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## Editorial



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# Teaching During Covid-19

**Prof Majeed Ch.**

## Introduction

The recent outbreak of COVID-19 has enormously affected every aspect of global arrangements with its fast and lethal reach. Originating from Wuhan, a Chinese city, this highly infectious virus has forced to impose nationwide closures in many countries impacting onsite educational systems to shut down. Considering the safety of students and following the steps taken by many infected countries, the Pakistan government initially closed all the educational institutions and later allowed partial opening of schools where 30 -50 % of students were allowed to attend classes in a cyclic manner. The direct and most immediate impact of this decision was an untimely break and loss of learning opportunities for all students. In order to continue with teaching and learning, Higher education commission, developed online tea-ching guidelines with the instructions to resume tea-ching, by following these guidelines. The guidelines included development and implementation of both online and hybrid curricula. Online teaching-learning is based on application of information technology tools to ensure access to learning resources for all students in the absence of face to face classes. It is conducted in the form of asynchronous or synchronous communication where- in asynchronous system tools like e-mail, discussion boards, learning newsgroups are used. For synchro-nous system webcasting, live chat and audio/video technologies are used for real-time class.

Hybrid learning can be defined as a learning approach that combines both remote learning and in-person learning to improve student experience and ensure learning continuity. One of the biggest advantage of both remote learning and later hybrid learning conducted by institutions following Covid-19 pandemic was resumption of educational activities. However, this advantage was associated with many challenges. A few of the cha-llenges are as follows

Difficulties with Student Engagement - One of the main challenge of hybrid learning is the concept of student engagement. Ii is a challenge to keep both the students who are physically present in the classroom and the students who are learning remotely as engaged as each other, in order to deliver an equal learning experience.

Technical Issues - Another possible problem that can lead to disruption of learning experience is the emergence of technical issues. These can take many different forms, but if members of a class or a course do experience difficulties in this area, it can not only disrupt their own learning, but also the learning of other students. Remote learners could have a range of different technical issues, from sound problems or difficulties connecting to a live stream, through to more complex issues with their computers or an inability to use software that is critical to the course. Depending on the severity, such issues can negatively affect the learning experience. Problems Facilitating Collaboration - In traditional classroom settings, learners can be physically placed into groups, but this is not viable when some students are learning remotely or in a hybrid setting thus making course delivery difficult. Challenge to Teachers - Many teachers have a fear of technology and often see a move to hybrid or online learning as a move to replace them as teachers and as a way to diminish the learning experience for students. Student attendance issues – In an online session teacher can never know how focused/attentive a student is during a session. Or even if the student is there even. Assessment issues - Lack of training of teachers to develop reliable and valid assessments and lack of student preparation to use the application correctly.

Monetary issues – online or hybrid learning is dependent on information technology tools. It requires investment in effective and latest IT tools and computers.

***Various Suggestions to Overcome these Issues are;***
Creating a formal faculty development program for teaching hybrid courses. Allocating the necessary time for instructors to redesign traditional courses

into hybrids . Preparing students to learn IT skills so they can learn effectively in hybrid courses. Allocation of funds for upgradation of IT facilitie. Developing effective communication between students and teachers.

The organizers need to make faculty overcoming the idea that blended learning is not as effective as traditional face-to-face learning. Redefining the role of the facilitator. Managing and monitoring participant progress.

In this challenging world both faculty and students have to learn to be conversant with the modern gadgets.

**Prof. Abdul Majeed Ch.**
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Original Article

# Morphological Pattern of Endometrial Biopsy in Women with Clinical Diagnosis of Abnormal Uterine Bleeding

**Nosheen Khurram, Nasim Aslam Ghumman, Noshin Wasim Yusuf**

**Abstract**

**Objectives:** This study was carried out to determine the underlying gynecological pathology with help of morphological pattern of the endometrial histology in women of different age groups with clinical diagnosis of abnormal uterine bleeding.

**Material and Methods:** This is a retrospective study of a series of one hundred and twenty cases of women with presenting complaint of abnormal uterine bleeding. This study was done in the Department of Pathology, Rashid Latif Medical College, in collaboration with Gynecology departments of Arif Memorial Hospital and Hameed Latif Hospital over period of one year. (July2018 to June 2019).

One hundred and twenty cases of endometrial curettage, with clinical impression of abnormal uterine bleeding were analyzed and reported by two histopathologists. Patients with complications of pregnancy were excluded from present study.

**Results:** Histopathological examination of endometrial curetting revealed spectrum of morphology from physiological changes to malignancy. Endometrium with normal cyclical changes were seen in 64 (53.33%) cases, followed by endometrial polyp 18 (15%) cases, endometrial hyperplasia 15 (12.5%), and disordered proliferative of endometrium 10 (8.33%) cases. Malignancy was noticed in 3 (2.5%) cases. Malignancy was diagnosed mostly in the postmenopausal age group.

**Conclusion:** The present study proves that on routine basis endometrial histopathological evaluation is a useful diagnostic measure to determine the underlying cause of abnormal uterine bleeding which ultimately help in accurate treatment.

**Keywords:** Abnormal uterine bleeding, polyp, hyperplasia, disordered proliferation, malignancy

## Introduction

The term abnormal uterine bleeding is related to any irregularity in the menstrual cycle including volume of blood flow, duration, or frequency. An average menstrual cycle is of 24 to 38 days and bleeding lasts 7 to 9 days.[1] Endometrial tissue sampling is not requirement of all women with presenting complaint of AUB but should be done on women who at risk of developing hyperplasia and malignancy. An endometrial biopsy is thought to be the preferred test in women with AUB who are above the age of 45 years. Endometrial biopsy should also be done in women of 45 years of age or even younger with unopposed estrogen exposure, obesity, diagnosed cases of polycystic ovarian syndrome (PCOS), and in cases of treatment failure or persistent bleeding.[2] Internationally, the women of reproductive age group show the prevalence of abnormal uterine bleeding from 3% to 30% of cases, with a higher occurrence at time of menarche and perimenopause. Results of many studies are confined to heavy menstrual bleeding (HMB), but when irregular and intermenstrual bleeding are also incorporated, the prevalence even rises up to 35% or even greater.[3] Overall prognosis of abnormal uterine bleeding is good, but it varies with the underlying pathology. The core purpose of endometrial evaluation and treatment of chronic AUB is to exclude malignancy and to improve the patient's quality of life along with perso-nalized current and future fertility goals. Prognosis also varies and it is established on bases of medical versus surgical treatment. Medical treatment with anti-fibrinolytic and non-steroidal anti-inflammatory

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medicine has shown very good results to reduce blood loss during menstruation.[4] In surgical options dilatation and curettage of the endometrial tissue is extremely helpful to determine various forms of AUB and exclusion of any organic pathology.[5]

## Methods

This is a retrospective study of all cases of endometrial biopsies with clinical impression of abnormal uterine bleeding received during period of one year from July 2018 to June 2019 at Department of pathology, Rashid Latif Medical College, Lahore. Ages of the patients were from 20 to 70 years. Those patients who were either on hormonal therapy, had bleeding due to complications of pregnancy or having cervical pathology were excluded from present study. Endometrial tissue was sampled by dilatation and curettage (D&C). Fixation was done with 10% formalin and sent to pathology laboratory for assessment. The gross morphology was noted, and the total tissue submitted was further processed in automated processor overnight. Paraffin block were prepared, and tissue section (4-6µ) were prepared. The sections were stained with hematoxylin and eosin stain (H&E) and microscopic examination was carried out by the pathologist.[6] The histopathological results by microscopy were noted and causes of AUB were grouped into func-tional and organic reasons. Normal menstrual phases (proliferative and secretory) of the endometrium and other physiological variations in the endometrium related to disturbance in hormonal level (atrophic endometrium and disordered proliferative endomet-rium) were included in functional causes while endo-metrial polyp, chronic endometritis, hyperplasia, and endometrial carcinoma were part of organic causes. Results were calculated by using SPSS 25.

## Results

The age of the patients ranged from 20 to 70 years. Maximum number of patients were in the age group of 41 to 50 years, 45 cases (37%) followed by 31 to 40 years, 38 cases (32 %). Only 14 cases (12%) were above the age of 50 years. Out of 120 cases, 112 (93.33%) were premenopausal whereas 8 (6.66%) were post- menopausal. (Figure 1). The predominant pattern of bleeding was menorr-hagia 44 cases (36.66%) followed by metrorrhagia 38 cases (31.66%), polymenorrhea 30 cases (25%) and post-menopausal bleeding 8 cases (6.66%). (Table 1)Histological examination showed proliferative endo-metrium (Figure 2) as the predominant finding 34 cases (28.33%) followed by secretory endometrium 30 cases (25%), endometrial polyp 18 cases (15%), hyperplasia 15 cases (12.5%), disordered prolifera-tion 10 cases (8.33%), endometritis 6 cases (5%) and atrophic endometrium 4 cases (3.33%). Malignant lesions comprised of 3 (2.5%) of the cases. (Table 2). In women 30 years or under, out of 23 cases, prolife-rative endometrium (47.82%) was main morpholo-gical pattern while in women 31 to 40 years, out of 38 cases secretory endometrium (34.21%) is the fore-most pattern on histopathology. Out of 18 cases of endometrial polyp (Figure 3), 13 cases were found in patients of up to 40 years of age and out of 15 cases of endometrial hyperplasia (Figure 4), 9 cases were between age group of 41 to 50 years. All 3 cases of malignancy (Figure 5) were seen in patients of 60 years of age or above and all of them presented with post-menopausal bleeding. There was statistically significant age difference of females with malignancy as underlying cause of blee-ding from females with Proliferative endometrium (p-value 0.008), Secretory endometrium (p-value 0.009), Polyp (p-value 0.018), Hyperplasia (p-value) and Disordered proliferation (p-value 0.010) whereas age difference of female with malignancy was not statistically significantly different from atrophic endometrium (p-value 0810). This showed that atrophic endometrium and malignancy is the main reason of abnormal uterine bleeding in older women with peri and post-menopausal period of their life.

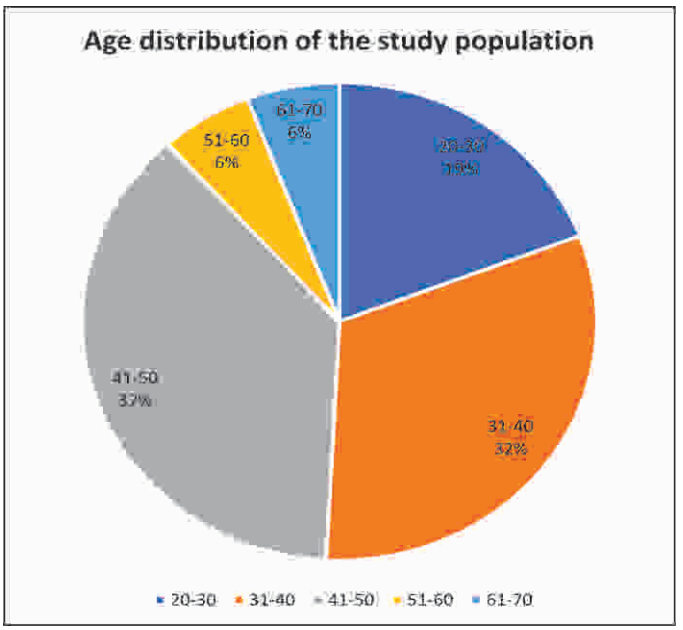



**Figure 1:** *Distribution of Cases According to Various Age Groups*

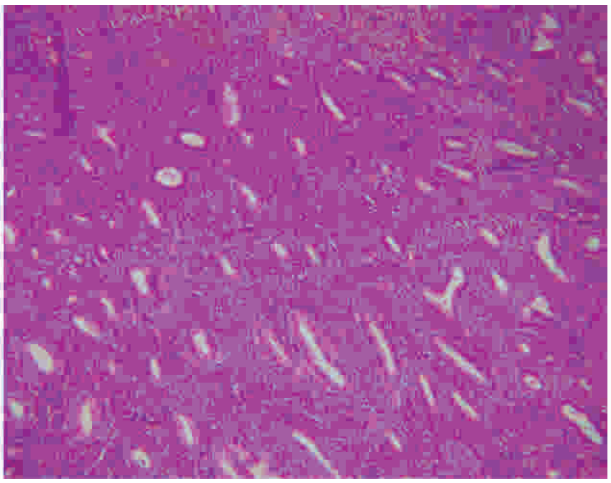


**Figure 2:** *Showing Proliferative Endometrium (H&E,10X)*

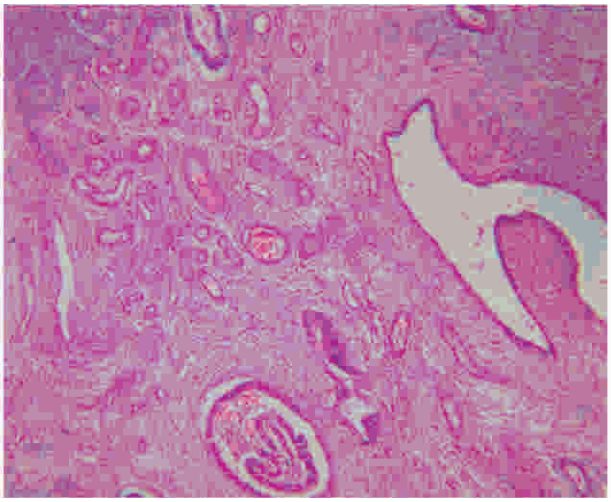


**Figure 3:** *Showing Endometrial Polyp (H&E,10X)*

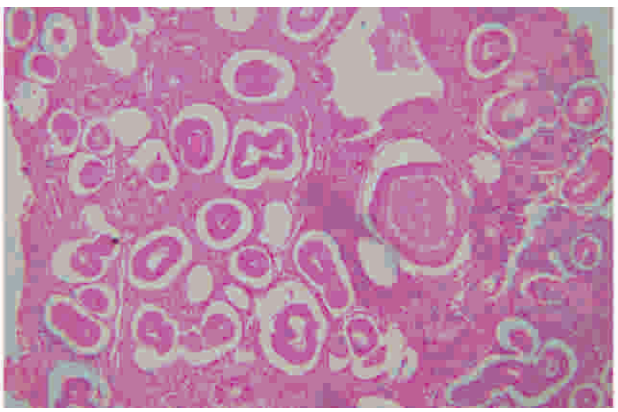


**Figure 4:** *Showing Endometrial Hyperplasia (H&E, 10X)*

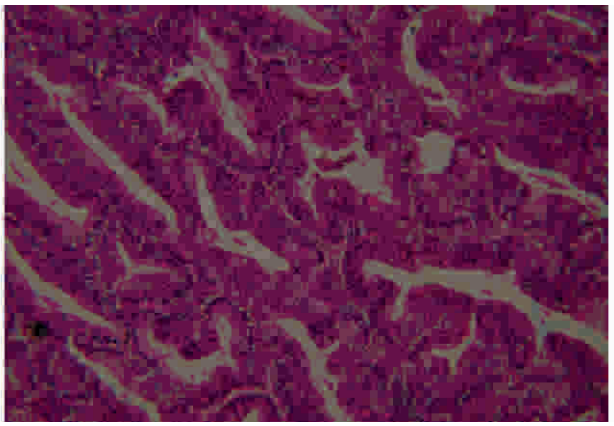


**Figure 5:** *Showing Endometrial Carcinoma (H&E, 10X)*

**Table 1:** *Breakup of Cases According to Presenting Complaint*

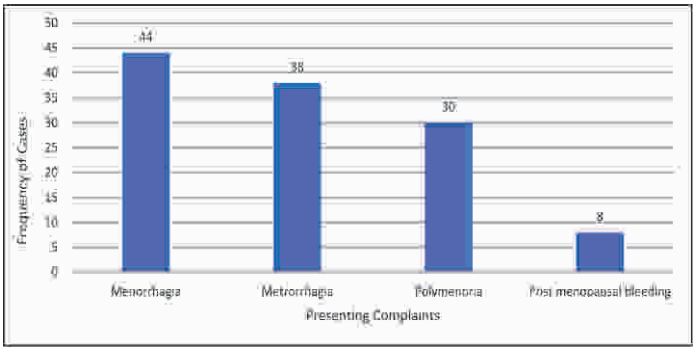
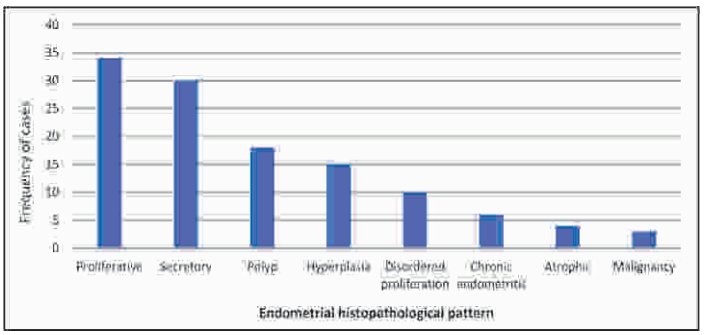



**Table 2:** *Distribution of Cases According to Endometrial Biopsy Findings*




## Discussion

Abnormal uterine bleeding is one of the commonly faced problem in gynecology department of our hospitals. It needs to be treated properly as it intervenes significantly with the quality of life in otherwise healthy women because of troubling symptoms like menorrhagia, metrorrhagia and polymenorrhea[7].

AUB incorporates both dysfunctional uterine bleeding (DUB) and bleeding from operationally treatable causes like endometrial polyps, hyperplasia, fibroids and malignancy. But in most of the cases dysfunctional uterine bleeding is manifestation of

anovulatory- cycle of menstruation.[8]

In present study, the commonly affected age group who presented with abnormal uterine bleeding was 41 to 50 years of age. This observation is comparable with many studies.[7,9,10,11,12,13] An increase in number of cases in this age group reveals that as women reach near their menopause age, the sum of ovarian follicles decreases and gonadotrophic hormone resistance increases which ultimately leads to low level of estrogen which is basic requirement of normal endometrial cycle[7]. Lowest number of patients belonged to age group of 61 to 70 years.

In current study most common presenting complaint was menorrhagia (36.66%). It is compatible with many other studies done worldwide, 51%,[7] 42%,[9] 28%[10] and 55.8%.[14]

Histopathological diagnosis showed wide range of patterns, ranging from physiological to pathological lesions of endometrium. In this study commonest histological pattern seen was proliferative (28.33%) and secretory (25%) phase of endometrium. Many studies showed the presence of predominantly these two patterns.[7,9,12,15] The cause of bleeding in the proliferative phase of endometrium is due to anovulatory cycles while bleeding in secretory phase is due to defect in the process related to regulation of menstrual breakdown of the endometrium.

Endometrial polyp was reported in 15% of cases. Literature showed quiet variability in its incidence. Few studies revealed 9.9%[16] to 17.64%[17] of cases as underlying cause of abnormal uterine bleeding while others showed only 0.6%,[15] 1.24%[12] and 2.46%[11] of the cases. Endometrial polyp was found more common below age of 40 years of age. This finding can be related to excessive use of hormones in this age for management of infertility.[16]

In present study incidence of endometrial hyperplasia (12.5%) was second common underlying pathology and this finding is comparable with another study done in Pakistan (12.6%)[15] and India (10.91%).[12] The possible reason could be that in our part of world most of the patients belong to poor socio-economic status and risk factors like diabetes, obesity and sedentary lifestyle is low. Other studies showed higher incidence, 16%,[7] 16.47%,[17] 18.03%,[11] 22.6%,[9] 26.7%.[10]

Results of cases with disordered proliferation of endometrium (8.3%) and chronic endometritis (5%) are like study done by Bhatta S and Sinha AK, 6.56% each. Endometrial atrophy is a consequence of absence of either exogenous or endogenous estrogen which is necessary for endometrial stimulation that leads to abnormal uterine bleeding whenever there is minor injury to thin atrophic endometrium. In present study atrophic endometrium was seen in 3.33% of cases. Many other studies showed almost same percentage.[10,12,14]

Endometrial biopsy is one of the significant requirements to ensure the presence of malignant and premalignant conditions. In present study incidence of endometrial carcinoma was 2.5%. This finding is almost the same as study done by Vaidya et al; (2.45%)[12]. In other studies, their finding were 0.4%,[15] 1.6%,[7] 3.3%,[10] 4.4%,[13] 5.74%,[11] and 5.88%.[17]

The prevalence of endometrial hyperplasia and endometrial cancer were more commonly present in the perimenopausal and post-menopausal females. Therefore, histopathological assessment of endometrium is especially advised in women of 40 to 50 years of age presenting with abnormal uterine bleeding to rule out any possibility of premalignant or malignant condition.[18] The sensitivity of endometrial biopsy for detection of endometrial abnormality is very high.[19]

A good clinic-radiological correlation is required in cases of abnormal uterine bleeding however histopathology remains the cornerstone to reach the actual underlying cause behind clinical diagnosis.[20]

## Conclusion

Endometrial evaluation should generously be advised in females of perimenopausal and postmenopausal age groups with presentation of AUB, to exclude possibility of any preneoplastic condition or malignancy as it is more common in women of 40 years or above and it is considered gold standard for ultimately deciding treatment plans.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## Authors Contribution

**KN:** Concept, Writing, Data Analysis

**GAN:** Data Compliation

YWN: Article Writing

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# Comparison of Analgesic Efficacy of Transversus Abdominis Plane Block Versus Infiltration of Local Anaesthetic into Surgical Wound In Emergency Laparotomies: A Randomized Control Trial

**Anum Anwar,[1] Hina Nabi Ahmed,[2] Lala Rukh Bangash,[3] Farah Arshad,[4] Sahira Nawaz,[5] Farida Sohail[6]**

**Abstract**

**Objective**

To compare mean pain score of bilateral TAP block versus infiltration of local anaesthetic into surgical wound on for emergency laparotomies.

**Method:** Randomized control trial. Emergency Operation Theatre in Department of Anaesthesiology at Mayo Hospital, Lahore from 1st April 2016 to 31st October 2016. laparotomy 150 patients were arbitrarily allocated two groups Group T (receiving bilateral TAP block) and Group L (local infiltration) by random number table method after informed consent. TAP block was administered bilaterally by using 20 ml of 0.25% bupivacaine in group T using a 21-gauge needle with the help of "Double Pop Technique" at midaxillary point at height of umbilicus. While in group L surgical incision site was injected with 20 ml of 0.25% bupivacaine immediately after closure of skin. Pain was evaluated by Visual analogue scale (VAS) at 6-hour interval postoperatively. Results were statistically analysed using SPSS version 20.0 and t-test was applied to compare mean pain score of two groups.

**Results:** Mean pain score in patients receiving bilateral TAP block 3.000±0.717 were significantly reduced (p value 0.003) versus mean scores in patients receiving infiltration of local anaesthetic into surgical wound in emergency laparotomies 6.08±1.171.

**Conclusion:** Bilateral TAP block reduced post-operative pain significantly in patients undergone emergency laparotomy.

**Key Words:** Emergency laparotomy, TAP block, local anaesthetic, bupivacaine, post-operative pain, analgesia.

## Introduction

Effective pain relief is required in patients who have undergone exploratory laparotomy since pain has many adverse effects on various systems of the body.[1] Respiratory complications are much more common due to inadequate post-operative analgesia after major abdominal surgery leading to inadequate respiratory effort that results in basal atelectasis and retention of secretions.[11,12] Post-operative pain if not addressed properly it may lead to delayed ambulation resulting in increased chances of deep venous thromboembolism.[2] Anxiety and distress related to pain affect quality of life of patient. Prolong hospital stays due to inadequate post-operative analgesia leads to financial burdens.[13] Thus, adequate post-operative analgesia leads to prompt ambulation, increases comfort level of the patient and helps him to return to regular routine of life earlier.[14]

Multimodal analgesia is considered as an efficient way to cater post-surgical pain and in reducing adverse effects associated with heavy doses of opioids and NSAID's.[3] With recent advancement in technology regional nerve blocks are gaining popularity. As component of multimodal analgesia, they reduce dosage requirements of analgesic drugs and many untoward side effects associated with them.[15] Along with peripheral nerve blocks administration of local anaesthetic into surgical wound is an ancient technique that is still in use by numerous surgeons and

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anaesthetists. There are various peripheral nerve blocks that have been used to reduce pain post operatively but TAP block has been found very effective in mitigating pain after major abdominal surgeries.[10,17] The anterior abdominal wall is supplied by dermatomes from T6 to L1 and TAP block numbs those nerves. This block was originally elaborated in the "lumbar triangle of Petit" in 2001 by Rafi by using conventional landmarks. Local anaesthetic is inoculated in the fascial plane that exists between two muscles transverse abdominis muscle and internal oblique muscle through which these sensory nerves pass. TAP block is an efficient analgesic method with additional benefit of intact motor and autonomic control in all abdominal procedures and permits early mobilization.[4,16,18] Parasa et al piloted an analysis in which efficiency of TAP block was evaluated post operatively after open abdominal surgeries. They found pain was less intense in patients receiving TAP block (48.07 ± 6.76) in comparison to those patients who don't get block (62.63 ± 6.66). They also concluded that this results in 36% reduction in entire tramadol intake in TAP block group. Thus, TAP block being a component of multi-modal analgesia has effective part in reducing post-surgical pain and doses of other analgesic drugs.[5,19] Though there were multiple studies available that prove pain-relieving efficacy[9] of TAP block but there were no studies available for comparison of mean pain score of transversus abdominis plane block versus infiltration of local anaesthetic into surgical wound in emergency laparotomies. So in this trial we compared effectiveness of bilateral TAP block with infiltration of local anaesthetic into surgical wound in emergency laparotomies. This study would provide baseline data for local population and would help to mitigate post-operative pain in patients undergoing emergency laparotomies.

## Methods

After endorsement from Ethical committee, randomized control trial was performed at Emergency department of Mayo Hospital, Lahore. Patients were included with non-probability consecutive sampling. Patients of either gender between 20 to 80 years, ASA I,II,III scheduled for emergency laparotomy for viscous perforation were included. Sample size of 150 cases (75 in each group) was calculated with 95% confidence interval, 80% power of test and taking expected mean ± standard deviation of mean pain scores in both groups at 6 hour post-operatively with 3.33 ± 1.51 in TAP block group versus 5.67 ± 1.31 in control group in patients undergoing emergency laparotomies.[5] Patients with established allergy to the study drug, with past account of opioid use or intolerance, obese (BMI>40), known bleeding disorder or renal or hepatic disease, known psychiatric disorder, infection at site of injection were excluded from the study. Informed consent was obtained. Brief history was taken and related physical examination was perfor-med. Investigations (complete blood count, platelet count, coagulation screening, and renal and liver function tests) were analysed. Patients were allocated randomly to Group T (receiving bilateral TAP block group) or Group L (local infiltration group) by using random number table in accordance with division ratio of 1:1. After shifting the patient to operating table, monitoring devices that includes pulse oximetry, electro-cardiographic monitoring and non–invasive blood pressure (NIBP) were attached and base line readings were obtained. Two large intravenous line were secured. Anaesthesia was induced with rapid sequence induction technique using injection propofol (2–3 mg/ kg) and injection succinylcholine (1.5mg/kg). For analgesia injection nalbuphine (0.1 mg/kg) was given just before incision. Anaesthesia was continued with isoflurane and 50% nitrous oxide in concentration of 50% in oxygen according to need of the patient.

After completion of surgery for patients with viscous perforation, just before extubation, TAP block is performed with blunted 21-gauge needle in group T using "double pop technique" in supine position of patient by single administrator experienced in blind technique of TAP block. In above mentioned technique the skin and subcutaneous tissue was penetrated in midaxillary plane at the height of umbilicus at right angle to the skin till resistance is felt. The needle was forced slightly through this resistance till it penetrated the external oblique aponeurosis. With slight further penetration second loss of resistance could be appreciated as needle passed through aponeurosis of internal oblique. To check the desired plane 1 ml of drug was injected after careful aspiration. The feeling of considerable resistance on injecting drug indicated misplaced needle tip obviating the need to reposition

it. After readjustment 20 ml of 0.25% bupivacaine was infiltrated. The same method was used to administer block on other side. While in group L surgical incision site was injected with 20 ml of 0.5% bupivacaine before skin closure by surgeon. In both groups dose did not exceed more than 1mg/kg/side of 0.5% bupivacaine.

All patients were extubated and transferred to the postoperative ward. Patients were shown and instructed about VAS in the preoperative period. One end of which was marked as '0' representing no pain and the other one as '10' signifying severe most pain. Patients were requested to highlight the value that best contemplated their pain. Postoperative pain was measured by VAS at 6-hour interim post-operatively and pain scores were collected. Inj Tramadol 50 mg was administered as rescue analgesia if VAS was more than 5 at 6 hour interval postoperatively. Designated proforma was used to collect all data.

All statistical data was recorded and analysed in SPSS version 20.0. Data was stratified for age, gender, ASA grading and mean pain score 6 hour post-operatively to deal with effect modifiers. Post-stratification t-test was applied.

## Results

In this study 150 patients that underwent emergency laparotomies were studies. There were no patients that were excluded from study. There were 10 ASA II patients, 134 ASA III and 6 ASA IV patients. (Table 2) Out of these 110 were males and 40 were females. (table 3)

Mean age in TAP block group patients was 56.85± 8.725 and mean age in patients receiving local anaesthetic infiltration into surgical wound was 57.71± 10.686. Mean pain score in TAP block group was 3.00±0.717 and mean pain score in patients getting local anaes-thetic infiltration into surgical wound was 6.08± 1.171. This difference in mean pain score was signi-ficant as p-value is 0.003(p-value<0.005).

## Discussion

The result of our study shows there is considerable reduction in mean pain scores in TAP block group in comparison to patients receiving infiltration of local anaesthetics. Mean pain scores in patients with TAP block were 3.000±0.717 as compared to group of patients receiving local anaesthetic infiltration 6.08± 1.171 with p value 0.003. Thus, TAP block causes more reduction in pain scores on VAS scale when compared to infiltration of local anaesthetic into surgical wound in emergency laparotomies. Paras et al. conducted a randomized control trial they include 60 patients from ASA state I to III that under-went emergency laparotomy. They administer TAP block before surgery in lumbar triangle of "Petit". They divided patients into two groups; one received 25ml of 0.25% bupivacaine and other got normal saline administered bilaterally. For post-operative pain tramadol was used along with intramuscular diclofenac sodium. Tramadol was administered with PCA (patient controlled analgesic) pump while dose of diclofenac sodium adjusted 12-hourly. The tramadol requirement at 2 hour and total given in 24 hours was measured along with assessment of pain and side effects of opioids. They found that TAP block group had mean pain scores 48.07 ± 6.76 with total tramadol intake in 24 hours 281.33 ± 69.66 mg when compared to the control group having mean scores for pain 62.63 ± 6.66 and tramadol intake 439 ± 68.59 mg. Thus, our study is in consistency with the fact that TAP block significantly reduces mean pain scores but, in our study, comparison is made between TAP block and local anaesthetic infiltration.

*Frequency Distribution of Asa Grading*

| ASA | Frequency | Percent |
|---|---|---|
| ASA II | 10 | 6.7% |
| ASA III | 134 | 89.3% |
| ASA IV | 6 | 4.0% |
| **Total** | 150 | 100.0% |

*Frequency Distribution of Gender Between Both Groups*

| Gender | Count/ percentage | Study groups | | Total |
|---|---|---|---|---|
| | | Local Infiltration | TAP Block | |
| **Male** | **Count** | 56 | 54 | 110 |
| | **%** | 51% | 49% | |
| **Female** | **Count** | 19 | 21 | 40 |
| | **%** | 47.5% | 52.5% | |

*Mean Age of The Patients with Standard Deviation*

| Study groups | N | Mean | Std. Deviation |
|---|---|---|---|
| LOCAL INFILTRATION | 75 | 57.71 | 10.686 |
| TAP BLOCK | 75 | 56.85 | 8.725 |

Similarly Vijayalakshmi et al. conducted study in patients undergoing gynaecological procedures in which open abdominal surgical approach used.[6] He

*Comparison of Mean Pain Scores of The Patient*

| Study groups | N | Mean | Std. Deviation | P - value |
|---|---|---|---|---|
| LOCAL INFILTRATION | 75 | 6.08 | 1.171 | 0.003 |
| TAP BLOCK | 75 | 3.00 | 0.717 | |
| There was statistically significant difference between MEAN PAIN SCORES of two study groups | | | | |

randomly allocated patients into group receiving TAP block and other group receiving local anaesthesia into surgical site. He administered 0.25% bupivacaine at dose of 0.6ml/kg bilaterally at height of umbilicus in triangle of "petit" after completion of surgery while other group got infiltration of local anaesthetic into surgical lesion just before extubation after placement of skin sutures .They recorded time at which patient demanded rescue analgesia and monitored intensity of pain at that moment by using VAS scale. They used morphine as rescue analgesia at dose of 0.1mg/kg and it was continuously administered thereafter with PCA pump for 24 hours. Total amount of morphine consumed in period of 24 hours post operatively calculated. They concluded that In Group T patients demanded foremost dosage of morphine considerably later and at that moment pain was not much intense as compared to other group (P = 0.001 and 0.003 respectively). Total intake of morphine in group receiving local anaesthetic was more as compared to TAP block group so the side effects of morphine also predominated in this group. Thus conclusion of their study was that transversus abdominis plane block is an effective modality to reduce pain with few adverse effects and their results are in line with our conclusion but we have done comparative study in patients undergoing exploratory laparotomy. Likewise, Priya et al conducted study in 60 patients who underwent major abdominal operations. They calculated doses of tramadol required post opera-tively at 24 hour time interval and at 48 hour time interval. According to their study, total amount of tramadol consumed in patients in TAP block in 24 hour time duration (210.05 ± 20.5 vs. 320.05 ± 10.6; P < 0.01) and at 48 hour interval (508.25 ± 20.6 vs. 550.25 ± 20.6; P < 0.01). They also concluded that time at which patient demanded first dose of analgesic drug was more as compared to other group (178.5 ± 45.6 vs. 23.5 ± 3.8; P < 0.001). Pain intensity measured at different intervals in 24 hours period post operatively. Pain scores were significantly less in TAP block group contrary to other group.[7] Thus, TAP block is very effective modality with crucial role in mitigation of pain post operatively. The results of our study add significance to above mentioned study and prove it to be more effective as compared to ancient technique of wound infiltration with local anaes-thetic. Ejas et al. performed randomized control trial in patients who underwent single incision laparoscopic cholecystectomy.[8] They performed TAP block under USG guidance with ropivacaine in concenteration of 0.375% bilaterally in mid axillary plane in one group while other group received local anaesthetic infiltration at site of insertion of ports. They calculated amount of morphine required post operatively in 24 hours. Morphine requirement in group receiving TAP block was 34.57 + 14.67 mg as compared to other group in which values were 32.76+14.34 mg. They found TAP block did not cause significant reduction in post-operative analgesic requirement as compared to conventional methods. This is contrary to our result in which we found TAP block more effective. There are certain limitations of our study that it does not measure time of administration of first dose of analgesia, total dosage requirements of analgesia 24 hour post-operatively and incidence of nausea and vomiting.

## Limitations

TAP block has more efficacy if it is performed under ultrasound guidance but unfortunately due to resources limitation we don't have access to ultrasound.

## Recommendations

The study can be expanded to include dosage requirements of analgesia in 12 hours of post-operative period and occurrence of post-operative nausea and vomiting.

## Conclusion

Outcome of our study shows substantial reduction in mean pain scores after bilateral TAP block infiltration in patients with emergency laparotomy. Mean pain scores remain less than 4 on VAS pain scale in patients with TAP block. Hence it is concluded that TAP block significantly reduces pains score on VAS scale as compared to surgical wound infiltration with local anaesthetic in patients with emergency laparotomies. TAP block is better modality as part of multimodal analgesia to reduce post-operative pain as compared to surgical wound infiltration with local anaesthetic.

## Author's Contribution

**AA:** Concept, Conduction of study, manuscript preparation and editing, literature review

**HNA:** Manuscript preparation, proof reading and critically reviewed the article

**LRB:** Statistical analysis of the data

**SNK:** Data collection

**FA:** Data collection

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# Acidosis Frequency in Children of Pediatric Acute Diarrhea

**Muhammad Zain Ul Abadin,[1] Arif Zaheer,[2] Shahla Tariq,[3] Muhammad Ans,[4] Kashif Mehmood,[5] Moazzam Farooq[6]**

**Abstract**

**Objectives:** To Found out the frequency of aidosis in patients of paediatric accute diarrhea.

**Methods:** Two hundred and eighty children fulfilling the inclusion/exclusion criteria admitted in Department of Paediatrics, Services Hospital, Lahore was taken. Informed consent of the parents of children was obtained to include their data in the study. Every children with acute diarrhea was followed through 1-2cc arterial sample sent to the hospital laboratory of the hospital.

**Results:** out of the total 280 patients, 83(29.5%) had acid base abnormality and 197(70.5%) had normal acid base imbalance. Out of 83(29.5%) patients who had acid base abnormality 50(17.5%) males and 22(8%) females had acidosis while only 8(3%) males and 3(1%) females had alkalosis.

**Conclusion:** Acidosis is the most common abnormalities. Its incidence increase with increase in duration of diarrhea.

**Key Words:** Acidosis, paediatric acute diarrhea

## Introduction

In developing countries, Diarrhea still plays key role in both morbidity and death among under-5 children and accounts for 9% of 5.9 million global under-5 deaths.[1] Children with diarrhea often present with respiratory difficulties with or without dehydration, and this is mainly due to the presence of metabolic acidosis[2] resulting mainly from a loss of bicarbonate in feces.[3] Dehydration is the most frequent and dangerous complication and is the main reason for metabolic acidosis in such children.[4]

The gastrointestinal tract (GIT) helps to regulate acid-base homeostasis. Large amounts of H+ and $HCO_3$ cross the specialized epithelia of the various components of the gut every day, but under normal conditions, only a small amount of alkali (approximately 30 to 40 mmol) is lost in the stool.[5] The small amount of alkali lost as a byproduct of these transport events is easily regenerated by renal net acid excretion, which is regulated by the kidney to maintain body alkali stores. Disruption of normal gut function, however, uncovers its power to overwhelm acid-base homeostasis. Acid-base disorders can vary from severe acidosis to severe alkalosis, depending on the site along the gastrointestinal tract affected and the nature of the losses that ensue.[6] These disruptions in acid base equilibrium are associated with disorders of either potassium imbalance or sodium imbalance.[7]

The type of diarrhea depends on which part of the GIT has been targeted and the causative agent.[8] Commonly observed acid base disturbances in diarrhea are hyperchloremic metabolic acidosis and metabolic alkalosis occurs in very few types.[9] In secretory diarrhea, like caused by Vibrio Cholera, there is hyperchloremic metabolic acidosis. Lactic acidosis may supervene as a result of tissue hypoperfusion.[10] In inflammatory diarrhea, there is no acid base disturbance initially as kidney is compensating for the loss, however, in severe cases, volume depletion and hyperchloremic metabolic acidosis may occur. In case of autoimmune diarrhea, incidence of metabolic alkalosis is more. [11] A study was conducted in Bangladesh reported higher incidence of morbidity

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and mortality in children who developed metabolic acidosis and suggested that early recognition of features of acidosis may help clinicians to have prompt management that may further help reduce mortality in such children. [12] As it is a common cause of morbidity and mortality in Pakistan, and limited literature is available in refe-rence to acid base imbalance and there is no research done on this important issue in my center. Young children die of this simple problem, so my rationale is to highlight the major cause which lead to death from this simple problem.

## Methods

It was a cross sectional study which includes 280 cases. Sampling was done by Non probability consecutive sampling technique. Our inclusion criteria was children between 3 months to 5 years of age and children with acute diarrhea (Passage of loose or watery stools at least 3 times in 24 hours, for less than 14 days). Children having any chronic GI illness like celiac disease and congenital adrenal hyperplasia and children having other systemic disease like renal (urea> 20mg/l, creatinine > 1.3mg/dl), gastrointestinal and metabolic diseases were excluded from the study because these cases will act as effect modifiers and if included in the study will introduce bias in the result. The collected data was entered and analyzed using SPSS version 16. The frequency and percentage of children with acid base imbalance whether acidosis or alkalosis were noted. Data was stratified for age, acid base imbalance, gender, duration of diarrhea to address the effect of modifiers. Chi-square test was used to compare qualitative data. $p < 0.05$ was considered as significant.

## Results

We found out that, out of 280 cases 140(50%) were in the age range of 3-12 months. When they were divided according to gender, 148(53%) were male and 132(47%) were females. When acid base balance was checked. Out of the total 280 patients, 83(29.5%) had acid base abnormality and 197(70.5%) had normal acid base balance. Out of 83(29.5%) patients who had acid base abnormality, 50(17.5%) males and 22(8%) females had acidosis while only 8(3%) males and 3(1%) females had alka-losis as shown in Table-1. Data was than stratified with age, number of diarrhea episodes and severity of dehydration using chi-square test as shown in Table-2.

**Table 1:** *Distribution of Acid Base Imbalance (n=280).*

| Acid Base Imbalance | Male | Female | Total | p-value |
|---|---|---|---|---|
| **Acidosis pH <7.35** | 50(17.5%) | 22(8%) | 72(25.5%) | 0.005 |
| **Alkalosis pH >7.45** | 8(3%) | 3(1%) | 11(4%) | 0.001 |
| **Normal pH 7.35-7.45** | 109(39%) | 88(31.5%) | 197(70.5%) | 0.054 |

## Discussion

Acidosis is the most common acid base imbalance in

**Table 2:** *Stratification of Acid Base Imbalance with Regard to Age Range, Number of Diarrheal Episodes and Severity of Dehydration (n=280).*

| Stratification of frequency acid base imbalance with regard to age range | Age Range | | | p-value |
|---|---|---|---|---|
| | 3 - 12 months (n=140) | 13 - 24 months (n=81) | 25 months - 5 years (n=59) | |
| **Acidosis** | 51(36.4%) | 20 (31%) | 6 (10%) | 0.025 |
| **Alkalosis** | 6 (4.5%) | 2(4.6%) | 0 (0%) | 0.300 |
| **Normal** | 90 (64.2%) | 62 (69%) | 53 (90%) | 0.001 |
| **Stratification of frequency acid base imbalance with regard to number of episodes** | **Number of episodes** | | | |
| | **1-3 (n=146)** | **4-5 (n=78)** | | |
| **Acidosis <7.35** | 21(25.5%) | 26 (28%) | 25 (38%) | 0.001 |
| **Alkalosis >7.45** | 4(4%) | 2 (2%) | 5 (7.6%) | 0.025 |
| **Normal 7.35-7.45** | 57(70%) | 65 (70%) | 25 (38%) | 0.005 |
| **Stratification of frequency acid base imbalance with regard to severity of dehydration** | **Severity of Dehydration** | | | |
| | **No dehydration** | **No dehydration** | **No dehydration** | |
| **Acidosis <7.35** | 11 (20%) | 30(18.3%) | 31(47%) | 0.001 |
| **Alkalosis>7.45** | 3(5%) | 2(1.9%) | 6(9%) | 0.025 |
| **Normal 7.35- 7.45** | 31(86%) | 87 (73%) | 26(40%) | 0.005 |

our study population. 25.5% who presented with diarrhea also had acidosis. In a study conducted by Sharifuzzaaman et al in 2017 in Bangladesh they reported acidosis in 96% of the children who presented with watery diarrhea.[12] These results are very higher than ours it may be due the fact that they have included patient only with complain of acute watery diarrhea whereas we included cases of diarrhea with any cause of origin. In a study conducted in Kathmandu, Nepal 94% children who presented with diarrhea had acidosis whereas only one 6% had alkalosis.[13] Similar results have been reported by Habib Ullah[14]. Narchi reported that there is no significant difference between the serum bicarbonate concentrations in relation to the degree of dehydration in diarrhea patients[15]. Shah reported that increase incidence of acidosis in diarrhea is due to more loss of bicarbonate from gastrointestinal tract[13]. When frequency of acidosis is stratified with age range, it is found that acidosis is more frequent in the 3-12 months age group. Similarly, in a study conducted by Eke C Bet al in Nigeria they reported Children less than 12 months of age were three times more likely to have acidosis (odds ratio = 3.098) than those above 12 months. This may be related to the high body surface area in the younger infants, thereby predisposing them to greater loss of fluid and electrolytes.[16] Acidosis is also more common in the group with diarrhea of more than 6 days (44.4%in the third group). This is due to the fact that as duration of diarrhea prolongs increase faecal losses of sodium, potassium and bicarbonate leads to more loss which are not being replaced properly due to the improper rehydration methods and lack of awareness about continuation of breastfeeding during diarrhea in Pakistani mothers, according to Bello DA.[17] This also suggest that early presentation and prompt correction of this derangement may reduce the duration of diarrhea and by extension associated mortality as corroborated by other studies.[18,19] Acidosis is present in the group with no dehydration The reason is that in these patients, loss of water was replaced by hypotonic solutions but the loss of electrolytes were not properly compensated. However, its incidence is much higher in the group with severe dehydration. Loss of more bicarbonate as compare to Hydrogen leads to increase incidence of acidosis in severely dehydrated patients.[20]

## Conclusion

Acidosis is the most common acid base abnormality in children with acute watery diarrhea. Children less than 2 years of age are most affected. Frequency of acidosis increases with an increase in duration of diarrhea and occur more frequently in patients who are severely dehydrated .All children especially less than 2 years of age must be properly dehydrated. ORS should be started immediately and in proper amounts once diarrhea starts.

### Limitations of the Study

The limitations of the study are we were unable to correlate it with blood urea and creatinine level as we didn't took blood samples of all the study population for these levels due to financial constraints. In addition, serum electrolytes of all the population was not collected due to kit constraints.

## Author's Contribution

**AZM:** Sampling, introduction & results
**ZA:** Critical review & hypothesis development
**TS:** Sampling & discussion
**AM:** Sampling & introduction
**MK:** Sampling & results
**FM:** Sampling & statistical analysis

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# Frequency of Vesicoureteral Reflux in Children having Recurrent Urinary Tract Infections

**Irum Aslam,[1] Muhammad Asif Siddiqui,[2] Fatima Zia,[3] Hafsa Qamar[4]**

**Abstract**

**Objective:** Repeated urinary tract infections are significantly related to anatomical abnormalities of urinary tract. Vesicoureteral reflux is quite common, under diagnosed anatomical abnormality, leads to renal scarring and chronic kidney disease. The objective of the study was to determine the frequency of vesicoureteral reflux in children having repeated urinary tract infections.

**Methods:** It is cross sectional survey conducted in department of Pediatric Medicine, The Children's Hospital & Institute of Child Health, Lahore, spanning from 20-5-2014 to 19-11-2014, using non-probability purposive sampling, a total of 140 patients included. Each child was screened and followed with repeated urinary tract infections for frequency of vesicoureteral reflux by detailed clinical examination and relevant investigation as defined in operational definition. To avoid any controversy, all the findings of UTI & vesicoureteral reflux was assessed by a single consultant. Data was managed using SPSS version 20.

**Results:** In this study the mean age of all patients was 5.64 ± 2.35 years. There were 42 (30%) males and 98(70%) females in this study with male to female ration 1:233. The mean number of episodes of urinary tract infections was 5.82 ± 1.95 per years. Frequency of vesicoureteral reflux in these patients was seen in 35(25%) of the patients. When we stratified the data over age, gender and number of episodes of urinary tract infection we found significant association of vesicoureteral reflux with age groups only (p-value < 0.05) while no association between vesicoureteral reflux versus gender and number of episodes of urinary tract infection (p-value > 0.05).

**Conclusion:** We found significant correlation between vesicoureteral reflux and repeated urinary tract infections. Cases with repeated urinary tract infections should be investigated thoroughly to address underlying cause, in order to prevent renal damage and long-term complications.

**Key Words:** Paediatric, Urinary tract infections, hydronephrosis, Vesicoureteral reflux

## Introduction

In paediatric population, urinary tract infections (UTI) are commonly seen. Symptoms for UTI include anorexia for fever, lethargy, urinary complaints and vomiting. 5% of children with repeated UTI are at risk of renal damage.[2] Children with UTI can present with pyelonephritis, urethritis or cystitis.[3] There are different organisms responsible for UTI, Escherichia coli in almost 80% of total cases.[4] Other include klebsiella, pseudomonas aeroginosa, enterobacter, and proteus.[5] UTIs and some congenital abnormalities may cause renal scarring.[6] Vesicoureteral reflux (VUR) is one of the common congenital anomalies, in which there is backward flow of urine from bladder towards kidneys. VUR is seen in 30 to 50% of children that are diagnosed with infections of urinary tract.[7] VUR causes hydronephrosis, increase risk of UTI and in presence of bacterial infection causes pyelonephritis. Kids suffering from hydronephrosis may require daily dose of antibiotic for prevention of UTI or surgical correction.[7]

VUR prevalence is between 22.7% to 26.4% in children, suffering from UTI.[8] Urine tract related congenital abnormalities should be suspected and diagnosed promptly in order to prevent irreversible renal damage. Renal ultrasonography, voiding cys-

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tourethrography (VCUG), Tc-99m Diethylene- triamine-penta-acetic acid (DTPA) Scan, Dimercapto-succinic acid Scan (DMSA) are used to diagnose urinary tract congenital abnormalities and extent of renal damage.[3] Purpose of this study was to see frequency of vesicou-reteral reflux in children with recurrent UTI. Whereas, Urinary tract infection was defined as pure growth of micro-organisms of >105 organisms/ml on urine culture. Recurrent urinary tract infection was defined as urinary tract infection twice in 6 months or ≥ 3 times in 1 year on urine culture. Vesicoureteral reflux was characterized by the retrograde flow of urine from the bladder into ureters or kidneys and was assessed by voiding cystourethrogram (VCUG) in terms of whether being present or not.

### Inclusion Criteria

1. Patients fulfilling operational definition of recurrent urine tract infections.
2. Age between 2 to 10 years
3. Both genders

### Exclusion Criteria

1. Children with known congenital anomalies of the kidney/urinary tract or having multiple anomalies like syndromic patients e.g. Down's syndrome

## Methods

This was cross sectional survey conducted in Department of Pediatric Medicine, The Children's Hospital & Institute of Child Health, Lahore with duration of Six months spanning from 20-5-2014 to 19-11-2014. Sampling technique was non probability, purposive with estimated sample size, calculated with 95% confidence level, 7% margin of error with an expected VUR frequency of 22%, is 140 children.[8] After an informed consent, patients fulfilling the inclusion criteria were enrolled. Collected data was entered and analyzed using statistical software SPSS version 20. Mean and ± SD was calculated for quantitative variables like age, number of episodes of urinary tract infections. Frequency tabulation and percentage was done for qualitative variables like vesicoureteral reflux in recurrent urinary tract infections. Data was stratified for age, gender and number of episodes of urinary tract infection. Chi-square test was applied post stratification with p-value ≤ 0.05 considered as significant.

## Results

In this study the mean age of all patients (n=140) in this study was 5.64 ± 2.35 with age range of 8 years (minimum age=2 and maximum age =10 years). The mean number of episodes of urinary tract infection was 5.82±1.95 with minimum and maximum number of urinary tract infection per years. (Table 1). When we stratified the data over age, gender and number of episodes of urinary tract infection we found that, among 35 patients with vesicoureteral reflux, there were 12 (343%) patients who were 2-5 years of age and 23(65.7%) patients were 6-10 years of age. There was significant association between vesicoureteral reflux and age groups of the patients, p-value 0.004. There was no significant association between vesicoureteral reflux and gender, p-value = 0.523. Likewise, there was no statistical association between vesicoureteral reflux and number of episo-des of urinary tract infection, p-value = 0.481.

## Discussion

If urinary tract abnormalities like vesicourethral reflux is diagnosed earlier in patients with repeated UTI the damage in kidney can be prevented either

**Table 1:** *Descriptive Statistics of Age (Years) and Number of Episodes of Urinary Tract Infection*

| | Mean | Std. Deviation | Range | Min. | Max. |
|---|---|---|---|---|---|
| Age (years) | 5.64 | ±2.35 | 8 | 2 | 10 |
| Number of episodes of urinary tract infection | 5.82 | ±1.95 | 6 | 3 | 9 |

**Table 2:** *Frequency and Comparison of Vesicoureteral Reflux with Respect to Age (Years), Gender and Number of UTI Episodes Frequency Distribution of Vesicoureteral Reflux in Recurrent UTI Patients*

| Yes | No |
|---|---|
| 35 (25%) | 105 (75%) |

**Comparison of Vesicoureteral Reflux with Respect to Age (Years), Gender and Number of UTI Episodes**

| | | Vesicoureteral reflux | | p-value |
|---|---|---|---|---|
| | | Yes | No | |
| Age groups (years) | 2-5 | 12(34.3%) | 65(61.9%) | **0.004** |
| | 6-10 | 23(65.7%) | 40(38.1%) | |
| Gender | Male | 12(34.3%) | 30(28.6%) | 0.523 |
| | Female | 23(65.7%) | 75(71.4%) | |
| Number of episodes of urinary tract infection | 3-6 | 20(57.1%) | 67(63.8%) | 0.481 |
| | 7-9 | 15(42.9%) | 38(36.2%) | |

with prophylactic antibiotics or with corrective surgery.[9] Symptoms for UTI in older children can be of urinary origin but in younger kids symptoms are usually nonspecific and sometime in infants they are difficult to observe. Urine dipstick analysis is important for ruling out of UTI in patients having low level of clinical suspicion. Although Urine culture is gold standard for diagnosis of UTI in children having high suspicion clinically, cloudy urine, positive leukocyte esterase or positive nitrate activity in case of urine dipstick analysis.[10]

For diagnosis of repeated UTIs related morbidities, we need detailed history, physical examination, renal as well as bladder sonography urine analysis and culture and contrast cystography, beside assessing other risk factors like bacterial virulence, antibiotic resistance.[11]

3% of girls in prepuberty phase and 1% of boys in prepuberty phase are diagnosed with UTI. The incidence for urine infection in childhood and infancy is high and also influenced by gender and age.[12] Average age for subjects was 27.15± 20.72 months.[13] 80(81.8 %) males along with 18(18.2%) females were included. Most subjects were of age 01.00 to 24.66 months in one study.[13] In our study average age of subjects was 5.64 ± 2.35 yrs. There were 42 (30%) males and 98(70%) females in this study with male to female proportion 1:2.33.

Risk of recurrent UTI is high in children anomalies like vesicoureteral reflex and neurogenic bladder or with poor hygiene habits.[14] In this study average number for episodes of UTI was 5.82 ± 1.95 with maximum and minimum number of UTI per years.

Primary vesicoureteral reflux is congenital with normal functioning of lower urinary tract, on other hand secondary vesicoureteral reflux is due to obstructive cause like posterior ureteral valve or neurogenic bladder.[15] Precise frequency for vesicoureteral reflux is not known because several children are asymptomatic but vesicoureteral reflux frequency is much higher in children suffering from repeated UTI 15-70%.[13,15,16,17]

In this study stratification of data was done for gender, age and episodes of UTI, we observed that in 35 patients suffering from vesicoureteral reflux 12(34 %) patients are with age group (2 to 5 years), whereas 23(65.7%) of are with age group (6 to 10 years). There is strong relationship between to the age and vesicoureteral reflux (p-value 0.004). There is no statistically significant relationship between gender, number of urine tract infections with vesicoureteral reflux.

We made conclusion from our study that congenital abnormalities of urine tract must be looked for in any age group of children presenting with repeated UTI, irrespective of gender and number of urine tract infections. Vesicoureteral reflux should be promptly suspected and treated accordingly, in order to prevent renal scarring.[18]

## Conclusion

We found significant correlation between vesicoureteral reflux and repeated urinary tract infections. Children with repeated urinary tract infections should be investigated thoroughly to address underlying cause, in order to prevent irreversible renal damage and long-term complications.

## Author's Contribution

**AI, SAM, ZF, QH :** Concept design, interpretation of data, :

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# Self-Reported Treatment Adherence in Patients of Diabetes Mellitus Type 2: A Cross-Sectional Study in Lahore, Pakistan

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**Abstract**

**Objectives:** Suboptimal adherence to therapy due to neglected self-care behavior in chronic diseases is a global crisis. The aim of this research was to gauge the prevalence of adherence and to assess the effect of age, sex, education level and socioeconomic status on adherence to self-care strategies.

**Methodology:** A cross-sectional study was conducted at Diabetes Management Centre, Services Hospital Lahore. 357 patients were administered a standardized questionnaire, the Diabetes Self-Management Questionnaire. A cut off value of 7 on a 0-10 scale was labeled as good adherence. The influence of age, sex, education and income on adherence was examined by multiple logistic regression analysis.

**Results:** The mean age of the sample was 49.76±12.5 years, 64.52% were female, 37% had no formal education, and 47.39% had monthly household income > Rs. 45000. The prevalence of good adherence as a marker of good self-care behavior was 42%. The mean Sum Scale scores were 6.63 ±1.48. Glucose Management subscale showed the highest mean score i.e. 6.65 ±2.07 while Physical Activity subscale showed mean lowest score i.e. 5.26 ±2.75. The sociodemographic factors being measured did not influence adherence significantly.

**Conclusion:** This study provides insight into the self-care behaviors of diabetic patients. This research highlights the immediate need to take steps to improve adherence among individuals. The sociodemographic factors were not found to influence adherence to self-care activities significantly in this sample. Further research is required to explore other factors that may increase the risk of suboptimal adherence among diabetics.

**Keywords:** Diabetes mellitus, adherence, factors, Pakistan

## Introduction

Over last few decades, diabetes has emerged as a pandemic. From developed to developing nations, its prevalence is increasing rapidly, with approximately 463 million cases reported globally in 2019 and a projected rise to 700.2 million cases till 2045. In 2019 alone, it claimed 4.2 million lives.[1]

In recent years burden of diabetes has rapidly increased in both developed and developing countries. In 2019, there were a dismal 19.4 million cases of diabetes and 159,000 diabetes related deaths in Pakistan.[1]

Diabetes is a chronic disease, and its management is a lifelong commitment. While a physician is responsible to draft a treatment plan, the onus of the execution is on the patients. 95% of the day-to-day management is carried out by the patient themselves,[2] which means that between clinic appointments there is very little a physician can do. The efficacy of the treatment relies on the personal resolve of the patients alone.

Diabetes requires a complex, multifaceted treatment including lifestyle modifications, often as a first-line defense, and pharmacotherapy. The selfcare behaviors have several domains: blood glucose measurement, dietary control, exercise, medication and keeping appointments with the physician. The primary outcome is glycemic control i.e. maintaining HbA1C at <7%.[3] Adherence to therapy is a significant predictor of treatment outcomes.[4–6] WHO defines adherence as: "The extent to which a person's behavior – taking

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medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider."[7] Several international studies have shown adherence to be suboptimal.[8–11] Regional research on this topic is limited, however non-adherence appears to plague patients in Pakistan as well. Studies conduc-ted in Karachi[12] and Multan[13], for example, found only 20% of participants fully adherent. Non adherence leads to poor glycemic control[6,14] and greater morbidity[15]. According to UKPDS 35, 1 percent decrease in HbA1c decreased risk of microvascular complications by 37%.[16] Predictors of non-adherence are classified as modi-fiable and unmodifiable factors. The latter include sociodemographic factors, including age, sex, educa-tion and socioeconomic status.[7] Literature provides conflicting reports on association of these factors with non-adherence, both national[12,17,18] and interna-tional.[11,19,20] These demographic characteristics can help physi-cians to forecast non-adherence in individuals. This can enable physicians to provide better attention to patients at risk of non-adherence and create personalized treatment plans for ideal outcomes. Local research on adherence is deficient, and to draw conclusions or comparisons a larger pool of data is required. In the present research, we attempted to determine the level of adherence in a local diabetic population sample and the effect of sociodemographic factors on adherence.

## Methods

A cross-sectional questionnaire-based study was conducted at an urban government tertiary care institution, over a period of 1 month, from 1st to 30th of September 2019. Participants included in this study were older than 30 years, with a diagnosis of Diabetes Mellitus Type 2 for a duration of at least 1 year, who had received a full treatment plan from their health provider. Patients taking oral medication only, insulin only as well as combination therapy as a part of their treatment were included. Participants were chosen by convenience sampling and each gave informed consent to take part in the study. Exclusion criteria included the inability to understand Urdu, mental incapacitation and type I or gestational diabetes. The sample size selected for this study was 357, for a confidence level of 95% and margin of error ±5%. The research involved the collection of two sets of data: the demographic characteristics of the population (Table 1), and the assessment of adherence. The demographic characteristics that were measured included age, sex, education and income as shown in Table 1. These were reported by the patient in a preliminary face-to-face interview. Treatment adherence was measured by a pre-valida-ted and reliable questionnaire (Cronbach's α= 0.96), the Urdu-version of Diabetes Self-Management Questionnaire (DSMQ) made by Schmitt[21] et al and translated by Bukhsh et al.[22] It was comprised of 4 sub-scales, namely Glucose Management, Dietary Control, Physical Activity and Health-care Use.[21] There was one additional question relating to overall selfcare. Patients rated their adherence using a Likert scale of 0-3 to, where 0 was 'does not apply to me' and 3 was 'applies to me very much'. The sub-scale scores and sum scale scores were compiled separately and each was converted to a 0-10 scale. Adherence was considered as a dichotomous variable; a score of 7 or above was considered "good adherence". The DSMQ was administered in paper form and as an interviewer-assisted questionnaire. In the latter case, it was read out to the illiterate participants verbatim and no further description was provided, to ensure validity. Data was analyzed using SPSS 25.0. Prevalence of non-adherence in the population was calculated and represented as a percentage of the total population. Data was analyzed by multiple logistics regression analysis to forecast the trends and predict the association between the independent variables i.e. the demographic characteristics, and the dependent variable i.e. adherence. The results were adjusted for employment status, duration of diabetes, type of treatment and presence of comorbidities. Value of p less than 0.05 was considered significant.

The purpose and components of the research were explained to each participant and informed consent was obtained. Ethical approval was obtained from the institution's ethical review board, Ref. No IRB/ 2019/ 570/SIMS.

## Results

In September 2019, 357 patients were administered the DSQM at the Diabetes Management Center, SHL. The mean age of respondents was 49.76±12.5 years. 231 (64.5%) were female and majority i.e. 133 (37.3 %) of the respondents had no education. 168 (47.3 9%) respondents had income > Rs. 45000 while 91

(25.49 %) had income between Rs. 35001 to Rs. 45000. The demographic and clinical characteristics of the population are summarized in Table 1.

Good adherence to therapy (sum scale score ≥7) was seen in 150 (42%) participants. The mean sum scale score was 6.63 ±1.48. Table 2 shows the mean scores for the individual sub-scales and sum scale; it also records the scores corresponding to the demographic variables. Sum scale scores were highest for 60-70 years age group followed by > 70 years; 51-60 age group showed lowest scores. Females had higher scores than males, i.e. 6.67 ±1.26 and 6.56±1.82 respectively. There was an overall increase in the scores with an increase in the level of education. The lower income groups obtained higher sum scale scores.

Glucose management, Dietary and Health-Care Use sub scales showed increased adherence with increasing age. Physical activity sub scale showed the opposite. Males demonstrated better glucose management and health care use but poorer physical activity and dietary management scores. Higher education showed an overall better glucose management and physical activity scores. Those with middle school education showed highest health care use scores. Lowest dietary control and physical activity scores were observed in the FSc./Class[11-12] category. Better physical activity scores were seen in higher income groups. In contrast there was a decrease in dietary control and health care use scores with an increase in income level. Glucose management was highest in lower income groups. Dietary control and physical activity were poor across all variables. Socio demographic factors affecting adherence are reported in Table 3. Good adherence was highest in 41-50 and 51-60 age groups. More males were adherent than females. 34.67% of the adherent indi-viduals had no formal education. Good adherence was highest in highest income group. A multiple logistic regression model was used to predict the influence of the demographic characteristics on the dependent variable i.e. adherence. The p values for all variables were greater than 0.05 and hence the varia-bles were insignificant. The p values are reported in Table 3.

**Table 3:** *Demographic Profile of the Sample*

| Demographic Characteristics | Frequency (n) | Percentage (%) |
|---|---|---|
| **Age (years)** 49.76±12.5 | | |
| 31-40 | 59 | 16.53 |
| 41-50 | 132 | 36.97 |
| 51-60 | 117 | 32.77 |
| 60-70 | 35 | 9.8 |
| >70 | 14 | 3.9 |
| **Gender** | | |
| Male | 126 | 35.29 |
| Female | 231 | 64.52 |
| **Education** | | |
| No formal education | 133 | 37.25 |
| Primary school/class 1 -5 | 52 | 14.57 |
| Middle school/class 6–8 | 41 | 11.48 |
| Matric/class 9-10 | 81 | 22.69 |
| FSc../class 11-12 | 23 | 6.4 |
| undergraduate | 27 | 7.56 |
| **Monthly household income (Rs.)** | | |
| < 5000 | 1 | 0.28 |
| 5000-15000 | 19 | 5.32 |
| 15000-25000 | 39 | 10.92 |
| 25000-35000 | 38 | 10.64 |
| 35000-45000 | 91 | 25.49 |
| >45000 | 169 | 47.39 |
| **Employment** | | |
| Employed | 117 | 32.77 |
| Unemployed | 240 | 67.23 |
| **Locality** | | |
| Urban | 242 | 67.79 |
| Rural | 115 | 32.21 |
| **Duration of diagnosis (years):** | 7.58 ± 6 | |
| **Type of treatment** | | |
| Oral hypoglycemics | 166 | 46.50 |
| Insulin | 125 | 35.01 |
| Combination | 66 | 18.49 |
| **Co-morbidities** | | |
| Yes | 240 | 67.23 |
| No | 117 | 32.77 |

## Discussion

Two out of five patients were found to have good adherence. This is a concerning statistic, as poor adherence is a major factor that contributes to poor glycemic control[8] and, consequently, complications[24] and mortality. Suboptimal adherence is pervasive in previous litera-ture. A study conducted in Islamabad in 2015 reported 62% non-adherence in patients.[17] The ENTRED study in France found suboptimal adherence to prescribed medications in almost 60% of the 3637 participants.[25] A study in Kerala, India found 74% of the rural population to be non-adherent.[26] Out of 257 patients in Karachi, 79.4% were reported to have low adherence.[12] A mere 20% of the population was found to be adherent at Nishtar Hospital, Multan.[13] 45.4% of the sample at the rural health training center of Tamil Nadu showed low adherence, which is lower than that observed in our

**Table 2:** *Mean Scores and Standard Deviation of the Sub-scales and Sum Scale Across the Categories of Sociodemographic Variables. Mean Score of the Sample in each Subscale and Sum Scale is also Shown*

| Demographics | Glucose Management Sub-Scale | Dietary Control Sub-Scale | Physical Activity Sub-Scale | Health-Care Use Sub-Scale | Sum Scale |
|---|---|---|---|---|---|
| **Age** | | | | | |
| 31-40 | 6.88 ±1.75 | 5.63 ±1.05 | 5.44 ±2.64 | 6.16 ±1.96 | 6.75 ±1.26 |
| 41-50 | 6.47 ±1.97 | 5.45 ±1.16 | 5.35 ±2.48 | 5.85 ±1.84 | 6.54 ±1.40 |
| 51-60 | 6.56 ±2.27 | 5.41 ±1.35 | 5.00 ±2.92 | 6.02 ±2.29 | 6.50 ±1.62 |
| 60-70 | 7.07 ±2.34 | 5.91 ±1.23 | 5.75 ±3.04 | 6.48 ±2.40 | 7.10 ±1.47 |
| >70 | 7.19 ±1.85 | 5.82 ±1.39 | 4.44 ±3.51 | 7.30 ±2.34 | 6.98 ±1.66 |
| **Gender** | | | | | |
| Male | 6.69 ±1.92 | 5.47 ±1.51 | 4.90 ±3.10 | 6.61 ±2.73 | 6.56 ±1.82 |
| Female | 6.63 ±2.33 | 5.56 ±1.05 | 5.45 ±2.53 | 5.78 ±1.60 | 6.67 ±1.26 |
| **Education** | | | | | |
| No Formal Education | 6.46 ±2.23 | 5.44 ±1.25 | 5.05 ±2.67 | 5.91 ±2.04 | 6.53 ±1.50 |
| Primary School/Class 1 -5 | 6.72 ±1.75 | 5.62 ±0.91 | 5.34 ±2.58 | 6.11 ±1.70 | 6.74 ±1.10 |
| Middle School/Class 6–8 | 6.59 ±2.01 | 5.51 ±1.14 | 5.34 ±2.91 | 6.61 ±2.34 | 6.61 ±1.37 |
| Matric/Class 9-10 | 6.88 ±2.03 | 5.69 ±1.20 | 5.57 ±2.92 | 6.27 ±2.31 | 6.83 ±1.44 |
| FSc./Class 11-12 | 6.87 ±2.42 | 5.19 ±1.66 | 4.78 ±2.10 | 5.46 ±2.04 | 6.23 ±1.99 |
| Undergraduate | 6.74 ±1.87 | 5.56 ±1.46 | 5.43 ±3.27 | 5.97 ±2.12 | 6.67 ±1.75 |
| **Monthly Household Income (Rs.)** | | | | | |
| < 5000 | 8.33 ±0.47 | 6.77 ±0.49 | 5.00 ±2.56 | 10.00 ±0.40 | 8.13 ±0.59 |
| 5000-15000 | 7.47 ±2.11 | 5.77 ±1.57 | 4.85 ±3.94 | 8.01 ±2.61 | 6.92 ±1.88 |
| 15000-25000 | 7.47 ±2.25 | 5.76 ±1.57 | 5.13 ±3.48 | 7.29 ±2.84 | 6.92 ±1.89 |
| 25000-35000 | 6.19 ±2.03 | 5.32 ±1.34 | 5.32 ±2.74 | 6.11 ±2.14 | 6.39 ±1.62 |
| 35000-45000 | 6.27 ±2.12 | 5.34 ±1.12 | 5.08 ±2.50 | 5.54 ±1.83 | 6.41 ±1.35 |
| >45000 | 6.68 ±1.96 | 5.57 ±1.12 | 5.42 ±2.54 | 5.81 ±1.70 | 6.69 ±1.34 |
| **Mean Score of the sample** | 6.65 ±2.07 | 6.39 ±1.71 | 5.26 ±2.75 | 6.08 ±2.10 | 6.63 ±1.48 |

**Table 3:** *Distribution of Frequency of Good Adherence Across the Categories of each Variable and Multiple Logistic Regression Significance Values. Comparison of Frequency of Good vs Poor Adherence in each Category is also shown.*

| Demographics | Good Adherence (n) | p Value | Poor Adherence (n) |
|---|---|---|---|
| **Age** | | .962 | |
| 31-40 | 25 | | 34 |
| 41-50 | 50 | | 82 |
| 51-60 | 49 | | 68 |
| 60-70 | 19 | | 16 |
| >70 | 7 | | 7 |
| **Gender** | | .674 | |
| Male | 97 | | 73 |
| Female | 53 | | 134 |
| **Education** | | .720 | |
| No Formal Education | 52 | | 81 |
| Primary School/Class 1 -5 | 23 | | 29 |
| Middle School/Class 6–8 | 19 | | 22 |
| Matric/Class 9-10 | 35 | | 46 |
| Fsc./Class 11-12 | 8 | | 15 |
| Undergraduate | 13 | | 13 |
| **Monthly Household Income (Rs.)** | | .684 | |
| < 5000 | 2 | | 0 |
| 5000-15000 | 11 | | 8 |
| 15000-25000 | 19 | | 20 |
| 25000-35000 | 15 | | 23 |
| 35000-45000 | 36 | | 55 |
| >45000 | 67 | | 101 |

sample.[23] Similarly, 42.3% were non-compliant in a study at Kolkata.[27] However, most of these studies measured adherence using instruments different from that used in the present research, hence, comparison is difficult to make.

Lowest adherence was reported for physical activity, which is an observation reported frequently in literature.[27–29] The sample population showed better glucose management. Among the self-care behaviors measured glucose management, dietary control and health care use were found to be better in older individuals, which could be explained by the availability of family support as well as time. There was a decrease in the adherence to physical activity with increasing age, probably due to comorbidities which limit mobility. However, in the multiple logistic regression model, age was not a significant factor ($p > 0.05$). Surveys at Islamabad[17], Tamil Nadu, India[23] and France[25] all demonstrated the effect of age on adherence to be insignificant. A positive relationship has, however, been found in others.[11,13,24,30]

In this sample population males had better adherence to therapy; 64.71% of the adherent individuals were males. Males showed better health-care use but poo-

rer physical exercise levels, confirming the results of a Saudi Arabian study.[31] Sex did not significantly modify adherence in our regression model. There have been mixed reports in the past regarding the association of sex with adherence. Some local[13,17] and global studies[20,32,33] have shown similar results to ours. Others have commonly shown males to have better adherence[11,30,34] 37.25% of the sample had no education, corres-ponding to the literacy statistics of Pakistan.[35] This population scored lower in all self-care activities. 34% of the adherent population had no formal education. The number of adherent vs non-adherent patients improved as the education level increased, however, there was no significant relationship found between the two variables. Researches at Aga Khan University Hospital, Karachi[28] and Rawal Institute of Health Sciences, Islamabad[17] demonstrated a neutral relationship. This was observed in Kenya[8] and Tamil Nadu, India[23] as well. Many regional surveys have found a positive relationship between education level and adherence, including studies at Quetta city[18], Islamabad[17] and Dhaka city[29], Bangladesh. The adherence for < 5000 income group was seen to be unusually high, which could be due to the very small sample. 44.64% of the adherent patients earned Rs. 45000 or more, however this result could be influenced by the fact that almost half the patients belonged to this income group. The adherent and non-adherent patients in each income bracket, other than < 5000, were approximately the same, indicating that income had no effect on adherence. Multiple logistic regression also confirmed this finding. Increase in adherence with better socioeconomic status has been overwhelming in past research.[11,13,25,27,36] A neutral relationship has been observed as well, for example in Quetta city[18] and Turkey,[33] which agrees with the findings of this study. This study presented local data regarding adherence in patients of Diabetes Mellitus. It showed that over-all adherence is sub-optimal among patients, high-lighting the necessity to address this issue. The non-modifiable demographic factors were not predictors of adherence. There is an urgent need for further research to explore other factors that could impede adherence, so that targeted treatment strategies can be developed to combat non-adherence and improve glycemic control and treatment outcomes. The instrument was a self-reported questionnaire, which could lend a recall and social desirability bias, leading to underestimation of poor adherence[37]. How-ever, self-reported questionnaires have been shown to be a reliable and convenient method to measure adherence related to clinical outcomes.[38] Our results have been derived from a sample chosen by convenience sampling. This could impart some level of sampling bias to our results. However, our results agree with several regional and global which contributes to its credibility. This study was conduc-ted in a central government tertiary care hospital, however, as the sample was chosen from only one institution, it may not be suitable to generalize these results to the national population.

## Conclusion

This study provides insight into the self-care behaviors of diabetic patients. Patients were most diligent about glucose management. Adherence to physical activity was seen to be the lowest. The sociodemographic factors were not found to influence adherence significantly in this population sample. There is a strong need to carry out further research on the barriers to adherence to therapy in order to improve compliance, self-care behaviors and treatment strategies.

## Authors Contribution

**RS:** Methodology, Literature Review, Data Collection, Article Writing
**AA:** Data Collection
**IF:** Supervision, Methodology
**RA:** Drafting Revising, Analysis
HA: Methodology and Statistics

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# Frequency and Severity of Premenstrual Syndrome Among Undergraduate Medical Students

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## Abstract

**Objective:** To find out the frequency and to assess the degree of severity of premenstrual syndrome among undergraduate medical students

**Methods:**Cross-Sectional Study conducted at Obstetrics and Gynecology department, Jinnah Hospital, Lahore in six months from June 2019-Nov 2019. Study was conducted in 161 female Students, aged 18-25 years from Allama Iqbal Medical College of 1st year to final year who had regular periods (28-35 days) for last 3 months before start of study, and voluntarily consented for participation. Female using hormonal contraception, any medication or having any organic pathology (Fibroid, Endometriosis) were excluded. PMS was diagnosed on the basis of a modified DRSP scale. A Questionnaire was designed on the basis of existing available literature. It was based on a list of symptoms and their severity during the 5 days before her periods. Female who fulfilled the following criteria were labeled as having PMS:

1. A score of > 50 on Daily record of severity problems scale (DRSP),
2. History that the symptoms end within 4 days after her period starts

**Severity of PMS:** It was diagnosed on the basis of DRSP scale.

- Mild: if the score on DRSP is 50-85
- Moderate: if the score on DRSP is 86- 120
- Severe: if the score on DRSP is >120

Data was analyzed by SPSS version 23. Frequency, percentage charting was expressed for variables like presence of PMS and severity of PMS. Quantitative variables like age and BMI were expressed by Mean ±S.D. Data was stratified for age, BMI, year of study, living status and marital status to deal with effect modifiers. Test of significance was applied i.e chi-square. A p-value ≤0.05 was considered significant.

**Results:** Subjects ranged between 18-25 years with mean age of 19.9±2.1 years. Majority of the students were between 18-20 years. Mean BMI was 19.9±1.9 kg/m2. Mean year of study was 2.4±1.3 year. Out of 161 subjects, 53 (32.9%) were living with parents while remaining 108 (67.1%) were far from parents. Married students were 10 (6.2%). Premenstrual syndrome was found to be in 31 females (19.2%), mild 4.3%, moderate 8.1% and severe 6.8%,and severity was more in 4-5 years students, p-value was found significant with variable years of study (p-value= 0.095).

**Conclusion:** PMS was found in 19.2% of undergraduate medical students. Early recognition and timely management can improve the quality of performance among undergraduates.


**Key Words:** DRSP scale, Premenstrual syndrome, Undergraduates

## Introduction

Definition of PMS varies over the years because of its unknown etiology and its related symptoms complex. Globally Physicians are having different opinions about this malady.[1] Reproductive age women often experience repeated psychological, physical and behavioral complexities occurring in second half of cycle and vanish by the end of menstruation.[2] These symptoms really interfere with household, social, and workplace activities, inter personal and even the sexual functioning of a woman, which are not related to any organic or functional


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ailment.[3] Some degrees of premenstrual problems are expe-rienced by even younger girls in initial years follo-wing menarche. Many Studies depicts that around 80% of women may experience some of premenstrual symptoms in their reproductive age.[4] When it is very severe, premenstrual syndrome is called as premens-trual dysphoric disorder (PMDD). The psychological symptoms are anger, frustration, emotional liability, depression and apprehension. Physical symptoms include weight gain, swelling, breast pain, headache, dizziness, and tingling sensations, so that psychiatric and endocrinal disorders must be checked before labelling a women PMS. Symptomatology which is triggered by ovulation, appears about one week before the start of periods and vanishes immediately after the start of periods.[5] Due to the severity of symptoms and its prolonged history it is associated with long term effects on the emotional health, relationships and impairment in work. Women suffering PMS report significant family disharmony, inability to perform at workplace along with frequent absence from work, school, or college. Very few Data is available on PMDD in young girls.[6] In a study, it was concluded that, the prevalence of premenstrual syndrome was 39.6%. The distribution of severity of symptoms was minimal 2.5%, mild 27.5%, moderate 42.5%, severe 25% and extreme 2.5%.[7] 1n another study, prevalence of PMS was found around 18.4% and moderate to severe PMS was found in 14.7%.[8]

## Results

Subjects ranged between 18-25 years with mean age of 19.9±2.1 years. Majority of the students were between 18-20 years. Mean BMI was 19.9±1.9 kg/m$^2$.

Mean year of study was 2.4±1.3 year. Out of 161 subjects, 53(32.9%) were living with parents while remaining 108 (67.1%) were far from parents. Married students were (6.2%) n=10. (Table -1) Premenstrual syndrome was found in 31 females (19.2%), mild 4.3%, moderate 8.1% and severe 6.8% (Table-2). Stratification for age, BMI, year of study and marital status was also done (Table-2) and p-value was found significant in 4-5 years of study (p-value= 0.095).out of total 125 students of 1-3 years PMS was found I 23 students (18.4%) and out of 36 students of 4-5 years it was found in 8 students (22.2%). Out of those 8 students In 4-5 years 5 had severe and 3 had moderate PMS. (table-2)

## Discussion

Many women in their reproductive age may experience physical or emotional symptoms before the start of periods. Amongst these, some are so badly affected that it impairs their mental and physical health, relationships, and quality education.[9] It is also observed that premenstrual syndrome (PMS) exists more among single women, between 35-44 years, and in women of low income groups living in deprived areas.[10,11] Multiple risk factors are revealed with PMS in several studies, including age, stress, marital status and body mass index. These risk factors were found to worsen the manifestations.[12] A significant number of women in Pakistan expe-rience PMS but they don't come up with this idea of suffering a disorder.[13] In our

**Table 1:** *Demographic Profile of Subjects*

| Variables n = 161 | | Frequency | Percentage % |
|---|---|---|---|
| Age Mean = 19.9±2.1 | 18 – 20 | 109 | 67.7 |
| | 21—25 | 52 | 32.3 |
| BMI Mean = 19.9±1.9 | ≤18 | 26 | 16.1 |
| | ≥18. 1 | 135 | 83.9 |
| Year of study | 1-3 Years | 125 | 77.6 |
| | 4-5 Years | 36 | 22.4 |
| Living Status | Parental House | 53 | 32.9 |
| | Independent/Boarding | 108 | 67.1 |
| Marital Status | Single | 151 | 93.8 |
| | Married | 10 | 6.2 |
| Pre Menstrual Syndrome | Yes | 31 | 19.2 |
| | No | 130 | 80.8 |
| Severity of Pre Menstrual Syndrome | Normal | 130 | 80.8 |
| | Mild | 7 | 4.3 |
| | Moderate | 13 | 8.1 |
| | Severe | 11 | 6.8 |

**Table 2:** *Pre Menstrual Syndrome & Independent Variables Cross Tabulation*

| Variables | | Pre Menstrual Syndrome | | | Total | P Value |
|---|---|---|---|---|---|---|
| | | Mild | Moderate | Severe | | |
| Age | 18-20 | 6 | 8 | 6 | 20 | 0.386 |
| | 21-25 | 1 | 5 | 5 | 11 | |
| | Total | 7 | 13 | 11 | 31 | - |
| BMI (Kg/m$^2$) | ≤18 | 1 | 1 | 1 | 3 | 0.890 |
| | ≥18. 1 | 6 | 12 | 10 | 28 | |
| | Total | 7 | 13 | 11 | 31 | - |
| Year Of Study | 1-3 | 7 | 10 | 6 | 23 | 0.095* |
| | 4-5 | 0 | 3 | 5 | 8 | |
| | Total | 7 | 13 | 11 | 31 | - |
| Marital Status | Single | 7 | 10 | 11 | 28 | 1.00 |
| | Married | 0 | 3 | 0 | 3 | |
| | Total | 7 | 13 | 11 | 31 | - |

country, menstruation and related feminine issues are taken as taboos and women are forced to accept that PMS is not a signi-ficant issue to be talked about or to seek advice for, even if it adversely affect their lives.[13] PMS is a symptom complex of physical and psycho-logical symptoms appearing prior to the onset of periods and resolves with the onset of menstruation or within few days of menstruation.[14] Our sample is comparable with past similar studies, and the mean age of all participants is 19.9±1.6 years and the majority of them are urban resident and single. The participants from previous studies were also from similar age group college students, had urban residence, and were unmarried. [15, 16, 17, 18] In current study, the frequency of PMS is 19.2% (14.9% for moderate to severe PMS and 4.3% for mild) among undergraduate medical students. It is in agreement with the study done by Rapkin and Mikacich[19] and other studies from Asian countries among this population.[20] This finding is also consis-tent with two other studies BY lentz & parry.[21, 22] The prevalence of severe and mild PMS in this study is not in agreement with the study by Steiner et al who reported 21.3% and 8.3%, respectively, and also differs from study by Chayachinda et al[23] who repor-ted 25.1% PMS among Thai nurses. The lower preva-lence in our study can be explained by influence of cultural norms, social factors, peer experiences, local practices and life stresses about menstruation in Pakistani context which affects both experiencing and reporting of the premenstrual symptoms.

In present study no statistically significant relationship was established amongst subjects in relation to age, BMI, marital status and living conditions, which is in consistent with study of Nour Bkhashani et al,[16] except age which showed higher prevalence in younger 18-20 years, which may be because in present study sample size smaller for that study.

## Conclusion

In conclusion, PMS was found in 19.2% of undergraduate medical students of government medical college of Pakistan. Frequency and severity of PMS was more in 4rth and final year students. Worldwide it is a common problem and awareness about the existence of this medical problem and early recognition along with timely management, among undergraduates the quality of their performance can be improved.

### Limitations and Challenges

This study only reflects one medical institute and such more studies should be conducted in other educational systems to better understand the true picture of existing data for this disorder and to establish the triggering factors and available management options. Another limitation of present study is use of subject's self-reported data due to which there is possibility of higher expression of disorder amongst subjects.

## Recommendations

- There is an immense need to create Adolescent awareness programs in colleges for better understanding of PMS, changing attitudes towards existence of disorder and knowledge about available pharmacological & non pharmacological therapies.
- Premenstrual calendars, diaries and questionnaires can be used as a tool to label PMS/PMDD.
- Lifestyle changes, behavioral therapies, and physical fitness workouts aerobic exercises should be adopted and gymnasiums must be there in colleges.
- Students should be evaluated for their eating behaviors. Eating well throughout the month is a better approach to PMS than tweaking your diet while suffering the symptoms.

## Authors Contribution

**YS:** Data Compilation, Writing
**BB:** Data Analysis
**FA:** Data Collection
**ZA:** Expert Advice

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# Diagnostic Accuracy of Gene Xpert on Bronchoscopy Washings in Patients with Suspected Pulmonary Tuberculosis

**Waseem A. Khan,[1] Nayyar Manzoor,[2] Asad Javaid,[3] M. Saqib Musharaf,[4] Nausheen Sohail,[5] Nighat Majeed[6]**

**Abstract**

**Objective:** The objective of this study was to determine the diagnostic accuracy of GeneXpert assay of bronchial washing in detecting pulmonary tuberculosis in suspected TB patients with no sputum production taking culture of bronchial washing as gold standard.

**Methods:** This is cross sectional study. Data was collected through structured questionnaire. Patients had bronchoscopy according to standard protocol. Their bronchial washings were sent for culture and GeneXpert assay for Mycobacterium Tuberculosis. Data analysis was done using SPSS 20 version.

**Results:** From one hundred and seventy patients the age was observed as 16-60 years. AFB was detected by GeneXpert assay in 45.3% patients. AFB was detected by culture report in 47.6% patients. The sensitivity of GeneXpert was observed as 87.65 %, specificity was 93.26 %, and diagnostic accuracy was calculated as 90.59%.

By using chi-square t-test, there was significant association found between GeneXpert and Culture report in both gender in all age groups with any duration of symptoms with p-value = 0.000.

**Conclusion:** The GeneXpert assay was highly effective for detecting pulmonary tuberculosis in suspected TB patients who do not have sputum production.

**Key words:** GeneXpert Assay, Culture Report, Bronchial Washing, Pulmonary Tuberculosis

## Introduction

Tuberculosis is caused by Mycobacterium species. The most common species is Mycobacterium Tuberculosis which usually infects humans in most cases. But other species can also infect humans like Mycobacterium bovis, Mycobacterium africanum, Mycobacterium microti and Mycobacterium canettii.[1] Tuberculosis is an air born infection and infectious droplets remain in environment when infected person speaks, sneezes and coughs.[1] All individuals who are exposed do not get infection. Whether the infection will spread to other individual depend on certain factors like immunity of individual, duration of exposure and infectiveness of the source.[1] It is the immunity of the individual which contain the infection and does not allow its spread. In about 5% individual infection is not controlled and individual develops active TB within 1-2 years.[2] This is called primary tuberculosis. In other 5% individuals the immune system contain infection to localized site but mycobacterium remains in dormant stage and reactivate later on when the immunity of individual becomes weak[(2)]. This category is named as postprimary or reactivation of tuberculosis. The remaining 90% of the individuals will harbor mycobacterium in tissue but will be asymptomatic and this category is called as latent tuberculosis. Tuberculosis infects one third of world population[3] and causes significant morbidity and mortality. It is major public health problem because it spreads through droplet infection.[3] Milllions of people get infected and a million people die each year because of this infectious disease.[1] Pakistan belongs to the countries which has highest burden of the disease in the world. Pakistan is 4th among the twelve countries with high number of missing TB cases.[6] Major diagnostic procedures

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employed for diagnosing pulmonary tuberculosis are sputum smear, culture for detection of Acid-Fast bacilli (AFB) and chest radiography. In those patients who are highly suspected of tuberculosis based on history and radiology it is pertinent to demonstrate presence of AFB through sputum smear to avoid unnecessary empiric therapy.

Active disease may manifest with minimal symptoms initially but as the disease progresses over months then overt symptoms develop.[4] Active tuberculosis manifests with symptoms of fever, productive cough, night sweats weight loss and fatigue. Sometimes patient may present with hemoptysis with typical symptoms.[4] The clinician should have high index of suspicion since the disease has insidious onset and nonspecific symptoms.

Extrapulmonary tuberculosis results from hematogenous spreads to different organs of body like pleura, lymph nodes and larynx. Most extrapulmonary disease is not contagious, but laryngeal tuberculosis is exception. Chest x-ray may be normal in cases of extrapulmonary TB. Miliary tuberculosis results from hematogenous route and can cause numerous tiny lesions throughout the lung field measuring 1-3mm and it can disseminate to other organs of body like central nervous system, eye and liver.

In postprimary TB patient, upper zones are involved usually.[5,7] The radiological features of postprimary TB includes patchy consolidation, dense consolidaion and cavitation involving apical and posterior segments of upper lobes and superior segments of lower lobes.[5] In 5% of postprimary TB patients only lung bases are involved.[2] Cavitation is common finding seen in 20%-45% cases. CT scan chest may be used when chest x-ray is not diagnostic but CT is not routinely required for diagnosing TB.[8]

Not all patients expectorate adequate sputum and it's minimal in amount some time that cannot be collected. In those cases where there is radiological evidence of lesion but no sputum production making diagnosis is a challenge. Patients who have smear negative tuberculosis they are less infectious than sputum smear positive patients.[9,10] However patients who are smear negative but culture positive tuberculosis they can spread mycobacterium tuberculosis.[11,12] In those cases where there is scanty sputum or no sputum production bronchoscopy can be helpful in making diagnosis. Bronchial washings can be taken and GeneXpert and culture can be done on sample. In previous study GeneXpert was done on bronchial washings and showed encouraging results. Out of 120 patients, 83(69.2%) patients were detected having active pulmonary tuberculosis on bronchial washings in sputum scarce TB patients.[13]

## Methods

This crossectional study was conducted in the department of pulmonology of Jinnah Hospital lahore. Suspected pulmonary tuberculosis patient of either sex having ages 16 to 60 years with fever and cough for more than 6 months but no sputum production were enrolled after approval from ethical committee of research at Jinnah Hospital. Patients who were diagnosed of pulmonary TB and received anti-tuberculosis medication for 2 weeks and those patients who fall in the definition of category-2 patients were excluded. Informed consent was taken and data was collected through questionnaire. Patients had bronchoscopy procedure according to the protocol. Their bronchial washings were sent for culture for Mycobacterium Tuberculosis, and GeneXpert assay for presence of AFB immediately to pathology laboratory of Allama Iqbal Medical College. Results of both GeneXpert assay and culture were collected. Pulmonary tuberculosis was diagnosed by both GeneXpert and positive culture for Mycobacterium Tuberculosis. Sensitivity, specificity and diagnostic accuracy of GeneXpert assay was calculated using culture as gold standard. Data analysis was done by using SPSS version 20.

## Results

From 170 patients the minimum age was observed as 16 years and maximum age was 60 years with Mean ± SD as 39.08 ± 13.74 years. The minimum duration of symptoms was observed as 6 months and maximum duration of symptoms was 18 months with Mean ± SD as 11.32 ± 3.24 months. AFB was detected by GeneXpert assay in 77 (45.3%) and by culture report in 81 (47.6%) patients. The sen-sitivity of GeneXpert was observed as 87.65 %, speci-ficity was 93.26 %, positive predicted value was 92.21%, negative predicted value was 89.25% and diagnostic accuracy was calculated as 90.59%. By using chi-square t-test, there was significant asso-ciation found between GeneXpert and Culture report in less than 40 years of

age group with p-value = 0.000. In more than 40 years of age group, there was significant association found between GeneXpert and Culture report with p-value = 0.000. There was signi-ficant association found between GeneXpert and Culture report in male with p-value=0.000. In female, there was significant association found between GeneXpert and Culture report with p-value = 0.000. There was significant association found between GeneXpert and Culture report in less than one year duration of symptoms

**Table 1:** *Diagnostic Accuracy of GeneXpert on Bronchoscopy Washings*

| GeneXpert | Culture Report | | Total |
|---|---|---|---|
| | AFB Detected | AFB not Detected | |
| AFB detected | TP=71 | FP=6 | 77 |
| AFB not detected | FN=10 | TN=83 | 93 |
| **Total** | 81 | 89 | 170 |

**Table 2:** *Stratification with respect to Age (n = 170)*

| Age | GeneXpert | Culture Report | | Total | P-value |
|---|---|---|---|---|---|
| | | AFB Detected | AFB not Detected | | |
| < 40 year | AFB detected | 27 | 3 | 30 | 0.000 |
| | AFB not detected | 10 | 35 | 45 | |
| | Total | 37 | 38 | 75 | |
| ≥ 40 year | AFB detected | 44 | 3 | 47 | 0.000 |
| | AFB not detected | 0 | 48 | 48 | |
| | Total | 44 | 51 | 95 | |

**Table 3:** *3 Stratification with respect to Duration of Symptoms (n = 170)*

| Duration of Symptoms | GeneXpert | Culture Report | | Total | P-value |
|---|---|---|---|---|---|
| | | AFB Detected | AFB not Detected | | |
| **< 1 year** | AFB detected | 34 | 3 | 37 | 0.000 |
| | AFB not detected | 5 | 41 | 46 | |
| | Total | 39 | 44 | 83 | |
| **≥ 1 year** | AFB detected | 37 | 3 | 40 | 0.000 |
| | AFB not detected | 5 | 42 | 47 | |
| | Total | 42 | 45 | 87 | |

group with p-value = 0.000. In more than one year duration of symptoms group, there was significant association found between GeneXpert and Culture report with p-value = 0.000.

## Discussion

The objective of this research is to determine the diagnostic efficacy of GeneXpert assay of bronchial washing in detecting pulmonary tuberculosis in suspected patients with no sputum production. In our study there was significant association found between GeneXpert and Culture report in both gender in all age groups with any duration of symptoms with p-value = 0.000.

Mostly pulmonary tuberculosis is diagnosed on clinical grounds and with radiology in patients when there is typical history. The diagnostic accuracy of different modalites have been studied before like clinical assessment, radiology and sputum microscopy. In previous study, out of 364 TB patients, 35.1% were diagnosed on clinical grounds and radiology, 20.8% on radiological, and 17.58% on the basis of clinical evaluation. Sputum smear examination for Mycobacterium tuberculosis was done in 85.6% patients, of these 31.9% were positive [14].

Previous studies have evaluated the efficacy of GeneXpert assay on pulmonary and extrapulmonary samples and results are very encouraging. For pulmonary samples the sensitvity and specificity were 90.6 % and 94.3%. For extrapulmonary samples they were 100% and 91.6%. For sputum smear negative samples the sensitvity, specificity, positive predictive value and negative predictive values were 86.3%, 93%, 79%, and 95.6%[15]. Our study has comparable results with previous study. In our study The sensitivity of GeneXpert was observed as 87.65%, specificity was 93.26 %, positive predicted value was 92.21%, negative predicted value was 89.25%.

In cases where there is no sputum production but high suspicion of tuberculosis, sputum induction and bronchoscopy can be done to collect sample. Bronchoscopy is accepted modality for diagnosis when saline induction is not helpful[16]. In one study where sputum was not produced but x-ray was showing active disease, flexible fiberoptic bronchoscope was used in making diagnosis. In that study, two hundred and seventy five suspected TB patients based on chest radiology, fiberoptic bronchoscopy was done and bronchial brushings and transbronchial biopsy samples colllected. 89(32.4%) were diagnosed as active pulmonary TB. In 60(67.4%) of these patients the diagnosis was made by bronchoscopy[17]. There are very few studies who have used bronchial washings and GeneXpert and using culture as gold standard in sputum scarce TB patients. In previous local study

bronchoscopy was done to collect bronchial washing sample and GeneXpert done[13]. Out of 120 patients eighty three patients were diagnosed as active pulmonary TB by this approach. Our study is unique in a way that it not only determines the role of GeneXpert on bronchial washing sample but also determine the efficacy of culture as well on same patient.

## Conclusion

The GeneXpert assay has high diagnostic accuracy for detecting pulmonary TB in suspected patients where x-ray is suggestive of active disease but there is no sputum production.

## Author's Contribution

**KAW:** Conceived Idea, study draft
**JA, MN:** Data Collection
**MSM:** Statistical analysis, interpretation
**SN:** Crtically reviewed manuscript
**MN:** Final review

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# Comparing the Efficacy of Hyaluronic Acid and Platelet Rich Plasma Treatment by using Visual analogue Scale in the Patients of Knee Osteoarthritis

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**Abstract**

**Objective:** To compare the efficacy of Hyaluronic acid (HA) and Platelet rich plasma (PRP) for treatment of Knee osteoarthritis.

**Methods:** A randomized controlled trial done at department of Orthopedics Unit-I, Mayo Hospital Lahore. 130 cases fulfilling inclusion criteria were enrolled. All patients were divided into two groups. In group-A, cases were treated with HA (1% sodium Hyaluronate mixed in a phosphate buffered saline). In group-B, cases were treated with 10ml of PRP extracted from 100ml of their blood. Before and after procedure pain and efficacy was recorded.

**Results:** The frequency of pain reduction ≥ 50% was statistically higher in PRP group as compared to HA group, p-value < 0.05.

**Conclusion:** Through the findings of this study we conclude that the efficacy of efficacy of PRP was high than HA for treatment of Knee osteoarthritis.

**Key Words:** Osteoarthritis, platelet-rich plasma, efficacy, hyaluronic acid.

## Introduction

Arthritis is of the most prevalent chronic conditions in cases with advanced age. The most commonest joint to be effected is the knee joint with a prevalence up to 41%, compared to the prevalence of 30% in hands and 19% in hips.[1] Kellgren-Lawrence (K/L) along with x-rays is utilized to diagnose and grade the severity of disease. Its overall score ranges from 0–4 with confirmed diagnosis of knee osteoarthritis at Grade 2.[2,3] There is an evidence of repairing cartilage by stimulation method and there are many other methods to reduce cartilage damage that is by inhibiting catabolic enzymes or supressing genes, use of growth factors or by artificial replacement of cartilage.[4] PRP injections is a platelet concentration above base line have a great acceptance in orthopaedics. [5,6,7]

According to a recent systematic review, short and long duration follow ups have shown that the treatment guidelines of injecting PRP inside the knee synovial cavity, is found to be more efficacious then only injecting injections of saline Hyaluronic acid, placebos, ozone and steroids.[8,9,10] Many physician do agree that by incorporating HA (viscosupplementation) into synovial cavity, it magically restore the physiological viscoelastic qualities of pathological synovial fluid.[11,12] Platelet contains growth factors: platelet-derived growth factors (a, b), transforming growth factor (TGF)-β, vascular endothelial growth factor, epidermal growth factor, fibroblast growth factor. [5,12]

A team of scientist have found that the severity of visual analogue score of 15 subjects (55.5%) falls to the half of their previous score at their third month of treatment with PRP and 8 patients who were treated with HA, also showed a significant decrease in VAS with p-value = 0.227.[4]

The rationale of this study is to compare HA and PRP

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for treatment of knee osteoarthritis in our local patients. We found no local study and global study reported high rate of reduction (<50%) in pain from baseline but on comparing with HA the difference was insignificant. On the basis of findings of this study we want to see its role in our local population so that in future PRP can be utilized to gain quick recovery of the cases if found to be more effective.

## Data Collection Procedure

It was a randomized controlled trial comprising 130 patients selected though non-probability consecutive sampling. 65 cases in each group were taken using percentage of < 50% decrease in VAS at 3 months. We used 80% power of study and 95% confidence level. Cases of age 30- 80 years of either gender with diagnosis of knee osteoarthritis (duration of symptoms more than 2 weeks) were included. Subjects having Hb <11 mg/dL, history of previous knee surgery (on clinical record), blood disorders like hemophilia, etc, Systemic disorders (diabetes mellitus; BSR >120), Rheumatoid arthritis {on clinical signs and symptoms and digital –rays (stage III & IV)}, history of severe cardiovascular diseases, infections, history of immunosuppressive drugs, patients receiving anticoagulants, use of non-steroidal anti-inflammatory drugs in the last 5 days before blood donation, were excluded.

All patients were divided into 2 equal groups. In group-A, cases were treated with HA in which a very clear solution of sterile 1% sodium Hyaluronate in a phosphate buffered saline. In group-B, a total of 100 mL of blood through venous was taken and PRP was extracted in a 10-mL syringe. Patients were called again after the duration of 3 months. Before and after procedure, pain and efficacy was recorded. All related information was recorded on attached proforma.

### Data analysis procedure:

All collected data was entered and analysed using SPSS version 22. Categorical data like gender and <50% reduction in pain was presen-ted in form of Frequency (%). Quantitative data (age, duration of pain, pain before and after 4 months) was presented as mean ± S.D. Chi-square test was applied to compare efficacy of procedure in both groups. P-value ≤0.05 was considered as significant.

## Results

The mean age of cases in PRP and HA group was 48.26 ± 13.32 and 46.71 ± 11.09 years respectively, there were 84(64.6%) male and 46(35.4%) female cases in whole sample, moreover there were 53(81.5 %) male and 12(18.5%) female in PRP group while in HA group there were 31(47.7%) male and 34(52.3%) female cases respectively. The mean duration of disease in PRP group was 10.74 ± 4.59 weeks and in HA group was 10.75 ± 4.93 weeks. In PRP group ≥ 50% reduction in pain was seen in 38(58.5%) cases and < 50% reduction seen in 27(41.5%) cases whereas in other group ≥ 50% reduction seen in 19(29.2%) cases and < 50% in 46(70.8%) cases. The frequency of pain reduction ≥50% was statistically higher in PRP group as compared to HA group, p-value < 0.05. Results of all demographic features (age, gender and obesity) showed that efficacy of PRP was higher than HA with p-value < 0.05.

**Table 1:** *Descriptive Statistics of pain at baseline and at 3rd months after treatment in both groups.*

| | Study groups | Mean | S.D | Min. | Max. |
|---|---|---|---|---|---|
| **Pain before** | PRP (n=65) | 5.97 | 1.86 | 4 | 10 |
| | HA (n=65) | 7.57 | 2.07 | 4 | 10 |
| | Total (n=130) | 6.77 | 2.12 | 4 | 10 |
| **Pain after 3 months** | PRP (n=65) | 3.32 | 1.52 | 2 | 6 |
| | HA (n=65) | 4.71 | 1.75 | 2 | 7 |
| | Total (n=130) | 4.02 | 1.77 | 2 | 7 |

**Table 2:** *: Comparison of efficacy of treatments in both groups with respect to duration (weeks) and VAS.*

| | | Efficacy | Study Groups | | Chi-square | p-value |
|---|---|---|---|---|---|---|
| | | | PRP | HA | | |
| **Duration (weeks)** | < 12 weeks | Yes | 22(59.5%) | 10(29.4%) | 6.462 | 0.011 |
| | | No | 15(40.5%) | 24(70.6%) | | |
| | 12 weeks or more | Yes | 16(57.1%) | 9(29.0%) | | |
| | | No | 12(42.9%) | 22(71.0%) | 4.761 | 0.029 |
| **Pain before** | 4-6 | Yes | 28(66.7%) | 15(57.7%) | 0.556 | 0.456 |
| | | No | 14(33.3%) | 11(42.3%) | | |
| | 7-10 | Yes | 10(43.5%) | 4(10.3%) | | |
| | | No | 13(56.5%) | 35(89.7%) | 9.134 | 0.003 |

## Discussion

Any joint of the body is susceptible to OA but the most common joints on the hit list of this disease are Knee, hip, spine, hand and foot. In 2011, the prevalence of osteoarthritis was 28% n Pakistani population.[13] A study complied few studies on (739 patients, 817 knees, 39% males, mean age of 59.9 years, with 38 weeks average follow-up) were

analyzed.[14] We in current study found that 84(64.6%) male and 46 (35.4%). Kohsiban and his fellow colleague conducted a study and found out that all those subjects who were treated with PRP showed more pain improvement that the subject who were injected with HA.[15] Meheux and his fellows did a systemic review in year 2015 and con-cluded that management of knee OA disease with PRP injection is far better than HA. Our research study had the results in line with the results of above mentioned worldwide studies.[14] Mendia et al. did a research study on patients of knee OA and findings favoured the treatment with PRP rather than with any placebo or steroids. Similar results were drawn out from a systemic review of six-teen studies done by Chang et al.[16,17] Kon E. & Bennell conducted the study on younger patients effected with cartilage lesions and extracted the same results from their studies as mentioned above.[18,19]

However, Filardo and his fellow colleagues used PRP and HA as treatment regime and found out that both are of equal importance in reducing OA symptom and severity with a significant p-value of <0.0005 and both drugs have shown similar trend for all clinical scores used.[20]

A study reported 50% decrease in VAS at 3 months in 15 (55.5%) treated with PRP and 8(30.7%) patients treated with HA with insignificant difference, p-value = 0.227.4 We in current study also found that in PRP group there were 38(58.5%) cases in which ≥ 50% reduction in pain was seen while in 27(41.5%) cases the reduction of pain was < 50%.

## Conclusion

Through the findings of this study we conclude that the efficacy of efficacy of PRP was high than HA for treatment of Knee osteoarthritis. In future PRP can be utilized to reduce the symptom, pain and to improve better functions of knee.

## Authors Contribution

**AM:** Concept, Data Analysis
**AMM:** Discussion Writing
**ZM:** Initial Drafting
**SF, SA:** Data Collection
**MF:** References writing and final proof reading

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# Efficacy of Autologous Platelet Rich Plasma in the Treatment of Male Androgenetic Alopecia

**Nadia Naeem,[1] Saadiya Siddiqui,[2] Atif Shehzad,[3] Kehkshan Tahir,[4] Marrium Manzoor[5]**

**Abstract**

**Objective:** To assess the outcome of autologous platelet rich plasma(PRP) for the treatment of androgenetic alopecia in male patients.

**Methods:** A total of61 male patients from Department of Dermatology, Lahore General Hospital Lahore with ages between 18-60 years were included in the study during a period of 6 months. PRP was prepared by double spin method and CaCl2 was used to activate platelets. PRP was injected, with a 30-G needle using Nappage technique. This descriptive case series study was carefully monitored. Protocol included three treatment sessions with an interval of four weeks. Number of hairs, and hair strength was assessed by dermoscopy and hair pull test. SPSS Version-21 was used for data entry and analysis.

**Results:** The mean age of patients was 42.67±8.63 years. Mean number of hair was 21.50±4.57 per dermatoscopic field, Post treatment number of hair was 78.10±16.24. mean duration of disease was 10.25±3.52 months. Majority of patients were in stage iv 19(31.1%) and in stage ii 16(26.2%). There was significant difference in number of hair before and after treatment.

**Conclusion:** PRP is an effective method to treat the patients with androgen alopecia.

**Key words:** Autologus platelet rich plasma, Androgen alopecia .

## Introduction

Androgens have a great effect on scalp and body hair. Scalp hair grows without effect of androgens while body hair growth is dependent on androgen presence. Androgens dependent hair fall is termed as androgenetic alopecia also referred as Male pattern hair loss (MPHL).[1] Alopecia is a dermatological disorder which is andro-gen dependent and with genetic predisposition. It generally starts by 20 years of age and effect up to 50 percent of men when they reach by their 50 years of life.[2] Alopecia involves an ongoing loss and thinning of scalp hair in a specific pattern causing a significant psychological effect on one's mental health and make it difficult for a person to cope up with his self-esteem. The two factors, testosterone metabolite dihydrotesterone and a receptor named as hair follicle-related androgen receptor challenging world's dermatologist, as these two are modulating this androgen-dependent disorder, whereas few studies have also found genetic involvement in this pathology.[3] Few treatment option available including minoxidil, 5-alpha-reductase inhibitors and hair transplantation but these modalities have many aftereffect including excessive body hair growth, birth defects, decreased libido and prolonged impotence.[4] The use of PRP methodology in the skin care and aesthetic medicine may prove as a revolutionary step of dermatological treatment in the near future. How-ever, the available published data is low in count to support this evidence.[5] Injection of PRP is easy, pocket friendly and convenient mode of method for treating this alopecia which is ensuring great patient overall satisfaction with few documented side-effects.[6] Rationale of this study is to assess the outcome of autologous PRP for the treatment of androgenetic alopecia in male patients in local population. This will improve the way of doing our practice and will also help to update the local management guidelines.

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## Objective

To assess the outcome of autologous platelet rich plasma for managing the male patients of androgenetic alopecia.

## Methods

This study was conducted at department of dermatology, Lahore general hospital, Lahore. 61 subjects were segregated from outpatient department on the basis of inclusion and exclusion criterion and enrolled in the study after informing them and getting their written consent forms. Name, age and duration of Androgenetic Alopecia of each patient was recorded on properly formulated proforma. Calculation of the sample size was done by consi-dering 95% confidence level, 12% margin of error and the estimated percentage of hair pulled out reduc-tion as 65% on hair pull test[7]. Study Design was Descriptive case series. Duration was 6 months (16-08-2017 to 17-02-2018) and non probability conse-cutive sampling Technique was used.

**Inclusion** criteria listed as patients of male gender between ages 18-60 years with mild to moderate androgenetic alopecia with Hmilton-Norwood score 1-5. **Exclusion** criteria as laid as; any patient not ensuring for follow check-ups, on the topical treatment (minoxidil, prostaglandin analogues, retinoids, and corticosteroid) or systemic treatments for Androgenetic Alopecia (such as finasteride, dutasteride, and antiandrogens) since last two months, patients with supressed immunity (malignancy, chemotherapy, steroid therapy), other dermatological disorders involving hair and skin of head, autoimmune disorders, hematologic disorders, platelet dysfunction syndrome and subjects under anticoagulation therapy (on medical record), active infection involving scalp and receiving drugs causing hair loss (retinoids, antidepressants, oral contraceptives, anticoagulants, lipid lowering drugs, B-blockers,ACE inhibitors) were excluded from study. PRP was carefully prepared by method of double spin and $CaCl_2$ poured to mixture in order to stimulate platelets. Affected area of scalp was sterilized with pyodine solution and anaesthetic agent was applied to the specified area which was going to be treated. PRP (0.5-01 ml/$cm^2$) was shifted to a one ml sterilized syringe with a thirty gauge needle and administered into the selected areas of the scalp using Nappage technique in a depth of 1.5-2.5mm of skin. Our proto-col included 3 treatment sittings after every 4 weeks. At each visit the number of hair monitored by derma-toscope (3Gen DermLite) using maximum magnifi-cation(10x) as standard and by gross photographs. Hair number in one dermatoscopic field using maxi-mum magnification was counted at each visit. Stren-gth of hair was assessed using hair pull test with more than 10% of hairs removed in a plucked bunch of hair considered positive. SPSS Version-21 was used to analyse data. The quan-titative variables i.e. age, number of hair and duration of androgenetic alopecia was presented as Mean and Standard deviation. Data was stratified for age, dura-tion of Androgenetic Alopecia and stage of alopecia to address the effect modifiers. In order to check the study significance, post stratification Independent t-Test was applied taking P-value ≤ 0.05 as significant.

## Results

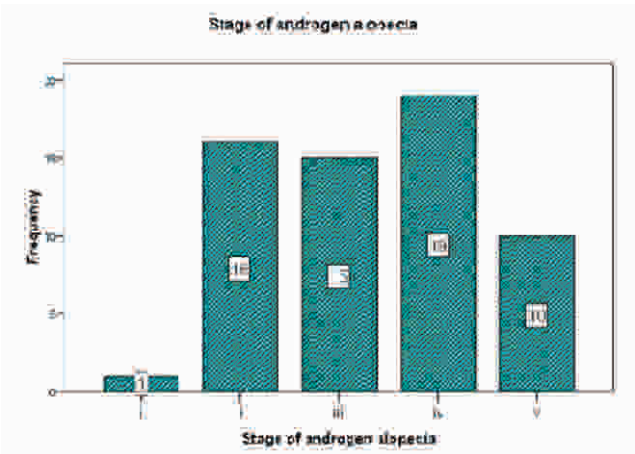
The mean age of patients was 42.67±8.63 years. Mean number of hair before treatment was 21.50± 4.57 per dermatoscopic field at maximum magnification and it was 78.10±16.24 post treatment (P-value <0.05) (Table 1). Mean duration of disease was 10.01 ± 3.46 months. Majority of patients were in stage ii, iii, and stage iv i.e. 16(26.2%) 15(24.6%) and 19(31.1 %) respectively. In stage i and v there were 1(1.6%) and 10(16.4%) patients respectively( Graph#1). Post treatment Hair pull test was negative in majority of the cases 48(78.7%) and mean hair pull score was significantly different pre (90.57) and post treatment (78.45) with p-value <0.05(Table#1). When data was stratified for the age it was noted that 19(76%) patients were in the age groups of 18-40 years and 29(80.6%) in 41-60 years age groups was having negative hair pull test after treatment. There was no significant impact of the duration of the disease for the negative hair pull test and stages of androgen alopecia (Table2). Figure#1 shows pre and post treatment dermatoscopic and gross photographs of few patients.

**Table 1:** *Descriptive statistics of Mean number of hair per dermatoscopic field(DF), Hair Pull Test status and Mean Hair Pull Score*

| | Number Of Hairs/DF | Hair Pull Test | | |
|---|---|---|---|---|
| | Mean | Frequency(%) | | Mean Score (sd) |
| | | Positive | Negative | |
| Pre Treatment | 21.50±4.57 | 38(62%) | 23(38%) | 90.57(6.11) |
| Post Treatment | 78.10±16.2 | 13(21%) | 48(78%) | 78.45(5.32) |
| P.Value= 0.001 | | | | |

**Table 2:** *Stratification of the Hair Pull Test with Respect to different Baselines Parameters*

| | | Hair Pull Test | | P-value |
|---|---|---|---|---|
| | | Positive | Negative | |
| **Age** | 18-40 year | 6(24%) | 19(76%) | 0.75 |
| | 41-60 year | 7(19.4%) | 29(80.6%) | |
| **Duration of Disease** | 1-6 Month | 1(8.3%) | 11(91.7%) | 0.43 |
| | >6 month | 12(24.5%) | 37(75.5%) | |
| **Group of Androgen Alopecia** | I-iii | 7(21.9%) | 25(78.1%) | 0.98 |
| | > iii | 6(20.7%) | 23(79.3%) | |




**Graph#1:** *Presentation of the Stages of the Androgen Alopecia in the Study Subjects*

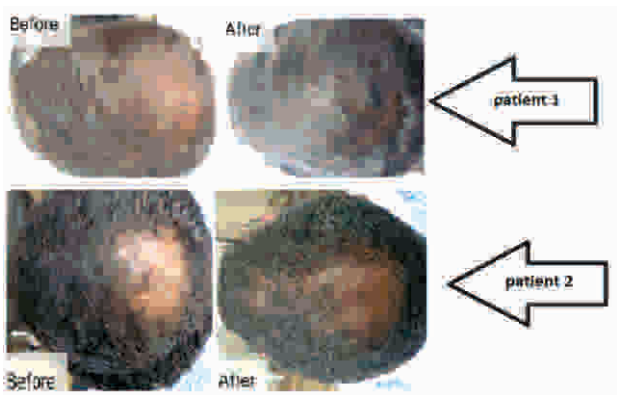
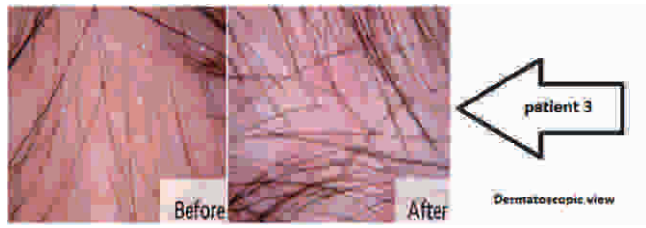



**Figure 1#** *Dermatoscopic and Gross photoghraphs of study population*

## Discussion

Platelet-rich plasma (PRP) is considered as a novelty in the field of biotechnology. It is a combination of cell-based therapy and tissue engineering. This therapy outlines an autologous preparation of plasma with distilled platelets. This mixture of platelet has a magical power to regenerate and repair the damaged body sites as it contain numerous factors of growth and cytokines. [8] Many medical specialities are getting benefits from this new technique including periodontal therapy, maxillofacial surgery,




orthopedics and sports medi-cine. For few recent years, dermatologist are laying their hands on this new modularity, particularly in relieving acne scars, fat grafting, wound healing and hair regrowth.[9] Researches has explored many beneficial outcomes of PRP in adipose precursor cell proliferation, wound healing, differentiation of cell and forming new blood vessels. A normal blood sample contains a proportion of around 93% red blood cells, 6% platelets and 1% white blood cells. However, what scientist do while preparing PRP, the reverse this proportion i.e. a 94% concentration of platelets and a 5% concentration of RBCs by centrifugation and it's the principal for making this incredible mixture. The exceptional high concentration of useful growth factors and cytokines in PRP basically make this mixture the most suitable selection for facilitating tissue rejuvenation and healing. The concentration of platelets with tissue reparative efficacy is found to be nearly 1 million platelets/µl, which is ~5 times the normal concentration of plate-lets.[10] Losing a body part, of any proportion, does have a negative impact on one's mind but especially losing hair means losing a chunk of your integrated perso-nality and it does have a great impact on one's psy-chological health. Unfortunate is that, this androgen dependent hair loss have very few treatment option including topical minoxidil and oral fenasteride (appoved by FDA) having many side effects,[11] making it more challenging for dermatologists to treat it.

PRP has already succeeded in drawing attention of many physicians and surgeons all around the world such as in plastic surgery, orthopaedic surgery and cardiac surgery because of its potential use in skin rejuvenating effects, rapid healing, reduced infection rate and decreased chance of hypertrophic keloids and scars.[12,13]

Certain growth factors are found to activate the proliferative phase and trans-differentiation of hair and stem cells and produce new follicular units. Papilla cells get proliferated under the influence of basic fibroblast growth factor (bFGF) in vitro and thereby

plays a key role in elongating hair shaft.[14] Our research work has reported that after performing three sessions of PRP the hair pull test becomes negative. This outcome is similar to the outcome of a study done by Bestiet al.[15] Who also have observed improvement in hair volume and coverage but according to our study, only mode-rate improvement in hair volume and coverage was observed by using dermatoscope to monitor it. In the previous studies, One of the studies show that baseline mean hair count 89.6±20.9 and at 3 months mean hair count was 123.2±33.7.[16] We have a little variation in the results of this study as compared to the previous study due to generalizability of the study population. A specific population which was studied previously had a pattern of alopecia while in our study it was advantage that we have to deal with the general population. Another study done by V.cervellietal showed baseline mean hair count 103.6±30.7 and at end of 3 months a mean increase was 121.6±34.1[7]. One study showed 100% positive hair pull test before treatment and pull test was negative in 81.81% at end of treatment and There is a marked increase of usual number of 71 hair follicles to 93 hair follicle units.[2,6] As sample size is an important factor for the validity of the results so the sample size in this study was high as compared to the previous studies.[6,7,16] Previously most of the studies were conducted on a sample size of less than 30 cases but in our study the sample size was 61 cases that is the advantage of this study. These findings of our are further supported by the results of a case-control study which states that there's a notable increase in hair number per $cm^2$ after treating subjects with PRP injection as compared to their controls (mean difference [MD] 14.38, 95% confidence interval [CI] 6.38–22.38, $P < 0.001$). Likewise, a crucial growth of hair thickness cross section per $10^{-4}$ $mm^2$ (MD 0.22, 95% CI 0.07–0.38, $P = 0.005$) added another plus point to PRP treated group. However study concluded that there isn't significant positive effect of PRP injection on under-study subjects, in terms of getting benefits in increase hair number (MD 18.79%, 95% CI − 8.50–46.08, P = 0.18), neither with hair thickness (MD 32.63%, 95% CI − 16.23–81.48, P = 0.19) which favours the results of current study.[17] In previous study lesser time was given and a booster dose was administered at the last injection which has led to biasness and changed results. But in our study almost same concentration of the plasma is administered so that actual results could be obtained. There's a published study who reported that their subjects have shown good results in term of increased hair density at six weeks (154.80±34.39 hairs per $cm^2$), at three months (170.70±37.81 hairs per $cm^2$) and at six months (156.23±37.75 hairs per $cm^2$), we did not have so long follow up, but the results were similar.[18] As it was a meta-analysis so it further strengthens the results of our study. Hence, on the basis of this study the PRP treatment could be a method of the choice in androgenic alopecia.

At present, we scientist have very limited published data regarding PRP's probable outcomes on hair growth .This study has added to that limited data. But still it should be conducted on a larger scale with involvement of the multiple hospitals/institutions. Moreover, in this study effects of the environment and hygienic conditions are not evaluated so further studies are needed.

## Conclusion

Our study hereby concludes that treating the patients of androgenic alopecia with PRP injectable comes out to be an effortless, pocket-friendly and practicable treatment modality for hair loss and it appear to be a novel valuable adjuvant treatment option for alopecia. With adequate published data as evidence for its effectiveness, this treatment option is still rooting itself in medical sciences. Clinical trials are fewer but due to its easy going approach and availability, it's an outstanding treatment option for worldwide dermatologists.

## Authors Contribution

**NN:** Research, Statistics, compliation of paper, practical work
**SS:** Supervisor, compliation of paper
**SA:** Supervisor, arrangement of all gadgets, selection of topic
**TK:** Supervisory Role

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# Comparison Between Tidal Volume and Vital Capacity Breathing Techniques of Preoxygenation in Patients with Ineffective Facemask Seal

**Farah Arshad,[1] Hina Nabi,[2] Fareeda Sohail,[3] Anum Anwar[4]**

**Abstract**

**Objective:** The purpose of this research was to compare the mean hemoglobin oxygen de-saturation time by using tidal volume breathing technique for three minutes and eight vital capacity breathing technique for pre-oxygenation in patients with ineffective face mask seal.

**Methods:** This study included 60 patients with beard, moustache, large nasal bridge, facial anomalies, nasogastric tube and edentulous patients. They were randomized into 2 groups after achieving documented informed consent. Group-A was preoxygenated with TV breathing technique for three minutes at an oxygen flow of 10 litres per minute. Whereas, Group-B was preoxygenated with eight VC breaths for one minute at an oxygen flow of 10 litres per minute.

**Results:** The age of the participants varied from 22 years to 65 years with an average of 44.63 ± 10.03 years. There were 29 (48.3%) male and 31 (51.7%) female patients in the research group. Both the groups were comparable in respect of mean age (p=0.839) and gender distribution (p = 0.796). The mean hemoglobin oxygen desaturation time was considerably longer in VC breathing group (6.77±1.10 vs. 3.43±.50 minutes; p=0.000) in contrast to TV breathing group regardless of age and gender of patients.

**Conclusion:** The mean hemoglobin oxygen desaturation time was substancially longer in vital capacity breathing group (6.77 ± 1.10 vs. 3.43 ± .50 minutes; p = 0.000) in contrast to tidal volume breathing group regardless of patient's age and gender in patients with ineffective face mask seal undergoing elective surgery.

**Key Words:** Ineffective Face Mask Seal, Preoxygenation Breathing Techniques, Vital Capacity, Tidal Volume, Mean Hemoglobin Oxygen Desaturation Time

## Introduction

Preoxygenation with 100% oxygren is accomplished prior to general anesthesia is induced. The purpose is to enhance oxygen reserves through displacement of nitrogen from functional residual capacity of lungs, thus preventing arterial oxygen desaturation and hypoxemia. Inadequate face mask seal causes a leak that leads to inflow of atmospheric air into the circuit. The frequently performed methods for preoxygenation are inhalation of 100% oxygen at normal tidal volume (TV) for three to five minutes or eight full deep vital capacity (VC) breaths in one minute. The available literature declares VC technique to be preferable to TV technique of preoxygenation in terms of mean hemoglobin oxygen desaturation time. However, not enough evidence is published locally. So TV technique for 3 min will be compared with 8 VC breathing technique for 1 min at an oxygen flow of upto 10 L/min and the measuring parameter for both techniques would be de-saturation time.

## Methods

The sample size was approximated as 60 cases by using 95% confidence level, 80% power of test with an expected mean time for haemoglobin oxygen desaturation as 3.73 ± 0.76 minutes in TV group and 5.21 ± 0.96 minutes in VC group11. Non-Probability, Purposive Sampling technique was used for selection of 60 patients belonging to either gender, between 18 to 65 years of age, ASA I or II, with Mallampatti class of I or II, scheduled for elective surgery with ineffective face mask seal in patients with beard, moustaches, facial anomalies, nasogastric tube, large nasal bridge and edentulous patients. But the patients who

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had cardiac disease, pulmonary disease, obesity, smoking history, pregnancy and who denied written informed consent were not incorporated in this research.

After endorsement from the local ethical committee all 60 participants were randomly catagorized into two groups by using random number table. Patients in group A were advised to breath normally for three minutes and the patients in group B were directed to take 8 deep breaths for 1 minute. All the patients were given anxiolytics with intravenous nalbuphine (0.1 mg/kg) and midazolam (2mg) prior to induction. Monitoring of peripheral oxygen saturation was done by pulse oximetry. After either technique of preoxygenation, induction for general anesthesia was initiated by injecting propofol (2mg/kg) and succinylcholine (1.5mg/kg) intravenously. Oxygenation via face mask was carried on until spontaneous breathing was ceased within 30 seconds after the injection of succinylcholine. The endotracheal tube was placed in trachea under direct vision and then initial end of the ETT was left open to room air. The time taken by hemoglobin oxygen saturation to fall from 100% to 95% was noted and then at this point ETT was attached to ventilator for positive pressure ventilation after the tube position was confirmed.

The entire statistical numbers and figures were recorded and scrutinized by using SPSS version 20.

- Numerical variables i.e age and time of desaturation have been presented by mean ± SD. Independent sample t-test been used to compare mean time of desaturation between the two groups taking $p \leq 0.05$ as significant.
- Categorical variables i.e. sex has been presented as frequency and percentage.
- Data has been stratified for age and sex to deal with effect modifiers. Post-stratification independent sample t-test has been used taking $p \leq 0.05$ as significant.

## Results

The age of the participants varied between 22 to 65 years with an average of 44.63 ± 10.03 years. There were twenty nine (48.3%) male and thirty one (51.7%) female patients in these research groups as demonstrated in Table 1. The two groups were comparable in respect of mean age ($p = 0.839$) and sex distribution ($p = 0.796$), illustrated in Table 2.

The mean hemoglobin oxygen desaturation time was considerably longer in VC breathing group (6.77 ± 1.10 vs 3.43 ± 0.50 minutes; $p = 0.000$) as compared to TV breathing group. This difference was appreciated across all age and sex groups as depicted in Table 3.

## Discussion

Inadequate face mask seal is the most frequent reason of not attaining a greatest alveolar oxygen concentration during preoxygenation prior to induction of general anesthesia that leads to inflow of atmospheric air into the circuit and decreases the concentration of

**Table 1:** *Baseline features of Study Population*

| Features | Participants |
|---|---|
| | n=60 |
| **Age (years)** | 44.63±10.03 (22 - 65) |
| **Sex** | |
| • **Male** | 29 (48.3%) |
| • **Female** | 31 (51.7%) |

**Table 2:** *Comparison of Baseline Features of Study Groups*

| Features | TVB (n=30) | VCB (n=30) | P value |
|---|---|---|---|
| **Age (years)** | 44.37±10.12 | 44.90±10.10 | 0.839 |
| **Sex** | | | |
| • **Male** | 14 (46.7%) | 15 (50.0%) | |
| • **Female** | | | 0.796 |
| | 16 (53.3%) | 15 (50.0%) | |

Independent sample t-test, Chi-square test, $p>0.05$
TVB: Tidal Volume Breathing
VCB: Vital Capacity Breathing

**Table 3:** *Comparison of Mean Hemoglobin Oxygen Desaturation Time (minutes) between Study Groups*

| Features | TVB (n=30) | VCB (n=30) | P value |
|---|---|---|---|
| **Overall** | 3.43±0.50 | 6.77±1.10 | 0.000* |
| **Age Groups** | | | |
| • **22-35 years** | 3.40±0.55 | 6.80±0.84 | 0.000* |
| • **36-50 years** | 3.44±0.51 | 6.76±1.20 | 0.000* |
| • 51-65 years | 3.43±0.54 | 6.75±1.17 | 0.000* |
| **Sex** | | | |
| • Male | 3.43±0.51 | 6.73±1.16 | 0.000* |
| • Female | 3.44±0.51 | 6.80±1.08 | 0.000* |

Independent sample t-test
* observed difference were statistically significant
TVB: Tidal Volume Breathing
VCB: Vital Capacity Breathing

oxygen present. The frequently performed methods for preoxygenation are inhalation of 100% oxygen at normal tidal volume (TV) for three to five minutes and eight full deep vital capacity (VC) breaths in one minute. The available literature declares VC technique to be preferable to TV technique of preoxygenation in terms of mean hemoglobin oxygen desaturation time. However, not enough evidence was available in locally published research. The aim of this research was to compare the mean time for hemoglobin oxygen desaturation by using tidal volume (TV) breathing technique for three minutes and 8 vital capacity (VC) breathing technique for pre-oxygenation in patients with ineffective face mask seal. A randomized controlled trial was carried out at Department of Anesthesiology and Intensive Care, Sir Ganga Ram Hospital, Lahore, six months after the acceptance of synopsis from 14th October, 2014 to 13th April, 2015. This study included 60 patients belonging to both genders of age between 18 to 65 years scheduled for elective surgery with inadequate face mask seal randomly divided in group A and group B. Group - A was preoxygenated by tidal volume (TV) breathing technique for three minutes at an oxygen flow of 10 litres per minute. However, Group B was preoxygenated with eight vital capacity (VC) breaths for 1 minute with oxygen flow of 10 litres per minute. A documented informed consent was achieved from every participant. The age of the participants varied between 22 to 65 years with an average of 44.63±10.03 years. An equivalent mean age has been stated previously by Rajan et al. in 2015 (47.90±12.17 years)[102], Kundra et al. in 2013 (40.40 ±12.40 years)[2], Ramkumar et al. in 2011 (46.20± 13.20 years)[5], Kang et al. in 2010 (42.20±2.30 years)[3], Delay et al. in 2008 (42.90±11.60 years)[8] and Singh et al. in 2006 (41.40±7.39 years)[103]. However, a much lower mean age of 29±5 years has also been noted by Taha et al. in 20094. There were twenty nine (48.3%) male and thirty one (51.7%) female participants in these research groups. A same female preponderance has also been pointed out by Kang et al. in 2010 (46.67% vs 53.33%)[3] and Delay et al. in 2008 (21.43 % vs 78.57%)[8]. However, an equal gender distribution has been noticed by Taha et al. in 2009 (50.0% vs 50.0%)[4]. Moreover, a male prevalance was observed by Ramkumar et al. in 2011 (53.33% vs 46.67%)[5]. The two groups were comparable in respect of mean age ($p = 0.839$) and sex distribution ($p = 0.796$). Thus there was no inherent bias among the research groups. The mean hemoglobin oxygen desaturation time was remarkably greater in vital capacity (VC) breathing group ($6.77 \pm 1.10$ vs $3.43 \pm 0.50$ minutes; $p = 0.000$) in comparison with tidal volume (TV) breathing group. This variation was appreciated among all age and sex groups. Our outcome is close to that of Rajan et al. in 2015 ($6.87 \pm 1.78$ vs $3.47 \pm 0.38$ minutes; $p < 0.001$)[102]. A similar considerably longer mean hemoglobin oxygen desaturation time has also been documented in vital capacity (VC) breathing by Singh et al. in 2006 ($4.70 \pm 0.27$ vs $3.70 \pm 0.44$ minutes; $p < 0.005$)[103] and Baraka et al. in 1999 ($5.21 \pm 0.96$ vs $3.73 \pm 0.76$ minutes; $p \leq 0.05$)[11] in contrast to tidal volume (TV) breathing technique. This research is the initial and earliest of its kind in local population and has noted that vital capacity (VC) breathing technique of preoxygenation is preferable to tidal volume (TV) breathing in respect of considerably longer mean hemoglobin oxygen desaturation time ($6.77 \pm 1.10$ vs $3.43 \pm 0.50$ minutes; $p = 0.000$) regardless of patient's age and gender in patients with inadequate face mask seal scheduled for elective surgery. The findings of this study thus recommend and encourage the use of Vital Capacity breathing technique for preoxygenation in patients with ineffective face mask seal going through elective surgery as it provides remarkably longer mean hemoglobin oxygen desaturation time deferring the occurence of arterial oxygen desaturation and hypoxemia during the apneic period after the general anesthesia is induced.

## Conclusion

The mean hemoglobin oxygen desaturation time was considerably longer in vital capacity (VC) breathing group ($6.77 \pm 1.10$ vs $3.43 \pm 0.50$ minutes; $p = 0.000$) in comparison to tidal volume (TV) breathing group regardless of patient's age and gender in patients with ineffective face mask seal going through elective surgery.

## Authors Contribution

**AF:** Concept, Conduct of study, Manuscript preparation, editing, Literature review
**NH:** Manuscript Preparation, Proof Reading, Critical Review
**SF:** Statistical Analysis of Data
**AA, BZ:** Data Collection

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# Clinical Audit of Obstetrical Hysterectomies for a Period of One Year in A Tertiary Care Hospital

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**Abstract**

**Objectives:** To audit the obstetric hysterectomies in a tertiary care hospital during one year.

**Methods:** It was an observational retrospective study design, where all the pregnant women were assessed for feto-maternal outcomes, indications and complications for peripartum hysterectomy. The records were retrieved from Jan 2015 to Dec 2015 by using hospital record system. The study duration was of one year. The venue of the study was Lahore General hospital, Lahore. The exclusion criteria included all unmarried women, women with chronic kidney disease or renal failure, past surgical history of heart disease, whereas all the women who delivered in hospital, private clinic or at home after atleast 28 weeks of gestational age and experience hysterectomy at the time of delivery or after delivery in the puerperium, were included in the study.

**Results:** The data over 32 women were retrieved from the hospital record system. The mean age of the women was 30.34+2.23 with range 26-34. The average number of parity was 3 of all females. The range of parity was 2 to 7. The average gestational age was 36.18 weeks. All the deliveries were done by cesarean section whereas 4 (12.5%) were elective and 28 (87.5%) were with emergency indications. 13 (40.6%) of the deliveries were in private clinic, 9 (28.1%) were done by LHV/ mid wife, 5(15.6%) were in private hospitals, 4(12.5%) were in LGH and only 1(3.1%) was at home. 18(56.3%) of the women were having at least one abortion in previous history.

**Conclusion:** We concluded that emergency peripartum hysterectomy is very vital procedure that saves lives and manage life threatening obstetrical hemorrhage when other methods failed to control it.The major indications for emergency peripartum hysterectomy were placental abruption, placenta praevia/accrete, uterine atony and ruptured uterus.

**Key Words:** Uterine artery embolization, Emergency peripartum hysterectomy, maternal morbidity and mortality, healthcare providers

## Introduction

The surgical removal of the uterus either at the time of cesarean section or subsequent vaginal deli-very, or within the puerperium period is known as Emergency peripartum hysterectomy. Mainly it is performed due to insistent and life threatening obstetric hemorrhage. Emergency peripartum hysterectomy can be rightly categorized as a near miss event. This is very vital to highlight the events as it explains the standards of healthcare providers and also assist to reduce the maternal morbidity and mortality. In 1876, the first cesarean hysterectomy was termed by Eduardo Porro of Milan for PPH resulting live baby and mother.[1] The leading cause is uterine atony (UA) in developing countries and abnormal placentation in developed countries. It is published and observed a change of trend in epidemiology in several studies.[2] Previously uterine atony and rupture were major indications of emergency peripartum hysterectomy which are now replaced by abnormal placentation that is caused by high cesarean section rate all over the world. Community based use of oxytocin, misoprostol, condom

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catheter balloon, and non-inflatable anti-shock garments for the hypovolemic shock management, B-lynch sutures, uterine artery and internal iliac artey ligation which termed as conservative medical and surgical methods has been supported effectively to control and manage the obstetric hemorrhage.[3] An option of uterine artery embolization was possible due to innovation in interventional radiology.[4] An increased risk of abnormal placentation and emergency peripartum hysterectomy was connected in various studies with previous uterine scar.[2] Literature review showed that the incidence of emergency peripartum hysterectomy ranges between 0.24 to 5.09 per thousand deliveries worldwide.[5] In comparison to non-obstetric morbidity and mortality, peripartum hysterectomy being an unplanned and emergency is associated with significant high rates.[6] The perfection in traditional methos of postpartum hemorrhage (PPH) and blood transfusion facilities has improved the outcome.[4] The main aim of study was to audit the obstetric hysterectomies in a tertiary care hospital during one year of time.

## Methods

It is an observational retrospective study design, where all the pregnant women were assessed for feto-maternal outcomes, indications and complications for peripartum hysterectomy. The records were retrieved from Jan 2015 to Dec 2015 by using hospital record system. The study duration was of one year. The venue of the study was Lahore General hospital,Lahore. The exclusion criteria include all unmarried women, women with chronic kidney disease or renal failure, past surgical history of heart disease whereas all the women who delivered in hospital, private clinic or at home after at-least 28 weeks of gestational age and experienced hysterectomy at time of delivery or afterwards within the defined period of puerperium, were included in the study. The retrieved information contained demographics along with diagnostic history of all the pregnant women. Ethical Committee of the hospital approved the study.

Statistical analysis: The collected data was electronically stored & analyzed by using SPSS version 20. Descriptive statistics were applied to calculate mean and standard deviation. Frequency distribution and percentages were calculated for qualitative variables like indication of caesarean section etc . A P- values less than 0.05 was considered statistically significant.

## Results

The data of 32 women were retrieved from the hospital record system. The mean age of the women was 30.34+2.23 with range 26-34. The average number of parity was 3 of all females. The range of parity was 2 to 7. The average gestational age was 36.18 weeks. All deliveries were done by cesarean section whereas 4 (12.5%) were elective and 28 (87.5 %) were with emergency indications. The detailed summary for previous scar uterus is given below in figure.

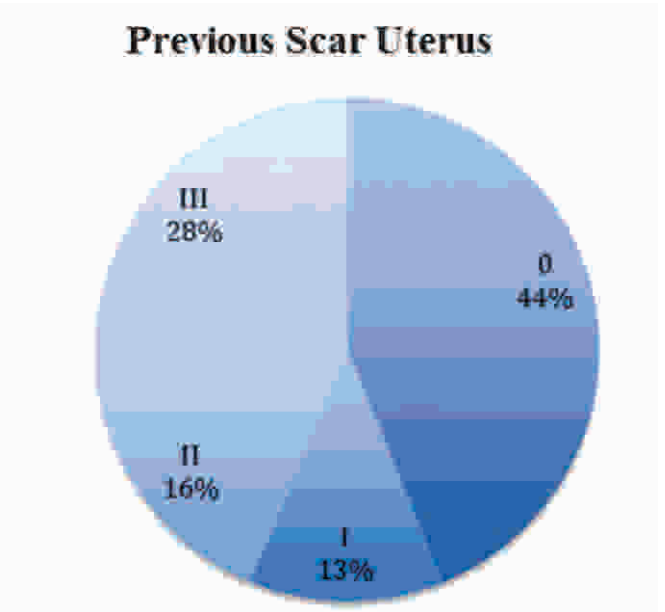


**Figure :** *Summary of Previous Scar Uterus*

13 (40.6%) of the deliveries were in private clinic, 9 (28.1%) were done by LHV/ mid wife, 5(15.6%) were in private hospitals, 4(12.5%) were in LGH and only 1(3.1%) was at home. 18(56.3%) of the women were having at least one abortion in previous history.

The complications observed in all mothers were summarized in table 1.

## Discussion

The study was planned to audit the obstetrical hysterectomies at a tertiary health care level. We not only report baseline characteristic for the patients but also the indication for hysterectomies along with its complications arisen as well. Inspite of advancement in surgery and medicine fields, PPH remains the prominent reason of maternal morbidity and mortality. To treat the life threatening obstetric hemorrhage, emergency peripartum hysterectomy is performed, because controlling with conventional methods

**Table 1:** *Summary of the complications.*

| Complications | |
|---|---|
| Hemorrhage | 29(90.6%) |
| DIC | 8(25.0%) |
| Bladder Injury | 11(34.4%) |
| Intestinal Injury | 1(3.1%) |
| Ureteric Injury | 1(3.1%) |
| Maternal Injury | 1(3.1%) |
| DVT | 1(3.1%) |
| Maternal death | 3(9.4%) |
| Hemorrhage | 6(18.8%) |
| Reopening due to hemorrhage | 1(3.1%) |
| Wound infection/ sepsis | 16(50.0%) |
| Pelvic Abscess | 1(3.1%) |

is difficult. The reported incidence of emergency peripartum hysterectomy ranges between 0.24 and 5.09 per 1000 deliveries.[5] The incidence reported in our study is supported by the above literature and other published studies.[7-8] We observed in our study that majority of the cases were with poor access to the healthcare. We also reported in our study the major indications of emergency peripartum hysterectomy which were abnormal placental localization, uterine atony and uterine rupture. We also observed in our findings the cases with adherent placentation; the percentages were supported by other published studies[8-9]. Due to previous history of cesarean section, adherent placentation become among one of the commonest indications. The study held by Kwee et al.,testified that both previous cesarean section and cesarean section in key pregnancy were associated with significant increased risk of emergency peripartum hysterectomy.[2] The effort to discrete the adhe-rent placenta can bring a massive hemorrhage. A timely decision to go with hysterectomy can lead to improved outcomes.[2] We reported in our study the majority of the cases with multipara who underwent emergency peripartum hysterectomy. This finding is supported with other previously published studies.[10-11] Among hysterectomy performed the majority of type was subtotal hysterectomy. The percentages available in literature ranges among 53-80%.[11] It is presumed that this type of hysterectomy involved with less blood loss, lessening the operative time and less complication in comparison to other types. Our study reported the risk factors like multiparity, placenta previa, previous cesarean section, and cesarean in index pregnancy. Other published studies available with similar risk factors.[2,12] We also have observed three maternal deaths in our study as a complication. Other emergency peripartum hysterectomy complications including mortality were studied and analyzed by Machado LS et al,[1] Contrary to our study he claimed the maternal morbidity ranging between 26 to 31% and the commonest was blood transfusion requirement and urinary tract injury.

## Conclusion

We concluded that emergency peripartum hysterectomy is very vital procedure that saves lives and manage life threatening obstetrical hemorrhage when other methods failed to control. The major indications for emergency peripartum hysterectomy were the abnormal placental localization, uterine atony and uterine injury or rupture.

## Author's Contribution

LF: Data analysis, computing, writing
IS, AH: Data collection
MS: Computing, interpretation of data
JZ: Data collection

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# Comparison of Ovulation Induction with Letrozole with Metformin Versus Letrozole Alone in Females Presenting with Polycystic Ovarian Syndrome

**Zubda Aiman,[1] Amna Khanam,[2] Mahliqa Maqsood,[3] Mehwish ayyaz,[4] Alia,[5] Tayyaba Kanwal[6]**

**Abstract**

**Objective:** To compare the frequency of Ovulation Induction after administration of Letrozole with metformin versus Letrozole alone in females presenting with Polycystic Ovarian Syndrome

**Methods:** This Randomized Controlled Trial was done in unit 5 of Lady Aitchison Hospital Lahore for 6 months. Total 200 females fulfilling the inclusion criteria were recruited from OPD. Lottery method was used for randomization of study subjects. Females in group A were given Letrozole 2.5mg once a day for five days (from third to seventh day)of the cycle for three consecutive months and metformin 1500mg (500mg 3 times a day) daily for three months, while females in group B were given Letrozole 2.5mg once a day for five days (from third to seventh day) le for three consecutive months. Then they were followed up in OPD for 3 cycles. In all 3 cycles TVS was done on day 12 to access the number of follicles and to measure the size of largest follicle, and on day 21 of cycle progesterone level will be assessed for confirmation of ovulation induction. The data was entered and analyzed through SPSS version 20. Mean and standard deviation was calculated for age and BMI. Frequency and percentage was calculated for Ovulation induction. Both groups were compared by using chi-square test taking p-value<0.05 as significant. Data was stratified for BMI (Normal, overweight and Obese).After stratification chi-square test was applied keeping a p value $\leq$0.05 as significant.

**Results:** In Group-A mean age of women was 28.18±6.58 years. In Group-B mean age of women was 27.08±5.15 years. In Group-A ovulation induction rate was much higher as compared to that of Group-B women. i.e. (89% vs. 60%). p-value=0.000. Ovulation induction rate was significantly higher with Letrozole+ Metformin in women who were having normal BMI, overweight & obese as compared to that of Letrozole alone.

**Conclusion:** Letrozole with metformin is more effective for the ovulation Induction females presenting with polycystic ovarian Syndrome as compared to letrozole alone.()

**Key Words:** Polycystic Ovarian Syndrome, Management, Ovulation Induction, Letrozole, Metformin

## Introduction

PCO is commonest hormonal disorder of females in reproductive age group and it has very high prevalence.[1] PCOS is the leading cause of anovulatory subfertility and it accounts for 70% of subfertility cases related to ovulatory disorder. 5-10% women of reproductive age group are affected by PCOS.[4]

The cause of this multifactorial condition is not comp-letely known and its phenotype expression varies. Clomiphene citrate (CC) is frequently used drug for ovulation induction. But one fourth of women do not give adequate response to this drug .These resistant cases are typically treated with administration of gonadotrophins but there are more chances of multi-fetal gestations and hyperstimulation of ovaries.[5]

Recently it has been found that Letrozole makes endometrium more receptive for implantation in addition to increasing ovulation rate therefore chances of success-ful pregnancy have increased in women presenting with this disorder.[6] Additional benefits of

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Letrozole are decreased number of multifetal gestations and less androgenic side effects and decreased cases of ovarian hyperstimulation so less frequent monitoring is requi-red as compared to gonadotrophins.[7]

PCOS is heterogenous disorder involving genetic, hormonal and environmental factors. No definitive treatment is available for this condition. Weight reduction and lifestyle modification is mainstay of the treatment.[8] First case of PCOS was recognised in 1721 in Italy.

Studies in different countries show prevalence of PCOS using Rotterdam criteria as follows, 6.3% in Srilanka, 2% in south China,5 % in Thailand, 8% in UK and 4% in USA(there is no difference among black and white women). [2]

Literature has reported that letrozole is effective in ovulation induction but there are conflicting results reported in literature. Moreover, there are no study conducted which compares letrozole in combination with metformin and letrozole alone and local magnitudes are also missing. Through this study we wanted to get local magnitudes and results which can be applicable and on the basis of which we can implement the use of letrozole with metformin for management of PCO instead of letrozole alone. Objective of this study is to compare the frequency of Ovulation Induction after administration of Letrozole with metformin versus Letrozole alone in females presenting with Polycystic Ovarian Syndrome. Hypothesis of the study was that there is some difference in frequency of Ovulation Induction with Letrozole with metformin versus letrozole alone in females presenting with Polycystic Ovarian Syndrome.

## Methods

This randomized controlled trial was done in Unit 5 of Lady Aitchison Hospital in 6 months time. Total of 200 cases (100 cases in each group was calculated with 80% power of test, 5% level of significance and taking expected percentage of ovulation induction i.e. 90.57% with Letrozole with metformin and 60.78% with Letrozole alone in females presenting with PCOs) were enrolled by Non-Probability, consecutive Sampling. Women age 18-39 years, BMI <35, Infertility due to anovulation, Polycystic Ovarian Syndrome (fulfilling two of the following three criteria atleast:Oligomenorrhea / amenorrhea, Hyper androgenaemia (testosterone≥ 2.5nmol/l) or free androgen index ≥ 5 or clinical evidence (acne/hirsutism), Ultrasound evidence of Polycystic Ovarian Syndrome (either ≥ 12 follicle measuring 2-9mm in dia meter or ovarian volume > 10ml)), Normal husband semen analysis (sperm count 20 million/ml, 60% are motile and 30% have normal morphology), Patency of both fallopian tubes by hysteroscopy and laproscopy, and No recent treatment within six months for induction of ovulation on history were included. Ovulation induction was measured as production of follicles confirmed on Ultrasonographic findings (follicles size >18mm at 12 day of menstruation) and day 21 progestrone level>3ng/dl for three cycles, if these findings were achieved then labelled as ovulation induction. Women with Uterine pathology by ultrasound, Hyperprolactinemia (<500 mIU/l), Hyperthyroidism (TSH<0.5Uu/ml)/ Hypothyroidism (TSH>6Uu/ml), FSH > 9mIU/mn (during early follicular phase), Previous surgery related to genital tract, Impaired hepatic (serum bilirubin level>2mg/dl)/ impaired renal functions (serum creatinine>1mg/dl), Diabetes Miletus / BSR > 140mg/dl were excluded.

After taking permission from instituitional review board/head of department, 200 females who are fit in the inclusion criteria were recruited from Outpatient department of Lady Aitchison Hospital Lahore. Informed consent and personal information (name, age, BMI and contact) was obtained. Lottery method was used for randomization. Females of both groups were counseled about dietary modification and encouraged to do brisk walk for 30 min twice a day. Females in group A were given Letrozole 2.5mg once a day for five days (from third to seventh day)of cycle for three months and metformin 1500mg (500mg 3 times a day) daily for three months, while females in group B were given Letrozole 2.5mg once a day for five days (from third to seventh day of cycle) for three consecutive months. Then they were followed up in OPD for 3 cycles. In all 3 cycles TVS was done on day 12 to access the number of follicles and to measure the size of largest follicle, and on day 21 of cycle progesterone level will be assessed for confirmation of ovulation induction. All the data was collected according to predesigned proforma. The data was entered and analyzed through SPSS version 20. Mean and standard deviation was calcu-lated for age and BMI.

Frequency and percentage was calculated for Ovulation induction. Both groups were compared by using chi-square test taking p-value <0.05 as significant. Data was stratified for BMI (Normal, overweight and Obese). After stratification chisquare test was applied keeping a p value ≤0.05 as significant.

## Results

In Group-A mean age of women was 28.18±6.58 years. In Group-B mean age of women was 27.08± 5.15 years. In Group-A minimum and maximum age of women was 18 and 39 years while in Group-B this was 18 and 37 years respectively. (Table-1)

In Group-A mean BMI of women was 28.05±2.82. In Group-B mean BMI of women was 27.54±2.54 Kg/ $m^2$. In Group-A minimum and maximum BMI of women was 23 and 32 while in Group-B this was 23 and 31.9 respectively. As per body mass index criteria in Group-A 20(20%) women were having normal BMI, 44(44%) were overweight and 36(36%) were obese. In Group-B 20 (20%) women were having normal weight, 59(59%) were overweight and 21(21%) were obese. In Group-A ovulation induction rate was much higher as compared to that of Group-B women. i.e. (89% vs. 60%). p-value=0.000(Table-2)

Ovulation induction rate was much higher with Letrozzole+ Metformin in women who were having normal BMI, overweight & obese as compared to that of Letrozzole alone i.e. Group-A (Ovulation induction Rate): Normal BMI Women: 95% vs. Group-B: 65% (pvalue = 0.018), Over Weight Women: Group-A:86.4% vs.55.9% (p-value=0.001)& Obese women: Group-A: 88.9% vs. Group-B:66.7% (p-value= 0.040). (Table-3)

**Table 1:** *Age Distribution Of Patients*

| | Group-A | Group-B |
|---|---|---|
| **n** | **100** | **100** |
| **Mean** | 28.18 | 27.08 |
| **SD** | 6.585 | 5.154 |
| **Minimum** | 18 | 18 |
| **Maximum** | 39 | 37 |

Group-A= Letrozole + Metformin
Group-B= Letrozole

**Table 2:** *Ovulation Induction In Study Groups*

| Ovulation Induction | Group-A | Group-B | Total |
|---|---|---|---|
| **Yes** | 89(89%) | 60(60%) | **149** |
| **No** | 11(11%) | 40(40%) | **51** |
| **Total** | 100 | 100 | **200** |

Chi-Square Test= 22.13 p-value= 0.000

**Table 3:** *Ovulation Induction In Study Groups Stratified For Bmi*

| BMI | Ovulation Induction | Group-A | Group-B | p-value |
|---|---|---|---|---|
| **Normal** | **Yes** | 19(95%) | 13(65%) | **0.018** |
| | **No** | 1(5%) | 7(35%) | |
| **Overweight** | **Yes** | 38(86.4%) | 33(55.9%) | **0.001** |
| | **No** | 6(13.6%) | 26(44. 1%) | |
| **Obese** | **Yes** | 32(88.9%) | 14(66.7%) | **0.040** |
| | **No** | 4(11.1%) | 7(33.3%) | |

## Discussion

PCOS is responsible for 75% cases of ovulatory disorders.[9] PCOS-related subfertility is treated appropriately by ovulation induction. Many treatment modalities including medical and surgical options have been employedto treat PCOS linked infertility. Medical options include Metformin, Clomiphene citrate, Letrozole and gonadotrophins.[10] Surgical options include ovarian drilling and wedge resection. Resistant cases to both medical and surgical treatments are offered Intrauterine insemination with stimulated cycle and In-vitro fertilization. [11]

About half of all women with PCOS show some degree of insulin resistance. Hyperinsulinemia ultimately leads to the hyperandrogenism, which is responsible for the clinical manifestation of disease. 77 Metformin increases insulin sensitivity and inturn decreases the production of androgens from ovaries, also improves quality of the egg and induces ovulation. However several studies showed that the combination of metformin plus Clomiphene Citrate in the CC-resistant patients was very effective in inducing ovulation in 68.6%– 77.7% of patients.78-80.[12]

Several case reports have shown the effective role of metformin in PCOS patients by enhancing conception rate and improving the metabolic profile.[13]

Clomiphene citrate does not give equal response in all patients for ovulation induction. It acts by antagonising the effects of estrogen and thus causes raised levels of gonadotrophins from pituitary gland, this in turn will stimulate growth of ovarian follicles and ovulation.[14]

Letrozole inhibits actions of enzyme aromatase. It blocks the conversion of androgens to estrogens in ovarian follicles, this will result in fall in circulating level of estrogen and rise in intraovarian androgens, this decreased level of estrogen inturn causes negative effect on hypothalamic–pituitary thus raising FSH level and it will enhance ovarian follicular development.[15] The effective role of letrozole in patients with clomiphene-resistant PCOS has been documented with the use of 2.5 mg daily doses on third to seventh day of menstrual cycle in various studies.[16]

In this study it was observed that women who were given Letrozole + Metformin among them rate of ovulation was 89% as compared to the women who were given Letrozole among them rate of ovulation induction was 60%. A statistically significant association was seen between ovulation induction with treatment groups. (p-value=0.000).[17]

Davar reported that with the use of Metformin+ letrozole as combination showed pregnancy rate per cycle in 8% women. Nahid L in his study reported an induction rate of 88% with the use of letrozole alone. Hatem Abu Hashim from Egypt reported rate of ovulation induction as 64.9% with the use of letrozole alone. Badawy et al. who had an ovulatory rate of 62% for letrozole cycles.[90] In other trials, Mitwally and Casper[91] had ovulatory rate of 75%, Al-Omari et al. had an ovulatory rate of 87.5%, whereas Elnashar et al. reported an ovulation rate of 54.6%.

Sohrabvand et al. added either CC or letrozole initially after 6–8 weeks of treatment with metformint in CC-resistant PCOS women, they found that the combination of metformin plus letrozole leads to more pregnancies. About 15–40 % of women with PCOS have CC resistance which can be ascribed to the antiestrogenic effect of CC on endometrium and cervical mucus or by hypersecretion of luteinizing hormone.

Although administration of Letrozole for induction of ovulation varies in many studies but overall Letrozole alone is effective in PCOS women. It is widely used for many years and various studies have proved its beneficial role for ovulation induction. In addition to it, it does not have adverse effect on endometrium and cervical mucus.[18]

In literature only one study was found who had used combination of these both treatment in PCOS women. Ibrahim Abd Elgafo in his study used metformin plus letrozole and reported an ovulation rate of 48.9%. To our knowledge, no studies have yet compared the effects of letrozole with combined metformin.[19]

This study is the first of its kind in our set up and in local literature which both these drugs have been used in combination. However different studies have used letrozole with CC.[20] But no such combination was adopted by studies done previously to see the efficacy of these two combination for successful outcome in women with PCOS.[16]

## Conclusion

Letrozole with metformin is more effective for the ovulation Induction in females presenting with polycystic ovarian syndrome as compared to letrozole alone.

## Authors Contribution

**AZ:** Concept, Design, analysis
**KA:** Analysis, Interpretation
**MM:** Interpretation
**AM:** Drafting Revising, Analysis
**A:** Analysis and Interpretation
**KT:** Design, Interpretation

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# Protective Effect of Enterococcus faecium SF68 and Saccharomyces boulardii in Acute Severe Diarrhea in Infants: Randomized Controlled Trial

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**Abstract**

**Objectives:** This study was done to observe the effect of Enterococcus faecium SF68 and Saccharomyces boulardii in acute severe diarrhea in infants.

**Methods:** It was a single blind, randomized controlled clinical trial done in Children Hospital, Lahore. The infants were selected between 6 months to 12 months of age. All the infants were suffering from acute diarrhea with severe dehydration. Total 105 infants were selected and randomly divided into three groups having 35 infants in each group. Infants in group A received standard treatment of diarrhea. Infants in group B and C received Enterococcus faecium SF68 and Saccharomyces boulardii respectively twice daily for five days along with standard treatment of diarrhea. All the infants were monitored for five days. The treatment response was observed in terms of frequency of diarrhea, duration of diarrhea, stool consistency and length of hospital stay.

**Results:** The frequency of diarrhea, duration of diarrhea and length of hospital stay were significantly reduced in both group B and C as compared to group A.

**Conclusion:** Enterococcus faecium SF68 and Saccharomyces boulardii helped to reduce the stool frequency, duration of diarrhea, length of hospital stay and also improved the stool consistency in acute severe diarrhea in infants.

**Key Words:** Probiotics, Enterococcus faecium SF68, Saccharomyces boulardii, Acute severe Diarrhoea

## Introduction

Diarrhea is defined as "the passage of 3 or more loose or liquid stools per day or more frequently than is normal for the individual."In acute diarrhea, there is sudden onset of excessively loose stools > 10ml/kg/day in children less than 1 year of age and >200 g/24 hours in older children, which lasts less than 14 days.[1] The data of World Health Organization (WHO) reveal that there are 2 billion cases of diarrhea throughout the world each year and 1.9 million children under the age of 5 years perish from diarrhea every year, commonly in developing countries. The fluid and electrolyte replacement is primary treatment of diarrhea. Zinc supplements are recommended along with oral rehydrating salt (ORS) in diarrhea as they decrease the duration of diarrhea. The antibiotic treatment is controversial in the treatment of diarrhea, but there are certain infections for which treatment is mandatory.[2]

Probiotics are live microorganisms, which maintain a balance between the immune system and gastro-intestinal tract. They are available in different forms as tablets, powders and capsules. They have anti-microbial activity against pathogenic bacteria and produce compounds which kill the pathogenic bacteria.[3] Enterococci are part of the microflora of intestine of animals and humans. Enterococcus faecium SF68 is the probiotic strain that can be used in the treatment of diarrhea. Saccharomyces boulardii is

included in the yeast familyand it is the principal

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probiotic yeast. The S. boulardii can be used in the management of acute diarrhea as well as antibiotic associated diarrhea.[4] The future studies should be done to put emphasis on best dosage of S. boulardii in diarrhea from different causes as some studies did not specify the dose of S. boulardii in diarrhea from various causes.[5] Trials with probiotic Entercoccus faecium SF68 in humans are limited and results show variations.

Few studies have been conducted in developing countries regarding the use of probiotics in diarrhea and most of the studies have not provided Zn as part of the treatment. Therefore well designed (randomized controlled trial) RCTs should be done in developing countries to compare the recommended treatment of diarrhea i.e. ORS, Zn supplements and continued feeding, with and without adding probiotics.[6] Most of the studies which have been done on probiotics included only mild to moderate diarrhea when there is no dehydration or some dehydration and the studies which were done on severe diarrhea showed no beneficial effect.[7] There is a need to study the efficacy of probiotics in severe diarrhea in developing countries. In this study the effect of two different probiotics i.e. Enterococcus faecium SF68 and S. boulardii have been evaluated in acute severe diarrhea in infants.

## Methods

It was a prospective, single blind, randomized controlled clinical trial. The trial was conducted in Children Hospital, Lahore from July 2016 to November 2016 after being reviewed and approved by Ethical Committee. The sample was calculated by using 90% power of study and 5% level of significance. It was calculated by taking mean ± SD of number of stools/day with standard treatment versus standard treatment with probiotic in children.[8] According to this formula sample size was 32. We included 35 infants in each group. The infants with age range of 6 months to 12 months suffering from acute diarrhea with severe dehydration were included in the study. Dehydration was severe (more than 10%) when there was rapid or weak pulse, low blood pressure, sunken eyes and lack of urine output. The exclusion criteria were; infants with any chronic disease, typhoid fever, blood in stools, infant having severe malnutrition and who have been given probiotics within last 10 days. Non-probability, purposive sampling was done for selec-tion of patients. An independent person not affiliated with this study randomized 105 infants into three groups of 35 infant in each group through simple randomisation by using random number list genera-ted by computer. The person who randomised the infants also prepared the envelopes in which treatment plan of the infants was present. The parents received sealed and packed envelopes according to randomisation list. The serial number of the infants with name and age was mentioned on the envelopes. The envelopes were opened, and the infants were put in their specific groups. In this way treatment plan was concealed from the researcher until intervention started. The parents of the infants were kept blind and they did not know in which group infants were put. After enrollment, baseline lab investigations i.e. complete blood count, serum electrolytes and renal functions tests were done for all infants. In group A, which was a control group, infants were given only standard treatment of diarrhea, i.e., ORS, IV fluids and Zn supplements. Antimicrobial treatment was only given when needed.[2] Infants in group B were given standard treatment as well as probiotic Enterococcus faecium SF 68, one capsule every 12 hours for five days. Contents of capsule were mixed in 20 ml water for administration.[9] Infants in group C were given standard treatment of diarrhea as well as probiotic S. boulardii, one capsule of 250 mg every 12 hours for five days. Contents of capsule were mixed in 20 ml water for administration.[10] The probiotics were given to the infants as soon as the infants were able to take orally. The following parameters were observed: Frequency of diarrhea, Duration of diarrhea, Stool consistency, Length of hospital stay. Infant was defined as recovered from diarrhea when 8 hours had passed after passage of stool with normal consistency or infant had been discharged.[8] Stool consistency was classified as normally formed stool, soft stool, semi liquid and liquid and was graded according to classification as 1, 2, 3, 4 respectively.[11] Infant was discharged when he or she was recovered from diarr-hea. If diarrhea was prolonged, infant was discharged after five days as we had monitored parameters for five days, but total duration of diarrhea was noted for which infants were inquired telephonically daily.

The data collected was processed by using Statistical Package for Social Sciences. The data was checked for normal distribution by Shaprio Wilk test. The data

was normally distributed. Quantitative variables were presented in mean and SD. ANOVA was used to analyze the significance between three groups and post hoc Tukey's test was used for pairwise comparison between the groups. Qualitative variables were presented as frequencies and proportions. Chi square test was applied for qualitative variables. *p* value <0.05 was considered significant.

## Results

The Table. 1 summarizes the mean ± standard deviation of various demographic parameters of all study groups. The infants were included with age range 6 to 12 months. Mean weight of the patients was in between 15th to 50th percentile

The Table. 2 summarizes the mean ± standard deviation of frequency of diarrhea and other associated symptoms in all study group at the time of admission. Almost all of the patients had more than ten episodes of diarrhea per day. The 100 % of patients had stool with liquid consistency.

Figure. 1 illustrates the post-treatment comparison of mean ± standard deviation of change in pattern of number of stools in all study groups over a period of 5 consecutive days.

The comparison of means of all groups by ANOVA revealed a significant difference between the group

**Table 1:** *Demographic Data of Patients in all Study Groups*

| Demographic data | Group A (Control) | Group B (*SF68*) | Group C (*S. boulardii*) |
|---|---|---|---|
| Age (months) (mean ± SD) | 8.64 ± 2.37 | 8.64 ± 2.18 | 9.3 ± 2.4 |
| Weight (kg) (mean ± SD) | 7.4 ± 0.93 | 7.41 ± 0.94 | 7.67 ± 0.85 |
| Male n (%) | 24 (68.6 %) | 21 (60 %) | 18 (51.4 %) |
| Female n (%) | 11 (31.4 %) | 14 (40 %) | 17 (48.6 %) |
| Rural Areaw n (%) | 14 (40 %) | 7 (20 %) | 6 (17.1 %) |
| Urban Area n (%) | 21 (60 %) | 28 (80 %) | 29 (83 %) |

means with a p value of <0.001.

The number of stools passed by the infants in group A was much higher as compared to infants in group B and group C. The difference was significant between group A and group B from day 1 (after 24 hrs) to day 5. The difference was not significant between group A and group C on day 1 (after 24 hrs) but difference was significant between group A and group C from day 2 to day 5.

**Table 2:** *History of diarrhea and associated symptoms at the time of admission*

| History of patients | Group A (Control) | Group B (*SF68*) | Group C (*S. boulardii*) |
|---|---|---|---|
| No. of stool before treatment of diarrhea (mean ± SD) | 12.71±3.25 | 11.28±3.01 | 11.25 ± 2.91 |
| Fever n (%) | 17 (48.6 %) | 12 (34.3 %) | 19 (54.3 %) |
| Vomiting n (%) | 29 (82.9 %) | 27 (77 %) | 31 (88.6 %) |

**Figure. 1:** *No. of Stools After Treatment*

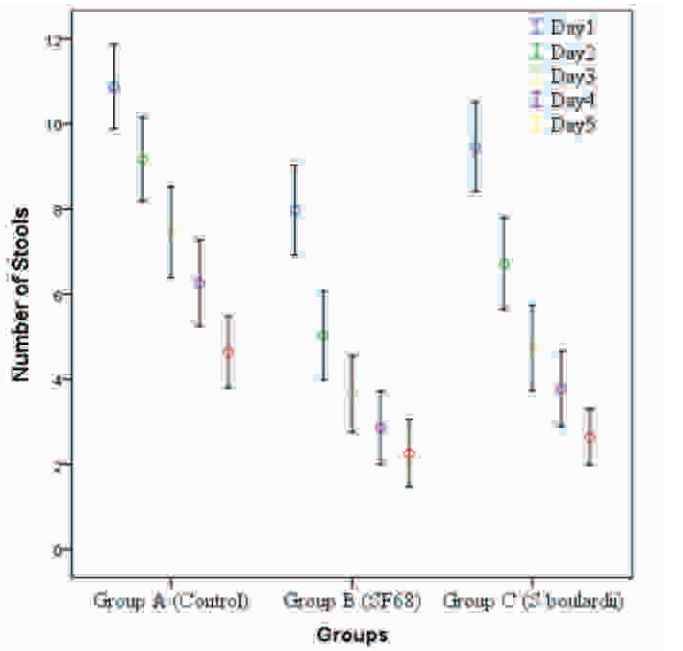


Table. 3 summarizes the post-treatment comparison of mean ± standard deviation of stool consistencies in all study groups over a period of 5 consecutive days.

There was significant difference in improvement of stool consistency among groups. Patients in group B and group C started passing normal stools earlier as compared to patients in group A. At day 5, 80 % of patients had normal stool in group B while 60 % of patients had normal stool in group C as compared to 23% in group A.

Table. 4 summarizes the post-treatment comparison of mean ± standard deviation of duration of diarrhea in all study groups. The duration of diarrhea was higher in group A as compared to group B and group C. There was no significant difference between group

**Table 3:** *Number (%) of patients with different stool consistencies*

| | Stool Consistency | Day1 | Day2 | Day3 | Day4 | Day5 |
|---|---|---|---|---|---|---|
| Group A (control) | Normal | | | | 3(8.6%) | 8(22.9%) |
| | Soft | | | 5(14.3%) | 6(17.1%) | 9(25.7%) |
| | Semi Liquid | 1(2.9%) | 7(20%) | 5(14.3%) | 15(42.9%) | 16(45.7) |
| | Liquid | 34(97.1) | 28(80%) | 25(71.4%) | 11(31.4%) | 2(5.7%) |
| Group B (SF68) | Normal | | | | 19(54.3%) | 28(80%) |
| | Soft | | 15(42.9) | 23(65.7%) | 11(31.4%) | 3(8.6%) |
| | Semi Liquid | 14(40%) | 10(28.6%) | 8(22.9%) | 2(5.7%) | 3(8.6%) |
| | Liquid | 21(60%) | 10(28.6%) | 4(11.4%) | 3(8.6%) | 1(2.9%) |
| Group C (S. boulardii) | Normal | | | 1(2.9%) | 10(28.6%) | 21(60%) |
| | Soft | | 7(20%) | 17(48.6%) | 13(37.1%) | 8(22.9%) |
| | Semi Liquid | 7(20%) | 9(25.7%) | 10(28.6%) | 8(22.9%) | 5(14.3%) |
| | Liquid | 28(80%) | 19(54.3%) | 7(20%) | 4(11.4%) | 1(2.9%) |
| ***p* value of Chi square test** | | 0.001 | <0.001 | <0.001 | <0.001 | <0.001 |

B and group C in terms of duration of diarrhea.

Table. 5 summarizes the post-treatment comparison of mean ± standard deviation of length of hospital stay in all study groups. The length of hospital stay was higher in group A as compared to group B and group C. There was no significant difference between group B and group C in terms of length of hospital stay.

Figure. 2 illustrates the post-treatment comparison of mean ± standard deviation of episodes of vomiting in all study groups over a period of 5 consecutive days. The comparison of means of all groups by ANOVA revealed a significant difference between the group

**Table 4:** *Duration of diarrhea (hours)*

| Groups | N | Mean | Standard Deviation | *p* value |
|---|---|---|---|---|
| Group A (Control) | 35 | 130.37 | 63.11 | <0.001 |
| Group B *(SF68)* | 35 | 54.26 | 56.36 | |
| Group C *(S. boulardii)* | 35 | 71.71 | 53.32 | |

means with a p value of <0.001. The patients in group B had less episodes of vomiting as compared to patients in group C at day 1 and at day 2 only.

**Figure. 2:** *Episodes of vomiting after treatment*

**Table 5:** *Length of hospital stay (days)*

| Group | N | Mean | Standard Deviation | *p* value |
|---|---|---|---|---|
| Group A (Control) | 35 | 4.16 | 1.14 | <0.001 |
| Group B (SF 68) | 35 | 2.18 | 1.38 | |
| Group C (*S. boulardii*) | 35 | 2.9 | 1.42 | |

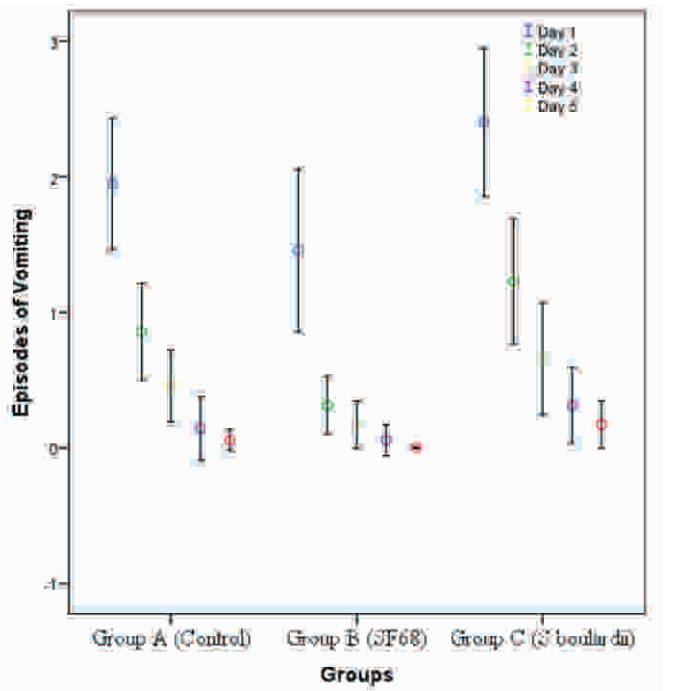


Figure. 3 illustrates the post-treatment comparison of mean ± standard deviation of body temperature in all study groups over a period of 5 consecutive days. The comparison of means of all groups by ANOVA revealed a significant difference between the group means with a p value of <0.001. Body temperature difference was significant only at day 2 after treatment when the patients in group A had high fever as compared patients in group B and group C while the difference was not significant between group B and group C.

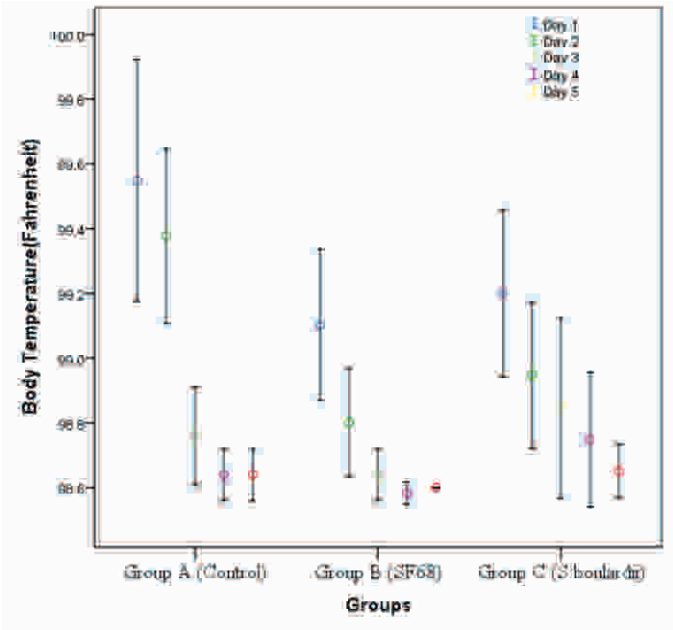


**Figure. 3:** *Body Temperature in Study Groups After Treatment*

## Discussion

This study was a single blind randomized controlled clinical trial carried out in Children Hospital, Lahore. Protective effects of two different probiotics in acute severe diarrhea in infants were compared with standard treatment of diarrhea as well as with each other. Total 105 patients were selected, and each group had 35 patients. The age of patients was between 6 to 12 months. This age group was selected as hospitalization associated with diarrhea is common in this age group.[12,13] The patients were having severe dehydration at the time of admission and needed IV fluids. All the patients were followed for a period of five days. All the patients received complete intervention. No patient was dropped from the study after selection. The patients in group A received only standard treatment of diarrhea and it was a control group. The patients in group B received standard treatment of diarrhea as well as probiotic Enterococcus faecium SF68 and patients in group C received standard treatment of diarrhea as well as probiotic S. boulardii.

Randomized controlled trials have been done on the effect of S. boulardii in diarrhea and most of these trials showed positive results in decreasing the duration of diarrhea.[14,15,16,17] Another study was done in Turkey to compare the effect of two probiotics i.e., S. boulardii and Bifidobacterium lactis in acute diarrhea in addition to standard treatment of diarrhea in children. However, in this study, there was no significant difference in duration of diarrhea and vomiting in control group and the group in which S. boulardii was given.[18] In present study, S. boulardii was given to patients of group C. There was significant difference in stool frequency between group A and group C as stool frequency was reduced in a group receiving S. boulardii. The mechanism by which S. boulardii decrease the duration of diarrhea depends upon the stimulatory effects on the mucosa of intestine, protective action against inflammation and inhibitory action of bacterial toxins.[19,20] Studies on effect of probiotic Entero-cccus Faecium SF68 in diarrhea in children are limited. One study was done in Switzerland to evaluate the efficacy of Enterococcus faecium SF68 in diarrhea and it showed a decrease in duration of diarrhea in children.[21] Another study was done in Italy to assess the efficacy of five probiotic preparations iin children suffering from.[9] Patients were randomly assigned to receive one of five interventions. The control group received only ORS. The other four groups were randomly assigned to receive one of four probiotic preparations in addition to standard treatment of diarrhea. However there was no significant difference in parameters between control group and the groups receiving S. boulardii and Enterococcus faecium SF68. This is contradictory to results of present study. Mechanism of action of Enterococcus faecium SF68 may depend upon the immune system of the body as one study done on animals showed that this probiotic stimulated the immune functions of the host as the group of animals which received the probiotic showed increased fecal IgG and IgA as compared to the animals in the control group.[22] In this study, Enterococcus faecium SF68 was given to group B. There was significant difference in stool frequency between control group and the group receiving Enterococcus faecium SF68 as stool frequency was reduced in a group receiving Enterococcus faecium SF68. In present study both probiotics i.e., S. boulardii and Entero-coccus faecium SF68 decreased the stool output, duration of diarrhea and length of hospital stay in infants in acute severe diarrhea. There was no significant difference in stool frequency, duration of diarr-hea and length of hospital stay between group B and group C. Both probiotics also improved the stool consistency and the percentage of infants forming normally formed stool was higher in a group receiving Enterococcus faecium SF68 as compared to

infants receiving S. boulardii. At day 5, 80% of patients formed normal stool in group B while 60% of patients formed normal stool in group C. There was also significant difference in vomiting between group B and group C. The episodes of vomiting at day 1 and at day 2 were less in a group receiving Enterococcus faecium SF68 as compared to group receiving S. boulardii. There are many advantages of this study like the concealment of allocation of infants into specific groups removed the bias. Some infants were discharged early from hospital, but the direct and continuous contact with physician maintained the quality and integrity of results. Like the advantages, there were some limiting factors of the study; the nutritional status and body weight of infants varied because the majority of patients reporting to government hospi-tals belong to low socioeconomic status and general health of infants is very important in terms of immunity. Moreover, the type of diarrhea (infective/ non infective) was not taken into account while selecting infants for study group.

## Conclusion

This is the first study which made the comparison of the effects of S. boulardii and Enterococcus faecium SF68 in acute severe diarrhea in infants. In developing countries, the people have less exposure about the benefits of probiotics. As the children in develo-ping countries are malnourished having decreased immunity, adding specific probiotics in acute diarr-hea will help in early recovery leading to socio-economic benefits.

## Authors Contribution

**KAF:** Concept, Design, Data Acquisition, Interpretation, Literature search, Manuscript writing
**KZM:** Literature search, Data Interpretation, Manuscript writing
**RMA:** Critical revision, Manuscript formatting
**IZ:** Literature search, Statistical Analysis
**PF:** Data Collection & Analysis
**CS:** Critical revision, Proof Reading

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# Various Histomorphologic Patterns of Urothelial Carcinoma in TURBT Specimen

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**Abstract**

**Objective.** To evaluate the various morphologic patterns of urothelial carcinoma in transurethral resection specimen of urinary bladder.

**Method:** One hundred ninty three biopsies of transurethral resection of bladder from different age groups without exception of sex and race were included in this study from year 2013-2019 in services hospital Lahore.

**Result:** Eighty-eight cases from 193 biopsies from services hospital Lahore in 2013 to 2019 were reported as high-grade urothelial carcinoma. While 52out of 193 cases were diagnosed as nested variant of urothelial carcinoma.03 cases neuroendocrine differentiation of urothelial carcinoma is identified and 21 cases having squamous and 12 cases with sarcomatoid differentiation of urothelial carcinoma is reported.

**Conclusion:** Urothelial carcinoma has many histological variants each having different prognosis and clinical implications. So accurate subtyping of the tumor is important for patient's better management.

## Introduction

Definition of histological variants is idiosyncratically dissimilar histomorphologic phenotypes of a particular neoplasm.[1]

Urothelial carcinomas are one of those tumors which demonstrate the numerous histological variants. Some of these variants have good prognosis and some are clinically aggressive. Almost 90% of bladder carcinomas are originate from the urothelium. While little proportion 7% of urothelial carcinomas represent as primary squamous cell carcinoma and another 2% represent as primary adenocarcinoma of the bladder.[1] As per literature out of 90% urothelial carcinomas 33% display some constituent of the deviating differentiation. This deviating differentiation includes squamous, glandular, small cell, rhabdoid differentiation and even rarely trophoblastic and Mullerian features. According to 2016 WHO categorization, urothelial carcinoma is reported with its ten histological variants so far. It includes nested, microcytic, micro papillary, lymphoepithelioma like, plasmacytoid, sarcomatoid, giant cell, poorly differentiated, lipid rich and clear cell.[8]

Some of the histomorphologic patterns of urothelial carcinoma are associated with poor prognosis more clinical aggressive as well as poor response to therapy.

Presence of various histology within the same tumor lesion can affect the diagnosis, management and prognosis of the patient. Therefore, it is critically significant to diagnose precisely the various morphological patterns of urothelial carcinoma. To notify the majority of these histomorphologic patterns co-exist with the conventional urothelial carcinoma and do not usually arise in pure form is necessary. Here we discuss some of the histomorphologic patterns of urothelial carcinoma are commonly found in our biopsies.

Nested/Solid histomorphologic pattern of urothelial carcinoma is low grade and rare variant, it has deceivingly bland appearance of tumor cells with mild cytological atypia and mild pleomorphic and occasional prominent nucleoli arranged in small and large nests.[5] However this innocent morphology has a definitive malignant behavior and can be presented as locally advanced or metastatic disease in a patient due

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to delay in diagnosis therefore 3 nested variant of urothelial carcinoma is at an advanced stage at the time of clinical presentation.[18] Diagnosis is not confirmed until muscle invasion is present. Nested/Solid pattern of urothelial carcinoma has good prognosis but the optimal treatment has not yet been resolute because of a rare histomorphologic pattern. Further research is required to define the effective approach.[18]

Next is the sarcomatoid pattern of urothelial carcinoma. It is high grade, display both epithelial and sarcomatoid morphology[2, 17]. Malignant spindle cells leiomyosarcoma-like or another nonspecific heterologous component such as osteosarcoma or chondrosarcoma demonstrate in the sarcomatoid component of this tumor.[17] and the epithelial component is the most commonly of conventional urothelial carcinoma. In some cases, malignant spindle cell component tends to occupy more than fifty percent of the tumor it is possible to lack any epithelial component, that will complicate the diagnosis. This pattern is rare and patients with sarcomatoid carcinoma usually presents with advanced stage and have worse prognosis as compared to conventional urothelial carcinoma. There is no optimal treatment option for this histomorphologic pattern of urothelial carcinoma because many patients develop metastasis after surgery. [14]

Now we discussed the neuroendocrine differentiation in the urothelial carcinoma. It is high grade variant of urothelial carcinoma. It includes small cell, large cell neuroendocrine carcinoma, well differentiated neuroendocrine carcinoma and paraganglioma. Small cell and large cell carcinoma arise from urothelial carcinoma and admixed either with the conventional carcinoma or any other morphologic pattern. Morphologically small cell carcinoma exhibits small cells with high nuclear to cytoplasmic ratio, nuclear molding abundant mitotic figures with necrosis and large cell carcinoma has larger cells with evident cytoplasm, finely stippled chromatin and prominent nucleoli. Overall survival rate is poor. Chemotherapy is the only established therapeutic regimen for treated neuroendocrine carcinomas.[8]

Quite a reasonable case of urothelial carcinoma is observed with definitive areas of squamous and glandular differentiation in high grade urothelial carcinoma and it should be distinguished from primary squamous cell carcinoma and primary adenocarcinoma.[9] The presence of in situ component of urothelial carcinoma indicated the exclusion criteria of primary squamous cell carcinoma or primary adenocarcinoma. As in the absence of any conventional urothelial carcinoma component, primary squamous cell carcinoma or adenocarcinoma should be considered. This pattern presented with worse prognosis and the only treatment option is new adjuvant therapy.[15] Various histomorphologic pattern along with the divergent histology is common in urothelial carcinoma and must be recognized quantified and reported accurately. There are still more fields of research regarding the biological predictive prognostic and treatment implications of urothelial carcinoma with histological variants. Proper recognition and consistent reporting of histomorphologic pattern in urothelial carcinoma is essential. For better defined treatment strategies as well as biomarkers of different variants of urothelial carcinoma more dedicated prospective clinical trials with definitive criteria, tumor registries data base recordings and biopsies are mandatory.

Cystoscopically resection remains the best treatment choice in noninvasive urothelial carcinoma and in some variants of urothelial carcinoma particularly in micro papillary, squamous, plasmacytoid and sarcomatoid. Neo adjuvant chemotherapy is in the chemo sensitive variants particularly in neuroendocrine and lymphoepithelioma like variants of urothelial carcinoma.

Recent research suggested that molecular composition of these urothelial carcinoma could be related to the expression of specific histomorphologic patterns and new subtypes could be identified with further investigation.

## Methods

This study is descriptive study held in Pathology Department of Services Institute of Medical Sciences Lahore. We assessed the urothelial carcinoma in 193 cases comes from patients who underwent transurethral resection of bladder in 2013 to 2019 (07 years data). The specimen was retrieved from the files of the Histopathology Department of Services Institute of Medical Sciences. The cases were chosen to represent urothelial carcinoma along with its various variants to be assessed. Good presentation of morphology is the only criteria of selection. Cauterized and quantitatively inadequate material was excluded

from the study. There were not consecutive cases. No patients reported a history of previous treatment. The tumors were diagnosed and reported along with their histological variants' counterpart.

## Results

we examined different histological variants of urothelial carcinoma obtained from transurethral resection of bladder from 193 patients in the year of 2013 to 2019 in services hospital Lahore (see Fig. 1). In that study eighty-eight (45.0%) cases were reported as urothelial carcinoma high grade and the remaining cases are represented as histomorphologic patterns of urothelial carcinoma. Fifty-two (49%) cases were nested; three (2.8%) cases were urothelial carcinoma with neuroendocrine differentiation. Twelve cases (11.4%) were reported as sarcomatoid differentiation of urothelial carcinoma and twenty-one cases (20.1%) were reported as urothelial carcinoma with squamous differentiation. Despite in apparent and recent rise in the incidence of variants of urothelial carcinoma the real epidemiology presentation and prognostic values are still not well established. 14So the aim of our study is to better understand the increase in the load of various variants of urothelial carcinoma.

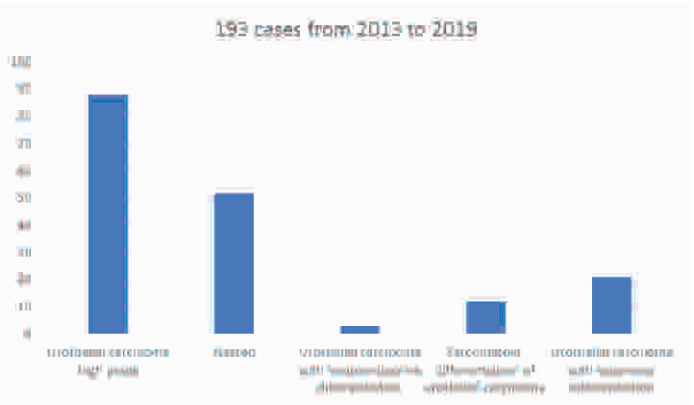


**Figure 1:** *Depiction of the Data through Histogram*

## Discussion

To choose the better treatment modalities and improvement in the cases of urothelial carcinoma, we should identify and report of the various histomorphologic patterns accurately and it is crucial to identify precise risk stratification of patients with bladder cancer. The presence of some morphological variants such as sarcomatoid differentiation, plasmacytoid and nested in bladder carcinomas are more aggressive and at the time of presentation and often are in advanced stage of disease.

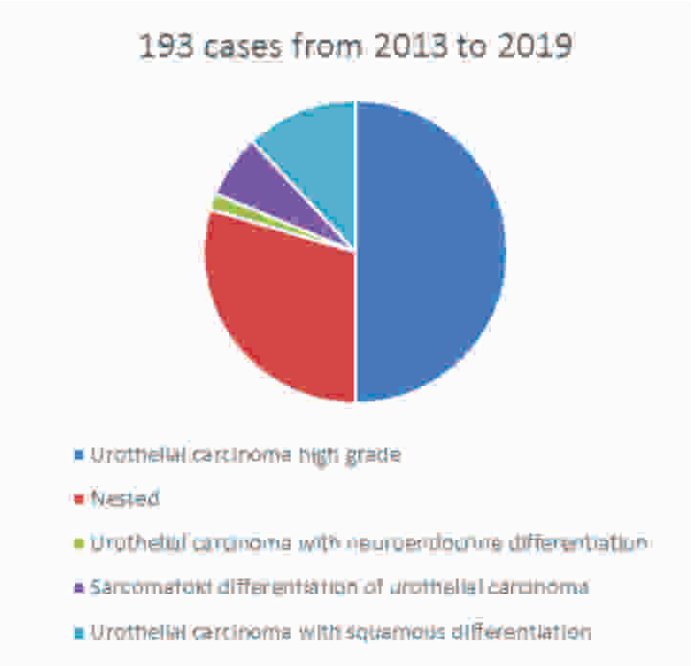


**Figure 2:** *Depiction of the Data through Pie Chart*

A single series of large cases has documented that many histomorphologic patterns are common in high grade urothelial carcinoma and that comprised forty percent of the cases in the series by Perez-Montiel D, 2006.[21] According to this study after squamous and glandular differentiation, sarcomatoid (7%) and micro papillary (3.7%) pattern were the common. Similarly, in our study 40% are of high-grade urothelial carcinoma and 11.4% is sarcomatoid variant but in contrast to this study nested variant is more common in our cases (49%) might be due to increase in incidence of this variants in our population as well as fail to collect data of reporting of micro papillary variant in subsequent other biopsies. Frequency of the various histomorphologic variants with respect to the conventional urothelial carcinoma is quite unavailable. Squamous differentiation is the second most common variant is seen in our cases (20%). The prognostic significance of squamous differentiation is unclear, although some studies of Budia Alba A in 1999, Zhai QJ in 2007 have suggested an adverse outcome.[2,17] Another study reveals that 60 to 70% cases were of nested variant of urothelial carcinoma[5,6,19,20,21] as in our study 49% nested variant. It is sufficiently clear that urothelial carcinoma has the ability for the divergent differentiation so for surgical pathologist it is important to be aware of this potential for multidirectional differentiation, as the correct characterization of tumors may have diagnostic, therapeutic or prognostic implications significantly impacting on the management of the patient.

## Conclusion

Upgrading in TURP procedures, devoted genitourinary pathologists and emerging genomic techniques for sub typing will lead to a better definition of each histomorphologic patterns of urothelial carcinoma along with related prognosis and treatment strategies.

## Author's Contribution

KH: Interpretation, compiling & article writing
JA, LT: Interpretation, compiling of data
NI, SS: Interpretation, review of data
LR: Review of data

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# Single-Stage Combined Surgery for Treating Neglected Bilateral Developmental Hip Dysplasia after Walking Age

**Abdul Latif Shahid,[1] Zulqarnain Butt,[2] Islam Hussain,[3] Farhad Alam,[4] Naila Asad,[5] Muhammad Nazir Awan,[6] Hana Khurshid[7]**

**Abstract**

**Objectives:** To determine outcome in Single Stage Surgery of Both Hips in Bilateral Developmental Dysplasia of Hip in Children after walking age.

**Methods:** This was a retrospective review of 20 hips in 10 patients (7 females and 3 males), operated at the children's hospital and the institute of child health, Lahore between 2014 and 2016. The age of patients was between 2 and 5 years. There were 10 hips in grade IV, 6 in grade III and 4 in grade II according to Tonnis classification. Both hips were operated in single stage. Open reduction of hip joint was done by anterolateral approach in all children. Salter osteotomy was done in every child while femoral shortening was needed in 10 hips. Outcome of single stage surgery was assessed by radiological assessment of Severin's scoring system and functional assessment of MacKay's scoring system at final followup after 2 years of suegery.

**Results:** There was no effect of age, gender, malnutrition, body mass index on outcome. According to Severin's scoring system, 14 hips (70%) were in grade I while 6 (30%) in grade II. Outcome was excellent in 6 hips (30%), good in 13 (60%) and fair in 1 (5%) by applying MacKay's scoring system. Hip spica of one child was changed after one month due to wetting with urine. There was no hip dislocation or subluxation in any case.

**Conclusion:** Single stage surgery of both hips can be done safely in bilateral developmental dysplasia of hip by anterolateral approach in late presented children.

**Key Words:** Developmental dysplasia of hip, Single stage surgery.

## Introduction

Developmental dysplasia of the hip (DDH) is a broad term having many aspects depending on patient's age at diagnosis and can lead to no problem in future and sometimes permanent disability.[1]

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The overall incidence worldwide ranges from 1 to 34 cases per 1000 births.[2] Hip screening of neonates by physical examination should be done for proper diagnosis. In younger children, ultrasonography is the best while radiographs should be diagnostic modality in older children[2]. The reason for late presentation of cases is delayed or missed diagnosis and failure in conservative or operative treatment.[3] The incidence of late presentation is high in developing countries like Pakistan due to lack of awareness and negligence of family. Significant changes occur in joint with time such as dysplasia of the acetabulum, constriction of the acetabular capsule, fixation of the inversion of the limbus, thickened round ligament, infiltration of the acetabulum by fibrous tissue and femoral anteversion. If the problem is not treated in time, it will lead to early onset osteoarthritis and significant morbidities.[4] Age of late presentation is different in different countries like after three months in Australia.[5]

Bracing, Traction, Closed reduction, Open reduction of hip with capsulorraphy and Pelvic or/and Femoral osteotomies are commonly used to treat DDH after walking age.[6] The purpose of the DDH treatment is to achieve a stable hip joint by providing concentric reduction. This will stimulate normal development of femoral head and acetabulum.[7,8] Children older than three years usually require open reduction combined with pelvic and femoral osteotomy.[7] The main objective of treatment is to provide ideal environment of both femoral head and acetabulum for their development[7]. Most popular surgical technique to correct the deformity is combined open reduction with femoral shortening.[9] Multiple studies have shown improved outcome in combination of open reduction, femoral shortening and pelvic osteotomies in single stage.[9] There is no conclusive evidence in the literature to support pre-treatment traction methods.[8] The rationale of my study is to determine outcome of single stage surgery of both hips in bilateral developmental dysplasia of hip in children after walking age. The result of this study will allow us to change our previous concepts regarding management of bilateral developmental dysplasia of hip in children after walking age.

## Methods

After approval from the ethical review committee of our hospital, this retrospective case series study was done. 10 patients with 20 hips who came in outpatient department of pediatric orthopedics of the Children Hospital and the Institute of Child Health, Lahore during 2014 and 2016 and fulfill the inclusion criteria were enrolled for this study. Our selection criteria were all patients aged 2-5 years with bilateral DDH. Children with age less than two years, who had taken initial treatment, paralytic, pathological, teratologic or traumatic dislocations and neuromuscular disease were excluded from the study. Informed consent and demographic profile (name, age, sex, and contact) was obtained. The procedure details, benefits and complications explained to parents. Preoperatively radiograph of pelvis including both hips anteroposterior view was taken and acetabular index was measured. Clinical data of all the patients like pain symptoms, range of hip joint motion, status of Trendelenburg sign and gait pattern were recorded for all the patients. The degree of dislocation of the femoral head was assessed by Tonnis classification system. A single surgical team carried out all procedures uniformly to reduce bias. Open reduction of both hip joints was done using anterolateral approach. Right side was operated first and then left side. Bilateral adductor tenotomy was done. Psoas tenotomy was done and intraarticular obstacles like pulvinar, ligamentum teres and transverse acetabular ligament were removed. Capsulotomy was done and femoral head was located within acetabulum. Decision about femoral shortening was made intraoperatively in case of difficulty in femoral head reduction. Salter osteotomy was performed if femoral head coverage was deficient. Capsulorrhaphy was done on both sides in all patients. After right side, left side was operated similarly. Bilateral hip spica was applied for a period of ten weeks. All data was collected on single proforma. Follow up period was 2 years. After ten weeks, hip spica and wires were removed under general anaesthesia. Union was assessed radiologically on every visit for 3-6months. Now full weight bearing was allowed and physiotherapy started assessing with radiological union. Dynamic compression plate used for femoral shortening was removed after one year under general anaesthesia. With evidence of occurrence of union on X-Ray, walking was advised. The outcome was assessed postoperatively by modified MacKay's criteria (table 1) and Severin's scoring system (table 2) at final follow up visit after 2 years.

## Results

A total of 10 patients (20 hips) were operated for bilateral DDH. There were seven females (70%) and 3(30%) males. 10(50%) hips were in grade IV, 6(30%) hips in grade III and 4 (20%) hips in grade II according to Tönnis classification. Mean preoperative acetabular index angles were 38.6° for right hips and 38.2° for left hips. After surgery, mean acetabular index angles were19.6° for right hips and 20.2° for left hips. According to Severin's scoring system, 14 hips (70%) were in grade I while 6 hips (30%) in grade II. No patients were seen with Severin's Grade III, IV and V. The clinical outcome was excellent in 6 hips (30%), good in 13 hips (65%) and fair in 1 hip (5%) by applying MacKay's scoring system. Hip spica of one child had to be changed after one month due to wetting with urine. There was no hip dislocation or subluxation in any case.

## Discussion

DDH is unilateral in 80% cases (60% on left side

while 20% on right side) and bilateral in 20% cases[7]. In unilateral cases, initial treatment is Pavlik harness, then closed reduction and hip spica if brace treatment fails. Open reduction of hip with capsulorrhaphy combined with femoral and pelvic osteotomies(triple procedure) is treatment of choice in children after walking age.[10] The results of our study found 70% hips in grade I and 30% in grade II of Severin scoring system. According to Mackay scoring 30% hips were in excellent condition, 60% good and 5% in fair condition. In our study no patient required subsequent operation for redislocation and subluxation. There was 50% reduction in mean acetabular index angles postoperatively. Several research works have evaluated the functional and radiographic outcomes of surgical reconstruction for DDH. Mansoor et al found excellent and good radiological and clinical results in the one-stage pro-cedure (open reduction and proximal femoral derota-tion osteotomy) in 15 patients with DDH. Compar-able to our study results he found 66.6% in Grade I and 26.6% Grade II of Severin scores in his patients. The difference was seen in Mackay scoring where his results showed excellent condition of hips in 40% vs 30% in our study, good condition in 40% vs 60 %.[11] Similar to our study Qadir I et al found single stage procedure of open reduction, femoral shortening and pelvic osteotomy for treatment of DDH in older children with good to excellent functional and radio-logical outcomes. The results of his retrospective analysis was 28.6% in excellent condition vs 30% in our results, 44 (57.1%) in good condition vs 60% of our study results. The only difference was that they found 9 (11.7%) hips in fair condition whereas we had 5% hips that were in fair condition and also we did not find any hip in poor condition while they had 2 (2.6%) in poor condition.[9] Contrasting results with 90% success rate have been documented by various researchers. In a case series study by Saqib et al, variation from our results was concluded. 34.8% of patients achieved grade I (excellent) of McKay's classification and 39.1% grade II (good) in single stage triple procedure of open reduction, femoral and pelvic osteotomy.[4] The disparity was also shown in Severin grading as they found 95.7% below grade III whereas none of the patients in our study were in grade III. This difference could be due to the follow up period of one year. Kashif et al studied the outcome of one stage correc-tion of developmental dysplasia of hip (DDH) in children older than three years of age. They reported 14% hips were in Severin grade III, 21% in grade II and 50% in grade I. According to Modified Mackay's scoring system clinical outcome of 50% hips were excellent (stable hips with pain free full range of motion, no limp and negative Trendelenburg sign), 32% hips were good, 11% hips were fair and 7% hips were poor.[7] The difference in their results from our study could be due to the time of clinical evaluation postoperatively as we had followed up for 24 months in contrast to their 12 month evaluation. Hung NN and Duc HH compared Outcome between Salter Innominate Osteotomy and Zigzag Osteotomy Combined Fibular Allograft for Developmental Dysplasia of the Hip in Children. Their results with Salter Innominate Osteotomy according to Modified Mackay's scoring system were excellent hips in 73.9 %, good in 18.3%, Fair in 5.3% and poor in 2.5%. Radiologically 77.1% were in Severin grade I, 14.8% in grade II, 4.9% in grade III and 2.5% in grade IV[6]. Their results were different than our study which could be due to different preoperative management techniques used.

Baki et al treated 32 hips (22 patients) with develop-mental dysplasia by a single-stage open reduction through Ferguson's medial approach and Pemberton acetabuloplasty. The clinical results were excellent in 30 hips (93.8%) and good in two (6.2%) as per Mackay scoring. Radiological assessment showed that 29 hips (90.6%) were rated as class I and three hips (9.4%) were class II by Severin classification[12]. This difference in results from our study could be due to difference in methodology of the operation as they operated via a medial approach. Hosny MM evaluate the clinical as well as the radio-graphic results of management of bilateral DDH cases with Salter and Dega osteotomy. The final clinical outcome results with Salter technique were excellent in 30% hips, good in 40%, fair in 25% and poor in 10%.[13] The advantage of choosing single stage operation was short hospital stay with no need of repeated immobi-lization and decreased joint stiffness. Also changes in the sacroiliac joint and pubic regions are limited in the single stage operation, and there is less damage to the pelvic inlet, birth canal, sciatic nerve and vessels.[14] The limitations of the present study comprise its retrospective nature and the limited number of children. Also it only represents the experience of a single institution without a comparative study. Future

studies can be done to compare different techniques and also with different institutions.

## Conclusion

The results conclude that single stage surgery of both hips can be done safely in bilateral developmental dysplasia of hip by anterolateral approach in children after walking age.

**Table 1:** *Modified McKay Criteria*

| | |
|---|---|
| **Excellent** | Stable, painless hip, no limp, negative Trendelenburg sign, and a full range of movement |
| **Good** | Stable, painless hip, slight limp, negative Trendelenburg sign, and a slight decrease in range of movement |
| **Fair** | Stable, painless hip, limp, positive Trendelenburg sign, and limitation of movement |
| **Poor** | Unstable or painful hip, or both; positive Trendelenburg sign |

**Table 2:** *Severin's Scoring System*

| | |
|---|---|
| **Grade I** | Normal appearance |
| **Grade II** | Mild deformity of the femoral head and neck or the acetabulum |
| **Grade III** | Moderate deformity of the femoral head and neck or the acetabulum or both |
| **Grade IV** | Subluxation of the femoral head |
| **Grade V** | Articulation of the femoral head with a false acetabulum |
| **Grade VI** | Redislocation |

## Authors Contribution

**SLA:** Manuscript Writing
**NZ:** Study Concept andDesign
HI, AF: Data Acquisition
**AN:** Statistical Analysis
**AANM:** Data Interpretation
**KH:** Manuscript Review

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# Mode of Delivery in Pregnant Females with Fibroid Uterus Presenting in Spontaneous Labour

**Uzma Aziz,[1] Madiha Afzal,[2] Hadia Shabbir[3]**

**Abstract**

**Objectives:** 1) To determine the mode of delivery of obstetric population with uterine fibroids presenting in spontaneous labor. 2) To determine the various indications for emergency cesarean section in pregnancies with uterine fibroids.

**Methods:** It was a Descriptive cross sectional study done at Obstetric unit of Arif Memorial teaching Hospital, from June 2019 to May 2020. 50 pregnant patients with uterine fibroids in spontaneous labor were included in the study with 95% confidence level and 5 % margin of error.

**Results:** In our study, 62 % (n=31) patients were between 20-30 years of age with 38 % (n=19) between 31-40 years with Mean age and SD 25.63 ±2.89 years. 68% (n=32) patients were between 34-36 weeks of gestation whereas 32% (n=18) were between 37-39 weeks with Mean gestational age and SD 29.66 ±1.59. 66 % (n=33) patients were Primigravida to Gravida 3 and 34% (n=17) were Gravida4 to Gravida 5. The frequency of emergency caesarean section in patients with uterine fibroids was 58% (n=29) whereas 42 % (n=21) cases with uterine fibroids had normal vaginal delivery. The most frequent indication for emergency cesarean section was labor dystocia i.e. (41.37%).

**Conclusion:** The frequency of emergency caesarean section amongst patients with uterine fibroids presenting in spontaneous labor is high particularly due to labor arrest. The number of fibroids has an impact on mode of delivery in these patients. Therefore each obstetric patient with uterine fibroids, must be evaluated thoroughly for the appropriate mode of delivery in prenatal period.

**Key Words:** Pregnancy, uterine fibroids, mode of delivery, cesarean section, spontaneous vaginal delivery

## Introduction

The fibroids are the benign tumors of smooth muscle cells of the uterus. They are the most frequent benign tumors found in females in their reproductive age.

The incidence of the uterine fibroids increases to 40%-60% by 35 years of age and rises to 70%-80% at 50 years of age but still the etiology of uterine fibroids is not exactly understood.[1] The incidence of pregnancy with fibroids is about 0.5% to 4%.[2] The prevalence of fibroids in pregnancy in Pakistan is 0.87%.[3] The frequency of uterine fibroid with pregnancy is increasing because of couple's tendency to delay first pregnancy till the age of 30. Due to increase in estrogen/ progestin levels, 15% - 30% of fibroids will enlarge in pregnancy. However most of the fibroids shrink in size during puerperium.[4] Less than 3cm Intramural and sub serosal fibroids are not clinically significant. Pregnancies associated with uterine fibroids are labelled as high risk pregnancies. Most of these pregnancies with fibroid uterus are usually uneventful but sometimes, serious complications can occur during the course of pregnancy, depending upon the size, site and location of the fibroid.[5] About 10%–30% of females with uterine fibroids face obstetric complications during pregnancy.[1]The recent evidence reports a higher rate of cesarean delivery particularly in women with large uterine fibroids when compared with normal vaginal deli-very rate i.e. 48.8% vs. 13.3% and the most common cause for

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emergency caesarean section was dysfunc-tional labor while malpresentation was the commo-nest indication for elective caesarean section in these patients.[6] Women with uterine fibroid have increased caesarean section rate due to distortion of uterine cavity or other obstetric reasons.[4] In such pregnancies caesarean section rate, postpartum hemorrhage and prolong hospital stay is found to be high and needs specific follow up.[7-9] Conversely, Vergani et al. reported a high vaginal delivery rate amongst laboring women with fibroids and concluded that pregnant women with fibroids should be counseled for the trial of labor.[10] Ciavattini et al. found high rate of emergency caesa-rean section in patients with multiple uterine fibroids as compared to pregnant females with single or no fibroids delivering vaginally.[11] The size, number and location of uterine fibroids have significant impact on the mode of delivery. So prior information is useful in assigning risk category of a pregnant female with fibroids.[12] Our study was aimed to determine the mode of deli-very in pregnant obstetric population with fibroid uterus presenting in spontaneous labour. In our study the mode of delivery of pregnancy with uterine fibroid was dependent on the size, number of fibroids that was comparable to the study of Poovathi and Ramalingam.[13] The inconsistent available data in the literature about the preferred mode of delivery in pregnancies with uterine fibroids provides the reason to carry out this research. As pregnant females with uterine fibroids have greater concerns to know about their mode of delivery, our study will be a good addition in previous available literature to determine the mode of delivery in these patients thus making counseling of these patients to be done appropriately regarding mode of delivery.

## Methods

It was Descriptive cross-sectional study which was conducted at Obstetric unit of Arif memorial teaching Hospital, Lahore from June 2019 to, May 2020 after taking approval from ethical committee of RLMC. 50 pregnant females with uterine fibroids having spontaneous labor were selected with a 95% Confidence level and 5 % margin of error with non-probability purposive sampling technique after fulfilling the inclusion criteria. Written informed consent was taken from the patients to use their data for this study. The collected data was analyzed by using SPSS version 17.

### Inclusion Criteria

- 20-40 years of age
- PG to Gravida 5
- with a Gestational age 34 weeks – 39 weeks
- single or multiple uterine fibroids > 3 cm
- having spontaneous labor

### Exclusion Criteria

- Pregnancy with maternal medical disorders
- Previous caesarean section
- Fetal malpresentation
- Placenta previa
- Cervical fibroids
- Inadequate pelvis
- Lower segment uterine fibroid of >8 cm were excluded from the study.

All patients were given a trial of labor and followed till their delivery. Their progress of labor was monitored with partogram and fetal condition was assessed by continuous fetal heart rate monitoring with cardiotocography.

## Results

A total of 50 cases fulfilling the study criteria were included to assess the rate of caesarean section in pregnant patients with uterine fibroids.

Age distribution of the patients showed that 62% (n=31) were between 20-30 years whereas 38% % (n=19) were between 31-40 years of age with mean and standard deviation of the patient's age as 25.63 ± 2.89 years. (Table No. 1)

68% (n=32) patients were between 34+0-36+6 weeks of gestation whereas 32% (n=18) were between 37+0-39+6 weeks while the mean and standard deviation for the gestation age was determined as 29.66±1.59. (Table No. 1)

66 % (n=33) patients were between Primigravida to Gravida3 and 34% (n=17) were between Gravida4 to Gravida5. (Table No. 1)

The frequency of caesarean section in patients with uterine fibroids was 58% (n=29) whereas 42 % (n= 21) cases with uterine fibroids had spontaneous vagi-

nal delivery. (Table No. 2)

The most frequent indication for emergency caesarean section was labor dystocia 12 (41.37%) followed by fetal distress 10 (34.50%), PROM with poor bishop score 4 (13.79%), cord prolapse 2 (6.89%), and placental abruption 1 (3.44%) being the least common indication for abdominal delivery. (Table 3)

**Table 1:** *Distribution of Age, Parity and Gestation Age*

| Age(in years) | No. of patients | Percentage |
|---|---|---|
| 20-30 | 31 | 62 % |
| 31-40 | 19 | 38 % |
| Total | 50 | 100 % |
| Mean ±SD | 25.63±2.89 | |
| **Gestational Age in weeks** | | |
| $34^{+0}$-$36^{+6}$ | 34 | 68 % |
| $37^{+0}$ – $39^{+6}$ | 16 | 32 % |
| Total | 50 | 100 % |
| Mean± SD | 29.66 ±1.59 | |
| **Parity** | | |
| Primigravida-Gravida[3] | 33 | 66 % |
| Gravida[4]-Gravida[5] | 17 | 34 |
| **Total** | 50 | 100 % |

Figure-I shows that 25 (86.20%) patients with multiple fibroids having trial of labor ended up in emergency caesarean section as compared to 4 (13.80%) patients with single fibroid who had caesarean section.

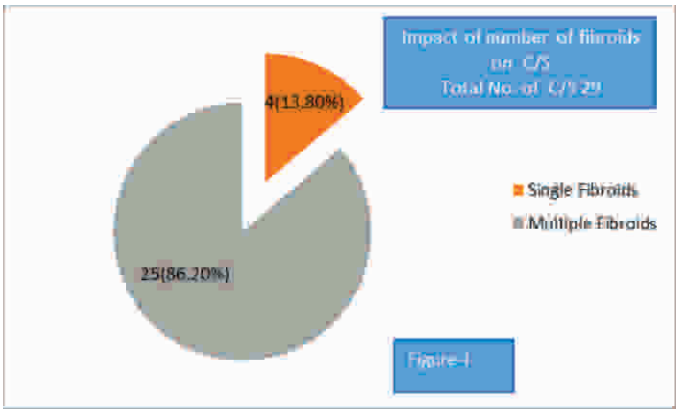
**Table 2:** *Mode of delivery in patients with uterine fibroids*

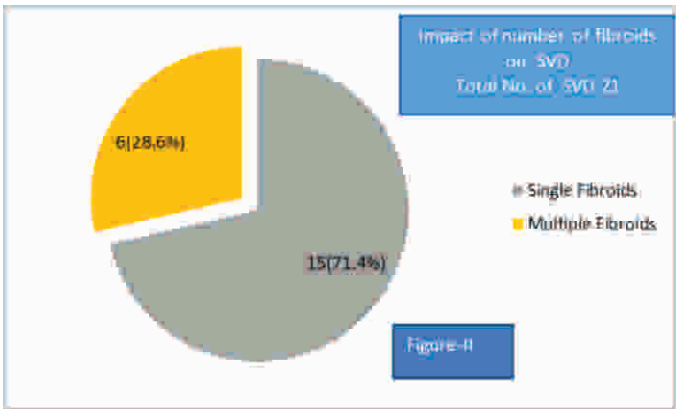
| MOD | No. of patients | Percentage |
|---|---|---|
| Caesarean section | 29 | 58 % |
| Spontaneous vaginal delivery | 21 | 42 % |
| **Total** | 50 | 100 % |

Figure-II shows that 15 (71.4%) patients with single fibroid delivered vaginally when compared to 6 (28.6%) patients with multiple fibroids delivering vaginally.

**Table 3:** *Indication for emergency Caesarean section in patients with fibroids*

| Indication | No. of Patients | Percentage |
|---|---|---|
| Labor Dystocia | 12 | 41.37 % |
| Fetal Distress | 10 | 34.50 % |
| PROM with poor bishop score | 4 | 13.79 % |
| Cord Prolapse | 2 | 6.89 % |
| Placental Abruption | 1 | 3.44 % |
| **Total** | 29 | 100 % |




## Discussion

Uterine fibroids are the commonest benign tumors of the female genital tract. They occur in 30-70% females in their reproductive ages.[14] These tumors have been implicated as a risk factor for increased caesarean section in pregnant women. The frequency of fibroids increases with the advancing age of the females and is generally most common among African American females.[15] The prevalence of uterine fibroid in pregnancy is 0.1%–10.7%.[16, 17] Presence of fibroids in pregnancy increases the likelihood of obstetric complication by 10%–30% while increasing the frequency of caesarean section up to 70%.[18] Past studies on delivery outcomes in females with uterine fibroids have shown disparities and inconsistent results. These studies show that in such pregnancies, the incidence of operative delivery increases.[19, 20] In our study, 62 % (n=31) of the patients were bet-ween 20-30 years of age. This finding is in compa-rison to the study of Javed M who concluded that 59% of the pregnant females with fibroid uterus presented at a younger age i.e. between 20-30 years of age.[5] The increased incidence of uterine fibroids in young pregnant obstetric population can be justified by quoting that estrogen and progesterone which stimulate the uterine lining during menstrual cycle in preparation for pregnancy appear to promote the growth of fibroids which contain more estrogen and progesterone receptors than normal uterine muscles do. In our study, 66 % (n=33) patients were between para 1 to para 3 and 34% (n=17) were between para 4 to para 5.

The fibroids are usually associated with nulli-parity. The relative risk of fibroids decreases with increasing parity and each additional term pregnancy, the risk is reduced to one fifth with five term preg-nancies compared with nulliparous females.[21] This is similar to the findings in nulliparous black females in whom there is a nine-fold increase in the incidence of fibroids. Females with uterine fibroids have had fewer term pregnancies and are generally of lower parity than the females without this problem.[22] The frequency of caesarean section in our patients with uterine fibroids was 58 % (n=29) and 42% (n= 21) patients with uterine fibroids had a normal vagi-nal birth. The results of the current research are in concurrence with the study done by Javed M indicating that the caesarean delivery rate was 63.5% in pregnancies with fibroid uterus.[5] One research shows that there is the strong associa-tion between the uterine fibroids and an increased risk of caesarean section, particularly with large size fibroid. Another study by Youssef A, recorded the caesarean section in 47.8% of the pregnant patients with fibroids which is less than that of our results.[23] The increased rate of emergency caesarean section in our study was noticed because of increased incidence of dysfunctional labor due to distorted uterine anato-my leading to failure to progress and large tumor volume. Also the most common indication for emergency caesarean section in our patients was labor dystocia i.e. 12 patients (41.37%), followed by fetal distress i.e. 10 (34.5%) patients, PROM with poor BISHOP score i.e. 4 (13.7%) patients, Cord prolapse i.e. 2 (6.8%) patients and placental abruption i.e. 1 (3.5%) patients. This finding of our study was comparable with the research done by NOOR S showing that failure to progress (39%) and fetal distress(38%), PROM (14%) were the most common indications and placental abruption(3.3%) the least common indication for emergency caesarean delivery.[24] Although previous literature and our study reports that uterine fibroids are associated with an increased rate of emergency caesarean section in patients having trial of labor.[25,26] We also determined the association between the number of fibroids and its impact on mode of delivery thus observing that our study population having multiple fibroids ended up more in emergency caesarean section than those having single fibroid who successfully ended in having vaginal delivery i.e. (86% vs. 71%). This finding is in comparison to the study of Zhao R who concluded that SVD rate is high in patients with single fibroids than patients with multiple fibroids.[12] However Valerie I et al didn't find difference in the mode of delivery (Normal vaginal Delivery and caesarean section) in females with multiple fibroids compared with those having single or no fibroids.[27] This finding was also supported by Stout et al in which females with single fibroid 5< cm didn't have an increased risk of a caesarean delivery when contrasted with females with multiple fibroids >5 cm.[28] The limitation of our study was that we didn't consi-der the location of the fibroids (subserosal, intramural or submucosal) to see the impact on mode of delivery.

## Conclusions

We concluded from our study that the rate of emergency caesarean section is higher among patients with uterine fibroids with labor dystocia the most common indication of emergency caesarean section. So it is recommended that

1. Each patient who presents with uterine fibroids, must be assessed at consultant level at term to determine the suitable mode of delivery.
2. Promote obstetric practice that multiple/ large fibroids are not absolute contraindication for trial of labor provided prior assessment of patient has been done in antenatal period to be eligible for trial of labor.

These strategies will help to reduce the frequency of caesarean section in pregnant patients with fibroid uterus thus increasing chances of normal vaginal delivery.

**Conflict of interest and Funding**

The authors declared that they have no conflict of interest and did not received any funding.

## Authors Contribution

**AU:** Literature Search, Study Concept & Design
**AM:** Data Collection
SH: Data Collection and Analysis

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# Comparison of R-CHOP with CHOP in Patients of Diffuse Large B Cell Lymphoma

**Faiza Rehman Lodhi,[1] Amjad Zafar,[2] Muhammad Abbas Khokhar,[3] Ali Waheed Goraya,[4] Sonia Ashraf,[5] Sobia Yaqub[6]**

**Abstract**

**Objective:** Diffuse large B cell lymphoma (DLBCL) is a lymphoid B cells neoplasm with a diffuse pattern and high proliferation rate. Cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP) was considered effective as other complicated regimens with more toxicity profile. Rituximab is a monoclonal antibody directed against CD20 positive B cell. It has good activity therapeutically in patients of DLBCL. It increases response rates and survivals when added to CHOP chemotherapy. Although R-CHOP is more effective but due to high cost of Rituximab it is usually not incorporated with chemotherapy in most of our patients and CHOP is still used extensively. Due to heterogeneity of disease and difference in ethnicity, there may be difference in outcomes of two regimens. This study will help us in tailoring our management plan that will result in better outcome of patients.

**MethodS:** 70 patients aged between 20-65 years having DLBCL were taken in this study. We rando-mized patients by lottery method into two groups. Group I received CHOP with dose of Cyclophosphamide 750mg/m2, Doxorubicin 50mg/m2, Vincristine 1.4 mg/m2 and prednisolone 40mg/m2.Chemotherapy was given on Day-1 while prednisolone was given for 5 days from Day-1 of chemotherapy. Group II received R-CHOP which includes same chemotherapy with same dosage. Rituximab was included in Group II with dose of Rituximab 375 mg /m2. Each cycle was given at three weeks interval. Response in terms of CR (Complete Response), PR (Partial Response), SD (Stable Disease) or PD (Progressive Disease) was evaluated as per leukemia network after 4 cycles of chemotherapy. The quantitative variables were calculated by taking mean and standard deviation. The response was assessed in percentage and frequencies and compared by applying chi square test.

**Results:** Group I had 37.1% while Group II had 68.6% complete response with p value of 0.019. Partial response was 48.6% in Group I while 20.0% in Group II. 14.3% in Group I and 8.6% in Group II either had stable disease or progressive disease.

**Conclusions:** R-CHOP has superior response rates as compared to CHOP, therefore, whenever possible Rituximab should be added as target therapy in chemotherapy.

**Key Words:** Diffuse large B cell lymphoma, CHOP, R- CHOP

## Introduction

Among non-Hodgkin's lymphomas, DLBCL is most common type present approximately 25 % in the developed countries[1]. Based on morphology of lymphoid tissue and immunophenotyping pathological diagnosis of DLBCL can be made. CHOP was considered effective as other complicated regimens with more toxicity profile based on number of serial clinical investigations[2]. DLBCL is a heterogeneous variety of tumors having large B cells that are transformed and having prominent nucleoli. Cells of DLBCL have basophilic cytoplasm, diffuse pattern of growth and high proliferation rate. Tumor cells in DLBCL expresses B cell antigens (CD19, CD20, CD22 and CD79a). Rituximab is monoclonal antibody directed against CD20 positive B cells. It has good activity therapeutically in patients of DLBCL. R-CHOP which includes Rituximab with CHOP chemotherapy is more effective therapy and has better

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responses and survivals[3]. Rituximab when incorporated with chemotherapy showed survival benefit in the GELA Trial. It also increase survival in British Columbia trial when added to CHOP chemotherapy[4,5]. There was no difference in response rate between R-CHOP and CHOP in another study but there was a significant difference in relapse rates between these groups[5]. This was in contrast to result of another study conducted on elderly patients, where the response rate was also increased with R-CHOP [3]. In a study, Li X et al analyzed retrospectively 437 patients of DLBCL who were newly diagnosed. In six university hospitals they received CHOP or R-CHOP therapy and followed up for assessment of response after treatment. Between R-CHOP and CHOP, significant differences in overall survival and progression-free survival were present. Median follow up was of 86 month in this study. Overall survival was 84.1% in R-CHOP group and 70.2% in CHOP group with p value of 0.018. While progression free survival was 81.5% in R-CHOP group and 66.7% in CHOP group with p value of 0.015. In this study, elderly patients with age greater than 60 years received higher overall survival as compared to younger population. Median follow up was 66 months in elderly population with overall survival 80.7% in R-CHOP group and 53.0% in CHOP group with p value of 0.011.Chemotherapy with rituximab did not showed significant effect on overall survival that is 85.5% in R-CHOP and 79.4% in CHOP group with p value of 0.428[6]. In another study by Afzar M et al showed CR for CHOP Group as 44.4% and for R-CHOP group as 48.2% while PR as 11.1% for CHOP group and 7.1% for R-CHOP [7]. Although R-CHOP is more effective but due to high cost of Rituximab it is usually not incorporated with chemotherapy in most of our patients and CHOP is still used extensively. There may be difference in outcomes of two regimens due to heterogeneity of disease and difference in ethnicity. This study will help us in in better outcome of patients by tailoring our management plan.

## Methods

After taking approval from hospital ethical committee, patients who fulfilled the selection criteria were enrolled and written informed consent was taken from them before commencement of treatment. Patients were randomized by lottery method into two groups. Group I received CHOP with dose of Cyclophosphamide 750mg/$m^2$, Doxorubicin 50mg/$m^2$, Vincristine 1.4 mg/$m^2$ and prednisolone 40mg/$m^2$. Chemotherapy was given on Day-1 while prednisolone was given for 5 days from Day-1 of chemotherapy. Group II received R-CHOP which includes same chemotherapy with same dosage. Rituximab was included in Group II with dose of Rituximab 375 mg / $m^2$. Each cycle was given at three weeks interval. Response in terms of CR (Complete Response), PR (Partial Response), SD (Stable Disease) or PD (Progressive Disease) is evaluated as per Lugano criteria with CT scan after four cycles of chemotherapy. We ensured follow up by taking patient's contact number. All the information was recorded on Performa by me. Data was entered on SPSS (Statistical Package of Social Sciences), version-10 software after being collected on Performa. Quantitative variables (age) were presented as mean and standard deviation. Qualitative variables (stage and disease response) were presented as frequency and percentage. Comparison between groups was made by applying chi-square test. We stratified the data for age, gender and stage of disease to describe effect modifiers. Chi-square test was used after stratification to assess significance with $p < .05$ as statistical significance.

## Results

70 subjects were randomly divided into Group I (CHOP n=35) and Group II (RCHOP n=35). Mean age of subjects was 45.24 years, SD 13.31 with minimum age of 20 years and maximum age of 78 years. 57.1% in Group I and 48.6% in Group II were of age 20 – 50 years and 49.2% in Group I and 51.4% in Group II were of age 51 – 80 years. 31.4% were females and 68.6% were male in Group I, 42.8% were females and 57.2% were male in Group II. 11.4% in Group I and 17.1% in Group II were in stage-1. 11.4% in Group I and 22.9% in Group II were in stage-2. 37.1% in Group I and 17.1% in Group II were in stage-3. 40.0% in Group I and 42.9% in Group II were in stage-4. 42.9% in Group I and 20.0% in Group II have no extra nodal involvement, 42.9% % in Group I and 62.9% in Group II had one extra nodal involvement and 8.6% in Group I and 17.1% in Group II had 2 extra nodal involvements. 37.1% in Group I and 42.9% in Group II had low risk (0-1), 28.6% % in Group I and 17.1% in Group II were having low intermediate risk, 22.9% % in Group I and 17.1% in Group II were having high interme-diate risk (=3) and 11.4% in Group I and 22.9% in Group II were having

high risk (4-5). 28.6% in Group I and 51.4% in Group II had comorbidities. Final outcome was compared among groups, 37.1% in group I and 68.6% in Group II had complete res-ponse with P<.019 which was statistically significant. 48.6% in group I and 20.0% in Group II had partial response, 5.7% in group I and 0.0% in Group II had a stable response, and 8.6% in both groups had prog-ressive disease.

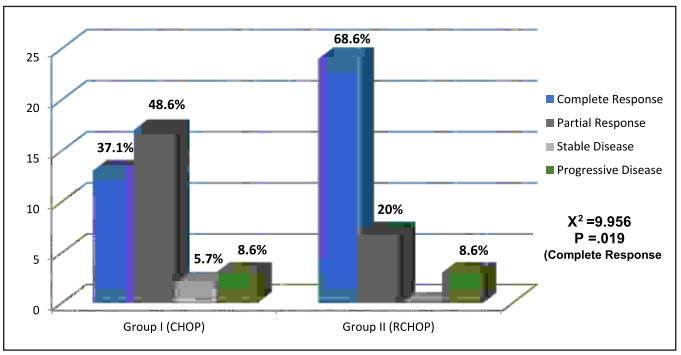


**Figure #1:** *Final Outcome of Treatment Among Groups*

**Table 1:** *Demographic Data of Patients included in the study.*

| AGE (Years) | Groups | |
|---|---|---|
| | Group I | Group II |
| Mean Age | 46.6 | 49.6 |
| Median Age | 47.00 | 52.00 |
| Std. Deviation | 14.485 | 11.950 |
| Minimum | 21 | 22 |
| Maximum | 70 | 72 |
| **An ARBOR STAGING** | **Groups** | |
| | **Group I** | **Group II** |
| STAGE1 | 4 (11.4%) | 6 (17.1%) |
| STAGE2 | 4 (11.4%) | 8 (22.9%) |
| STAGE 3 | 13 (37.1%) | 6 (17.1%) |
| STAGE4 | 14 (40.0%) | 15 (42.9%) |
| **EXTRANODAL SITE** | **Groups** | |
| | **Group I** | **Group II** |
| ≤ 1 SITE INVOLVEMENT | 30 (85.8%) | 29 (82.9%) |
| ≥ 2 SITE INVOLVEMENT | 5 (14.2%) | 6 (17.1%) |
| **IPI SCORE** | **Groups** | |
| | **Group I** | **Group II** |
| 0-2 LOW & LOW INTERMEDIATE RISK | 23 (65.7%) | 21 (60%) |
| 3 – 5 HIGH & HIGH INTERMEDIATE RISK | 12 (34.3%) | 14 (40%) |
| **COMORBIDITIES** | **Groups** | |
| | **Group I** | **Group II** |
| No | 25 (71.4)% | 17 (48.6%) |
| Yes | 10 (28.6%) | 18 (51.4%) |

## Discussion

DLBCL is the commonest variety of non-Hodgkin's lymphoma. It is clinically very heterogeneous lymphoma. Only 40% patients show good responses to current therapy and have survival benefit, whereas others don't respond well. This clinical heterogeneity and difference in natural history is due to molecular heterogeneity among tumors. CHOP is standard chemotherapy for patients with DLBCL. Rituximab is monoclonal antibody directed against CD20 positive B cells. It has good activity therapeutically in patients of DLBCL. We conducted a randomized trial and compared responses of R-CHOP with CHOP in patients of DLBCL.

Rituximab when added to CHOP chemotherapy increases complete responses and survival of patients in older patients with diagnosis of DLBCL as per study by Coffier et al. There was no significant increase in toxicity seen with addition of Rituximab.[3]

Most of patients of DLBCL are of greater than sixty years[8]. Only half of patients responded with CHOP chemotherapy which was considered standard for years for all age groups of DLBCL.[10] Multiple attempts were made by adding other chemotherapy agents to increase the efficacy of therapy but it did not succeed. Regimens with increase doses of chemotherapy imp-rove responses only in younger patients who have bad prognosis.[11] These intensified therapies were not tolerated by elderly population of patients. CHOP is also sometimes not tolerated by elderly patients. For this purpose easily tolerated chemotherapy regimens were designed for old patients, but these are less beneficial as compared to CHOP.[10]

Rituximab is a monoclonal antibody directed against CD20 positive B cells, it was first given on relapse and refractory low grade lymphomas. It was then found to have activity in relapse and refractory DLBCL.[12] CD20 is surface protein on lymphoid cells that is present only on mature B cells. The antibody is a chimeric because it is made up of human IgG1 portion with genetic engineered portion of mouse antibody which has CD20-binding site on it. Studies were conducted in which rituximab combined with CHOP chemotherapy showed 90 percent responses in all lymphomas.[13]The Groupe d'Etude des Lymphomes de l'Adulte (GELA) group studied and compared R-CHOP with CHOP in elderly population of patients

with DLBCL. This was a randomized trial comparing both the effectiveness and safety of rituximab when combined with CHOP with CHOP alone in patients of DLBCL. Higher responses rates and survivals were found among patients of DLBCL treated with R-CHOP. Patients treated with R-CHOP had fewer relapses after complete response and less rate of progression of disease that is why having longer survival. R-CHOP was tolerated well and no serious side effect was observed. In conclusion, R-CHOP chemotherapy when we give to elderly population of patients with newly diagno-sed DLBCL increases responses to therapy, decreases failures with treatment and relapse of disease. It also improves survivals when compared with CHOP che-motherapy alone. There was no significant gain in toxicities with this addition.

## Conclusion

R-CHOP has superior response rates as compared to CHOP, therefore, whenever possible Rituximab should be added as target therapy in chemotherapy.

## Authors Contribution

**LRF:** Article writing

**ZA, KAM:** Data Collection

**GWA, AS, TS:** Data analysis

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# Assessment of Knowledge About Autism Spectrum Disorder Among Paediatricians

**Fatima Zia,[1] Hafsa Qamar,[2] Irum Aslam,[3] Muhammad Asif Siddiqui[4]**

**Abstract**

**Objective:** To evaluate the frequency of Paediatricians who have good knowledge for diagnosis of Autism Spectrum Disorder (ASD).

**Methods:** It is cross-sectional study conducted in department of Paediatric Medicine, Children Hospital, Lahore, Jinnah Hospital and Services Hospital Lahore, in 6 months duration, spanning from June 27, 2016 till December 27, 2016. A total of 89 doctors fulfilling the inclusion criteria were registered after informed consent. Demographic data (including age, sex, qualification and duration of clinical experience) was taken. Doctors were given a questionnaire to assess their knowledge of ASD. The questionnaire was a nineteen-item self-administered questionnaire divided into four domains namely, social interaction (Domain 1), impairment in communication (Domain 2), repetitive behavior (Domain 3), characteristics of autism as a disorder and its comorbidities (Domain 4). The KCAHW sore ≥15 was considered as good. Data was entered and analyzed in (SPSS) version 22.0.

**Results:** The mean age of subjects was 30.67 ± 2.80 years with 31(31%) physicians male and 69(69%) were females. The mean KCAHW score was 15.07 ± 3.54 with minimum and maximum score of 7 and 19. According to operational definition a total of 62(62%) subjects had good knowledge while 38(38%) physician had score < 15.

**Conclusion:** Though 68% of paediatricians had good knowledge about childhood autism according to our study. The physicians who had poor knowledge, must be considered for different educational activities to enhance their knowledge regarding ASD, which may help in early diagnosis and improving prognosis of children with ASD.

**Keywords:** Paediatricians, Autism spectrum disorder

## Introduction

Autism Spectrum Disorder (ASD) constitutes several clinical disorders, ranging from mild behavior disturbances to severe disability. Abnormal social interaction as well as communication plus repetitive and restrictive pattern of activities and behaviors are important features of ASD. Normal daily functioning of child may be affected and symptoms can be noted at an early age.[1,2] ASD incidence is increasing dramatically in children. In past it was rare, 1st case was described by Kanner in year 1943[3] but now prevalence is reported to be around 62/10,000.[4,5] Many factors are responsible for this increase like well-defined diagnostic criteria even in mild forms for autism, awareness of both parents plus physicians and increase of true preva-lence.[6] Due to this high prevalence many pediatri-cians are now able to suspect and diagnose ASD during 18 to 36 months of life in children with abnor-mal communication, socialization or stereotypic behaviors.[7] For early intervention, we need early diagnosis of the disease based on adequate know-ledge, diagnostic criteria and availability of screening tools. Age of the child at which ASD is diagnosed first time is dependent on treating physician knowledge.[8] According to a study average age for diagnosis of ASD was 4 years and 10 months.8 In one study, out of 167 participants, 51% of participants had good knowledge, 49% had poor knowledge for Autism.[9]

In Pakistan, some of healthcare workers lack proper knowledge regarding ASD.10 Similarly other studies

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suggested different levels of knowledge (causes, treatment, prognosis, cognitive profiles of autism) for people having different professions or roles (health professionals, parents, teachers) involved in diagnosis of autism. Among healthcare professionals, pediatricians are more important because they are the first point of contact where children are reporting first time with abnormal behavior. Main focus of our study is to assess the knowledge of pediatricians required for diagnosis and treatment of autistic spectrum disorder. [9]

## Methods

This is a Cross-Sectional Study conducted in departments of Paediatric Medicine, Children Hospital, Lahore, Jinnah hospital and Services Hospital Lahore in 6 months durations from June 27, 2016 till December 27, 2016. 100 paediatricians was included with 95% confidence interval, 10% margin of error and taking expected percentage of good knowledge i.e. 51% of pediatricians for diagnosis of ASD, using non probability purposive sampling technique. Whereas paediatricians with age range 26-35 years of both genders, having more than 1-year clinical experience in teaching hospital were included. Doctors who are not practicing for more than 6 months or doctors who are not permanently positioned in paediatric ward were excluded. 100 doctors fulfilling the inclusion criteria after informed consent were registered for the study.

Demographic data (including age, sex, qualification and duration of clinical experience) was taken. Doctors were given a questionnaire to assess their knowledge of ASD. Knowledge about Childhood Autism among Health Workers (KCAHW) Questionnaire was used. The questionnaire was a nineteen-item self-administered questionnaire divided into four domains namely, social interaction (Domain 1), impairment in communication (Domain 2), repetitive behavior (Domain 3), characteristics of autism as a disorder and its comorbidities (Domain 4), the total score ranges 0-19 and good score was labelled as > 15. Data was entered and analyzed in (SPSS) version 22.0. The quantitative variables age, years of experience and KCAHW score were expressed as mean and standard deviation. Frequency and percentage were calculated for qualitative data like gender and good knowledge i.e. KCAHW score ≥ 15. Data will be stratified for age, gender, duration of experience (1-5, > 5 years) and qualification to deal with effect modifiers. Post stratification Chi-square test was applied taking p-value ≤ 0.05 as significant.

## Results

The mean age of subjects was 30.67 ± 2.80 years with minimum and maximum age of 26 – 35 years. There were 37(37%) subjects aged 26-29 years and 63(63 %) doctors were 30-35 years old. A total of 31(31%) physicians male and 69(69%) were females. According to duration of experience, 58(58%) subjects had 1-5 years of clinical experience and 42(42%) subjects had > 5 years of experience. There were 18(18%) students who were only graduate while 82(82%) were PG trainee as well. The mean KCAHW score was 15.07 ± 3.54 with minimum and maximum score of 7 and 19. A total of 62(62%) subjects had good knowledge while 38(38%) physician had score < 15. When data was stratified for age, gender and duration of experience, we found significant association of good score with these effect modifiers, p-value > 0.05.

## Discussion

Autism spectrum disorder is one of the fastest increasing disorders in children throughout the whole world and it is lifelong disorder affecting neuronal development in children hence can be characterized by the symptoms like impaired non-verbal and verbal communication, impaired socialization and restricted behavior and interest patterns.[11] There are many studies in current age that are being done related to this disorder but these studies suggest different

**Table 1:** *Descriptive Statistics of Age (years) and KCAHW Scores*

| | Mean | S. D | Range | Min. | Max. |
|---|---|---|---|---|---|
| Age (years) | 30.67 | ±2.80 | 9 | 26 | 35 |
| KCAHW* | 15.07 | ±3.54 | 12 | 7 | 19 |

*Knowledge about Childhood Autism among Health Workers (KCAHW) Questionnaire

**Table 2:** *Comparison of Good KCAHW Score and Age Groups*

| | | Good knowledge | | p-value |
|---|---|---|---|---|
| | | Yes | No | |
| Age groups (years) | 26-29 | 21(33.9%) | 16(42.1%) | 0.408 |
| | 30-35 | 41(66.1%) | 22(57.9%) | |
| Gender | Male | 20(32.3%) | 11(28.9%) | 0.728 |
| | Female | 42(67.7%) | 27(71.1%) | |
| Duration of experience (years) | 1-5 | 34(54.8%) | 24(63.2%) | 0.413 |
| | >5 | 28(45.2%) | 14(36.8%) | |

variation and levels of knowledge in healthcare workers and professionals that directly influences treatment diagnosis and prognosis of this disease.[12]

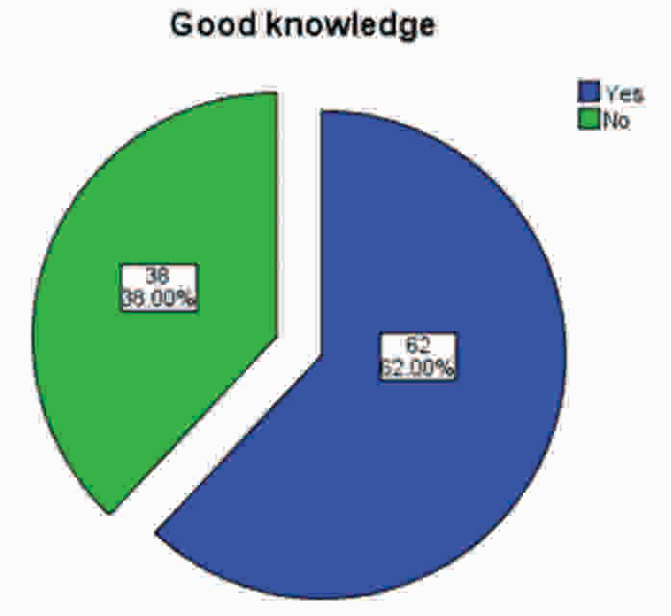


**Fig-1:** *Distribution of Good Score*

Variations of knowledge regarding Autism, may present in primary health care providers for example family physicians and family pediatricians and in comparison to specialist like speech therapist child psychiatrist and psychologist according to one survey done in United States.[13] Professionals of healthcare in countries that are underdeveloped also have low levels of knowledge regarding ASD.[14] Pediatricians are first point for contact, so they must have proper knowledge regarding autism spectrum disorder.[15] In Pakistan healthcare professionals still have questionable assessment regarding this disorder.[16]

In the year 2011, one study observed baseline misconceptions and knowledge related to autism in healthcare professionals of Pakistan.[10] In this study mean subjects age was 30.67 ± 2.80 yrs. with 31(31 %) male and 69 (69%) physicians females. Accurate knowledge regarding DSM IV TR criteria of diagnosis regarding autism was main focus of the study but in different professionals' variations were noted related to proper use of this criteria in diagnosis of autism. Non physicians had more chances of diagnosing autism correctly than physicians. (P value <0.001).[10] Similar results were seen in another study done in one of the African countries.[17] Our study was done on paediatricians only with mean KCAHW score as 15.07 ± 3.54 with maximum and minimum score as 19 and 7 only. Total 62% of res-pondents had good knowledge and 38% of physicians had less than 15 score. So, our study showed 38% paediatricians had poor knowledge regarding autism spectrum disorders, which in turn may affect early diagnosis and prognosis of children with autism spectrum disorder. There is need to conduct studies on larger scale prospectively with imparting learning of autism spectrum disorder using different educa-tional activities and comparing pre- and post-educa-tional activities results regarding knowledge of autism spectrum disorder in health care workers.

Hence it is concluded that some pediatricians may need to improve their knowledge regarding autism spectrum disorder.[18]

## Conclusion

Though 68% of paediatricians had good knowledge about childhood autism according to our study. The physicians who had poor knowledge, must be considered for different educational activities to enhance their knowledge regarding ASD, which may help in early diagnosis and improving prognosis of children with ASD.

## Author's Contribution

**ZF, QH, AI, SAM:** Concept, design, interpretation, drafting

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# Histological Changes in Proximal and Distal Convoluted Tubules of Kidney of Albino Rats after Exposure to Mosquito Coil Smoke Inhalation

**Nazia Siddique,[1] Masooma Ahmed,[2] Maria Ilyas,[3] Rukhsana Jabeen,[4] Abdul Hannan Jawad,[5] Zafar Iqbal[6]**

**Abstract**

**Objective:** To evaluate the effects of the mosquito coil smoke (MCS) inhalation on histology of proximal (PCT) and distal (DCT) convoluted tubules of kidney in Wistar Albino rats.

**Design:** Experimental study, randomized control trial.

**Methods:** This study was approved by the Ethical Committee of PGMI, Lahore. 24 Wistar rats were selected and randomly divided into 3 groups, each containing eight animals. Group A was control; Group B and C were experimental groups and were exposed to mosquito coil smoke inhalation for 8 hours/day for two and four weeks respectively. Kidney tissue of albino rats was dissected, examined and analyzed histologically.

**Results:** The results of MCS inhalation in histological sections of group B and C showed marked cellular necrosis and vacuolization in PCT (proximal convoluted tubule) of the kidney as compared to the group A. protein cast was absent in PCT of all groups. DCT (distal convoluted tubules) in group B and C showed marked necrosis, vacuolization and protein cast. Necrosis was more marked in group C treated with mosquito coil smoke for 4 weeks.

**Conclusion:** The results indicate that pyrethroids in mosquito coil smoke though considered least toxic pesticides, are very harmful. Exposure of pyrethroids can induce adverse changes in tubules of kidney.

**Key Words:** MCS Mosquito Coil Smoke, Pyrethroids, PCT Proximal convoluted tubules, DCT Distal convoluted tubules.

## Introduction

Mosquitoes are the main agent which can cause various vector-borne diseases. Most common diseases in Pakistan are Malaria and Dengue Fever. During the second decade of 21st century the Pakistan encountered the dengue epidemics. As no vaccine is available against dengue fever the only way of protection is prevention. People tend to wear long sleeved clothes with long trousers to prevent mosquito bites, sleep under bed nets, use topical repellent and burn repellent coils. As mosquito coils are cheap and easily available so it is most commonly used method to kill mosquitos[1]. Previous studies suggested that mosquito coils containing pyretheroid as an active ingredient can help in controlling mosquito borne diseases[2]. Mosquito coils smoke contain pyrethrin, d -trans-allethrin, aldehyde etc. Traditional coils are made from pyrethrum extracted from chrysanthemum cinnerariae folium plant. Pyrethrin is a natural pyrethrum and pyretheroids are synthetic derivatives of pyrethrins.[3]

One of previous study estimated that smoke produced by burning one mosquito coil was equivalent to smoke produced by burning approximately 75 - 137 cigarettes[4]. It was discovered that in some developing countries the use of unauthorized mosquito coils may induce human poisoning.[5] Pyretheroid poisioning produced a defect in cardiac conduction.[6] Vacuolar degeneration, necrosis, thrombosis and vasculitis in heart were also reported. Sore throat, nausea, vomiting and abdominal pain are acute effects of Pyretheroid ingestion.[7]

Pyretheroid based mosquito coils induce neurotoxi-

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city by oxidative damage in brain.[8] According to previous studies the action on voltage gated sodium channel and receptor gated ion channels are main cause of neurotoxicity.[9] The decrease in motor activity was produced by Pyrethroid.[6] Prolonged and uninterrupted exposure to mosquito coil smoke containing allethrin induces toxic changes in males testis including destruction of tubular archi-tecture, epithelial cell disruption, increase in the size of the lumen and necrotic spermatozoa.[10] In female, Pyrethroid may disrupt the estrous cycle, endocrine glands may have showed increase in weight especially thyroids and adrenals.[11] Pyrethrin and pyrethroids enter the body by many routes including ingestion with food, inhalation via coil smoke or burning or directly in contact with the skin. These chemicals are metabolized very rapidly in human body. Nervous system is the main primary target of the pyrethroid toxicity.[8] Chronic exposure of pyrethroides produce many toxic effects including skin allergy, asthma, irritation of nose, throat and damages heart, lungs, liver and kidneys.[8,9] Pyrethroids (DTA) are prone to induce toxicity at cellular levels leading to necrosis and tissue damage. Neurotoxic effects of chemicals emitted via mosquito coil smoke are extensively reported[10]. Many of the studies conducted in the past have established morphological, biochemical and cellular toxicity in the gastrointestinal and especially in the inhalants respiratory system.[11] Prolonged coil smoke exposure lead to adverse behavioral and neurological side effects in rat's offspring during prenatal and early postnatal period.[12] It decreased sperm concentration and induced liver toxicity.[7] This study was designed to observe the toxic effects mosquito coil smoke on histology of kidney.

## Methods

The animal study was conducted in the animal house of Anatomy department, PGMI, Lahore. The study protocol and procedures were approved by the Ethical Committee of PGMI, Lahore.

This was an experimental study, randomized control trial. Albino rats of Wister strain were obtained from animal house, PGMI, Lahore. Inclusion criteria were healthy animal of mix gender with average weight of 180-200 grams. Animals were weighed and examined thoroughly for any gross morbidity. They were individually kept in climate-controlled conditions of temperature 23 ± 0.5˚C and 12 hours light / dark cycles in an undisturbed well ventilated room. They were provided with standard rat food and water ad libitum. Rats were acclimatization in their cages for 15 days.

### Procedure and Histological Analysis

After acclimatization, the animals were randomly divided using Stat Trek random number generator into three groups A, B and C. Each group contained 8 rats. Group A was not exposed to mosquito coil and served as control. Group B and C were experimental group and were exposed to mosquito coil smoke.

During the experiment rats were kept in their designated cages and allowed to inhale the MCS as whole body inhalation. The mosquito coil was burnt and then placed in the center of room. The animal cages were positioned equidistant from the mosquito coil so that all rats inhale equal amount of MCS. Group A was control and was not exposed to any mosquito coil smoke. Group B and group C were experimental and were exposed to mosquito coil smoke for 8 hours/ day for two and four weeks respectively.

All animals were sacrificed under deep anesthesia 24 hours after exposure to their last dose. Kidneys (right and left) were dissected out. Weight of both kidneys was recorded carefully on electronic weighing scale. All the animals were euthanized by decapitation. Their bodies were disposed-off by burying in burial ground at PGMI, Lahore. Kidneys were washed with normal saline and fixed in 10 ml of neutral 10% buffered formalin. Tissue processing was done by using automatic tissue processor and then embedded in paraffin. 3 – 4 µm thick serial paraffin sections were obtained and stained with standard haematoxylin and eosin (H&E) reagent for the histopathological examination. Slides were examined under light microscope (ACCU-SCOPE 3000-LED Microscope) at 10X and 40X magnifications. Proximal and distal convoluted tubules were obser-ved in 5 fields of view in each kidney. The cells of proximal and distal convoluted tubules were exa-mined for the presence of cellular necrosis, cellular vacuolization and protein cast.

### Statistical analysis

The observations were recorded in MS Word® and Excel® data sheet. Data was analyzed using SPSS 21·0. Qualitative analysis of parameters was carried

out by using Pearsons chi square test or/and fisher exact test, at 5 % level of significance. A p-value ≤ 0·05 was considered as statistically significant.

## RESULTS

Proximal convoluted tubules were lined by simple cuboidal epithelium with prominent brush border, round nuclei with prominent nucleoli. The cell size and cell shape remain constant in PCT when three groups were compared. Necrosis of PCT was absent in group A while present in group B and C and was statistically significant when all the three groups were compared. (Table 1, figure: 1) Cytoplasmic vacuoles were observed in PCT cells in treated groups and statistically significant when compared with control (Figures 2, 3, 4). Protein cast was not significant statistically in PCT. Cellular necrosis, cytoplasmic vacuoles and luminal protein cast in PCT and DCT were absent in group A. Distal convoluted tubles were recognized by larger more clearly defined lumen, lined by simple cuboidal epithelium, closely packed nuclei and lack of brush border. The cell size and shape remain constant in all three groups. Group A showed no signs of cellular necrosis, vacuolization and protein cast. Cellular mecrosis, vaculization and protein cast were present in both group B and C and were statistically significant. (Table 2) (Figure 2,3,4)

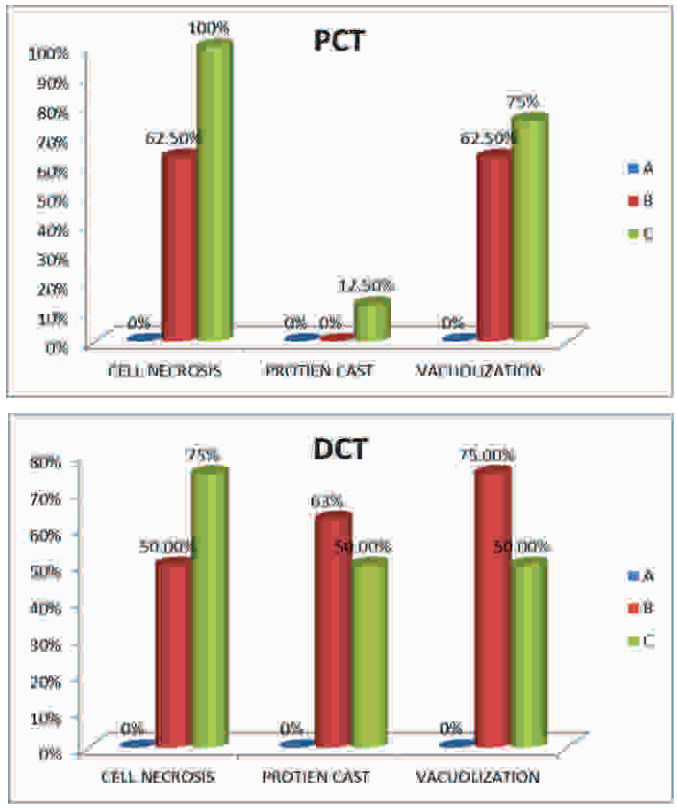


**Figure 1:** *Bar Chart Showing Comparison Percentage of Necrosis, Vacuolization and Protein Cast in PCT and DCT between Groups I, II, III.*

**Table 1:** *Showing Percentage of Cellular Necrosis, Protein cast and Vacuolization in PCT in Group A, B and C.*

| PCT | Status | Group A | | Group B | | Group C | | $\chi^2$-test (p-value) |
|---|---|---|---|---|---|---|---|---|
| | | n | % | N | % | N | % | |
| Cell necrosis | Normal | 8 | 0 % | 3 | 62.5% | 0 | 100% | 0.000*** |
| | Necrotic | 0 | | 5 | | 8 | | |
| Protein cast | Absent | 8 | 0 % | 8 | 0% | 7 | 12.5% | 0.352 |
| | Present | 0 | | 0 | | 1 | | |
| Vacuolization | Normal | 8 | 0 % | 3 | 62.5% | 2 | 75% | 0.006** |
| | Vacuolized | 0 | | 5 | | 6 | | |

*p-value ≤ 0.05 is considered to be statistically significant.

**Table 2:** *Showing Percentage of Cellular Necrosis, Protein Cast and Vacuolization in DCT in Group A, B and C*

| DCT | Status | Group A | | Group B | | Group C | | $\chi^2$-test (p-value) |
|---|---|---|---|---|---|---|---|---|
| | | n | % | n | % | N | % | |
| Cell necrosis | Normal | 8 | 0% | 4 | 50% | 2 | 75% | 0.008** |
| | necrotic | 0 | | 4 | | 6 | | |
| Protein cast | Absent | 8 | 0% | 3 | 62.5% | 4 | 50% | 0.024* |
| | Present | 0 | | 5 | | 4 | | |
| Vacuolization | normal | 8 | 0% | 2 | 75% | 4 | 50% | NA |
| | Vacuolized | 0 | | 6 | | 4 | | |

*p-value ⩽ 0.05 is considered to be statistically significant.

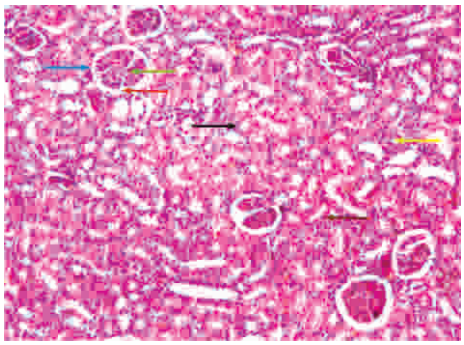

**Figure 2.** *Photomicrograph of the Kidney from the Control group A Showing PCT Lined by Cuboidal Epithelium with Brush Border (Brown Arrow) and DCT lined by cuboidal epithelium (black arrow) Renal corpusle (blue arrow) with central glomerulus (green arrow) surrounded by bowman's space (red arrow) and blood vessels are also present (yellow arrow). H&E stain 10 X*

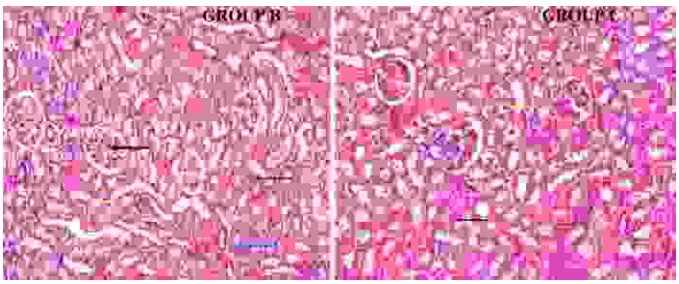


**Figure 3.** *Photomicrograph of the kidney from the group B (right) and group C (left) showing necrosis of both PCT (yellow arrow) and DCT (blue arrow). Cytoplasmic vacuoles are present (green arrow). Congested glomerulus (black arrow) and interstitial hemorrhage (brown arrow) is seen. Protein casts are present in DCT (red arrow). H&E stain .10 X*

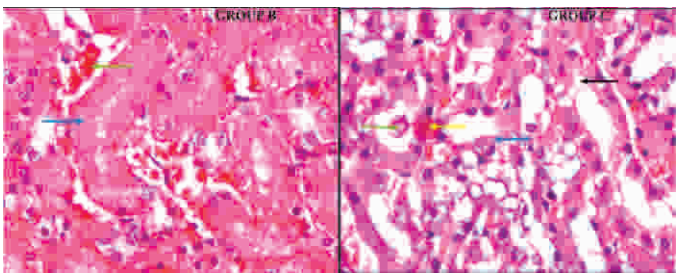

**Figure 4:** *Photomicrograph of the kidney from the group B(right) and group C (left) showing necrosis of renal tubules (blue arrow) and interstitial hemorrhage (green arrow). Cytoplasmic vacuolization of tubular epithelium (black arrow) and protein casts in DCT (green arrow) are seen H&E stain.40X*

## Discussion

The current study was designed to see the effects of mosquito coil smoke exposure on kidney tissue, using rat as a model. The experimental results demonstrated Pyrethroids (DTA) based mosquito coils are toxic in nature. Previously conducted studies have demonstrated that mosquito coil smoke inhalation shows signs of toxicity in liver and lung.[9] many previously conducted studies proved adverse effects of prolonged inhalation mosquito coil smoke. Current study has focused on the histopathological effects on the hictoarchitecture of kidneys.[5,8,13]

The histological observations on kidney from treated groups B and C showed marked toxic changes. The kidney tubules of rat treated with mosquito coil smoke inhalation showed necrosis and vacuolization. This tubular necrosis and vacuolization was due to the accumulation of phospholipids, lipids and cholesterol deposits in the cell[13]. Studies have shown that Pyrethroids act as potent inhi bitors of the mitochondrial complex I and oxygen, leading to their toxic effects on the mitochondria. The increased oxygen consumption causes an increase in the oxidative stress. It induces lipid peroxidation, protein oxidation and depletion of multiple antioxidant enzymes, which include glutathione, glutathione peroxidase, and catalase and superoxide dismutase activities14. The increased oxygen consumption increases mitochondrial oxygen usage. Pyrethroids inhibit the ATP production by the cellular mitochondria. A principle molecular mode of adverse action of the synthetic pyrethroids is alteration of sodium potassium (Na+/ K+) pump kinetics[15]. The sodium and water transport into cellular interior increases causing cellular fluid overload, disturbed protein synthesis and altered mechanical functions. These disturbed Na+/ K+ pump causes impairment of the oxidative phosphorylation that eventually results in hydrophilic degeneration, cellular swelling and vacuolization in the cytoplasm of renal tubular and parenchymal cells.[14] Pyrethroids increase free radical formation which damages body cell. The formation of oxygen free radical is one of major factor in toxicity of pesticides[15]. Voltage - gated sodium channels are mainly reported to be the primary target for toxicity of these coil smoke chemicals in humans. Research studies have depicted that all types of mammalian calcium channels are targets for allethrin at concentrations almost same as that reported for interaction with sodium channels[16]. The micro molar concentration of both compounds inhibited glutamate and succinate sustained state 3 respirations in a concentration - dependent manner. This inhibition is due to the effect of pyrethroids on mitochondrial transport system and also on the components of the respiratory chain.[14]

In our study we observed intraluminal cast formation in renal tubules. The matrix from the necrotic epithelial cell is the main cause for formation of this cast.[17]

This cast formation further obstructs the lumen of tubules. These findings suggest that inhalation of mosquito coil smoke cause nephrotoxicity. Their continuous usage causes harmful toxic effects in kidney. As these agents are easily absorbed in the body through inhalation.

## Conclusion

The observations and results of present study clearly indicate that despite of being the least toxic pesticide, pyrethroids still have harmful and necrotizing effects, as exposure to pyrethroids cause nephrotoxicity. Present study will produce an awareness of the dangers of the excessive use of mosquito coils and restriction of unlimited use of pyrethroid insecticides especially at living places.

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**Declaration of interests:** We declare no conflict of interests. This study was taken from thesis.

**Funding disclosure:** No funds were obtained for this study from any external source.

**Conflict of interest:** None

## Author's Contributions

**SN:** Principal investigator, data collection, study design & concept

**AM:** Literature review, data collection and interpretation of analysis.

**IM:** Data collection, critical evaluation, final editing of manuscript

**JR:** Data interpretation & tables

**JHA:** Data collection & statistical analysis

**IZ:** Manuscript writing

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# Pattern of Anemia among Primigravida Attending the Antenatal Clinic of Tertiary Care Hospital

**Natasha Bushra,[1] Ahmad Zunair Wasim,[2] Jamshid Feroze,[3] Maria Masood[4]**

**Abstract**

**Objectives:** To determine the frequency of anemia, severity, its various types and determinants among primigravida attending the antenatal clinic of tertiary care hospital.

**Methods:** It was cross sectional study conducted in Antenatal clinic, Gynecology and Obstetrics department, Services Hospital Lahore for duration of one year from 01-07-2017 to 30-06-2018. All primigravida presenting to antenatal clinic for their first antenatal visit uptil 24 weeks were included in study. Blood samples of the patients was sent in complete blood count vial to pathology laboratory. Patients having hemoglobin level less than 11 gm/dl were labelled as anemia and typing was done according to RBC indices, S. Ferritin and hemoglobin electrophoresis if required. Characteristics of patients anemic and nonanemic patients were compared. Severity of anemia was also noted.

**Results:** Total 210 primigravida were screened and 53 (25.2%) patients were found to be anemic. Iron deficiency anemia was noted in 40(75.5%) patients, beta thalassemia in 9(17.0%) patients and megaloblastic anemia in 4(1.9%) patients. Mild anemia was seen in 28(52.8%), moderate anemia in 19(35.8%) and severe anemia in 6(11.3%) primigravida. The mean age of the patients was 25.68±4.68 years in patients without anemia and 26.47±4.76 in patients with anemia. The mean gestational age at booking was 16.15±4.87 weeks for non anemic patients and 22.23±3.67 weeks for anemic patients ($p<0.05$). Mean hemoglobin in anemic patients was 9.2+0.8 mg/dl while 11.1+0.6mg/dl in nonanemic patients ($p<0.05$). Illiteracy, low socio-economic status and no intake of iron supplementation had significant association with anemia ($p<0.05$).

**Conclusion:** The frequency of anemia among primigravida attending the antenatal clinic of tertiary care hospital was 25.2% and the most common type was iron deficiency anemia. Poverty, illiteracy, late booking and no iron and folic acid intake were significant determinants of anemia.

**Key Words:** Anemia, Primigravidas, Iron deficiency anemia

## Introduction

Anemia affects quarter of global population with South Asia, Central and West Africa having highest anemia prevalence in the world.[1] Anemia is an important risk factor for health and development of women and children. Anemia in pregnancy constitutes a major public health problem and it is estimated that 56% of pregnant women in developing countries are anemic.[2] Anemia not only affects women health with fatigue and decreased working capacity but anemia in pregnancy is associated with high morbidity and mortality.[3] Maternal anemia is associated with fetal anemia and is important cause of perinatal mortality[4]. WHO classifies anemia into three categories i.e. mild anemia with hemoglobin 10-10.9gm/dl, moderate anemia with hemoglobin of 7-9.9gm/dl and severe anemia with hemoglobin< 7gm/dl.[5] The prevalence and disease burden of anemia in pregnancy has shown great variation in different developing countries ranging from 35.1% to 76.5%.[6,7] Poor socioeconomic conditions and repeated pregnancy burden with depletion of iron stores is characterized as reason for development of anemia.

All of these studies shows the disease burden of anemia in pregnant population where majority of the sample size consist of multigravida females. It is generally thought that primigravida do not have

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anemia as they didn't experience pregnancy burden which drains maternal iron stores. They are considered a low risk group and taken to hospital late for booking. Not many studies have been published which address frequency of anemia, its types and determinants in primigravida. First pregnancy is generally the first exposure of girls to a health care facility and many ailments are diagnosed for the first time. Primigravida constitute a very important obstetric cohort which, in which thalassemia minor can be diagnosed for the first time. Moreover their anemia will have different corelates as compared to multigravida. We planned this study to determine the frequency of anemia, its types and determinants among the primi-gravida presenting to the antenatal clinic of the tertia-ry care hospital. To our knowledge this is the first local study from Pakistan which addresses anemia in primigravida patients. This would also indirectly highlight the disease burden of anemia among female population as primigravida with anemia are more likely to be having pre-existing anemia . This will be useful in formulating the guidelines for young patien-ts who are getting married regarding their screening of anemia and prophylactic iron supplementation. Moreover, this study will provide baseline data for further research to be conducted regarding the risk factors and strategies for the management of anemia with respect to its public health importance to dec-rease the morbidity and improved feto-maternal out-come.

## Methods

It was a cross sectional study conducted in obstetrics department, Services Institute of Medical Sciences, Services hospital Lahore after taking approval from IRB. All primigravida presenting to antenatal clinic for their first antenatal visit uptil 24 weeks were included in study. All patients fulfilling the selection criteria was approached and an informed consent was taken from them before enrolling in the study Detailed history regarding age, education, socioeconomic status, previous ailments and dietary habits particularly intake of mutton or beef 2-3 times/week and iron plus folic acid tablets daily was taken. Family history of thalassemia was also recorded. The patients who were not willing to participate in the study and with bleeding disorders were excluded from the study. All the Information regarding their age and contact no was obtained by the researcher and noted in the proforma. Blood samples of the patients was taken by using aseptic techniques and was sent in complete blood count vial to pathology laboratory of Services Institute of medical sciences, Lahore for measurement of hemoglobin level and RBC indices. Results were collected by the researcher next day and were labeled anemia if hemoglobin was less than 11gm/dl. Females with low hemoglobin and RBC indices showing hypochromic, microcytic anemia were offered serum Ferritin to see iron stores and Hemoglobin electrophoresis to confirm beta thalassemia. Patients were classified as Iron deficiency anemia, thalassemia and megaloblastic anemia depending on RBC indices. All patients with anemia were categorized into mild, moderate and severe anemia according to WHO criteria with mild anemia (Hemoglobin level 10-10.9g/gl), moderate anemia (Hemoglobin level 7-10g/dl) and severe anemia (Hemoglobin level less than 7gm/dl). All patients were offered management of anemia according to the standard protocol. Characteristics of patients with & without anemia was compared. Sample size of 210 cases was calculated with 95% confidence level, 4% margin of error and taking expected percentage of primigravidas with anemia as 9.6%. Data was entered into computer through SPSS version 23, and it was analyzed by descriptive statistics. Qualitative variables like presence of anemia and type of anemia was presented in the form of frequency and percentages. Data was stratified for the age, trimester of pregnancy, educational status and total family income to control the effect modifier. The comparison between qualitative variables was done by using chi square test or fisher Exact test where appropriate. Chi square was applied post stratification and p value $< 0.05$ was taken as statistically significant.

## Results

In our study, 210 primigravida were screened out of which 53 were found to be anemic giving frequency of 25.2%. Iron deficiency anemia was noted in 40(75.5%) patients, beta thalassemia in 9(17.0%) patients and megaloblastic anemia in 4(1.9%) patients. Stratification of type of anemia done and 28(52.8%) were having mild anemia (Hemoglobin level 10-10.9g/gl), moderate anemia (Hemoglobin level 7-10g/dl) in 19(35.8%) and severe anemia (Hemoglobin level less than 7gm/dl) in 6(11.3%) primigravida were seen. (Table1)

The mean age of the patients was 25.68±4.68 years in patients without anemia and 26.47±4.76 in patients with anemia. The mean gestational age at booking was 16.15±4.87 weeks for non anemic patients and 22.23 ± 3.67 weeks for anemic patients ($p<0.05$). Mean hemoglobin in anemic patients was 8.2+0.8 mg/dl while 11.1+0.6mg/dl in nonanemic patients ($p<0.05$). Educational status showed that 36 (67.9%) of anemic patients were illiterate while 58/157 (36.9 %) of nonanemic patients were having elementary or no education( $p<0.05$). Low socioeconomic status had significant effect on prevalence of anemia ($p=0.476$). Mean gestational age of delivery was 35.5± 1.0 weeks in anemic and 37.6±1.7 weeks in nonanemic patients($p<0.05$)Table II.

## Discussion

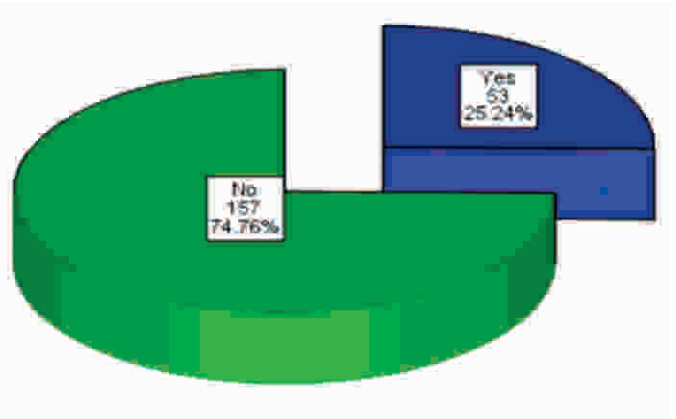
The frequency of anemia among primigravidas was found to be 25.2% which is quite high considering the cohort. The prevalence of anemia in pregnant patients reported in studies from Africa ranges from 25.3% - 53.09%.[8-11] These studies report 19- 25% patients to be primigravida but none of them have studies proportion of primigravida having anemia. One study from Malaysia has reported prevalence of 19.5% anemia in primigravida which is less than our study.[12] Study from Turkey report prevalence of 20% in pregnant patients at booking.[13] Malaysia and Turkey are developed countries with higher per capita income and less population burden from Pakistan hence better nutritional status of women. Studies from Pakistan report a high prevalence of anemia in pregnancy ranging from 74.8–93.2%.[14-16] Iron deficiency anemia was the commonest anemia seen in patients in our study. It is the commonest anemia reported worldwide.[8-11,14,15] Anemia in primigravida is alarming and depicts general status of women in society. Poverty with no intake of meat and protein being expensive although richest source of iron is a crucial reason. Gender bias have a role to play in low middle income countries as girls are definitely underfed.[2] Adequate knowledge about prenatal nutrition is also lacking among girls as is reported from study from Sindh.[14]

**Table 1:** *Frequency distribution of type & severity of anemia*

| | | Frequency | Percent |
|---|---|---|---|
| **Type of Anemia** | Iron deficiency Anemia | 40 | **75.5** |
| | Beta thalassemia | 9 | **17.0** |
| | Megaloblastic Anemia | 4 | **1.9** |
| | Total | **53** | **100** |
| **Severity of Anemia** | Mild anemia | 28 | 52.8% |
| | Moderate anemia | 19 | 35.8% |
| | Severe anemia | 6 | 11.3% |

**Table 2:** *Demographic & Maternal Characteristics*

| Parameters | Anemic =53 | Non anemic=157 | P value |
|---|---|---|---|
| Age | 26.68±4.68 years | 25.68±4.68 | 0.350 |
| Gestational Age at presentation (weeks) | 21.23±3.67 weeks | 16.15±4.87 | 0.000 |
| Education | | | |
| Illiterate / Elementary | 36 (67.9%) | 58 (36.9%) | |
| Secondary | 10 (18.8%) | 65 (41.4%) | 0.029 |
| Higher secondary | 7(13.3%) | 34 (21.6%) | |
| Income/month | 38(71.6%) | | 0.036 |
| <Rs.25,000 | | 92(58.5%) | |
| >25,000 | 15(28.3%) | 65(41.4%) | |
| Iron/folic acid intake | 15 (28.3%) | 52(33.1%) | 0.045 |
| Intake of meat | 5(9.4%) | 22(14.0%) | 0.574 |
| Hemoglobin at enrolment | 9.2±0.8 | 11.1±0.6 | 0.004 |




**Fig#1:** *Frequency Distribution of Anemia*

Mild anemia was seen in 52.8% of patients while 35.8% had moderate and 11.3% had severe anemia in this study. Studies from Pakistan have also reported majority of cases to be having mild to moderate anemia in women ranging from 52.5 to 69.9% with severe anemia in fewer cases.[14-16] Studies from Ethiopia and South Africa also report mild to moderate anemia to be more prevalent in pregnant women.[8,11] Study from Turkey reports significantly less anemia with mostly mild cases in pregnant patients at booking as most of the patients belonged to affluent socioeconomic class.[13] Severe anemia is generally related to acute blood loss while mild to moderate anemia depicts nutritional deficiency which is prevalent in Africa and South Asia. Thalassemia was the

second commonest anemia in our study seen in 17.9% of patients. Prevalence of 4.9% is reported from Islamabad while a study from Lahore reports 7.5% prevalence.[17,18] High prevalence in our study might be related to screening only primigravida. Screening for thalassemia should be mandatory for all young girls pre martially so that early screening can be offered to patients and prevention of major thalassemia is possible. A study by Anchang-Kimbi et al documented that 57% frequency of anemia. Moreover, it was seen that 75% of the anemic females had iron deficiency anemia while 17.3% and 5% suffered from beta thalassemia and megaloblastic anemia respectively.[19]

Mean gestational age at booking was significantly late for anemic women. We enrolled the study participants uptil 24 weeks as incidence of anemia increases with gestational age due to progressive hemodilution and more demand from the fetus. Early booking leads to appropriate iron supplementation and dietary counselling of patients which is evident in our study as iron and folic acid intake was significantly better in nonanemic patients. Incidence of iron deficiency anemia has progressively decreased in India over 15 years due to increasing iron intake of population along with iron fortification of salt.[20] This is especially important in young girls who will be mothers in near future so that they have adequate stores to start pregnancy. Knowledge about nutrition in pregnancy should be imparted to general public especially addressing myths and misconceptions about iron intake. A study from Ghana reports that patients were four times more anemic in third trimester and reason being inadequate iron supplementation due to lack of knowledge about micronutrient needs in pregnancy[21].

Poverty and illiteracy were significantly associated with anemia in our study. Both go hand in hand as poor families cannot afford education which is not provided by the State in LMIC. All studies from Africa and South Asia report illiteracy and poverty as major cause of anemia.[6-10,14,15,16] Education empowers women to take decisions regarding diet, iron supplementation and spacing during pregnancies. Mean hemoglobin of 9.2 was too low for a primigravida in early pregnancy. Anemia in pregnancy is not only responsible for adverse maternal outcome but childhood stunting is irreversible outcome of inadequate nutrition during pregnancy. Stunting has long-term effects on individuals and societies, including: diminished cognitive and physical development, reduced productive capacity. Children born to anemic mothers have low IQ and have poor school outcomes[22]. WHO has set global targets to achieve 50% reduction of anemia in women of reproductive age and 40% reduction of the global number of children under five who are stunted by 2025.[23]

It is recommended that government should focus on giving education regarding importance of micronutrients to all adolescent girls. Adequate nutrition, beginning in early stages of life, is crucial to ensure good physical and mental development and long-term health of our nation.

## Conclusion

The frequency of anemia among primigravida attending the antenatal clinic of tertiary care hospital was 25.2%. Iron deficiency anemia was the commonest followed by beta thalassemia and megaloblast anemia. Poverty, illiteracy, late booking and no iron and folic acid intake were significant determinants of anemia.

### Conflict of interest

There is no conflict of interest.

## Author Contribution

**NB**: Conceptualized the study and wrote initial manuscript.
**AZW:** Data analysis.
**JF:** Reviewed initial manuscript and wrote final manuscript.
**MM:** Maintained database.

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# Association of Antidiabetic Treatment with the Type of Obesity in Type 2 Diabetic Patients

**Jawariea Ali, Sheikh Sajjad Ali, Muhammad Imran, Tuba Tariq, Umair Mahmood, Junaid Iqbal**

**Abstract**

**Objective:** To find association between antidiabetic treatment and the type of obesity in type 2 diabetic patients.

**Methods:** The study was conducted in National Institute of Diabetes & Endocrinology (NIDE), Karachi, over a period of 6 months, ie. from January to June, 2018. It was an observational analytical study, for which 59 patients were selected via non-probability sampling, as per inclusion and exclusion criteria. Data was collected through detailed history, examination. A database was developed and analyzed on SPSS 17. A p-value <0.05 was taken as statistically significant.

**Results:** Fifty nine patients fulfilling the inclusion criteria were included in this study. While 30 (50.8%) had generalized obesity, 29 (49.2%) were not having generalized obesity. Further it was observed that 35 (59.3%) had abdominal obesity, while 24 (40.7%) were not having abdominal obesity. A total of 39 (66.1%) were on insulin, while 20 (43.9%) were not on insulin. Finally, 41 (69.5%) were on oral hypoglycemic drugs, while 18 (30.5%) were not on oral hypoglycemic drugs. P-values were not significant for the study parameters.

**Conclusion:** There is no association between antidiabetic treatment and type of obesity in type 2 diabetic patients.

**Key Words:** diabetes, obesity, body mass index, insulin, oral hypoglycemic drugs

## Introduction

Obesity is intercontinental issue.[1] In USA alone, more then 2/3rd of population is morbidly obese.[2] A study conducted in 2006 suggested that a quarter of the Pakistani population falls in the overweight or obese category.[3] This was calculated by quantifying them according to Indo-Asian specific BMI cut off values. According to the 2016 World Health Organization (WHO) statistics, 20.8% of the population is overweight and 4.8% is obese.[4] Studies done in Pakistan have labeled obesity as an epidemic.[5]

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The relationship between human fat and metabolic disorders are not completely understood, although excess body fat is linked with cardiovascular disease risk.[6] Obesity is directly related to BMI and adiposity is amount of human fat accumulated and it represents excess load of human body fat.[7] Body mass index is a measure for human body shape based on an individual's mass and height.8 According to the World Health Organization, normal BMI is ≤ 25.0 kg/m$^2$ and generalized obesity is defined as BMI of or more than 30. And according to a WHO expert consultation on appropriate BMI for Asian population, the range for acceptable normal or optimum BMI should be narrowed to 18.5–23 kg/m$^2$, but the criteria for obesity is still BMI 30 or more.[9] Abdominal obesity is defined as WC of 90 cm or more for men and 80 cm or more for women according to the International Diabetes Federation for Asian populations. Abdominal obesity, also known as belly fat or clinically as central obesity, is considerable abdominal fat around the stomach and abdomen.[10]

## Methods

The study was conducted in National Institute of

Diabetes & Endocrinology (NIDE), Karachi, over a period of 6 months, i.e. from January to June, 2018. It was an observational analytical study. A sample size of 59 was calculated using standard formula: $n = z^2$. P (1 - P) / $m^2$, where n is the sample size, z is the confidence level at 95% (standard value of 1.96), P is the prevalence of disease, and m is the margin of error at 5% (standard value of 0.05). The sample size was verified by the help of computer software PASS (Power Analysis and Sample Size) version 2015, at 90% power of the test and an alpha of 0.05. Patients, coming to OPD of NIDE, were selected via non-probability (convenient) sampling, as per following criteria:

### Inclusion Criteria

Type 2 diabetes
Both male and female individuals
Age > 40 years
Weight > 70 kg
Abdominal waist > 80 cm
BMI > 25
On insulin and/or oral hypoglycemic drugs for at least 10 years

### Exclusion Criteria

Type 1 diabetes
Gestational diabetes
Hypothyroid patients
Other co-morbidities (eg. CRF, CLD etc)

Data was collected through detailed history and examination (general physical, systemic examination, biometrics). Data source included the records of diabetic patients treated in NIDE, Karachi and the data was used to categorize the patients according to type of obesity and the type of anti diabetic treatment. A database was developed and analyzed on SPSS 17. Mean and SD was calculated for age. Frequency and percentages were calculated for gender, waist circumference, BMI, use of insulin and use of oral hypoglycemic drugs and outcome variable ie. generalized and abdominal obesity. Effect modifier was controlled through stratification of age, gender, insulin use and oral hypoglycemic drugs. It was done to see their effect, on outcome variables, applying chi square test. A p-value of < 0.05 was taken statistically significant.

### Results

In this study, 59 diabetic patients, both males and females, fulfilling the inclusion criteria, were included. On analysis of demographics data it was observed that 42 (71.2%) were males while 17 (28.8%) were females. A total of 36 (61%) patients were below 60 years of age while 23 (39%) were 60 years or above of age. While 30 (50.8%) had generalized obesity, 29 (49.2%) were not having generalized obesity. Further it was observed that 35 (59.3%) had abdominal obesity, while 24 (40.7%) were not having abdominal obesity. A total of 39 (66.1%) were on insulin, while 20 (43.9%) were not on insulin. Finally, 41(69.5%) were on oral hypoglycemic drugs, while 18(30.5%) were not on oral hypoglycemic drugs. Stratification and analysis of observed data is given in Tables 1-4:

### Discussion

Our study compared the type of antidiabetic treatment on the type of obesity, using 59 diabetic patients. We observed that generalized obesity was more in our patients than abdominal obesity. It was an unfortunate finding that abdominal obesity was invariably present in users of both type of treatments. Hollander in 2007 compared insulin and different oral hypoglycemic drugs in diabetics and concluded an overall weight gain in exclusive insulin users.[11] One important factor that has been shown to increase abdominal obesity with insulin therapy is hypoglycemia. Frequent hypoglycemia and treatment, often overtreatment, can cause weight gain.[12] There is also evidence that

**Table 1:** *Analysis of Insulin use with Generalized Obesity*

| Insulin use | Generalized obesity | | P - value |
|---|---|---|---|
| | Yes (30) | No (29) | |
| Yes (39) | 13 | 26 | 0.09 |
| No (20) | 17 | 03 | |

**Table 2:** *Analysis of Oral Hypoglycemic Drugs use with Generalized Obesity*

| Oral hypoglycemic drugs | Generalized obesity | | P - value |
|---|---|---|---|
| | Yes (30) | No (29) | |
| Yes (41) | 16 | 25 | 0.06 |
| No (18) | 14 | 04 | |

**Table 3:** *Analysis of Insulin use with Abdominal Obesity*

| Insulin use | Abdominal obesity | | P - value |
|---|---|---|---|
| | Yes (35) | No (24) | |
| **Yes (39)** | 24 | 15 | 0.17 |
| **No (20)** | 11 | 09 | |

**Table 4:** *Analysis of Oral Hypoglycemic Drugs use with Abdominal Obesity*

| Oral hypoglycemic drugs | Abdominal obesity | | P - value |
|---|---|---|---|
| | Yes (35) | No (24) | |
| Yes (41) | 24 | 17 | 0.54 |
| No (18) | 11 | 07 | |

insulin may play a direct role in fat creation and deposition.[13] Anderson et al. compared lispro and regular insulin at mealtimes and found no difference in weight gain between the two groups of patients with type 2 diabetes. Reduction in A1C also did not differ between the two groups.[14] Cheng in 2011 considered different pharmacotherapeutic options in type 2 diabetics and proposed that the treatment of diabetes should not only focus on glycemic control as its sole intention, but it should take into consideration the effect of antidiabetic treatment on weight as well, since obesity aggravates insulin resistance, beta cell failure, and cardiovascular risk.[15] Rosenstock et al. compared the efficacy of insulin analogs detemir and glargine when added to oral glucose lowering agents in insulin-naive type 2 diabetes subjects with baseline HbA1c of 8.6% in a 52-week, open-label treat-to-target trial. Treatment with insulin detemir (n = 291) and glargine (n=291) resulted in a comparable decrease in HbA1c from 8.6 to 7.2 and 7.1%, respectively. However, there were modest reductions in weight gain seen with detemir versus glargine (+3.0 kg versus +3.9 kg, P=.01).[16] Holman et al. conducted an open-label multicenter trial to evaluate the efficacy of basal insulin, prandial insulin, and biphasic insulin in type 2 diabetes patients inadequately controlled (mean HbA1 ~ 8.5%) on oral hypoglycemic agents[24]. Patients randomized to prandial insulin (n = 239) had a greater weight gain of 6.4 ± 0.5 kg compared with patients on biphasic insulin (n = 235) with weight gain of 5.7 ± 0.5 kg and basal insulin (n = 234) of 3.6 ± 0.5 kg.[17] Jacob et al. conducted a multicenter double-blind, placebo-controlled study in which overweight or obese patients with type 2 diabetes (mean HbA1c ~ 8.5%; BMI ~ 37 kg/m$^2$) on either metformin, sulfonylurea, and/or insulin were randomized to treatment with orlistat 120 mg three times daily (n = 1279) or placebo (n = 1271). Patients treated with orlistat had a statistically significant greater decrease in body weight (−3.8 kg) than placebo-treated patients (−1.4 kg) and a larger decrease in HbA1c compared with placebo (−0.74% versus −0.31%). In addition, patients with minimal weight loss (<1% of baseline body weight) were also found to have a significant improvement in glycemic control with orlistat (HbA1c −0.29%) compared with placebo (±0.14%) suggesting that improvement of glycemic control associated with orlistat may be independent of weight loss.[18] Clearly, the weight gain associated with insulin is a major drawback for treating diabetes, especially patients with type 2 diabetes mellitus.

## Conclusion

There is no association between antidiabetic treatment and type of obesity in type 2 diabetic patients. Diabetics have more abdominal as well as generalized obesity, which is not related to the drug they are taking for control of diabetes.

## Author's Contribution

**JA:** Author; Data collection
**ASS:** Conceived the article; Proof reading
**IM:** Data analysis
**TT:** Data analysis, Results compilation
**MU:** Write up and formatting
**IJ:** Statistical analysis

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# A Comparison between Bupivacaine Alone and Bupivacaine with Tramadol in Epidural Block for Postoperative Pain Management

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**Abstract**

**Objective:** This study was designed to compare the mean pain score with bupivacaine versus tramadol plus bupivacaine in patients undergoing surgery under general anesthesia. Randomized Controlled Study. Anesthesia department of SIMS medical college/Services Hospital, Lahore. Duration is 13 months from 20th August2017 till 24th September 2018.

**Method:** 80 patients aged 20-60 years of ASA I & II status, undergoing elective surgery were selected. Patients were randomly divided into two groups (Group A and B) of 40 each, using random numbers table. An epidural catheter was placed at L3-L4 intervertebral level. Group A was given 30 ml of 0.125% bupivacaine and Group B was given 25mg Tramadol plus 0.125% bupivacaine mixture in the same volume. General anesthesia was induced with IV Propofol 2mg/kg and atracurium 0.5mg/kg. After recovery from anesthesia, patients were shifted to HDU. Post-operative pain was assessed using the 10-point VAS score. Injection nalbuphine 0.1mg/kg was given as rescue analgesic when VAS score became more than 4.

**Results:** The mean age of patient in Group A was 37.5 ± 9.1 years and 38.6 ± 7.0 years in Group B. Mean BMI in Group A was 33.2 ± 4.3 and 32.2 ± 4.2 in Group B. The mean pain score after 12 hours of surgery was 3.6 ± 0.8 in Group A and 1.5 ± 0.9 in Group B, p value was significant.

**Conclusion:** Thus, the present study concludes that epidural administration of tramadol as adjuvant with bupivacaine is more effective in postoperative pain relief as compared to bupivacaine alone.

**Key Words:** Bupivacaine, Epidural, Postoperative pain, Tramadol.

## Introduction

Surgical patients require effective intra operative as well as post-operative pain control. The aim of postoperative analgesia is to provide patient comfort, early ambulation and recovery of motor function.[1] Effective postoperative analgesia decreases the incidence of respiratory and cardiovascular complications, improves patient satisfaction, speeds up recovery and discharge from hospital.[2,3,4,5] High severity of postoperative pain increases the incidence of hospital stay duration, surgical morbidity and mortality.[3]

Regional analgesia with the local anesthetic drug via epidural catheter is established method of satisfactory postoperative pain management.[1,6] Epidural block gives better control of the level of analgesia, lesser hemodynamic changes and can be used for postopera-tive pain relief by using different drugs.[6,7] The choice of individual drug used for epidural analgesia depends upon the factors like severity of pain, pre-sence of co morbid conditions and general condition of the patient.[4] Bupivacaine is a local anesthetic which belongs to the amide group of anesthetic agents that has been widely used for peripheral nerve blocks, spinal and epidural anesthesia. Various adjuvants have been added to the local anesthetic to minimize their side effects and prolong the duration of intra-operative and postoperative analgesia.[7] Opioids are considered the best option as adjuvants to local anes-thetics for

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postoperative analgesia because of easy availability and convenient use.[8] Tramadol is a cen-trally acting opioid analgesic and is similar in struc-ture to morphine and codeine with both active enan-tiomers. It augments the pain transmission inhibition via neurotransmitters modulation: the (+)-enantio-mer inhibits serotonin reuptake, whereas the (–)-enantiomer inhibits norepinephrine reuptake and has no neural toxicity when given intrathecal or in epidural anaesthesia.[9,10] In addition, the (+)-enantiomer and the primary metabolite of tramadol, (+)-O-desmethyl - tramadol, both act as μ-opioid receptor agonists.[11] The different properties of the tramadol enantiomers create synergistic analgesic effects, which improves tolerability by decreasing various side effects common to other opioids, such as respiratory depression, constipation, and abuse potential.[12]

The rationale for managing post-operative pain is to improve the outcome of surgery along with increased patient satisfaction. Earlier studies have revealed the use of systemic and regional analgesics with minimum side effects to be effective in relieving pain. We designed this study to compare the mean pain score with bupivacaine versus tramadol plus bupivacaine in patients undergoing surgery under general anesthesia.

**Study Design;** Randomized, Controlled Trial.

**Study Duration;** 13 months from 20th August 2017 till 24th September 2018.

**Venue;** Anesthesia Department of SIMS Medical College/Services Hospital.

## Methods

After approval from hospital ethical committee, 80 patients aged 20-60 years of ASA I & II status, undergoing elective surgery were selected through wards of Department of Surgery, Services hospital, Lahore. Written informed consent was taken. Patients with absolute contra indication for epidural block like bleeding disorder or receiving anticoagulants, allergic to study drugs, infection at the site of injection and neurological deficit were excluded from study. Patients were randomly divided into two groups (Group A and B) of 40 each using random numbers table. A 20G cannula was passed and standard monitors were applied after receiving the patient in operation theatre. Before administering general anesthesia, an epidural catheter was placed with Tuohy needle after loss of resistance technique at L3-L4 intervertebral space level. After a test dose of 3 ml xylocaine containing epinephrine (1:200,000), Group A was given 30 ml of 0.125% bupivacaine and Group B was given 25mg Tramadol plus 0.125% bupivacaine in the same volume of 30 ml. Anaesthesia was then induced with IV Propofol 2mg/kg and tracheal intubation was done with atracurium 0.5mg/kg. General anaesthesia was maintained with 50% $O_2$ + 50% $N_2O$ and 1.2% isoflurane with IPPV. At completion of surgery, patients were recovered from anesthesia and shifted to high dependency unit, where they were followed-up for 12 hours. After 12 hours, post-operative pain was assessed using the 10-point VAS score. No pain-0, 1–3-mild pain, 4–7-moderate pain, and 8–10-severe pain. Injection nalbuphine 0.1mg/kg was given as rescue analgesic in patients with VAS score of more than 4.

## Data Analysis

SPSS version 21 was used to enter and analyze the data. Quantitative variable like age, BMI and post-operative pain were represented by mean ± SD. Qualitative variable like gender were presented by calculating frequency and percentage. Both groups were compared for postoperative pain by using independent sample t-test. P-value≤0.05 was considered as significant.

## Results

The mean age of patient in Group A was 37.5 ± 9.1 years. In group B mean age was 38.6 ± 7.0 years. Age was comparable for both groups. Mean BMI in Group A was 33.2 ± 4.3 and 32.2 ± 4.2 in Group B. BMI distribution was equal in both groups. Table 1.

There were 38 males and 42 females making 47.5 % and 52.5 % of sampled population. Male female distribution was almost equal. (Figure:1) The mean pain score after twelve hour of surgery was 3.6 ± 0.8 in Group A and 1.5 ± 0.9 in Group B, p value was significant. Table 2.

Data stratification for age group and mean pain score was not significant. Table 3

## Discussion

More than 80% of patients suffer from acute post-operative pain after surgical procedure. The severity of pain is categorized as moderate, severe or extreme by 75% of patients. Adequate pain relief has been

reported in literature by less than half number of patients. Persistent postsurgical pain leads to increased risk of post-surgical complications, delay in recovery and thus quality of life will be affected with inadequate control of pain.[13,14] The goal of modern postoperative pain management is to minimize suffering and enhance recovery and rehabilitation through blunting maladaptive reflexes.[15] Many preoperative, intraoperative, and postoperative strategies are being used to control postoperative pain.[13,14] Most commonly used is epidural analgesia because of its various advantages. The major advantage is the use of lower doses of analgesic drugs with prolonged duration of action and minimal side effects.[15]

**Table 1:**

| | Group A (Bupivacaine) | Group B (Bupivacaine &Tramadol) |
|---|---|---|
| Age | 37.15±9.11 | 38.65±7.04 |
| BMI (kg/m$^2$) | 33.26±4.36 | 32.29±3.31 |

**Table 2:**

| | Group A (Bupivacaine) | Group B (Bupivacaine&Tramadol) | p-value |
|---|---|---|---|
| Pain Score Mean ± SD | 3.650±0.833 | 1.525±0.960 | 0.000 |

**Table 3:**

| Age (years) | Group A (Bupivacaine) | Group B (Bupivacaine&Tramadol) | p-value |
|---|---|---|---|
| 20-35 | 3.94±0.63 | 1.50±0.61 | 0.438 |
| 35-60 | 3.40±0.90 | 1.54±1.18 | 0.609 |

In our study lower VAS scores were found with combination of bupivacaine plus tramadol administered epidurally ($p<0.05$). Similar results were seen by Saxena D et al who also noticed lower pain scores with epidural tramadol+bupivacaine and concluded that it provided better analgesia than bupivacaine alone in patients undergoing lower limb surgeries.[6]

Comparable observations were seen by Pavithra who conducted study on pediatric population and compared bupivacaine alone versus tramadol plus bupivacaine. Duration of analgesia was maximum in combination therapy and there was less need for rescue analgesia in combination therapy group.[16] Likewise, Akhtar N et al supported the tramadol-ropi-vacaine combination to be effective than ropivacaine alone in lowering the pain scores when used in supraclavicular block for upper limb surgeries.[11] Singh et al. also revealed significant lower VAS scores with epidural tramadol as adjuvant to 0.2% ropivacaine in upper abdominal surgeries.[1] Consistent with our results, Imam A et al observed lower VAS pain scores in their study with tramadol via epidural route when compared to bupivacaine for postoperative analgesic effect in gyneacological surgeries.[17] In agreement to our study results, Yadhuraj MK et al found lower pain scores after 12 hours. He compared tramadol with pentazocine when given epidurally for postoperative analgesia in lower abdominal surge-ries.[18] Conflicting results have been seen in few studies which could be attributed to choice of local anesthetics, choice of adjuvants used and methodology. Higher VAS scores were seen by Agarwal et al with Tramadol-bupivacaine (4.4) after 4.5 hours undergoing TKR and THR surgeries under combined spinal epidural anesthesia.[2] Patil et al did not find mean VAS score to be lower in tramadol-bupivacaine when compared to fentanyl-bupivacaine group. This was contradictory to our study results which could be due to variation in methodology.[4] Contrary to our study results, Deo et al also found VAS scores to be significantly higher in Tramadol group. The reason for this variation could be that comparison was done with Butorphanol-bupivacaine combination and not with bupivacaine alone.[15] There were few limitations in our study like sedation score and adverse effects of Tramadal were not mea-sured in our study. Moreover, we could not compare its analgesic effects with other opioid and nonopioid adjuvants. Future studies can be done with other newer drugs to assess their efficacy for epidural analgesia.

## Conclusion

Thus, the present study concludes that epidural administration of tramadol as adjuvant with bupivacaine is more effective in postoperative pain relief as compared to bupivacaine alone.

**Conflict Of Interest;** None.

## Author's Contribution

**KS:** Basic design
**AA:** Data analysis
**SS:** Discussion writing
**BMM:** Iterpretation & data analysis
**MA:** Final drafting of manuscript
**JUM:** Final approval of revision

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# Association of Vitamin-D levels with Sleep Disturbances

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**Abstract**

**Objective:** Vitamin-D insufficiency and sleep disturbance, both are common problems worldwide and much more common in our part of world. Two problems are associated with each other, which make the situation worse especially locally where over the counter use of even sedatives is common. Vitamin D levels and sleep quality index has been measured and association recorded in our study.

**Methods:** This cross-sectional analytic study was conducted in Division of Medicine, CMH Lahore from 5th April 2019 to 5th Sep 2019. A total of 106 patients presenting to medicine OPD with symptoms of Vitamin-D insufficiency& low Vitamin-D levels were included in the study. PSQI score was calculated. Post treatment follow up Vitamin-D levels and Pittsburgh Sleep Quality Index score were recorded. Data was entered and analyzed by using spss software version 20.

**Results:** Following 106 patients presenting to medical OPDs with Vitamin-D insufficiency, Mean Vitamin-D levels at first visit were ±20.30 with standard deviation of ±13.14 (CI 95%) , PSQI score in first visit was 7(SD ±2.66, CI 95%) Mean Vitamin-D levels in second visit after treatment was 83.5(SD ±20, CI 95%). PSQI score mean 3.1(SD 1.8, CI 95%). Odds ratio of 3.9(95% CI: 1.20, 12.7), Chi-Square 5.62 with p value .018 was found in first visit and 8.3 (95% CI: 3.15, 22.0) ,Chi-Square 20.9 with p value <.001 for second visit indicating significant association of Vitamin-D deficiency with poor sleep score.

**Conclusion:** Sleep disturbance is associated with low Vitamin-D levels depicting as high Pittsburgh score whereas score decreases with increasing Vitamin-D levels.

**Key Words:** Pittsburgh Sleep Quality Index (PSQI), Vitamin D levels (Vitamin-D level), Sleep disturbances

## Introduction

Vitamin-D is one of the fat-soluble vitamins and is essential for bone health. Its discovery dates back with the discovery of rickets type bone disease in 1600-1800 as the prevalence of rickets in children increased from 40-60 % in urban and crowded areas and later on in mid-1800 s it was found to be associated with poor sunlight exposure leading to cod liver oil replacement for treatment and finally to discovery of Vitamin-D.[1]

Vitamin-D has 2 forms i.e. D2 (ergocalciferol) mainly from plant source and D3 (cholcalciferol) obtained from diet like deep sea fish, egg yolks, liver or from synthesis in skin by Ultraviolet B light exposure to skin. Because of last two-decade insufficiency of Vitamin-D main sources are supplements and fortified foods all over the world.[2] Activated Vitamin-D is formed by 1,25 hydroxylation in liver and kidney and absorbs calcium and phosphate from gut. Vitamin-D status is measured by measuring 25(OH) D. Different methods of measurement were used by different investigators and till now values defined are level of 25(OH) D <10ng/ml (25nmol/l) is considered deficiency, 11-30ng/ml (26-75nmol/l) insufficient and more than 30ng/ml (75nmol/l) is considered sufficient.[3-6]

Vitamin-D deficiency results from poor dietary intake, inadequate sunlight exposure, dark skin, obesity, malabsorption, liver and kidney disease etc.[7,8] It has been associated with bone pains, bone diseases like rickets in kids and osteomalacia in adults. Vitamin-D insufficiency has been found to be an added risk factor with certain extra skeletal diseases like diabetes, cardiovascular disease, and malignan-

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cies and sleep disorders.

Vitamin-D supplementation is found to reduce musculoskeletal pains, 9 risk of bone disease, fractures, obstructive sleep apnea syndrome, cardiovascular mortality, diabetes, risk of cancer, infertility, autoimmunity etc.[10-12] Sleep is an essential component of human life and disturbance leads to poor function of the body.[13] Sleep problems are associated with Vit D deficiency so treating Vit D deficiency might help patients with sleep disturbances and decrease need of sedatives.[14] Several different scales have measured sleeping hours and quality. Sleep –wake activity inventory (SWAI), sleep impairment index scale (SII), sleep disorder questionnaire, Wisconson sleep Questionn-aire (WSQ), Epsworth sleepiness scale, Pittsburgh sleep quality index (PSQI) etc are the common used scales.[15] PSQI is good and detailed account of Patients sleep of last 1 month. Patient can fill the Performa or Questionnaire him/herself and final score from all components can be calculated. A poor sleep score is Pittsburgh score>5.[16] This study was designed, as there is no local data on the association of Vit D insufficiency with sleep disturbances in Pakistan. So identification of insufficient Vit D cases and sleep problems associated might relieve burden of disease and bring good quality sleep with less use of sedatives by proper replacement.[17]

## Methods

This study was conducted in Division of Medicine, CMH Lahore, from April 2019 to September 2019, after approval from Institutional Review Board (IRB), CMH Lahore (Ref No. 58/ERC/CMHLMC, dated June 9, 2020). A total of 106 patients were selected from outpatient department after calculating the sample size (95 % Confidence level, 10 % margin of error and taking frequency of Vitamin D deficiency as 30 % (14-59%). All these patients presenting in OPDs with muscle pains and lethargy and having low Vitamin-D levels were included. While those subjects who had symptoms because of some other medical illness like rheumatologic disease or uncontrolled diabetes mellitus, respiratory, psychiatric, neuropathic or myopathic problems, complicated liver, kidney or heart disease was excluded from the study.

Written informed consent was taken from each patient for participation in study and confidentiality was maintained. Their demographic profiles (i.e. age, sex, occupation) were also noted using a structured questionnaire.

Vitamin-D levels were recorded and grouped according to levels i.e. Deficiency (<26 nmole/L), Insufficiency (26-75nmole/L).[3-6] Co-morbid conditions and medications were recorded. All other causes which could cause sleep disturbances and any co morbid condition which was active with clinical or lab abnormalities were excluded. Patients were asked about sleep disturbances and the ones having problem were given Pittsburgh sleep quality index score questionnaire. Pittsburgh sleep quality index has seven components; Out of this first 4 components have questions about time to bed and actually sleeping hours whereas component no 5 assesses quality of sleep and awakening, component 6 marks need of medication for sleep, 7&8 measure effect of sleep problems on patients health and 9 is about overall quality of sleep .Each component is scored 0-3 according to severity. Total score more than 5 marks poor sleep. PSQI score was calculated from the answers about previous month sleep quality. Patients were treated with inj vitamin D3 20000 IU, PO monthly with vit D3 oral tablet 1000 units daily for 2 months followed up after two months. Vitamin d levels and PSQI score was calculated at in follow up visit.

All the collected information was entered into SPSS version 20.0 and analyzed. Age, Vitamin-D levels, Pittsburgh sleep quality index score of first visit and 2 months follow up visit were presented as mean and +/- standard deviation. Frequency tables were made for gender, co morbid conditions, sleep disturbances, medications; Vitamin d levels were correlated with sleep disturbances both for first visit and 2 months follow up visit using Odds ratio and Chi-Square. Confounders like co morbid conditions, age and gender were analyzed by using Logistic regression analysis and adjusted odds ratio was calculated.

P value <0.05 was considered significant.

## Results

A total of 106 patients were enrolled according to inclusion criteria having symptoms and low vitamin D levels. Out of these 29 (27.7%) patients were males whereas 77(72.6%) were females. From 106 individuals, 27 patients (25.5%) were of age group 13-30, 77(72.6%) were of age group 31-60 and 2 (1.9%)

patients were of age 61-90. Majority of patients (67.9%) had no co-morbid condition or medical illness

In first observation Vitamin-D deficiency (level less than 26 nmole/L was seen in 90 (84.9%), 16 patients (15.1%) had level between 26-75 (Vitamin-D insufficiency). Sleep recording of previous month showed that 18 patients (16%) had Pittsburgh sleep quality index score of 1-5 (mild to moderate problem) and 88(83%) had Pittsburgh sleep quality index score of >5(poor sleep, severe problem). Use of sedatives was seen in 34 whereas 51 were not using any medication. In co morbid record, 6 patients (5.7%) had Diabetes mellitus, 11(10.4%) had hypertension, 4(3.8% patients had thyroid disorder 1 patient was asthmatic of mild intermittent type, 10 patients had some rheumatologic disorders out of which 5 had osteoarthritis, 3 Fibro-myalgia, 1 of gout and 1 of rheumatoid arthritis in remission with DMARDS, Two patients had other medical illnesses including heart disease and liver disease in each and none had neuropathy. All of these patients were stable and in remission as account of their disease control with no active clinical or lab abnormality thus ruling out possibility of sleep distur-bances by these problems All 6 patients with associa-ted diabetes mellitus had Vitamin-D level<26 and all-11 patients having hypertension also showed Vit D deficiency with level <26 nmole/L

Mean a Vitamin-D level at first visit was ±20.30 with standard deviation of ±13.14 (CI 95%), Pittuburgh scale in first visit was 7(SD ±2.66, CI 95%. (Table-I). There was negative correlation between vitamin D levels with Pittsburgh sleep scale of -0.15(p <0.05) (Table-I). In second observation after treatment with Vitamin-D 3 20000 IU monthly PO for two months Vitamin-D deficiency (level less than 26 nmole/L was seen in 38(35%), 68 patients (65%) had level between 26-75 (Vitamin-D insufficiency).

Sleep recording of previous month showed that 78 patients (73%) had Pittsburgh sleep quality index score of 1-5 (mild to moderate problem) and 28(26%) had Pittsburgh sleep quality index score of >5(poor sleep, severe problem). Use of sedatives was seen in 34 whereas 51 were not using any medication. Significant association was found between sleep disturbance with Odds ratio of 3.9 (95% CI: 1.20, 12.7), Chi square 5.62 and p value .018. Adjusted odds ratio was 3.85 with p value .02 in logistic regression analysis with confounders. (Table-II)

Mean Vitamin-D level in second visit was 83.5(SD ± 20, CI 95 %). PSQI score mean 3.1(SD ± 1.8, CI 95 %,). Odds ratio of 8.33 (95% CI: 3.14, 22.0) with Chi-Square 20.9,p value .000 was found in second visit indicating significant association of vitamin D deficiency with poor sleep score. Adjusted Odds ratio was 8.48 with p value .000(<. 001) (Table-III)

## Discussion

This is study from a tertiary care hospital establishing sleep disturbances in Vitamin-D deficient patients. We found that in absence of other causes of sleep disturbances Vitamin-D patients had decreased sleep hours and poor sleep quality with odds ratio of 3.9 in first visit and 8.3 in second visit. Sleep is very important for wellbeing of any person and factors affecting poor sleep need proper evaluation and treatment accordingly. Vitamin-D deficiency is common all over the world and more in our region because of dark skin and inadequate fortification of food like seen in developed world. Moreover, poverty keeps people in circle of finding basic food items and deprives them

**Table 1:** *Demographic Details and Disease Characteristics*

| | Mean | Standard Deviation |
|---|---|---|
| Age | 41.11 | 15.04 |
| Vitamin-D level first visit | 20.30 | 13.14 |
| Pittsburgh sleep quality index first visit | 6.62 | 2.66 |
| Vitamin-D level 2nd visit | 83.51 | 20.74 |
| Pittsburgh sleep quality index 2nd visit | 3.11 | 1.90 |

**Table 2:** *Risk of Sleep Disturbances in Vitamin-D Deficiency First Visit.*

| | | PSQI score | | Total | OR | Adjusted OR | Chi-Square | P-value |
|---|---|---|---|---|---|---|---|---|
| | | >5 | <5 | | | | | |
| Vitamin-D Deficiency | <25 | 78 | 12 | 90 | 3.9 | 3.9 | 5.62 | .018 |
| | 26-75 | 10 | 06 | 16 | | | | |
| | | 90 | 16 | 106 | | | | |
| Total | | 100.0% | 100.0% | 100.0% | | | | |

**Table 3:** *Risk of Sleep Disturbances in Vitamin-D Deficiency 2nd Visit.*

| | | PSQI score | | Total | OR | Adjusted OR | Chi-Square | P-value |
|---|---|---|---|---|---|---|---|---|
| | | >5 | <5 | | | | | |
| **Vitamin-D Deficiency** | <75 | 20 | 18 | 38 | 8.33 | 8.48 | 20.9 | .000 |
| | >75 | 08 | 60 | 68 | | | | |
| | | 28 | 78 | 106 | | | | |
| **Total** | | 100.0% | 100.0% | 100.0% | | | | |

with so-called luxury of nutrient rich food like fish. Vitamin D deficiency is affecting Pakistani population irrespective of age gender or area and cases recorded are only tip of the iceburg.[18,19] Vitamin-D deficiency has been proven to be associated with many diseases and sleep disturbances Sleep deprivation or disturbance is also found to be associated with increased risk of certain diseases and all-cause mortality.[20] Vitamin-D deficiency has been found to be related with severity of liver disease in local population.[21] Considering that, Vitamin-D replacement can reduce risk of diseases, severity of certain diseases, can decrease analgesic and sedatives use and can improve sleep quality.[22,23]

Cheng et al. found that severe Vitamin-D deficiency is associated with sleep disturbances odds ratio calculated was 4.14(CI 95% 2.01,8.52) p-value <0.001) in pregnant females in Singapore.[17] Eckini et al. conducted a study on pediatric population to know link between Vitamin-D and vitamin B12 deficiency with sleep disturbances and an association was found OR 1.93(95% CI,0.65-5.76,P<0.001).[24] similar link was found by Jung YS et al where an OR of 1.36 was found(95%CI,1.01,1.83) in fixed day field workers in the electronics manufacturing industry in Korea.[25] Piovezan RD found an association of obstructive sleep apnea as well as short sleep duration with Vitamin-D deficiency with OR 2.15(CI 95%, 1.21, 3.81). In our study we used Pittsburgh sleep quality index which measures sleep duration, quality of sleep and need for medications. It measures record of previous month sleep and is better marker of any kind of sleep disturbances. A negative correlation was found in our study of Vitamin-D levels with sleep disturbances. Higher Vitamin-D levels showed lower PSQI score and lower Vitamin-D levels showed higher PSQI scores. There are no local studies to find this asso-ciation although two studies as mentioned above have been reported from Korea and Singapore. The prob-lem is worst in developing countries as developed world has almost overcome the problem by fortifica-tion of food, healthy diet facilities, education and good health care services.

As prevalence of Vitamin-D deficiency and its association with bone diseases, sub-fertility, liver disease, cardiovascular disease, tuberculosis etc. has been studied in Pakistani population[18,21], Our study will add its association with sleep disturbances in literature which in turn might help patients by finding cause of their sleep disturbance and treatment by vitamin D replacement so that patient will get rid of sedatives use and addiction

## Conclusion

Higher frequency of sleep disturbances is observed in patients with vitamin D deficiency. Vitamin-D deficiency is found at any age younger to older individuals but seen more common in females having more sleep disturbances getting worse during pregnancies.

## Author's Contribution

**FS:** Design manuscript, statistical analysis
**SS:** Data collection
**MH, IJ:** Statistical analysis

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# Frequency of Weight Gain and its Impact in Adults during Lockdown: A Cross-Sectional Study

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**Abstract**

**Objectives:** The current lockdown in the country has led to a sedentary lifestyle because of a shift of daily activities online and a fear of contracting the illness leading to isolation inside homes; Hence an expected change in weight of the general population. This study aims to determine the frequency of weight gain and its impact in adults during the current lockdown of COVID-19.

**Methods:** Participants selected from the ages of 18-25 from different universities of Pakistan were sent questionnaires via WhatsApp, posted online using Microsoft Forms. A total of 157 responses were attained.

**Results:** Among the 157 participants the average weight before the lockdown was 61.95 kgs and after the lockdown was 64.99kgs so there was an increase of 3.016 kgs whereas 18.5% of the sample maintained their weight and 37.6% were reported to have lost weight. The results also depict a 1.6% increase in impairment of body image.

**Conclusion:** We concluded that the Lockdown due to the COVID-19 pandemic has caused a gain in the weight and lowered self-esteem with regard to body image of most young adults in Pakistan due to many factors including higher food intake, lack of exercise and also emotional distress.

**Key words:** Obesity, Weight gain, Lockdown, Body Image.

## Introduction

On March 11, 2020 WHO Director General declared COVID-19 a global pandemic, the first ever pandemic caused by the coronavirus species.[1] As governments, started to lockdown there countries, the stress and anxiety among the populations raised, as Brooks et al. found in their review a positive correlation of increased mental health problems during this pandemic. The factors leading to this rise include the long duration of isolation, fear of infection, inadequate supplies, boredom and frustration surrounding financial situations due increasing unemployment.[2] The article published by Zachery et al. May 2020, found that 22% of the subjects gained 5–10 pounds during self-isolation as they spent 20-24hrs inside the house.[3] Furthermore, this study also found that a significantly higher percentage of people that gained weight were eating in response to stress or snacking after dinner.[3]

As the uncertainty surrounding and duration of the pandemic increases, people tend to make unhealthier lifestyle choices. People tend to choose foods with longer shelf life that are highly processed and rich in calories.[4] This not only affects adults but also children. As schools, workplaces and gyms closed down, opportunities for physical activity also declined. Furthermore, people also have an unhealthier sleeping pattern during holidays. All of these factors i.e. unhealthy diet, lack of physical activity and poor sleeping habits lead to a heightened risk of obesity.[3]

As it is well known, obesity is linked to heightened morbidity and mortality. Obesity causes a low-grade systemic inflammation that leads to the development of metabolic dysfunction.[5] According to Bary et al. dysfunctional subcutaneous fat deposition lead to increased free fatty acids and decreases triglycerides which in turn causes ectopic fat deposition. This lipid deposition in various systems of the body lead to

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cardiovascular disease, diabetes mellitus and dyslipidemia. On the other hand there is increase in cytokines release and angiotensin which causes hypertension.[6] Furthermore, there is an increased risk of breast cancer, endometrial cancer and other forms of cancer.[7–9] Obesity also modifies the immune responses of the body, making the immune system more vulnerable to infections and less responsive to vaccinations, antivirals and antimicrobial therapies.[10] It has with higher incidences of respiratory tract infections as well as rhinitis, sinusitis and pha-ryngitis/ laryngitis in obese individuals.[11] A greater incidence of bronchitis, pneumonia and influenza like illness has also been reported in obese individuals.[12–14] In addition, according to Lee et al. and Delvin et al. there is a rise in mental health problems as obese people are more prone to weight based bullying, body image issues, depression and eating disorders.[15,16] Keeping in view all these factors, this study was aimed to determine frequency of weight gain and its impact in adults during the current lockdown of COVID-19.

## Methods

After approval by the ethical committee of CMH LMC & IOD, participants both male and female, age group of 18-25years, belonging to different universities of Pakistan were offered to be enrolled in the study. The sample size was calculated to be 157 using the Rao soft formula with 95%confidence interval and 5%margin error. The population size used was calculated by using values of Zachary et al.[2]

Questionaries' were administered online using Microsoft Forms by sending the link for the form to WhatsApp groups. The questionnaires were adapted using Impact of Weight on Quality of Life (IWQOL)[17] and Body Image Questionnaire (BIQ)[18]. The questions designed included questions from four areas: physical function, self-esteem, public distress and body image, respectively. Question 1 to 6 collected biodata of the participants. Question 7-16 were adapted from the IWQOL. Each question was rated on a three-point Likert scale with 'Never' scoring 0 points, 'Sometimes' scoring 3 points and 'All the time' scoring 5 points. The scores are additive and higher scores mean lower impact of weight gain on physical function, self-esteem, public distress. Question 17 - 21 were adapted from the Body Image Questionnaire (BIQ).[18] This part consist of 5 questions related to body image. Each item for this part was scored from 1 i.e., impaired to 5 i.e., most impaired. The total score was achieved by summing all scores. The total scores ranged from 6-30 with a higher score reflecting greater impairment of body image. All data was analyzed using SPSS software (version 26; IBM). Results were presented in frequency and percentages. Chi- square test was used for comparison of categorical variables. P value <0.05 was statistically significant.

## Results

One hundred and fifty-seven people completed the survey of which 109 were females and 48 males. The average weight before lockdown was 61.95 kgs and after lock down was 64.966 kgs, an increase of 3.016 kgs. Stable weight was maintained by 18.5 % of the sample while 37.6 %and 11.5 % reported to have gained less than 5 kilograms and more than 5 kilograms respectively. This data is presented in figure 1.

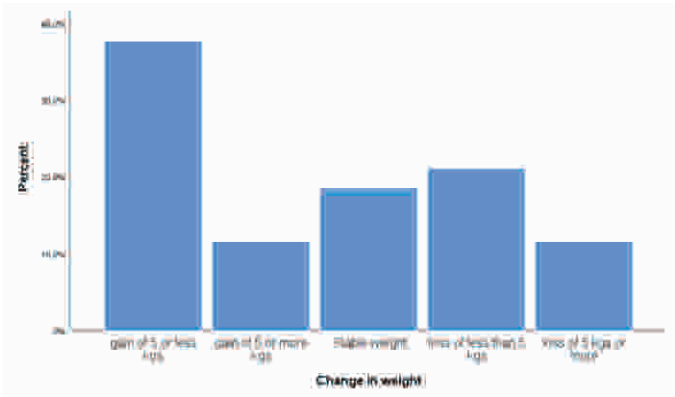


**Figure 1:** *Change in Weight by Percentage of Population*

The average score for part 1 of the survey assessing quality of life was 12.185 before lockdown and 12.86 after lockdown (Table 1). The increase in this score shows that the overall quality of life worsened during lockdown however this difference is not significantly high. As represented by Table 1, physical function declined in two variables, trouble with moderate exercise i.e., trouble climbing stairs/running with a P-value of 0.033 and trouble with stiff joints i.e. I am troubled by painful or stiff joints with a P- value of 0.002. The area of self-esteem also showed significant p-values for the variables 'Because of my weight, I am afraid of being rejected' and 'Because of my weight, I avoid looking in mirrors or seeing myself in photographs' with p- values of 0.04 and 0.033 respectively. The P- value was also significant for the varia-

ble concerning the area of work i.e. trouble getting things accomplished or meeting my responsibilities (0.02). The average score for part 2 of the survey assessing impairment in body image was 12.796 before lock-down and 13.701 after lockdown (Table 1). This demonstrates that there has been an increase in the likelihood of impaired body image. Assessment of impairment of body image demonstrate an increased impairment in some variables.

Table 2 represents the variables with significant p-values when populations were compared according to their change in weight. People were significantly self-conscious because of their weight after lockdown with a p-value of 0.026. Experience of being ridiculed, teased, or receiving unwanted attention increased in population with gain in weight, while it declined in those that lost weight(0.06).

**Table 1:** *Scores and Standard Deviation for Assessment of Quality of Life and body Image*

| | Assessment of quality of life | | Assessment of body image | |
|---|---|---|---|---|
| Average Score | Mean | Std | Mean | Std |
| Before lockdown | 12.1847 | 3.2420 | 12.7962 | 4.0884 |
| After lockdown | 12.8599 | 3.8886 | 13.7006 | 4.8417 |

For the area of body image after lockdown, p-value was significant for "How noticeable do you feel your weight was/is/will be to a stranger(0.043). From the population with gain of 5 kgs or more 4 people reported feeling that their weight was markedly noticeable to a stranger; however, this number doubled to 8 after lockdown.

## Discussion

This cross-sectional study shows the association between weight gain (obesity) and lockdown during the Covid-19 pandemic in Pakistan. The population studied ranged from 18-25 years with mostly students who stayed home from Mid-March of 2020 to 15th September, 2020. The results how weight gain affected the physical and mental health of people. 49.1% of the participants gained weight and the rest of the 50.9% either had stable weight or had weight loss. We have focused on the effects of weight gain which may be due to poor physical activity as weren't allowed to go outside and many people prefer gyms/outdoors over home exercises, increased screen time, high fatty diet, and less vegetables. Another important reason was that the lockdown period was associated with a higher level of stress and people resorted towards "stress eating" as a coping mechanism as set by prior research of Zachary 2020.[3]

The most common side effect of weight gain was reduction in physical activities. Of those who gained weight 12 participants had trouble performing daily activities, 8 had difficulty in climbing stairs and 14 reported and an increase in joint pain. This showed that quite a few numbers of participants had side effects of obesity on their health. This can lead to complications later, if obesity is not controlled, such as Diabetes, PCOS in young women, atherosclerosis etc. An article reported that women were at a greater risk of gaining weight due to stress-related eating.[19] This also brings attention to a relatively ignored population during this pandemic; women with PCOS, the most frequent endocrine disorder in women of reproductive age.[20] According to Barber et al. Even though postprandial thermogenesis was significantly lower in women with PCOS, it cannot be linked to weight gain as the resting metabolic rates remain similar to those without PCOS.[21] However, as established by Deeks et al. PCOS is a significant contributor to anxiety and depression.[22] Anxiety and depression, however have are linked to higher BMI, especially in women.[23] With the rise in anxiety due to the pandemic, there may be an increased risk of obesity in women, especially those with an underlying metabolic disorder like PCOS. Ultimately, this may attribute towards the fact that the amount of weight gain might have led to increased levels of inflammatory mediators like TNF,IL-1,IL-6, resulting in osteoarthritis as mentioned previously by Vincent HK.[24] The problem of osteoarthritis linked with obesity was more commonly seen in women; it affected the larger stabilizing joints mostly like knee, back and hip, that are important in performing physical activities like climbing stairs as presented also by Elizabeth M Badley in 2020.[25]

In our society particularly the South Asian society weight gain comes with a social stigma that has a considerable amount of negative effect on the mental health of slightly obese and obese people. People tend to lose self-confidence, self-esteem and start avoiding their own body image. This has been highlighted in our results as well. Before lockdown 60.1% people were self-conscious about their weight and 61.7% were self-conscious after lockdown. More number of

**Table 2:** *Significant Variables for Different Range of Weights*

| | | | Population with gain of less than 5 kgs | Population with gain of 5 kgs or more | Stable weight | Population with loss of less than 5kgs | Population with loss of 5kgs or more | P-value |
|---|---|---|---|---|---|---|---|---|
| **Physical Function** | | | | | | | | |
| Because of my weight, I have trouble tying my shoes, putting on/taking off clothes, crossing my legs etc. | Before | Never | 57 | 16 | 27 | 29 | 12 | 0.021 |
| | | Sometimes | 2 | 2 | 2 | 2 | 6 | |
| | | Always | - | - | - | - | - | |
| | After | Never | 48 | 8 | 27 | 30 | 16 | 0.0001 |
| | | Sometimes | 10 | 8 | 1 | 3 | 2 | |
| | | Always | 1 | 2 | 1 | - | - | |
| I am troubled by painful or stiff joints | Before | Never | 44 | 10 | 21 | 20 | 8 | 0.312 |
| | | Sometimes | 10 | 6 | 5 | 9 | 8 | |
| | | Always | 5 | 2 | 3 | 4 | 2 | |
| | After | Never | 35 | 6 | 19 | 19 | 13 | 0.018 |
| | | Sometimes | 24 | 9 | 10 | 12 | 5 | |
| | | Always | - | 3 | - | 12 | - | |
| **Self esteem** | | | | | | | | |
| Because of my weight, I am self-conscious | Before | Never | 26 | 8 | 16 | 11 | 6 | 0.874 |
| | | Sometimes | 23 | 7 | 8 | 17 | 10 | |
| | | Always | 10 | 3 | 5 | 5 | 2 | |
| | After | Never | 23 | 4 | 16 | 9 | 8 | 0.026 |
| | | Sometimes | 22 | 6 | 10 | 15 | 8 | |
| | | Always | 14 | 8 | 3 | 19 | 5 | |
| Because of my weight, I avoid looking in mirrors or seeing myself in photographs | Before | Never | 49 | 11 | 23 | 25 | 10 | 0.108 |
| | | Sometimes | 8 | 6 | 23 | 8 | 7 | |
| | | Always | 2 | 1 | - | 33 | 1 | |
| | After | Never | 42 | 6 | 25 | 26 | 13 | 0.001 |
| | | Sometimes | 16 | 8 | 5 | 5 | 15 | |
| | | Always | 1 | 4 | 1 | 2 | - | |
| Because of my weight, I experience ridicule, teasing, or unwanted attention | Before | Never | 44 | 8 | 18 | 16 | 5 | 0.002 |
| | | Sometimes | 13 | 10 | 10 | 15 | 10 | |
| | | Always | 2 | 18 | 1 | 2 | 3 | |
| | After | Never | 39 | 5 | 19 | 17 | 11 | 0.066 |
| | | Sometimes | 18 | 11 | 8 | 12 | 5 | |
| | | Always | 2 | 2 | 2 | 4 | 2 | |
| **Body Image** | | | | | | | | |
| How noticeable do you feel your weight was/is/will be to a stranger (if you do not camouflage yourself e.g. with clothes and/or makeup) and the feature has not been pointed out to them? | Before | Not at all | 25 | 5 | 11 | 12 | 1 | 0.015 |
| | | Slightly | 3 | 6 | 7 | 12 | 6 | |
| | | Moderately | 9 | 3 | 5 | 8 | 6 | |
| | | Markedly | 2 | 4 | 6 | 1 | 4 | |
| | | Very | 3 | - | - | - | - | |
| | After | Not at all | 18 | 2 | 11 | 10 | 2 | 0.043 |
| | | Slightly | 19 | 4 | 7 | 12 | 8 | |
| | | Moderately | 14 | 3 | 5 | 8 | 5 | |
| | | Markedly | 4 | 8 | 5 | 2 | 1 | |
| | | Very | 4 | 1 | 1 | 1 | 2 | |
| How much do you feel your weight/body shape is the most important aspect of who you are? | Before | Not at all | 8 | 1 | 6 | 5 | 1 | 0.964 |
| | | Slightly | 16 | 5 | 7 | 10 | 6 | |
| | | Moderately | 20 | 10 | 7 | 10 | 6 | |
| | | Mostly | 13 | 2 | 7 | 8 | 5 | |
| | | Totally | 2 | 18 | 2 | - | - | |
| How much do you feel your weight/body shape is the most important aspect of who you are? | Before | Not at all | 8 | 1 | 6 | 5 | 1 | 0.964 |
| | | Slightly | 16 | 5 | 7 | 10 | 6 | |
| | | Moderately | 20 | 10 | 7 | 10 | 6 | |
| | | Mostly | 13 | 2 | 7 | 8 | 5 | |
| | | Totally | 2 | 18 | 2 | - | - | |
| How much do you feel your weight/body shape is the most important aspect of who you are? | After | Not at all | 10 | 1 | 7 | 4 | 2 | 0.311 |
| | | Slightly | 13 | 3 | 6 | 9 | 5 | |
| | | Moderately | 22 | 6 | 8 | 12 | 7 | |
| | | Mostly | 10 | 5 | 6 | 7 | 4 | |
| | | Totally | 4 | 3 | 2 | 1 | - | |

people feared social rejection based on their body weight after lockdown than before lockdown. This led them to avoid looking at their body image in mirrors (self- avoidance). Other contributory factors were peer victimization, unwanted teasing, societal pressure as given in prior research of Lowry in 2007[26] and has also been shown in our results. There was a gradual increase in number of young adults who were facing teasing and ridiculing due to weight gain after lockdown, whereas it decreased for people who lost weight after lockdown which depicts the strength of peer pressure on overweight individuals.

We lived in a difficult time during the Covid-19 pandemic with a lot of people reporting mental health issues they faced during lockdown and post lockdown. Weight gain could be a contributing factor. The limitations of our study include the questionnaires being sent online there might be a chance that these were not solved by the individuals themselves which may lead to ambiguous results. A proper identification procedure must have been added to avoid such discrepancy. A broader spectrum of age groups should have been used to get an accurate idea about how the weight altered within individuals. Based upon the number of responses, especially the huger share contributed by adults with less than 5 kg gain of weight, it may be suggested that they immediately switch to less fatty diet and observe healthier activities to cover up this short range of weight gain easily. Another limitation that the female responses were not segregated during data collection for the variables and hence the ratio of young females being affected by stiff joints, cannot be deciphered.

## Conclusion

In conclusion, it is seen that the community-wide quarantine during COVID-19 pandemic has caused weight gain in adults. This weight gain has occurred due to availability of calorific processed foods, lack of physical activity, emotional distress and overall a sedentary lifestyle that seem to dominate the COVID-19 isolation. Such weight gain is not only deleterious for those who are already overweight, obese, immunocompromised or suffer from severe mental illnesses but also those who were of normal weight pre lockdown, immunocompetent neurotypicals. Our research clearly depicts the substantial changes in weight i.e., an increase of 3.016kg weight on average, post lockdown and an increase of 1.6% in impairment of body image among adults falling in 18-25 age group. With above mentioned results, there's no doubt that covid-19 isolation has not only led to stagnancy causing weight gain in young adults but also low self-esteem and negative body image ultimately giving rise to unhealthy individuals with mental health issues. So, the question arises are we really ready to deal with a low esteemed debilitating generation when the pandemic is finally over?

## Author's Contribution

**BU:** Literature search, study design & concept, questionaire design, data collection

**SU:** Literature search, study design & concept, questionaire design, data collection, data analysis

**TS, KKS, SF:** Literature search, study design & concept, questionaire design, data interpretation, drafting

**AB:** Data analysis, data interpretation, drafting

**IF:** Overall supervision, drafting, revision & final approval

**AKR:** Data analysis, data interpretation, drafting

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# Shoulder Tip Pain in Laparoscopic Cholecystectomy with Active vs Passive Evacuation of Pneumoperitoneum

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**Abstract**

**Objective:** The objective of the study was to compare the frequency of severity of shoulder tip pain after active (gas suctioning) and passive removal of pneumoperitoneum among patient undergoing laparoscopic cholecystectomy.

**Methods:** This Observational comparative study was directed in general surgery department of DOW university hospital beginning from February 2016 to February 2017. Two hundred and six patients undergoing standard 4 port laparoscopic cholecystectomy were enrolled equally in either groups. The surgeon evacuated the abdomen by using a multiporous suction tube limiting the negative suction pressure to - 40 mmHg for 2-5 minutes under direct vision in active aspiration group, while in control group, $CO_2$ was removed passively. Pain scores were recorded using visual analog score at 16 hours post-operatively by residents of surgery blinded to the study.

**Results:** Mean VAS pain score at 16 hours in intervention group was much inferior than control group 1.00 ±2.09 vs. 3.06 ± 2.58 ( $p < 0.001$).

**Conclusion:** Active aspiration of CO2 is an effective method that removes most if not all gas from the abdominal cavity. This will cause statistically significant decrease post-operative discomfort, pain and decrease need of rescue analgesics.

**Key Words:** Laparoscopic cholecystectomy, Pneumoperitoneum, Active Aspiration, shoulder tip pain, post-laproscopic cholecystectomy pain

## Introduction

Laparoscopic cholecystectomy has largely replaced conventional open cholecystectomy.[1] It provides great satisfaction to patient and at the same time beneficial for the operating surgeon as well in terms of high grade visibility minimum operative time, minimum anesthesia time, less postoperative pain, early mobilization, earlier discharges , and return to activities of daily life.[2,3] Out of many reasons, patients prefer laparoscopic cholecystectomy over open cholecystectomy because of less post-operative pain most common of them are shoulder tip pain and right hypochondrium pain. Assortment of shoulder tip pain reported incidentsare from 35% to 80% and may last for greater than 72 hours post-operatively. [4]

Post-operative shoulder pain and abdominal pain due to residual pneumoperitoneum leads to unpleasant discomfort and delay mobilization in spite of multiple doses of analgesics.[2,5] It also leads to reduced intra operative urinary output, respiratory compliance, reduced cardiac output and decreased venous blood flow.[3,5] The etiology of shoulder tip pain is multifactorial.[2] The shoulder tip pain due to residual $CO_2$ is also caused by stretching of diaphragm muscles and phrenic nerve irritation.[2] Therefore reduction in post laparoscopic cholecystectomy pain can be done by multiple methods like low pressure pneumoperitoneum, instillation of NSAIDS, instillation of intra-

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peritoneal local anesthesia, infiltration of wound with local anesthesia and removal of residual pneumoperitoneum.[3,5,6,7] Various methods have been introduced like pulmonary recruitment maneuver consisting of two to five insufflations, at the end of procedure active suctioning of $CO_2$ or filling the abdomen with warm saline.[1,4,8] Patient receiving abdominal filling with saline voided noticeable amount of urine following the immediate post-operativenight, disposes the patient to fluid overload and its time consuming.[3,9] Pulmonary recruitment maneuvers carries risk of pneumothorax and increased morbidity.[12] It implies that none is proven to be as assuring to be a standard method. Since no local data is available, and there is no standard technique, the rationale of the study was to see the effect of active aspiration of $CO_2$ as a superior technique. The objective of the study was to compare the frequency of severity of shoulder tip pain after active (gas suctioning) and passive removal of pneumoperi-toneum among patient undergoing laparoscopic cholecystectomy.

## Methods

This observational comparitive study was performed in general surgery department, DOW university hospital, from February 2016 to February 2017 over a period of one year after approval from research and training cell of CPSP . A total of 216 patients of either gender, age ranged between 20 to 60 years and undergoing interval laproscopic cholecystectomy were included in the study. Pregnant females, HTN, COPD and DM, laparoscopic cholecystectomy converted to open cholecystectomy, ended in common bile exploration and Placement of drains were excluded. The Rao soft software was used for "sample size calculaton|. Proportion of the incidence of shoulder pain varies from 35% to 80% and ranges from mild to severe with confidential interval of 95 %and margin of error of 9% sample size was n=108 in each group.[4] All patients undergoing standard 4 port laparoscopic cholecystectomy were recruited in either of the 2 groups. Intervention group was labelled as group A and control group as group B. In Group A, the surgeon evacuated the abdomen by using a multiporous suction tube limiting the negative suction pressure to -40 mmHg for 2-5 minutes under direct camera view, while in group B, $CO_2$ was removed passively, trocars were removed and incisions were closed. Pain scores were recorded using visual analog score at 16 hours post operatively by residents of surgery blinded to the study Those patients, who experience moderate to severe pain in spite of routine analgesics received a single bolus dose of Diclofenac sodium 75mg intramuscular or injection Nalbuphine 5 mg intravenous maximum thrice in 24 hours if needed.

Statistical package of social science software, SPSS, version 16 was used for data analysis. Frequency and percentage quantitative variables and mean and SD of qualitative variables was calculated. To compare both groups, the chi-square test was used. P value of $\leq 0.05$ was considered statistically significant.

## Result

The study is based on total of 216 patients and none of them were excluded. Out of them, 108 were allocated I neither group by sealed envelod method. Demographic variables are mentioned in table 1.

It was observed that 107 ( 91.1% ) patients in control and 28 ( 25.9% ) patients in case developed pain. P value $< 0.001$ for both groups.

The pain intensity was further characterized as no pain, mild moderate and severe pain based on Visual Analog Scale from 0 to 10. The results are as shown in graph 1. Over all Mean VAS score at 16 hours after laparoscopic cholecystectomy was $2.03 \pm 2.56$. The score in control group which was much higher than case group ($3.06 \pm 2.58$ vs. $1.00 \pm 2.09$).

After stratification in the context of effect modifiers, age, height, weight, BMI and period of surgery, it was found that all of them effect pain outcome. However it was observed that in age group between 20 – 30 years, no significant association was found with pain score (p value 0.77). Severity of pain score had significant association with age and BMI (p value $<0.001$). However, BMI of range between 20-25 $kg/m^2$ had no association with the severity of pain (p value 0.438).

## Discussion

Pain after laparoscopic surgery can occur in abdomen ,either upper or lower , back or either shoulders.[10,11,12] It can be transient or lasting up to days.[10]

Shoulder tip pain was documented in 99.07% of the control group and 32.85 % of case group in our study. This shows that over all pain score in case group was significantly lower (p value $< 0.001$).

**Table 1:** *Description Of Patient's Characteristics (n=216)*

| CHARACTERISTICS | CONTROL | CASE | P value |
|---|---|---|---|
| | n 108( %) | n 108 ( %) | |
| **AGE GROUPS** | | | |
| 20 – 30 | 72 ( 66.7) | 12 (11.1) | <0.001 |
| 31 – 40 | 18(16.7) | 31(28.7) | |
| 41 – 50 | 18( 16.7) | 65(60.2) | |
| **SEX** | | | |
| Male | 48 ( 44.4) | 17(15.7) | <0.001 |
| Female | 60(55.6) | 91( 84.3) | |
| **BMI** | | | |
| 20-25 | 61 | 31 | |
| 25-30 | 41 | 22 | <0.001 |
| 35-40 | 6 | 55 | |
| **DURATION OF SURGERY** | | | |
| < 30 mins | 0 | 6(5.6) | |
| 30-60 mins | 54( 50%) | 41(38) | <0.001 |
| 61-120 mins | 54(50%) | 9(8.3) | |
| > 121 mins | 0 | 52(52) | |

**Table 2:** *Description Of Analgesic Requirement N = 31*

| CHARACTERISTICS | CONTROL n(% ) | CASE n(%) | P-value |
|---|---|---|---|
| **ADDITIONAL ANALGESICS NAMES** | | | |
| Toradol | 18(58) | 13(41.9) | <0.01 |
| Toradol and Nalbuphine | 18(58) | 2(6.4) | |
| **ADDITIONAL ANALGESICS FREQUENCY** | | | |
| Once | 18(58) | 13(41.9) | <0.01 |
| multiple | 18(58) | 2(6.4 ) | |

Similar study conducted by Jasmin et al showed no pain 86.2% in the case group.[4] The results are comparable with our study in which 78.8% of intervention group had no pain. In another research done by Fredman B et al., the active aspiration (AA) group in which gas was actively aspirated by suction, while no efforts, in the non-active aspiration (NAA) group, were made.[13] Throughout the initial post-operative hour, lesser stresses were made by AA patients for morphine in comparison to those who belong to NAA group (15.3 +/- 15.7 vs 31.3 +/- 26.2) and also obtained a smaller dose of PCA morphine (2.7 +/- 1.3 mgvs3.9 +/- 1.9 mg) P = 0.056. This concluded that residual pneumoperitoneum was one of the important contributing factor leading postoperative pain as shown in previous studies in literatrure.[13,14]

In a recent international study, patients experiencing mild, moderate and severe pain were 15.5%, 49.3 % and 35.2% from control group and 13.8% from intervention group experienced mild pain. However, none of the patient experienced moderate and severe pain.[4] Whereas in our study, 7.4 % of Group A patient had mild pain whereas 12% and 1.9% patients moderate and severe pain. One of the explanations can be difference of suction pressure used in either studies. It can be concluded to question the efficiency of various proposed method and some more trials should be conducted to decide which is the suitable one.

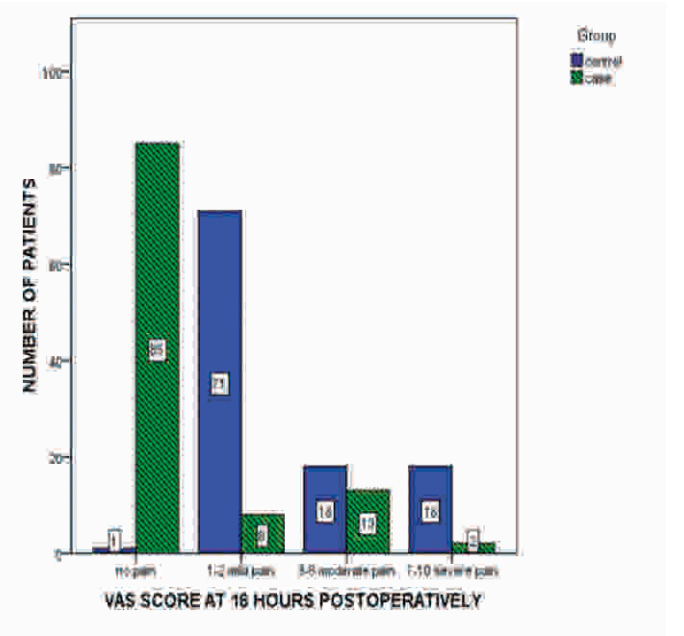


**Fig 1:** *Stratification According to Pain and Severity of Pain*

Results of our study are comparable with study conducted by Jasmin S et al. in which rescue analgesia was required by 33.1 % of the study population in contrast to only 14.3 % in our present study.[4] Out of these, in contrast, their requirement of analgesia by control and case group were 50 % and 42.3% which was significantly higher than our study.[4,15] This brights to highlight that patient's decrease demand of additional analgesia is an indirect measure of our maneour to evacuate pneumoperitomeum .

Since no local data is available in our country, we do not have any standard guidelines for our population. The limitation f our study was a single center study with small sample size. Further studies are required so that a concerte guideline can be postulated and new standards of care can be postulated for the best intrest of patient.

## Conclusion

Active aspiration of $CO_2$ is an effective method that removes most if not all gas from the abdominal cavity. This will cause statistically significant decrease postoperative discomfort, pain and decrease need of

rescue analgesics

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None

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None

## Author's Contribution

**AA:** Manuscript writing & data collection
**NS:** Manuscript writing & data processing
**KAM:** Data collection
**KWA:** Proof reading & correction
**BMA:** Proof reading & supervision
**IHS:** Data collection

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# COVID-19: Myths and Facts

**Sofia Manzoor,[1] Saima Chaudhary,[2] Sara Humayun,[3] Naheed Akhtar,[4] Shamsa Humayun[5]**

**Abstract**

The stormy spread of novel coronavirus around the world bewildered everyone. On 11th March 2020, WHO declared it a Global Pandemic. The progressing nature of COVID-19 disease with rising morbidity and mortality created panic and fear around the world which generated confusion, anxiety and misconceptions regarding its origin, nature, spread and treatment. These misconceptions among public favored negative practices leading to rapid disease spread, delay in acquiring the appropriate medical help and consequently increased morbidity and mortality. The facts and fictions surrounding the COVID-19 and the scientific evidence to resolve these misconceptions is necessary to lessen the morbidity and mortality of the disease by seeking timely and authentic medical advise. COVID-19 spreads by respiratory droplets. Different home remedies have only supportive role in recovery. The only solution to problem is dispelling the myths and strict practicing of respiratory and hands hygiene, physical interindividual distancing and avoidance of crowds as preventive measures.

**KEY WORDS:** COVID-19, facts and fictions

## Introduction

Covid-19 originating from Wuhan city of China shocked the world with its stormy spread and deadly nature. On 11th March 2020, WHO declared it a pandemic. The dubious nature of disease with associated morbidity and mortality created panic and fear around the globe which generated confusion, anxiety and misconceptions regarding its origin, nature, spread and treatment. These misconceptions among public favored negative practices lead to rapid disease spread, delay in acquiring the appropriate medical help and consequently increased morbidity and mortality. The aim of this paper is to explore the facts and fiction surrounding the COVID-19 and the scientific evidence generated to resolve these misconceptions and misbeliefs.

**MYTH #1:** Corona Virus is a bioweapon, deliberately compounded in Wuhan laboratory.

**FACT:** The controversy surrounding the origin of COVID-19 generated heated debate among the superpowers. The mere fact that the epidemic was first reported in Wuhan, Hubei province, alone does not necessarily mean that it is humanly prepared bio-weapon in China[1]. Dr. Lau and colleagues concluded "there is currently no evidence showing that SARS-CoV-2 is an artificial recombinant."[2]

The public health scientists from the United States, Europe, and Asia further substantiated in The Lancet: "We stand together to strongly condemn conspiracy theories suggesting that Covid-19 does not have a natural origin[3].

**MYTH #2:** It is transmitted to humans through bats and Wuhan market sea food.

**FACT:** Coronaviruses is a large group of family affecting different species of animals. According to CDC, it can rarely pass between humans and animals as in MERS and SARS. Initially, this novel coronavirus was thought to have started in wet market of Wuhan, suggesting animal-to-human transmission. But a large number of people diagnosed with the virus didn't have exposure to the wet markets, so it is clear that virus has person to person transmission[4].

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"Although the Wuhan market was initially suspected to be the epicenter of the epidemic, the immediate source remains elusive," Dr. Lau and colleagues wrote. The possibility that new combination of virus has developed, if bats carrying corona virus were mixed in the Wuhan market. However, no animal samples from the market were reported to be positive, neither the first identified case in a human nor other early patients had visited the market, all these suggesting the possibility of an alternative source.[5]

The plausible explanation could be that humans packed live bats in unhygienic conditions with other wild species which might have served as intermediate hosts. This may be the reason at Wuhan wet market where many experts believe COVID-19 emerged[6].

**MYTH #3:** Extremes of temperature can kill the Virus.

**FACT:** There is no proven correlation between temperature variation and corona spread. In a French research, heating the virus at 56°C-30min and 60°C-60min did not significantly affect the number of detectable RNA copies.[7]

According to report of The National Academies of Science, warm weather in summer would have little impact on the spread of coronavirus in the United States. There is some evidence that it may transmit less efficiently in warmer temperature, but it still be rendered as insignificant because of lack of host immunity globally.[8]

The WHO also states that there is no reason to believe cold weather can kill the new coronavirus.[9]

**MYTH#4:** It targets only older people, not children.

**FACT:** SARS-CoV-2 can infect people of any age. Children are usually mildly affected, and it has affected 2% of children under the age of 18 years worldwide[10]. Older people and those with comorbid conditions like asthma, diabetes, cardiac disease and compromised immune system have serious complications.[4]

**MYTH#5:** It is transmitted through urine and faeces.

**FACT:** Coronavirus is present in faeces[11]. However, there are no reports of feco-oral transmission of the COVID-19 virus to date.[12] According to Prof. John Edmunds, from the London School of Hygiene & Tropical Medicine. Every time we swallow, we swallow mucus from our upper respiratory tract. In fact, it is an important defensive mechanism which sweeps viruses and bacteria down into our gut where they are denatured in the acidic environment of our stomach and when excreted in stool no more infectious to others.[13]

**MYTH #6:** It is transmitted through house flies and mosquito bites.

**FACT:** The existing evidence does not favor its transmission through houseflies and tick bites. According to WHO and Centre for Disease Control and Prevention it is not an air born disease and spreads by respiratory droplets.[4,9]

**MYTH #7:** It is transmitted by 5G Radiations.

**FACT:** In The Guardian, mobile network representative stated that they have noticed cases of vandals setting fire to mobile masts, disrupting critical infrastructure, and spreading false information suggesting a connection between 5G and the COVID-19 pandemic".[14] Ahmad et al reported that it is just a conspiracy theory and has no link to reality of coronavirus transmission of by 5G radiations.[15]

**MYTH #8:** Home remedies help in prevention and elimination of coronavirus.

**FACT:** There is no evidence that eating garlic, ginger and onion prevent or cure novel coronavirus. Garlic has different antimicrobial properties. Food can only boost immune system to combat the disease.[9,16]

Drinking hot water every 15 minutes, taking lemon, honey, hot pepper soup, and gargling with warm salty water provide soothing effect on one's throat rather than elimination of virus. There is no role of hot baths in prevention of corona virus. Rather hot baths can damage and burn the skin.[9]

There is limited evidence that regular rinsing of nose with saline help people recover quickly from common cold but currently no scientific evidence exists that it can ward off novel coronavirus.[4,9,16]

**MYTH # 9-** Holding breath for 10 seconds is diagnostic test for coronavirus.

**FACT:** No evidence exists to prove this breathing

exercise in diagnosis of coronavirus. It is diagnosed by lab test.[9]

**MYTH # 10-** Thermal scanners can diagnose coronavirus infection.

**FACT:** Thermal guns only detect temperature which can be raised due to other infections as well. It alone necessarily cannot diagnose coronavirus infection[9].

**MYTH #11-** Overseas ordering and buying can spread novel coronavirus.

**FACT:** According to WHO, humidity, temperature changes and shipping conditions make it difficult for viruses to survive longer on objects such as letters or packages, so there is very low risk of spreading coronavirus from products or packaging that are shipped over a period of days or weeks[9].

**MYTH#12-** Drinking methanol, ethanol or gargling with bleach can prevent coronavirus Infection.

**FACT:** Drinking alcohol is injurious to health and disinfecting the nose or mouth with bleach is also harmful. All these measures do not prevent from novel coronavirus infection[9].

**MYTH# 13-** Coronavirus infection is a simple flu.

**FACT:** coronavirus is far deadlier than flu. Simple flu can infect 0.1% of population and it is infecting about 3-4%. In severe cases, patients need hospitalization for ICU care.[17]

**MYTH # 14-** Once infected with coronavirus, infection cannot resolve.

**FACT:** Most people infected with novel coronavirus had mild signs and symptoms and recovered with symptomatic care.

**MYHT # 15-** Chloroquine and macrolides can be used for prevention and treatment of coronavirus.

**FACT:** Chloroquine and hydroxychloroquine are considered as immunomodulatory agents. In a non-randomized trial, Gautret et al. reported that hydroxychloroquine has shown significant viral load reduction until viral disappearance and this effect was enhanced by the macrolide azithromycin.[18]

The Lancet stated that neither Hydroxychloroquine nor chloroquine benefitted patients of COVID-19 and even raised the risk of death due to arrhythmias or problems in heart rhythm. But this study has been retracted, so use of these drugs need further research[19].

**MYTH #16-** Pneumonia and H Influenza vaccines can protect from coronavirus.

**FACT:** Pneumococcal and H Influenza vaccines provide no protection against novel coronavirus. This virus is new and should have its own vaccine. The process of new vaccine production is under research and very well supported by WHO.[9]

**MYTH #17-** Antibiotics prevent or cure novel coronavirus infection.

**Fact:** Antibiotics can cure bacterial infections; they have no role in prevention or treatment of this viral infection. Though, empirical antibiotics can be useful for coexisting bacterial infections.[9]

**MYTH # 18-** Ibuprufen use can worsen the novel corona infection.

**FACT:** Initially WHO warned against the use of Ibuprufen use but later took it back as no evidence showed any harm with the use of ibuprofen and other anti-inflammatory pain killers.[9]

**MYTH # 19-** ACE inhibitors worsen novel coronavirus infection.

**FACT:** American College of Cardiology, American Heart Association, and Heart Failure Society of America suggest that people should not stop taking angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs), as these drugs don't worsen the novel corona infection.[20]

The only effective preventive strategies recommended by WHO and Centre for Disease Prevention and Control are:

- Frequent hand washing with soap and water for 20 seconds or rubbing with alcohol-based sanitizer.
- Avoid touching eyes, nose, and mouth.
- Practice of physical interindividual distancing of about 3 feet.
- Avoid going in crowded places.
- Observe good respiratory hygiene, cover mouth

and nose with bent elbow or tissue with cough or sneeze and dispose off the used tissue immediately and wash your hands.

- Stay home and self-isolate even with minor symptoms such as cough, headache, mild fever, until you recover. Have someone bring you supplies. If you need to leave your house, wear a mask to avoid infecting others.
- Healthcare workers caring for infected individuals should practice contact and airborne precautions which include PPE (N95 or FFP3 masks, eye protection, gowns, and gloves) to prevent transmission of the pathogen.

In conclusion, as health care professionals it is our moral obligation to resolve these misconceptions and create public awareness based on the scientific evidence. This is the only way forward to curb the disease spread and harmful practices among the public. The existing evidence holds that strict observation of preventive measures can protect from novel coronavirus and to date only supportive treatment is available till vaccine is produced.[9]

## Authors Contribution

**MS:** Article concept, design and draft writing.

**CS:** Draft Writing

**HS:** Literature Search

**AN:** Draft Review

**HS:** Final Approval of Draft and all review

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