosupplement substances, NSAIDs, and glucocorticoids have been conducted all over the globe. In a murine model of OA, the goal of this project was to relate the chondroprotective effects of hyaluronic acid (HA), a viscosupplement material, and piroxicam (PIRO), an NSAID. When the scores of gait and histology of the control and HA groups were evaluated after the interventional procedure was completed, we identified significant changes that confirm the chondroprotective benefits of HA. Our results matched those of Zhenqinq's study from 2018. He compared rabbit HA-interrupted OA models to a disease group and concluded with a substantial p value of 0.05.[19] Yunus Emre used a 27 mm drill bit to cause chondrocyte abnormalities in rats' knees. In contrast to control group mouse mice, he discovered that HA had regenerating effects on cartilage (p-value 0.001). 20 Similarly, our findings are corroborated by a 2020 study by Li Jung Kang and colleagues, who developed a surgically induced OA mouse model and discovered that HA had chondroprotective effects (p value 0.01) when compared to a vehicle-treated group.[21] When the Gait and histology scores of the PIRO and control groups were matched, we discovered statistically considerable results which proved PIRO's chondroprotective effectiveness. Similarly, Park and his colleagues found the same outcomes in their investigation. In comparison to saline-treated rats, their research found statistically significant changes (p value 0.05) in joint swelling ratings in IA PIRO intervention rats.[22] Meanwhile, Ijaz ul Haq and colleagues observed a regenerative effect of PIRO (p value 0.05) in rodent OA models, which supports our findings.[23] Similarly, Aziza's study has revealed that PIRO intramuscular treatment lowers articular swelling and arthritis score statistically substantially (p 0.05) in vehicle-induced arthritis in mice.[24] Her results corroborated previous research on PIRO's chondroprotective properties. After comparing the chondroprotective efficacy of the HA and PIRO groups, we discovered that both drugs have equal chondroprotective efficacy. Our work is unusual in that both medicines are routinely recommended by doctors for the treatment of OA, and no in vitro, animal, or human investigation has examined the chondroprotective effectiveness of these two treatments to our knowledge.

## Conclusion

In rat models, intra-articular injection of hyaluronic acid and piroxicam decreased the severity of OA, as shown by better mean gait and histopathological scores. Both medications have identical chondroprotective effectiveness, according to the comparison.

**Conflict of Interest** *None*

**Funding Source** *None*

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## Authors Contribution

**NI:** Conceptualization of Project
**MS :** Data Collection
**ZS:** Literature Search
**SG:** Statistical Analysis
**NA:** Drafting, Revision
**ZR:** Writing of Manuscript

# Bacteriological Quality of Drinking Water Supplies in Different Areas of Lahore

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**Abstract**

**Objective:** The aim of this study was to assess the bacteriological quality of drinking water in different areas of Lahore.

**Method:** It was a cross-sectional study conducted from April 2021 to September 2021. A total of 150 water samples were collected from different localities of the Lahore city with different socio-economic conditions. The samples were collected in sterilized containers from water taps and filtration units and brought to the laboratory within two hours of collection. Membrane filtration technique was used to determine the presence of total coliforms and faecal coliforms.

**Results:** Tap water samples positive for bacterial contamination were 74 (86.0%) of the 86 samples tested and from the filtration unit, out of the 64 samples 38 (59.3%) tested positive for contamination with highly significant difference between contamination rates of tap water and water from filtration unit (p value <0.001). Bacterial contamination was highest in areas with low socioeconomic status, 91.9%, followed by 65.5% in intermediate socioeconomic status and 56.6% in areas with high socioeconomic status. The difference was statistically significant between areas with low and high socioeconomic status (p<0.001).

**Conclusion:** A considerable number of water samples in Lahore didn't meet the standard guidelines and thus highlights the importance of strict monitoring and control systems.

**Keywords:** Bacterial contamination, socioeconomic status, drinking water

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## Introduction

Safe and readily available water is fundamental to human development and well-being. One of the most effective ways in promoting health and reducing poverty is by providing access to safe drinking water. In 2020, approximately one in four individuals did not have access to safe drinking water in their dwellings and nearly half the world's population had inadequate sanitation measures according to World Health Organization (WHO).[1] In Pakistan, increased population, rapid urbanization and conventional agricultural activities are leading to increased water contamination issues with time. The conventional knowledge and approaches cannot be used to overcome these issues.[2,3]

Poor sanitation and contaminated water supplies has been known to cause water borne diseases like cholera, typhoid, polio, diarrhea and dysentery. Inadequate sanitation facilities along with unsafe drinking water supplies not only take a toll on community's health but also puts an extra burden on health care. Insufficient management of industrial, agricultural and urban waste means the drinking-water of hundreds of millions of people is hazardously polluted.[4] It is estimated that each year, 829 000 people die from water borne diseases that result from consumption of contaminated drinking water, poor sanitary facilities, and lack of hand hygiene. However, this can easily be prevented and can save the lives of 297 000 children under the age of five each

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year.[5] The sources of water contamination are multiple, comprising of natural chemicals and minerals, land fill and waste disposal mechanisms, industrial activities, and sewer overspills or mixing of water supplies with sewage.[6,7]

Given the importance of clean drinking water, drinking water is routinely tested to assure its safety for consumption. As a result, normal intestinal organisms are utilized as a faecal contamination indicator. The presence of indicator bacteria means fecal pollution and thus posing greater threat of water borne diseases in the community.[8,9]

One of these indicators is the total coliforms. They are suitable indicators as these are easy to recognize and count in water. Coliforms are found abundantly in soil and decomposing vegetation, however, they can be associated with human or animal faecal pollution, so coliforms essentially do not provide indication of fecal contamination.[8] However, Escherichia coli is always indicated as a sign of direct or indirect faecal contamination.[9] It can be found in huge numbers in the flora of human intestines.[10] According to WHO, total coliforms and Escherichia coli, should not be detectable in any 100 mL of drinking water sample.[10-12] In Pakistan, only 20% of the total population has access to safe & reliable drinking water. The remaining 80% of population is compelled to use water that is unsafe for human consumption due to the paucity of safe and reliable water sources.[3] Therefore, it is imperative to conduct water surveillance studies frequently, so that adequate measures can be taken in order to prevent water borne diseases.

We undertook this study to assess the bacteriological quality of drinking water in different areas of Lahore.

## Material and Methods

Our study was a cross-sectional descriptive study carried out in the Pathology Department of CMH Lahore Medical College, Lahore from April 2021 to September 2021. The study was approved by the ethical committee of CMH Lahore Medical College IRB no. 544/ERC/CMH/LMC. A total of 150 samples were collected from different areas of Lahore. These areas were divided into High, Intermediate and Low based on the socioeconomic conditions (SEC). High SEC areas included Faisal Town, Wapda town, Model town, Bahria town, Askari X, Askari V, Iqbal town, Cavalry ground and Garden town. Intermediate SEC areas included Bedia Road, Ichra, Firdous Market, Berni Road, Thokar Niaz Baig, Malik Park, Rizwan block, Hassan town, Azam Garden, Sabzazar, Sadar Bazar, Press club, Margzaar colony, Rana town, Awan town, Mansoora bazar, Shaam Nagar, R.A bazar, Guldasht town and Garhi Shahu. Low SEC areas included Badami bagh, Shadbagh, Farooq Ganj, Wasan pura, Usman Ganj, Singh Pura, Anarkali, Mochi gate, Mayo hospital, Saanda, Shahdara, Baghbanpura, Begumpura, Singhpura, Delhi gate, Mohni Road, Lohari gate, Peer Maqi, Mozang Chungi, Tajpura.

From each site, water samples were aseptically collected in 200 ml capacity sterile screw capped bottles. The water samples were collected from the water taps and filtration units. The samples were transported to the Pathology Laboratory of CMH Lahore within 2 hours of collection. In the laboratory all the samples were processed within 24 hours of collection. Aseptic techniques were practiced during the analysis process to avoid sample contamination. Membrane filtration technique was performed for bacteriological analysis of water samples according to the guidelines of American Public Health Association (APHA).[13] The analysis involved passing water samples through sterile 0.45µm filters. The membrane filters were then placed on Chromogenic coliform agar (Bio life) plates and incubated at 35°C for 24 hours. Number of cell growth was expressed as colony-forming units per 100 milliliters (CFU/100ml). The results were interpreted according to the manufacturer's instructions (Bio Life). All pink to red colonies were considered as presumptive coliform bacteria but not E. coli. All dark-blue to violet colonies were considered as E. coli. The total coliform count was the sum of both pink/red colonies plus dark-blue/violet colonies that were oxidase negative (Fig-1). The data was analyzed by computer software program SPSS 22.0. Frequencies and percentages were calculated. Chi square test was used to estimate statistical significance.

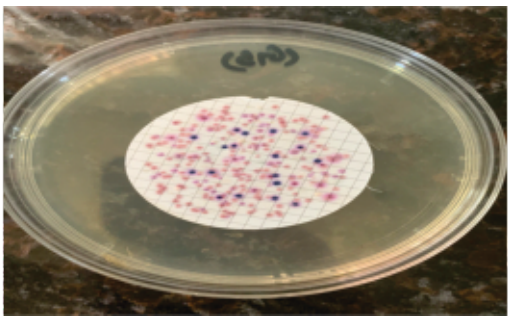

**Fig-1:** *Chromogenic coliform agar showing pink colonies (coliforms) and blue colonies (E. coli)*

**Table 1:** *Breakup of results of Bacteriological testing of drinking water system of Lahore (n= 150)*

| Parameters | | No. of tests | No. (%) of samples unfit for drinking (as per WHO 1993) |
|---|---|---|---|
| **Types of water samples** | | | |
| | Tap water | 86 | 74 (86.0%) |
| | Filter water | 64 | 38 (59.3%) |
| **Socioeconomic status** | | | |
| | High | 30 | 17 (56.6%) |
| | Intermediate | 58 | 38 (65.5%) |
| | Low | 62 | 57 (91.9%) |

**Table 2:** *Frequency of Total coliforms and E. coli in drinking water samples from Lahore (n= 150)*

| Parameters | | No. of Samples | No. (%) of samples positive for Total coliforms | No. (%) of samples positive for E. coli |
|---|---|---|---|---|
| **Types of water samples** | | | | |
| | Tap water | 86 | 74 (86.0%) | 34(39.5%) |
| | Filter water | 64 | 38 (59.3%) | 18 (28.1%) |
| **Socioeconomic status** | | | | |
| | High | 30 | 17 (56.6%) | 9 (30.0%) |
| | Intermediate | 58 | 38 (65.5%) | 12 (20.6%) |
| | Low | 62 | 57 (91.9%) | 31 (50%) |

## Results

In the present study, a total of 150 water samples were tested from the tap water and filtration unit. Tap water samples positive for bacterial contamination were 74 (86.0%) of the 86 samples tested. From the filtration unit, out of the 64 samples 38 (59.3%) tested positive for contamination as shown in Table 1. There is highly significant difference between contamination rates of tap water and water from filtration unit (p value <0.001). The number of samples positive for E. coli were 34 (39.5%0 from tap water and 18(28.1%) from filtration unit as shown in Table 2. No significant difference was found between numbers of E. coli in tap water and filtration unit water samples (p-value >0.05). The water samples collected from different localities of Lahore were divided into areas with high, intermediate, and low socioeconomic status. Bacteriological contamination was highest in areas with Low SEC 91.9%, followed by 65.5% in Intermediate SEC and 56.6% in areas with High SEC as shown in Table 1. The difference was statistically highly significant between areas with Low SEC and High SEC (p<0.001) and non-significant between areas with Low SEC and Intermediate SEC (p> 0.05) as well as between Intermediate SEC and high SEC (p>0.05). E. coli positive samples from areas of different SEC were highest (50%) in Lower socioeconomic status areas. Significant difference was found between Intermediate and Low SEC areas for E. coli positivity.

## Discussion

Due to its immense significance, access to safe drinking water was included in both the Millennium Development Goals and the Sustainable Development Goals introduced for the period 2016-2030. Quality of drinking water is directly related to disease outbreaks especially diarrheal diseases.[14] According to an estimate, 1.8 billion of the total population worldwide utilize a source of drinking water which is fecally contaminated.[15] Every year, 1.5 million people die from diarrheal diseases, including 360,000 children under the age of 5, predominantly in low-income nations. Unsafe water supplies, poor sanitary conditions and inadequate hygiene are responsible for approximately 58% of diarrheal diseases.[14]

The current study undertook the assessment of the bacteriological quality of drinking water in different areas of Lahore. Presence of both Escherichia coli and total coliforms in water sources were considered as sufficient proof of exposure to faecal contamination. In the present study, a total of 112 (74.67%) samples out of 150 samples were positive for faecal contamination. In a similar study conducted in Karachi by Fatima et al. 313 (64.66%) samples out of 484 were positive for faecal contamination.[16] In another study conducted in Nepal, out of a total sample of 243, 160 (66%) samples had faecal contamination.[17] Whereas, another study conducted in the area of Saggiyan, Lahore showed 95% of the water samples were polluted with fecal coliforms.[18]

In the current study, 74% of samples from tap water and 38% from filter water were contaminated with faecal coliforms whereas 34% of samples from tap water and 18% samples from filter water showed the presence of E. Coli. These results are similar to a study conducted in Bangladesh, in which, 73.96% samples were contaminated with faecal coliforms and 34.7% with E. coli.[19] In another study conducted in Lahore, 51% of the filtered and 93% of the unfiltered water samples were found to be fecally contaminated and unsuitable for consumption.[20] Another study which compared the

coliforms existence in filtered and boiled water found 16.67% faecal coliform contamination of filtered water.[21]

The present study also correlated the quality of drinking water samples with the socioeconomic status of the people. Accordingly, samples were collected from different localities designated as areas with high, intermediate, and low socioeconomic conditions. Bacterial contamination was highest in areas with low socioeconomic conditions 91.9%, followed by 65.5% in intermediate and 56.6% in areas with high socioeconomic conditions. These results concurred with a similar study conducted in Rawalpindi and Islamabad which concluded that people living in poor socioeconomic conditions were more prone to waterborne diseases as there was a strong association between hygienic status and waterborne diseases.[22] Contamination of drinking water creates a significant burden on public health in countries like Pakistan with poor socioeconomic conditions, due to water-related diseases. This study highlights the importance of water surveillance studies, so that preemptive measures can be taken in order to prevent water borne diseases.

## Conclusion

A considerable number of the samples that were obtained did not meet the quality standards which poses an issue concerning the microbiological quality of drinking water and emphasizes the significance of rigorous monitoring and regulatory mechanisms. Since the total viable count in the majority of the tested samples was much higher than the permitted range defined according to the national and international requirements, further preventative measures must be seriously considered in order to enhance the quality of drinking water.

**Conflict of interest** *None*

**Funding Source** *None*

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## Authors Contribution

**MSA:** Conceptualization of Project
**KHC, FH, MR :** Data Collection
**FH, MR:** Literature Search
**FH, KHC:** Statistical Analysis
**AS, AS:** Drafting, Revision
**FH, KHC:** Writing of Manuscript

# Post-Traumatic Stress Disorder (PTSD) in COVID Patients After Discharge from COVID-Intensive Care Unit (COVID-ICU) at a Tertiary Care Hospital

**Muhammad Hussain,[1] Syed Mazhar Ali Naqvi,[2] Madiha Gohar,[3] Aneeqa Tahir,[4] Namra Nadeem,[5] Sarwat Asif,[6] Maryam Naveed[7]**

**Abstract**

**Objective:** To evaluate the PTSD in patients who suffered from COVID 19, received treatment, and stayed at COVID ICU.

**Method:** Study was conducted in COVID-ICU SHL Lahore after 1st wave of COVID (May to August 2020). Among 100 sick Patients 60 discharged from the ICU and 34 participants were included in the study, who responded to our telephonic calls after 6-8 weeks of Discharge from ICU. Rest of the patients were excluded due to different reasons mainly wrong contact number/inadequate information by person interviewed. A Patient Health Questionnaire (PHQ- 9) was used to grade the symptoms of PTSD in the participants telephonically after taking informed consent. The PSDT was categorized into four categories as mild, moderate and severe categories.

**Results:** Forty-one %(n=14) patients had mild PSDT followed by 'moderate' 23%(n= 8) and minimal 20%(n=7). Fifteen out of 34 participants were of age 50-60 years. Highest PSDT was noted in short stayed patients.

**Conclusion:** High depression/PSDT in covid ICU discharged patient is alarming. All patients being discharged after covid should undergo depression screening and prescribe prompt treatment for mental health issues.

**Keywords:** TSD, post-traumatic stress disorder, mental health, COVID 19

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## Introduction

COVID-19 Pandemic originated from China and spread out to more than 230 countries causing almost 800,000 deaths all over the world. Diseases remained a big health care burden with millions of ICU admissions and prolong hospital stay. Though mortality reduced over time, ICU stay and barriers affected the mental health of medical care staff.[1,2] ICU stay can be traumatic and complex, which can lead to extraordinary and tiresome physical, psychological, cognitive, and functional consequences for both patients and families.[3] Deep-rooted physical and psychological reverberations are seen influencing the standards of life when survivors of ICU treatment are called for long-term follow-up.[4]

Aggravating or new-onset dysfunction in physical, cognitive, or mental health after ICU medical care is known as post-intensive care syndrome (PICS). The PICS components, such as anxiety, depression, and post-traumatic stress disorder, are some major psychopathological conditions and are believed to occur in up to one-third of ICU survivors.[5] The precise clinical entity of posttraumatic stress disorder (PTSD) is developed due to a person's reaction to a disturbing incident affected by character traits, psychiatric pre-morbidity, gender, peri-traumatic dissociation, extended disability after a

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stressful event, deficient social support, and ineffective coping methods used by distressed individuals.[6,7]

This may also lead to depression and diminishing interest in practical life (especially social), and have substantial consequences on the quality of life.[8] A follow-up of 150 patients, who were admitted to ICU, was done for one year, which showed indefinite depressive symptoms related to an increasing rate of re-admissions in hospitals as well as to emergency sector visits.[9] Several factors are contributory for ICU anxiety, for example, respiratory inadequacy, pain with endotracheal tube placement, suctioning, the strain on the hypothalamic-pituitary-adrenal axis, release of inflammatory cytokines, administration of exogenous catecholamines, and inability to communicate.[10] COVID-ICU are sealed ICU with isolation, which means no physical contact with family is allowed. Moreover, Hazmat suits are used by doctors and paramedics, which also increase patient stress levels during ICU stay. We had 32 bedded well equipped ICU, centrally monitored by bedside monitors and overhead cameras for each patient. Dedicated ICU team including one consultant, 1 Pulmonology post graduate trainee (PGT) and one anesthesia PGT was present round the clock in ICU. We had 2:1 or 3:1 nurse to patient ratio. Every patient was managed according to treatment protocol designed by head of ICU after multidisciplinary input.

## Material and Method

Covid ICU services hospital Lahore between May to August 2020. This is a Prospective Cohort Study. Among 100 sick patients admitted to this during Amy to end of August 2020, 60 patients were discharged. They were contacted by the phone numbers in the record and information were taken either directly from patients or the person directly taking care of patient. If the responding person wasn't involved in direct care he was excluded from study and labelled as non-responder. A total of 34 patients or care-givers responder and rest were non-responder due to multiple reasons like incorrect number, responder wasn't involved in direct care, death of patient. We used a shortened version of Patient Health Question-naire-9 (PHQ- 9) for depression with an additional question about daily work-related difficulties (make it 10 questions in total) to measure symptoms of post-traumatic stress disorder. This tool was used as it was translated in Urdu and validated tool to screen, rate and monitor depression in Pakistani population. Each question has 4-point scores from 0-4. All patients were called by phone and their answers were recorded after an informed consent; all questions were asked from the patients directly or a care giver directly looking after patient and the response was noted in a proforma. All data was noted along with demographics, patient's disease severity, and ICU stay. Data were analyzed by

| Total Score | PTSD Severity |
|---|---|
| 0-5 | Minimal PSTD |
| 6-10 | Mild PSTD |
| 11-16 | Moderate PSTD |
| 17-22 | Moderately severe PSTD |
| 23-30 | Severe PSTD |

SPSS 19.0. Severity was calculated as per PHQ-10 standard guidelines.

## Results

Total of 34 patients were able to complete study and were included for data analysis. in the study, 17 males and 17 female patients. All were discharged home after variable ICU stay. Their age, length of ICU stays and comorbidities are tabulated in Table-1. Highest number

**Table 1:** *Age distribution, gender, ICU stay, co-morbidity and degree of hypoxia at presentation. NRM= non-rebreathing mask, NC= nasal canula, NIPPV=*

| Age | | n | Percen -tage |
|---|---|---|---|
| | Younger than 50 years old | 14 | 41.% |
| | 50 to 60 years old | 15 | 44.% |
| | Older than 60 years old | 5 | 14.7% |
| **Gender** | | | |
| | Male | 17 | 50% |
| | Female | 17 | 50% |
| **Duration of Stay** | | | |
| **short** | 3-15 days | 21 | 62% |
| **intermediate** | 16-30 days | 8 | 23% |
| **Long** | >30 days | 5 | 15% |
| **Co-Morbidities** | | | |
| | DM | 11 | 32 |
| | HTN | 15 | 44 |
| | IHD | | |
| | Chronic lung disease | 5 | 14 |
| **Saturation on presentation** | | | |
| | 92-95% with 10-15L NRM | 12 | 35% |
| | 92-95% with NRM+ NC | 15 | 44% |
| | 88-92% with NIPPV | 7 | 21% |

of patients developed mild PTSD 41%(n=14) followed by moderate 23.5%(n=8) and minimal 20.6(n=7). There was direct correlation of duration of stay and severity of PTSD as 85%(18) of short stay has mild to moderate PTSD while 100% (n=5) among those who stayed longer had moderate to severe PSTD. Degree of hypoxia at presentation was a contributary factor but it was associated with prolong stay and it is difficult to assess which factor is more important. Comorbidities were diabetes and hypertension and both had almost same number and severity of PTSD.

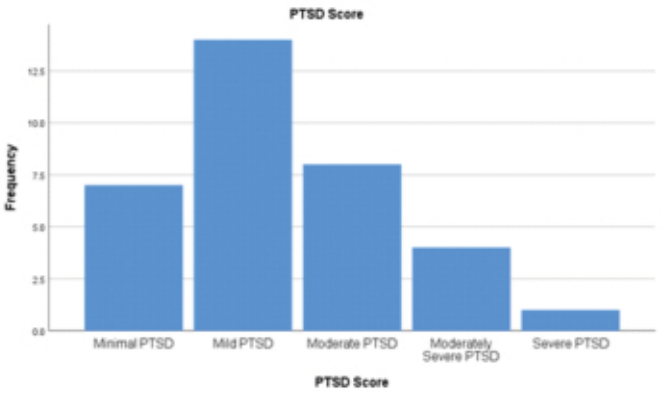


**Fig 1:** *Distribution of PTSG Severity among COVID Survivors.*

## Discussion

This prospective cohort study is carried out on 34 COVID survivors, who were discharged after stay in the COVID ICU. In all the respondents, symptoms of PTSD were found on different severity levels. If we talk about the history of PTSD after being sick from a deadly disease, in 2003, an outbreak of SARS erupted in Hong Kong in which it was reported that the prevalence of PTSD was 5% in patients who were monitored for 3 months. But, when the observance window was increased, the PTSD had reached 25.6%.[1] The reason for this high rate could have been the fear of dying in the patients who had recovered, which is a similar case in the COVID outbreak since it spreads at a very high rate and its mortality rate is also very high.

In this study, the highest recorded PTSD severity was 'mild severity' which was presented by 14 participants. The second highest PTSD severity was 'moderate severity' which was presented by 8 participants. 15 out of 34 participants were of age 50-60 years. The highest PTSD that developed was during the short stay, after which 7 participants experienced mild PTSD symptoms. Presently, some studies and surveys are being conducted to figure out the prevalence of PTSD in COVID survivors. 603 people belonging to Tunisia were examined for after-discharge PTSD. It was noted that 33% of participants suffered from PTSD.[11] Similarly, 898 adults belonging to the USA were assessed for PTSD symptoms. The prevalence rate of PTSD in them was 31.8%.[12] 2286 people from Italy were diagnosed with PTSD, where the prevalence rate was 29.5%.[13] All of these studies had such participants who were diagnosed or who were not diagnosed with COVID 19. In our study, only those subjects were included who were diagnosed, treated, and discharged from the hospital. This study has small sample size and larger study is require to validate the results with different tools apart from PHQ-9

## Conclusion

Generally, there is a risk of PTSD in COVID patients, particularly those who stayed in ICU even those who stayed for short duration. Counseling, psychological therapy and family support may minimize the risk.

**Conflict of interest** *None*

**Funding Source** *None*

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## Authors Contribution

**MH, AT:** Conceptualization of Project
**NN:** Data Collection
**AT:** Literature Search
**SM, AN:** Statistical Analysis
**SM:** Drafting, Revision
**AT, AN:** Writing of Manuscript

# Common Causes of Non-Compliance in the Use of Inhalers in Children 5 to 12 Years of Age with the Diagnosis of Asthma

**Awais Zafar,[1] Sonia Saleem,[2] Muhammad Affan Arif Butt,[3] Muhammad Abdullah Butt,[4] Shahid Mahmood,[5] Muhammad Maaz Arif[6]**

**Abstract**

**Objective:** To determine the common causes of non-compliance when using inhaler therapy in pediatric population at Gulab Devi Teaching Hospital, Lahore.

**Method:** In cross-sectional study, the Random sampling (purposive sampling) technique was used. The study was carried out in the pediatrics department, Gulab Devi Teaching Hospital Lahore, Pakistan. SSPS version 21 was used to evaluate the data.

**Results:** The present study comprised 100 Asthmatic patients, with an average age of 9.12 and a standard deviation of 2.38. Out of a total of 100 patients, 37 (37%) were male and 63 (63%) were female patients. 26 % had shown good compliance with the medication and 74% had shown noncompliance. Common factors of non-compliance were affordability (40%), poor inhaler technique (19%) and social issues (15%).

**Conclusion:** Inhaled medications are the mainstay of treatment for asthma. Compliance of the patients especially in the paediatric age group remains a great challenge. Common factors that were observed for non-compliance were affordability, poor inhaler technique and social issues.

**Keywords:** Asthma, inhaler, inhaler technique, drug compliance

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## Introduction

Asthma is a chronic obstructive pulmonary illness that presents with a different constellation of signs and symptoms including cough, difficulty in breathing, wheezing sound from the chest, feeling of tiredness and chest congestion. The patient may present with acute exacerbation of symptoms in conditions with infections involving the respiratory tract and exposure to a sensitized allergen which may lead to respiratory failure in extreme conditions.[1]

Worldwide, it is estimated that around 300 million people suffer from asthma and the number affected is increasing especially in the paediatric population. World Health Organisation states that in one year, almost 15 million disability-adjusted life years are wasted.[2] and another survey shows that asthma results in the loss of tens of millions of schooling days per year.[3]

Hyper-responsiveness of the respiratory passage increased mucus production, immune dysregulation and remodeling of the respiratory passage are all linked to asthma. In the immunologic pathways of asthma, both innate and adaptive immunity play a role. Asthma is a common chronic lung condition in children that produce wheezing, dyspnea, chest tightness, and coughing. These symptoms can frequently be managed by avoiding or lowering asthma triggers (allergens and irritants) and adhering to medical advice (starting asthma control

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drugs or changing the present treatment regimen as needed).[4] A prevalent characteristic of asthma is type 2 asthma with eosinophilia. It can happen with or without a noticeable allergy. Non-type 2 asthma is the second major subtype of asthma, which includes a diverse range of endotypes and phenotypes such as exercise-induced asthma, obesity-induced asthma, and so on. Infections, cigarette smoke, and pollution can cause neutrophilic asthma, which is not caused by allergens.[5] Dyspnea, which is occasionally linked with 'respiratory pain,' cough, and wheezing are the key symptoms used to diagnose asthmatic illness. A qualitative score (mild, moderate, and severe) or a visual analogue scale are occasionally used to quantify these symptoms (VAS).[6] Airway hyperresponsiveness (AHR) is the underlying cause in asthmatic patients that leads to narrowing and remodeling of the bronchial tree over time. There is hypertrophy of the smooth muscles encircling the air passages and an increased number of mucus-producing cells that explain many of the symptoms observed in asthmatic patients.[7]

In the paediatric age group, asthma is a challenge both for the parents and the pediatrician. Though allergen-induced cases are common and obvious, and seasonality may become apparent with time but virus-induced asthma is still widespread.[8] The relative impact of each trigger on disease activity may fluctuate depending upon the child's age. This is because smaller airways and flexible rib cage are more pliable and hence more prone to airway obstruction.[9] Atopy is favored in paediatric population due to immature and developing immune system.[10] During the initial years of life, interactions between immune system maturation and lung growth and development appear to be critical in the development of asthma.[11] All of these events are impacted by the combination of genetic, developmental, and environmental variables.[12]

Inhaled corticosteroids either alone or in combination with long-acting beta 2 agonists are the mainstay of therapy in asthmatic patients with persistent symptoms.[13] Combination inhalers have the advantage of treating asthma with lower corticosteroid doses, are relatively cost-effective and may ensure compliance with the medication as provide better control of symptoms than corticosteroids alone.[14] Adherence to the inhaler is a challenge, especially in the paediatric population suffering from asthma. According to a study, it was estimated that less than 50 percent of the paediatric patients show adherence to the prescribed medication for asthma.[15] Thus pediatricians should strain to identify and deal with the factors resulting in non-adherence to inhalation therapy as it is the mainstay of therapy in asthma. The objective of our study is to determine the common causes of non-compliance when using inhaler therapy in paediatric population at Gulab Devi Teaching Hospital, Lahore.

## Materials and Methods

This cross-sectional study was carried out in the pediatrics department, Gulab Devi Teaching Hospital Lahore, Pakistan. The duration of the study was of six months. The sample size determined was 100 with 95% confidence interval and 5% margin of error. Non-probability sampling technique was used. Children of ages 5 to 12 years, diagnosed with asthma and prescribed inhaler therapy were included in the study. While children less than 5 years and more than 12 years, those not using inhaler for asthma control and those in whom wheezing episodes were due to causes other than asthma were excluded from the study. One hundred cases with diagnosed asthma and on inhaler therapy in the specified age group presenting to the paediatric department of Gulab Devi Hospital were included in the study. Demographic information including name, age, sex and weight were recorded and informed consent were taken from their parents. Compliance with the treatment and reasons for noncompliance were recorded with the help of a proforma. All collected data was statistically analyzed by using SPSS 21 version. Descriptive statistics like Mean, Median, Mode and S.D were applied. Frequency was studied by statistical test. Qualitative and quantitate data were presented in the form of figures and tables.

## Results

The current study showed a mean weight of 22.39 of the patients involved in the study with a standard deviation of 5.043 (Table 1). The subjects involved in this study had an age and mean±SD of 2.38±9.1237. For gender distribution, 37(37%) were males and 63(63%) were females. In this study, 55(55%) patients belonged to poor families, 24(24%) patients belonged to rich families and 21(21%) patients belonged to middle-class families. In this study, 9(9%) patients had asthma for 1 week, 15(15%) patients had asthma for 2 weeks, 20(20%) patients had asthma for 3 weeks, and 26 (26%) patients had asthma since 1 month while 30 (30%) patients had asthma for 2 or more months. In this study, all patients were prescribed inhaler therapy out of which 44(44%) patients had used inhaler previously while 56(56%) patients had not used inhaler. In this study, 54(54%) patients were not using

inhaler at all, while 18(18%) patients were using inhaler for 1 week, 12(12%) patients were using inhaler for 2 weeks ,11(11%) patients were using inhaler for 3 weeks and 5(5%) patients were using inhaler for almost 1 month. In this study, 19(19%) patients were having improper inhaler technique while 81(81%) patients inhalation technique was proper. Out of 100 patients 26(26%) had shown proper compliance to inhaler technique and 74(74%) had shown non-compliance (Fig 1). Out of 74 patients the reason for non-compliance in 15(15%) patients were because of social

**Table 1:** *Statistical Analysis of Patients*

| No. of patients | Mean | Median | Mode | S.D | Skewness |
|---|---|---|---|---|---|
| **100** | 22.39 | 22 | 25 | 5.04304 | -.303 |

issues (misinforms), 19(19%) patients was because of their poor technique and in 40(40%) patients was because of affordability (Fig 2).

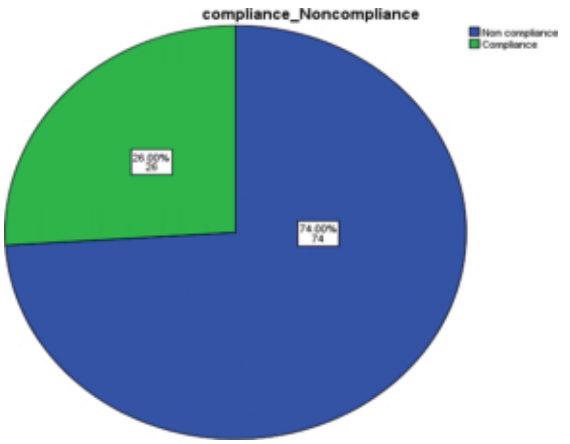


**Fig-1:** *Frequency Distribution of Compliance & Noncompliance*

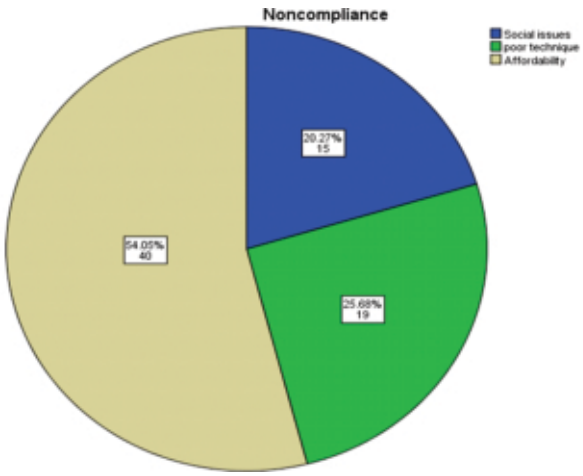


**Fig-2:** *Frequency Distribution of Noncompliance*

## Discussion

Asthma is a chronic obstructive pulmonary disease that presents with different signs and symptoms of the respiratory system. Asthma is more of a problem in the paediatric age as it results in absence from school, impacts the growth of the developing child, results in behavioral problems and causes a lot of anxiety and concern for the parents as well. One of the reasons for poor asthma control in this age group is poor compliance with the inhaled medication. Doctors treating asthmatic patients should have a good knowledge about the factors responsible for poor adherence to the therapy, so they can counsel the patient and parents accordingly.

The present study emphasizes affordability of the medication to be the main factor for non-compliance. Pakistan like other developing countries has a vast majority of people below the poverty line and cost of medication is an extremely important factor for non - compliance in setup. Parveen et al came to the same conclusion that cost of the inhaled medication is the most important reason for non-compliance with a percentage of 41 percent (comparable to the present study's percentage of 40 percent). Same study showed that 15.6 percent patients stopped using inhaler due to difficulty in learning the correct technique.[16] It can be related to the present study's conclusion of poor technique of 19 percent causing non-compliance. Another related study shows poor education of the patient on the use of inhaler medication to be a reason for non-adherence to treatment.[17]

In Developed countries, studies show cost to be not a major factor for non-compliance but the main reasons for concern were side effects of the medication (58 percent) and the perception of addiction to inhaler therapy (31 percent).[18] In another study conducted at Lahore, 38.4 percent patients were showing poor compliance due to forgetfulness and 34.5 percent discontinued the medication on their own when the symptoms improved.[19]

One factor that is an important reason for non-compliance is the social stigmata of the disease.15 percent patients stopped using the medication as per the present study's results. Bisko et al showed defiance behavior and peer pressure to be important factors resulting in stopping the therapy.[20]

## Conclusions

Asthma is a chronic lung condition especially in the

modern developed era. Inhaled medications are the mainstay of treatment. Compliance of the patients especially in the paediatric are group remains a great challenge. In the present study, about 100 asthmatic patients 26 % had shown compliance and 74% had shown noncomp-liance. Common factors that were observed of non-compliance were affordability, poor inhaler technique and social issues.

**Conflict of Interest** *None*

***Funding Source*** *None*

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## Authors Contribution

**:** Conceptualization of Project
**:** Data Collection
**:** Literature Search
**:** Statistical Analysis
**:** Drafting, Revision
**:** Writing of Manuscript

# Frequency of Persistent Pre-diastolic Notch on Uterine Artery Doppler in Diagnosed Cases of Pre-Ecclampsia

**Rukhsana Nasim,[1] Ali Zafar Sheikh,[2] Abeer Yasin,[3] Seema Samreen[4]**

**Abstract**

**Objective:** To determine the frequency of persistent pre-diastolic notch on uterine artery Doppler in diagnosed cases of pre-eclampsia.

**Method:** Descriptive Cross Sectional study, carried out in the Radiology Department Lahore General Hospital, Lahore. Study duration was 6 months, 01-01-2022 to 30-06-2022 A total of 160 cases that fulfilled inclusion/exclusion criteria were enrolled Doppler ultrasound was performed. Patients who had still prediastolic notch at 24 weeks, then persistent prediastolic notch was labeled. All the information was recorded on a predesigned proforma. Data was entered and analyzed by using SPSS version 20.

**Results:** The mean age of patients was 30.07±6.94years. The mean gestational age was 29.61±3.87weeks. There were 37 (23.1%) females with parity 0, 50 (31.3%) had parity 1, 30 (18.8%) had parity 2, 23 (14.4%) had parity 3 and 20 (12.5%) had parity 4. The mean BMI was 26.65±4.58kg/m2. There were 57 (35.6%) females who had persistent pre-diastolic notch on uterine artery Doppler ultrasound while 103 (64.4%) did not show persistent pre-diastolic notch.

**Conclusion:** Incidence of persistent pre-diastolic notch is high in pregnant females diagnosed with preeclampsia.

**Keywords:** Persistent pre-diastolic notch, uterine artery Doppler, preeclampsia

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## Introduction

Hypertensive disorders account for the three common causes of perinatal as well as maternal mortality and morbidity in both under-developed and developed countries.[1] Pre-eclampsia (PE) which is defined as a combination of maternal hypertension and proteinuria at 20 weeks of gestation, complicates about 3–8% pregnancies in the western world.[1,2] Majority of these complications include 13-26% of small-for-gestational age newborns and 16-21% of preterm births leading to perinatal deaths and long-term morbidity in neonates.[3]

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Depending on ethnic group, the incidence of PE in healthy nulliparous women ranges from 3% to 7% and in multiparas from 1% to 3% globally.[4] In Pakistan this incidence is 1.2%. According to an estimate of World Health Organization (WHO) 12% or maternal mortality is attributed to PE in Asia.[5]

In an uneventful pregnancy the resistance of the uterine artery (UA) flow reduces reciprocally with progressing gestational age.[6] If a low resistance-circulation is not achieved, risk of adverse pregnancy outcome increases, one of them being PE, which is a multi-system disorder.[7,8] Utero-placental perfusion can be determined by performing Doppler studies of bilateral uterine arteries and studying their waveform and flow velocities.[9]

Pre diastolic notch appears in the first trimester of pregnancy and represent normal high resistance flow in placental vessel during early pregnancy; it usually disappears after 22 weeks of pregnancy. The presence of

this notch late in pregnancy indicates increased uterine vascular resistance and hence, impaired uterine circulation. This indicated that the pregnancy is complicated by maternal PE.[10] Previous studies have demonstrated an improvement in the screening of adverse pregnancy outcomes utilizing UA Doppler alone in the first and second trimester of pregnancy with different sensitivity and specificity.[11]

The presence of notch in bilateral uterine arteries in second trimester has sensitivity and specificity of 36.1 and 97% respectively, while these measures were 57.5 and 98.2% in third trimester for the prediction of PE.[10-12]

The rationale of this study was to find out the frequency of persistent prediastolic notch in the uterine arteries utilizing Doppler study and pulse waveforms in diagnosed cases of PE in our population, as these tools are readily available in virtually all the obstetric set ups locally. Unfortunately the timely utilization of these tools for early detection of PE and consequent clinical intervention to reduce its complications remains low in our region.

## Material and Methods

This was a descriptive cross sectional observational study and it was conducted in Radiology Out Patient Department (OPD) of Lahore General Hospital from 1st January till 30th June, 2022, after letter of approval from the ethical board. The sample size was n=160 calculated by the formula $n=z^2pq/d^2$ where z=1.96, p=88.2% and d=5. Patients referred from Obstetrics OPD of the same hospital, fulfilling the inclusion criteria; parity <5, ges-tational age of 20weeks (assessed on ultrasound), clini-cally diagnosed to have pre-eclampsia (Bp≥ 140/90 mmHg at least on two determinations 1-7 days apart and ≥ 2+ protein on at least one dipstick measurement in urinalysis) with presence of pre-diastolic notch on uterine artery Doppler done at 20 weeks of gestational age (assessed on ultrasound) were enrolled in our study after getting written informed consent. The patients were also booked for a follow up Doppler ultrasound on 24th week of gestation in the same visit.

Females who were known cases of chronic hypertension (BP≥ 140/90mmHg) before conception, gestational or chronic diabetes (BSR>186mg/dl), females with twin pregnancy (on ultrasound), females suffering from anemia (Hb<10g/dl) or renal impairment (creatinine >1.2mg/dl) and liver diseases (ALT>40IU, AST> 40IU) were excluded from the study. Demographic details (name, age, parity, Body Mass Index, gestational age at presentation) were recorded. Then UA Doppler ultrasound was performed using GE Logic S8 ultrasound machine having a 2.3–4 MHz trans-abdominal transducer. All scans were done by at least three qualified radiologists having at least 4 years of experience in ultrasound and Doppler. The right and left uterine arteries were identified in patients at 20 weeks of gestation using grey scale and colour Doppler in an oblique plane of the pelvis with the patient lying in supine position. The Doppler signals were sampled at the level where the uterine arteries cross over the external iliac arteries. At least three consecutive waveforms were obtained to identify the pre-diastolic notch in uterine artery evident as a trough-like notch in between the systolic and diastolic phases. The patients who had the notch in bilateral uterine arteries were assessed again at 24th week of gestation using the same technique and parameters. Re-demonstration of the pre-diastolic notch in bilateral uterine arteries at 24 weeks of gestation was labeled as persistent pre-diastolic notch. All this information was recorded on a predesigned preforma.

Data was entered and analyzed by using SPSS version 20. Quantitative data including maternal age, gestational age, height, weight and BMI was presented by mean and standard deviation (SD). Qualitative data like parity and persistent pre-diastolic notch was presented as frequency and percentages. After this chi-square test was applied to check the significance of the results with p-value ≤ 0.05.

## Results

During the study 160 patients with singleton pregnancy and clinical diagnosis of PE underwent ultrasound at 20 weeks and again at 24 weeks of gestation.

The mean age of patients was 30.07±6.94years and the mean gestational age was 29.61±3.87weeks. There were 37 (23.1%) females with parity 0, 50 (31.3%) had parity 1, 30 (18.8%) had parity 2, 23 (14.4%) had parity 3 and 20 (12.5%) had parity 4. The mean BMI was 26.65 ± 4.58kg/m$^2$.

There were 57 (35.6%) females who had persistent pre-diastolic notch on UA Doppler ultrasound while 103 (64.4%) did not show persistent pre-diastolic notch. Figure 1, 2

Data was stratified for age of patients. In patients aged

18-30years, persistent pre-diastolic notch was present in 45 (54.2%) patients. In patients aged 31-42years, persistent pre-diastolic notch was present in 12 (15.6%) patients. The difference was in significant range ($p<0.05$). Table 1

Data was stratified for gestational age of patients. In patients presented at gestational aged 24-30weeks, persistent pre-diastolic notch was present in 30 (31.9%) patients. In patients presented at gestational aged 24-30 weeks, persistent pre-diastolic notch was present in 27 (40.9%) patients. The difference was insignificant ($p>0.05$). Table 2

Data was stratified for parity of patients. In nulliparous patients, persistent pre-diastolic notch was present in 23(62.2%) patients. In primiparous patients, persistent pre-diastolic notch was present in 20 (40.0%) patients. In multiparous patients, persistent pre-diastolic notch was present in 14 (19.2%) patients. The difference was significant ($p<0.05$).

Data was stratified for BMI of patients. In normal weight patients, persistent pre-diastolic notch was present in 20(29.9%) patients. In overweight patients, persistent pre-diastolic notch was present in 21(42.9%) patients. In obese patients, persistent pre-diastolic notch was present in 16 (36.4%) patients. The difference was significant ($p<0.05$).

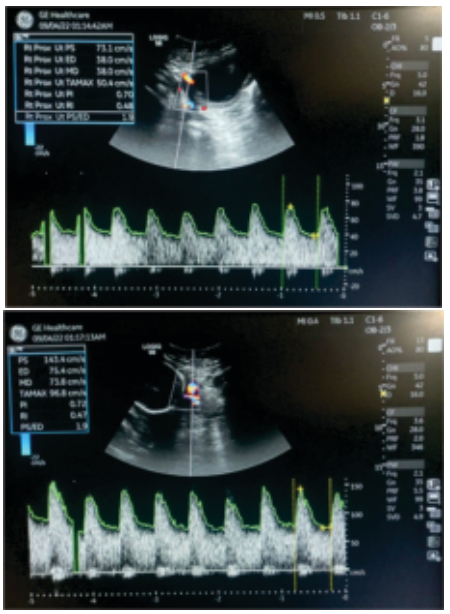

**Figure 1** *Right and Left uterine artery Doppler and pulse waveform of a diagnosed patient of preeclampsia at 25 weeks of gestation with absent pre-diastolic notch.*

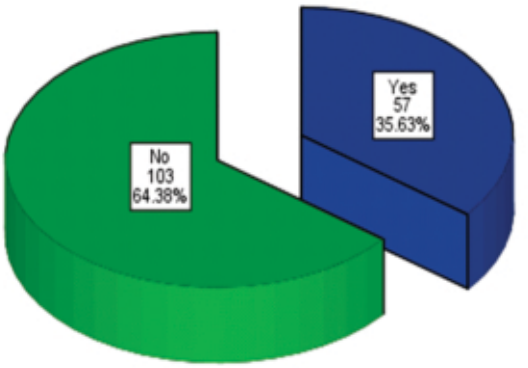


**Figure 2** *Distribution of persistent pre-diastolic notch*

## Discussion

In our study, there were 57 (35.6%) females who had persistent pre-diastolic notch on uterine artery Doppler ultrasound. One international study showed that the frequency of persistent prediastolic notch on uterine artery Doppler was 22.6% in females with preeclampsia.[13] Another study showed that the frequency of persistent prediastolic notch on uterine artery Doppler was 36% in females with preeclampsia.[14] This high frequency of abnormal UA Doppler studies was also reflected by another Pakistani study done by Tabassum S., et al however in their study obesity was reported in 18.8% of the patients while in our study it was 35.6%.[15] The difference can be attributed to a increased incidence of obesity in general population in Punjab compared to Sindh, where their study was conducted.[16]

A recent local study done by Shahid N., et al, showed the mean maternal age to be 27.65 and mean gestational age of 23.88 which is in correspondence to our study.[17]

**Table 1:** *Comparison of persistent pre-diastolic notch in age strata*

| | | Age (years) | | Total |
|---|---|---|---|---|
| | | 18-30 | 31-42 | |
| Persistent pre-diastolic notch | Yes | 45 (54.2%) | 12 (15.6%) | 57 (35.6%) |
| | No | 38 (45.8%) | 65 (84.4%) | 103 (64.4%) |
| Total | | 83 (100%) | 77 (100%) | 160 (100%) |

*Chi-Square Test = 25.994: p-value = 0.000 (Significant)*

**Table 2:** *Comparison of persistent pre-diastolic notch in gestational age strata*

| | | Gestational Age (weeks) | | Total |
|---|---|---|---|---|
| | | 24-30 | 31-36 | |
| Persistent pre-diastolic notch | Yes | 30 (31.9%) | 27 (40.9%) | 57 (35.6%) |
| | No | 64 (68.1%) | 39 (59.1%) | 103 (64.4%) |
| Total | | 94 (100%) | 66 (100%) | 160 (100%) |

*Chi-Square Test = 1.368: p-value = 0.242 (Insignificant)*

The presence of pre-diastolic notch in the second trimester has been linked to a high probability of developing pre-eclampsia.[18] In a study conducted by El-Hamedi A., et al, the disease was predicted in almost 75% of the most severe cases who had developed pre-eclampsia before eighth month of gestation. This suggests that the clinical value of UA doppler is favorable in predicting severe forms of adverse outcomes in patients at a higher risk for pre-eclampsia.[19,20]

## Conclusion

Thus the incidence of persistent pre-diastolic notch in UA Doppler is high is diagnosed case of PE . We will recommend the gynecologists to utilize UA Doppler studies as a non-invasive, quick and affordable screening tool for early detection of PE so that timely clinical interventions can be made to prevent its grave complications.

**Conflict of Interest** *None*

**Funding Source** *None*

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## Authors Contribution

**RN:** Conceptualization of Project
**SS:** Data Collection
**AZS:** Literature Search
**SS:** Statistical Analysis
**AY:** Drafting, Revision
**AY:** Writing of Manuscript

# Comparison of Hemodynamic Parameters of Propofol and Sevoflurane During Cardiopulmonary Bypass Time in Patients Undergoing Coronary Artery Bypass Graft: A Randomized Control Trial

**Kaneez Ume Farwa,[1] Fatima Sakina,[2] Bukhsh Ahmad,[3] Fatima Majeed,[4] Waseema Afzal,[5] Muhammad Jahangeer[6]**

**Abstract**

**Objective:** To compare hemodynamic parameters of propofol and sevoflurane during cardiopulmonary bypass time in patients undergoing coronary artery bypass graft (CABG) surgery to avoid increase in lactate level.

**Method:** One hundred and twenty-six patients were included. Non probability consecutive sampling was used. Patients were divided in two groups, propofol was given to group 1-P, and sevoflurane to group II-S. Age, clamp-time, bypass-time, mean arterial blood pressure on bypass machine, lactate level (pre-cross clamp lactate level and post-rewarming lactate) and flow-rates on CPB were compared between two groups. SPSS version 24 was used and p value ⩽ 0.05 was considered as significant.

**Results:** The mean pre-cross clamp lactate level, post- rewarming lactate, total noradrenaline dose used, MAP (Mean Arterial Pressure) during CPB, flow-rate, total bypass-time and cross clamp-time of Group-I was 1.79±0.58 mmol/L, 4.67±0.98 mmol/L, 0.088±0.04µg/kg, 65.37±2.14 mmHg, 5.23±1.06L/min=(CI×BSA), 109.04± 3.08 minutes and 67.90±2.08minutes , respectively. The mean pre-cross clamp lactate level, post- rewarming lactate, total noradrenaline dose, MAP during CPB, flow-rate, total bypass-time and cross clamp-time of Group-II was 1.88±0.62 mmol/L, 4.75±0.22 mmol/L, 0.18±0.12µg/kg, 69.69±2.22 mmHg, 4.66±2.29L/min=(CI×BSA), 110.12±2.82minutes and 68.63±2.47minutes , respectively. The differences were statistically insignificant, except total Noradrenaline dose (p=0.000) and MAP during CPB (p=0.000).

**Conclusion:** Study reveals that hemodynamic stability in both groups remained same but mean arterial pressure was low which required higher flow-rate. Group II showed increase requirement of vasopressors.

**Keywords:** Propofol, Sevoflurane, hemodynamic stability, Lactate level, CABG

**How to cite:** *Farwa KU, Sakina F, Ahmad B, Majeed F, Afzal W, Jahangeer M. Comparison of Hemodynamic Parameters of Propofol and Sevoflurane During Cardiopulmonary Bypass Time in Patients Undergoing Coronary Artery Bypass Graft: A Randomized Control Trial. Esculapio - JSIMS 2022;18(03):305-309*

***DOI: https://doi.org/10.51273/esc22.2518313***

## Introduction

Among intravenous anesthetics propofol is frequently and widely used anesthetic with high lipid solubility.[1] Pharmacokinetics of propofol allows rapid induction, proper maintenance and early recovery of conscious level at the time of reversal given. On other hand sevoflurane is also widely used volatile and haloginated anesthetic with low blood gas solubility which allows rapid onset of action.[2] Sevoflurane is isopropyl flurinated methyl ether with pleasant fragrance, hemodynamicaly stable and fast emergence in body. Cardiac anesthesiologists recommended sevoflurane in comparison with isoflurane.[3] During cardiac bypass sevoflurane have vasodiator effect due to its smooth muscle ralaxant action on vascular resistance and reduces the

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output of sympathetic system without any effect on smooth muscle stimuli of any other origin.[4] Lots of controversial studies are available in use of sevoflurane and propofol for cardiac stability. Some authors concluded no difference between propofol and sevoflurane use.[5] All above of these conclusions and controversies both drugs are widely in practice in cardiac surgery because of their hemodynamic stability.[6] Lactic acid is an end product of anaerobic metabolism which causes lactic acidosis and leads to tissue hyoperfusion.[7] Measurement of lactic acid can be done with blood lactate level which is helpful for assessment of tissue perfusion and its adequacy in body.[8] Tissue hyoperfusion is a risk of CPB during surgery and after surgical procedure. Increase of decrease in lactate level may be due to degree and duration of hypothermia, duration of CPB, pump flow rate means oxygen delivery, and intraoperative maintenance of anesthesia or hematocrit value.[9]

High lactate level after cardiac operation is a predictor of many complications like prolong ventilatory support and inotropic support which increase the morbidity and mortality rate at the time Icu admission.[10] This study was conducted to correlate the hemodynamic effect of propofol and sevoflurane in terms of hemodynamic stability, blood lactate level, perfusion pressure and complications after and during surgical procedure.

## Material and Methods

This study was a randomized control trial, that was conducted in the cardiac surgery department of Chaudhary parvaiz Elahi Institute of cardiology, Multan from May 2017 to May 2018 under supervision of senior staff of cardiac surgery and intensive care unit. One hundred and twenty six patients were included in this study. The sample size was calculated from reference study ( Gravel etal, 1999, that was randomized control trial) published in Canadian journal of anesthesia, with the help of www.openepi.com online sample size calculator, with confidence interval of 95% and power of study 80%. Study was started after ethical approval from ethical board of institution, letter NO:06, JAN, 2017. This study has been registered in clinical trial registry (Clinical Trials.gov Identifier: NTC05004545). Informed consent was taken from patients. Non probability consecutive sampling technique was used for collection of data. Patients with history of uncontrolled hypertension, diabetes, any chest trauma or surgery, emergency surgery, known history of drugs used in trial and who were refused to give informed consent were excluded from the study.

All patients who were advised elective coronary artery bypass graft surgery under standard anesthesia and hospital protocols included in the study. Fentanyl 5-15 micrograms/kg, propofol 1-1.5 mg/kg, midazolam 0.05 - 0.1 mg/kg and 0.5 mg/kg atracurium was used for induction of anesthesia. Anesthesia was maintained with isoflurane and additional doses of atracurium and fentanyl till the time of cardiopulmonary bypass. Patients were divided into two equal groups I and II. Group I was given propofol infusion with doses of 75-125 micrograms /kg/min and maintained. In group II sevoflurane 1-2% was given with vaporizer which is connected with CPB pump oxygen supply system. Supply was constantly delivering 3 liter per mint of oxygen and sevoflurane mixture. Once CPB started hypothermia of 32 degree was monitored with hemotherm stockertand monitored through nasal probe. Perfusion pressure monitored through invasive blood pressure monitoring, flow rate monitored according to body surface and cardiac index maintained at 2.4 L/min/$m^2$. Blood lactate level and hemoglobin monitored with arterial blood gasses on hourly basis through blood gas analyzer ABL 800. Anterograde and retrograde cardioplegia was applied, hemoglobin level maintained at 8 to 9 grams/dl and final lactate level was obtained before rewarming. Cross clamp time and bypass time was recorded. All data was collected and recorded by another person who is unaware of study variables.

Data was recorded and analyzed by using SPSS version 24. Mean and standard deviation were calculated for quantitative variables like age, clamp time, bypass time. Frequency and percentages were calculated for qualitative data like gender. Student t test and chi square test was applied to see association between variables. P value $\leq 0.05$ was taken as significant.

## Results

One hundred and twenty-six patients of both genders were included in this study. The patients were divided into two groups; n= 63 in Group-I and n=63 in Group-II. The mean age and weight of Group 1-P was 46.09 ± 3.06years and 66.34±4.11kg, respectively. There were more males than females i.e. n=43 (68.3%) and n=20 (31.7%), respectively. While, the mean age and weight of Group II-S was 48.84±2.96 years and 71.14±4.88 kg, respectively. There were more males than females i.e. n=50 (79.4%) and n=13 (20.6%), respectively. The difference of age and weight were statistically signifi-

cant, (p=0.000) and (p=0.000), respectively (Table. I).

The mean pre-cross clamp lactate level, post- rewarming lactate, total noradrenaline dose, MAP during CPB, flow rate, total bypass time and cross clamp time of Group-I was 1.79±0.58 mmol/L, 4.67±0.98 mmol/L, 0.088±0.04μg/kg, 65.37±2.14 mmHg, 5.23± 1.06 L/min = (CI×BSA), 109.04±3.08minutes and 67.90±2.08 minutes, respectively. While, The mean pre-cross clamp lactate level, post- rewarming lactate, total noradrenaline dose, MAP during CPB, flow rate, total bypass time and cross clamp time of Group-II was 1.88±0.62 mmol/L, 4.75±0.22 mmol/L, 0.18±0.12μg/kg, 69.69±2.22 mmHg, 4.66±2.29L/min=(CI×BSA), 110.12±2.82minutes and 68.63±2.47minutes , respectively. The differences were statistically insignificant, except Total Noradrenaline dose (p=0.000) and MAP during CPB (p=0.000). (Table. II). P-value ≤0.05 was considered as significant.

**Table 1:** *Demographic Variables*

| Variable | Group I-P n=63 | Group II-S n=63 | P-value |
|---|---|---|---|
| **Age (years)** | 46.09±3.06 | 48.84±2.96 | 0.000 |
| **Weight (kg)** | 66.34±4.11 | 71.14±4.88 | 0.000 |
| **Gender** | | | |
| **Male** | n=43 (68.3%) | n=50 (79.4%) | 0.156 |
| **Female** | n=20 (31.7%) | n=13 (20.6%) | |

**Table 2:** *Hemodynamic Parameters among the Groups*

| Variable | Group I-P n=63 | Group II-S n=63 | P-value |
|---|---|---|---|
| Pre-cross clamp lactate level (mmol/L) | 1.79±0.58 | 1.88±0.62 | 0.407 |
| Post- rewarming lactate (mmol/L) | 4.67±0.98 | 4.75±0.22 | 0.534 |
| Total Noradrenaline dose (μg/kg) | 0.088±0.04 | 0.18±0.12 | 0.000 |
| MAP during CPB (mmHg) | 65.37±2.14 | 69.69±2.22 | 0.000 |
| Flow rate (L/min = (CI×BSA)) | 5.23±1.06 | 4.66±2.29 | 0.073 |
| Total bypass time (Minutes) | 109.04±3.08 | 110.12±2.82 | 0.081 |
| Cross clamp time (Minutes) | 67.90±2.08 | 68.63±2.47 | 0.075 |

## Discussion

Hemodynamic stability and lactate level control is the main requirement during anesthesia which leads to better outcomes in postoperative period. It is well established truth that hemodynamicaly unstable patients during anesthesia may have high lactate level. In a study by Ranucchi et al[11] it was observed that there was no linearity between association of lactate level and mean CPB time during cardio pulmonary bypass. In his study cut off value for CPB was 96 minutes.

In another study conducted by Shinde et al, it was[12] reported that there was a relationship between CPB and lactate level when cut off value for CPB was 96 minutes, but this relationship among both variables is not linear. Another study was conducted by Essa J et al[13] and was reported that patients in both propofol and sevoflurane group remain hemodynamicaly stable. There was no difference observed regarding noradrenalin dose and lactate level. In propofol group low MAP was observed (63.1 ± 2.6 mmhg).

Another study was conducted by Khare A et al[14] on comparison of sevoflurane and propofol and reported that hemodynamic stability and recovery profile of sevoflurane is equal to propofol. He recommended that sevoflurane can be used as an alternative of propofol in laparoscopic procedures. Heart rate is also same in both groups. In terms of hemodynamic stability of propofol and sevoflurane this study is compareable with our study, but it was performed in different group of patients. Another study was conducted by Likhvanta VV et al[15] and reported that sevoflurane control the cardiac biomarkers release and reduce the hospital stay of patients when compared with propofol infusion in coronary artery bypass graft surgery in which patient was kept for CPB. Use sevoflurane also reduce the 1 year mortality rate by reduction of post-operative complications. Recovery time is also rapid after use of sevoflurane. This study is also comparable with our study. In this study lactate level during and after use of CPB was not monitored.

Another study was conducted by Tang L et al[16] and on use of sevoflurane in inhalational anesthesia for hemodynamic stability and reported that sevoflurane is superior to any other anesthetic agent. Recovery time was not effected with use sevoflurane. Bharti N et al[17] also conducted study on comparison of sevoflurane and propofol and reported that emergence time, recovery time and extubation time was assessed and concluded that there was not markable difference between both groups.

Robba C et al[18] also conducted a similar study on comparison of sevoflurane and propofol anesthesia and reported that induction of anesthesia is safe and fast in both groups, but mean arterial pressure drop is associated

with both groups which can leads to hypoperfusion of spinal cord. In a study conducted by Husedzinovic et al[19] reported that myocardial contractility increased to significant range in sevoflurane group when Doppler echo was performed. Hemodynamic stability and hypertension remains same in both groups at the time of induction and after induction.

Orhon ZN et al[20] conducted a study between propofol and sevoflurane and reported that hemodynamic parameters, spo2 values were not significantly different between two groups. Sevoflurane is as effective as propofol both groups when compared in terms of heart rate and blood pressure. This study is also comparable with our study. Two main factors were reported for responsibility of hemodynamic instability; one blood loss during surgery and second is inadequate anesthesia. It is very important to evaluate the cause hemodynamic instability. Bleeding cause can be corrected with intravenous fluids (colloids, crystalloids) and for anesthetic cause depth of anesthesia should be revaluated.

Tang et al[21] conducted a study using sevoflurane and propofol in patients undergoing cardiopulmonary bypass, they found no difference in adverse events, in terms of low cardiac output and post thoracotomy bleeding, after use of these drugs. These results are comparable with our study. They have studied cardiac output, decline in it is responsible for increase in lactate level.

Maintaining acid-base balance during cardiopulmonary bypass in CABG surgeries is one of the main strategies of management. The metabolic acidosis, as shown by increases in lactate level can be prevented by maintaining adequate perfusion. We compared Sevoflorane and Propofol for studying hemodynamic parameters with their use. That showed both drugs are same in this respect, however higher flow rates are required together with use of noradrenaline to maintain adequqte mean arterial blood pressure and cardiac output, that is mandatory to prevent ischemic injury to body organs and increase in lactate level. Maintaining adequate level of hemoglobin is also part of it. Myocardial pharmacological support in terms of Noradrenaline use was higher in sevoflurane group showing its higher cardiac depressant effect.

Some factors may have been important, affecting our results, like left ventricular ejection fraction at time of surgery, blood loss before onset of CPB machine, that were managed with use of pharmacological support and packed red blood cell transfusion.

**Limitations of the study:** Our study have certain limitations, that is flow rates and use of inotropes are affected by vasodilation that is caused by various medications used by patient in preoperative period and anesthetics during procedure. Inflammatory response to CPB circuit also causes vasodilation. For maintaining adequate perfusion, and lactate level all these things must be considered.

Results of our study reveal that hemodynamic stability in both groups remains same but mean arterial pressure was low which required high flow rates and vasopressors during cardiopulmonary bypass time. To maintain adequate level of mean arterial blood pressure significantly higher amount of vasopressor was used in group II, that shows more cardiac depressant effect of sevoflurane. During CPB lactate level remained same in propofol infusion and sevoflurane groups during cardiopulmonary bypass graft surgery. Further controlled trialed studies required to justify the superiority.

**Conflict of Interest** *None*

**Funding Source** *None*

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## Authors Contribution

**KUF:** Conceptualization of Project

**FS:** Data Collection

**BA:** Literature Search

**FM:** Statistical Analysis

**WA:** Drafting, Revision

**MJ:** Writing of Manuscript

# Heart Rate Variability- A Predictive Tool for Analysis of Autonomic Dysfunction in Covid-19 Vaccinated Individuals

**Somia Iqbal,[1] Sumaira Iqbal,[2] Sumera Gul,[3] Atayyab Shaukat,[4] Komal Saher[5]**


## Abstract

**Objective:** To determine the association between gender and HRV values in COVID-19 vaccinated participants and the difference in HRV in male and female COVID-19 vaccinated individual as compared to standard value of HRV in healthy individuals

**Method:** An experimental, randomized control study was carried out in the department of physiology of Wah Medical College, Wah Cantt, Pakistan for 3 months (April 2021 to June 2021). A total 100 vaccinated students of 1st year and 2nd year MBBS were divided into 2 groups, Female (Nf= 50) and Male Group (Nm= 50). Then were further divided into three groups: (Group 1-HRV in above normal range), (Group 2- HRV in below normal range), and (Group 3- HRV in normal standard range).

**Results:** 64.0% females had HRV value within standard reference range whereas 36.0% were below the range. 44.0% males had HRV value within standard reference range, 28.0% were below the range and 28.0% were above range. There was significant association ($p < 0.001$) between gender and HRV values in COVID-19 vaccinated participants. The average HRV of male and female COVID-19 vaccinated individuals were significantly different ($p<0.001$). The HRV of female vaccinated individuals was significantly different where no difference was found in male vaccinated individuals, when compared with standard values.

**Conclusion:** COVID-19 vaccinated females are more prone to disturbance in autonomic modulation as compared to males vaccinated individuals, thus at momentarily risk of cardiovascular events.


**Keywords:** COVID-19, Heart rate variability, Gender, Vaccine

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## Introduction

COVID-19 virus, first identified in China in December 2019, was communicated globally imprudently.[1-2] For more than one year, authorities across the world have encountered multifaceted challenges to battle this ailment. Due to an imperative necessity to thwart the further blowout of COVID-19 infections, the conservative measures for consent of new vaccines could not be trailed, and these vaccines were given as an emergency endorsement.[3] This creates a solid motive for gathering detailed scientific evidence for these vaccines by monitoring the adversative responses reports in the population, after vaccination.[4-6]

Most vaccines work by exposing the body's combat system to antigens and generate a comparable immune response as if it was exposed to the actual virus.[7] Thus, after getting a vaccine, augmented inflammation levels caused by stimulation of our immune system may lead to a short-lived unevenness in the autonomic innervation of the heart. Decrease in parasympathetic action and extreme sympathetic activation effect the functions of ANS, thus causes cardiovascular dysfunction, arrhythmias and sudden death.[8]

Heart rate variability (HRV) is an easily manageable, accessible, and noninvasive physiological tool, regulated by the autonomic nervous system (ANS). It is used

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for decades to evaluate general well-being in various clinical settings.[9] Decrease in HRV below the normal range is risk factor for disruption in normal cardiac events like such as arrythmias, angina, myocardial infarction and can be a warning of an impending cardiac complication. It helps to diagnose earlier than other currently employed laboratory tests.[8,9]

Presently, there is dispersed information regarding the disparate events about the reporting and scrutiny of adverse measures following the COVID-19 vaccination. This study analyzes whether there is any association between gender and HRV values in COVID-19 vaccinated participants and there is difference in HRV of male and female covid-19 vaccinated individual as compared to standard value of HRV in healthy individuals. Hence, by using heart rate variability as a predictive tool, we will try to analyze that whether the COVID-19 vaccination is associated with cardiac illness state evolution or not. In addition, this study helps to generate a safety signal for COVID-19 vaccines at an early stage and form the foundation of other studies for creating and assessing the safety data of COVID-19 vaccines.

## Material and Method

This cross-sectional experimental randomized control trial was conducted in Department of Physiology, Wah Medical College, Wah Cantt after getting approval from ethical review board.

A total of hundred students from first year and second year MBBS were enrolled in the study via random sampling. The study was proceeded after informed and written consent from the participants. Data was collected within 20 days after complete vaccine protocol. The students who received inactivated COVID-19 vaccines were included in the study. Equal number of male and female participants were included/To control the factor of gender in our study, we used the equal allocation stratification technique. Students who were less than 17 years or more than 21 years and who have history of hypertension, or any other cardiac disease were excluded from the study. Students taking anti-asthmatic drugs, cold medicine, decongestant, antihypertensive drugs, anti-depressants, anti-anxiety, or thyroid medicines were also excluded from the study. Students after 20 days of vaccination was not included in the studies. Subjects were requested to avoid coffee, tea, cola drinks, and smoking for 12 hours before data collection procedure. Heart rate variability was obtained during deep breathing in early morning by Lead II electrocardiographic recording for 1 minute using an electrocardiograph.

For measuring heart rate variability, we used the commonly used time domain method by RMSSD which is the square root of the mean squared differences of successive NN intervals.[10]

The root mean square of successive differences between normal heartbeats (RMSSD) was obtained by first calculating each successive time difference between heartbeats in milliseconds(ms). Then, each of the values was squared and the result was averaged before the square root of the total was obtained.[11] The RMSSD reflects the beat-to-beat variance in heart rate and is the primary time-domain measurement used to estimate the vagally mediated changes reflected in HRV.[10]

The normal value of heart rate variability in young healthy adults if measured by time domain method (RMSSD) is 42+15ms.[12,13] Individuals with HRV less than 27ms were considered to have low heart rate variability and was allocated the Group 1, Group 2 individual with HRV more than 57ms were considered to have high HRV and individuals with HRV more than 27ms and less than 57ms were considered to have normal HRV and were allocated in Group 3.

Data was collected on data collection proforma (given in Annexure A) and then was analyzed by using Statistical Package for the Social Sciences (SPSS 20.0 version software program). Covid-19 vaccination was an independent variable and Heart rate variability was dependent variable.

Results of COVID-19 vaccinated participants are divided into 2 sets of Female (Nf=50) and Male Group (Nm= 50). Then result of each set is further divided into three groups; (Group 1-HRV in above range), (Group 2- HRV in below range), and (Group 3- HRV in normal standard range) and were expressed in terms of percentage. Chi square test was applied to test the significant association between gender and HRV values in COVID-19 vaccinated participants. Independent sample T test was applied to observe the gender difference in the variance and average HRV of COVID-19 vaccinated individuals. One sample T test was applied to observe the difference in HRV of male and female COVID-19 vaccinated individual when compared to standard value of HRV in healthy individuals. P value of $< 0.05$ was regarded as significant.

## Results

The HRV values in females (Nf= 50) and males (Nm=

50) were expressed in Table 1.1 Results after applying Chi Square test displayed that p value is <0.001 that showed a significant association between gender and HRV values in COVID-19 vaccinated participants.

The mean HRV values in male and female students were 48.6639 + 4.43ms and 31.1422 + 0.94ms respectively. Table-2 shows that the variance for HRV of male COVID-19 vaccinated individuals is statistically different from HRV of female COVID-19 vaccinated individuals. Table-3 showed that it means there is no significant difference in HRV of male COVID-19 vaccinated individual as compared to standard value of HRV in healthy individuals. However, the HRV of female COVID-19 vaccinated individual as compared to standard value of HRV in healthy individuals was found significantly different.

**Table 1:** *Heart Rate Variability (HRV) of COVID-19 Vaccinated Individual*

| | | HRV of Covid-19 Vaccinated Individual | | |
|---|---|---|---|---|
| | | Above | Below | Normal |
| **Participants Of COVID-19 Vaccinated Individual Count (N=100)** | Female Participants Of COVID-19 Vaccinated Individual (%) | 0.0% | 36.0% | 64.0% |
| | Male Participants Of COVID-19 Vaccinated Individual (%) | 28.0% | 28.0% | 44.0% |

**Table 2:** *Comparison of Variance of HRV of Male and Female COVID-19 Vaccinated Individuals*

| | | Levene's Test for Equality of Variances | | Significance | |
|---|---|---|---|---|---|
| | | F | Sig. | One-Sided p | Two-Sided p |
| **HRV values of COVID-19 vaccinated individuals** | Equal variances assumed | 24.830 | <.001 | <0.001 | <0.001 |
| | Equal variances not assumed | | | <0.001 | <0.001 |

**Table 3:** *Comparison of HRV of Female and Male COVID-19 Vaccinated individuals with standard reference value*

| | Significance |
|---|---|
| HRV values Female COVID-19 Vaccinated individuals | <.001 |
| HRV values Female COVID-19 Vaccinated individuals | .070 |

## Discussion

Investigational evidences recommend that autonomic indicators such as heart rate variability (HRV) is advantageous and suitable way of estimating the autonomic modulation.[14] Low HRV has been documented as a solid pointer of risks linked to adversative proceedings, indicating the importance of autonomic nervous system in sustaining health.[14-16] Our study showed a notable association between gender and HRV values in COVID-19 vaccinated participants and showed a significant difference between the average HRV of male and female COVID-19 vaccinated participants. Our findings were similar to the results of Umetani et al., (1998) and Lutfi & Sukkar., (2011) that showed that there were gender variances in autonomic modulation. The underlying mechanisms of the gender difference in cardiac autonomic function are still not clea.[17,18] However, Umetani et al., (1998) and Koenig & Thayer., (2016) proposed that the detected gender differences show lower parasympathetic activity in female and this view is supported by the fact that females have an increased heart rate as compared to males.[17,19]

Our study showed that HRV in female COVID-19 vaccinated individual is significantly low as compared to standard HRV value in healthy individuals.[12,13] It is probably due to the fact that the vaccine may generate an inflammatory provocative response that is controlled by the autonomic nervous system.[8,9] This association is mediated to a large degree by the vagus nerve.[9] The vagus nerve not only plays an imperative role in regulation of inflammation but also acts as a bidirectional street between the brain and the rest of the body as it is also forming the autonomic innervation of the heart.[9,10] Therefore, after getting a vaccine, augmented inflammation levels caused by stimulation of the immune system may lead to a short-lived irregularity in the autonomic innervation of the heart.8 Therefore, it can be hypothesized in the light of our findings that vaccinated females are more prone to disturbance in autonomic modulation as compared to males vaccinated individuals. These results were similar to results of Lanza GA et al., (2011) that showed that vaccine for Influenza A virus also induce cardiac autonomic dysfunction and may momentarily increase the risk of cardiovascular events.[20] However, our study showed no significant change in HRV of male vaccinated participants, rather showed dominant parasympathetic activity in the form of high HRV. Lutfi & Sukkar., (2011) study also showed significantly higher HRV values in males as compared

to females.[18] In addition, the results of Umetani et al., (1998) also revealed lower HRV in female compared with male subjects at age less than 30 years old.[17] Khan, Hussain & Aleem., (2010) study showed that population of Pakistan have increased parasympathetic activity further strengthened our results.[13] However, pros of vaccine administration are way more than the cones and a study with bigger sample size is required to be done to determine further validity and reliability of our results. Furthermore, follow up data can also help in further strengthening or nullifying our findings.

## Conclusion

Our study showed that COVID-19 vaccinated females are more prone to disturbance in autonomic modulation as compared to males vaccinated individuals, thus at momentarily risk of cardiovascular events.

**Conflict of Interest** *None*

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## Authors Contribution

**SI:** Conceptualization of Project

**SI, AS, KS:** Data Collection

**SI:** Literature Search

**SI:** Statistical Analysis

**SI:** Drafting, Revision

**SI, SI:** Writing of Manuscript

# Socio-Demographic Factors and Abuse in Attempted Suicide and Deliberate Self-Harm

**Sumira Q Bokhari,[1] Rehma S Alam,[2] Qambar M. Bokhari,[3] Rabia Majeed,[4] Aysha Butt[5]**

**Abstract**

**Objective:** The objective of this study was to find out the socio-demographic factors and causes of Deliberate Self-Harm and suicide attempt.

**Method:** Cross-Sectional research design and purposive sampling was used to collect data from Department of Emergency and Department of Psychiatry, Services Hospital, Lahore. Data was comprised of 100 patients with suicidal attempt, with age-range of 13 to 65 years (M = 25.65, SD = 11.15). A semi-structured interview was conducted with the participants and Traumatic Experience Checklist (Nijenhuis, Van der, Kruger, 2002) was administered to determine the occurrence, and impact of any trauma experienced by them.

**Results:** The data was analyzed through descriptive statistics, and frequency and percentages of age, gender, educational status, and professional status, causes and ways of Deliberate Self-Harm, history of psychological illness, family history of Deliberate Self-Harm and psychological illness, and scores of participants on Traumatic Experience Checklist were determined. The results of study showed that medicine intake (43%), acid intake (22%) and cuts and injuries (25%) were the most common ways of Deliberate Self-Harm and family conflicts (56%) and psychological illness (28%) were the commonest causes of Deliberate Self-Harm.

**Conclusion:** It can be concluded from the findings of the study that experiencing one or more trauma, family conflicts and psychological illness are some of the major causes of Deliberate Self-Harm in patients with suicide attempt.

**Keywords:** Deliberate self-harm, suicide, trauma, abuse.

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## Introduction

One of the serious mental health problems are suicidal behaviors and deliberate self-harm.[1,2] In every country, including Pakistan, fatal attempts of suicide is positioned among top ten reasons of death in all age group. It is one of the three major causes of death in the age group 15-35.[1] According to the World Health Organization report (2001) about 10 to 20 million people attempted to commit suicide, and about one million became successful in their attempt of suicide. Moreover, the prevalence rate for suicide over the world ranges from 5 to 30 lakhs population per year. Suicide is described as a multidimensional and multifactorial sickness and dissatisfaction.[3] The acts of suicide are recognized as the social problems, and therefore, mental health conditions are given equivalent conceptual status with conflicts in family, maladjustment in social settings etc. For about 43% of the suicide cases, the cause is unknown.[4] The survey of World Health Organization reported that the complex interaction between biological, psychological, social and situational factors result in suicide. Similarly different medical, social and psycho-

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logical conditions, along with early age of 15 to 24 years, female gender, lack of education, unavailability of employment opportunities, loneliness and history of socio-economic deprivation were reported to be the potential risk factors of suicide.[5] In addition to suicide, Deliberate self-harm (DSH) is defined as the intentional injuring to one's own body. It could be with or without apparent intention of suicide.[6] Currently DSH is one of the major community health problems in Pakistan, as the estimated figures of intentional harm to self were reported to be more than 100000 per year.[7] Therefore it is essential to deal with the increasing cases of DSH, as its number is 10 to 20 times higher than completed suicides.[8] Thompson and Kaslow (2002) attempted to study the risk factors of suicidal attempts in African American women who were experiencing recent intimate partner violence (IPV). The results of the study showed that participants with suicidal attempt were more likely to have hopelessness, higher levels of depressive symptomatology, abuse of drugs, and history of childhood abuse and neglect during childhood, as compared to those who did not report any suicidal attempt.[9] Devries, et al., (2013) found that in women with IPV, IPV was associated with the occurrence of depressive symptoms. Similarly IPV was also related with the incidents of suicidal attempts.[10] Moreover Lauw, How and Loh (2015) identified that adolescents who were at the risk of harming self intentionally are likely to experience common stressful events which included problems in friendship or relationship issues, study related stress, bereavement, physical or psychological abuse.[11]

Spokas, Wenzel, Stirman, Brown, Beck (2009) studied the role of childhood sexual abuse (CSA) as a risk factor for suicidal behavior among participants with recent suicidal ideation. The study showed that men who recently attempted suicide, had a history of CSA, and had higher scores on hopelessness and suicidal ideation than men without a CSA history. Men with a CSA history were also more likely to have made multiple suicide attempts.[12]

In addition to this Hunuscin, et al., (2018) conducted another study to identify the ways of self-inflicted harm in US population. The study showed that firearm usage, cutting/piercing, jumping from high places, anoxic injuries and poisoning were the most common ways of inflicting harm to self.[13] Moreover another study was conducted by Bazargan, et al., (2017) identified that participants who were involved in deliberate self-harm were more likely to be suffering from substance abuse and various mental health problems i.e., episodic mood disorders (49.3%), depressive disorders (19.2%), anxiety disorders (11.2%) and schizophrenia (10.8%).[14] Similarly Hawton (2002) also concluded that people with deliberate self-harm tend to have a history of recent attempt of self-harm done by friends or family members, abuse of drugs, depressive symptoms, anxiety, lack of impulse control, and self-esteem issues.[15]

A review of currently available indigenous literature on DSH reported the prevalence rates of attempted self-harm from private and public sector hospitals[16], however the results of these studies could not be reported due to the differences in research design, time frame of research, size of sample, age of participants etc. Therefore, the current study was designed to determine the socio-demographics characteristics of participants with attempted suicide /DSH, and the causes and ways of Deliberate Self-Harm in patients who presented to the Emergency and Psychiatry Department Services hospital Lahore.

## Material and Methods

The data was collected from 100 patients with attempted suicide, Deliberate Self-Harm, from the Emergency department and Department of Psychiatry in Services Hospital Lahore, Pakistan. The data was collected in duration of 6 to 12 months. Patients with age-range of 13 to 65 years were included in this study with the history of attempted suicide, deliberate self-harm. Patients with critical condition and who were unable to talk about their deliberate self-harm were not included in this study. The data was collected through Purposive Sampling and cross-sectional research design was used. 100 patients with attempted suicide, DSH, were taken from the emergency department and department of Psychiatry. Informed consent was taken in writing from the participants as part of the ethical consideration for guidance on human subject research as specified in the Helsinki Declaration. To collect study-related information from research participants, a demographic information questionnaire was designed by the researcher. The questionnaire was comprised of information regarding age, gender, educational and professional status, marital status, ways of attempted suicides, causes of attempted suicides, DSH. Moreover, Traumatic Experience Checklist (Nijenhuis, Van der, Kruger, 2002) was also administered to determine the occurrence and impact of any traumatic event experienced by the

research participants. Traumatic Experience Checklist (TEC) (Nijenhuis et al., 2002) is a self-report measure assessing possibly traumatizing events.[17] Scores for emotional, physical and sexual abuse was calculated by summation of item scores. For the current research, translated version of the checklist was used which was translated by Yaqoob and Sitwat (2015).

## Results

Our results showed that ways of attempted suicide/ Delibrate Self-Harm in research participants were medicine intake (43%), acid / poison intake (22%), cuts and injuries (25%), jumped over a roof (4%), setting self on fire (2%) and hanging self (4%). While the causes of Self-Harm include academic problems (3%), family conflicts (financial problems and relationship problems) (56%), psychological issues (Anger 6%) and psychiatric illnesses (28%), and unknown reason (7%). It was also evident from the results that 60% of the participants had a previous history of Self-Harm, and 42% of the participants had a history of psychological issues and psychiatric illnesses, which consisted of anger issues (6%), bi-polar disorder (4%), conversion disorder (2%), depression (19%), obsessive compulsive disorder (4%), psychosis (3%), and unknown (4%). It was also identified from the descriptive statistics that 14% of the research participants had a family history of psychiatric

**Table 1:** *Shows the descriptive statistics for the socio-demographic characteristics of participants*

| Demographic Characteristics | Frequency | Percentages |
|---|---|---|
| **1.** Gender | | |
| Men | 27 | 27 |
| Women | 73 | 73 |
| **2.** Education | | |
| Un-Educated | 14 | 14 |
| Primary | 16 | 16 |
| Middle | 11 | 11 |
| Secondary | 26 | 26 |
| Intermediate | 13 | 13 |
| Graduation | 14 | 14 |
| Other | 6 | 6 |
| **3.** Profession | | |
| Un-Employed | 12 | 12 |
| Student | 13 | 13 |
| Housewife | 34 | 34 |
| Labourer | 8 | 8 |
| Government Employee | 3 | 3 |
| Private Job | 30 | 30 |
| **4.** Marital Status | | |
| Married | 49 | 49 |
| Un-Married | 49 | 49 |
| Divorced | 2 | 2 |
| **5.** SES | | |
| Lower | 37 | 37 |
| Lower Middle | 2 | 2 |
| Middle | 60 | 60 |
| Upper | 1 | 1 |
| **6.** Religion | | |
| Islam | 94 | 94 |
| Christianity | 6 | 6 |

**Table 2:** *Shows the descriptive statistics of Deliberate Self-Harm related variables in participants*

| **1. Ways of DSH** | **Frequency** | **Percentages** |
|---|---|---|
| Medicine Intake | 43 | 43 |
| Acid/Poison Intake | 22 | 22 |
| Cuts & Injuries | 25 | 25 |
| Jumped over a Roof | 4 | 4 |
| Fire-Setting | 2 | 2 |
| Hanging Self | 4 | 4 |
| **2.** Causes of DSH | | |
| Academic Problems | 3 | 3 |
| Anger Issues | 6 | 6 |
| Family Conflicts (Financial Problems & Relationship Problems) | 56 | 56 |
| Psychiatric Illnesses | 28 | 28 |
| Reason Unknown | 7 | 7 |
| **3.** History of DSH in Past | | |
| Yes | 60 | 60 |
| No | 40 | 40 |
| **4.** History of Psychological issues and psychiatric Illnesses | | |
| Yes | 42 | 42 |
| No | 58 | 58 |
| **5.** Type of Psychological/psychiatric Illness | | |
| Anger Issues | 6 | 6 |
| Bi-Polar Disorder | 4 | 4 |
| Conversion Disorder | 2 | 2 |
| Depression | 19 | 19 |
| OCD | 4 | 4 |
| Psychosis | 3 | 3 |
| Not Known | 4 | 4 |
| **6.** Psychiatric Illness in Family | | |
| Yes | 14 | 14 |
| No | 86 | 86 |
| **7.** History of DSH in Family | | |
| Yes | 9 | 9 |
| No | 91 | 91 |

illness, and 9% of them had a family history of Self-Harm. The scores of participants on Traumatic Experience Checklist (TEC) showed that all the research participants have experienced traumatic events in different numbers as evident by Table-1

The participants of current research experienced the emotional abuse in their life, as evident by the descriptive statistics, as 30 participants have experienced it once in their life, 20 participants have experienced it twice in their life and only 6 participants have experienced it three times in their lifetime. However, the prevalence of physical abuse was comparatively less than emotional abuse, as evident by Table-2. It was revealed from the research statistics that there were 24 participants who have experienced physical abuse once in their life, and only 5 and 1 participants had experienced it two and three times, respectively.

Moreover, the scores of participants on Traumatic Experience Checklist also showed that 7 of the research participants have experienced sexual abuse once in their life, while 1 of them have experienced twice and three of the research participants have experienced it thrice in their life. Table-3

**Table 3:** *Shows the descriptive statistics of Traumatic Experience Checklist for Emotional, Physical and Sexual Abuse*

| Number of Emotional Abuse | Frequency | Percentages |
|---|---|---|
| **0** | 44 | 44 |
| **1** | 30 | 30 |
| **2** | 20 | 20 |
| **3** | 6 | 6 |
| **Number of Physical Abuse** | | |
| **0** | 70 | 70 |
| **1** | 24 | 24 |
| **2** | 5 | 5 |
| **3** | 1 | 1 |
| **Number of Sexual Abuse** | | |
| **0** | 91 | 91 |
| **1** | 7 | 7 |
| **2** | 1 | 1 |
| **3** | 1 | 1 |

## Discussion

The results of the current study showed that the significant ways of self-harm in research participants were medicine intake, acid / poisonous substance intake and cuts and injuries. These findings can be significantly supported by the study of Hanuscin, et al[13]., and Shekhani, et al[18]. who revealed that patients who were involved in self-harm tend to use firearms, cutting/piercing, jumping from high places, anoxic injuries and poisoning as ways of causing harm to self. However, in the current study firearm usage was not reported to be a way of causing self-harm which may be due to the unavailability of firearms easily.

The current study also revealed that the causes of Self-Harm include academic problems (3%), family conflicts (financial problems and relationship problems) (56%), psychological illness (34%), and unknown reason (7%). These results of current study can be significantly explained by the study of Thompson and Kaslow[9], Devries[10] and Lauw, How and Loh[11]. These studies showed that people who attempted suicide and deliberate self-harm were more likely to have high levels of depression, drug use, psychological/ psychiatric illness, relationship problems, academic stress and physical or psychological abuse. In addition to this, deliberate self-Harm can also be caused by the previous history of deliberate self-harm, and family history of psychological/psychiatric illness and deliberate self-harm, as evident by the results of current study. These findings are also in line with the results of Hawton[15], who claimed that participants who reported to commit intentional self-harm tend to have a history of recent self-harm by friends, family members, misuse of drugs, symptoms of depression, anxiety, impulse control problem and low self-esteem issues.

For the current study Traumatic Experience Checklist[16] was also administered to determine the number of various traumas and their impact on the research participants with deliberate self-harm. The results showed that 93% of the participants had experienced any traumatic event in their life one or more time in their life. These results can further be strengthen by the findings of Devries, et al.[10] Lauw, How and Loh[11] and Spokas, et al.[12], who concluded that participants with intimate partner violence, physical or psychological abuse, and childhood sexual abuse were at higher risk of doing deliberate self-harm and multiple suicidal attempts.

It can be concluded from the results of current study that there are number of causes and associated factors that lead to suicide and eventually death, as deliberate self-harm can be severely life-threatening and can cause life-time injuries and damage. Therefore, while treating patients with deliberate self-harm or suicide attempt it is necessary to rule out the underline causes of deliberate self-harm so that patient's quality of life can be improved, and future self-harm can be prevented .[19]

## Limitations of the Study

The age-band of participants for the current study was too broad therefore it was recommended to study the identified factors and associated causes of DSH and attempted suicide for specific age group. Moreover, it was also recommended to study the personality correlates of people with DSH and attempted suicide.

**Conflict of Interest** *None*

**Source of Funding** *None*

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## Authors Contribution

**SB:** Conceptualization of Project
**RM, QB:** Data Collection
**RA, QB:** Literature Search
**RM :** Statistical Analysis
**AB, SB :** Drafting, Revision
**RM, RA:** Writing of Manuscript

# Impact of COVID-19 on Lifestyle Factors among Residents of Twin cities, Pakistan-A Cross-sectional Study

**Farah Rashid[1], Nadia Tariq[2], Sadia Zafar[3], Usman Zafar[4], Shehla Farhin[5], Syed Shoaib Hussain Shah[6]**

**Abstract**

**Objective:** COVID-19 pandemic has played havoc with millions of lives worldwide, affecting not only physical health but also mental and social wellbeing. The objective of this study was to assess effect of Covid-19 on factors related to mental health and life style.

**Method:** It was a cross sectional study conducted among residents of Islamabad and Rawalpindi above 18 years of age, from July-August, 2020.The sample size was 886. Data was collected through a self-designed pre -tested structured questionnaire with crohnbach's alpha value 0.89. It was posted on various social media platforms. Data was entered and analyzed through SPSS version 26.

**Results:** The mean age of the sample was 29.63+9.361. 26.6% (236) reported to have fear of death from covid-19 while 33.9% (300) felt hopeless. Increase in domestic disputes was reported to be 31.7% (281). 68.1% (603) participants performed physical activities during the lockdown. Eating habits were altered as well with 30.8% (273) participants reporting less appetite and 34.3% (304) increased appetite. 38.1% (338) had trouble falling asleep while 31% (275) said that they tended to stay asleep longer. During the lockdown, majority of the social media users (45.5%) reduced their social media usage, 21.7% (192) stopped using it completely, and 32.8% (291) continued using social media without any change.

**Conclusion:** Covid-19 pandemic impacted noticeably mental health and life style factors including eating habits, sleep patterns, physical activity and social media usage

**Keywords:** Impact, COVID-19, mental, lifestyle, factors, Pakistan, sleep, eating habits, physical activity, social media

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## Introduction

The Covid-19 first began in the city of Wuhan, China. It is now established that it is a public health emergency at the global level. The disease has been found to be associated with a variety of psychological illnesses such as anxiety, depression, loneliness, domestic, child and substance abuse.[1,2] The pandemic has been a challenge for psychiatrists and other health professionals. The pandemic has impacted and raised number of people worldwide who need psychiatric help. In comparison to natural disasters, such as earthquakes or tsunamis, cases are distributed everywhere and not localized to a given area.[3,4] Main factors responsible for affecting psychosocial functioning are un certainty and un predictability of this disease, impaired social functioning due to isolation and quarantine and interpersonal issues. Situation in Pakistan is even worse due to existing poor health infrastructure. Therefore, holistic and comprehensive approach is required to tackle this problem.[5] Since Pakistan is a low middle-income and 5th most populous country, economic instability and financial

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challenges have badly affected the mental health of people, along with the direct effects of the pandemic. As this pandemic has played havoc in Pakistan as in the rest of the world, its mental health effects need to be researched along with its physical and financial consequences. This study was conducted to assess the effect of Covid-19 on factors related to mental health, physical lifestyle factors on financial hardships.

## Materials and Methods

It was a cross-sectional study conducted among residents of Islamabad and Rawalpindi above 18 years of age. The study duration was 2 months. The sample size was calculated by using the formula n = [DEFF*Np(1-p)]/[(d2/Z21-α/2*(N-1)+p*(1-p)] (95% confidence level, 5% precision, 50% assumed prevalence to get maximum sample size and design effect 2). Sample size was inflated by 15% for data errors to get an overall sample size of 886. Sampling technique was non-probability consecutive. As per the guidelines given by the World Health Organization and the Government of Pakistan to minimize physical social interaction, respondents were electronically invited by sharing google forms link on various social media platforms (Facebook, WhatsApp groups). They were requested to further share the link in their friends and family circles. The first 886 completed forms were included in the study. A self-developed pre-tested structured questionnaire was used for data collection. Cronbach's alpha for the tool was calculated to be 0.89. It comprised of socio-demographic profile, items related to mental health, various life style factors and financial situation. Data was analyzed using SPSS v 26. Percentages were calculated for categorical variables. Continuous variables were analyzed using mean, median and standard deviation. Inferential statistics were performed using Chi-square test and logistic regression (taking p-value less than 0.05 as significant).

Study was undertaken after approval from the Institutional review board of Islamabad Medical and Dental College. The study was self-financed. Informed consent was taken from the participants, explaining the objectives of the research in the form of a disclaimer statement. Confidentiality and anonymity was ensured. Automatically generated random IDs were given to each form filled by the participants. For data security, Google Forms ensured password protected access to the database.

## Results

The data was collected from 886 participants, out of which 65.7% (582) were males and 34.3% (304) were females. The mean age of the sample was 29.63+9.361. Regarding marital status, 52.6% (466) were unmarried, while 47.4% (420) were married. Majority of the respondents (77.7%) belonged to urban areas while 22.3% (198) were from rural areas. During the Covid-19 lockdown, 68.1% (603) reported working from home. Covid-19 pandemic adversely affected the mental well-being of people all over the world. In our study, 26.6% (236) reported to have fear of death from covid-19. 63.1% participants had little interest in daily life activities while 33.9% (300) felt hopeless. 28.2% (250) agreed that they developed feelings of being a failure during lockdown. Anxiety about future uncertainty developed in 55.3% (490), 48.9% (433) reported feelings of restlessness while 39.8% (353) felt angrier than before. On cross-tabulation, all the variables related to mental well-being, that is, fear of dying from covid infection, little interest and pleasure in daily activities, feelings of hopelessness and failure, tendency to be angrier and restless and future anxiety were more in females (p-value<0.05). Financial insecurity was more in males (65.1%) as compared to females (37.2%) with a significant p-value of 0.000. All these variables were reported to be more among the unmarried participants with significant p-values except financial insecurity which was found to be more (64%) among married respondents. (p-value 0.000). The results of cross-tabulation are shown in table 1. Covid-19 also had drastic effects on lifestyle factors. Our study reported that 68.1% (603) participants performed physical activities during the lockdown. Eating habits were altered as well with 30.8% (273) participants reporting less appetite and 34.3% (304) feeling hungrier. Regarding sleeping habits, 38.1% (338) had trouble falling asleep while 31% (275) said that they tended to stay asleep longer. Role of social media has been debatable during the Covid-19 pandemic. Our results portrayed that majority of the respondents (31.8%) found social media depressing during this period, 16.8% found it panicky and fearful, 17% reported it to have a negative impact, while 34.3% felt that it had a positive impact. During the lockdown, majority of the social media users (45.5%) reduced their social media usage, 21.7% (192) stopped using it completely, and 32.8% (291) continued using social media without any change. On cross-tabulation, table 2 depicts that staying asleep for longer hours was reported more among females and unmarried (p-value 0.000). Less appetite was more among unmarried (p-value 0.033) and greater appetite was more among females and unmarried (p-value 0.000). Majority of the males (74.9%) and married

participants (80%) agreed that social media caused stress during Covid-19 infection. When asked about reducing social media usage, decreased usage during pandemic was reported more among males (46.9%) and married (48.6%) with significant p-value (p=0.00).

## Discussion

Covid 19 pandemic is not just a medical phenomenon but has devastating impact on the life style and its quality affecting individuals as well as communities leading to social dysfunction.6 In order to determine the impact of COVID-19 on psychological wellbeing and quality of life, a Chinese study revealed 52.1% of participants were terrified and apprehensive due to the pandemic and 46.7% of the participants felt helpless.[7] There was no significant difference between males and females in their fear of the disease while the age group 18-30 years feared more as compared to older age groups. Our study results show that 26.6% of participants have fear of dying from Covid 19 with no significant difference between males and females as well as participants having different marital status. 33.9% of the participants feel hopeless with females and unmarried people feeling hopeless more. This difference in fear of death and hopelessness with the Chinese study may be due to the fact that people of this area are more resilient or may have strong religious beliefs.

Feeling of being a failure is present among 28.2% with 33.9% having little interest or pleasure in doing things. Females and unmarried people reported little interest more. There was a high (17.9%) prevalence of psychological symptoms such as depression and anxiety among people who experienced lockdown during the COVID-19 pandemic as shown by a nationwide survey conducted in Japan.[8] The prevalence rates of depressive symptoms and anxiety symptoms were 10.5% and 38.2%, respectively during lockdown according to an online survey conducted in India.[9] This shows that lockdown period has led to increase in depression and anxiety. It is more in Pakistan and India. This may be due to the reason that people of these countries faced more financial constraints during lock down period. The COVID-19 crisis has hit developing countries like Pakistan which may lead to extreme economic and social turmoil in future. Any destructions in economic cycle leads to lower gross domestic product and higher unemployment rates in a country.[10] Our study shows 55.5% respondents have financial in security during lock down which was more in males. It is justified as mostly male members of the family have financial responsibilities in this region of the world. According to a study done in UK, working people were found to have more financial insecurity as compared to non-working which is consistent with our study due to the same reason.[11]

Social media along with playing a positive role, has also lead to a surge of various rumors and misinformation regarding the etiology, outcomes, prevention, and cure of the disease. Such spread of misinformation is promoting wrong practices leading to poor physical and mental health outcomes. Misinformation regarding remedies and cure led to panic buying also. Our study shows the same with 72.2% of respondents agreeing that social media played a negative role and contributed to increase in stress and anxiety.[12]

Sleep plays a pivotal role in the onset and exacerbation of chronic illnesses. A recent survey, conducted by King's College London (KCL) with 2250 UK respondents revealed that 38% reported sleeping less or less well than normal before the country was placed on lockdown. This is consistent with our study that shows 38.1% of participants have trouble falling asleep and 31% sleep for longer hours. The results are also comparable with another study conducted in Karachi, Pakistan in which one third of the participants reported trouble falling asleep.[13] Females and un married people tend to sleep longer during lock down as per our study. Energy intake is one of the most fundamental behaviors pertaining to health. Since the outbreak of COVID-19, there have been several media reports of stockpiling of household items. If the population is buying more food items, then they may be preparing more home-cooked meals. Indeed, Kantar World panel estimated a 38% increase in the number of meals consumed at home during the lockdown period.[14] In our study 30.8% reported to have less appetite in this period with 34.3 % reporting increased appetite.

Increase in domestic disputes was reported by 31.7% of the participants with maximum reporting increase in verbal abuse (85.5%) followed by physical (11%). It has been shown internationally that family violence can escalate during and after large scale disasters. A rise of 40% or 50% increase in family violence was reported in Brazil. In one region of Spain, the government claimed that calls to its helpline had risen by 20% in the first few days of the confinement period and in Cyprus, calls to a similar hotline rose 30% in the week after the country confirmed its first case of coronavirus. Calls to the UK Domestic Violence Helpline increased by 25% in the seven days following the announcement of tighter social distancing and lockdown measures by

the government as reported by Refuge, one of the leading domestic abuse organizations in UK.[15-17]

The results of our study relate to the studies done in the other parts of the world. There is a change in life style factors since Covid-19 strengthened its roots.

## Conclusion

There was rise in depression, anxiety, financial insecurity during lock down period. Social media played a negative role by exacerbating stress and anxiety. Dietary habits, sleep pattern were disturbed and there was a rise in domestic disputes.

**Conflict of Interest** *None*

**Funding Source** *None*

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# Effect of N-Acetylcysteine Therapy on Mortality Rate in Patients of Acute Aluminium Phosphide Poisoning

**Shahbaz Ashraf,[1] Tazeen Nazar,[2] Bilal Aziz,[3] Hussain Farooq,[4] Numreen Nazar,[5] Nazia Mumtaz[6]**

**Abstract**

**Objective:** To determine the effect of N-acetylcysteine therapy on mortality rate in patients of acute aluminium phosphide poisoning.

**Method:** This Randomized Controlled Trial was conducted in the Department of Medicine, , King Edward Medical University/ Mayo Hospital, Lahore from January 2018 to March 2019. Ninety-six patients with acute aluminium phosphide poisoning were selected via simple random sampling technique. The patients were divided into two groups, group A received supportive management and group B received N-acetylcysteine therapy along with supportive care. The patients were followed up to the primary end points of the study i.e. either discharge from hospital after recovery or death. Relevant information was recorded on a pre-designed proforma. Data analysis was done using SPSS Version 23.0.

**Results:** Out of a total of 96 patients, 50(52.1 %) were males and 46(47.9 %) were females. Mean age of the patients was 27.5± 9.8 years. In Group A (supportive therapy), 29(60.4%) patients died while 19(39.6%) were discharged after recovery. In Group B (N-acetylcysteine + supportive therapy), 17(35.4%) patients died while 31(64.6%) were discharged after recovery. N-acetylcysteine therapy significantly reduced mortality in patients with acute aluminium phosphide poisoning (p=0.024)

**Conclusion:** N-acetylcysteine in combination with supportive therapy significantly reduced mortality rate in patients with acute aluminum phosphide poisoning compared to supportive therapy alone.

**Keywords:** Aluminum Phosphide, N-acetylcysteine, Supportive Therapy.

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## Introduction

Aluminum phosphide(AlP) tablets, commonly referred to as Wheat Pills are used as fumigant, rodenticide and pesticide in closed grain storages in rural areas.[1] Because it is inexpensive and readily available, it is commonly used for suicide especially by people of third world countries leading to hundreds and thousands of deaths yearly.[2] India reported its first cases of AlP poisoning in 1980s. Ever since, innumerable cases of AlP poisoning have been reported in Pakistan, India, Iran, Sri Lanka, Morocco and other developing countries. Effectees are mainly inhabitants of rural areas and mostly young males and females.[3]

AlP exerts its toxicity through phosphine gas which is released when its tablet reacts with atmospheric moisture. The powder residue left after phosphine gas is released consists of aluminium hydroxide which has a low potential for causing toxicity.

The proposed mechanisms of phosphine toxicity include overactive acetylcholine signaling, reduction of cellular metabolism and increased production of free radicals.[4]

Once ingested, AlP reacts with water and acid in stomach,

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producing phosphine gas which causes local and systemic toxicity.[5] Local effects are mainly corrosive including gastric irritation, epigastric pain, nausea, vomiting, diarrhea and later on dysphagia and esophageal strictures.[6] Findings on upper gastrointestinal endoscopy include gastric and duodenal erosions and hyperemia of gastric mucosa. Cases of upper gastrointestinal bleed and acute liver failure have also been reported. [7]

Systemically, it increases oxidative stress that triggers apoptosis and eventually cell necrosis.

Cardiac manifestations result from toxicity of cardiac myocytes leading to atrial and ventricular dilatation resulting in reduced left ventricular ejection fraction.[8] This toxic myocarditis causes hypotension which is refractory to inotropic support. Persistent cardiogenic shock leads to acute kidney injury and further worsens metabolic acidosis. Cardiac myocyte dysfunction can also lead to cardiac dysrhythmias. Restlessness, anxiety, seizures, coma, hypo or hyperglycemia, electrolyte imbalance, aspiration pneumonitis, acute respiratory distress syndrome also occur.[5,9] Cases of methemoglobinemia and intravascular hemolysis secondary to AlP have also been reported in literature.[10]

Diagnosis of AlP poisoning is based on history, presence of the material ingested and silver nitrate test.[11] Management of AlP poisoning is mainly supportive.[5,12] On presentation, firstly gastric lavage with edible oil, diluted potassium permanganate (1:10000) or sodium bicarbonate is done.[13] Specific treatment includes magnesium sulphate that reduces frequency of cardiac dysrhythmias and reduction in overall mortality, from no reduction to significant reduction in mortality rates.[14] In a study by Goharbari MH et al, liothyronine 50µg when administered through nasogastric tube, improved arterial blood pressure, pH and lipid peroxidation.[15]

Another study conducted by Halvaei Z et al showed improved systolic blood pressure, oxidative stress and mortality rate with antioxidant vitamin E therapy.[16] Mohan B et al showed significantly reduced mortality rate in patients who received extracorporeal membrane oxygenation therapy along with supportive therapy as compared to the patients who received only supportive treatment.[17] On the basis of its important role in mitochondrial electron transport chain, coenzyme Q10 therapy has been proposed by Marashi SM et al for management of acute AlP poisoning.[18] Numerous studies have shown the beneficial effect of N-acetylcysteine (NAC) mainly attributable to its antioxidant effect. Results have also shown comparatively reduced rates of mortality in patient groups treated with oral or intravenous NAC but reduction was not shown to be statistically significant. One study by Bhalla A et al showed no mortality benefit of intravenous NAC therapy.[19]

## Material and Methods

This Randomized Controlled Trial was conducted in the Department of Medicine, King Edward Medical University/ Mayo Hospital, Lahore from January 2018 to March 2019. A sample size of 96 patients (48 patients in each group) was taken using 90% power of test, 5% level of significance and by taking expected percentage of mortality with supportive therapy and supportive therapy + NAC therapy as 81.8% and 54.2% respectively.[20] Simple random sampling technique was applied in selecting the patients. Patients of either sex between the age of 14-60 years with history of AlP (wheat pill) ingestion, confirmed with silver nitrate test or material documentation and presenting within 24 hours of ingestion were included in the study. History of ingestion of multiple poisons, known hypersensitivity to NAC and cardiopulmonary resuscitation on presentation resulted in exclusion from the study. After getting approval from the Board of Studies (BOS) and Institutional Review Board (IRB) of King Edward Medical University, 96 patients conforming to the inclusion criteria were enrolled in the trial. Informed written and verbal consent was taken from the patients or their first degree relatives. Patients' demographic data was obtained. At the time of presentation to medical emergency, initial resuscitative measures including stomach wash was done. The patients were then divided into two groups A and B by computer generated method. Patients in group 'A' received supportive care, that included intensive monitoring, adequate hydration, MgSO4 2g I/V 4-6 hourly, inotropic support (dopamine, dobutamine, norepinephrine) and ventilatory support as required. While the patients in group 'B' received N-acetylcysteine therapy (140mg/kg PO loading dose followed by 70mg/kg PO, 4 hourly for 72 hours) in addition to supportive care. Laboratory investigations like complete blood count (CBC), Liver function tests(LFTs) including serum ALT, AST, alkaline phosphatase and bilirubin levels, Renal profile including serum creatinine, blood urea nitrogen, cardiac biomarkers like serum LDH, serum CK-MB, arterial blood gas analysis, urine complete and electrocardiography were carried out at the time of presentation. The patients were followed up to the primary end points of the study i.e. either discharge from hospital after recovery or death. The study variables

included age, gender, outcome (death or discharge after recovery), number of ingested tablets, time after ingestion till presentation to emergency room and blood pressure at presentation. All this information was recorded on a predesigned proforma. Data was analyzed using Statistical Package for Social Science (SPSS) Version 23.0. Quantitative variables like age, number of tablets ingested, time after ingestion till presentation to hospital, systolic and diastolic blood pressure at presentation were presented as mean±SD. Qualitative data like gender and primary outcome were presented as frequency tables, percentages and appropriate charts. Chi-square test was used to compare mortality between the two groups. P value<0.05 was considered significant.

## Results

Out of a total of 96 patients, 48 (50%) in each group, 50(52.1 %) were males and 46(47.9 %) were females with a mean age of 27.5± 9.8 years. Mean time taken from ingestion to presentation to Mayo Hospital was 4.94± 4.11 hours. Mean systolic and diastolic blood pressure at presentation was 88.75± 40.73 mmHg and 55.31± 29.62 mmHg respectively. Out of 96 patients, 46(47.9 %) died in hospital while 50(52.1 %) were discharged after recovery. In group A, 29(60.4%) patients died while 19(39.6%) were discharged after recovery while in group B, 17(35.4%) patients died while 31 (64.6%) were discharged after recovery. Means of variables along with their standard deviation is depicted in Table 1 and comparison of means between the two groups analyzed with Independent Sample t-test is shown in Table 2. Table 3 shows therapy outcome.

**Table 1:** *Means of Variables*

| | Age (years) | No. of Tablets Ingested | Time from ingestion to presentation (hours) | Systolic BP (mmHg) | Diastolic BP (mmHg) |
|---|---|---|---|---|---|
| **Mean** | 27.5 | 1.37 | 4.94 | 88.75 | 55.31 |
| **Std. Deviation** | 9.8 | 0.83 | 4.11 | 40.73 | 29.62 |

**Table 2:** *Comparison of Means in Therapy Groups*

| Variable | Mean in supportive therapy group | Mean in NAC + Supportive therapy group | Sig. (2 tailed) |
|---|---|---|---|
| Age | 27.13± 10.21 | 27.83± 9.42 | 0.73 |
| Tabs ingested | 1.44 ± 0.94 | 1.3 ± 0.7 | 0.41 |
| Time to presentation(hours) | 4.61 ± 3.12 | 5.26 ± 4.92 | 0.44 |
| Systolic BP | 83.74 ± 45.5 | 93.33 ± 34.89 | 0.25 |
| Diastolic BP | 52.92 ± 30.73 | 57.29 ± 28.41 | 0.47 |

**Table 2:** *Comparison of Means in Therapy Groups*

| | | | Outcome | | Total |
|---|---|---|---|---|---|
| | | | death | recovery | |
| Therapy | NAC+ supportive | Count | 17 | 31 | 48 |
| | | % within Therapy | 35.4% | 64.6% | 100.0% |
| | supportive | Count | 29 | 19 | 48 |
| | | % within Therapy | 60.4% | 39.6% | 100.0% |
| **Total** | | Count | 46 | 50 | 96 |
| | | % within Therapy | 47.9% | 52.1% | 100.0% |

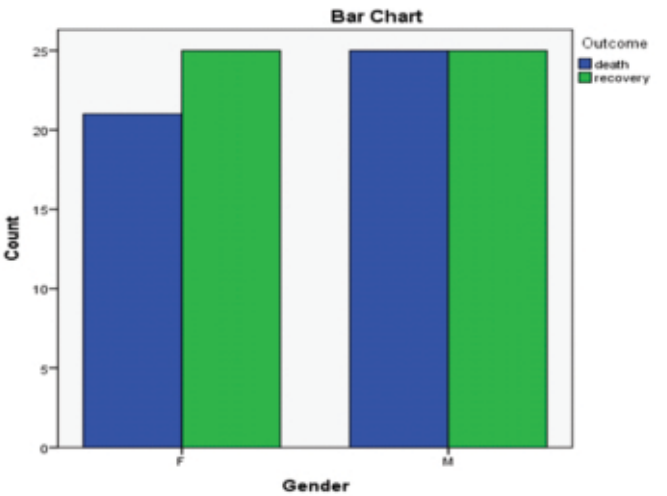


**Fig-1:** *Gender and outcome distribution*

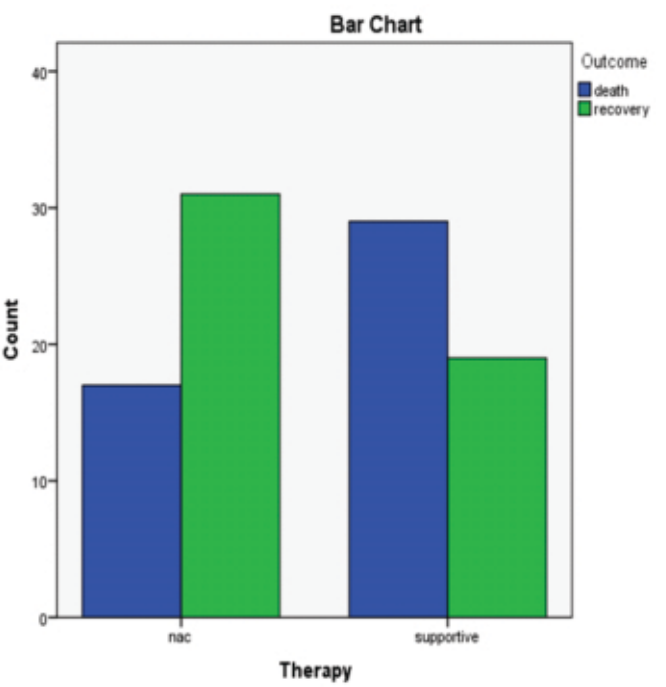


**Fig-2:** *Therapy and Outcome Distribution*

## Discussion

This study was conducted to determine the effect of N-acetylcysteine (NAC) therapy on mortality rate in patients of acute aluminium phosphide poisoning and a significant improvement in primary outcome (mortality rate) was observed. Mortality rate was 60.4 % in supportive therapy group and 35.4 % in patient group treated with NAC along with supportive therapy, with p value of 0.024, hence showing statistically significant reduction of 25% in mortality rate. The results were comparable to the previous studies conducted by Tehrani H et al and Agarwal A et al, who observed 24% and 27% reduction in mortality rates, respectively, with NAC therapy.[21,22] However the results differed greatly to the study by Taghaddosinejad F et al who did not observe any statistically significant reduction in mortality rate with NAC therapy.[19] Overall mortality rate was 47.9%, in line with the range of 33% to 87% reported in literature.[8,9]

Most of the patients in this study were young and there was no gender predominance. This was opposed to the observation in the study by Agarwal A et al that predominantly involved male patients.[22] No significant gender bias was noted in relation to outcome (mortality rate). Mean values of age, number of tablets ingested, time taken from intake to presentation, systolic and diastolic blood pressure at presentation were comparable in both groups leading to reduction in bias. Aluminum phosphide poisoning has very high mortality rates ranging from 33% to 87% according to different studies.[8,9] Intake of more than one tablets, hypotension, cardiac dysrhythmia, metabolic acidosis, development of acute kidney injury, high Sequential Organ Failure Assessment (SOFA) score, high Acute Physiologic Assessment and Chronic Health Evaluation (APACHE) II score and need for mechanical ventilation have been shown to be important predictors of mortality.[8] The patients that survive the acute episode make good recovery without any major long term organ dysfunction. Some survivors may develop gastrointestinal symptoms due to local damage caused by phosphine gas. Cases of esophageal stricture and tracheo-esophageal fistula formation after Aluminium phosphide poisoning have been reported.[6] Survivors also need psychosocial counselling to avoid further incidence of self-harm.

Aluminium phosphide tablets are increasingly being used as poison for self-harm in rural areas of Pakistan. Given its high rates of mortality, it is important to strive for finding further modalities of treatment in order to minimize mortality from aluminium phosphide poisoning. No specific antidote has been described to date. Melatonin has shown promising results in animal studies. In a study by Halvaei Z et al, vitamin E therapy significantly improved antioxidant capacity and survival.[16] A case report by Oghabian Z et al described successful treatment of a case of aluminum phosphide poisoning with combination of NAC and vitamin C.[23]

Although the interventions described above show protective effects to various degrees, the mortality rates are still very high even with the use of these therapies. Even in this study, although mortality rate was reduced with NAC therapy but it was still too high at 35%. Better interventions are needed to reduce mortality rates further with a goal to bring survival rates to near 100%. Reduction of oxidative stress is an important target for further research. While the search for better interventions is ongoing, NAC has shown promising results in current scenario. Protective role of NAC needs to be studied further. Double blind randomized controlled studies and meta-analysis of currently available data is needed to produce better quality evidence in favor of routine use of NAC therapy in patients of acute AlP poisoning. Synergistic effect of NAC therapy in combination with other interventions like vitamin E, vitamin C, Melatonin, early CRRT and IOBP, also needs to be further explored. And finally, the supply side dynamics need to be improved. Easy availability of AlP tablets needs to be checked. Use of alternative, less toxic fumigants needs to be encouraged.

## Conclusion

Aluminum phosphide (wheat pill) is a lethal toxin with high in-hospital mortality rate. Currently, supportive therapy is the mainstay of management in such patients. In this study, statistically significant reduction in mortality rate was observed with oral N-acetylcysteine therapy. Beneficial effect of NAC therapy alone and in combination with other emerging interventions needs to be further explored.

**Conflicts of interest** *None*

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## Authors Contribution

**SA:** Conceptualization of Project
**BA:** Data Collection
**BA:** Literature Search
**BA:** Statistical Analysis
**HF, NN:** Drafting, Revision
**HF, NN:** Writing of Manuscript

# Geographical, Clinical and Morphological Features of Molar Pregnancy in Pakistan

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## Abstract

**Objective:** To determine the association of molar pregnancy with age, geographical distribution, clinical presentation and morphological features in our population.

**Method:** It is a 5-years retrospective cross sectional study commencing from 1st January 2015 to 31st December 2019 on uterine evacuation samples submitted for histopathology at Chughtai's Institute of Pathology (CIP) and Central Park Teaching Hospital (CPTH), Lahore, Pakistan. Case records of all reported molar pregnancies during the study period were retrieved from computer files.

**Results:** A total of 462 cases of hydatidiform mole were diagnosed during this period. These constituted of 313 cases (67.74%) of complete hydatidiform mole (CHM) and 149 cases (32.25%) of partial hydatidiform mole (PHM). Maximum number of cases were received from the province of Punjab constituting of 242 cases (52.38%) followed by 132 cases (28.57%) from Khyber Pakhtunkhuwa (KPK). However, maximum cases of complete moles were reported from the province of KPK constituting of 110 cases (83.33%) out 132 submitted samples. Geographical distribution of molar pregnancy was observed as a statistically significant associated factor regarding morphological features (X2 = 23.732, p-value=0.000). Females ranging in age from 16 to 58 years were included in the present study. Maximum cases were reported in the 21-30 years age group comprising of 272 cases (58.87%) of which CHM constituting a maximum figure of 200 cases i.e 73.52% (p-value=0.004). Maximum specimens comprising of 265 cases (57.35%) showed grape like clusters on gross. The most common clinical presentation was vaginal bleeding constituting of 395 cases (85.49%). Incidental molar pregnancy was seen in 79 cases (17.09%).

**Conclusion:** Females with molar pregnancy can be cured and their reproductive function preserved provided their initial treatment and follow-up is timely and appropriate. Histopathological examination of molar tissue is the gold standard for its definite diagnosis & categorization as CHM & PHM.


**Keywords:** Hydatidiform mole, histopathology, trophoblast, chorionic villi, vesicles.

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## Introduction

Gestational trophoblastic disease (GTD) constitutes a heterogeneous group of interrelated diseases arising from tissues of placental origin which includes partial hydatidiform mole (PHM) and complete hydatidiform mole (CHM), invasive mole, choriocarcinoma and placental site trophoblastic tumor (PSTT).[1] Molar pregnancy represents the maximum burden of disease in the spectrum of GTD. The word "hydatid" is a Greek word meaning droplet and the word "mole" indicates the burrowing nature of the trophoblastic tissue into the uterine wall.[2]

The incidence of GTD varies in different regions of the world with the highest figures reported in the South-East Asian countries as compared to the western nations.

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In Europe, the incidence of molar pregnancy is 1/1000 pregnancies, in Japan and South East Asia it is 2/1000 deliveries and in Taiwan it is 1/125 pregnancies.[3] The highest incidence of molar pregnancy is reported in Turkey with an incidence of 12.1/1000 deliveries.[4] The malignant potential of this disease is also highest in South East Asia ranging from 10-15% whereas in the Western nations it ranges from 2-4%. The reasons for these geographical variations are indefinite.[5] The incidence of GTD in Pakistan is not known, however in one study the reported frequency is estimated as 28 per 1000 live births.[6]

The etiology of the disease is uncertain, however cytogenetic studies indicate a strong genetic association. CHM is characterized by having 46 chromosomes (46XX karyotype) all of paternal origin whereas the PHM is triploid, having a 69 XXX or 69 XXY karyotype.[7]

On morphology, CHM appears as grossly visible grape like vesicles and histologically is characterized by dilated chorionic villi surrounded by circumferential trophoblastic proliferation. Fetal parts, blood vessels and nucleated red blood cells (RBCs) are not seen in complete moles whereas the PHM grossly shows an admixture of some hydropically dilated villi and some normal villi with polar trophoblastic proliferation. Fetal parts with blood vessels containing nucleated RBCs are a prominent and diagnostic feature of PHM.[8] Presenting complains include vaginal bleeding and increased uterine volume during the 1st trimester of pregnancy with the disease ultimately ending in a miscarriage.[9]

Well documented risk factors for molar pregnancies include extremes of maternal age, previous molar pregnancy and a history of spontaneous abortions having a 2-3 fold increased risk of molar pregnancy compared with normal pregnancies. Women with a previous molar pregnancy have a risk of 1-2% in the next pregnancy.[9] Other risk factors includes low socio-economic status, dietary deficiency of protein, vitamin A, folic acid and iron. A nutritional deficiency during the 1st trimester may lead to the formation of a hydatidiform mole.[10]

The diagnosis of hydatidiform mole is greatly facilitated in the first trimester of pregnancy with ultrasound findings typically showing a "snow storm" appearance. The combination of ultrasound and markedly elevated serum β- HCG levels as expected for the gestational age is highly suggestive of molar pregnancy.[7] However histopathological examination of the evacuated uterine contents remains the ultimate gold standard for accurate diagnosis of molar pregnancy.[9] A hydatidiform mole is considered benign, but is premalignant having a definite potential to become malignant and invasive.[11] The risk of malignant potential is approximately 15% in CHM, while it is much lower in PHM reported as 0.5- 1%.[10]

An important diagnostic immunohistochemical marker differentiating between partial and complete mole is p57, which is a paternally imprinted inhibitor gene. Its absence supports the diagnosis of complete mole. In contrast partial mole which has a maternal contribution is p57 positive.[11]

The treatment of hydatidiform mole includes evacuation of the uterine contents by suction dilatation & curettage under ultrasound guidance in young females who desire fertility. However, hysterectomy is a preferred option in females older than 40 years of age and those who do not desire child bearing options.[12]

The objective of this study is to determine the occurrence of molar pregnancy in the different provinces of Pakistan and its relationship with different age groups and morphological features.

## Materials and Methods

The present study is a 5-years descriptive cross – sectional study conducted from 1st January 2015 to 31st December 2019 on uterine evacuation samples received at Chughtai's Institute of Pathology (CIP) and Central Park Teaching Hospital (CPTH), Lahore. Samples at CIP were received from the collection centers located in the different provinces of Pakistan.

Record and data of patients during this 5-year period was retrieved from computer files and entered in a proforma showing age, clinical features, gross and microscopic diagnosis alongwith address showing the province wise geographical location. Approval for the study was taken from the Ethical Review Board of CPMC (vide letter number CPMC/IRB-No/1312, dated February 09, 2022). Specimens with suspected molar tissue on gross examination, ultrasound and elevated β- HCG levels were included in the study. Products of conception (POC's) without molar change on gross examination and endometrial curettings of non-pregnant females were excluded.

Molar tissue fixed in 10% buffered formalin was processed using standard protocols: following fixation the entire specimen was transferred to tissue cassettes

and processed using an automatic tissue processor. Routine 5-micron sections were stained with hematoxylin and eosin, and prepared slides were evaluated by two consultant histopathologists.

Data obtained was analyzed using SPSS version 24 and frequencies and percentages were calculated. p-values were calculated by using a chi-square test to observe the association of molar pregnancy with age, geographical region, gross morphological features and clinical presen-tation. A 5% level of significance was used.

## Result

A total of 462 cases of hydatidiform moles were diagnosed during a 5-year period commencing from January 2015 to December 2019. These constituted of 313 cases (67.74%) of CHM and 149 cases (32.25%) of PHM giving a ratio of 2.10:1. (Figure:1-3)

Females ranging from 16 to 58 years were included in the study and categorized in four age groups. Maximum cases were seen in the age range of 21-30 years which constituted 272 cases (58.87%). Among this age category of 21-30 years, a maximum of 200 cases (73.52%) were reported as CHM and 72 cases (26.47%) as PHM. There were 21 cases (4.54%) of molar pregnancy in females above 40 years of age. These constituted 9 cases of CHM and 12 cases of PHM (Table1). Age distribution was significantly associated with molar pregnancy (X2 = 13.163, p-value=0.004).

Regarding geographical distribution, specimens of molar tissue were received from the four major provinces of Pakistan (Baluchistan, KPK, Punjab and Sindh) as well as from Azad Jammu and Kashmir and Gilgit Baltistan. Maximum number of molar pregnancy cases were received from Punjab, constituting 242 specimens (52.38%) followed by 132 cases (28.57%) from KPK, of which complete molar cases constituted of 110 cases (83.33%). This figure represents the maximum number of cases reported as CHM from KPK followed by Punjab in which 150 cases (61.98%) out of 242 cases were categorized as CHM. In Sindh, 48 cases (58.53%) out of 82 cases were diagnosed as CHM. Very few cases were received from Baluchistan (2 cases), Gilgit Baltistan (2 cases) & Azad Jammu and Kashmir (2 cases) constituting a combined total of 6 cases of which 5 were reported as complete moles (Table1) Geographical distribution of molar pregnancy was observed as a statistically significant associated factor regarding morphological features (X2 = 23.732, p-value=0.000).

Gross features included 265 cases (57.35%) with exclusive grape like vesicles, 141 cases (30.51%) showing a few grape like structures and 56 cases (12.12%) with no gross abnormality. Molar pregnancy was statistically significantly associated with these gross morphological

**Table 1:** *Cross tabulation of molar pregnancy with age, province, morphological features and clinical presentation (n= 462)*

| Factor | Category | Molar Pregnancy | | Number of cases (Percentage) 462 (100%) |
|---|---|---|---|---|
| | | Complete (313 cases) 67.74% | Partial (149 cases) 32.25% | |
| Age Distribution | < 20 years | 46 (60.53%) | 30 (39.47%) | 76 (16.45%) |
| | 21 – 30 years | 200 (73.52%) | 72 (26.47%) | 272 (58.87%) |
| | 31 – 40 years | 58 (62.37%) | 35 (37.63%) | 93 (20.12%) |
| | > 40 years | 09(42.86%) | 12(57.14%) | 21 (4.54%) |
| Province | Baluchistan | 01(50%) | 01(50%) | 02 (0.43%) |
| | KPK | 110 (83.33%) | 22 (16.67% | 132 (28.57%) |
| | Punjab | 150 (61,98%) | 92 (38.02%) | 242 (52.38%) |
| | Sindh | 48 (58.53%) | 34 (41.46%) | 82 (17.74%) |
| | Gilgit Baltistan | 02 (100%) | 0 (0%) | 02 (0.43%) |
| | Azad Jammu & Kashmir | 02 (100 %) | 0 ()%) | 02 (0.43%) |
| Morphological Features | Exclusively grape like clusters | 182 (68.68%) | 83 (31.32%) | 265 (57.35%) |
| | Few grape-like clusters | 108 (76.60%) | 33 (23.40%) | 141 (30.51%) |
| | Normal products of conception | 23(41.07%) | 33 (58.93%) | 56 (12.12%) |
| Clinical Presentation | Vaginal bleeding and increased uterine volume | 294(74.43%) | 101(25.57%) | 395/85.49% |
| | Abdominal pain and hyperemesis | 19(28.36%) | 48 (71,64%) | 67/14.50% |

features (X2 = 23.395, p-value=0.000).

The commonest presenting feature was vaginal bleeding and increased uterine volume seen in 395 cases (85.49%). Other nonspecific symptoms included abdominal pain and hyperemesis seen in 67 cases (14.50%). Clinical suspicion of molar pregnancy was suspected in 383 cases (82.90%) whereas 79 cases (17.09%) were unsuspected incidental findings. Clinical presentation was significantly associated with morphological features (X2 = 55.649, p-value=0.000) (Table 1).

**Figure. 1:** *Gross image showing numerous grape-like vesicles in a complete hydatidiform mole (CHM).*

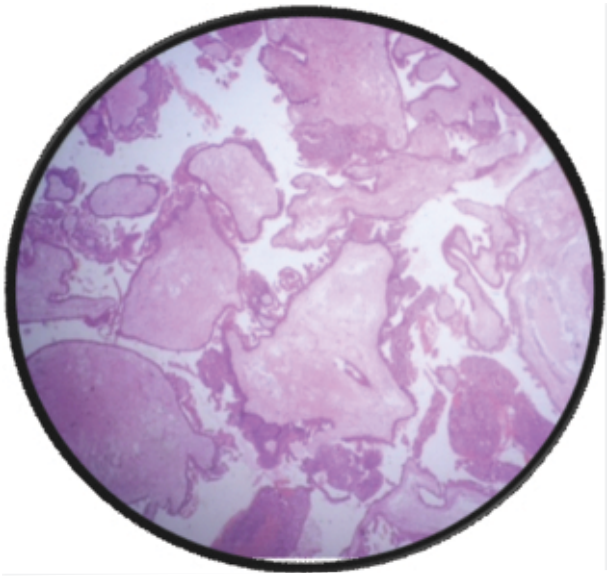

**Figure. 2:** *Light microscopic view of complete hydatidiform mole (CHM) showing dilated chorionic villi with circumferential trophoblastic proliferation (Hematoxylin and Eosin x 200).*

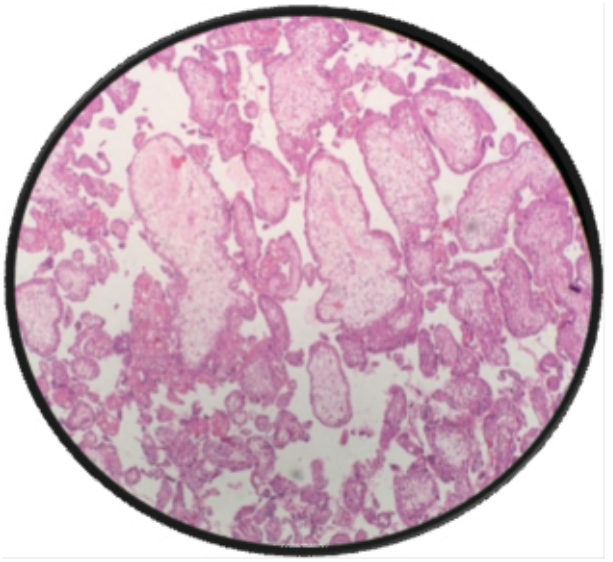

**Figure 3:** *Light microscopic view of partial hydatidiform mole (PHM) showing intermixed population of large and small chorionic villi with polar trophoblastic proliferation (Hematoxylin and Eosin x 200).*

## Discussion

GTD is among the rare human tumors that can be cured despite the presence of metastatic disease.[13] Complete and partial moles are genetically abnormal pregnancies and can be distinguished on the basis of morphological features, cytogenetic origin, clinical presentation and subsequent prognosis.[14]

Distinction between a molar conceptus from normal POC's by histopathology is extremely important as the patient's management and prognosis are based on this distinction. In addition, both entities have different potentials for clinical persistence, recurrence and malignant transformation.[7]

The diploid CHM is the premalignant form of gestational trophoblastic neoplasia[14] whereas the triploid PHM has a reduced chance of malignant transformation, the risk being 1 in 200 pregnancies as compared to 1 in 12 for CHM.[15]

In the present study, CHM constituted 313 cases (67.74%) compared to PHM comprising of 149 cases (32.25%). A local study by Nousheen Aziz in 2012 quoted figures of 79.48% cases of CHM and 5.12% cases as PHM.[1] highlighting the increased frequency of CHM as compared to PHM.

In a study by Olivier Mulisya in 2018 on 181 patients, the prevalence of hydatidiform mole was 6.1 % (11 cases out of 181).[16] All cases were CHM and there was no

PHM in his study. However, some other studies have reported contradictory figures in which PHM outnumber CHM. In a recent study by Talat Zehra in 2020 from Karachi all molar tissue were diagnosed as PHM[4] and another study conducted in West Indies in 2013, PHMs constituted of 61.1% of molar pregnancies.[17]

Age is considered a significant risk factor for the development of molar pregnancy. The relative risk with odd ratio (OR) is quoted as 2.14 for females younger than 20 years and 7.39 for females above 35 years of age by Nargese J. Talati, Karachi.[15] In the present study maximum number of 272 cases out of 462 cases (58.67%) diagnosed with GTD ranged from 21-30 years. Similarly, Talat Zehra also reported maximum number of GTD cases in 21-35 years of age.[4] In their study no case was seen in females less than 20 years, while in our study 76 cases (16.45%) were seen in females less than 20 years of age with mean age of 25.5 years.

A study in India (2019) by Jyoti R Chandran shows a mean age of 24.65 years for molar pregnancies.[18] Similarly, a study by Saleem Sadiq at JPMC, Karachi reported maximum of 111 cases (45.5%) in 21-30 years of age with mean of 27 years,[19] which is in accordance to our study.

According to a study in 2013 by Savage PM regarding age distribution, higher frequency of molar pregnancies was observed in females younger than 20 years and older than 45-50 years.[20] In our study maximum number of 272 cases (58.87%) were observed in the 21-30 years age range followed by 31-40 years age group which constituted of 93 cases (20.12%). However, 76 cases (16.45%) were also reported in females less than 20 years. Three cases of CHM were reported in females aged 16 years, all reported from KPK. At the other extreme, 21 cases (4.54%) were reported in females more than 40 years of age. The maximum age reported was 58 years diagnosed as CHM from KPK and a case of a 50-year female was reported from Punjab.

The global prevalence of molar pregnancy is almost 1 for 4 abortions (24.7%).[21] Its incidence varies by geographical region, being high in developing countries, females younger than 20 years and older than 40 years of age. It is more common in patients of low socioeconomic status with its associated dietary deficiency of protein, folic acid and carotene. A history of abortion is associated with increasing chances of developing a subsequent molar pregnancy.[22]

Out of a total 462 cases, 454 cases were diagnosed and treated with suction curettage, 6 cases were diagnosed and treated with hysterectomy and two placentae were received. All hysterectomies were reported as CHM with an age range of 25-45 years reported from Punjab and KPK. Both placentae were received with a fetus and diagnosed as PHM.

In present study 85.49% cases presented with vaginal bleeding during the first trimester and 14.50% had other symptoms of increased uterine fundal height, abdominal pain, distention and hyperemesis. A study in 2021 from Italy by Giampiero reported 87% cases with abnormal vaginal bleeding.[9] These findings are in accordance to our study.

In this study pre-evacuation clinical suspicion of molar pregnancy was seen in 383 cases (82.90%) whereas 79 cases (17.09%) were unsuspected of being molar pregnancies. They were assumed to be normal POC's but on histology were reported as hydatidiform moles highlighting the importance of histopathological examination being the gold standard for the diagnosis of molar pregnancy. In the study by Olivier Mulisya in Uganda, clinical diagnosis of molar pregnancy was suspected in 13 patients, of which 9/13 cases were confirmed as CHM histologically. Two cases were clinically unsuspected and diagnosed after surgical evacuation for abortion.[16]

A rare and interesting occurrence consisting of a twin pregnancy with a normal fetus and a coexistent associated mole is estimated to occur in 1 in 22,000 – 100,000 pregnancies. This occurrence can be seen with both CHM and PHM.[23] The diagnosis can be established antepartum by ultrasound and such patients with a twin pregnancy having a normal fetus with a concomitant molar pregnancy should be warned about a high risk of hemorrhage, hypertension and other complications including persistent GTN.[23] Such patients also have higher chances of metastatic disease requiring multidrug chemotherapy.[23]

In our study there were two twin pregnancies both with fetuses and the second sac was associated with CHM. In some cases, these types of twin pregnancies are incidentally discovered on examination of the placentae after delivery.

As this is a retrospective study, we could not get the post-treatment radiological features, serum β- HCG level and subsequent follow-up of these cases of molar pregnancy as regards their further progression towards malignant change or subsequent normal pregnancies.

## Conclusion

Of the two types of molar disease, CHM has a greater propensity for being persistent and recurrent with a subsequent progression to choriocarcinoma in 2.5% cases, whereas only less than 0.2% of partial moles will undergo this complication.

It is strongly suggested that all products of conception whether suspected or not of being molar pregnancy should be evaluated by histopathological examination especially if there is a strong clinical suspicion and if relevant risk factors like history of previous molar pregnancy or recurrent abortions are present. In addition, early diagnosis with subsequent follow-up helps in management and treatment of such patients with a subsequent decrease in complications and mortality associated with this entity.

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## Authors Contribution

**SR, KB, SN:** Conceptualization of Project
**SR, KB, SN:** Data Collection
**MA, NM:** Literature Search
**SN, KB:** Statistical Analysis
**MA, SN, ASC:** Drafting, Revision
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# Effect of Various Commercially Available Mouthwashes on Color Stability of IPS Empress Ceramic Restoration: An In-vitro Study

**Lama Alkhudair,[1] Shazia Nawabi,[2] Abida Saleem,[3] Nusrat Jabeen,[4] Asma Ejaz Khan,[5] Syeda Ridaa Fatima[6]**

**Abstract**

**Objective:** This study aims to compare the color stability of IPS EMPRESS direct (Ivoclar Vivadent) ceramic restorations after exposure to two commercially available mouth rinses.

**Method:** Thirty disc-shaped specimens (10x4 mm) of IPS IMPRESS direct (Ivoclar Vivadent) ceramic restoration was prepared. The specimens were separated into three groups (n=10) randomly. Commonly used mouthwashes, chlorhexidine0.2 %, and Listerine were used as experimental groups. Distilled water was used as the control group. Specimens were immersed in 10 ml of each, for 20 minutes every day for 30 consecutive days. The color values of each were measured before and after immersion by the NIX color sensor according to the CIELAB color scale. Their color change value was calculated. Data were analyzed and interpreted using IBM SPSS version 22. A two-way analysis of variance at a significance level of .05 was used for further evaluation of the collected data.

**Results:** There was a significant difference in the color change of restorative material following immersion in mouthwashes.

**Conclusions:** Following immersion in mouth rinses, ceramic restorative materials revealed a color difference.

**Keywords:** IPS EMPRESS ceramic, color stability, chlorhexidine0.2%, listerine, esthetic failure, NIX color sensor.

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## Introduction

Esthetics has played a fundamental role in the field of prosthetic dentistry and the demand for esthetics has always been challenging and inescapable for dental professionals in their routine dental practice.[1] Modern materials have been created to restore teeth to their most natural state.[2] Dental ceramic is one of them. They are increasingly being used in clinical settings due to their close appearance to natural teeth.[3] They also have several other desirable characteristics, including low thermal conductivity, biocompatibility, abrasion resistance, and low bacterial adhesion. Over the last few years, ceramics have become the most dominant material used in the fabrication of fixed prosthesis.[4] The systematic review of clinical data shows a comparatively higher clinical survival rate for metal-ceramic restoration (94.4 %) as compared to all-ceramic restoration (88.6%) over five years. However, the latter is more desirable among patients. This is mainly attributed to the excellent esthetics of the all-ceramic restorations.[5]

However, all these properties of dental ceramics are desired to be preserved throughout their functional lifetime in an oral environment, where they may interact with different plaque-controlling agents to reduce periodontal diseases and dental caries. For any crown, bridge, and veneering material,[6] color constancy is an essential physical quality.[7] The ability of a mate-rial to retain its

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color over some time in a particular environment is termed color stability.[8] In 2019, Gresnigt et al reported that the majority of patients complain regarding restorations attributed to discoloration of restoration and accounts for the failure of esthetic restoration.[9] Several conditions, both intrinsic and extrinsic, might induce discoloration of restorative materials.[10] The material's discoloration is one of the intrinsic characteristics.[11] Staining by adsorption or absorption of colorants from exogenous sources such as coffee, tea, nicotine, drinks, and mouthwashes are examples of extrinsic causes.[12] This study aims to evaluate the effects of different commercially available mouthwashes on the color sta-bility and strength of IPS EMPRESS ceramic restora-tions. In this study, the null hypothesis was that daily mouthwash use impacts the color stability and strength of ceramic restorative materials.

## Materials and Methods

A total of 30 ceramic discs of IPS IMPRESS Direct (10mm in diameter and 4mm in thickness) were constructed in a standardized manner.[13] Samples were divided into three main groups (n=10). All specimens were fabricated using a CNC milling machine and electric Iso Met micro saw 4000.[14] They were seated in a central motor machine CNC Jr. Tabletop Mill XD series vertical CNC milling machine which fabricates restorations utilizing subtraction manufacturing technology.[15] All specimens were cut into discs of 4mm thickness using a diamond saw disc at the speed of 2500 rpm under water coolant. A digital caliper was used to verify the dimensions. Standardized immersion solutions were prepared for all groups. All disc samples were tested twice before and after immersion in the solutions. The baseline shade of the ceramic samples (N=30) was measured using a NIX color sensor before immersion in the solutions. Group 1:0.2% Chlorhexidine gluconate mouthwash. Group 2: Listerine® mouthwash, and Group 3: distilled water which is control. To evaluate color stability, the specimens were immersed in mouthwash agents and distilled water (control) at 37◦C, daily for 18 consecutive days. Immersion lasted for 20 minutes every day. This time interval is equivalent to 2 min of mouthwash per day for six months. Each specimen was then washed for 120 sec with tap water and then air-dried. The shade of the samples was measured again using a NIX color system.

## Results

Statistical analysis was done using IPM SPSS 22 version. Mean and Standard deviation was calculated before and after immersion (Table1, Table2). Paired T-test was carried out to determine if there was any significant difference between the measurements before and after the immersion (Table 3). One way ANOVA test was also applied to analyze the difference between groups at a 0.05 significant level (Figure 1). The paired t-test determined that there is a significant (p=.043) difference in the groups before and after immersion (Table 3). Therefore, the first part of the null hypothesis "The mouth-rinse will affect the color stability of restoration" is accepted.

A significant difference is observed through one way ANOVA test between chlorhexidine and Listerine groups (p= 0.299) regarding the discoloration of resto-rative material (Figure 1).

**Table 1:** *Standard Deviation of groups before immersion*

| Groups | Mean | Standard deviation | N |
|---|---|---|---|
| **1** | 100 | 0 | 30 |
| **2** | 100 | 0 | 30 |
| **3** | 100 | 0 | 30 |

**Table 2:** *Standard deviation of groups after immersion*

| Groups | Mean | Standard deviation | N |
|---|---|---|---|
| **1** | 120 | 41.404 | 30 |
| **2** | 106.67 | 25.820 | 30 |
| **3** | 113.33 | 34.575 | 30 |

**Table 3:** *Paired t-test for analysis of difference before and after immersion*

| | Mean | Standard deviation | Standard error mean | 95% confidence interval of the difference | | Significance |
|---|---|---|---|---|---|---|
| **Pair before - after** | -13.333 | 34.575 | 6.312 | Lower -26.244 | Upper -4.23 | 0.43 |

**Fig 1** **ANOVA**

| | Sum of Squares | Df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| Between Groups | 1333.333 | 1 | 1333.333 | 1.120 | .299 |
| Within Groups | 3333.333 | 28 | 1190.476 | | |
| Total | 34666.667 | 29 | | | |

**Figure 1:** *One way ANOVA test for analysis of the difference between groups at a 0.05 significant level*

## Discussion

The growing accessibility of media and online information has increased the demand for superior dental aesthetics.[16] The success of an aesthetic restoration is based on the replication of tooth shape and shade. It is also vital that the selected shade is maintained in the harsh oral environment throughout the functional life of the prosthesis.[17] Keeping this in view, dental ceramics are the material of choice and they have widely been used to replace missing teeth due to their superior optical properties of color translucency, opalescence, sound biocompatibility, and good wear resistance.[18] An extremely homogenous leucite-based ceramic is used to form IPS EMPRESS Ceramic. It is capable of scattering light like natural enamel and therefore, it blends well with its surroundings. Apart from this highly desirable property, its mechanical properties and strength have made it the material of choice for permanent restoration.[19] However, both dentists and patients need to be educated about the gradual discoloration of ceramics that occurs when these materials are exposed to different conditions and various oral hygiene products.[20] In 2014, Sarikaya I studied the effects of various surface treatments on different types of dental porcelains. He reported that glazed porcelain is much more likely to retain its color in the oral environment than polished porcelain[21]. In 2015, Tekce N et al studied the effects that different drinks have on the color stability of different restorative materials and reported the subsequent change in their shades.[22] In 2017, Van den Breemeret et al conducted a retro perspective case study to assess the clinical performance of monolithic lithium disilicate posterior restorations and discussed in detail, the changes observed after one year, two years, and five years.[23] The present study observed the effects of two commercial mouth rinses on the color stability of IPS EMPRESS ceramic restoration. Mouthwashes are of paramount importance where prevention and reduction of periodontal diseases and dental caries is concerned. However, these mouthwashes may cause discoloration of the restorative materials.[24] In this study, a statistically significant difference is observed between the groups after immersion in mouthwashes.[25]

## Conclusion

Although mouthwashes are important in the reduction of periodontal diseases and dental caries, they may result in discoloration of the restorative materials as a side effect. However, follow-up at regular intervals and clinical studies are required to evaluate their effects on color stability.

**Conflict of Interest** *None*

**Funding Source** *None*

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## Authors Contribution

**LA:** Conceptualization of Project
**SN:** Data Collection
**AS:** Literature Search
**AS:** Statistical Analysis
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# Association of Maternal Anemia with Low Birth Weight

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**Abstract**

**Objective:** To determine the frequency of anemia in women who were pregnant and attended a hospital with tertiary care facilities, and to compare the neonates' low-birth-weight frequency, with vs without anemia in pregnant women.

**Method:** A Descriptive case series study was conducted from 11th December 2021 to 10th June 2022 in Obstetrics and Gynecology Department, Services Hospital Lahore. After getting ethical review committee approval with letter reference no: IRB/2022/990/SIMS, venous blood samples of 196 women with singleton pregnancy of gestational age 37-42 weeks were collected to determine hemoglobin, red cell indices and frequency of maternal anemia. Just after delivery, neonatal weight at birth was measured to determine low-birth-weight frequency.

**Results:** In this study, 20 to 40 years was the range of age, and mean was 30.61 ± 4.24 years. Patients counted 113 (57.65%) were 31-40 years old. Gestational age had 38.63 ± 1.24 weeks mean while mean parity was 3.24 ± 1.31. Mean height was 157.87 ± 13.25 cm while mean weight was 71.28 ± 7.87 kg. Mean BMI was 29.26 ± 3.44 kg/m2. In this study, frequency of anemia in pregnant women was found in 89 (45.41%) patients. The frequency of LBW was 52.81% in anemic women versus 31.78% in women who did not have anemia.

**Conclusion:** This study resulted that, pregnant women have quite high anemia frequency and anemic women have high frequency of low-birth-weight neonates as compared to women without anemia.

**Keywords:** Pregnancy, Anemia, Low-Birth-Weight

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## Introduction

Amongst hematological manifestations during pregnancy, Anemia is a major element that cause worldwide health issues, including Pakistan and has a major impact on women with lower socioeconomic class with lack of health facilities.[1,2] Pregnant women of countries like United Kingdom, United states of America, Germany and Australia, which are considered developed countries, are also effected by Anemia, ranging between 9% to 51%.[3,4] While in countries like Pakistan, India, Sudan, Ghana, which are developing countries, there is 44% to 81% anemia prevalence in pregnant women.[5,6]

Iron in ionic form facilitates new hemoglobin generation and it is major source of oxygen supply to vital body organs. Absence of iron availability for erythropoiesis in extracellular portion and infection in body affect the metabolic phenomenon of hemoglobin formation. Usually hemoglobin concentrations below 11g/dL is diagnostic of anemia in pregnancy. Low-birth-weight occurs due to intrauterine growth restriction caused by low hemoglobin concentration, which leads to reduced oxygen supply to fetus and affects angiogenesis of placenta. There is higher risk of low-birth-weight neonates in women who have hemoglobin levels below 10 g/dL during pregnancy vs women without anemia during pregnancy.[7]

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Amongst infants' mortality and morbidity risk factors, low-birth-weight is considered a major factor and has been studied well. The risk of morbidity and mortality is far more in infants having birth weight less than 3000 grams as compared to the infants with birth weight of 3000 grams or more.[8]

The exact mechanism which links low-birth-weight and anemia in pregnancy is not well known, despite of the fact that determinants of both are similar.[9] A study by Anwar et al. reported maternal anemia in 53.18% women with pregnancy with a strong low-birth-weight (LBW) association. The frequency of LBW was 36.3% in anemic women versus 14.6% in women without anemia.[10] While a study by Kumari did not report any significant association between maternal anemia and LBW. They reported LBW in 32.9% anemic women versus 32.4% in non-anemic women including overall frequency of anemia 78.45%.[11]

Socioeconomic and demographic factors affect maternal anemia. Therefore, local population should be identified for association between maternal anemia and low-birth-weight. As low-birth-weight contributes as major factor for infants' mortality, this study is aimed to determine maternal anemia in women who attended the hospital with tertiary care facilities, as well as its association with low weight at birth.[12] So, by early identification and treatment of anemia, we will be able to reduce the burden of low-birth-weight infants as well.

## Material and Methods

In Obstetrics and Gynecology Department, a descriptive study from 11 December 2021 to 10th June 2022 was conducted. After the ethical review committee gave approval, Aa total of 196 pregnant women having age 20-40 years with singleton pregnancy having 37-42 weeks of gestation, were included through non probability, consecutive sampling.

Women having hemoglobin (Hb) <10 g/dL were labelled as anemic. Low Birth Weight (LBW): Neonates having birth weight <2500 grams were labelled as LBW. Birth weight of each baby was measured immediately after birth using a digital weight scale specified for measurement of neonatal birth weight in grams. Patients with multiple like twins or more preg-nancies, co-morbidities such as eclampsia or gestational diabetes were excluded. World Health Organization (WHO) software was used to calculate sample size with the following assumptions: Confidence level=95%, Proportion of Anemia in pregnant females=53.18%[14], Absolute Precision= 7%. A written consent was taken from each participant. A performa was for each patient that contained age, gestational age, height, weight, parity and BMI of the pregnant women who were inclu-ded in the study. Venous blood samples were drawn which were sent to hematology laboratory to determine the frequency of maternal anemia. Till neonate's birth, all patient were followed. Birth weight of neonate was measured just after birth to determine the LBW. The collected information was analyzed with SPSS version 25. For continuous variables like age, gestational age, parity, BMI, height and weight, descriptive statistics were applied for standard deviation and mean calculation while for categorical variable such as maternal anemia and LBW, percentage and frequency was found out. For determination of maternal anemia association with LBW, Chi Square test was used. Through stratification, effect modifiers, e.g., BMI, parity, age and gestational age, were controlled. To determine the association of these effect modifiers with maternal anemia and association of maternal anemia with LBW, post-stratification Chi square test was applied. P-value < 0.05 was considered as significant association.

**Table 1:** *Distribution of Patients (n= 196) according to age, gestational age, parity and BMI*

| **Age (in years):** **Mean ± SD = 30.61 ± 4.24 years** | **No. of Patients** | **%Age** |
|---|---|---|
| 20-30 | 83 | 42.35 |
| 31-40 | 113 | 57.65 |
| Total | 196 | 100.0 |
| **Gestational Age (in weeks):** **Mean ± SD = 38.63 ± 1.24 weeks** | | |
| 37-39 | 145 | 73.98 |
| 40-42 | 49 | 26.02 |
| Total | 196 | 100.0 |
| **Parity:** **Mean ± SD = 3.24 ± 1.31** | | |
| **Primiparous** | 35 | 17.86 |
| **Multiparous** | 161 | 82.14 |
| **Total** | 196 | 100.0 |
| **BMI (kg/m $^2$):** **Mean ± SD = 29.26 ± 3.44 kg/m$^2$** | | |
| **⩽27** | 73 | 37.24 |
| **>27** | 123 | 62.76 |
| **Total** | 196 | 100.0 |

## Results

This study includes 20 to 40 years age range, with 30.61 ± 4.24 years, mean age. Patients counted 113 (57.65%) were 31-40 years old. Gestational age had mean of 38.63 ± 1.24 weeks, while mean parity was 3.24 ± 1.31. Mean height was 157.87 ± 13.25 cm while mean weight was 71.28 ± 7.87 kg. Mean BMI was 29.26 ± 3.44 kg/m$^2$. With respect to age groups, gestational age, parity and BMI, Anemia stratification is shown in Table No. II. Frequency of anemia in pregnant women was found in 89 (45.41%) patients as shown in Figure I. The low birth weight (LBW) frequency was 52.81% in women having anemia versus 31.78% in women who did not have anemia as shown in (Table III).

**Table 2:** *Stratification of Anemia with respect to age groups, gestational age, parity and BMI*

| Age in Years | Anemia | | p-value |
|---|---|---|---|
| | Yes | No | |
| 20-30 | 41 (49.40%) | 42 (50.60%) | |
| 31-40 | 48 (42.48%) | 65 (57.52%) | **0.336** |
| **Gestational Age (weeks):** | | | |
| 37-39 | 65 (44.83%) | 80 (55.17%) | |
| 40-42 | 24 (48.98%) | 25 (51.02%) | **0.614** |
| **Parity** | | | |
| Primiparous | 11 (31.43%) | 24 (68.57%) | |
| Multiparous | 78 (48.45%) | 83 (51.55%) | **0.067** |
| **BMI (kg/m$^2$)** | | | |
| ⩽27 | 43 (58.90%) | 30 (41.10%) | |
| >27 | 46 (37.40%) | 77 (62.60%) | **0.004** |

**Table 3:** *Comparison of the frequency of low birth weight in pregnant women with vs without anemia.*

| Anemia | low birth weight | | p-value |
|---|---|---|---|
| | Yes | No | |
| **Yes** | 47 (52.81%) | 42 (47.19%) | **0.003** |
| **No** | 34 (31.78%) | 73 (68.22%) | |

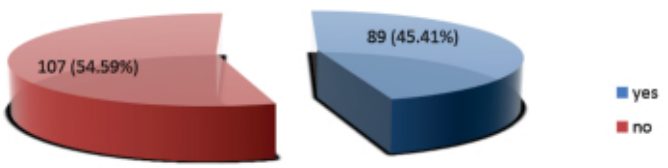


**Figure I:** *Frequency of anemia in pregnant women (n=196).*

## Discussion

Low-birth-weight occurs due to intrauterine growth restriction caused by low hemoglobin concentration, which leads to reduced oxygen supply to fetus and affects angiogenesis of placenta.[13] There is higher risk of low-birth-weight neonates in women who have hemoglobin levels below 10g/dL during pregnancy vs women without anemia during pregnany.[13] In 2011, it was estimated that 38.2% was the prevalence of anemia in pregnancy. Including North America, where is reaches up to 20%, this phenomenon affects the pregnant women worldwide. In Europe, maternal anemia was found to be 24.5 %, where as in Africa, it was 44.6%. Asia and Oceania had 39.3% and 29% maternal anemia prevalence respectively while in Caribbean and Latin America it was found to be 28.3%.[14] Anemia in pregnancy occurs worldwide, affecting not only pregnant women but also leading to undesirable gestational outcomes,[14] that's why it demands prime attention for identification and treatment. Considering the reviews that included women of diverse regions with varying socioeconomic statuses, there is limited study in this aspect. A systemic review, established up to 2014, showed only cohort study, established the association of different outcomes of gestation with various socioeconomic status ranging between lower to middle class.[15] Another review which included cohort as well as case-control methods, was concluded up to 2010 and published in 2013. This review established association of anemia in pregnant women with low weight at birth of infants.[16] Different reviews published between 2012-2015 emphasized the role and effect of iron supplementation associated with low-birth-weight.[17] My study shows that 89(45.41%) pregnant women had anemia. The frequency of LBW was 52.81% in anemic women versus 31.78% in non-anemic women. The linking mechanism of anemia in pregnancy with LBW is not well understood. However, studies done previously have shown that the resultant weight of new born might be affected due to intrauterine growth restriction which is secondary to development of anemia in pregnancy.[18] During the second trimester of pregnancy, about 30-40 ml/Kg plasma is produce physiologically which leads to development of hypervolemia. Contrary to this, the blood cells do not form to this extent, and hemodilution happens which may lead to anemia in pregnancy. Fetal hypoxia is the result of affected angiogenesis of placenta which is stimulated by decreased hemoglobin concentration levels.[19] As placental transportation of nutrients and oxygen to fetus is reduced due to decreased hemoglobin levels,

the potent stimulus for fetal and uterine growth depletes and it results in reduced uterine blood perfusion, increased vascular resistance and restricted growth of trophoblastic surface, that ejects arterial blood of mother into placenta. Resultantly, a compromised fetal-placental connection leads to reduction in gas exchange across placenta and eventually, low-birth-weight occurs.[20] Goldenberg et al,[21] described in study that presence of anemia in pregnant females leads to detrimental effects on their newborns. As the nutritional supply to the growing fetus is compromised to varying extent, the results depend upon severity of anemia in pregnant females. Presence of maternal anemia has a direct relation with gestational age. The most affecting duration is first trimester, in which the growing fetus gets more affected as compared to second or third trimester. Similarly, the resultant effects regarding premature delivery due to premature rupture of membranes associated with low birth weight and post-natal risks of prematurity are much higher in pregnant females who have severe maternal anemia during first trimester as compared to second or third trimester. Mavalankar et al,[22] found that there was greater risk in pregnant females who had anemia during pregnancy to have low-birth-weight babies as compared to those women who did not have anemia during pregnancy. Jones et al,[23] studied and found that there was increased incidence of anemic mothers having low birth weight babies. But on the other hand, its difference from group containing non-anemic mothers was not significant ($p= 0.11$). Badshah et al,[24] found in study that pregnant women having anemia belonging from tribal areas of Pakistan had a strong positive association with low-birth-weight infants showing difference ($p<0.01$) as compared to infants of those mothers who did not have anemia during pregnancy. Moreover, it was also established that there was increased small for gestational age risk in pregnant women with anemia as compared to the women without anemia. Lone et al,[25] in a multi-disciplinary study, showed 1.9 times increased (95% Confidence interval (CI): 1.0-3.4) risk of low-birth-weight incidence in pregnant women with anemia.

## Conclusion

This study resulted that, pregnant women have quite high anemia frequency and anemic women have high frequency of low-birth-weight neonates as compared to women without anemia. So, we recommend that public awareness programs should be arranged regarding this major public health issue among women of reproductive age group and for treating clinicians as well, for early screening and management of maternal anemia in order to reduce the low-birth weight neonates.

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## Authors Contribution

**EO, RBN:** Conceptualization of Project
**EO, SW:** Data Collection
**EO, MST:** Literature Search
**EO, RBN:** Statistical Analysis
**EO, FT:** Drafting, Revision
**EO, FT:** Writing of Manuscript

# Role of Prophylactic Antibiotics on Surgical Site Infection in Elective Laparoscopic Cholecystectomy

**Sehrish Siddique,[1] Sidra Mehmood Dar,[2] Usman Qureshi,[3] Sidra Ahmad,[4] Jahangir Sarwar Khan[5]**


## Abstract

**Objective:** To compare the frequency of post-operative surgical site infection in patients receiving prophylactic antibiotics and without prophylactic antibiotics after elective laparoscopic cholecystectomy.

**Method:** Randomized Controlled Trial carried out at Surgical Unit-1, Holy family Hospital, Rawalpindi. Duration of this was 1st May 2019 to 31st Oct 2019.

Total 218 patients were enlisted according to the inclusion criteria of the study. Patients were randomly divided into two equal groups. Group A was given prophylactic antibiotic before surgery and Group B was considered as placebo. Outcomes were measured in terms of frequency of postoperative surgical site infection in patients of both groups. A p-value of 0.05 was considered statistically significant.

**Results:** Mean age (years) in the study was 45.62+12.66 whereas there were 128 (58.1%) male and 90 (41.3%) female patients. Frequency and percentage of post-operative surgical site infection in patients among both the groups was 9 (8.3%) and 2 (1.8%) respectively which was statistically significant (p-value 0.03).

**Conclusion:** The study concluded that there is a difference in frequency of surgical site infection in patient receiving prophylactic antibiotics and those with not receiving antibiotics, undergoing laparoscopic cholecystectomy. This is likely to be happen because of the overuse of antibiotics which are the key factors contributing to antibiotic resistance. Hence, it would be advisable that general public and doctors should play a role in order to avoid unnecessary exposure of antibiotics to the patient which don't play any significant role on post-operative surgical site infection.


**Keywords:** Antibiotics, laparoscopic cholecystectomy, Prophylactic, Surgical site infection.

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## Introduction

For decades surgical site infection (SSI) has contributed a major burden in increasing morbidity and mortality over the surgical floor. According to studies, incidence of SSI is approximately 3-4 %.[1] In order to improve the outcomes of surgery, prevention of such infection is the key factor. One way to decrease the incidence of SSI is the use of prophylactic antibiotics. In clean contaminated and contaminated procedures, preoperative antibiotics significantly reduce bacterial contamination and thus SSI.[4]

Nowadays, laparoscopic cholecystectomy (LC) is the procedure of choice for symptomatic gallstones. Although it is minimal invasive but laparoscopic cholecystectomy has incidence of SSI, correlating with intraoperative findings and comorbidities of the patient[2]. Studies have proved that infection rate after LC is far lesser than open cholecystectomy.[1,6,7] Most occurring infective complications after open cholecystectomy are seroma formation, wound infection and wound dehiscence. Therefore, prophylactic antibiotics are routine practice

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at most surgical departments.[2,3]

In elective LC, studies suggest that antibiotics should be given prior to surgery in high risk patients[6]. But the benefit of prophylactic antibiotics in low risk cases is still a subject of debate. Recent studies now suggest that low-risk patients do not require antibiotics before surgery.[2-5]

The aim of this research proposal is to compare the frequency of post-operative surgical site infection in patients receiving prophylactic antibiotics and without prophylactic antibiotics after elective laparoscopic cholecystectomy. The rationale of this proposal is that although antibiotics decrease morbidity postoperatively but overuse has aggravated the problem of drug-resistance, the accurate measure of magnitude and frequency of drug resistance needs further studies. Hence, by implementing this study in our routine practice, it will prevent patient from unnecessary exposure of antibiotics and it would be cost effective as well. This study will help a lot to avoid unnecessary exposure of antibiotics to the patient which don't play any significant role on post-operative surgical site infection.

## Materials and Methods

Ethical committee approval received for the study and a Randomized Controlled Trial was done in Surgical Unit-1, Holy family Hospital, Rawalpindi of six months duration i.e. 1st May 2019 to 31st Oct 2019. Sampling Technique was consecutive non probability sampling. There were 109 patients in each group with a total of 218 patients.

Both male and female patients aged 18-60 years undergoing elective Lap cholecystectomy.

Acute cholecyctitis, Empyema GB, Contaminated surgery, Body mass index ≥30, Diabetes mellitus; BSR>200mg/dl, Use of antibiotics within one week of the planned LC (As it may create a bias in one group) current study. All the patients has been fulfilling the selection criteria presenting at surgical unit – I, Holy Family Hospital, Rawalpindi were acknowledged about the study and written informed consent was taken. A random number list was generated for 218 patients randomly assigned them group A or Group B (109 patients each) using SPSS software. Every patient fulfilling the selection criteria was assigned study ID number in chronological order and after corresponding to the ID number of mentioned study group SPSS generated random number list was allocated to the patient. The surgical procedural elements and the surgeon performing procedures was standardized to eliminate any potential confounding effect. All surgeries were done by consultant having >1year post fellowship experience.

Group A was given prophylactic antibiotic 1gram ceftriaxone30 minutes before surgery and group B was given 0.9% normal saline 5 ml (placebo). Postoperative surgical site infection was recorded as per operational definition on the day 7, 14 and 28 days follow up after surgery. All the information of patients were recorded.

Data was entered and analyzed in SPSS version 26. Qualitative variables like wound infection, gender and previous history of acute cholecyctitis were measured as frequency and percentage. Quantitative variables like age, BMI were presented as mean+standard deviation. Surgical site infection in the two study groups were analyzed using chi square test. P-value of <0.05 would be considered statistically significant. For effect modifier like age, gender and previous history of acute cholecyctitis, BMI stratification were done and post stratification chi square test was applied at 5 % level of significance.

## Results

Mean age (years) in the study was 45.62+12.66years. There were 128 (58.1%) male and 90 (41.3%) female patients. Mean body mass index in the study was 28.36 +5.35kg/m$^2$. There were 30 (27.5%) patients who were presented with history of acute cholecyctitis. Frequency and percentage of post-operative surgical site infection in patients receiving prophylactic antibiotics and without prophylactic antibiotics after elective laparoscopic cholecystectomy was 9 (8.3%) and 2 (1.8%) respectively which was statistically significant (p-value 0.030) as shown in Table-1

**Table 1:** *Comparison of Post-operative surgical site infection in patients among both the groups*

| Parameters | | Two Groups | | Total N (%) | P-value |
|---|---|---|---|---|---|
| | | Group A (antibiotics) N (%) | Group B (placebo) N (%) | | |
| Surgical Site Infection (post operatively at day 28) | Yes | 9 (8.3%) | 2 (1.8%) | 11 (5%) | 0.03 |
| | No | 100 (91.7%) | 107 (98.2%) | 207 (95%) | |
| Total | | 109 | 109 | 218 | |

**Table 2:** *Effect modifiers stratification with Comparison of Post-operative surgical site infection in Acute Cholecyctitis patients among both the groups*

| Parameters | | Surgical Site Infection (post operatively at 28 day) | Group-A (n=35) | | Group-B (n=35) | | P value |
|---|---|---|---|---|---|---|---|
| | | | n = 109 | % | n=109 | % | |
| Age (years) | 18 - 40 | Yes | 5 | 13.2% | | 2.7% | 0.095 |
| | | No | 33 | 86.8% | 36 | 97.3% | |
| | 41 - 65 | Yes | 4 | 5.6% | 1 | 1.4% | 0.167 |
| | | No | 67 | 94.4% | 71 | 98.6% | |
| Gender | Male | Yes | 4 | 5.7% | 1 | 1.7% | 0.246 |
| | | No | 66 | 94.3% | 57 | 98.3% | |
| | Female | Yes | 5 | 12.8% | 1 | 2% | 0.041 |
| | | No | 34 | 87.2% | 50 | 98% | |
| BMI | < 23 | Yes | 2 | 7.1% | 0 | 0% | 0.165 |
| | | No | 26 | 92.9% | 26 | 100% | |
| | > 23 | Yes | 7 | 8.6% | 2 | 2.4% | 0.08 |
| | | No | 74 | 91.4% | 81 | 97.6% | |
| Previous history of acute Cholecyctitis | Yes | Yes | 8 | 26.7% | 0 | 0% | 0.549 |
| | | No | 22 | 73.3% | 1 | 100% | |
| | No | Yes | 1 | 1.3% | 2 | 1.9% | 0.753 |
| | | No | 78 | 98.7% | 106 | 98.1% | |

For effect modifier like age, gender, BMI and previous history of acute cholecyctitis, stratification was done and compared with the frequency of post-operative surgical site infection in patients receiving prophylactic antibiotics and without prophylactic antibiotics after elective laparoscopic cholecystectomy as shown in Table-2

## Discussion

The purpose of using prophylactic antibiotics is controversial in low-risk cases. Many studies strongly believe on the efficacy of preoperative antibiotics in low-risk patients.[13–17] On the other hand, many research proposals discourage the use of antibiotics preoperatively undergoing laparoscopic cholecystectomy.[8-12] Furthermore, decline in infectious complications was the main reason of antibiotic use in such patients[14–17]. But the recent studies and clinical trials now conclude that rate of infection is very low in low-risk patients, so it does not alter the rate of postoperative SSI.[8–12]

In a study by Jae Do Yang, five hundred and nine laparoscopic cholecystectomies were performed on low-risk patients. It was observed that antibiotics given before the procedure did not alter the rate of infection post-operatively.[3]

In a study conducted by Pankaj Kumar, patients were divided into two groups. First group received antibiotics before the procedure while second group received placebo (saline injections). It was observed that the rate of SSI was equal in both groups. It was also observed that SSI rate was not related to spillage of bile during the procedure. So antibiotics are not required in low-risk cases.[4]

Similarly, Chong ju, described in his study that four hundred and seventy-one patients underwent LC and the rate of SSI was 1.69%. The incidence of SSI was comparable for patients 5 out of 279 (1.79%) in group 1, who received second generation cephalosporin 1 gram I/V before surgery and 3 of 192 patients (1.56%) in group 2 (p=0.973), who were not given prophylactic antibiotic.[5]

Spaziani E study showed that preoperatively patients were divided into three groups. Group 1 patients (n=41) were given ampicillin-sulbactam; Group 2 patients (n=40) received ciprofloxacin while Group 3 patients (n=53) received no antibiotic. It was observed that there was infection in total 11 patients (8.2%) in all groups. Six patients developed infection in Group1 and Group 2 (three in each group 7.3%) while five patients (9.4 %) developed infection in Group 3 (p=0.916).[8]

The impact of biliary spillage during LC on the frequency of SSI is also a matter of discussion in many studies. One group of authors mark bile spillage and bactibilia as an important factor in causing wound infection in low-risk patients.[15] So they suggest antibiotic use pre-

operatively. Anderson DJ concluded in his study that third generation cephalosporin decrease bactibila and thus postoperative infection[14]. In our study, we concluded that the rate of SSI is not influenced by the presence of bacteria in bile or perforation of gallbladder causing spillage.

Study conducted by Chong Ju7 showed that average age of patients in his study were 44.6+23.4 with gender distribution 15% and 85% respectively, the study showed that surgical site infection among both the groups was 4.41% and 2.63% respectively showing that the rate of postoperative SSI is not altered by giving antibiotics preoperatively and thus not an essential component in low-risk patients of LC.

## Conclusion

The study concluded that there is a difference in frequency of surgical site infection in patient receiving prophylactic antibiotics and those with not receiving antibiotics, undergoing laparoscopic cholecystectomy. Hence, it would be advisable that patient should be prevent from unnecessary exposure of antibiotics which will be cost effective. Thus, general public and doctors should play a role in order to avoid unnecessary exposure of antibiotics to the patient which don't play any significant role on post op surgical site infection.

**Conflict of Interest** *None*

**Funding Source** *None*

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## Authors Contribution

**SS:** Conceptualization of Project
**SS, SA:** Data Collection
**SMD:** Literature Search
**UQ:** Statistical Analysis
**JSK:** Drafting, Revision
**SMD:** Writing of Manuscript

Original Article

# Correlation between Stress and Meaning in Life in Early Career Doctors in Pakistan

**Samiya Iqbal**[1]

**Abstract**

**Objective:** To assess the correlation between stress and meaning in life in early career doctors in Pakistan

**Method:** It was a cross-sectional study carried out using non-probability convenience sampling from March to May 2021 with early career doctors in Pakistan. The data was collected using a form distributed online that included demographic variables, Purpose in Life (PIL) test and Perceived Stress Scale (PSS). SPSS 26.0 was used for data entry and analysis.

**Results:** The average score on PIL test was 67.64±15.20 and PSS was 20.20±5.88. Female doctors reported higher perceived stress (18.82±6.11) than male doctors (20.75±5.07). There was a significant negative correlation between the PIL and PSS, $r(215) = -.610$, $p < 0.01$. $r = -0.610$ represents a large effect size.

**Conclusion:** Higher meaning in life is associated with lower perceived stress in doctors. Interventions that focus on meaning in life may help improve the well-being of doctors.

**Keywords:** Stress, Psychological Distress, Meaning in Life, Purpose in Life, Doctors.

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## Introduction

Doctors experience significant stress in their everyday occupational activities. Firth-Cozens[1] reported that compared to 18% of the working population as a whole, approximately 28% of doctors exhibit above-threshold levels of stress. The prevalence of stress among doctors ranges from roughly 24-64%, according to recent studies from India[2], Iran[3], Malaysia[4], and Egypt[5]. This is supported by the available statistics from Pakistan.[6,7] There are several reasons for this. The nature of work involves confrontation with disease and death under the threat of experiencing violence and the possibility of strict scrutiny and litigation while working long work hours with irregular sleep and meal schedules, pressure to complete tasks in a timely manner and little work life balance. Moreover, doctors tend to put high demands on themselves, can be perfectionistic and may have interpersonal relationship difficulties with peers and seniors. In addition, unavailability of adequate resources and personnel, insufficient compensation for the service and hostile work environment play a role.[8,9] Because the COVID-19 pandemic added to the burden on the healthcare system and doctors were faced with uncertainties about the disease and personal safety, stress levels increased. This stress can have detrimental personal and professional consequences for the doctor with increased rates of physical illnesses and mental health issues, problems in marital and social life as well as dissatisfaction with career, compromised quality of patient care and medical errors.[8,9] Neurobiological research suggests chronic, uncontrollable stress impairs the functioning of the prefrontal cortex leading to decreased motivation and difficulty in making decisions.[10] Despite this, most practitioners experience a career in medicine as meaningful.

Southwick et al[11] proposed that meaning in life affects on the stress response, resilience, ability to endure adverse circumstances and post-traumatic growth. They draw on Viktor Frankl's Logotherapy, which posits that life is potentially meaningful under all conditions. Even under the most miserable situations, meaning can be discovered by exercising the freedom to choose one's attitude to inescapable suffering and self-transcendence.

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This allows one to have optimism, altruism, spiritual grounding, social relationships and active coping, which are well known to mitigate stress. From the perspective of health, a greater sense of purpose in life is associated with better cardiovascular indicators, endocrine profiles, cognitive aging and restorative sleep as well as reduced mortality in both young and older adults.[12] Moreover, stress exposure was associated with depression when the presence of meaning in life was low but with high meaning, the association does not hold.[13] The sense of meaning decreases negative appraisals of the situations[14] and repetitive negative thinking after an unpleasant event, leading to healthier coping strategies.[15] It enhances positive affect[16], subjective well-being and life satisfaction.[17]

Apart from the indirect effects on the response to stress, empirical evidence suggests a direct effect meaning has on subjective distress experienced by the individuals. A study conducted on palliative care professionals demonstrated that meaning of work and perceived stress were negatively correlated.[17] Similarly, presence of meaning was related to less mental distress in hospice nurses.[16] Moreover, several recent studies confirmed that meaning in life and meaning-centered coping alleviated the coronavirus pandemic stress.[18,19]

However, there were no available studies that investigated the effect of meaning in life on stress experienced by Pakistani doctors. This study was planned to pave the way for further empirical research in this area and if the findings are consistent with the literature presented above, meaning-centered interventions can eventually be designed to improve the well-being of doctors, especially in the aftermath of the global pandemic.

## Material and Methods

This study used a cross-sectional survey research design. The sample size was calculated using Sample Size Calculators for designing clinical research with the following parameters: level of significance = 5%, confidence interval=95%, and correlation coefficient r = -0.52 from a previous study.[20] Data were collected from early-career doctors working in Pakistan between March and May 2021 recruited using convenience sampling. The inclusion criteria were that participants (i) were early career doctors (i.e. those working for 10 years or less) and (ii) were working for a minimum of past 6 months. Those who were currently under treatment for a psychiatric disorder were excluded. After obtaining ethical approval from the hospital ethical review committee, all participants were asked to complete an online survey, which was created with Google Forms and distributed through social media networking sites. It began with information about the study's objectives. Participants were assured of confidentiality, anonymity, and that any information they provided would be used solely for research purposes. All participants provided informed consent to participate in this study. The survey included information about the participants' sociodemographic characteristics, including information about age, gender, marital status, education, designation at job, total duration of work and whether they worked in COVID units or not. Psychological variables collected included the Purpose in Life (PIL test and the Perceived Stress Scale (PSS).

PIL test was developed by Crumbaugh & Maholick in 1964. This is a 20 item self-rated psychometric scale designed to assess level of meaning in life. Each question has a range from 1-5; the higher the score on the test, the higher the level of meaning in life.

Perceived Stress Scale (PSS) is a measure of the degree to which the situations in one's life are regarded as stressful. It is a 10-item scale with a range of responses from 0-4. PSS scores are obtained by reversing responses to the four positively stated items (items 4, 5, 7, & 8) and then summing across all scale items. Higher scores indicate a greater level of perceived stress.

Statistical analyses were performed using SPSS version 26.0. Categorical variables were described using frequencies and percentages. Quantitative variables were described with mean (M), standard deviation (SD). The internal consistency of each subscale was assessed using Cronbach's alpha and a value higher than. 7 was considered acceptable. Analysis of variance and t test were run to assess the impact of demographic characteristics on perceived stress and meaning in life. Pearson's correlation test was applied and Pearson product-moment correlation coefficient was calculated along with p value $<0.05$ taken as significant.

## Results

Average age of the participants was 27.45±2.82 years and the average duration they had worked as a doctor was 3.88±2.62 years.

Table 1 reveals that more women doctors (n=155, 71.4%) participated in the study compared to men (n=62, 28.6%). A greater proportion of doctors (n=129, 59.4%) were

**Table 1:** *Sociodemographic Characteristics of the Participants*

| Baseline characteristic | Frequency | Percentage |
|---|---|---|
| **Gender** | | |
| Female | 155 | 71.4 |
| Male | 62 | 28.6 |
| **Marital status** | | |
| Single | 129 | 59.4 |
| Married | 82 | 37.8 |
| Separated | 1 | 0.5 |
| Divorced | 4 | 1.8 |
| Widowed | 1 | 0.5 |
| **Highest educational level** | | |
| MBBS | 197 | 90.8 |
| BDS | 4 | 1.8 |
| Postgraduate qualification | 16 | 7.4 |
| **Job designation** | | |
| House Officer | 69 | 31.8 |
| Medical Officer | 29 | 13.4 |
| Postgraduate Trainee | 101 | 46.5 |
| Consultant/Specialist | 12 | 5.5 |
| Lecturer/Demonstrator | 5 | 2.3 |
| Public Health Specialist | 1 | 0.5 |
| **Specialty** | | |
| Medicine & Allied | 124 | 57.1 |
| Surgery & Allied | 68 | 31.3 |
| Non-clinical specialties | 7 | 3.2 |
| General Practice | 13 | 6.0 |
| Dental specialties | 5 | 2.3 |
| **Worked/working in COVID Units** | | |
| Yes (Frontline Workers) | 125 | 57.6 |
| No | 92 | 42.4 |

single than married (n=82, 37.8%). Majority of the doctors had MBBS as their highest qualification (n= 197, 90.8%) and were working as postgraduate trainees (n=101, 46.5%). Over half of the doctors had worked in or were working in COVID units (n=125, 57.6%) while the rest had not (n=92, 42.4%).

The Cronbach's α value for Perceived Stress Scale (PSS) and Purpose in Life (PIL) test were .85 (>.80) and .93 (>.90), which indicated good reliability of the scales administered.

The mean score on PIL test was 67.64±15.20 and PSS was 20.20±5.88.

To compare the mean PIL scores of male and female participants, as well as those of frontline workers and others, independent sample t-tests were used. In either comparison, there were no significant differences in PIL scores between the groups. Independent sample t-tests were also used to compare the mean PSS scores between genders and frontline workers versus others. PSS scores differed significantly between males (M = 18.82, SD = 5.07) and females (M = 20.75, SD = 6.11); t(215) = -2.198, p = 0.03. There were no significant differences in PSS scores between those who worked in COVID units and those who did not.

The effect of marital status, highest educational level, job designation, and specialty on PIL and PSS scores was compared using one-way ANOVA tests. There were no statistically significant differences in either score between the groups.

Pearson correlation coefficient was calculated to assess the linear relationship between purpose in life (PIL) and perceived stress (PSS) scores of the participants. There was a significant negative correlation between the PIL and PSS, r(215)=-.610, p<0.01. r=-0.610 represents a large effect size. Age and the duration of work as a doctor showed a significant positive correlation with PIL scores, although the effect size was small.

**Table 2:** *Correlations*

| Variables | Age | Duration | PIL | PSS |
|---|---|---|---|---|
| Age | 1 | .844** | .202** | -.115 |
| Duration | - | 1 | .175** | -.050 |
| PIL | - | - | 1 | -.610** |
| PSS | - | - | - | 1 |

**Correlation is significant at the 0.01 level (2-tailed).

## Discussion

The primary aim of the study was to assess the effect of meaning in life on stress experienced by early career doctors working in Pakistan. A statistically significant negative correlation was found between stress and meaning in life in the population researched in the current study.

This study supports the findings of the existing international literature. Ostafin et al15 showed that meaning was inversely with distress, r(88)=−.53, p<.001. Similarly, Park and Baumeister23 demonstrated those having a greater sense of meaning in life described lesser current stress, r(153) = −0.28, p = 0.001. Hill et at[13] indicated that sense of purpose is not only associated with lower levels of perceived stress but also with decreased secretion of cortisol, even though the amount of daily stres-

sors experienced does not decrease. This may mean that meaning fosters an optimistic attitude and active coping. The research conducted on specifically on medical professionals points in the same direction. Moreno-Milan et al[17] also reported that palliative care workers who found greater meaning in their work scored lower on the measure of perceived stress, which increased their satisfaction with life. Another study conducted on hospice nurses frequently dealing with mortality revealed the presence of meaning in life was associated with less stress, burnout and negative emotional states, as well as with more positive emotional states.[16]

The only other published study done on Pakistani doctors reported a significant negative correlation between perceived stress and psychological well-being among doctors. Even though this used the Ryff psychological well-being scale, it did not report the correlation between the purpose in life subscale and stress.[21] Another local study looked at the same variables as the current study but the population investigated was that of medical students. The reported correlation coefficient was found to -0.52, $p<0.05$.20

Even though it was not the primary goal of the study to report on the level of stress in doctors and its relationship with the demographic variables, an important finding was that female doctors reported being more stressed than male doctors did but there was no statistically significant difference between the two genders with respect to meaning in life. Moreover, older doctors with longer duration of medical career experienced greater meaning in life. Interestingly, marital status, highest educational attainment, job designation, specialty and frontline work in COVID-19 pandemic were found to have no significant difference effect on perceived stress or meaning in life.

A study done in Pakistan found out a higher overall mean PSS score was 26.09±8.141 than the current study. Also, age and the number of years at work were negatively correlated with stress in contrast to what this study found. However, they also reported that the females had significantly higher perceived stress scores compared to the males and that the effects of marital status and specialty on stress were not significant.[22] Another study from Faisalabad, Pakistan also confirms the higher degree of stress in female doctors but also suggested that being married was associated with greater stress.[7] Arif et al24 showed that stress index from top to bottom was observed in house officers, medical officers/ post-graduate trainees and consultants/ specialists but this was not consistent with the current study. The differences with the present study may be explicable by the personality factors and sociodemographic variables that were not accounted for in this as well as the previous studies.

Let us now consider the strengths and limitations of the study presented above. It has been especially useful as it opens a new avenue for research on the mental well-being of our target population in Pakistan, since there were no other studies on the topic available. The sample included both men and women with a wide distribution of doctors across job designations and specialties. However, correlational studies cannot conclusively prove the relationship between variables and self-reported measures can introduce bias. We hope that future research would rectify these shortcomings. The current time has been significantly stressful for doctors, making such research the need of the hour, so that we have more interventions in our arsenal that enable better stress management.

## Conclusion

Experiencing higher meaning in life leads to lower perceived stress in early career Pakistani doctors.

**Conflict of Interest** *None*

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## Authors Contribution

**SI:** Conceptualization of Project
**SI:** Data Collection
**SI:** Literature Search
**SI:** Statistical Analysis
**SI:** Drafting, Revision
**SI:** Writing of Manuscript

# Effects of Avocado Aqueous Seed Extract on Liver Biochemical Markers in Rats with Hepatotoxicity Induced by Isoniazid

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**Abstract**

**Objective:** To observe the improvement in serum biomarkers of liver function (LFTs) by using aqueous Avocado seed extract with isoniazid (INH) in Albino rats.

**Method:** It was an experimental research conducted at KEMU from January to June 2019. The study included thirty six male Sprague Dawley Albino rats divided into 4 group using lottery method, each group having 9 animals. All animal groups were administered treatment by gavage method for 30 days. Blood sample of each animal for biochemical markers analysis was collected 24 hours after the last dose of drugs by cardiac puncture. The collected data from the four groups was entered in Statistical package for social sciences (SPSS) version 26 for analysis. Mean and standard deviation were calculated for quantitative characteristics. One way ANOVA was used to make the comparison between all groups. Pair wise comparison was performed using Least square difference (LSD) Test. P-value <0.05 was considered significant.

**Results:** Serum alanine aminotransferase (ALT), serum aspartate aminotransferase (AST), serum alkaline phosphatase (ALP), and serum bilirubin showed a significant difference upon co-administration of aqueous Avocado seed extract with INH among all the groups.

**Conclusion:** The current study indicates a significant dose-dependent improvement in serum biomarkers of liver function when INH and avocado aqueous seed extract are used together.

**Keywords:** Avocado seed, Isoniazid-induced hepatotoxicity, LFTs, Albino rats.

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## Introduction

Avocado is a dicotyledonous plant belonging to the order Ranales and the family Lauraceous.[1] Avocado seeds make up a significant portion of the total fruit. Phenolic acids, falvinoids and condensed tannins are essential phytochemicals present in avocado seeds.[2] Ethanol extracts of leaf and fruit contain important phytochemicals that produce apoptosis of tumor cells by inhibiting growth signals within these cells.[3] The biological benefits of aqueous seed extracts of Avocado have been implicated in hypertension observed on rat models by reducing heart rates.[4] The aqueous seed extract has also been found effective in the treatment of hyperglycemia in diabetic rats.[5]

Tuberculosis (TB) is a major contributor to the disease burden in Pakistan and 75% of TB patients are in productive age group.[6] Prompt and complete treatment of TB is strongly indicated. Isoniazid (INH) is one of the most important drugs used to treat TB. But it has been associated with severe hepatotoxicity and fatal liver injury by causing necrosis and steatosis of hepatocytes.[7,8]

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The reported liver toxicity with isoniazid is 1.6%.[9]

The research on biological effects of Avocado seed is still in its early stages. The present study was conducted to monitor the improvement in serum biomarkers of liver function by using aqueous Avocado seed extract and INH together in INH-induced hepatotoxic albino rats.

## Material and Method

It was an experimental study conducted on thirty six adult male Albino rats after taking approval from the IRB (letter # 205/RC/KEMU) and ASRB (letter# 10220/KEMU/2018), KEMU. The study was carried out at Experimental Research Laboratory (Animal House) of Postgraduate Medical Institute, Birdwood Road, Lahore in collaboration with Anatomy department and Histopathology laboratory of KEMU from January 2019 to June 2019.

A total of 36 male Sprague Dawley Albino rats of 8-12 weeks age, weighing between 200-250 grams were randomly divided into 4 groups by lottery method. Each group had 9 animals and each group was housed in a separate cage labeled according to the animal groups. Animals were allowed to acclimatize for 1 week before start of experiment. Any rats that became inactive or stopped eating during acclimatization were excluded. The animals were fed tap water ad libitum and standard diet.

Group 1, Control group (CG) received only1 ml/kg/day distilled water in morning.10 Group 2, Isoniazid group (INHG), received only isoniazid 100 mg/kg/day dissolved in 1ml distilled water as a single dose in the morning.[11] Group 3, Isoniazid-Avocado (low dose) group (INHAV low) was given Isoniazid 100 mg/kg/day dissolved in 1 ml distilled water as a single dose in morning,[11] and Avocado seed extract (aqueous) 250mg/kg/day dissolved in 2 ml distilled water as a single dose in the morning, one hour after INH.[10] Group 4, Isoniazid-Avocado (high dose) group (INHAVhigh) received Isoniazid 100 mg/kg/day dissolved in 1 ml distilled water as a single dose in the morning,[11] and Avocado seed extract (aqueous) 500 mg/kg/day dissolved in 4 ml distilled water in two divided doses of 2 ml each. 1st dose was given in morning, one hour after INH and 2nd dose in the afternoon. All the doses were given by gavage method for 30 days.

Blood sample of each animal for biochemical markers analysis was collected 24 hours after the last dose of drugs by cardiac puncture. Almost 2 ml blood was collected in sterile syringe & transferred to vial containing sterile gel. The vials were transported to Biochemistry laboratory, KEMU with utmost care. Blood was allowed to clot for 1 hour. Serum was separated and centrifuged at 3000 revolutions per minute for 10 minutes. The centrifuged serum samples were stored at -20°C in autoclaved tubes till they were used for LFT's estimation (Serum ALT, AST, ALP and Total Bilirubin for all groups). Statistical Package for the Social Sciences version (SPSS) 26 for data analysis. Mean and standard deviation were calculated for quantitative characteristics. One way ANOVA was used to make the comparison between all groups. A pair wise comparison was performed using the Least square difference (LSD) Test. P-value <0.05 was considered significant.

**Table 1:** *Comparison of LFTs among Study groups (One Way ANOVA)*

| LFTs | | Sum of squares | df | Mean square | F | P-value |
|---|---|---|---|---|---|---|
| Serum Alanine aminotransferase (ALT) | Between groups | 69806.779 | 3 | 23268.926 | 85.732 | 0.000* |
| | Within groups | 8685.245 | 32 | 271.414 | | |
| | Total | 78492.024 | 35 | | | |
| Serum Aspartate aminotransferase (AST) | Between groups | 80544.673 | 3 | 26848.224 | 37.190 | 0.000* |
| | Within groups | 23101.447 | 32 | 721.920 | | |
| | Total | 103646.120 | 35 | | | |
| Serum Alkaline phosphatase (ALP) | Between groups | 95465.715 | 3 | 31821.905 | 58.772 | 0.000* |
| | Within groups | 17326.233 | 32 | 541.445 | | |
| | Total | 112791.948 | 35 | | | |
| Serum Bilirubin | Between groups | .530 | 3 | .177 | 15.212 | 0.000* |
| | Within groups | .372 | 32 | .012 | | |
| | Total | .902 | 35 | | | |

*Significant P-value <0.05

## Results

The mean serum Alanine aminotransferase (ALT) for the four groups was 17.50±5.17u/l (CG), 140.97±28.04 u/l (INHG), 89.66±9.97 u/l (INHAVlow) and 73.69± 13.16 u/l(INHAVhigh). Serum ALT was highest in INHG and lowest in CG. When compared among groups, serum ALT was significantly different among groups (P value= 0.000 (Table-1).

The mean serum Aspartate aminotransferase (AST) for the four groups was 50.49±12.29 u/l (CG), 172.48±36.12 u/l (INHG), 136.31±32.19u/l (INHAVlow) and 158.03± 19.88u/l (INHAVhigh). Serum AST was highest in INHG and lowest in CG. One-way ANOVA showed that the difference between the groups is significant (P value= 0.000) (Table-1).

The mean serum Alkaline phosphatase (ALP) for the four groups was 91.26±8.33 u/l (CG), 221.79±22.35 u/l (INHG), 205.32±30.93 u/l (INHAVlow) and 198.63± 25.29 u/l (INHAVhigh). Serum ALP was highest in INHG and lowest in CG. Difference in serum ALP among groups was significant (P value= 0.000) by One Way ANOVA (Table-1). The mean serum bilirubin for the four groups was 0.40±0.07 mg/dl (CG), 0.74±0.09 mg/dl (INHG), 0.59±0.14mg/dl (INHAVlow) and 0.52 ±0.10 mg/dl (INHAVhigh). Serum bilirubin was highest in INHG and lowest in CG. Comparison between groups by one way ANOVA showed that the difference in serum bilirubin between groups was significant. (P value= 0.000) (Table-1).

## Discussion

The Avocado seed makes up about 13-18% of the whole fruit which is discarded as such despite being a natural and good source of carbohydrates, fats, proteins and important minerals like calcium, potassium, magnesium and phosphorus.[12,13] Although, it is mainly used for germination but it is also a rich source of nutrients and phytochemicals.[14]

This study was performed to observe the hepatoprotective effects of avocado seed aqueous extract on hepatic biochemical markers in isoniazid-induced hepatotoxicity in albino rats. Levels of serum transaminases and bilirubin were the highest in INHG, indicating severe hepatic insult. Several studies have proved the hepatic injury evident by elevated liver enzymes and serum bilirubin by using INH alone or in combination with other anti-TB drugs.[15-18] However, the levels of serum transaminases (ALT &AST) and serum bilirubin were found significantly reduced in INHAVlow (P value < 0.05) when compared with INHG but the reduction in serum ALP levels was not statistically significant. In INHAV high group, serum biochemical markers showed significant improvement (P value < 0.05) in comparison to INHG. It is worth emphasizing that there was an improvement in serum AST level in INHAVlow group more than INHAVhigh group which was quite unexpected. These findings in current study point towards a hepatoprotective role of avocado seed extract (aqueous) in both low and high doses.

The results of our study are consistent with the results of a study by Brai et al (2014) on aqueous leaf extract of avocado. They tried to find out what role it plays in liver damage from carbon tetrachloride in albino rats. Results indicated significantly low levels of liver enzymes and serum bilirubin in rats pretreated with aqueous leaf extract when compared to other groups which did not receive the extract.[19] In another study done by Jibril et al., (2015), the effects of avocado seed homogenates on liver enzymes were studied in albino rats as a co-treatment with first line Anti-TB drugs. Result showed a significant reduction in hepatic enzymes in the presence of avocado seed homogenate when compared with rats which received only Anti-TB drugs.[10] These results are also in accordance with findings in current study. A study by Cemaluk et al., conducted in 2018 showed that serum AST and ALT activity decreased in rats liver damaged by Monosodium glutamate (MSG) following administration of ethanolic Avocado seed extract. The study also reported similar decreasing levels of alkaline phosphatase and total serum Bilirubin upon administration of ethanolic Avocado seed extract. Tugiyanti et al. demonstrated in their study that powder supplement of Avocado seed improved the liver function in culled female quail. These studies strengthen the findings of our study.[20,21]

In a study by Zakariya et al., the hepatotoxic effects of aqueous and phenolic extracts from avocado seeds were compared in Wistar Albino rats. The study reported that serum levels of ALT, AST, and ALP were significantly higher in the aqueous and phenolic extract groups than in the control group with no extracts given.[22] The study results are in contrast to the present study.

## Conclusion

There is a significant dose-dependent improvement in serum biomarkers of liver function when INH and avocado aqueous seed extract are used together showing its hepatoprotective effects.

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**ZB, SQA, RT:** Conceptualization of Project
**ZB, SQA, AA:** Data Collection
**SQA:** Literature Search
**ZB, RT:** Statistical Analysis
**GM, SK:** Drafting, Revision
**ZB, SQA:** Writing of Manuscript

# Variations in Knowledge and Awareness of Stroke Signs and Symptoms Amongst the High Risk Adult Population of Lahore

**Rizwana Kitchlew,[1] Rimsha Tahir,[2] Masooma Bakhtiari,[3] Aiza Anwar [4]**


## Abstract

**Objective:** The objective of this study is to assess the knowledge of signs, symptoms and response to stroke in the high risk adult population of Lahore. We aim to analyze any possible associations to help conduct successful stroke awareness campaigns.

**Method:** Cross sectional study was conducted on the high risk adult population for stroke at Combined Military Hospital Lahore. Adequate knowledge of stroke was determined if five correct signs and symptoms were identified from a twenty-two component list. Descriptive analysis of participants' demographics variables, of stroke/signs and response to stroke was reported. The Pearson Chi-squared correlation coefficient was used to determine the correlation between adequate knowledge of stroke signs and symptoms with possible associative factors. Data was analyzed using IBM SPSS Software version 24.

**Results:** A total of 398 participants were included. Adequate knowledge of stroke was expressed by 287 (75.5%) respondents. Most common sign identified was sudden weakness in one half of the body by 316 (79.4%) patients. Majority expressed adequate stroke response of calling 1122 70 (17.6%) and going to hospital immediately 228 (57.3%). Statistically significant association of gender, education level, social class and appropriate response to stroke with adequate knowledge of stroke signs and symptoms was revealed ($p<0.05$).

**Conclusions:** Knowledge of stroke signs and symptoms in the high risk population of Lahore is sufficient. This outcome is a result of the high education level and social class in our study population.


**Keywords:** adult, association, education of patients, high risk, knowledge, stroke, signs and symptoms.

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## Introduction

Stroke is defined as a sudden onset of focal neurological deficit due to underlying compromise of cerebral perfusion.[1] It is identified worldwide as a major cause of death and long term morbidity.[2] In 2018, a study conducted in Pakistan on the epidemiology of stroke reported a stroke prevalence of 4.8%, revealing pregnancy and prolonged contraceptive use as the most rampant risk factor among females.[3] Other impor-tant and preventable risk factors included: overweight patients with concomitant diabetes mellitus and hypertension (49%), smokers (41.70%), patients with ischemic heart disease (34.50%), etc. However, despite the rampant prevalence of stroke in the country, there is no research available that correctly identifies whether or not the Pakistani population is well equipped with the know-ledge to identify stroke danger signs.

In a country where the estimated prevalence of diabetes mellitus is 19.9% amongst ages 20-79, and that of hypertension is reported to be 46.2%, there is an imperative need for stroke education due to the large number of high risk individuals. Timely reporting to healthcare facilities is the most important prognostic factor in the

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management of stroke. According to the American Heart Association/American Stroke Association guidelines, an intravenous infusion of tissue plasminogen activator (tPA) is the recommended treatment option for patients who present within 3 hours of symptom onset.[5] The rationale behind the use of intravenous thrombolytic in stroke management is derived from the findings of the National Institute of Neurological Disorders and Stroke (NINDS) tPA trial. Patients who had received tPA had a 30% greater chance of having minimal disability or no disability at all after 3 months.[6]

In Pakistan, TPA had previously not been approved by the Drug Authority of Pakistan. Consequently, the drug was only available privately at an exuberant price, rendering it all but impossible for the common man to purchase. However, in October 2020, Alteplase was registered under section 7 of the Drugs Act 1976 making it economically more accessible.

The purpose of our study was twofold: to assess the awareness of stroke signs and symptoms among the high risk adult population of Lahore, and educate them regarding the danger signs. We wish to utilize this data to hold public education campaigns that would assist the common population in effectively recognizing stroke signs and symptoms. A multidimensional approach involving early intervention via early recognition and early reporting is not only cost effective, but also an essential to combat this stroke epidemic. This leads to timely medical admissions and effective thrombolysis alleviating the major consequences of stroke.

## Material and Method

This cross sectional study was conducted at CMH Lahore and Institute of Dentistry, Pakistan through April 2021 till October 2021. After approval from the institutional 'Research Ethical Review Committee' a sample size of 349 was calculated.

The questionnaire was pilot tested on 30 volunteers who were not part of the final study sample. No changes were required in the structure of the questionnaire. Informed consent was taken and using non probability conve-nience sampling a total of 398 participants were inter-viewed in a semi structured approach allotting 20-30 minutes on each. Patient confidentiality was maintained via the informed consent section of the questionnaire and a sequential code was used during data entry, analysis and interpretation. Inclusion criteria for both male and females comprised of adults aged 18 years and older who had any of the following stroke comorbidities: overweight (BMI greater than or equal to 25 kg/m^2), smokers, ischemic heart disease, hypertension, dysrhythmias, diabetes mellitus, valvular/rheumatic heart disease, pregnant females and individuals using oral contraceptive pills.

We excluded from our study individuals with prior stroke history, barriers in verbal communication and healthcare professionals. The questionnaire consisted of 3 sections. Section 1 was allotted to information regarding demographic details. Section 2 was a table containing stroke and non-stroke signs and symptoms. The participants selected "yes" or "no" whether to their knowledge the listed variable pertained to stroke. Section 3 gauged participant response to stroke symptoms from a list of available options.

Section 2 of the study questionnaire was taken from a previous study 'Stroke Recognition Questionnaire" and following permission from corresponding author it was modified to fit our study requirements. Cronbach's alpha for the modified scale was 0.935 with fair internal consistency. Statistical analysis of the study was performed using version 24 of SPSS (Statistical Package for the Social Sciences) for Windows. In all the cases, $P<0.05$ was established as statistically significant. Shapiro-Wilk's test was used to assess the normality of age for both male and female participants. Non-normally distributed quantitative variables were reported as medians and interquartile ranges (IQR: Q3-Q1). A descriptive analysis of the variables of stroke that were assessed in the study was undertaken. Independent sample t test was undertaken to assess for any significant difference in ages of male and females. To assess whether or not participants reported an appropriate response to stroke, one point was given to each correctly identified stroke sign and symptom from the list below and expressed as a cumulative frequency:

- Diplopia, confusion, sudden weakness in one limb, sudden weakness in both legs and arms, numbness of face, difficulty in walking, sudden severe headache, slurred speech, pain in one arm, trouble controlling body movements, sudden unexplained dizziness

We deemed participants to have 'Appropriate Stroke Knowledge' if their score was greater than 5 (the cutoff point used in a previous research.[9] Indi-viduals having an appropriate knowledge of stroke underwent

Pearson's rank correlation analysis to assess the association with gender, education, previous stroke occurrence in a relative, social class, appropriate response to stroke (i.e. call 1122, go to hospital immediately).

## Results

Of the total 398 participants, there were 218 (54.8%) females and 180 (45.2%) males. The overall median (IQR) age of the participants was 54 (21). The independent sample t test revealed a significant difference for age p=0.000. Of the total sample, 170 (42.7%) individuals reported 'Yes' and 228 (57.3%) individuals reported 'No' to "Has anyone closely known to you suffered from a stroke?". Further demographic details are presented in Table 1. Table 2 reports descriptive frequencies of stroke signs and symptoms and response to stroke reported by the participants of the study. After calcula-ting the cumulative scoring of appropriately identified stroke signs and symptoms it was revealed that adequate knowledge was expressed by 287 (75.5%) respondents. The Pearson Chi-squared correlation coefficient was used to determine the correlation between adequate knowledge of stroke signs and symptoms with associative factors. As shown in Table 3, a statistically significant association of gender, education level, social class and appropriate response to stroke with adequate knowledge of stroke signs and symptoms exists.

**Table 1:** *Socio-demographic and clinical characteristics of participants*

| Socio-demographic | n (%) |
|---|---|
| Education level: Uneducated | 94 (23.6) |
| Education level: Primary School | 81 (20.4) |
| Education level: High School | 102 (25.6) |
| Education level: University | 81 (20.4) |
| Education level: Postgraduate | 40 (10.1) |
| Urban Residence | 309 (77.6) |
| Rural Residence | 89 (22.4) |
| Upper Class | 26 (6.5) |
| Upper Middle Class | 73 (18.3) |
| Middle Class | 151 (37.9) |
| Lower Middle Class | 104 (26.1) |
| Lower Class | 44 (11.1) |

*Obesity is defined as a BMI greater than 25kg/m$^2$.
n= number of individuals

**Table 2:** *Descriptive frequencies of Stroke Signs and Symptoms and response to Stroke.*

| Stroke Signs and Symptoms | Yes n (%) | Insufficient Knowledge n (%) | No n (%) |
|---|---|---|---|
| Diarrhea | 19 (4.8) | 35 (8.8) | 344 (86.4) |
| Difficulty Breathing | 98 (24.6) | 36 (9) | 264 (66.3) |
| Confusion | 148 (37.20) | 47 (11.8) | 203 (51.0) |
| Chest Pain | 77 (19.3) | 35 (8.8) | 286 (71.9) |
| Diplopia | 104 (26.1) | 55 (13.8) | 239 (60.1) |
| Sudden Weakness in One limb | 282 (70.9) | 44 (11.1) | 72 (18.1) |
| Sudden weakness in left or right side of the body | 316 (79.4) | 35 (8.8) | 47 (11.8) |
| Sudden weakness in both legs or arms | 218 (54.8) | 54 (13.6) | 126 (31.7) |
| Swollen Ankles | 62 (15.6) | 35 (8.8) | 301 (75.6) |
| Numbness on One side of the face | 192 (48.2) | 61 (15.3) | 145 (36.4) |
| Heartburn | 48 (12.1) | 35 (8.8) | 315 (79.1) |
| Dizziness or Loss of Balance | 176 (44.2) | 65 (16.3) | 157 (39.4) |
| Difficulty in Walking | 235 (59) | 36 (9) | 127 (31.9) |
| Sudden Severe Headache | 154 (38.7) | 51 (12.8) | 193 (48.5) |
| Fever | 58 (14.6) | 35 (8.8) | 305 (76.6) |
| Slurred Garbled Speech | 237 (59.5) | 42 (10.6) | 119 (29.9) |
| Cough | 43 (10.8) | 37 (9.3) | 318 (79.9) |
| Sudden Pain in One arm | 149 (37.4) | 39 (9.8) | 210 (52.8) |
| Leg Cramps | 109 (27.4) | 37 (9.3) | 252 (63.3) |
| Sudden Unexplained Dizziness | 149 (37.4) | 68 (17.1) | 181 (45.5) |
| Chronic Fatigue | 123 (30.9) | 37 (9.3) | 238 (59.8) |
| Trouble Controlling Body Movements | 150 (37.7) | 70 (17.6) | 178 (44.7) |
| Response to Stroke Signs and Symptoms | | | n (%) |
| Tell close family member | | | 115 (28.9) |
| Go to Hospital Immediately | | | 228 (57.3) |
| Call 1122 | | | 70 (17.6) |
| Wait For a Few Hours | | | 62 (15.6) |
| Schedule a Doctor's Appointment | | | 41 (10.3) |
| Alternate Medicine | | | 19 (4.8) |
| Do Nothing | | | 17 (4.3) |

**Table 3:** *: Pearson Chi-Squared Test: Correlation of adequate stroke knowledge with associated factors*

| | Gender | Education Level | Previous Stroke Occurrence in a relative | Social Class | Appropriate response to stroke-Call 1122 | Appropriate response to stroke – Go to Hospital immediately |
|---|---|---|---|---|---|---|
| **Adequate Stroke Knowledge** | | | | | | |
| **Value** | 4.034 | 13.201 | 1.862 | 13.071 | 26.655 | 11.661 |
| **Sig.** | **0.045*** | **0.010*** | 0.172 | **0.011*** | **0.000*** | **0.003*** |

*** p-value <0.05 is considered statistically significant**

## Discussion

Identifying patients who are more prone to cerebrovascular accidents and acknowledging the need to raise adequate awareness amongst them is a key step towards alleviating burden on healthcare facilities. The general impression is that people lack adequate knowledge regarding stroke signs and symptoms. The previous studies conducted in west support this notion.[10,11,12] Surprisingly, in our study population overwhelming majority possessed ample knowledge in this respect. These results are in stark contrast to previous studies. Multiple reasons can explain the conclusion of these results. Foremost being over half (56%) of the respondents in our study having an education level of high school or above and 62.8% belonged to the middle class or higher. Therefore, the number is representative of the educated class as opposed to Pakistani population as a whole. This hypothesis is further attested by the fact that there was a significant correlation with education and social class of adequate stroke knowledge (table3).

The commonly recognized, and correctly so, symptom of stroke was sudden weakness in one half of the body (79.4% of the respondents). This is one of the most poignant manifestations of stroke and also the most widely identified symptom in previous research data.[13] In contrast, the incorrect symptom that was most confusing for people was chronic fatigue. Including fatigue was a tricky question, because fatigue is a common post stroke symptom but does not occur at the time of stroke.[14] Nevertheless, the correlation is not completely irrelevant. It is equally important for healthcare professionals to guide patients regarding incorrect symptoms of stroke (e.g. diarrhea) to avoid unnecessary panic and overburdening of the emergency department. As to our knowledge, no previous studies conducted on stroke awareness focus on recognizing that patients also have incorrect information regarding the subject that needs to be addressed.

Our study also revealed over half of the respondents selected the correct responses to stroke, which were immediately go to the hospital or calling rescue 1122. The association between adequate stroke knowledge and appropriate response is understandable as someone who is familiar with the presentation of stroke would most likely recognize its emergent nature as well. However, it is disconcerting that a number of people with adequate stroke knowledge chose the wrong option, such as waiting for a few hours or trying alternate methods. This may be due to the hesitance amongst the population due to factors such as unexpected complications or unexpected deaths.[15] Furthermore, private medical hospitals charge an exuberant amount of fee, which only the affluent can afford. In contrast, government hospitals are free, but have long waiting lines and an overall lower quality of services.[16] Due to these reasons, even the people who chose 'tell a close family member' as their primary response may be at risk as family member may harbor these doubts and hinder patients from seeking timely treatment. Keeping these obstacles in mind, it is incumbent upon doctors in Pakistan whilst counselling the patients to stress upon the importance of timely intervention, especially now that tPA is available at government institutes. Although the cost is still high, spending money on prevention and early intervention is still better than spending it on rehabilitation.[17] Interestingly, there was no correlation between respondents who had adequate knowledge of stroke and had a relative or friend who suffered from stroke, despite the fact such respondents made up over half of the sample size. This lack of association also prevailed in previous researches, which found that majority of stroke patients and their caregivers had inadequate knowledge regarding strokes.[18] This could be because they were too panic stricken to notice the

individual symptoms aside from the one or two glaringly obvious ones. However this is alarming, as it highlights the need for educational campaigns to increase awareness of stroke. Personal experience is not enough to understand the correct course of action that must be taken should the patient experience any stroke symptoms.

One of the major reasons behind us undertaking this endeavor was to educate the high risk population about signs and symptoms of stroke, along with counselling them regarding the appropriate response. All our respondents belonged to a high risk category of stroke, with a majority of hypertensive and diabetic patients. According to previous research studies, educational campaigns are one of the most effective methods of spreading aware-ness regarding stroke, alongside television advertise-ments and stroke screening.[19] Our educational campaigns should aim to not only educate the masses regarding the correct symptoms of stroke, but also clarify which symptoms are not lethal or not indicative of an emer-gency situation. Additionally, the general population needs to be encouraged to report to the doctor imme-diately should they experience any stroke symptom, to maximize the benefit of tPA and limit morbidity.

A limitation of our study is being a single center study which may not provide full representation of the population. Furthermore, majority of our patients were educated thus the figures cannot be used to generalize the response of the overall population of the country.

## Conclusion

To the best of our knowledge, this was the first report of an initiative taken to create awareness regarding one of the most serious complications associated with diabetes and hypertension in the Pakistani population. The mentioned diseases are highly prevalent in our demographic population and are responsible for healthcare financial burdens due to high mortality and morbidity. The results of our study revealed the need to educate the common population regarding signs and symptoms that were not characteristic of stroke in order to avoid panic and burden at healthcare facilities.

**Conflict of Interest** *None*

**Funding Source** *None*

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## Authors Contribution

**RK, RT, MB, AA:** Conceptualization of Project
**RK, RT, MB, AA:** Data Collection
**RK, RT, MB:** Literature Search
**RT:** Statistical Analysis
**RK, RT, MB, AA:** Drafting, Revision
**RK, RT, MB, AA:** Writing of Manuscript

# Outcome of Open Repair with ON LAY Mesh Hernioplasty in Patients Presenting with Ventral Hernia -A Retrospective Analysis

**Abdul Basit Qureshi,[1] M Nadeem Aslam,[2] Muhammad Abdullah Qureshi[3]**

**Abstract**

**Objective:** To determine the outcome of ON LAY mesh hernioplasty in patients presenting with ventral and incisional hernias.

**Method:** The study is a descriptive case series carried out in Surgical Unit 1, Services hospital Lahore from January 2012 to December 2021. Data of 197 patients fulfilling the inclusion criteria who had ON LAY mesh hernioplasty were collected . Demographic as well as all other information was recorded on a Performa. All patients underwent ON LAY mesh hernioplasty under general anesthesia. Duration of surgery was noted. After surgery patients were shifted to ward and observed for immediate postop complications. Then patients were discharged and were follow-up for assessment of complications like wound infection, seroma formation and recurrence.

**Results:** Out of 197patients 47 (23.85%) had para umbilical hernia,16(8.12% )had epigastric hernia, 79(40.1%) had incisional hernia and 55(27.91%)had recurrent incisional hernia Mean age of patients was 41.15 years. There were 132(67%) females and 65(32.9%) males. Mean operative time was 145.65±29.33 minutes. There were 11(5.58%) patients who had wound infection 8 female(4.06%)and 3 male(1.52%).Seroma formation was seen in 7(3.55%) patients, 5(2.53%)females and 2(1.01%)males. Maximum duration of drains was 16 days and minimum was 8 days with mean duration 10.78±2.04 days. Recurrence was seen in 5(2.53%) patients,4(2.03%)females and 1 (0.507%) male.

**Conclusion:** Based on the results of this study it can be said that ON LAY mesh hernioplasty is a safe, convenient and very effective method of treating ventral and incisional hernias having minimum complications and recurrence with excellent long term results .

**Keywords:** ON LAY mesh hernioplasty, Ventral and incisional hernia repair, Seroma formation, Wound infection

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## Introduction

Abdominal wall hernias are frequently encountered in surgical practice accounting for 15% - 18% of all surgical procedures. Worldwide, more than 20 million hernias are operated per year.[1] Abdominal wall hernias have been reported more prevalent in low socioeconomic status.

Primary or secondary ventral hernia of abdominal wall is a fascial defect through which intraabdominal or preperitoneal contents protrude out continuously or intermittently[2]. Primary are true ventral hernias, whereas secondary are acquired (incisional or recurrent) hernias. Ventral hernias can also be described as reducible, incarcerated and strangulated. Cause of primary ventral hernia is multifactorial and evidence of connective tissue disorder favors familial predisposition[3]. Acquired her-

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nias may become clinically evident late but actual fascial separation starts in very early postop period [4].

Ventral Incisional Hernias (VIH) are a well-known complication after abdominal surgery and the incidence after laparotomy reported in literature ranges from 10% to 20%.[5] Early diagnosis, easily accessible health facilities and health education are important to prevent complications.

Despite advances in surgical technique and prosthetic technologies, the risks for recurrence and infection are high following the repair of ventral incisional hernias. High-quality data suggest that all ventral hernia repairs should be reinforced with prosthetic repair materials.[6]

Repair of ventral hernias can be done with open method as well as laparoscopically. Open repair of ventral hernias with mesh instead of sutures have become a standard procedure with excellent outcome[7]. It is associated with risk of wound infection ,seroma formation and chronic pain[8]. Complications of open ventral hernia repair (OVHR) are related to location of mesh placement e.g. mesh coming in contact with abdominal contents have more chances of intestinal obstruction and fistula formation[9]. Mesh can be placed ON LAY, SUB LAY or IN LAY in OVHR. All the locations have advantages and disadvantages. Most of the literature support the SUB LAY (retro muscular) location with low rate of infection, seroma formation and recurrence and it is considered as gold standard[10]. ON LAY technique can be used in OVHR with meticulous dissection and good hemostasis along with precautionary measures like thorough saline wash at the end of procedure, prolonged drainage and abdominal binder with excellent outcome[11].

## Material and Methods

The study is a descriptive case series carried out in Surgical Unit 1, Department of Surgery, SIMS Services hospital Lahore from January 2012 to December 2021. Total no of 197 patients were included in the study. Inclusion criteria was patients age 25-60 years of either gender with ventral hernia, BMI 18-40 Kg/$m^2$ and ASA status I-II. Patients with Diabetes Mellitus (BSR> 186 mg/dl), abnormal clotting profile (PT>20sec, APTT> 15 sec, INR>2) and ASA III or IV were excluded from the study.

Data of 197 patients fulfilling inclusion criteria were retrieved from database of surgical ward 1 Department of Surgery, Services hospital, Lahore. The demographic information like age, sex and address were noted. All patients underwent open ON LAY mesh hernioplasty under general anesthesia. After surgery patients were shifted to ward and managed with antibiotics, analgesia, I\V fluids and other supportive treatment. Patients were discharged with drains between 5$^{th}$ to 7$^{th}$ postop day and called for follow up in the ward after 3 to 4 days for wound examination, change of dressing, drain measurements. Drains were removed when output is reduced to 20 to 30 ml anywhere between 10 to 16 days. Then patients were follow-up in OPD fortnightly for three months to look for any delayed wound infection or seroma formation and then every six months for recurrence. All the data was collected on a pre-designed proforma (attached).

The data was entered and analyzed in SPSS version 20. Quantitative variables like age was calculated as mean and standard deviation. Qualitative variables like gender and complications were calculated as frequency and percentage.

Outcome was measured in terms of mean hospital stay, mean operative time, wound infection, seroma formation and mean duration of the drain requirement in days. Hospital stay was measured in days taking operative day as day 0 and patients were discharged when they were oral free and pain free. Operative time was from the incision till the end of the last stitch and was calculated in minutes by using stop watch. Wound infection (redness, erythema, pus discharge at site of wound) was graded according to Southampton wound grading system. It was labelled +ve if grade >3. It was assessed 10 days postop. Seroma was a localized collection of fluid detected clinically and with the help of ultrasound which needed drainage. It was assessed 10 days postop. Drains were removed when volume was less than 30 ml/24 hours and duration of drains were calculated in days.

## Results

Out of 197 patients, 47 (23.85%) had para umbilical hernia,16(8.12%) had epigastric hernia,79 (40.1%) had incisional hernia and 55(27.91%) had recurrent incisional hernia (Table 1). Mean age of patients was 41.15 years. Minimum and maximum age of patients was 25 and 60 years. (Table-2). There were 132 (67%) females and 65 (32.9%) males. Mean BMI of patients was 21.4 ± 1.75 (Table-2). Mean operative time was 145.65±29.33 minutes ranging from100 to 200 minutes. (Table-2). Maximum duration of drains was 16 days and minimum

was 8 days with mean duration 10.78±2.04 days. Mean drain volumes for right and left side drain were 198.04 ± 79.45 and 193.61±74.27 ml. (Table-2). As shown in Table 3 and Figure 1, 11 (5.58%) patients had wound infection including 8 females (4.06%) and 3 males (1.52%). Recurrence was seen in 5 (2.53%) patients, 4(2.03%) females and 1(0.507%) male (Table 3). Seroma formation was seen in 7 (3.55%) patients, being 5 (2.53%) females and 2 (1.01%) males (Table 3, Figure 1).

**Table 1:** *Types of hernia (n = 197)*

| Type | Number of patients | Percentage (%) |
|---|---|---|
| Paraumbilical hernia | 47 | 23.85 |
| Epigastric hernia | 16 | 8.12 |
| Incisional hernia | 79 | 40.12 |
| Recurrent incisional hernia | 55 | 27.91 |
| **Total** | 197 | 100 |

**Table 2:** *Characteristics of patients (n=197)*

| Item | Mean | SD | Min. | Max. |
|---|---|---|---|---|
| Age (years) | 41.15 | 11.05 | 25 | 60 |
| BMI (Kg/m$^2$) | 21.47 | 1.75 | 19 | 25 |
| Operative time (minutes) | 145.65 | 29.33 | 100 | 200 |
| **Drain volume** | | | | |
| Right side (mL) | 198.04 | 79.45 | 53 | 428 |
| Left side (mL) | 193.61 | 74.27 | 74 | 376 |
| Duration of drain | 10.78 | 2,04 | 8 | 16 |

**Table 3:** *Types of complications (n=197)*

| Complication | Number of patient | Frequency (%) |
|---|---|---|
| Recurrence | 5 | 2.53 |
| Seroma formation | 7 | 3.55 |
| Wound infection | 11 | 5.58 |

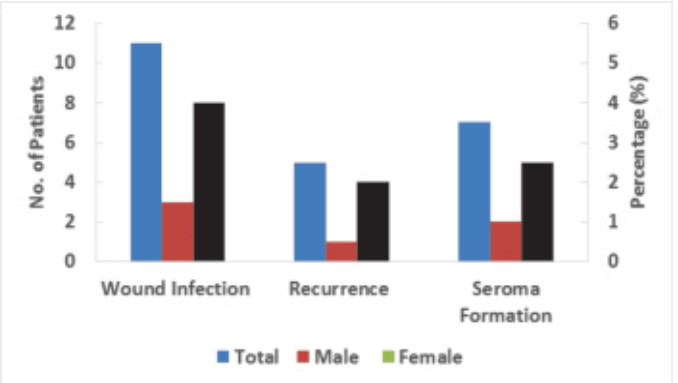


**Figure 1:** *Showing the frequency distribution of complications*

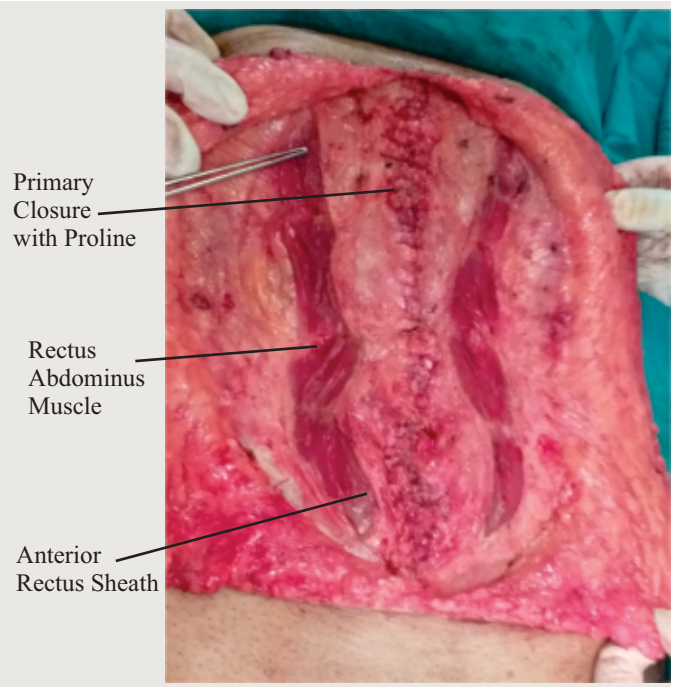


**Figure 2:** *Showing primary closure with sutures*

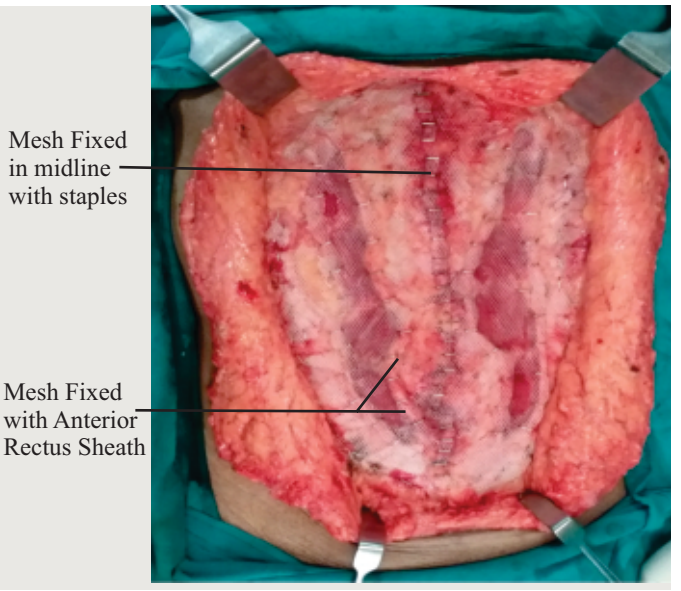


**Figure 3:** *Showing mesh fixed with staples*

## Discussion

The mean age of our cohort was about 41.15 years that is very comparable with other studies like Singh et al. (47±8.54), Bhattaria et al. (47 years), Ellis et al (49.4 years), Odeh JM et al (50.5 years) and Dhaigude et al (49.46 years)12-17. However, another study of Garg N et al found that mean age was quite less compared to our study.[16]

In our study, more prevalence of ventral hernia was

noted in female as compared to male (1:2.03) patients which is quite similar to other studies like Singh et al[17]. Similarly, Odeh JM and Garg N also reported that male to female ratio were 25:39 and 37:63 respectively[14-16].

Our results showed that wound infection occurred in 11(5.58%) patients that was similar as reported by Dhaigude et al and his co-workers (6.0%), but higher (12.5%) as recorded by Singh and his colleagues[15-17]. A body of evidences also demonstrated that incidence of wound infection rate ranged between 6 to 12%.[18-20] In another study conducted in Pakistan, 9.23% patients showed wound infection[21].

Seroma developed in 7 (3.55%) patients in our cohort. Dhaigude et al observed seroma formation in 8% patients[15]. A quite high incidence was reported by Singh et al (30%), kaafrani HM (23.3%), Poelman et al (28%), Ibrahim et al (15%)17, 22-24. In a study carried out in Quetta City during July 2016 to December 2017 by Manzoor et al seroma developed in 20% of patients[21].

Recurrence in the present study was found in 5 (2.53%) patients. Dhaigude et al noted recurrence in 1%, Saber et al in 3%, Ibrahim et al in 5%, Poelman et al in 16% patients[15,23-25]. Leithy et al found 2% recurrence in patients treated with ON LAY mesh hernioplasty[20]. No hernia recurrence was noted in studies by Singh et al and Manzoor et al.[17,21]

## Conclusion

Based on the results of this study it can be said that ON LAY mesh hernioplasty is a safe, convenient and very effective method of treating ventral and incisional hernias having minimum complications and recurrence with excellent long term results.

**Conflict of Interest** *None*

**Funding Source** *None*

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## Authors Contribution

**ABQ:** Conceptualization of Project
**ABQ:** Data Collection
**ABQ:** Literature Search
**ABQ:** Statistical Analysis
**ABQ:** Drafting, Revision
**ABQ:** Writing of Manuscript

# To Determine the Frequency of Different Grades of Breast Cancer in Obese Women

**Muzaffar Aziz,[1] Muhammad Ayub[2], Abdul Hannan Javaid,[3] Hajra Khan,[4] Umama Hayat Qureshi,[5] Khalid Hussain Qureshi[6]**

**Abstract**

**Objective:** To determine the frequency of different grades of breast cancer in obese women.

**Method:** This desctiptive cross sectional study, carried out in the department of General Surgery Nishtar Medical College, Multan from 2nd August 2021 to 1st February 2022. A total of 94 obese women with breast carcinoma and age 30-70 years were included. Patients who were already taking chemotherapy or operated for breast carcinoma were not included in this study. Informed consent was taken from each patient. The tumor grade was recorded after biopsy/ FNACs per-operational definition. All this information (age, duration of lump, height, weight, BMI, menopausal status, marital status, family h/o breast cancer, hormone replacement therapy and tumour grade was recorded by the researcher on a pre-designed proforma.

**Results:** Patients between 30 to 70 years were included in this study with mean age of 49.35 ± 10.88 years. Most of the patients 50 (53.19%) were 30 to 50 years of age. In this study, we have found the grade 1 in 16 (17.02%) obese women, grade 2 in 57 (60.64%) women and grade 3 in 21 (22.34%) obese women.

**Conclusion:** This study concluded that most frequent grade of breast carcinoma in obese women is grade 2 followed by stage 3 and 1 respectively.

**Keywords:** Breast cancer, obese, grade.

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## Introduction

Of the most common malignancies of women, carcinoma of the breast is one the most common malignancy, affecting approximately about 1.4 million women of the total population of the world in 2008 and leading to approximately 0.45 million deaths each year.[1] There have been significant advancement in the management of breast cancer during the last decade; with 5 year survival rate of 89.3 % and 10 year survival rate of 78.8%in the Chinese patients.[2] Breast cancer usually represents as adynamic and a complex disease. There are many prognostic factors to stage the breast carcinoma such as size of tumor, nodal status, histological grading, ER, PR & HER-2 neu receptor status and hematogenous spread.[3]

Carcinoma of the breast remains as the most prevalent cause of morbidity and mortality in women worldwide. Prevalence of breast carcinoma is 23% among all the cancers in women.[4] Advanced age is the major risk factor of breast carcinoma in women. As per recent studies, around half of patients with breast cancer presents after their 6th decade of life.[5] Mostly women die of breast carcinoma over the age of 65 due to advanced disease and poor prognosis.[6]

Long-term estrogen exposure is the only well-established risk factor among obese women for breast carcinoma as it is related to the initiation and progression of tumor.[7,8] The levels of free estrogen are inversely related to the levels of sex hormone binding globulin (SHBG). In case of breast carcinoma, the levels of SHBG were found low.[9] Peripheral aromatization of androgens to

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estrogen is the most common cause of increase estrogen production in post-menopausal women.[10]

Obesity is the bad prognostic risk factor of breast carcinoma among postmenopausal women.[11,12] Obesity (BMI >30kg/$m^2$) has negative affects on disease free survival period after diagnosis of breast carcinoma.[13] As compared to non-obese patients, obese patients tend to have advanced age, larger tumor size and poor nodal status.[14] According to a research, percentages of breast carcinoma in the obese pre-menopausal women were found to be 12.1% in grade 1, 68.2% in grade 2 and 19.7% in grade 3 and in obese post-menopausal women, the ratios were 17.3% in grade 1, 61.2% in grade 2 and 21.4% in grade 3.[15] While another study shows the proportion of 57.6 of grade 1 or grade 2 and proportion of 42.4 of grade 3 of CA breast.[16]

Obesity is becoming a major health concern worldwide due to its rapidly increased prevlance among the population. Multiple complications and comorbidites are the main concerns regarding the management and treatment plan of breast cancer in the obese patients. Although there is no direct relation between BMI and clinical management of breast cancer but as per recent studies, the measures against weight control should be prioritized before conducting any appropriate interventions. As per today, there is no available local study available on this topic, so I have decided to conduct this study to determine the frequency of different grades of breast cancer in obese women in local population. My study will going to be a promising addition to the existing literature and will be helpful in reducing the mortality and morbidity rates among the obese breast carcinoma patients by providing an empirical approaches and strategical plans regarding management of these specific patients.

## Material & Methods

Study design was Descriptive, Cross-sectional study. Study was conducted at Deptt. Of General Surgery, Nishtar Hospital Multan. This study was carried out from 2nd August 2021 to 1st February 2022. The calculated sample size is 94 with 5% level of significance, 10% margin of error and taking expected percentage of grade 3 in obese patients as 42.4%. Sampling technique is Non-probability, consecutive sampling. Inclusion Criteria is (a)Women with breast carcinoma (as per-operational definition) (b) Obese women (as per-operational defi-nition) (c) Age 30-70 years and exclusion criteria is (a)Patients already operated for breast carcinoma (b) Patients taking chemotherapy for breast carcinoma.

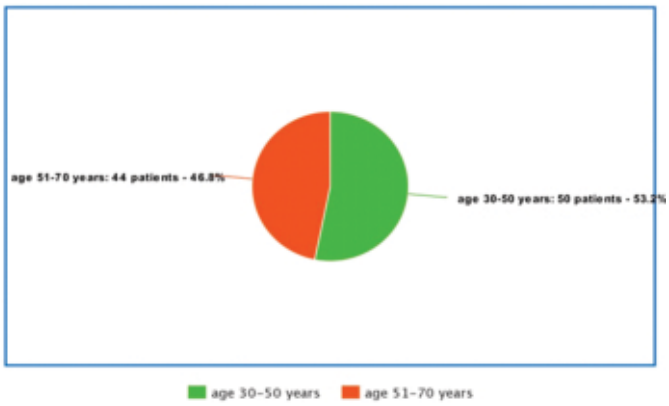
All women who presented with lump in breast >3 months duration and proved to be breast cancer on FNAC (pleomorphic cells with hyperchromasia, increased nuclear to cytoplasmic ratio (>1:1) and irregular nuclear contours that have breached the basement membrane) were included. BMI was calculated by following formula. BMI = weight in kgs / height in meters$^2$. Weight is measured by weight machine & height is measured by audiometer & 30 was to be considered as obese and <30 as non -obese. tumor grading was assessed according to Scarf-Bloom-Richardson grading system[17] for breast carcinoma as follows on microscopy of biopsy/FNAC; cancer cells with mitotic rate of <10%, small nuclei, and are arranged in tubular pattern. cancer cells with mitotic rate of 10%-50%, small nuclei, pleomorphism and arranged in solid clusters. cancer cells with sheets and solid nests and are highly pleomorphic with bizarre cells and mitotic rate of <50%. This study was reviewed by ethical review committee of Nishtar medical university and Hospital Multan and after approval from the committee, all those 94 patients who were completing the inclusion criteria were admitted to the Department of General Surgery, Nishtar Hospital, Multan. All of the patients were informed about the study and consent was taken from them. The tumor grade was recorded after biopsy/FNAC as per-operational definition. All this information (age of the patient, duration of breast lump, height, weight, BMI,pre-menopausal and post-menopausal status, married or un married, family history of breast cancer (yes/no), HRT (yes/no) & tumor grade was recorded by the researcher on a pre-designed proforma (Annexure).

Data that was collected via pre-designed proforma was analysed by SPSS version 20.0. Age, duration of lump and BMI were presented as mean and standard deviation. Married or unmarried, positive or negative family history of breast cancer, menopausal status and tumor grade (1/2/3) were presented as frequency and percentage.

Effect modifiers like age, duration of lump, BMI, marital status, family h/o breast cancer and menopausal status were addressed through stratification of data. Post-stratification chi square was applied to see their effect on tumor grade and p-value ≤0.05 was taken as significant.

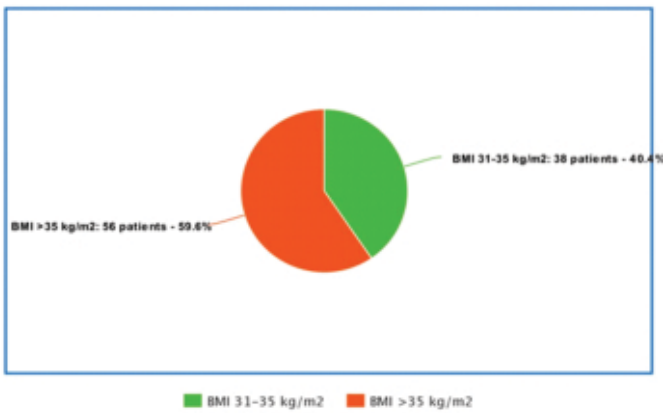
## Results

Patients having age between 30 to 70 years were included in this study with mean age of 49.35 ± 10.88 years. 50 patients (53.19%) were having age of 30 to 50 years as shown in Table II. Mean BMI was 36.03 ± 2.46 kg/m$^2$ (Table III). In this study, I have found the grade 1 in 16 (17.02%) obese women, grade 2 in 57 (60.64%) women and grade 3 in 21 (22.34%) obese women. Different grades of breast cancer were stratified according to age and BMI.




**Picture 1:** *Age Distribution of Patients (n=94).*

**Mean ± SD = 49.35 ± 10.88 years**




**Picture 2:** *Distribution of Patients According to BMI (n=94).*

**Mean ± SD = 36.03 ± 2.46 kg/m2**

## Discussion

Obesity affects approximately 13% of the world population.[17] In developed countries, such as the USA obesity affects >36% of adult population.[18] As a lot of research studies has been done and are of conclusion that diabetes and heart diseases have very well association with obesity, but association of breast cancer with obesity is not very well understood as a lot work and studies has been done in the recent past and further work needs to be done to reach the conclusion and to affect the clinical approach to the patients regarding this association.[19,20] Recent studies have shown that obesity and overweight patients have significant risks of having cancers like carcinoma of esophagus, stomach, thyroid, pancrease, uterus, breast, ovaries, colorectal carcinoma and multiple myeloma.[25] Adipose tissue which is abundant in obese individuals produces certain factors like inflammatory cytokines and mediators that helps in the invasion of carcinoma and its metastasis.[21,22] As we know that carcinoma of the breast is the most frequent carcinoma in women in the world. In developed countries the second most frequent cause of cancer related deaths is carcinoma of the breast. It is necessary to understand the association of obesity with carcinoma of breast so that awareness can be started at public level.[23]

I have conducted this study to determine and assess the frequency of different grades of carcinoma of breast in obese women. Mean age of this study was 49.35 ±

**Table 1:** *Frequency of different grades of breast cancer in obese women*

| | Frequency (%) | |
|---|---|---|
| **Grades of breast cancer** | Yes | No |
| **1** | 16 (17.02%) | 78 (82.98%) |
| **2** | 57 (60.64%) | 37 (39.36%) |
| **3** | 21 (22.34%) | 73 (77.66%) |

**Table 2:** *Stratification of different grades of breast cancer with respect to age.*

| | | 30-50 years (n=50) | 51-70 years (n=44) | P-value |
|---|---|---|---|---|
| **1** | Yes | 09 | 07 | **0.788** |
| | No | 41 | 37 | |
| **2** | Yes | 30 | 27 | **0.893** |
| | No | 20 | 17 | |
| **3** | Yes | 11 | 10 | **0.933** |
| | No | 39 | 34 | |

**Table 3:** *Stratification of different grades of breast cancer with respect to BMI.*

| | | 31-35 kg/m$^2$ (n=38) | >35 kg/m$^2$ (n=56) | P-value |
|---|---|---|---|---|
| **1** | Yes | 03 | 13 | **0.052** |
| | No | 35 | 43 | |
| **2** | Yes | 23 | 34 | **0.985** |
| | No | 15 | 22 | |
| **3** | Yes | 12 | 09 | **0.076** |
| | No | 26 | 47 | |

10.88 years having age range between 30-70 years. 53.19% (50) of the patients were having age between 30 to 50 years of age. As per results of this study the grade 1 was found in 16 (17.02%) obese women, grade 2 in 57 (60.64%) obese women and grade 3 in 21 (22.34%) obese women. In previous study, breast cancer grade in obese pre-menopausal women was found to be grade 1 as 12.1%, grade 2 as 68.2% and grade 3 as 19.7%. The same author has found the breast cancer grade in obese post-menopausal women as grade 1 in 17.3%, grade 2 in 61.2% and grade 3 in 21.4%.[15] In another study, breast cancer grade in obese women was found to be grade 1/grade 2 as 57.6% and grade 3 as 42.4%.[16] In another study it was observed that there is significant risk of invasive breast carcinoma in patients who were overweight or obese as compared to normal weight women. Of obese patient's risk was greatest for patients that have obesity grade $\geqslant 2$ (BMI> 35kg/$m^2$). In patients with BMI> 35kg/m2, biopsy of their specimen showed strong association with ER/PR + breast cancer. There is also association of large size tumor, positive lymph nodes, regional/ distant metastasis and deaths after breast carcinoma in patients with BMI> 35kg/$m^2$.[24]

It is observed in recent studies worldwide that the post-menopausal use of Hormonal therapy has effects on relationship between obesity and breast cancer with the understanding that Hormonal therapy obscurers the hazardous effects of obesity over the carcinoma of the breast particularly in relation to their effects on circulating hormonal levels.

## Conclusion

After analyzing the results of this study it concludes that grade 2 is the most common grade of breast cancer in obese women followed by stage 3 and stage 1 respectively. So we recommend that there must be public awareness programs on national and regional levels to create awareness among public regarding the association of obesity with breast cancers and to also maintain a healthy life style. This will also help the treating clinicians to counsel the patients regarding the risks of obesity with breast cancer and how to reduce morbidity and mortality associated with it.

**Conflict of Interest** *None*

**Funding Source** *None*

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**MA:** Conceptualization of Project
**MA:** Data Collection
**AHJ:** Literature Search
**HK:** Statistical Analysis
**UHQ:** Drafting, Revision
**UHQ:** Writing of Manuscript

# Perceived Barriers to Covid Testing

**Hina Ahmed,[1] Fatima Aqeel,[2] Jahanzeb Akhtar,[3] Faiza Ashraf,[4] Irsa ul Rehman,[5] Hamza bin Ashraf[6]**

**Abstract**

**Objective:** To determine the perception of medical students regarding the barrier toward Covid testing.

**Method:** It was a cross-sectional study enrolling 428 medical students (1st - 4th-year MBBS) through convenient sampling. After formal IRB approval, data was collected through google forms through WhatsApp groups from willing students. The data was compiled and analyzed by using SPSS software 26. The Chi-square test was applied to determine the relationship between the variables by keeping the study power at 80%.

**Results.** Out of 428 respondents, 301(70.3%) were females. The mean age of the participants was 21+3years. Out of all the participants, 127(29.7%) had a suspicion of covid, while 237(55.4%) had flu-like symptoms, and 122(28.5%) got themselves tested. Painful experience100(35%),37(13%) fear of side effects,207(72%)lack of guidance,135(47%)limited access, and 170(59%) cost were significant barriers toward covid testing. More than 50% agreed that social media's role was ineffective in spreading correct information.

**Conclusion:** The fear of getting a positive result, painful experience, side effects, cost, lack of awareness and access to the covid testing facility, fear of contracting the disease, lack of motivation, and poor role of social media in spreading awareness of covid testing were the significant barriers towards covid testing.

**Keywords:** Covid testing, PCR, fears, barriers.

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## Introduction

The Centers for Disease Control and Prevention (CDC), on Jan 22, 2020, confirmed the first laboratory- case of novel Coronavirus.[1] So far, Coronavirus has affected 175,183,965 people around the globe and claimed 3,777,286 deaths.[1] The number of cases and the death toll is increasing, offered every possible effort is to delay or stop the spread of the pandemic.[2] The importance of detecting cases is essential through the testing for SARS-CoV-2.3 The PCR testing plays a pivotal role in active, asymptomatic cases detection, contact tracing, and knowledge of regional and national infection rates to inform the public health authorities.[1] Samples can be taken through nasal, nasopharyngeal, oral, and oropharyngeal routes. Its diagnostic accuracy varies from 32% to 93%depending upon the size and quality of the sample.[4] The first quantitative test for the early diagnosis and detection of SARS-CoV-2 was distributed worldwide in January 2020 by the WHO[1] The PCR testing plays a vital role in the early identification of infected cases and subsequent management of the patients and implementation of mitigation strategies for prevention of the spread of disease.[5] Despite its importance, availability, and efficacy, the general public has observed resistance to getting tested.[6] Pakistan's government also provides PCR testing facilities at multiple governments and private health facilities.[7] The only difference at these facilities is that the govern-

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ment setting is doing free-of-cost testing while the private is charging at a cost that is beyond the reach of an ordinary man.[7] It is a common observation that affording people are going for private testing after exposure as they do not want to face the hassle of government settings.[8] While it comes to the commoner, they will not go for testing but instead will be in denial of getting the infection. A possible reason for the spread of the disease.[7] In a country like Pakistan, where the literacy rate is 59% and monthly wage of an unskilled worker is less than Rs 15,000.,[9] It is unrealistic to expect that people will be going for Covid testing when exposed.

Moreover, several misconceptions and myths make people hesitant about taking these tests.[10] In some areas of Pakistan like other countries, COVID-19 is not accepted as a disease. Instead taken as "a government conspiracy". Most people are unaware of public and private institutes where PCR testing is available in different cities.[11] Furthermore, tests done in government sector laboratories are considered unreliable. Some people are simply afraid of testing positive as a stigma. In contrast, others are afraid of the procedure of PCR.[12] Moreover similar trend seems prevalent in developing countries even though they have well-developed health systems. Many people are unaware of the importance of PCR testing in controlling the spread of this disease.[12] So, the rationale of this study is to determine the perception of the medical student regarding the barrier to covid testing. The study results will help fill the knowledge gaps and identify the areas that need behavior change through health education.

## Material and Methods

It was a cross-sectional study enrolling 1st-4th year MBBS students of Central Park Medical College. The study was completed in 6 months duration. Through a convenient sampling technique, data collection was done. After taking the IRB approval(CPMC/IRB-No/1273) and informed consent, MBB S students from 1st -4th year willing to participate in the study were asked to complete a structured questionnaire. However, the 4th-year MBBS student conducting the research project were excluded from the study. Using the WHO sample size calculator to keeping the prevalence at 50%, the calculated sample size was 385 medical students. All medical students fulfilling the inclusion criteria and giving consent were enrolled. The students were asked about their year of discipline and perception of the factors which act as a barrier to Covid testing through a struc-tured questionnaire disseminated to the medical students through a WhatsApp group using an online google proforma. The response time was one week

Once the data was collected, the compiled excel sheet from online google pro forma was transferred to SPSS software version 26 for further analysis. Means and standard deviations were calculated for quantitative variables like age, while frequencies of each variable were calculated. The Chi-square test was applied to determine the relationship between the variables. Data were presented as frequencies tables. The significance level was set at 95% ($p < 0.05$) and the power of the study at 80%.

## Results

Out of 428 respondents, 301(70.3%) were females. The mean age of participants was 21±3years. Out of all, 127 (29.7%) had a suspicion of covid, while 237(55.4%) had flu-like symptoms, and 122(28.5%) got themselves tested (Table -1). More than half feared getting positive after Covid testing(Table-2) (p=0.001). Considering barriers, 100(35%) said it was painful, 37(13%) had a fear of side effects,207(72%) (p=0.000) had a lack of guidance,161(56%)(p=0.037) considered unawareness of the location of the covid testing center, 135(47%) (p= 0.027) said limited access. Fifty percent considered that they might get an infection from the covid center. One hundred and thirty-three

**Table 1:** *Frequency distribution of experience of covid infection and testing*

| Responses | Yes n(%) | No n (%) | Not sure n(%) |
|---|---|---|---|
| Suspicion of Covid infection during the past year | 127(29.7) | 198(46.3) | 103(24.1) |
| Experience of Flue like symptoms during the past year | 237(55.4) | 158(36.9) | 33(7.7) |
| Thought of getting Covid tested | 123(28.7) | 288(66.6) | 17(4) |

(46%) and 170(59%) (p= 0.002) said that the covid test was unreliable and costly (Table-2). Lack of motivation was significantly asso-ciated with not getting themselves tested(Table-2). More than 60% agreed that social media played a nega-tive role in spreading correct information about covid testing(Table-2).

**Table 2:** *Cross Tabulation between the Thought of Getting Tested and different Barriers*

| Variables | Responses | Thought of getting Covid (PCR) tested | | | |
|---|---|---|---|---|---|
| | | No n(%) 288(67) | Not Sure n(%) 17(4) | Yes n(%) 123(29) | p-value |
| **Fear of side effects** | No | 210(73) | 8(47) | 94(76) | 0.000** |
| | Not sure | 41(14) | 7(41) | 6(5) | |
| | Yes | 37(13) | 2(17) | 23(19) | |
| **Lack of motivation** | No | 116(40) | 3(18) | 68(56) | 0.001** |
| | Not sure | 40(14) | 7(41) | 16(13) | |
| | Yes | 132(46) | 7(41) | 39(32) | |
| **Fear of getting positive** | No | 68(24) | 9(53) | 15(12) | 0.001** |
| | Not sure | 35(12) | 2(12) | 12(9.8) | |
| | Yes | 185(64) | 6(35) | 96(79) | |
| **Cost** | No | 88(31) | 8(47) | 30(25) | 0.002** |
| | Not sure | 30(10) | 6(35) | 15(12) | |
| | Yes | 170(59) | 3(18) | 78(63) | |
| **Lack of knowledge of COVID testing Centers** | No | 57(20) | 6(35) | 18(15) | 0.037* |
| | Not sure | 24(8.4) | 4(24) | 14(11) | |
| | Yes | 207(72) | 7(41) | 91(74) | |
| **Limited access to the locations** | No | 105(37) | 3(18) | 49(40) | 0.027* |
| | Not sure | 48(17) | 8(47) | 23(19) | |
| | Yes | 135(47) | 6(35) | 51(42) | |
| **Lack of role of social media** | No | 75(26) | 6(35) | 29(24) | 0.012* |
| | Not sure | 40(14) | 7(41) | 25(20) | |
| | Yes | 173(60) | 4(24) | 69(56) | |
| **Unawareness of the location of Covid centers** | No | 71(25) | 5(29) | 34(28) | 0.103 |
| | Not sure | 56(19) | 7(41.2) | 31(25) | |
| | Yes | 161(56) | 5(29) | 58(47) | |
| **Acquisition of Covid infection from vaccination center** | No | 85(30) | 6(35) | 34(28) | 0.68 |
| | Not sure | 54(19) | 4(24) | 30(24) | |
| | Yes | 149(52) | 7(41) | 59(48) | |
| **Reliability issues** | No | 77(27) | 5(29) | 35(28) | 0.85 |
| | Not sure | 78(27) | 6(35) | 30(25) | |
| | Yes | 133(46) | 6(35) | 58(48) | |
| **Painful experience** | No | 117(41) | 7(41) | 51(42) | 0.28 |
| | Not sure | 71(25) | 7(41) | 24(20) | |
| | Yes | 100(35) | 3(18) | 48(39) | |

Significant results **Highly significant

## Discussion

The research was conducted among the medical students at Central Park Medical College (CPMC) to determine medical students' perceptions regarding the perceived barriers to covid testing. Of the 428 responses, 55.4% thought they experienced flu-like symptoms during the past year. The literature shows that Flu and Covid -19 are highly contagious respiratory infections with similar symptoms.[13] Mostly, people getting the Covid infection develop flu-like symptoms, which lead to confusion about whether to go for Covid PCR testing or not.[13] The results from studies around the globe suggest that only people with good health-seeking behavior can perhaps get themselves tested; this observation is not generalizable.[14] The high false-negative results and general reliability issues have been the leading cause

of making people hesitant to get themselves tested.[12] Furthermore, the casual attitude of public both in developed and underdeveloped countries has been the main reason for the spread of disease.[15] People getting flu-like symptoms acceptability issues exists toward covid infec-tion.[13] Furthermore, the results of the current study showed that only 28.5% of people got themselves tested for COVID 19 when they developed symptoms. The reason for this small percentage might be the lack of awareness. It is worth emphasizing that people from the western world also have the same behavior as depicted in our results. However, they generally have vital scree-ning programs that help in contact tracing.[8] Generally public avoids unnecessary testing due to common ailments.[10] Even in developed countries, people lack cautious behavior towards others at work and in society.[16] Individuals generally perceive that flue usually subsides on its own. They have faulty attributes like eating or drinking, which leads to sore throat or flue. Even if they have Covid infection, they will remain in the phase of denial.[17]

Our participants (35%) believed that the Covid Testing procedure was painful. Many studies suggest that the nasal and oropharyngeal specimens taken for PCR testing are painful procedures. Thorough nasal or oropharyngeal brushing are required to decrease false-negative results.[4] Moreover, the specimen-taking procedure can lead to a less painful experience when explained before-hand and taken by an expert.[18] The results of our study indicate that 13% of respondents feared the side effects of PCR.[10] It is seen in different studies that a semi-skilled or unskilled person taking a PCR specimen can result in side effects ranging from nose bleeding to a cerebrospinal fluid leak.[4] Another documented factor identified is the uncooperative behavior of the patients.[4] In numerous studies, people feared PCR testing due to many misconceptions.[17] Health awareness through different portals should be ensured for the general public regarding the steps of PCR specimen collection.[19] More-over, assurance of proper training of staff involved in specimen collection to avoid such complications.[2]

Another critical barrier in our results was the lack of knowledge regarding the testing center's location in public and private settings. Our results show that more than half of the respondents believe there is a gap in knowledge regarding the availability of covid testing facilities among the general public. The barrier of limited access is one of the major hindrances to getting tested.[20] The cost of PCR testing is one main barrier to getting tested. The government of Pakistan, like many developed countries, has provided free-of-cost Covid testing facilities at some hospitals in major cities of the states.[11] Standing in long queues waiting to get tested in designated facilities is usually discouraged by our people, even if it is free of cost.[11] Moreover, people lack a sense of responsibility in getting tested. Furthermore, another barrier was the fear of getting the infection from the testing laboratories. Globally the fear of getting an infection among people has been aggravated during the pandemic.[1] Statistics have shown that the disease can spread when Standard Operating Procedures (SOPs) are not followed at the testing laboratories and during home sample collection.[14]

Moreover, false-negative results also contributed to lack of motivation to get themselves tested. More than half of our participants thought that PCR testing was a costly procedure. The government hospital provides a free-of-cost testing facility but has long waiting hours, while private laboratories charge heavy amounts.[11] Perhaps an individual whose average daily income is less than a dollar will be reluctant to spend money on a screening test. Therefore, getting tested by government laboratories will be the least priority.[9] Therefore, Pakistan's government should provide reliable testing facilities at more centers and regulate the testing charges at private laboratories.[7] It is worth emphasizing here that health awareness should be created among our general public so that they can avail themselves free of cost PCR testing from the designated centers of the government of Pakistan.[7] Moreover, the information provided by social media regarding the importance of covid testing is not effective in minimizing the fears. Perhaps it has been instrumental in creating false information and fears among the general public.[12] Social media should play a pivotal role in removing myths regarding covid testing19.[19,20] In this way sense of responsibility can be created among the general public that it is their responsibility to get themselves tested to curtail the spread of infection.[20]

## Conclusion

The fear of getting a positive result, painful experience, side effects, cost, lack of awareness and access to the covid testing facility, fear of contracting the disease, lack of motivation, and poor role of social media in spreading awareness the covid testing were the significant barriers towards covid testing.

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## Authors Contribution

**HA:** Conceptualization of Project
**HA, FA, JA, HA:** Data Collection
**HA, JA, HA:** Literature Search
**FA,JA:** Statistical Analysis
**FA, HA:** Drafting, Revision
**HA:** Writing of Manuscript

# Histological Effects of Ajwa on Oviduct after Nicotine Induced Toxicity in Adult Albino Rats

**Faeza Rauf,[1] Muhammad Suhail,[2] Aleena Sohail,[3] Tayyaba Muzaffar,[2] Shagufta Nasreen,[4] Attya Zaheer[5]**


## Abstract

**Introduction:** Nicotine changes histology of uterine tube and Ajwa stops nicotine from causing toxicity.

**Objectives:** To study the damages produced by nicotine in the oviduct of adult female albino rats and its protection by Ajwa fruit extract.

**Methods:** Three equal groups of 30 rats were made and maintained in the animal house of Punjab Postgraduate Medical Institute, Lahore. The control group A received no treatment except distilled water while among the two treated groups, group B received intraperitoneal nicotine injection (0.1 mg/kg body weight) for 28 days. The rats of group C were given 1000mg/kg body weight Ajwa fruit extract by gastric intubation plus 0.1mg/kg body weight intraperitoneal nicotine injection for 28 days.

**Results:** In nicotine treated rats of group B, mucosa of the fallopian tubes showed flattening of infoldings along with inflammatory cells and degenerated epithelial cells. Fibrosis and blood vessel congestion was present in serosa. Near normal restoration of oviduct structure was seen with Ajwa plus nicotine treated group C.

**Conclusion:** Nicotine can cause reversible injury to fallopian tubes and Ajwa improves oviduct histology, so it may be beneficial to recover sterility or subfertility caused by nicotine in women.


**Keywords:** Nicotine, Phoenix dactylifera, vascular congestion.

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## Introduction

Nicotine is present in many plants of family Solanaceae. Nicotine arrives in the human body as a part of tobacco smoke. 7 to 22 mg of nicotine is present in a cigarette.[1] In the United States, 35% men and 30% women of reproductive age are cigarette smokers.[2] In a national report in united states, 24.2% women left smoking before becoming pregnant, 11% of women smoked in the 3 months before pregnancy and 75.8% of these women smoked during pregnancy.[2]

Extensive destructive effects of nicotine on fertility are recognizable. Moreover, there are notable damaging effects from passive/side-stream smoking. Female smokers withstand a four time greater threat of ectopic pregnancy than nonsmokers, and this connection is independent of other causative factors.[3] Female who smoked more than 20 cigarettes daily had an odd ratio (OR) of 3.5 for ectopic pregnancy relative to nonsmokers.[4]

Nicotine acts on nicotinic cholinergic receptors to ease neurotransmitter release (dopamine and others), producing happiness, excitement, mood adjustment. α4β2 receptor, predominant in human brain, mediates nicotine dependence.[5]

Nicotine causes degeneration of ovary and endometrium.[6] Smoking disrupts transport of the, sperm for

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fertilization, reproduction and embedding.[7] Nicotine administration affects sperm count and motility, reduces the spermatogenic cell line and causes anomalies of the sperm head.[8] A decrease in ciliary beat frequency is noted upon introduction of smoke solutions in hamster infundibulum, which is revocable upon washout of the smoke solution.[9] In rabbit, smoke inhalation affect electrical activity of oviduct.[10] Smoke inhalation momentarily effect patency of human Fallopian tube.[11]

Antioxidant property of the date palm increases reproductive function and fertility. Male flowers of Phoenix dactylifera L or date palm pollen can produce a suitable condition for oogenesis and maintain effective fecundity in female mice and is a useful nutraceutical for potentiation of fertility.[12] Gonad stimulating potency of Date palm pollen (DPP) have already confirmed by Egyptian scientists. Date palm pollen suspension contains cholesterol, carotenoids, rutin and estrone which increase FSH and LH and exhibit gonadotrophic activity.[13]

Date extracts raise plasma levels of testosterone and estrogen, diameter of seminiferous tubules, increase sperm count, spermatogenesis and in male rats improve fertility.[14]

## Materials and Methods

Adult female albino rats were maintained at the Animal House of Punjab Postgraduate Medical Institute, Lahore. Rats were given a standard commercial diet, and water. Rats of each group were kept in separate cages. Rats were acclimatized for two weeks prior to experiment. Ajwa fruit extract was prepared by adding 1liter distilled water to coarsely pounded date fruit (3:1). This was kept at 4°C with infrequent stirring.[14]

Group A were given distilled water by gastric intubation in addition to ordinary diet for 28 days. To group B, daily intraperitoneal injection of nicotine was given. To group C, each rat was given nicotine intraperitoneally and Ajwa fruit extract by gastric intubation for 28 days.

All animals were euthanized 48 hour after last dose and uterine tubes were removed, kept for 2 days in 10% neutral buffered formaldehyde solution. 5 µm thick sections of oviduct were cut, stained with Hematoxylin and Eosin and were watched under the light microscope. Comparison was made between group A, B and C. Masson Trichrome stained slides were observed for fibrosis.

Data was analyzed by using SPSS soft-ware package 20. Comparison among groups was performed by using ANOVA (one way). Tukey's test was used where necessary. P-value ≤0.05 was considered significant.

## Results

In group A, the oviduct showed folded mucosa each lined by ciliated columnar and non-ciliated secretory cells, surrounded by definite thick muscularis mucosae and serosa. (Fig. 1 & 2) All 10 animals of group B showed flattening of mucosal folds. Abundant degenerated epithelial cells and Inflammatory cells were present in mucosa, muscularis and serosa. Interstitial edema was seen with blood vessel congestion, and fibrosis in serosa (Fig.1 & 2, Table 1 & 2). In group C, flattening of mucosal folds was present in 2 rats, degenerated epithelial cells, inflammatory cells infiltrate and interstitial edema reduced in outer layers. (Fig. 1 & 2)

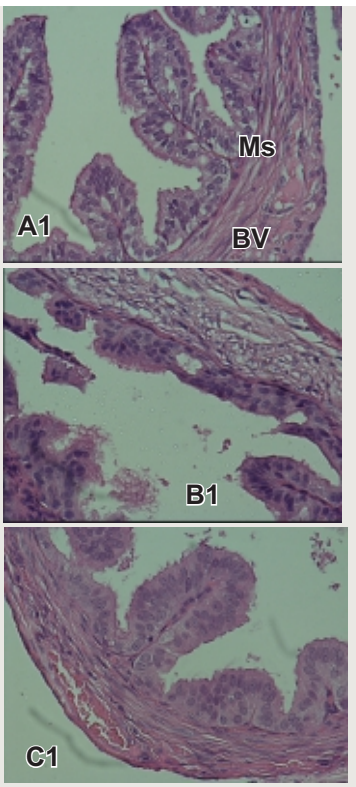


**Figure 1:** *Photomicrograph A1 of ampulla of oviduct of albino rat of control group A, showing well developed mucosal folds lined by ciliated and nonciliated columnar epithelium, muscularis (Ms) and serosa (S) with blood vessel in interstitial tissue. Photograph B1 shows decreased mucosal fold composed of less columnar cells with few cilia and more basal cells, edema and fibrosis (F) in serosa. In photomicrograph C1, folds are near normal with ciliated and nonciliated columnar epithelium, muscularis (Ms) and serosa (S) with congested blood vessels (CBV) in interstitial tissue. (10X, H & E)*

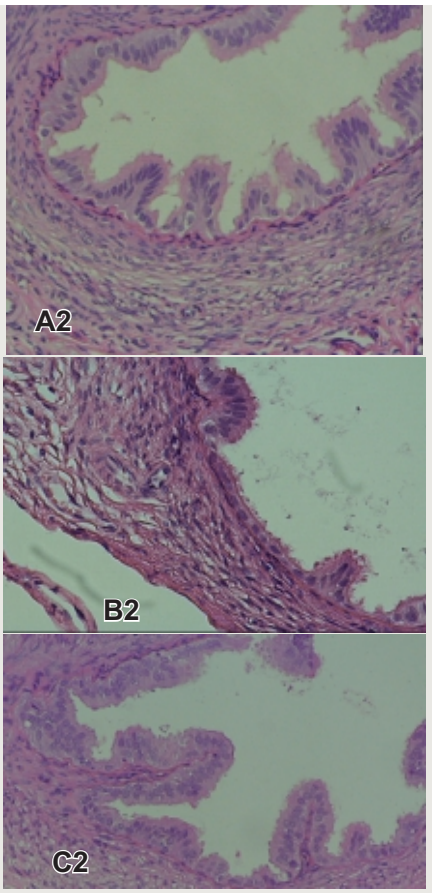


**Figure 2.** *A photomicrograph of isthmus of oviduct A2 of group A, showing well developed mucosal folds lined by ciliated and nonciliated columnar epithelium. A photomicrograph of isthmus of fallopian tube B2 of group B, long black arrow showing more basal cuboidal cells and less no of columnar cells and straightening of mucosal folds. A photomicrograph of isthmus of fallopian tube C2 of group C, showing well developed mucosal folds lined by ciliated and nonciliated columnar epithelium near to control group. (40X, H & E)*

## Discussion

In control group, tall mucosal folds, distinct muscularis mucosae and a thin serosa covered by mesothelium was present. Oviducts of rats of group B showed flattening of mucosal folds and inflammatory cell infiltration extended to the muscular and serosal layers. Degenerated epithelial cells were abundant. Edema was also present with blood vessel congestion and fibrosis in serosa. Increase in the formation of new collagen fibers dominate when recurrent injury occurs, and degradation of the already formed fibers decrease. Fibrosis occurs due to imbalance between fibrogenesis and fibrolysis. Inflammation and edema as effect of smoking on oviduct were also noted by Raieni[15] and there was no decrease in either the ciliated cells or the cilia.

Results of present study are partly in agreement with study performed by Morsy[16] on the fallopian tubes treated with methotrexate. Morsy noted blending and decline

**Table 1:** *Distribution of Congestion of Blood Vessels among groups*

| | Ampulla | | | | Isthmus | | | |
|---|---|---|---|---|---|---|---|---|
| **Congestion of Blood Vessels** | **Group A n (%)** | **Group B n (%)** | **Group C n (%)** | **P value** | **Group A n (%)** | **Group B n (%)** | **Group C n (%)** | **P value** |
| **Absent** | 9 (90.0%) | 0 (0.0%) | 5 (50.0%) | .000** | 10(100.0%) | 0 (0.0%) | 6(60.0%) | .000** |
| **Present** | 1 (10.0%) | 10 (100.0%) | 5 (50.0%) | .000** | 0 (0.0%) | 10 (100.0%) | 4(40.0%) | .000** |

**Table 2:** *Distribution of Fibrosis among groups*

| | Ampulla | | | | Isthmus | | | |
|---|---|---|---|---|---|---|---|---|
| **Fibrosis** | **Group A n (%)** | **Group B n (%)** | **Group C n (%)** | **P value** | **Group A n (%)** | **Group B n (%)** | **Group C n (%)** | **P value** |
| **Absent** | 10 (100.0%) | 0 (0.0%) | 6 (60.0%) | .000** | 10 (100.0%) | 0 (0.0%) | 5 (50.0%) | .000** |
| **Present** | 0 (0.0%) | 10(100.0%) | 4 (40.0%) | .000** | 0 (0.0%) | 10 (100.0%) | 5 (50.0%) | .000** |

**Table 3:** *Distribution of Inflammatory cell infiltrate among groups*

| | Ampulla | | | | Isthmus | | | |
|---|---|---|---|---|---|---|---|---|
| **Inflammatory cell infiltrate** | **Group A n (%)** | **Group B n (%)** | **Group C n (%)** | **P value** | **Group A n (%)** | **Group B n (%)** | **Group C n (%)** | **P value** |
| **Absent** | 10 (100.0%) | 0 (0.0%) | 3 (30.0%) | .000** | 10 (100.0%) | 0 (0.0%) | 5 (50.0%) | .000** |
| **Present** | 0 (0.0%) | 10 (100.0%) | 7 (70.0%) | .000** | 0 (0.0%) | 10 (100.0%) | 5 (50.0%) | .000** |

in number of mucosal folds, inflammatory cells in mucosa and serosa, interstitial edema and blood vessel congestion in serosa. Eweka[17] noted disruption of the basement membrane, hemolysis in connective tissue cells, vacuolations and hypertrophied columnar epithelium in monosodium glutamate treated fallopian tubes.

Similarly, Sodium Fluoride treated oviduct showed some mononuclear cells infiltration, blood vessel congestion in an experiment by El-abd.[18] Similar results were noticed by Ghaly[19] where nicotine caused dilated and congested portal veins, degenerated hepatocytes and periportal inflammatory infiltration of mononuclear cells mainly lymphocytes. Increased prostaglandin synthesis due to nicotine toxicity caused dilated blood vessels by relaxation of smooth muscle and through releasing other vasodilator substances in blood.[20] The presence of infiltrating lymphocytes might be explained as a defense reaction in response to the nicotine toxicity.[21]

In 8 rats of group C, near normal mucosal folding, degenerated cells and inflammatory cells were less in number, thickened muscularis layer and blood vessel congestion was seen which was in agreement with the findings of Morsy[16] on oviduct when low dose methotrexate was given for longer period of time. Infiltration of inflammatory cells played a role in the reversible changes. Sodium fluoride decreased fibrosis in serosa in a study by El-abd.[18] Ajwa date extract (ADE) in combination with CCL422 decreased the area occupied by collagenous fibers. Similar results were noticed by Wahdan[23] when monosodium glutamate induced degenerative changes in oviduct were treated with vitamin C. Findings of Ali[14] were also in agreement with above study where ochratoxin induced tubular damage was improved by Date fruit extract. Date stands as a useful food component and aqueous extract of date fruit causes inhibition of superoxide and hydroxyl radicals.[24]

The present study highlights the awareness to change towards the use of natural food and declares the protective potentials of the aqueous extract of Ajwa fruit on oviduct damaged by nicotine in rats. Active and passive smokers of reproductive age should be made aware of the possible hazards in smoking and how smoking could disturb their reproductive ability.

## Conclusion

In smoking women nicotine present in cigarettes either change structure or purpose of epithelial cells in the fallopian tube, which can result in infertility, ectopic pregnancy or spontaneous abortion. Ajwa fruit extract normalized the damaged fallopian tube and can be used as a beneficial remedy to treat reproductive disorders.

**Conflict of Interest** *None*

**Funding Source** *None*

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## Authors Contribution

**FF:** Conceptualization of Project
**MS:** Data Collection
**SN:** Literature Search
**TM:** Statistical Analysis
**AZ:** Drafting, Revision
**AS:** Writing of Manuscript

# Association of Students Self-Efficacy Scores with Academic Performance in Health Care Students

**Emaan Ahsin,[1] Sadia Ahsin,[2] Hira Ashraf,[3] Madiha Imran[4]**

**Abstract**

**Objective:** To record self - efficacy scores of first year MBBS and BDS students using Student Self -Efficacy Scale & to identify association between self-efficacy scores and academic performance of first year MBBS and BDS students in their first block/term exam.

**Method:** This cross sectional study was carried out at Foundation University School of Health Sciences, after ethical approval using non-probability convenience sampling. First year MBBS and BDS students (n= 200) were asked to respond on a validated 10 item SSE scale. Students' Physiology performance in exam was grouped as 1) High 75% and above, 2) Average 50-74%, 3) Low below 50%. The SSE scores were labeled as 1) High above 30, 2) Average 20-29 and 3) Low below 20. SPSS 21 was used for calculating descriptive statistics and correlation.

**Result:** Data of 178 received responses on SSE scale and term exam scores showed students falling in High SSE scores were 42.1 % (n=75), average 49.4 % (n=88) and low 8.4 % (n=15). Total High performers were 26.9 % (n=48), average 57.8 % (n=103) and low 15.1 % (n=27). A significant positive association between SSE and the academic scores (r=0.64, P = 0.00) was found using Pearson Correlation Coefficient.

**Conclusion:** Study indicates that higher the self-efficacy score of the students, the higher their exam scores.

**Keywords:** Students Self-efficacy score, Academic Performance

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## Introduction

Students, especially in their first year of medical school are exposed to high level of stress. Stress can result in poor academic performance, resulting in more stress. However, where some students may need mental and social support, others facing the same level of stress successfully cope and do not become part of the vicious circle.[1] Perhaps, while facing challenging workload, the student performance may not be just dependent on intelligence, teaching or learning techniques, gender, socioeconomic background or daily study hours. Personality profiles of medical students and doctors have been related to their performance outcomes in clinical environment.[2] It has been shown in a literature review carried out by Eva M D where four studies showed that the relationship between personality traits and performance becomes increasingly significant as students' advance through medical training years. In addition to personality variables, researchers also consider personal determinants like ones self-efficacy belief as an indicator of performance.[3] General self-efficacy is the belief in one's competence to cope with a broad range of stressful or challenging demands.[4] The Student Self -Efficacy (SSE) Scale specifically covers four main domains of students' academic challenges, namely academic performance, coping with academic stress, knowledge and skill development and social interaction with faculty. These academic challenges differ from those that other students face in daily life. As an educator, there is a need to understand how

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Acceptance Date: 31-08-2022

to support students meet these challenges[5]. A student reporting higher levels of self-efficacy takes difficult assignments as challenges to overcome, rather than threats to be avoided, which could impose stress on him. Some scholars believe that students with high self-efficacy show superior performance.[6] Current study is planned to comprehend the influence of student self-efficacy on academic performance of students.

## Methods

A cross sectional study was carried out at Foundation University School of Health Sciences after ethical approval using non-probability convenience sampling. The inclusion criteria were a total of 200 students of first year MBBS and BDS. After informed consent, students of first year MBBS and BDS were asked to fill a Student Self-efficacy Scale taken with permission from Rowbotham et al[5]. This scale consisted of 10 items which measured self-efficacy in four main areas namely a) academic performance b) knowledge and skill development c) social interaction d) coping with academic stress. The scale was answered on a four-point response format: (1) not at all true; (2) hardly true; (3) moderately true; (4) exactly true. Hence, score ranging from 10-40; 40 indicated higher student self-efficacy and vice versa. Students physiology first block/term exam scores were grouped as 1) High performance 75% and above, 2)Average performance 50-74%, 3) Low performance below 50%. The student self-efficacy (SSE) was labeled as 1) High SSE for scores above 30, 2) Average SSE for scores between 20-29 and 3) Low SSE for below 20.

## Results

Out of 200 students who were asked to fill the Student's Self-Efficacy (SSE) scale, 178 filled it in the given time. The collected data was entered in SPSS 21. Pearson correlation was computed to evaluate the association between self-efficacy score and academic performance of the MBBS and BDS students (Table I).

**Table 1:** *Association between Self-Efficacy Score and Exam Scores of the Students (n=178)*

| Pearson's co-efficient | *p- value* |
|---|---|
| 0.64 | 0.00* |
| *p< 0.05 | |

This result reveals highly significant positive relationship between two variables (r=0.64, p=0.00). It indicates that higher the self-efficacy score of the students, the higher their exam scores.

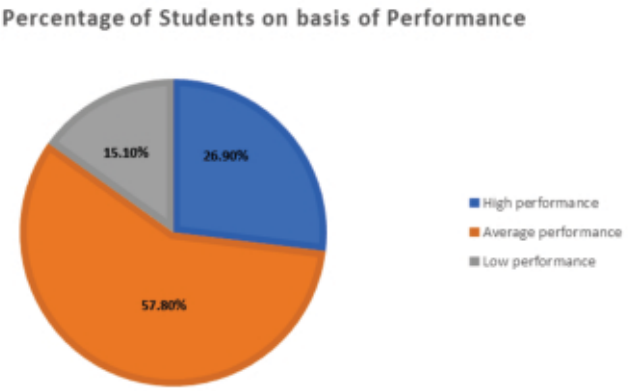


**Fig. 1**

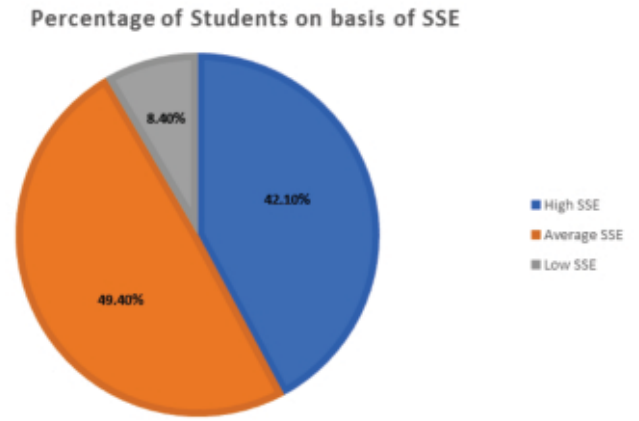


**Fig. 2**

The percentage of students scoring high, average and low results are shown in figure-I

The percentage of students scoring high, average and low SSE are shown in figure-II

## Discussion

The present study explores relationship between self-efficacy and academic achievement among students from first year of MBBS and BDS. Healthcare students starting university often find themselves overwhelmed and experience increased levels of stress and find difficulty managing their time and vast coursework[7,8]. Despite this, there are students who perform better than others. While this may be attributed to other factors, over the years, self-efficacy has been an area of growing interest for educators with increasing research being done on it[9]. A study conducted by Zheng et al compared self-efficacy, self-regulation and academic motivation as

predictors of academic achievement in medical students and showed that only self-efficacy was a direct predictor of students' academic achievements[10]. This may indicate that self-efficacy is more relevant when assessing health-care students which could be due to the fact that health-care students are required to master a certain set of skills and learn to develop rapport with patients[8]. These two factors i.e. skills development and social interaction are a vital facet of self-efficacy[5].

This study revealed that there was a positive correlation between the academic scores of high achievers and their self-efficacy scores. This indicates that students who have higher self-efficacy are more likely to score better in in examinations. These results are in agreement with the findings in similar studies conducted at various education levels[10-12]. However, these studies vary in methodology and target population. For example, a study on self-efficacy in Tehran[7] focused on research self-efficacy in post graduate students. Our study is specifically focused on first year medical and dental students because these students have freshly graduated from high school and have thus made the drastic transition from school to university life. This change of environment, institution, and increased workload can be a cause of significant stress and poor overall health[7,13,14]. In fact, literature indicates that there is higher levels of stress amongst first year students[15]. Furthermore these factors have found to be what students perceive to be the cause of academic failure, specifically in preclinical years[14]. In contrast there are some students who perform exceptionally despite these changes. Present study may indicate that self-efficacy levels in students is a significant factor which can aid in overcoming these challenges which hinder better academic performance.

It is important to note that while some studies do have findings in favor of self-efficacy and academic performances, there are studies which contradict this[16]. In study conducted by Wu et al[16], there was no significant relationship between self-efficacy scores and academic performance. Instead, it was intrinsic motivation which independently affected academic results. This brings into question whether improving self-efficacy is an effective intervention. Furthermore, a review on the self-efficacy beliefs of health sciences students conducted by Klassen et al showed that 46% of the articles reviewed were not in accordance with the guidelines derived from self-efficacy theory[9]. This may imply that the relationship between self-efficacy and academics still needs to be further researched and that the impact of self-efficacy on students may be worth expanding on.

While the information provided in this study is valuable, like all studies, it has its limitations. To further research the association between self-efficacy and academics, the study may be repeated with a larger sample size and by comparing results of more than one subject. Moreover, the self-efficacy scores and results can be evaluated again in the same students after providing counselling and employing methods to improve self-efficacy for a fixed duration of time.

## Conclusion

Present study revealed a positive correlation between high self-efficacy scores and high academic scores in first year MBBS and BDS students. This indicates that increasing self-efficacy in students may show an improvement in their academic results.

**Conflict of Interest** *None*

**Funding Source** *None*

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## Authors Contribution

**EA:** Conceptualization of Project

**SA, HA:** Data Collection

**EA:** Literature Search

**HA, MI:** Statistical Analysis

**HA, MI:** Drafting, Revision

**EA:** Writing of Manuscript

# Efficacy of Combination Therapy Sofosbuvir Plus Velpatasvir in Treatment of HCV

**Shahzad Latif,[1] Wafa Qaisar,[2] Hafiza Qaria Bushra Saleem,[3] Tariq Waseem,[4] Zartasha Hanan Khan[5]**

**Abstract**

**Objective:** To assess the treatment response and tolerance in HCV patients without doing genotypes.

**Method:** An interventional study was conducted to evaluate the efficacy and sustained virologic response (SVR) of 200 patients suffering with hepatitis C after an intervention of once-daily Sofosbuvir 400 mg plus Velpatasvir 100 mg for 12 weeks at Akhtar Saeed Trust hospital and Farooq Hospital Lahore between December 2019 to December 2021.The sample size was calculated by using keeping margin of error at 5%, confidence level at 95%, population size 20000 and response rate at 30%. Patients were followed up on weekly basis with CBC, LFTS and RFTS and HCV RNA by PCR at 4th week and six months after completion of 12 weeks treatment. With SPSS 23, Chi square test was applied and p-value of < 0.05 was considered significant.

**Results:** In this interventional study out of 200 hepatitis C positive patients 139(63.5%) were males and 61(27.9%) were females. A significant association was observed between gender (p=0.000), presenting complaints (p =0.002) abdominal ultrasound findings (0.004), status of patient (p=0.015), comorbidities (p= 0.042) and lab investigations (p=0.000). Various side effects were reported by 69(31.5%) experienced headaches, 60(27.4%) experienced dyspepsia, 57(26%) experienced nausea as a result of this combination therapy.

**Conclusion:** Twelve weeks of treatment with combination therapy of sofosbuvir and Velpstasvir is well tolerated and has high SVR in HCV patients with all types of genotypes.

**Keywords:** Combination therapy, Efficacy, Hepatitis C

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## Introduction

The hepatitis C virus (HCV), a single-stranded RNA virus of the family Flaviviridae with six major genotypes, infects more than 200 million people worldwide, representing more than 3% of the world's population.[1,2] According to the World Health Organization (WHO) estimates, Southeast Asia has considered a high-risk region for HCV with a prevalence of 2.15%[3] Chronic HCV infection causes progressive liver fibrosis, which can lead to cirrhosis, hepatic decompensation, and hepatocellular carcinoma.[4] As many as half a million people die annually from liver disease associated with chronic HCV infection.[5] HCV prevalence is highest in Egypt at more than 10% of the general population and China has the most people with HCV (29.8 million) and the ongoing transmission appears to be widespread, occurring in both healthcare and community settings.[6] Understanding HCV epidemiology in Pakistan is critical in developing and targeting cost-effective prevention and treatment interventions against HCV, in order to meet the global target of HCV elimination.[7] Pakistan

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is enduring an HCV epidemic of historical proportions as one in every 20 Pakistanis has been already infected with this infection playing a major role in the liver disease burden in this country.[8] Since 2014, the United States Food and Drug Administration (FDA) has approved a new wave of direct-acting antiviral (DAA) oral medications that has revolutionized the landscape for hepatitis C virus (HCV) treatment as this therapy is more effective, easier to tolerate, and significantly shorter in duration.[9] In addition, the newer DAA-based therapies are highly effective in traditionally more difficult-to-treat patients, including those with cirrhosis, HIV co-infection, renal failure, or prior HCV treatment experience.[10]

The development of a ribavirin-free single-tablet regimen of short duration that is effective in a broad range of patients with HCV infection would simplify clinical decision-making and reduce the need for pretreatment testing and monitoring during therapy.[11]

Sofosbuvir is a nucleotide analogue inhibitor of the HCV NS5B polymerase approved for the treatment of HCV in combination with Velpatasvir is a new pan-genotypic HCV NS5A inhibitor with antiviral activity against HCV replicons in genotypes 1 through 6.[12] Patients being treated with the combination therapy should be monitored and assessed for compliance with therapy and adverse effects.[13] HCV is one of the most common chronic infections in Pakistan and a major burden on the healthcare system. Measures should be taken at the national level to identify its actual burden and to control factors responsible for its spread. This study is aimed to find out the efficacy of combination therapy Sofosbuvir plus Velpatasvir in the treatment of HCV in Pakistan.

## Materials and Methods

An interventional study was planned to evaluate the efficacy and sustained virologic response (SVR) of patients suffering with hepatitis C after an intervention of once-daily Sofosbuvir 400 mg plus Velpatasvir 100 mg for 12 weeks at Akhtar Saeed Trust hospital EME Society and Farooq Hospital west-wood branch Lahore. It was conducted between December 2019 to December 2021.

A sample of 200 patients suffering from Hepatitis C was recruited in the study. It included both previously treated and untreated patients, infected with HCV genotype 1, 2, 4, 5, or 6, including those with compensated and decompensated liver cirrhosis. The sample size was calculated by using Raosoft online sample size calculator keeping margin of error at 5%, confidence level at 95%, population size 20000 and response rate at 30%. All those patients who were HCV positive by PCR between age of 18-75 years were included in sample. It included all patients who were newly diagnosed, relapsed, non-responders, treatment left, with compensated or decompensated liver disease. All those patients who were at End stage liver disease, End stage Hepatitis C Cirrhosis, diagnosed with hepatitis other than hepatitis C, had acute Psychiatric illness, end stage kidney disease and Tuberculosis were excluded. All those patients who showed Hypersensitivity for Sofosbuvir & Velpatasvir were also removed from interventional trial. Those who did not give consent to participate in trial or to share their data were also excluded. After recruitment of patients who gave written consent for trial, they were treated and then were followed up for 6 months. This follow up was done on weekly basis with CBC, LFTS and RFTS and HCV RNA by PCR at 4th week and six months after completion of 12 weeks treatment.

## Results

In this current study, 200 patients after screening for HCV positive by PCR without doing genotyping were included as open-labeled after written and informed consent, only one patient due to raised s. creatinine was excluded from the safety analysis and so left follow-up. The Bivariate analysis of PCR at 24 week (in Table: 1) showed significant association of gender (p=0.000), presenting complaints (p =0.002) abdominal ultrasound findings (0.004), status of patient (p=0.015), comorbidities (p= 0.042) and lab investigations (p=0.000).

Out of 200 patients, 69(31.5%) experienced headaches, 60(27.4%) experienced dyspepsia, 57(26%) experienced nausea. 14 (6.4%) complained of insomnia after soughing treatment.

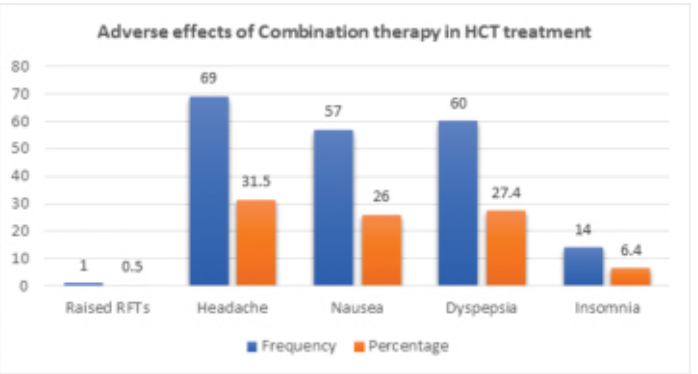


**Fig: 1** *Shows the side effects of Sofosbuvir plus Velpatasvir in Treatment of HCV*

**Table 1:** *Cross tab at PCR 24 weeks:*

| Variables | Frequency (n) | Percentage (%) | p-value |
|---|---|---|---|
| **Gender** | | | |
| Male | 139 | 63.5 | 0.000* |
| Female | 61 | 27.9 | |
| Presenting complaints | | | |
| HCV positive | 120 | 70 | 0.002* |
| Lethargy | 47 | 18 | |
| Weakness | 33 | 11.5 | |
| Ultrasound Abdomen findings | | | |
| Normal | 145 | 20.7 | 0.004* |
| Liver cirrhosis | 51 | 28.7 | |
| Hepatocellular carcinoma | 4 | 44.5 | |
| Status of patients | | | |
| Non- cirrhotic | 156 | 71.2 | 0.000* |
| Cirrhotic | 24 | 11 | |
| Relapse | 14 | 6.4 | |
| **Left treatment** | 6 | 2.7 | |
| **Comorbidities** | | | |
| **Diabetes Mellitis(DM)** | 21 | 9.6 | 0.001* |
| **Hypertension (HTN)** | 20 | 9.1 | |
| **Both DM and HTN** | 19 | 8.7 | |
| **IHD** | 2 | 0.9 | |
| **No comorbidity** | 139 | 63.5 | |
| **Hemoglobin** | | | |
| **Less than 10** | 25 | 12.5 | 0.000* |
| **10-13** | 147 | 73.5 | |
| **More than 13** | 28 | 14 | |
| **Platelets** | | | |
| **Less than 50** | 8 | 4 | 0.000* |
| **50-100** | 34 | 17 | |
| **100-150** | 23 | 11.5 | |
| **More than 150** | 135 | 67.5 | |
| **Bilirubin** | | | |
| **Normal** | 200 | 100 | 0.000* |
| **raised** | 0 | 0 | |
| **Albumin** | | | |
| **less than 2** | 13 | 6.5 | 0.000* |
| **2-3** | 49 | 24.5 | |
| **More than 3** | 138 | 69 | |
| **Left treatment** | | | |
| **yes** | 3 | 1.5 | 0.901 |
| **no** | 197 | 98.5 | |

## Discussion

HCV infection can lead to liver cirrhosis, hepatocellular carcinoma, and death. In this therapeutic interventional study, conducted on hepatitis C-positive patients, the combination therapy of sofosbuvir and velpatasvir was found effective and safe with no major adverse effects.

In this study, the percentage of the male and female population is 63.5% and 27.9% while another study conducted in China showed that HCV positive rates in males and females were 51.66% and 35.93%, respectively.[14] The ultrasound findings in this study reveal that 28.7% of patients developed liver cirrhosis and 44.5% developed hepatocellular carcinoma while another study conducted in Bangkok, Thailand showed that 40% of patients developed cirrhosis and the prevalence of hepatocellular carcinoma is 57% in Northern America.[15,16] The main comorbidities, found in this trial, were hypertension (9.1%) and diabetes mellitus (9.6%) while another study conducted in Brazil reported arterial hypertension in 30.4%, and diabetes mellitus in (24.6%) patients.[17]

Serum albumin and platelet count with (p-value <0.01) were observed in this study, similarly, in a Japanese study, the serum albumin and platelet count were significantly improved with combination therapy of sofosbuvir and velpatasvir (p-value<0.01).[18] In lab investigations, the platelet count ranges from 15-100/µL in 17% of HCV patients whereas a study conducted in Germany showed that 53% of the patients receiving antiviral therapy had platelet counts <90.000/µL.[19]

In the current study, for those who received antiviral therapy, liver function parameters such as serum bilirubin improved significantly in 100% of patients. In contrast, a study conducted in Egypt showed that the majority of patients who received sofosbuvir also showed improvement in bilirubin levels.[20]

In this study, no serious side effects to patients with end-stage renal disease were reported establishing the combination therapy with sofosbuvir and velpatasvir as safe, as well as effective in the management of hepatitis C patients with end-stage renal disease.[21]

In this trial, three patients left treatment while in a prospective open-label interventional trial conducted in Pakistan which investigated the efficacy of sofosbuvir and velpatasvir in hepatitis C patients, only two patients were lost to follow-up.[22]

## Conclusion

Once-daily sofosbuvir plus velpatasvir for 12 weeks provided high rates of sustained virologic response (SVR) among both previously treated and untreated

patients infected with HCV genotypes 1, 2,4, 5, or 6, including those with compensated and decompensated liver cirrhosis.

**Conflict of Interest** *None*

**Funing Source** *None*

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## Authors Contribution

**SL:** Conceptualization of Project
**WQ:** Data Collection
**HQBS:** Literature Search
**ZHK:** Statistical Analysis
**ZHK:** Drafting, Revision
**TW:** Writing of Manuscript

# Angiomatoid Fibrous Histiocytoma: A Rare Cause of Anemia in a Child

**Jawaria Ghazanfar[1], Amna Idrees,[2], Muhammad Ali Sheikh,[3] Muhammad Zaeem Khalid[4], Amna Ikram[5]**

**Abstract**

Angiomatoid fibrous histiocytoma (AFH) is a rare soft tissue tumor of intermediate potential and is usually found during first two decades of life. It is located mainly in extremities presents as a painless, slow growing mass with extensive blood supply. Embryologically, it arises from a pluripotent mesenchymal cell. Histologically, the tumor has thick pseudo capsule with chronic inflammatory infiltrates and hemorrhagic cystic areas. We present a case of AFH which caused severe anemia in a child with a non-healing ulcer on the medial aspect of left knee. Multiple blood transfusions, incision and drainage and biopsies were done however; only complete surgical resection proved to be fruitful. The biopsy is EMA positive, cytokeratin AE1/AE3 & Desmin are focal positive. CD21 highlights meshwork of follicular dendritic cells. Yearly follow up is advised. Angiomatoid Fibrous Histiocytoma should be kept in the differentials while managing hematoma-like lesions in the extremities. It is often misdiagnosed thus prompt treatment is usually delayed. The prognosis after complete surgical resection is good but chemotherapy should be considered in recurrent cases.

**Key words:** Angiomatoid fibrous histiocytoma, AFH, soft tissue tumor, children, Anemia

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## Introduction

Angiomatoid fibrous histiocytoma (AFH) was first described in 1979 by Enzinger, as a malignant form and then was changed to a tumor of intermediate potential. Histologically tumor is seen as a thick pseudo capsule with chronic inflammatory infiltrates and hemorrhagic cystic areas. In 2002, the World health organization (WHO) removed AFH from the malignant fibrous histiocytoma subtype of sarcoma and changed it to the category of tumors of uncertain differentiation as AFH.[1]

Angiomatoid fibrous histiocytoma is a rare, low grade, soft tissue tumor more common in young, usually a slow growing tumor and it rarely metastasizes.[2] Most of the time, it appears as a painless soft tissue mass in the subcutaneous or deep dermal layers of the body.[3]

Clinically and radiologically the tumor can be confused with hematoma or soft tissue hemangioma.[1] It is a unique borderline neoplasm with inert behavior, predominantly arising in the superficial tissues in the extremities.[4] It presents as a mass in subcutaneous region in extremities. The prognosis is generally good, the rate of recurrence is about 15% and the rate of metastasis is less than 1%.[5] Symptoms include anemia, weight loss, fever; pain or tenderness are extremely rare. Embryologically, AFH arises from a pluripotent mesenchymal cell because morphologically it shows vascular, histiocytic, smooth, and striated muscle differentiation. Microscopically, AFH shows solid arrays or nests of histiocyte-like cells, hemorrhagic cyst-like spaces, and aggregates of chronic inflammatory cells. Multifocal recent and old hemorrhages and inflammatory cells are distinctive feature of this tumor. A thick pseudo capsule with germinal centers makes it resemble with a lymph node.[1] Most common treatment option is wide surgical excision and has proven to keep the patient disease free in most of the cases.[5] Chemotherapy has shown significant results in the recurrent cases of AFH.[9]

This case report will present a rare cause of severe anemia

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due to AFH and its various clinical, radiological and histopathological findings along with the definitive treatment that was provided for AFH.

## Case

A 4-year-old male presented to Shaikh Zayed Medical Complex, Lahore in January 2021 through outpatient department with complaint of a non-healing wound on medial side of left knee that was oozing blood for last 4 months. The child was previously taken to a tertiary care hospital in Lahore where incision & drainage was done but the operative findings were not available. After that the patient developed a non- healing wound. Patient was taken to different hospitals and biopsy was taken, that showed a benign ulcer with granulation tissue.

In the meantime, patient continued to ooze blood from the affected area and developed severe anemia for which he received blood transfusion three times over 4 months. Hematologist was consulted as well and the patient was investigated extensively for bleeding disorders but no bleeding disorder was found. There was no history of bleeding disorder in family or patient. No history of weight loss, anorexia or fever. Rest of the history was unremarkable.

On physical examination there was marked pallor, small mobile, left sided inguinal lymph nodes were palpable. Local examination showed a profusely bleeding ulcer about 5×5cm, oval shaped with irregular margins and a granulation tissue pouting out of the floor of ulcer, that bled on touch. (Fig.1)

**Fig 1:** *Ulcer at the Time of Presentation*

Investigations done at the time of admission showed Hemoglobin level of 4g/dl. Bleeding factors, clotting time, bleeding time and rest of the baseline tests were within normal range. Arteriovenous Doppler ultrasound of left leg pointed out a large superficial bleeding wound on medial aspect of left knee joint with underlying cellulitis and mild joint effusion measuring 2.2*1.2*2.5 cm, approximate 34ml. Multiple large left sided inguinal lymph nodes were also mentioned. Short axis diameter was 1cm and showed some necrosis. Rest of the ultrasound was normal.

Excision of the tissue was done under general anesthesia. The lesion was extending up to deep fascia but was superficial to muscles with tendency to bleed. The sample was sent for histopathology. (Fig. 2)

**Fig 2:** *Wound at the time of first debridement containing vascular tissue.*

The biopsy showed benign ulcer with granulation tissue.

On follow up after 15 days, patient had superficial wound infection. However, there was no history of bleeding and he did not require blood transfusion. The wound was cleaned. (Fig. 3)

**Fig 3:** *Infected wound on follow up*

A soft inguinal swelling was noted on left side after

about 22 days of initial resection. On examination the swelling was 2*2cm, non-tender, non-erythematous with overlying skin discoloration. Ultrasound of inguinal swelling revealed enlarged lymph node with increased vascularity. Patient was admitted again for excisional biopsy of inguinal swelling. (Image. 4)

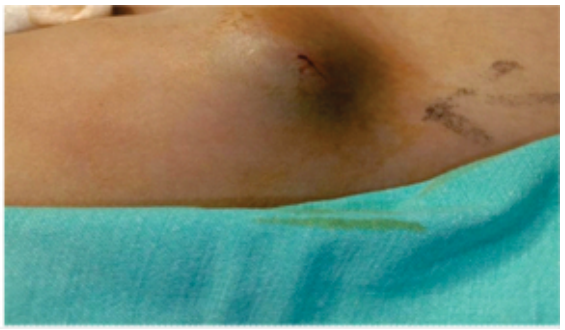

**Fig 4:** *Inguinal swelling*

**Fig 5:** *Intraoperative image showing inguinal swelling*

The inguinal swelling was aspirated before excision and frank blood was drained. Intraoperative findings showed highly vascularized lymph nodes with surrounding vessels. Lymph node was completely excised. Sample was sent for histopathology. EMA, cytokeratin AE1/AE3, Desmin, ASMA, CD34, Myogenin, SALL-4, CD21 stains were done on the specimen. EMA was positive, cytokeratin AE1/AE3 & Desmin were focal positive. CD21 highlighted meshwork of follicular dendritic cells. The final histopathological diagnosis was Angiomatoid fibrous histiocytoma. On three months follow-up the patient was in good health, inguinal swelling had disappeared, primary wound had healed, no blood transfusion was required. Patient was referred for the opinion of the oncologist who advised regular folowup only.

## Discussion

This case report demonstrates a very rare cause of soft tissue mass in the pediatric age group. AFH can easily be confused with hematoma, hemangioma, lipoma, leiomyosarcoma. AFH is a low grade and usually a slow growing tumor, more common in extremities with a good prognosis. AFH is composed of blood or fluid filled cystic spaces.[1] The pathological examination of the lesion may also be confused with metastatic carcinoma or melanoma, regardless of the presence of peculiar morphology.[6] Our case presented with severe repeated anemia due to the blood loss from the lesion and patient also required multiple blood transfusions.

A study carried out in 2011, showed that the rate of recurrence is about 15% and the rate of metastasis is about 1%.[7] In our case the disease involved local inguinal lymph nodes and after complete surgical resection of the primary as well as the inguinal swelling no other lesion was noted. According to a study conducted in 1991, immunohistochemistry demonstrates AFH to be positive for CD 68 and desmin.8 However, recent cytogenic studies have shown WSR1-CREB1 fusion gene reported in many cases.5 In our case, EMA was positive, cyto-keratin AE1/AE3 & Desmin were focal positive. CD21 highlighted meshwork of follicular dendritic cells.

Surgical resection proves to be beneficial in majority of the cases.[1] Most of the studies have shown wide surgical excision as a definitive treatment and patients remained disease free in most of the cases[5]. Our case report demonstrates complete surgical resection alone to be fruitful without chemotherapy and the child was asymptomatic thereafter.

Chemotherapy is not mainly used for the initial disease but has shown significant results in the recurrent cases of AFH along with regional lymph node metastases that occurred after wide local excision of primary lesion.[9]

According to a case reported in 2018 at Texas Children's Cancer Center, Tocilizumab which is an IL-6 receptor inhibitor antibody has shown good response in a child with treatment-refractory metastatic AFH with EWSR1-CREB1 fusion and elevated serum IL-6 as compared to the other chemotherapeutic agents. The disease reappeared after discontinuing tocilizumab for one year. Tocilizumab is generally well tolerated and is a suitable alternative for recurrent or metastatic AFH in comparison

to the conventional chemotherapeutic agents.[10]

A case series of seven cases compiled in Japan reports two out of the total cases to metastasize to distant sites, one of whom died due to these complications.[11] Literature shows AFH to recur in 15% of patients,[12] but metastasize in only less than 1%.[13] Very few of AFH lesions are primarily diagnosed as AFH even after complex imaging such as Magnetic Resonance Imaging (MRI) which shows homogenous hypointense lesions on T1 and hyperintense heterogenous lesions on T2.14 Although some studies have shown a 'double-rim' sign as a classical finding of AFH on MRI.[15] this has not been backed up by other case reports which claimed it to be present just due to the pseudocapsule and the subsequent peritubular edema. Costa et al reported local recurrence being associated with the irregularities in the border of the tumor and metastasis being in direct relation with the depth of the tumor.[15] Morgan et al reported a secondary paraneoplastic platelet function disorder that resulted in bleeding and intractable anemia.[16]

Substantial number of cases have been reported and research work has been done internationally but limited data is available in Pakistan. According to recent literature, the best diagnostic indicator for AFH is the presence of lymphoplasmacytic infiltrate around the tumor,[17] a feature rarely present in other tumors. Although it is also present in gastrointestinal shwannomma.[18] In addition, the location of these tumors is diverse, including but not limited to soft tissues, brain, lung, mediastinum, omentum and bone but most commonly occurring in the deep dermal or the subcuticular layer of extremities in the younger population.[19] It is expected that more locations will be added in the future owing to its diverse immunohistochemistry and pathophysiology. Furthermore, Chen at al from China indicates a high degree of probability of it being misdiagnosed as myofibroblastic tumors, dendritic cell sarcoma or poorly differentiated meningioma.[20] Hence, AFH has a morphological spectrum ranging from granulomas to both benign and malignant neoplasms.[21] extensive research is required to properly define the diagnostic criteria to aid in its better recognition and management.

This case represents the clinical, hematological, radiological and histopathological features of AFH. AFH often tends to be misdiagnosed so inadequate treatment can be provided sometimes by the physicians but the surgeons should keep this tumor in mind while treating any such mass. This case presented as a non-healing wound which bled profusely leading towards severe anemia. The incidental diagnosis made it clear that even the minor non healing wounds should not be taken lightly. As this tumor is of intermediate potential, therefore, yearly follow up and radiological surveillance is advised.

## Conclusion

This case study shows that even the minor non healing wounds should not be taken lightly and unusual causes should always be kept in mind when treating such cases and anemia without any apparent medical cause should be extensively investigated.

**Conflict of interest** *None*

**Funding Source** *None*

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## Authors Contribution

**AI:** Conceptualization of Project
**AI:** Data Collection
**MZK:** Literature Search
**:** Statistical Analysis
**MAS:** Drafting, Revision
**JG:** Writing of Manuscript

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