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Recommended Biosafety and Infection Control Practices in Autopsy Lab Keeping in View Autopsy of Confirmed or Suspected COVID 19 Case

Prof. Arif Rasheed
Department of Forensic Medicine, Services Institute of Medical Sciences, Lahore.

Biosafety is the most significant measure for medical & paramedical staff who are in contact with human remains with confirmed or suspected COVID-19, or other infectious diseases.

Autopsy Precautions and Procedures

Medical & paramedical staff who have contact with human remains, including those performing autopsy and collecting or handling specimens, are at risk for exposure to infectious agents, such as SARS-CoV-2, that may be present in tissues, blood, and other bodily fluids of the deceased person. Additionally, personnel might be exposed to residual surface contamination. Autopsy should be undertaken by using appropriate biosafety measures and procedures. All autopsy facilities should have written biosafety policies, site-specific risk assessments, and procedures, and all participating personnel should receive prior training in policies and procedures.

- Autopsy room must have a precautionary sign posted on the entry door (e.g., "Autopsy in Progress", "Authorized Personnel Only", "SARS-CoV-2 Awareness", "Proper PPE Required").
- Personnel must wear appropriate PPE.
- Number of personnel working in the autopsy suite and on the human body should be limited to the minimum number of people necessary to safely conduct the autopsy.
- Use a biosafety cabinet Class II or higher for the handling and examination of specimens and other containment equipment whenever possible.
- AGPs such as use of an oscillating bone saw should be avoided for confirmed or suspected COVID-19 cases. Consider using hand shears as an alternative cutting tool. If an oscillating saw is used, attach a vacuum shroud to contain aerosols.
- Use caution when handling needles or other sharps; (e.g. never recap, bend, or cut needles), and dispose of contaminated sharps in puncture-proof, labeled, closable sharps containers.
- A register including names, dates, and activities of all workers participating in the postmortem care and cleaning of the autopsy suite should be kept and available for future follow up, if necessary. The names of custodial staff entering after hours or during the day, should also be included in the register.
- Cleaning and disinfection procedures of the autopsy room, surfaces, and equipment must be performed below.

Engineering Control Recommendations and Facility Design for Autopsies

Autopsies on decedents with confirmed or suspected COVID-19 optimally should be conducted in Airborne Infection Isolation Rooms (AIIRs). If not available, other autopsy suites with adequate air-handling systems may be used. These rooms must:

- Maintain negative pressure relative to surrounding areas with no air recirculation to adjacent spaces.
- Provide a minimum of 6 air changes per hour (ACH) for existing structures and 12 ACH for renovated or new structures.
- Have air exhausted directly to unoccupied areas outside the building.
- Have local airflow control in place (i.e., laminar flow systems) directing air from around the autopsy table downwards and away from personnel.
- Have a Certified Class II Biosafety Cabinet.

Work surfaces should have integral waste containment and drainage features that minimize spills of body fluids and wastewater.

In addition, doors to the autopsy room should be kept closed except during entry and egress. Entry and egress should be limited to prevent interruptions in airflow. A portable high-efficiency particulate air (HEPA) recirculation unit could also be placed in the room to provide further air filtration. If use of an AIIR or HEPA unit is not possible, the procedure should be

performed in the most protective environment possible. AIIR room air should never be recirculated in the building, but directly exhausted outdoors, away from windows, doors, areas of human traffic or gathering spaces, and from other building air intake systems.

PPE Recommendations for Autopsies

The following combination of PPE is recommended for autopsy procedures:

- Surgical scrub suit worn under impermeable gown or apron with full sleeve coverage
- Double surgical gloves interposed with a layer of cut-proof synthetic mesh gloves
- At a minimum, a NIOSH-approved disposable N95 respirator should be worn; however, due to the likelihood of generation of contagious aerosols during various autopsy procedures, powered air-purifying respirators (PAPRs) equipped with N95 or HEPA filters are recommended.
  - PAPRs should be considered for personnel who cannot wear N95 respirators because of facial hair or other fit limitations.
  - PAPRs with high efficiency filters may provide increased comfort during extended autopsy procedures.
  - When respirators are necessary to protect workers, employers must implement a comprehensive respiratory protection program as per international standards.
- Eye protection such as goggles or face shield that covers the front and sides of the face
  - Proper eye protection must be selected to ensure that the N95 respirator does not interfere with the correct positioning of the eye protection, and the eye protection does not affect the fit or seal of the respirator.
  - Protective eyewear (e.g., safety glasses and the face shield) without gaps between glasses and the face to protect eyes from splashes and sprays.
- Surgical caps.
- Shoe covers with non-slip tread.

PPE should be worn following required don, use, and doff protocols to avoid self-contamination and to mitigate risk of carrying the virus outside the autopsy suite or adjacent anteroom.

After removing PPE, discard the PPE in the appropriate laundry or waste receptacle. Reusable PPE (e.g., goggles, face shields, and PAPRs) must be cleaned and disinfected according to the manufacturer's recommendations before reuse. Immediately after doffing PPE, wash hands with soap and water for 20 seconds. If soap and water are not available, an alcohol-based hand sanitizer that contains 60-95% alcohol may be used. However, if hands are visibly dirty, always wash hands with soap and water before using alcohol-based hand sanitizer. At all times avoid touching the face with hands Ensure that hand hygiene facilities are readily

Training and Delivery of Pediatric Surgical Services in Pakistan

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Pakistan produces world class doctors despite limitation of resources and lack of a mature infrastructure in the super specialties. Pediatric surgery is amongst the rapidly growing specialties owing to the exponential increase in population. Training good quality pediatric surgeons in Pakistan is possible but delivering high quality service in this field requires a very mature infrastructure. The College of Physicians and Surgeons of Pakistan (CPSP) is responsible for organizing and regulating the training in this specialty. At present, there are 12 institutions that are recognized for MCPS and FCPS training in Pakistan.[1]

Training

I have been fortunate to train and work in pediatric surgery between Ireland, UK, New Zealand and the UAE. I have, therefore, been a trainee, trainer and a service provider in 4 advanced health care systems. The advanced training degrees in Pakistan are MS and FCPS. The training structure of FCPS is not very different from that of the United Kingdom. In UK, those aspiring to train in pediatric surgery first complete 2 years of core surgical training in which they rotate through basic medical, surgical and orthopedics and trauma departments. They then compete for a national training number (NTN) to be able to enter the specialist training in pediatric surgery. This is a 6-year programme where, in the first 4 years the candidates gain knowledge to pass the FRCS (Paeds Surg) exam and competencies to manage routine and moderately complex pediatric surgical conditions.[2] In the final two years of training the candidates consolidate knowledge and advanced technical skills to be able to work independently at a consultant level and provide a safe service to their patients. They are also encouraged to apply for fellowships in their areas of intertest either in the bigger centres in UK or abroad. Throughout their training, they undergo a very structured assessment process every 6 months. The assessments are a combination of summative and formative assessment tools. A log book demonstrating that the trainee has participated in a minimum number of index pediatric surgical cases is also maintained and presented at these assessments. During their training, each candidate, ideally, has to rotate between 3 centres in their training consortium. They are also expected to complete some basic courses like Advanced Pediatric Life Support (APLS) and Care of Critical Ill Surgical Patient (CrRisp). Experience in a neonatal unit is also desirable to be able to understand the premature neonate's physiology.

The Pediatric Surgery training programme in Pakistan is also well structured. The CPSP oversees and regulates the training to ensure high standards. The Pakistani trainees undergo a rigorous 5 years training programme. (Intermediate module is 2 years and pediatric surgery training is 3 years). Similar to the UK training programme, the Pakistani pediatric surgeons in training also undergo 6 monthly assessments. In addition, they also have to pass a mid-training and end of training exam. Whilst the CPSP and Pakistani pediatric surgical trainers also encourage the trainees to move between high and low volume centres but due to a multitude of factors, few trainees are able to actually complete these inter centre rotations. Similarly, the access to courses like the APLS, CrRisp, wet and dry labs and national training days is not always possible. Despite many of the above limitations, the surgical exposure of the Pakistani trainees is far more as compared to their counterparts in the western world and this is purely volume based. This high-volume exposure provides increased confidence and sometimes better surgical technique to the Pakistani pediatric surgeons. However, owing, to such large volumes adequate senior supervision is not always possible and as a result, the outcomes many times are not comparable to the international standards.[3]

Service Provision and Delivery

The American Pediatric Surgical Association (APSA) recommends 2 pediatric surgeons per million or 1 per 100,000 patients between the age of 0-15 years.[4] Due to the large population and lack of resources, in Pakistan, there are only 0.26 pediatric surgeons per 100,000 children of above ages.[5] To add to this scarcity of pediatric surgeons is the small number of tertiary pediatric surgery centres. The above combination alone is a big reason for less-than-ideal outcomes for pediatric patients requiring specialized surgical care. Very frequently, the families cannot afford to take their child to a far-off tertiary centre due to financial reasons. As a result, they attend a tehsil or district hospital where the expertise, experience and resources do not allow for optimal care of this very unique group of patients. It is widely accepted that evidence-based care provided by adequately trained pediatric surgeons in tertiary centres results in far superior outcomes as compared to the care received in smaller centres like the ones mentioned above.[6-11]

Another major limitation in provision of good quality specialized pediatric surgical care is the existing poor infrastructure for these patients. By poor infrastructure, I mean lack of associated specialists required during the diagnosis and treatment of these patients. For example, a 500-gram premature neonate requires a trained neonatologist to ventilate him, an experienced radiologist to help with his imaging, a highly specialized anesthetist to give him general anesthesia during his surgery and highly qualified nursing staff in the intensive care units to look after them during and after surgery. The operation theatres need to be equipped to ensure these babies remain warm during surgery and have the appropriate adjuncts and surgical instruments required for surgery. Good quality service comprises of pre, intra and post operative care as a package. No matter how good a job the pediatric surgeon has done but if the intensive care is either not fully equipped or the staff are not competent to deal with these extra special group of patients (as is the case many times) then the poor outcomes cannot be prevented and are not comparable to the outcomes in the developed world.

How Can We Improve the Quality of Pediatric Surgical Care in Pakistan?

Whilst the training standards are very high there is still room for improvement. By increasing the number of training posts and centres, a higher number of trained pediatric surgeons will be available. These can then be deputed in some of the smaller hospitals. In parallel, other necessary resources like anesthesia and ICU staff will also need to be increased for these projects to be successful.

Sponsored Exchange training programmes for our surgeons in training will refine their approach and training. This in addition to their high-volume exposure will most certainly make them better surgeons than many of their counterparts in the western centres. The concept of out reach clinics where the specialist surgeons go and operate in smaller centres will serve 2 purposes. It will not only improve the quality of care and outcomes but we can also train their resident surgeons to deal with common conditions appropriately. International visiting surgeons with joint operating sessions with Pakistani surgeons will not only improve the outcomes but also enhance the experience of local surgeons.

Without good post operative care in the neonatal intensive care, the surgical outcomes will remain poor. I have spoken to a few local pediatric surgeons and they strongly believe that results for some of the congenital malformations like esophageal atresia or congenital diaphragmatic hernia can be improved very significantly if the post operative intensive care is improved. Hence, the CPSP may need to look at collaborating with their local training boards responsible for improving the standards of training for physicians and nurses that work in the neonatal intensive care units.

We cannot take away any credit from the service being provided by the locally trained pediatric surgeons. They work their heart out with very limited resources and despite that provide a decent level of care to the population of Pakistan. However, there is a huge room for improvement in the infrastructure required by them to provide an even better quality of care to the pediatric surgical patients in Pakistan.

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Comparison of Efficacy of Combination of Acitretin and Narrow Band Ultraviolet B versus Narrow Band Ultraviolet B Alone in the Treatment of Chronic Plaque Psoriasis

Faiqa Qadeer,[1] Hira Tariq,[2] Shahbaz Aman[3]

Abstract

Objective: To compare the efficacy of combination of narrow band ultraviolet B (NBUVB) and Acitretin (ReUVB) versus NBUVB alone in the treatment of moderate to severe plaque psoriasis.

Material and Methods: This randomized clinical trial was conducted at the Department of Dermatology Services Hospital, Lahore from October 2020 to April 2021. After getting approval from Ethical Review Committee, 100 patients of moderate to severe plaque psoriasis were enrolled. They were divided into two groups of fifty patients each. Group A patients received both acitretin and NBUVB therapy while group B received NBUVB therapy alone for 8 weeks. PASI 50 was set as the efficacy end point. PASI scores and photographs taken before and after treatment were analysed.

Results: Mean age of patients was 34.99 ± 9.28 years. In group A, 46 (92%) patients achieved PASI 50 while in group B, 19 (38%) patients achieved PASI 50. Therefore, the efficacy of combination of acitretin and NBUVB was significantly higher compared to NBUVB alone. Statistically significant effect of age, gender, body mass index and duration of disease was found on efficacy.

Conclusion: Narrow band Ultraviolet-B therapy is a useful treatment modality in moderate to severe psoriasis. However, combining it with acitretin can significantly enhance its efficacy.

Keywords: Efficacy, Acitretin, Narrow band Ultraviolet-B, Chronic plaque psoriasis

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Introduction

Psoriasis is a common skin disorder caused by an aberrant immune system. Its prevalence varies from 2 to 3% in different parts of the world.[1] Due to the disability caused by the disease and cost of the therapeutic modalities used to cater them, there is significant impact on healthcare system.[2] Therefore, choice of therapeutic options as well as strategies to improve their efficacy is of utmost importance in management of this chronic debilitating disease.

The major pathogenetic factors leading to manifestations of psoriasis involve an aberrant innate and acquired immune system that leads to release of cytokines that damage target tissues including skin and joints. This leads to activation of nuclear factor-κB (NF-kB) signalling pathway and leads to differentiation of T helper cells toward Th1 and/or Th17 cells.[1] To counter this complicated cascade, various topical and systemic agents are in use worldwide depending on disease severity and patient factors. Among these, Phototherapy especially narrowband Ultraviolet-B (NBUVB) is very useful, since it lacks systemic toxicity and can be used in combination with other topical and systemic agents safely.[3] NBUVB (311nm) replaced the broadband UVB (290-320nm) due to its ability to target only the diseased skin and sparing the normal tissues.[4] The mechanism of action of UVB in clearing psoriatic plaques is still uncertain. However, immunomodulation caused by UVB has been postulated to induce death of diseased epidermal cells and T cells. This has been suggested

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by reduced amounts of cytokines and interleukins of Th-17 pathway after treatment with NBUVB.[5,6] The usual dosage of NBUVB is started with minimal initial dose that is 50% of the minimal erythema dose (MED) administered thrice a week.[7] Acitretin is a second-generation retinoid and active metabolite of etretinate.[8] It selectively agonises retinoic acid receptor (RAR) leading to suppression of inflammation and regulation of keratinocyte differentiation and proliferation.[9] It also suppresses vascular endothelial cells of dermal vessels and migration of neutrophils.[10]

Combination of acitretin and NBUVB (ReUVB) therapy has been shown to be superior in treating psoriasis than either modality alone.[11] The combination has been proposed to regulate release and expression of Matrix metalloproteinase 13(MMP13) which is a key modulator of inflammation and epidermal proliferation in psoriasis.[12] However, there is little clinical data on the efficacy of the combination of the two modalities in our part of the world. We conducted this study to evaluate the role of the two treatment options in our population as it may reduce the dose of either modality and its side effects and help in earlier and better management of patients.

Methods

After getting approval from Ethical Review Committee, this randomized clinical trial was carried out in the Department of Dermatology, Services Hospital Lahore from October 15, 2020 to April 15, 2021. Patients of both genders and ages between 18 and 50 years, having moderate to severe psoriasis (PASI > 10) diagnosed clinically, were included after taking written informed consent. Patients were selected by non-purposive consecutive sampling. Patients less than 18 years of age, pregnant or lactating females, females of child bearing age not willing for contraception, patients having renal, hepatic, lung or neurological disease, photosensitivity or photo aggravated diseases or cutaneous malignant or premalignant lesions were excluded. Patients who had received oral retinoids, phototherapy or other immunosuppressive agents in last two months were also excluded. Detailed history and thorough physical and cutaneous examination of all patients was done. Pretreatment Psoriasis Area and Severity Index (PASI) scores were calculated and photographs were taken. Relevant serological tests including renal and liver function tests and fasting lipid profiles were carried out to rule out contraindications to acitretin.

The patients were randomly divided by lottery method into two equal treatment groups as follows. Group A was given acitretin at a dose of 0.5mg/kg daily along with NBUVB thrice weekly using whole body exposure chamber of Daavlin Phototherapy Unit, fitted with 12 Philips 100 W TL-01 lamps (FDA approved device) for eight weeks. Minimal erythema dose (MED) was tested on upper back of every patient before starting treatment. Group B was treated with NBUVB alone using the same protocol for eight weeks. Post treatment assessment was done at the end of eighth week, PASI scores were calculated and photographs were taken. Demographic and clinical data was recorded on a predesigned proforma. Efficacy was defined as achievement of PASI 50 i.e. at least 50% reduction in PASI score after treatment.

Data was entered and analysed using IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp. Numerical variables like age, body mass index (BMI), baseline and post treatment PASI scores were presented as mean±standard deviation. Qualitative variables like gender and efficacy were presented as frequencies and percentages. Data was stratified for age, gender, duration of disease and BMI to evaluate the role of effect modifiers. Post stratification Chi-square test was applied to check the significance with p-value≤0.05 as significant.

Results

This randomized therapeutic trial was carried out with the aim of comparing efficacy of combined treatment with acitretin and NBUVB versus NBUVB alone. Total 100 patients were enrolled; fifty each were allocated randomly to each treatment group. The mean age of all the patients was 34.99 ± 9.28 years, while the mean ages in group A (oral acitretin and UVB therapy) and group B (NBUVB therapy) were 34.72±9.20 years and 35.26±9.45 years respectively. In group A, 50% patients (25) were males and 50% were females. In group B, 21 patients (42%) were males and 29 (58%) were females. The mean BMI in group A was 30.62 ±4.05 and in group B was 30.26±4.71. The mean PASI score at baseline in group A was 42.14±13.18 and in Group B was 39.64±11.66. At the end of 8th week the mean PASI score in group A was 14.84 ± 8.86 and in group B was 23.38 ±11.38. In group A, 46(92%) patients achieved PASI 50 and in group B, it was achieved in 19(38%) of the cases, this difference was statistically significant (p-value≤0.001). It is evident that combination of acitretin and UVB led to significantly better disease

clearance than UVB alone (Table 1, Fig 1). Data stratification indicated that efficacy was also affected by age, gender, BMI and duration of disease since p-values

Table 1: *Demographic Data of Patients*

			No. of Patients (n = 194)	
			n	%
Gender	Group A	Male	25	50
		Female	25	50
	Group B	Male	29	58
		Female	21	42
Age	Group A	18–34 years	22	44
		35-50 years	28	56
	Group B	18–34 years	21	42
		35-50 years	29	58
Body mass index	Group A	Obese	15	30
		Non-obese	35	70
	Group B	Obese	18	36
		Non-obese	32	64
Duration of disease	Group A	< 2 years	34	68
		≥2 years	16	32
	Group B	< 2 years	33	66
		⩾2 years	17	34

were either significant (≤0.05) or highly significant (≤0.001).

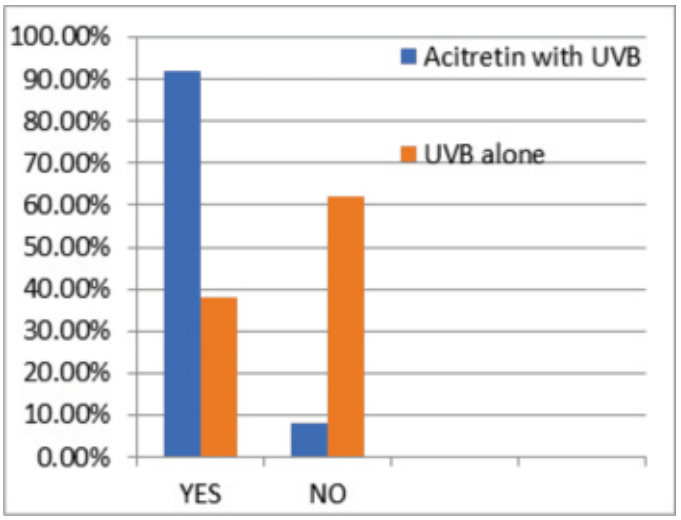

Fig-1: *Comparison of Efficacy between Treatment Groups*

Discussion

Due to the chronicity and significant psychosocial distress associated with psoriasis,[13] many treatment modalities have been used and developed over time for effective and timely cure of the disease. Phototherapy is a cost effective and relatively safe option among them. However, due to the potential theoretical risk of

Table 2: *Comparison of Efficacy between Treatment Groups*

Demographic parameter		Efficacy (PASI 50 Achieved)	Groups		Total	Chi-square	p-value
			Group-A (Acitretin plus UVB)	Group-B (UVB)			
Overall Efficacy		Yes	46(92%)	19(38%)	65(65%)	32.044	<0.001
		No	4(8%)	31(62%)	35(35%)		
Age (years)	18-34	Yes	18(18%)	5(23.8%)	23(23%)	14.532	<0.001
		No	4(18.2%)	16(76.2%)	20(20%)		
	35-50	Yes	28(100%)	14(48.3%)	42(42%)	19.655	<0.001
		No	0(0%)	15(51.7%)	15(15%)		
Gender	Male	Yes	25(100%)	8(38.1%)	33(33%)	21.573	<0.001
		No	0(0%)	13(61.9%)	13(13%)		
	Female	Yes	21(84%)	11(37.9%)	32(32%)	11.803	0.001
		No	4(16%)	18(62.1%)	22(22%)		
Body Mass Index	Obese	Yes	12(80%)	7(38.9%)	19(19%)	5.661	0.017
		No	3(20%)	11(61.1%)	14(14%)		
	Non-obese	Yes	34(97.1%)	12(37.5%)	46(46%)	27.633	<0.001
		No	1(2.9%)	20(62.5%)	21(21%)		
Duration of disease	< 2 years	Yes	33(97.1%)	12(36.4%)	45(45%)	27.973	<0.001
		No	1(2.9%)	21(63.6%)	22(22%)		
	⩾2 years	Yes	13(81.2%)	7(41.2%)	20(20%)	5.544	0.019
		No	3(18.8%)	10(58.8%)	13(13%)		

P-value ⩽0.05=significant

developing skin cancer associated with it,[14] patient compliance may be reduced. Combining it with retinoids, may reduce this risk because of tumour suppressive effects of retinoids.[15]

We found that significantly higher proportion of patients in the combination (ReUVB) group achieved efficacy end point (92%) compared to patients getting UVB alone (38%). Similar results were documented by Saeed et al in Chinese population who reported efficacy in 82.5% patients treated with ReUVB versus 55% patients treated with UVB alone.[16] They reported 80 to 100% improvement in clinical disease. Mean age of their patients was similar to our patients. However, they didn't find any significant effect of age or gender on efficacy. This can be attributed to different ethnicities of the study populations.

Iest et al disease clearance in 89% patients following ReUVB therapy compared to 62.5% patients treated with UVB alone.[17] Spuls et al reported more than 75% clearance in 72.5% patients after ReUVB in American patients.[18] Ruzicka et al compared the efficacy of ReUVB versus placebo and UVB in Wst Germany. They found a reduction in PASI of 79% in ReUVB group versus 35% in patients receiving placebo and UVB. This efficacy was achieved with significantly lower dose of UVB.[19] Therefore, the combination therapy may help in dose reduction of both treatments leading to a better safety profile of both modalities.

Kampitak et al also reported marked improvement in the ReUVB combination group in their study in Thailand.[11] Lebwohl also highlighted better efficacy of combination of acitretin and UVB along with reduction in doses and duration of both treatment modalities.[20]

We found combination of acitretin and UVB therapy more effective than UVB alone in management of moderate to severe psoriasis. However, the patients' compliance to the treatment might be hampered because of frequent visits to hospital for phototherapy, which might weaken his/her confidence in the therapy and the treating dermatologist. This can be countered by using home-based phototherapy devices which have given promising results in many studies.[2]

Conclusion

The combination of acitretin and NBUVB has many advantages including better and faster improvement in clinical disease achieved with lower dosage of both treatment options. This leads to better safety profile and more compliance. Hospital-based phototherapy may lead to reduced compliance especially for patients who live far from the source. They may benefit from home-based phototherapy devices. Combination therapy may also benefit those in whom other treatment options like biologics or methotrexate are contraindicated. Better and faster disease clearance with the combination therapy may increase patient compliance, satisfaction and adherence to treatment, which is inevitable in treating diseases like psoriasis.

Conflict of interest *None*

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Authors Contribution

FQ, SA: Conceptualization of Project
FQ: Data Collection
FQ: Literature Search
FQ: Statistical Analysis
SA, HT: Drafting, Revision
HT: Writing of Manuscript

Neurological Manifestations of COVID-19 Patients in Tertiary Care Hospital of Lahore

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Abstract

Objectives: This study was done to find out the neurological manifestations of COVID-19 patients presenting in Services Hospital Lahore.

Methods: It is a prospective observational study done at Services Hospital Lahore where a total 194 patients were enrolled in the study through consecutive sampling.

Results: 99(51%) of them were male and 95(49%) of them were female. Neurological manifestations of COVID-19 infection in our patients included myalgia which was present in 95(49.0%), headache was present in 87(44.8%), dizziness was seen in 38(19.6%), anosmia was reported by 31(16%), 19(9.8%) patients were confused, 9(4.6%) patients had neuropathic pain, 7(3.6%) patients had loss of vision, 4(2.1%) patients had Ischemic Stroke, 3(1.5%) patients had ataxia, 3(1.5%) presented with seizures, 3(1.5%) had a axonal neuropathy, 1(0.5%) patient presented in a coma, 1(0.5%) had encephalitis, 1(0.5%) had a haemorrhagic stroke, and 1(0.5%) patient presented with demyelinating neuropathy.

Conclusion: It is evident from a review of literature that many researches have highlighted similar neurological manifestations associated with COVID-19 infections as our study. Clinicians should be aware about the diverse neurological presentations of COVID-19 infections. Presentations without typical risk factors or in atypical age groups should especially prompt diagnostic testing for COVID-19 Infection.

Keywords: COVID-19, neurological manifestations, myalgia, dizziness, headache

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Introduction

COVID-19 has spread worldwide into a pandemic and caused great mortality and morbidity. One of the greatest challenges in this pandemic has been the varied signs and symptoms which have led to the presentation of COVID-19 cases. While respiratory system involvement has been classically associated with the greatest mortality and morbidity associated with the infection, COVID-19 infection also has a predilection to affect the nervous system. COVID-19 infection is associated with various central and peripheral nervous system findings.[1] This is due to the direct neurotropic affects of the virus and also due to the immune response as a result of the viral infection.[2]

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Methods

This study was a prospective observational study done at Services Hospital Lahore between July to September 2021. 194 patients admitted in Services Hospital Lahore between 18 to 80 years and had a positive COVID-19 PCR through a nasal swab were included in the study via consecutive sampling technique. Patients or their close attendants were interviewed by a neurologist after

informed consent. The Neurologist completed the 38 item questionnaire for all the interviewed patients. The data was then analysed using SPSS for Windows version 28.0.1. Frequencies/Percentages were calculated for the co-morbidities and clinical symptoms of the patients and the data displayed in the form of tables.

Results

Total 194 patients were enrolled in the study. 99(51%) of them were male and 95(49%) of them were female. The most common clinical symptom of the patients was Shortness of Breath which was present in 168(85.6%) of patients, 149(76.8%) patients had cough, 145(74.7%) had fever, 71(36.6%) patients had a sore throat, abdominal pain was present in 31(16%) patients and 23(11.9%) had loose stools. The most common neurological manifestation of COVID-19 infection in our patients included myalgia which was present in 95(49.0%), headache was present in 87(44.8%) of the patients, dizziness was seen in 38(19.6%), anosmia was reported by 31(16%), 19(9.8%) patients were confused, 9(4.6%) patients had neuropathic pain, 7(3.6%) patients had loss of vision, 4(2.1%) patients had Ischemic Stroke, 3(1.5%) patients had ataxia, 3(1.5%) presented with seizures, 3(1.5%) had a axonal neuropathy, 1 0.5%) patient presented in a coma, 1(0.5%) had encephalitis, 1(0.5%) had a haemorrhagic stroke, and 1(0.5%) patient presented with demyelinating neuropathy.

Table 1: *Gender of Patients Included in the Study*

Gender	Frequency (Percentage)
Female	99 (51.0)
Male	95 (49)

Table 2: *Co-morbidities of Patients Included in the Study*

Comorbidities	Frequency (Percentage)
Hypertension	83 (42.8)
Diabetes	80 (41.2)
Ischemic Heart DIsease	35 (18)
Chronic Kidney Disease	14 (7.2)
Chronic Obstructive Pulmonary Disorder	2 (1.0)
Asthma	2 (1.0)
Smoking	1 (0.5)

Table 3: *Neurological manifestations of the patients included in the study.*

Neurological Manifestations	Frequency (Percentage)
Myalgia	95 (49)
Headache	87 (44.8)
Dizziness	38 (19.6)
Anosmia	31 (16)
Confusion	19 (9.8)
Neuropathic Pain	9 (4.6)
Loss of Vision	7 (3.6)
Ischemic Stroke	4 (2.1)
Ataxia	3 (1.5)
Seizures	3 (1.5)
Axonal Neuropathy	3 (1.5)
Coma	1 (0.5)
Encephalitis	1 (0.5)
Haemorrhagic Stroke	1 (0.5)
Demyelinating Neuropathy	1 (0.5)

Discussion

Our research showed that patients presenting to Services Hospital Lahore and having positive COVID-19 tests showed a wide range of Neurological manifestations. The most common neurological manifestation we saw was Myalgia. Myalgia is one of the major symptoms of most viral infections and COVID-19 in particular and it was calculated by a meta-analysis done by Lippi et al.[3] that Myalgia is seen as symptom of onset in around 36% of COVID-19 patients. 49% of our patients had myalgia. Headache was seen in 44.8% of our cases. COVID-19 infection has been consistently associated with headache throughout the pandemic. This has more often been a bifrontal or holocephalic, pressing in nature and moderate to severe in intensity. Patients with migraine have seen a worsening in their headache frequency and have had attacks that are longer and more intense.[4] Interestingly headache has been associated with a lower mortality rate in COVID-19 patients and associated with lower CRP levels.[5]

Like in our study dizziness due to COVID-19 infection has been a common symptom, with countless studies showing the association.[6] Interestingly it is being increasingly recognised that these cases may be due to the increased incidence of Benign Paroxysmal Positional Vertigo with hyper coagulability and micro thrombus formation playing a part.[7]

Anosmia was one of the first symptoms linked to COVID-19 infection and our study showed that 16% of our patients had the same. Some of the earlier studies reported anosmia to be present in around half of COVID-19 patients8 and it was used as a clue and an indicator of infection earlier on in the pandemic. COVID-19 has also been associated with delirium and encephalopathy. The encephalopathy in particular has

been associated with the cytokine storm and interleukin mediated damage.[9] It is one of the worst manifestations of COVID-19 associated with a high mortality, with best treatment options still up as a matter of debate and research. Our study had patients present with such symptoms including 19 with confusion, 3 with seizures, 1 with coma and 1 with encephalitis.

7 of our patients has loss of vision associated with COVID-19 infection and while this has been an uncommon manifestation there are numerous case reports which highlight the various causes of such a presentation including Ischemic Stroke, increased intracranial pressure, retinopathy among others.[10-12]

Coagulopathy, Cardiac Embolisation, and Endothelitis due to COVID-19 has led to its association with multiple types of stroke including Ischemic Stroke, Cerebral Venous Sinus Thrombosis and Haemorrhagic Strokes.[13,14] Our study group also included 1 patient with Ischemic and 3 with Haemorrhagic strokes. It has been seen that many of these patients lack the usual risk factors for stroke and COVID-19 seems to play a major causative role in these patients. These patients are being managed as per the usual protocols for these illnesses.[15]

Lastly we saw patients with COVID-19 showing symptoms of Neuropathy including 9 with neuropathic pain, 3 with axonal neuropathy and 1 with demyelinating neuropathy. Neuropathy on the other hand has been associated with immune mechanisms as well as due to drugs used for COVID-19 treatment and pressure due to compression due to bedding during ICU/hospital stay.[16] It is evident from a review of literature that many researches have highlighted similar neurological manifestations associated with COVID-19 infections as our study. However the frequencies have differed in different studies and populations. There is still a lot of room to research the best treatment options for these manifestations, and if they adhere to or differ from similar manifestations due to the usual causative factors.

Conclusions

Clinicians should be aware about the diverse neurological presentations of COVID-19 infections. Presentations without typical risk factors or in atypical age groups should especially prompt diagnostic testing for COVID-19 Infection. Further research is needed in this area to determine all the neurological manifestations of COVID-19 and to find best treatment options and management strategies in these cases.

Limitations

The limitations of our study include that only hospitalised patients with positive COVID-19 PCR reports were included. Keeping the pandemic of COVID-19 in mind there are many more patients who do not present with symptoms severe enough to present in hospitals. Cases may go unrecognised with the patient not being tested for COVID-19 leading to missing some of the neurological manifestations associated with the illness. Considering the pandemic nature of the disease larger trials in a more diverse population is needed to get a true estimate of all the neurological manifestations of COVID-19 and their frequency among cases.

Conflict of Interest: *None*

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Authors Contribution

MAA, QB: Conceptualization of Project
MJM, MU: Data Collection
GMA: Literature Search
MJM, MU: Statistical Analysis
MAA, QB: Drafting, Revision
MAA, QB, MJM: Writing of Manuscript

Prevalence of Digital Eye Strain in the Gaming Community of Pakistan during First Countrywide COVID Lockdown

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Abstract

Objective: This cross-sectional study was conducted to explore the prevalence of Digital Eye Strain (DES) signs and symptoms among the video gamers in Pakistan, during the period of 1st countrywide COVID lockdown (March 2020 to September 2020) imposed by the government.

Methods: This survey was circulated via Google Forms on major social media gaming forums in Pakistan. Non-probability convenient sampling technique was used to collect data via an anonymous questionnaire regarding the signs and symptoms of DES and the gaming routines of the participants. Data was analyzed using SPSS 24.

Results: There were 201 (89.7%) males and 23 (10.3%) females with a mean age of 20.72±3.78 years and mean gaming of 12.59±11.40 hours per week. Out of all the signs and symptoms, tired eyes (50.2%) was the most common, followed by neck and/or shoulder pain (39.9%), headache (33.5%) and watery eyes (29.1%). The symptom considered the most disturbing was Neck and/or Shoulder pain (18.3%). 112 (50%) participants had a reduced visual acuity as well, and among them, the incidence during the lockdown was of 22 (19.6%) responders. Only the people showing four or more than four signs and symptoms were considered Digital Eye Strain positive.

Conclusion: Signs and Symptoms of DES were more common among participants who did video gaming for increased hours than with those who did less, and the difference was significant (p value = 0.03). Distance from the screen had an insignificant effect on the signs and symptoms.

Keywords: Digital Eye Strain (DES), Video game, Video gamers, COVID Lockdown

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Introduction

Since the step of government to impose lockdowns due to covid pandemic initiated, there was a surge in screen time for everyone globally, not only due to e-learning but also because public found substitute of outdoor sports and entertainment in using electronic gadgets[1]. Video Gaming encompasses a major part among all other leisure activities at home[2] and is one of the leading causes of vision related problems and physical distress.[3]

Digital Eye Strain (DES) is defined as a range of disorders related to vision, that outcomes from extended screen time, and is considered a major health problem since more than 2 decades.[4] Computer Vision Syndrome (CVS) mostly describes this same condition.[4] The signs and symptoms prevalent among the affected are, but not limited to blurred or double vision, dry or watery eyes, tired, burning, or itching eyes, frequent eye rubbing and redness in eyes, increased sensitivity to light or

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poor vision in dark, feeling that you cannot keep your eyes open, headache, neck and/or shoulder pain, poor vision in dark, difficulty concentrating.[5-7]

These signs and symptoms are thought to increment with increasing gaming hours and/or having a less distance between the eyes and the display screen, and can be reduced if breaks are taken in between the gaming sessions[3]. Furthermore, the High Energy Visible-light (HEV), especially from the blue/violet spectrum, is radiated from the screens of TVs, monitors, mobile phones, VR (virtual reality) Headsets or other handheld consoles and is believed to have an increased ocular penetration with proven damaging effects like Macular Degeneration.[8] Moreover, decreased visual acuity is also linked with prolonged gaming periods.[9]

Literature review showed that although majority of the researches had been done regarding the association of vision related difficulties and excessive screen usage, yet very few were centered towards gaming. Hardly any work has been done regarding it in Pakistan. Our study aims to investigate the prevalence of DES and its major causative factors among gamers in Pakistan, and to find a relationship between distance from video displays and gaming hours with the frequency of DES signs and symptoms among these gamers.

Methods

This cross-sectional study was initiated after the ethical approval from CMH Lahore Medical College, Lahore, from March 2020 till September 2020. According to Raosoft, sample size was 224 with 95% confidence level[10]. Non-probability convenient sampling technique was used to collect data. The questionnaire used was from Hoya Vision USA regarding DES signs and symptoms[7] and was circulated throughout the country-wide gaming communities via social media groups on Facebook and WhatsApp, using Google Forms link. The questionnaire was divided into 5 sections. The first, second and third sections consisted of the purpose of the questionnaire, declaration of consent and bio data of the participants, respectively. It also asked whether the signs and symptoms improved in any manner. Fourth and fifth sections consisted of 10 questions on video gaming habits of participants and 8 questions about different visual signs and symptoms observed by the participants, respectively. The responses were compiled using Microsoft Excel and the data was analyzed with IBM SPSS 24. Descriptive statistics in terms of frequency and percentages were used to describe qualitative variables like platform of gaming used and usage of blue light filter/glasses. Mean along with standard deviation was calculated for quantitative variables for example age, distance from screen, average gaming hours and so on. While qualitative variables were presented as frequency and percentages. Chi-square was used to determine association between variables and p-value less than 0.05 was taken significant.

Results

There were 201 (89.7%) males and 23 (10.3%) females with a mean age of 20.72 ± 3.78 years. Mean gaming

Table 1: *Demographic Data and Characteristics of Participants*

Parameters	Frequency	Percentage
Total Participants	224	100
Gender		
Male	201	89.7
Female	23	10.3
Occupation Status		
Student	204	91.1
Employed	16	7.1
Part Time Employed	4	1.8
Do you wear glasses/lenses while gaming?		
Glasses	86	38.4
Lenses	1	0.4
Sometimes Glasses, Sometimes Lenses	3	1.4
No	134	59.8
Do you use blue light filter or wear blue light glasses/specialized computer glasses?		
Yes	42	18.8
No	182	81.3
Do you experience any of the Signs & Symptoms of DES?		
Yes	202	90.2
No	22	9.8
If yes, do these symptoms decrease when you spend less time gaming/take breaks? (Out of 210 'Yes' responses)		
Yes	139	66.2
No	71	33.8

Table 2: *Table 2: Average Gaming Hours per Week and Average Distance from the Display*

Parameters	Mean
Gaming Hours per week	12.59 ± 11.40
Distance from the display in feet (top 3 platforms)	
PC/Laptop	2.53 ± 1.80
Console on TV	5.44 ± 3.63
Mobile Phone	1.09 ± 0.44

Table 3: *Relationship of Gaming Hours/Week and Distance from Screen with Digital Eye Strain (DES) Positivity (anyone with 4 or more Signs and Symptoms was Considered DES positive)*

Variable	Digital Eye Strain		P-Value
	Positive	Negative	
Gaming Hours			
⩽10 Hours per week	24	74	**0.03**
10 < x ⩽ 20 Hours per week	17	39	
20 < x ⩽ 30 Hours per week	7	26	
>30 Hours per week	18	19	
Distance from the display in feet			
⩽2 Feet	31	92	**0.48**
2 < x ⩽ 4 Feet	21	40	
4 < x ⩽ 6 Feet	8	16	
>6 Feet	6	10	

hours before the lockdown were 6.6 ± 7.4 hours per week and they increased to mean gaming of 12.59 ± 11.40 hours per week as the lockdown started. Most (91.1%) of the participants were students and others consisted of employed and part time employed (Table 1).

For the platform used primarily for gaming, 38.6% of the responders depended on a PC/Laptop, 28.7% had Mobile Phones, and 22.4% preferred consoles on TV. Other (10.3%) of the platforms included VR headsets, handheld consoles e.g Switch and physical VR gaming e.g HTC Vive. The average distance from the displays of 3 most common platforms is given in (Table-2). Furthermore, only 18.8% of the participants preferred to use a blue light filter or specialized computer glasses to protect their eyes from the excessive HEV exposure. The prevalence of DES signs and symptoms was reported by 202 (90.2%) participants, and 139 (68.8%) of them experienced decrease in signs and symptoms as they reduced their screen time. Out of all the signs and symptoms, Tired Eyes (50.2%) was the most common, followed by Neck and/or Shoulder Pain (39.9%), Headache (33.5%) and Watery Eyes (29.1%). The symptom considered the most disturbing was Neck and/or Shoulder pain (18.3%) and was difficult to deal with by the affected. 112 (50%) participants had a reduced visual acuity, and among them, the incidence during the lockdown was of 22 (19.6%) responders. To test whether there was any relationship between total gaming hours per week and distance of eyes from the screen with increase in the frequency of signs and symptoms, the data was divided into 4 groups each, as shown in (Table 3). Those with 4 or more than 4 DES signs and symptoms were considered DES Positive. Using a Chi-squared test and p=0.05 as a reference, it was found that the increase in gaming hours significantly increased the frequency of signs and symptoms among gamers (p< 0.05) however, the distance from the screen did not have a statistically significant relationship (p>0.05).

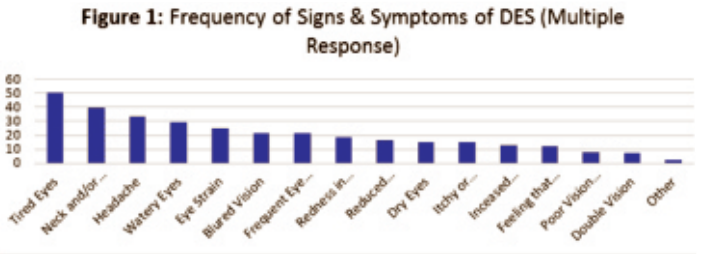

Figure 1: *Frequency of Sign and Symptoms of DES*

Discussion

Due to the advancement in technology, people are now more absorbed in playing video games to an extent that it has become a huge industry and a great source of income for many young adults. However, excessive screen times and exposure to radiations have adverse effects on the health. The widespread use of digital screens in devices used throughout the day have led to the emergence of "digital eye strain" as a new clinical syndrome that affects every individual who spends a large period fixated on multiple screens, for work or leisure.[11] Due to excessive leisure time staying home during the lockdown, the average gaming hours increased among the Pakistani gaming community, according to our survey, and so did it increase in other countries like Canada.[12]

In our study, 89.7% participants were males and 10.3% were females which is similar to a literature review article by Chen KH, Oliffe JL, Kelly MT which showed majority of video gamers were males[13] but slightly different from a study conducted nationally in Rawalpindi where 30.6% video gamers were females.[8] The most common symptom of tired eyes (50.2%) in our study is similar to a study conducted in South Korea,[3] however the next symptom in their study was blurred vision whereas our study showed shoulder/neck pain and headache as the most common symptoms after tired eyes.

The most disturbing symptom in our study was neck/shoulder pain which shows video gaming not only has ocular symptoms but as well as effects on physical health as well, which has also been indicated in a South Korean study[3] which showed that in the physical discomfort domain, the score for neck discomfort after

the gaming session was the highest (before gaming 0.44 ± 0.81 and after faming 1.92 ± 1.21, both values are significant), followed by the scores for shoulder discomfort, headache, and back discomfort. It was also seen that DES symptoms improved in 66.2% of the participants when less time was spent in gaming or breaks were taken in between. Ophthalmologists should set a certain time range for screen time after which DES symptoms may develop. Regular exercise should also be advised to promote a healthy lifestyle.

Due to the lockdown and using video gaming as a source of income, many young people have prolonged screen times and are developing ocular as well as extra ocular symptoms. Increased computer-related activities are an independent risk factor for Neck/Shoulder Pain (NSP) and Lower Back Pain(LBP) in adolescence. It is possible, even obvious, that with these modern leisure activities adolescents are confronted with a new health risk. NSP and LBP are signs of physical and mental loading[14,15]. Neck/shoulder pain can lead to severe postural health problems later in their lives that will not only affect their health but worsen their quality of life as well. In the study of Alabdulwahab et al.[16] a significant relationship was found between the Smartphone Addiction Scale (SAS) and the Neck Disability Index (NDI). In their study, Hakala et al. examined adolescents in Finland and reported that more than 2–3 hours of computer use per day increases the risk of NSP.[17] Silva et al. stated that musculoskeletal complaints were more frequent in individuals with who used electronic devices more frequently and the pain in the cervical and thoracolumbar area increases when the duration of these devices' usage increased to more than 4 hours per day[18].

Conclusion

The survey helped to establish that there are significant ocular or vision related effects on the gamers as they spend more time gaming, however, the distance from the screen did not significantly affect the visual signs and symptoms. Gamers may need to rest in between the gaming sessions to reduce the side effects and ocular fatigue.

Limitations

- Our study is a cross sectional carried over a period of few months. A study carried out over a longer period will give more accurate results.
- Our sample size was small; a larger sample size can assess DES symptoms more accurately as video gaming is an emerging leisure activity in Pakistan.
- Most of the participants were males so the signs and symptoms observed in females needs a bigger female participation.

Conflict of interest: *None*

The authors have no conflicts of interest to declare.

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Authors Contribution

IM: Conceptualization of Project
FI: Data Collection
US: Literature Search
FY: Statistical Analysis
RKA: Drafting, Revision
MF, FI: Writing of Manuscript

Estimation of Pulmonary Function Tests in Pre and Post-menopausal Women

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Abstract

Objective: To ascertain if post-menopausal women are more susceptible to a decline in pulmonary functions (PFTs) as compared to premenopausal women.

Methods: This cross-sectional comparative study was conducted at Physiology Department, FPGMI, Shaikh Zayed Hospital, Lahore from May 2019-May 2020. We recruited one hundred and twenty premenopausal women in age range of 40-50 years (group 1) and one hundred and twenty postmenopausal women with upper age limit of 55 years (group 2). After informed written consent, a detailed questionnaire regarding demographic data was recorded. Pulmonary functions were estimated by spirometry and compared between the two groups. Data were analyzed by SPSS version 20.

Results: Pulmonary functions were markedly declined in postmenopausal women as compared to premenopausal women. Percent predicted value for age for FEV1, FVC and FEV1/FVC in group 1 were 83.01±2.69%, 83.49±2.55% and 0.897 ±0.004% respectively. In group 2 these were 78.49±1.19%, 78.13±1.38% and 1.03 ±0.01% respectively. The differences between two groups were statistically significant (independent sample t test for FEV1 and FVC (p = 0.001 &0.002 respectively and Mann- Whitney U test for FEV1/FVC 0.0002)

Conclusion: It was concluded that pulmonary functions are compromised in post-menopausal women.

Keywords: Menopause, Pulmonary functions, spirometry.

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Introduction

Menopause is a natural physiological process resulting from gradual decline of primordial follicles due to aging and marks the end of a women's reproductive life.[1] It is defined as the permanent stoppage of menstrual cycles for minimum of 6 months, not less than 182 days since last menstrual period or fewer than 3 cycles in the last one year, or removal of both ovaries.[2]

Due to profound hormonal changes menopause is associated with low energy levels, hot flushes, disturbed sleep pattern, irritability and increased susceptibility to chronic conditions.[3]

Since sex hormonal receptors are also manifested in lung tissue, menopause is linked with increased risk of respiratory disorders.[4] A decline in lung function with menopause is likely related to decreasing estrogen levels.[5]

Estrogen and progesterone support pulmonary functions by alpha 2 adrenergic mediated bronchial smooth muscle relaxation and progesterone mediated central respiratory drive. These hormones also maintain bone mineral density maintaining thoracic cage and intrathoracic space.[6] Low levels of estrogen increase the risk of systemic inflammation as well as inflammation in the lungs.[7] The protective role of estrogen may be induced by synthesis of anti-inflammatory mediator secretory leukocyte protease inhibitor (SLPI) and inhibition of pro inflammatory interleukin(IL-33) synthesis

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in lung parenchyma by type II alveolar epithelial cells (AECII).[8] Due to its association with altered inflammatory responses, menopause can be a triggering factor for late onset asthma with increased exacerbations and poor response to anti-inflammatory treatments.[2] As estrogen receptors are also expressed in air way smooth muscles, estrogen causes bronchodilation by reducing intracellular calcium levels in air way smooth muscles through enhancement of cAMP signaling.[9] Postmenopausal women treated with estrogen as hormone replacement therapy have shown improvement in lung functions in terms of FEV1 and FVC.[10] Progesterone improves upper respiratory tract function and aids in breathing by enhancing the activity of pharyngeal dilator muscle. Estrogen up-regulates progesterone receptors, so combination of estrogen and progesterone enhances lung functions.[6]

Relation between respiratory fitness and reproductive aging and associated factors need further evaluation.[2] Future studies are required to illuminate the influence of menopause on lung function.[11] To our knowledge no data is available comparing pulmonary functions in pre and postmenopausal women in Pakistani population. The objective of this study was to find a link between lung function decline and menopause. As life expectancy is increasing far beyond menopause it is important to know how to maintain respiratory health in later life in a large and increasing number of women.

Methods

This cross sectional comparative study was carried out in physiology department, FPGMI, Shaikh Zayed Hospital, Lahore over a period of one year. The study was approved by Institutional Review Board Shaikh Zaid Hospital (IRB:1556). Post-menopausal and pre-menopausal subjects were recruited from relatives of patients coming to the in & out patients department of Shaikh Zayed Hospital, Lahore. Two hundred and forty women in the age range of 40 to 55 years were included in this study. Group 1included 120 self-reported healthy premenopausal women having regular menstrual cycles and age 40 years and above. Group 2 included 120 self-reported healthy postmenopausal women having no menstruation for last 12 months with maximum age of 55 years.

Women with history of hypertension and Heart disease, diabetes mellitus, tuberculosis, asthma, shortness of breath, cough, allergic rhinitis, COPD, on chemotherapy or on hormone replacement therapy, smokers, known bone and joint disease, obesity, use of systemic corticosteroids in last six months were not included in study.

After written consent demographic data was recorded. History, general physical and systemic examination was conducted and findings were noted. Height and weight were measured using measuring tape and digital weight machine. Body mass index of each subject was estimated using formula BMI = body weight (Kg) / height $(m)^2$.

Pulmonary function tests were performed on the participants using Spirolab III Diagnostic Colour Spirometer (made in Italy). Three acceptable values of FVC, FEV1 and FEV1/FVC were obtained using repeatability criteria (ATS criteria) i.e. the difference between the two largest values of FVC must be <150 ml and the difference between the two largest values of FEV1 must be <150 ml.[12] The percentage predicted values of PFTs for age were noted to rule out the effect of age and body mass index. (Normal range between 80-120 percent).[13]

The data was analyzed using IBM SPSS (Statistical Package for Social Sciences) version 20. Data were checked for normality of distribution by Shapiro Wilk's test. Data were considered to be normally distributed if p value was ≥ 0.05 and vice versa. The mean ± SD was given for normally distributed variables. The median and interquartile range (IQR) was given for non normally distributed variables. For quantitative variables with normal distribution independent sample t test was applied and Mann Whitney U test was applied on non normally distributed variables.

Results

Most of our study population was from urban areas (83.3% in group 1 & 88.3 % in group 2), and house wives (66.7% in group 1& 90 % in group 2). Group 1 was relatively more educated than group 2 (58% graduates verses 16 %). In Group 1 mean values of body mass index, percent predicted value of FEV1 and FVC were significantly normally distributed. Age and percent predicted value of FEV1/FVC were not normally distributed. In group 2 body mass index, percent predicted value of FEV1 and FVC were significantly normally distributed. Age and percent predicted value of FEV1/FVC were not normally distributed in both groups.

Independent sample t test applied on mean values of percent predicted value of FEV1 and FVC in group 1 and group 2 confirmed a statistically significant difference between group 1 and group 2.

Mann- Whitney U test was applied on percent predicted

Table 1: *Distribution of Demographic and Laboratory Data in Group 1(120 Premenopausal Women) & Group 2(120 Post menopausal Women)*

Parameters	Group1(120 premenopausal women)		Group2(120 postmenopausal women)	
	Mean ± SD	*p*- value	Mean ± SD	*p*- value
Age	46.13 ± 2.64	0.023*	54.12± 1.69	0.003**
BMI	23.99 ± 2.83	0.289	24.25± 2.59	0.359
FEV1 %	83.01 ± 2.69	0.079	78.49± 1.19	0.43
FVC%	83.49 ± 2.55	0.103	78.13±1.38	0.159
FEV1/FVC	0.897± 0.004	0.002*	1.03 ± 0.01	0.004**

*Distribution; not normally distributed (p value $\leqslant$ 0.05).

Table 2: *Independent Sample T Test for Pulmonary Function Tests between Group 1 and Group 2*

Characteristics	Groups	Mean ± SD	t-test value	Df	*p*- value
FEV1%	Group 1	83.01 ± 2.69	8.837	117	0.001**
	Group 2	78.49 ± 1.19			
FVC %	Group 1	83.59 ± 2.65	9.274	118	0.002**
	Group 2	78.13 ± 1.38			

**Significant difference between group 1 and group 2 at 0.01 level (2 tailed)

value for age of FEV1/FVC for comparing their mean values between group 1 and group 2 which showed a statistically significant difference between two groups.

Table 3: *Mann- Whitney U Test between Group 1 and Group 2*

FEV1/ FVC	Mean ± SD	Min.	Max.	Mann-Whitney U test	Asymp. Sig. (2-tailed)
Group 1	0.897 ± 0.004	0.97	1.00		
Group 2	1.03 ± 0.01	0.98	1.03	1012.0	0.0002**

**Significant difference between group 1 and group 2 at 0.01 level (2 tailed)

Discussion

Menopause is a normal physiological phase in the life of women leading to persistent cessation of menstrual cycle due to permanent loss of ovarian functions. Menopause is linked with decline in serum concentrations of progesterone and estrogen which may lead to increased risk of respiratory disorders. In our study, pulmonary functions were measured in premenopausal and postmenopausal women.

This project was undertaken to evaluate the status of lung functions in menopausal women and whether it differed from premenopausal females.

Mean BMI of premenopausal women was 23.99 ± 2.83 whereas that in postmenopausal women was 24.25 ± 2.59. Although BMI of both groups was within normal range as per inclusion criteria but a slightly higher BMI was noted in postmenopausal group. This is in accordance with the work of Noh et al.,2019.[14] They documented BMI in premenopausal group 22.35 ± 3.17 whereas 23.47 ± 2.99 in postmenopausal group and they attributed it to decline in estrogen levels affecting fat distribution in the body.

In this study, mean percent predicted value of FEV1 was noted to be lower in postmenopausal group (78.49 ± 1.19) than in premenopausal group (83.01±2.69). This difference in mean values was found to be statistically significant on applying independent sample t test with p value 0.001. It is in accordance with the findings of Memoalia et al., 20184 who documented significantly better percent predicted value of FEV1 in premenopausal as compared to postmenopausal women (124.85 versus 72.40%, p value < 0.0001). It may be due to decreased levels of estrogen and progesterone in postmenopausal women.[15] These results are however not in line with those of Triebner et al., 2017[3] who found no statistically significant association between FEV1 and menopause. This difference may be due to differences in geographical, environmental, nutritional and anthropometric parameters and sample size tested.[4] Similarly, in this study mean percent predicted value of FVC was noted to be lower in postmenopausal group (78.13 ± 1.38) as compared to premenopausal group (83.49 ± 2.55). This difference in mean values was found to be statistically significant on applying independent sample t test with p value of 0.002. These results are in accordance with Triebner et al., 2017[3] and Amaral et al., 2016[16] who noted a rapid decline in FVC in postmenopausal women as compared to premenopausal women. Similarly, Memoalia et al., 2018[4] documented FVC 3.27 ± 0.64 in premenopausal women as compared to 2.83 ± 0.78 in postmenopausal women concluding a statistically significant decline in postmenopausal women (p value 0.00). However, this study did not confirm the results of study conducted by Campbell et al., 2020[11] who documented that FVC has no significant difference between pre and postmenopausal groups (p value 0.353). This difference may be due to differences in ethnicity,

nutritional and anthropometric parameters and relatively small sample size compared to Amaral et al., 2016[16]. Mean percent predicted value of FEV1/FVC in group 1 was 0.897 ± 0.004 as compared to 1.03±0.01 in group 2 (indicating a restrictive pattern of lung function decline). These means were compared between group 1 and group 2 by Mann- Whitney U test. It showed a statistically significant difference between two groups with Mann- Whitney U value of and 1012.0 p value of 0.0002. These results are in accordance with Triebner et al., 2017[3] suggesting more marked decline for FVC than for FEV1, showing a restrictive pattern. These results are also consistent with Campbell et al., 2020[17] showing evidence that menopause at an early age leads to reduced pulmonary functions in a restrictive pattern. This is in contrast to the results of Memoalia et al., 2018[4]. They documented a significantly higher percent predicted value for age in premenopausal women as compared to that of postmenopausal women (93.24% vs. 62.15%, $P < 0.0001$) suggesting obstructive pattern.

Conclusion

Based on the results of this study it is concluded that postmenopausal women have a significantly increased risk of decline in pulmonary functions.

Conflict of Interest: *None*

Funding Source: *None*

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Authors Contribution

ZS: Conceptualization of Project
SM: Data Collection
ZH: Literature Search
RS: Statistical Analysis
ZS: Drafting, Revision
BAF: Writing of Manuscript

Determination of Post Mortem Interval by Insect Succession on Decomposing Rat Carcasses; an Experimental Study

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Abstract

Objective: Forensically relevant insect species identification in relation to environmental factors and habitat to rule out post mortem interval of putrefied, unknown human bodies.

Methods: Twelve dissected dead rats (n=12) were placed in 2 cartons in groups of six rats in each, placed over the roof of university animal lab. Changes in temperature and humidity were recorded daily for 31days. Insect succession was observed and correlation of temperature and humidity affecting insects' growth and their ability to approach the carcasses was established by statistical analysis using SPSS version 20.0.

Results: Two species of family Sarcophagidae (flesh flies), and one Calliphoridae (blow flies) were identified from the larvae reared in the lab at room temperature. The identified species were Sarcophaga albiceps, Sarcophaga ruficornis and Chrysomya megacephala. There was a positive correlation of their growth with temperature and humidity.

Conclusion: The results indicate that shortening or lengthening of life cycles of dipteral species in relation to temperature and humidity can lead to genuine assembly of a method to determine reverse timeline for determination of post-mortem interval. Studying insect succession for local insect species that feed on all dead matter can be used as comparison study for insect succession on human bodies.

Keywords: Post mortem interval (PMI), University of Health Sciences (UHS), Forensic Entomology, Insect succession, Calliphoridae, Sarcophagidae

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Introduction

The determination of time since death has decisive value in forensic investigations to solve the legal mysteries involved.[1] All rate methods have helped the legal experts in solving cases.[2] Amidst concurrent methods insect succession on the corpse is relied upon here. With the diverse groups of insects, their habitat and the place of death can be pin pointed.[3,4]

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The type and developmental stage of insect stage may provide an estimate of duration of planting a corpse at a given location.[5] Entomology has an extensive utilization to calculate the age of corpses based on the stage of the insects development.[6] The insect species and their developing stage while feeding on animal carcasses offer investigative standards that can be utilized forensically.[7] Insects get to feed on carcasses as the environmental and physicochemical factors vary speedily in such a tiny habitat.[8] The Diptera order has over 120,000 species. The relevant are species of Calliphoridae, Sarcophagidae and Muscidae, commonly called Blowflies, Flesh flies and House flies respectively.[9] They're differentiated by their morphological features and more accurately with the advanced used of Genetic testing.[10-12] Having strong sense of smell ranging up to 16Km (10 miles) blow flies are initial successors of organic remains

where females lay eggs, maintaining 50:50 gender ratio, with exception of the Chrysomya species that are either arrhenogenic or thelygenic. These flies prefer ovipositing eggs in the moist regions infesting the bodily orifices, mucosae and wounds.[13] Ecological succession is more reliable especially during the late putrefaction, i.e. after 48-72 hours.[2] A process classified by Payne to include fresh, advanced decay, bloated and skeletal or dry remnants,[1] the rate is affected by local and environmental factors i.e., temperature and moisture.[1,2,14] Forensic entomologists study the succession on decaying animal models organs such as blood, liver and kidneys of various cattle.[3,15] Many scientists have studied the effects of various abiotic factors like temperature and humidity to calculate time since death.[1, 16] We have taken a step in furthering this knowledge, so more studies have to be done with an aim to provide a more reliable/accurate estimation of the post mortem interval and its' correction based on environmental variables in the region of Pakistan.[1,13]

Methods

The rats were kept at the roof top of animal house of University of Health Sciences (UHS), Lahore during the month of March, 2016. The location of UHS is 31.50741, 74.30962. Twelve dissected dead albino rats (n=12) were placed in 2 cartons six in each, having holes carved, placed over dry sunny roof of animal house. The study was done in spring season and the temperature and humidity was calculated by thermo-hygrometer. The carcasses were observed for 1/2hr between 10-12pm every day to observe flies and larvae. Weather conditions were observed with a combined Celsius thermometer and humidity sensor and data was compared with nearest meteorological center in Lahore. The post-feeding larvae/pupae were collected and reared, then identified at emergence with morphological keys published by Meigen, 1926 for S.albiceps, Fabricius, 1794 for S.ruficornis and Fabricius, 1784 for C.megacephala. The study included incised rats to attract both blow and flesh flies and excluded live laboratory rats. The reason dissected rats were used was to attract both blow flies and flesh flies, as flesh flies feed and lay eggs on exposed flesh while blow flies are more keen on smell rather than flesh.

Statistical Analysis:

SPSS (V: 20) was used to estimate the correlation by Pearson correlation test, between postmortem interval and temperature and with humidity. The variables were post mortem interval in days, temperature in Celsius and humidity in percentage.

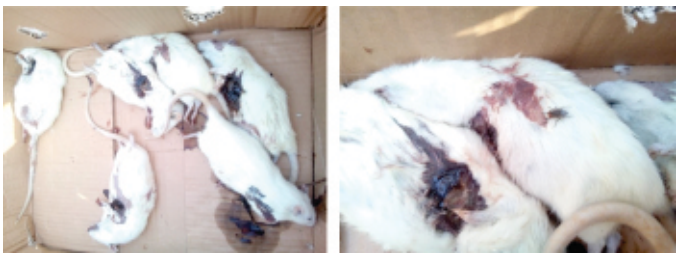

Fig No.1 & 2: *Dead Rats in carton in Fig 1. Sarcophagi fly on dead carcass in Fig 2.*

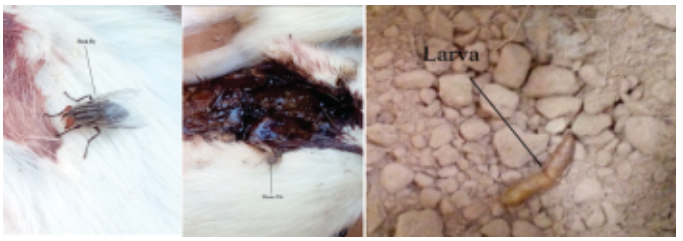

Fig No.3: *Flesh fly. Fig No. 4: House Fly. Fig No. 5: Succession and rearing of larvae on dry soil*

Results

The study was conducted in spring in the city of Lahore, Pakistan, as it has temperature closest to room temperature. 18 to 30°C were extremes, while average temperature throughout study was nearly 24.78°C and humidity 58.35%, ideal to observe insect succession. There are 7 genera and 23 species of Calliphoridae in Lahore, representing Oriental fauna and Chrysomya megacephala seems to appear on dead bodies as a common blow fly.[17] Regarding flesh flies, there are 4 genera and 23 species of Sarcophagidae in Lahore and S.albiceps and S.ruficornis are common flesh flies in Lahore.[18]

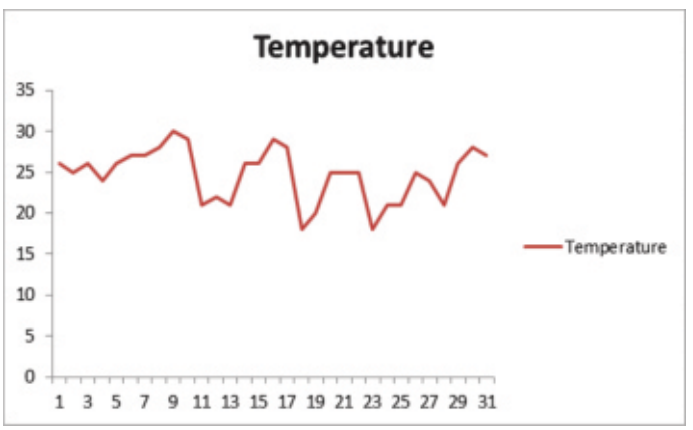

Fig. No.3: *Showing Plot between Temperature and PMI with PMI Values Along x Axis and Temperature values in Celsius Along y Axis.*

Table 1: *Data collection According to PMI*

No. (days)	(PMI) days	Temperature	Humidity %	Eggs (+ for presence, - for absence)	Larvae (+ for presence, - for absence)	Pupae (+ for presence, - for absence)
1	2	26	46	-	-	-
2	3	25	51	-	+	-
3	4	26	57	+	+	-
4	5	24	68	+	+	-
5	6	26	55	+	+	-
6	7	27	39	+	+	-
7	8	27	46	-	+	+
8	9	28	46	-	+	+
9	10	30	32	-	+	+
10	11	29	45	-	+	+
11	12	21	68	-	+	+
12	13	22	76	-	+	+
13	14	21	44	-	+	+
14	15	26	54	-	-	+
15	16	26	38	-	-	+
16	17	29	31	-	-	+
17	18	28	77	-	-	+
18	19	18	83	-	-	+
19	20	20	91	-	-	+
20	21	25	54	-	-	+
21	22	25	67	-	-	+
22	23	25	68	-	-	+
23	24	18	79	-	-	+
24	25	21	69	-	-	+
25	26	21	79	-	-	+
26	27	25	53	-	-	+
27	28	24	60	-	-	+
28	29	21	46	-	-	+
29	30	26	51	-	-	+
30	31	28	62	-	-	+
31	32	27	92	-	-	+

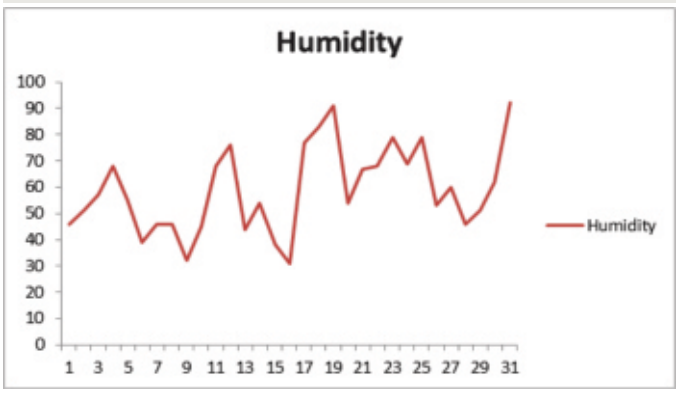

Fig No.4: *Showing Plot between Humidity and PMI with PMI Values along x Axis and Humidity Values in Celsius Along y Axis.*

Table 2: *The Correlation Among Temperature and PMI, PMI and Humidity*

		Temperature	Humidity	PMI
Temperature	Pearson Correlation	1	-.565**	-.254
	Sig. (2-tailed)		.001	.167
	N	31	31	31
Humidity	Pearson Correlation	-.565**	1	.397*
	Sig. (2-tailed)	.001		.027
	N	31	31	31
PMI	Pearson Correlation	-.254	.397*	1
	Sig. (2-tailed)	.167	.027	
	N	31	31	31

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

*. Correlation is significant at the 0.05 level for Humidity (2-tailed).

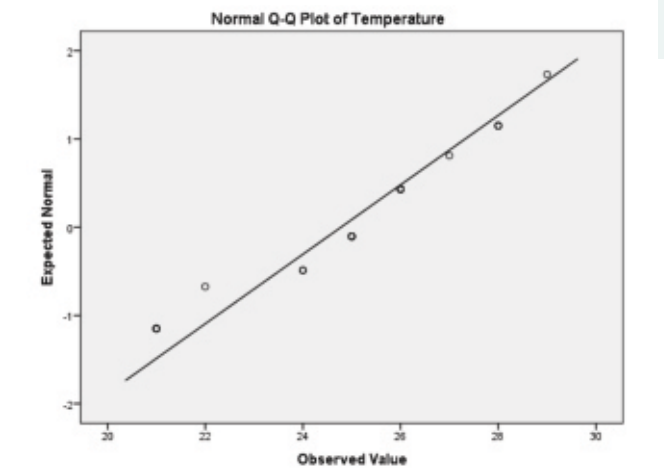

Table 3: *Plot between PMI and Temperature*

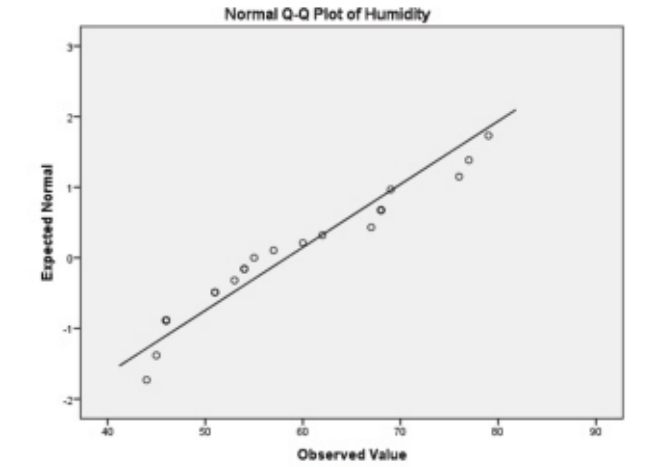

Table 4: *Plot between PMI and Humidity*

The insect succession by these flies was observed everyday for 2 hours for 31 days. Including 72 hours of the putrefaction time the total duration of study with carcasses was 34 days. There was rainfall for two consecutive days that increased levels of humidity between 83-91%, and decreased temperature between 18-20˚C. Other than these two days the mean temperature was 25˚C and humidity 58%. Table 1 shows observation of temperature and humidity values and appearance of insect larvae and shuffling of growth stages of flies.

The post feeding larvae collected were successfully reared inside the laboratory under controlled temperature of 25˚C. The flies that emerged from pupae were mounted and studied for anatomical identification with the help of morphological keys. The following 2 species of Sarcophaga(flesh flies) were collected by us on the carcass of freshly sacrificed rats to breed, S. Albiceps and S. Ruficornis. One species of Calliphoridae was identified; C.megacephala. The study showed a positive correlation of temperature and humidity as shown by Table 3 and 4, with the post mortem interval in days, with temperature showing stronger readings as compared to humidity. Table 2 gives a significant P value of 0.05 for temperature showing temperature significantly affects life cycles of blow and flesh flies.

Discussion

In order to determine post mortem interval by entomological time line, certain factors can shorten or prolong the life cycles of blow flies and flesh flies. The most important of these factors are temperature and humidity. Other factors that change behavior and egg laying process of these flies are rainfalls, sun light, shade, night time and condition of the carcass. This study included temperature and humidity as primary factors to study along with the life cycles of the blow and flesh flies. The weather of spring was chosen for one particular reason of keeping a comparatively constant temperature closest to the room temperature of 25˚C. Watson and Carlton (2003) observed insect succession on deer and swine carcasses in the season of spring for same reasons in Louisiana. Though, humidity varied considerably for few days due to rainfall that altered the temperature to a certain degree.[19]

We observed flesh flies as first flies to be spotted over carcasses. This is a novel finding and it has not been seen or investigated. One reason could be due to incised chests of the rats to enhance smell of putrefied rats that were placed outside after 72 hours after being euthanized. The blow flies were seen a day after. The city of Lahore has a semi-arid climate. Regarding stable and undisturbed life cycles of insects the spring season is the best with temperature and humidity within constant standard range.

Previously it has been shown that the presence of insects greatly affects the rate of decomposition[(12)] nevertheless, no inter-successional waves were observed, as flies being more abundant and were accompanied by Hymenoptera (ants) and in later stages Coleoptera (beetles), all nearly in same time zone as previously observed by Moura and colleagues (2005).[20] Maggots or larvae are frequently found on abandoned dead bodies that have been exposed to external environment for more than 24 hours and our observation was consistent with those recorded by Joseph and colleagues (2011) that forensically relevant larvae or eggs belong to order Diptera or flies including blow flies (Calliphoridae), flesh flies (Sarcophagidae) and house flies (Muscidae).[21] However we could not identify house flies in our study, may be, partially due to samples being placed on the roof as compared to ground level. Moreover, there have been reported different insect species in different demographic areas.

The succession of necrophagous flies that lay eggs or deposit larvae on the dead carcasses is affected by various factors per se. The most important factor is the environmental temperature that can affect post mortem interval estimation by lengthening or shortening of insect life cycle which is primarily used to give entomological PMI. Other factors like season, variations in time of the day, placement and posture of the carcass or corpse, superior predators, abundance of specific insect species in a particular area can greatly affect maggots and flies, their time of depositing eggs and growing into adult flies near the carcass or corpse as suggested by a study conducted by Anderson (2000).[22] Our study was consistent with these findings with temperature as a major influencing factor on insect development on the carcasses. This can easily be compared with entomological findings on the human corpses as insect species that scavenge the vertebrate dead carcasses are all the same according to Verma and Paul (2013).[23]

The current study showed promising results with daily temperature variations and these were similar to study conducted by Verma and Paul, (2013).[23] They established that duration of decomposing carcasses' decay was influenced by the climate changes, more specifically

the temperature alterations, even on yearly basis. The corpses decomposed comparatively faster in summer than in winter and spring season. Rise in environmental temperature in summers speeds up insect succession also, while slows down in winters. Two fly species, C. megacephala and rufifacies are found all the year round according to Verma and Paul, (2013).[23] Our findings of better correlation of PMI with temperature are consistent with study mentioned above. It is essential to know local predatory insect species where putrefied bodies are found. Their life cycles give an accurate estimate of time since death by calculating life cycle of insect and adding time of putrefaction.[24] The method is not error free but needs trained entomologists on the crime scene in the future.

Conclusion

The study indicates that shortening or lengthening of the life cycles of dipteral species in relation to temperature and humidity can lead to genuine assembly of a method to determine reverse timeline for determination of time since death. In cases where time elapsed since death exceeds, the determination by regular methods, entomology aides in assessing postmortem interval unerringly with the help of proper identification of insect species and knowing their life cycle.

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Conflict of Interest *None*

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Authors Contribution

ZS: Conceptualization of Project

SM: Data Collection

ZH: Literature Search

RS: Statistical Analysis

ZS: Drafting, Revision

BAF: Writing of Manuscript

Portal Vein Thrombosis in Hepatocellular Carcinoma: Where the CT Leads Us? Role of CT in PVT

Sadaf Arooj,[1] Sehrish Sharif,[2] Ali Mansoor,[3] Mahjabeen Masood,[4] Mahwash Mansoor,[5] Ume Kalsoom[6]

Abstract

Objective: To study the prevalence of Portal Vein tumor thrombosis in patients of Hepatocellular Carcinoma and to differentiate it from bland thrombus.

Methods: Prospective study was done in the Department of Radiology and Medical Imaging, Mayo hospital, Lahore from Jan 2019 to Jan 2020. 66 patients diagnosed with Hepatocellular carcinoma having portal vein thrombosis were selected and triphasic CT scan was carried out. Both Arterial and Portal venous phases of CT scan were read on Picture Archiving Computerized System (PACS). We used two criteria for labelling a thrombus as tumor thrombus. First, arterial enhancement and second, increased diameter i.e. greater than 18 mm on coronal images.

Results: We studied 66 patients. Thrombus in 20 patients (30%) turned out tumoral portal vein thrombosis and 46 patients (70%) were labelled bland portal vein thrombosis.

Conclusions: In our population bland portal vein thrombosis is more prevalent than tumor thrombosis in patients of HCC.

Keywords: Portal vein thrombosis, Hepatocellular carcinoma, CT scan, neoplastic vs bland.

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Introduction

Liver cancer proved to be 6th commonest cancer worldwide. Hepatocellular carcinoma is the most common liver cancer. The incidence was highest in East Asia and led to 905,677 new cases and 830,180 deaths during 2020. The incidence as well as mortality is higher in men. The prognosis of HCC is poor. The five year survival rate is 18.4%.[1-3] Its most important cause being cirrhosis of liver. Vascular thrombosis is a common complication in many types of malignancy and an important cause of increased morbidity and mortality in such patients. It not only affects the overall prognosis of the patient but also influences management decisions. Vascular thrombosis can be bland or tumoral.[4,5] Patients present in different ways. It can be asymptomatic or range of clinical presentation may include portal hypertension (upper gastrointestinal bleed).[6] Benign disease can be seen in Cirrhosis as well as Non cirrhotics mostly having chronic myeloproliferative disease or infections. Both have different clinical significance, management and prognosis.[7] Bland thrombus develops due to sluggish blood flow and can be treated by various methods like anticoagulants or thrombolytics whereas tumoral thrombus develops when neoplastic cells invade into the vessels. Therefore even the aggressive treatment of tumor thrombosis cannot help the patient mostly as it also makes the actual neoplasm unresectable.[8]

Portal vein thrombosis commonly occurs in patients of hepatocellular carcinoma due to portal hypertension. It can be intrahepatic and extrahepatic and may extend to splenic or mesenteric veins.[3] To differentiate the PVT

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as malignant or benign/ bland is important for precisely differentiating tumor stages and determining different treatment strategies for hepatocellular carcinoma patients. While bland tumoral thrombosis affects management to some extent, presence of tumoral thrombosis changes the whole scenario shifting the treatment from curative to palliative. The prevalence of portal vein thrombosis in patients of HCC is reported to be up to 35%.[7] Among these patients, the frequency of neoplastic PVT is approximately 33% while bland PVT is seen in 20% of patients.[4]

Many imaging modalities can be used to diagnose and differentiate neoplastic or bland portal vein thrombosis including Doppler Ultrasonography (USG), Dynamic CT scan, Dynamic MRI, Diffusion weighted MRI and Susceptibility weighted MRI.[5-9]

USG and Doppler have been identified as first line of investigations. These detect sonographic signs of portal hypertension as well as direct visualization of thrombus. Ultrasound is noninvasive and non-contrast method of evaluation. The limitations of USG being operator dependent and non-availability of large data recognizing tumor thrombosis.[10]

MRI with triphasic protocol as well as newer techniques like Diffusion weighted imaging is another important investigation for differentiating benign and malignant PVT.[9]

Presence of vascularity in the thrombus, dilatation and direct invasion of the portal vein are independently diagnostic of malignant PVT on CT and MRI.[11] Although the definitive diagnosis relies on fine needle aspiration cytology but it is an invasive procedure and contraindicated in coagulopathy and ascites. Triphasic CT is considered most helpful in making this crucial diagnosis[6] as it is a non-invasive technique and is readily available as compared to MRI which is more costly modality, may not be done in patients with claustrophobia and those with implanted metal devices in body.[14] HCC is a common malignancy in our part of the world due to high prevalence of HCV infection. Differentiating between these 2 types of vascular thrombosis in cases of HCC has important prognostic implications. However, there is a lack of availability of data from our part of the world regarding this vascular complication in HCC patients.

Methods

This Descriptive case series is carried out on Radiology Department Mayo hospital, Lahore from February 2019 to February 2020. Patients were selected through non probability convenient sampling who were biopsy proven hepatocellular carcinoma, whose alpha fetoprotein levels are >1000ng/ml, and who underwent triphasic CT abdomen. Patients who were taking anticoagulants due to any reason, who underwent any surgical treatment for HCC, who underwent Transhepatic Arterial Chemo embolization(TACE) for HCC were excluded from the study. Sample size of 66 patients was estimated by 95% confidence interval, 8% absolute precision with expected percentage of portal vein thrombosis in HCC as 12.5%. Therefore 24 females and 42 males were included in the study.

Thrombus Parameters

We considered a thrombus was considered neoplastic when there was arterial enhancement and/or increased diameter of portal vein ≥ 18mm on coronal images.[15]

CT SCAN PROTOCOL

Multiphasic CT scan Abdomen was done in all cases. Machine in our department was 150 slice MDCT (Toshiba). Following phases were done; Plain Non Enhanced (NECT), early arterial, late portal and delayed phases. Non ionic contrast Iohexol 300mg/ml was used, through injection rate being 5ml/sec through automatic dual head injector. Single breath hold technique was used.

We collected data on proforma and used SPSS version 26.0. Quantitative variable like age was presented as mean and standard deviation. Qualitative variable like gender was presented as frequency and percentage.

Results

Of the 66 subjects included in the study 36 % were female and 64 % were male with mean age of 61 ±6.6 yrs. Twenty (30 %) of patients came out as tumor portal vein thrombosis and forty six (70 %) proved bland portal vein thrombosis on CECT. Out of these twenty patients 3 patients who had tumor thrombus had single focal defect in liver and 17 patients had multiple focal defects in liver with tumor thrombus. While in the category of bland thrombus 12 patients were unifocal and 34 patients were multifocal.

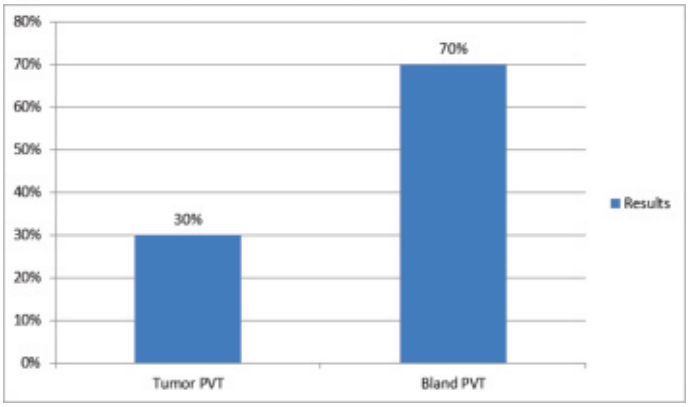

Fig-1:- *Percentage of Bland and Tumor PVT. PVT: portal vein thrombosis*

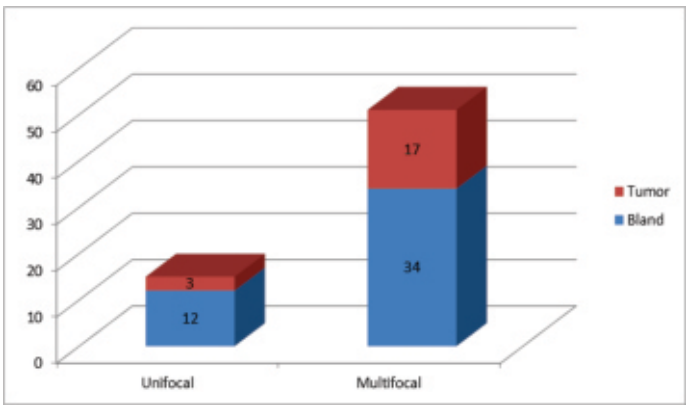

Fig-2: *Frequency of HCC Focal Defects in Bland and Tumor PVT.*

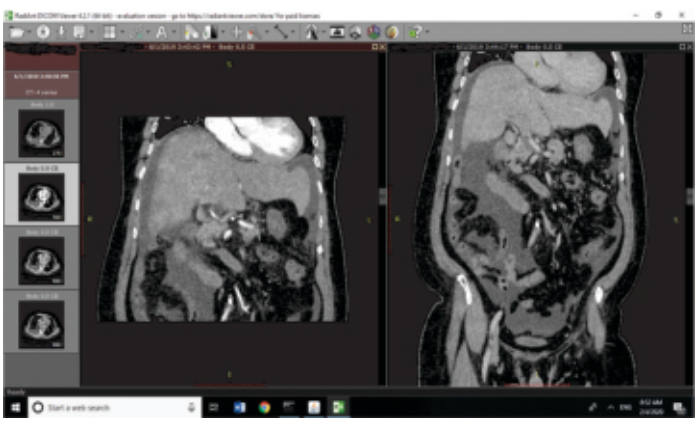

Fig-3: *This is the Image from Triphasic CT taken from One of the Patients who was Biopsy proven HCC Positive with AFP of 2016 ng/ml has a Filling Defect in Portal Vein that shows no Enhancement on Arterial Phase(Yellow Arrow) and Hence no Washout on Portovenous Phase. Case of Benign PVT.*

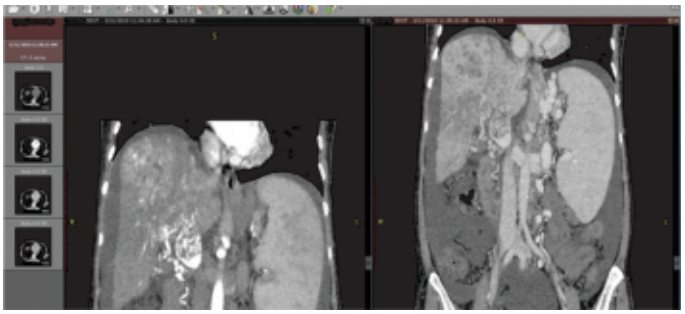

Fig-4: *Coronal CT of a Patient from this Study Diagnosed as Malignant PVT shows Significantly Dilated Portal Vein, Enhancement of Thrombus on Arterial Phase (Yellow Arrow) and Washout on Portovenous Phase (Orange Arrow). Enlarged Liver with Multiple Arterial Enhancing Focal Defects, Splenomegaly and Ascites are also Noted*

Discussion

Portal vein thrombosis is a common complication encountered in cirrhosis patients. Malignant portal vein thrombosis has incidence 36-44%. Benign PVT has 0.6-26% incidence in cirrhosis.[16]

HCC with malignant PVT is associated with poor prognosis.[17]

Some bacterial infections, thrombophillic disorders and sluggish portal blood flow accounts for increased prevalence of portal vein thrombosis. As cirrhosis is a hypercoagulable state; the imbalance between formation of pro and anticoagulable proteins due to impaired hepatic synthesis play a role in the formation of thrombus.[18,19] In Pakistan HBV and HCV infections are the leading causes of cirrhosis and HCC in which HCV has the severe complication of acute hepatitis, chronic hepatitis, carrier state and HCC. In HCV 50% patients develop chronic liver disease.[20] C Sofia et al evaluated the importance of color Doppler, dynamic CT scan and diffusion weighted imaging (MRI) in differentiating malignant and benign PVT. This study included 50 patients with PVT selected on USG, underwent color Doppler imaging, dynamic Contrast Enhanced CT scan and MRI. In comparison with our study, all three diagnostic modalities were compared. They proved that CT scan has sensitivity of >90%.[21]

Reena C et al discussed different portal vein pathologies. It encompassed acute on chronic PVT, congenital absence of portal vein, septic thrombophlebitis, obliterative portal venopathy, portal biliopathy, hepatic masses and tumor in portal vein.[22] PVT leads to worsening of overall prognosis in patients of HCC. They studied

1317 patients for the extent of invasion by using Liver Cancer Study Group of Japan Classification after performing CECT and MRI. They concluded that even minor PVT can lead to poor prognosis.[23]

Triphasic CT scan of liver and Doppler were done and results were compared to fine needle aspiration cytology. Neovascularity, arterial enhancement and portal vein expansion were seen in 87% patients. Their results showed that out of 16 patients diagnosed with tumor thrombus, 12 patients had direct invasion of PV by HCC (75%). That finding was not present in any one of the 4 patients who were having bland PVT accompanying HCC, thus rendering the specificity of this CT sign, approximately 100%. Consequently, if a vascularity, arterial enhancement of thrombus, PV enlargement > 23 mm, or direct invasion of PV by tumor was evident on CT, then the specificity for the diagnosis of malignant PVT approaches 100%.[24]

Another study proposed that above mentioned findings accompanied by increased AFP level were highly recommended to evaluate patients who were candidates for liver transplant.[25]

Limitations of the study include small sample size. This study may further be continued to overcome this limitation. We have not compared it with any other imaging modality which could have added more worth to our study.

Conclusion

In our population bland portal vein thrombosis is more prevalent than tumor thrombosis in patients of HCC. Thus Triphasic CECT would be very helpful for diagnosis and further treatment.

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Authors Contribution

SS, SA: Conceptualization of Project

AM, MM: Data Collection

ZH: Literature Search

MM, UK: Statistical Analysis

Assessment of Different Contraceptives and determinants among eligible couples attending out Patient Department of Hayat Memorial Hospital, Lahore

Amara Usman Tahseen,[1] Muhammad Naeem[2]

Abstract

Objectives: To evaluate the different Contraceptives and the variables among eligible couples.

Methods: A Cross-Sectional Descriptive Study was carried from the eligible couples attending the gynecology and obstetrics outpatient department of Hayat Memorial Hospital, Lahore. Study duration was from June 2021 to September 2021. Sample size was calculated by using prevalence of the most widely use contraceptive choice (Male condom) among eligible couples in Pakistan.

Results: Mean age of the patients was 26-30 years. 95% education level was seen in women. Male condom was the favored method of contraception and was practiced. Doctors were the main source of information (69.1%). On the other hand, the reasons for non-using contraception, mostly had feared due to pressure from husband or other family (3.3%). 28.5% eligible couples were using due to preference of doctor, 27.3% due to the cost of contraception.

Conclusion: The study about concern topic is to "assess different contraceptives and determinants among eligible couples attending the gynaecology and obstetrics out patients department of Hayat Memorial Hospital Lahore" that showed that the majority of contraceptive users are in middle age (26-30 years). The majority 95.9% were having the knowledge of different methods of contraception. Whereas the 89.8% couples are using different contraceptive methods. It was depicted that practices regarding barrier method are found highest. The male condom is preferred by majority of couples (53.9%). The least used method is emergency contraceptive pills (0.6%).

Keywords: contraceptive use, eligible couples, choices, reasons

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Introduction

The increasing population especially in developing countries has erected an alarming sign overall the world. The developed countries have achieved the target in controlling the growth rate in their countries and some of the countries having negative growth rate. This is an effort offset by rapid growth in developing countries. India is the second most famous country in the world after the China and with present growth rate is likely to leave behind China by 2050.[1,2] Population growths in Pakistan present very significant challenges. Pakistan is currently experiencing a clear imbalance in population needs.[3] There are many researches and theories that there is very negative effect of early pregnancies are indicated as the warning signs on the health of women on any age of groups. The use of contraception in early age group is very low and behind this there are many factors like lack of knowledge, awareness, poorly use of contraception, and availability, and less resource.[4] Contraceptive prevalence rates and fertility rate have largely remained unmark able, and have shown very

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slow and ineffective improvements during last two decades.[4,5]

A burden of population in developing countries with limited recourses and funds such as Pakistan make funds allocation to health and development all the more difficult in the presence of other challenges and barriers. The challenge of high population growth in Pakistan essential for use and implementation of creative plans that are effectual in the future increase in population.[7] Pakistan rank the 7th populous country with a population of 82 million and a growth rate of 2.0%. If remain unbounded it can reach 336 million by 2050.[8,9] Pakistan is having very high Total Fertility Rate and very highest maternal (MMR) and infant mortality rate (IMR). Many of developing nations are fighting the conflict against burden of increasing population among which, one is Pakistan.[10] Pakistan has a total fertility rate of 4.5% and a maternal mortality ratio of 298 per 100 000 lives births and National Institute of population studies Islamabad, Pakistan, making it one of the six countries devoting to more than 55 % of all maternal deaths overall the world. The birth spacing reduces the fertility rate and also enhances the mother health. The time immemorial that our need is to increase the contraceptive practice and pregnancy spacing in our country.[11] In Pakistan the total fertility can be decreased to 3.0 births per woman if 15% unwanted births are controlled. The required demand in Pakistan of family planning is 55.5% and contraceptive prevalence rate is 35% and having unmet need of 20%. Pakistan was running its family planning program in 1950 where in 1990 the Government set up a population welfare program for the providing of maternal and reproductive health services.[12] Orderly to decrease this ratio of maternal death, the Safe Motherhood Initiative has recognized family planning as one of the four pillars or supports of the inventiveness through with antenatal care, postnatal care and safe method of delivery.[13] Reproductive health care is one of the basic parts of the 3rd Sustainable Development Goal which accentuates on universal access to reproductive health-care services such as family planning, knowledge and education.[14]

The family planning programs and reproductive health remarkably put up to plummet fertility and improving maternal and child health in the low developed countries.[15] Trimming up the fertility is a necessary element that defines economic recovery and better health. The Fertility reduction and reduction in maternal and child mortality has a significant association.

Spontaneous pregnancies carry a major agonize in developing nations with 122 million women giving childbirth while their actual demand is to ceil family size.[16] Pakistan has one of the inflated fertility rates and stunted contraceptive use rate in the middle of all of its adjacent areas. The mean contraceptive prevalence rate in South Asian countries is 54% while Pakistan has least rate 35%. The amenities of family planning facility and instructing to consumer is a major chore assigned to Lady health workers of the National Program for Family Planning and primary health care which widely familiar as Lady Health Worker programs and is the great community formed on public sector reproductive health serving almost 66% to 73% of women of rural and remote population.[17]

In the Sustainable development goals, target 3.5 calls on countries by 2050, to make sure comprehensive to reproductive health care services, including family planning, education, information and the integration of reproductive health into national strategies and programs. The assessment of progress towards this target requires monitoring of family planning indicators, including the range and types of contraceptive methods used.[18] FP (family planning) practices help women/men or eligible couples to get definite objectives such as to keep away from unwanted birth, to propose about wanted birth, and to maintain birth spacing and to control the rhythm and to determine the number of children in the family.[19] Condoms and oral contraceptives are the most commonly practiced methods in the developed world. On other hand, situation is different for developing countries.

Female sterilization makes 36%, intrauterine device (IUD) stands at 30%, and Oral contraceptives pills account for 12%, condom make 11% and male sterilization is 4 %[20]. Contraceptive prevalence rate (CPR) is an indicator of women health, development and empowerment. Access to reproductive health services is also measured through contraceptive prevalence as a proxy indicator.

A cross-sectional study on assessing predictors of contraceptive use and demand for family planning services in undeserved area of Punjab was conducted by Azmat S, Temmerman M, (2015).The result showed that mean age was 30 years .The women visit private sector for reproductive health services, accessibility of services and good performance of staff were the predictors for helping the women in choosing contraceptive methods. Condom and female sterilization were the most common

methods. And the factors such as education, monthly income, women age had a significant association with current contraceptive usage.[8]

A cross-sectional study on assessing the knowledge of family planning among Pakistani couples attending a tertiary care hospital was conducted by Jaffery HO, Tufail S, Aslam P et al (2019). The result showed that mean age of women was 25-35years. The 89% had knowledge of contraception but only 67% were using contraception. Most commonly used method was barrier method 60%. The source of information were the doctors 28.2% .[11]

A descriptive cross sectional study on assessing the prevalence and predictors of contraception usage in Karachi was conducted by M. Siddiqui, K. Fatima; S. N. Ali et al (2020). The mean age was 18-25 years. There was a significant association between number of children, education status, and monthly income with currently using contraception. The most widely used method were male condom 65.5% followed by withdrawal method 28%. The main source of information were the healthcare providers.[21]

A cross sectional study on contraceptive awareness in antenatal women attending outpatient department in a tertiary care hospital was conducted by Adma HS, Anita V, (2019). The results showed that mostly women with age of 26-30 years and 95% were having knowledge of contraception and 85% were using different type of contraceptive methods. The male condom was the most famous method friend and neighbors were the main source of information.[22]

Based on the literature review and the aim, this study gives the knowledge for the practices of different contraceptive methods and reasons of adopting these methods among currently married women of age 15-49 years visiting gynecology/ obstetrician out patient's department in Hayat Memorial Hospital, Lahore. This all can be done with trial of spreading information and knowledge among the community. The need of the hour is to educate all the couples about the contraceptive methods of family planning, and tries to create awareness among women for decision making to have their own choices about the size of family. Population pyramid of Pakistan shows broad base, so there is a need to do work on family planning and contraceptive use and to improve policy making that depicts for health planning in this context.

Methods

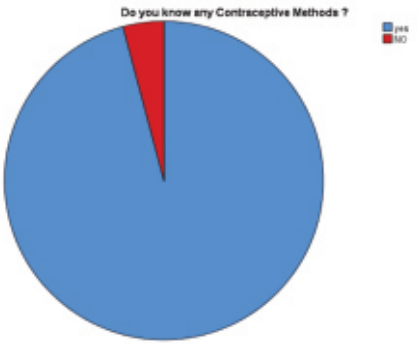
A Cross-Sectional Descriptive Study was carried from the eligible couples attending the gynecology and obstetrics outpatient department of Hayat Memorial Hospital, Lahore. Study duration was from June 2021 to September 2021. Sample size was calculated by using prevalence of the most widely use contraceptive choice (Male condom) among eligible couples in Pakistan: 38% at 5 % margin of error and 95 % confidence level using following formula:

$$n = \frac{n^2_{1-\frac{\alpha}{2}} p(1-p)}{d^2}$$

A self-structured questionnaire was used to collect data. The questionnaire included questions on practices of couples towards different contraceptive methods, reasons. Data was collected with Non-probability purposive sampling. The Statistical Package for the Social Sciences (SPSS) version 25 was used to analyze the data. Categorical data was presented as frequency distribution tables and figures. The "p" value less than or equal to 0.05 was taken as significant. All those couples who were in reproductive age group from 15-45years. Those couples who were prepared to join and give informed consent. Those eligible couples whose women had Hysterectomy. Eligible couples who were unable to conceive after 1 year of marriage suspected to be suffering from infertility.

RESULTS

A cross-sectional study was done to assess the different Contraceptives and deteminants among eligible couples visiting gynaecology/ Obstetrics out patient's department in Hayat Memorial Hospital, Lahore. Mean age



of the patients was 26-30 years. 87% of the women were educated. Knowledge regarding contraception was noted in 95.9% of the women. Male condom was the

most favorable method. The main source of information was the doctors (69.1%). The results were as following

Table 1: *Frequency Distribution of Eligible Couples according to Source of knowledge regarding Contraception*

Source of knowledge regarding contraception	Frequency	Percentage
Doctor	250	69.1
Lady Health Worker	44	12.2
Local Health care provider	6	1.7
Family Relative	47	13.0
Total	362	100.0

in our study.

Fig. 1. *Frequency Distribution pie Chart of Eligible Couples according to Knowledge Regarding Contraceptive Methods*

Table 2: *Frequency Distribution of Eligible Couples Regarding using Types of Contraception*

Using types of contraception	Frequency	Percentage
Male condom	195	53.9
oral contraceptive pills	32	8.8
Hormonal injections	21	5.8
IUCDS	50	13.8
Implant	3	0.8
Bilateral Tube Ligation	20	5.5
withdrawal method	3	0.8
Emergency contraceptive pills	2	0.6
Total	326	100

The Figure 1 shows that 95.9% eligible couples were having knowledge of contraception.

Table 1 shows that 69.1% women were get knowledge from doctors, 13% from family relatives, 12.2% from Lady Health workers and 1.7 % from local health care provider.

Table 2 shows that 53.9% were using Male condom, 8.8% oral contraceptive pills, 5.8% hormonal injections, 13.8% IUCDS,5.5% had bilateral Tubal ligation.

Calculated value of x^2 in Table 10 is = to 146.401 at 4 df and p value is 0.00 it shows that the association between currently using contraceptive and source of knowledge about contraception is significant.

Discussion

In our study, mean age was 26-30 years. The majority (95.5%) had knowledge of contraceptive methods and 89.8% practiced method of contraception. Practice regarding barrier method was highest. 53.9% was using male condoms, 8.8% oral contraceptive pills, 5.8% hormonal injections, 13.8% IUCDS, 5.5% had bilateral tubal ligation which was the least used method. Another Study that was conducted in Rawalpindi hospital showed that 96% women had knowledge of contraceptives but only 87% women were using them. As many studies showed that mostly eligible couples are aware of modern contraceptive methods especially male condom.

In our study, as for as decision to choose types of contraceptive was concerned, majority were using contraceptives according to advice by their doctors (28.5%) and 27.3% due to cost of contraceptives, 15.5% due to preference of husbands, 10.5% due to easy to use, 5.5% due to preference of wives, 1.7% due to availability and 0.3% due to any other reasons.

It is very important to see who promote information regarding contraceptive methods. The lack of knowledge regarding contraception has conclusively bad affect. In our study, the common sources were the doctors as and relatives. 69.1% women got knowledge from doctors, 13% from family relatives, 12.2% from Lady Health Workers and 1.7 % from local health care providers. Another study was conducted in Punjab province

Table 3: *Currently using any contraceptive method*knowledge about contraception Cross tabulation*

Are you currently using any Contraceptive method? * From where did you get the knowledge about contraception? Cross tabulation								X^2 value	p-value
		From where did you get the knowledge about contraception?					Total	146.4	0.00
		Doctor	Lady Health Worker	Local Health care provider	Family Relative	No knowledge			
Are you currently using any Contraceptive method?	yes	241	40	5	39	0	325		
	No	9	4	1	8	15	37		
Total		250	44	6	47	15	362		

also revealed that the common sources were hospital/ clinics and from a private sector or the relatives.[24]

In our study regarding the reasons to avoid contraception majority of females (3.3%) were not using any contraception due to pressure from husband or other family members and 3% were not using due to insufficient knowledge about contraceptive methods. It is overall assert that religious beliefs in Pakistan are not in favor of practicing any contraceptive methods and it shows to a lack of self-reliance in limiting family size. There are many religious and socials barriers and constraints which are supposed to responsible for low contraceptive prevalence rate in Pakistan.

Our study shows that 2.5% females are not using any contraceptive methods due to religious beliefs. The other studies have also highlighted the religions as an important factor affecting the couple's decision to adopt contraceptive methods. This is simultaneously similar with Pakistan DHS 2012-13 results which shows that contraceptive use increases with the number of children and gets the impeccable level when the couples have achieved their desired number of children. In our study, 29% women were having 3 children and 0.3% was having children.

WHO defines the concept of family planning as it's an ability of individuals and couples to predict and attain their desired numbers of children and the timing and spacing of their pregnancies in order to promote the women and child health.

The different strategies or plans to increase contraceptive use must include improving delivery of right and adequate information about the availability and accessibility of contraceptive methods. Education of women is considered to play an important role in decision making. In our study 7.7% women had stop using contraceptive methods due to allergic problems and 5.8 % due to missed periods and only 3.6% due to weight gain. Another study was conducted in Karachi; the most common side effect was followed by weight gain 4.4%.[25] In our study educational level of husbands was concerned, it showed that 25.1% were primary, 28.5% were intermediate and 27.9% were graduated whereas the education status of wives showed that 40.3% were primary and 20.2% were intermediate and 20.2% were graduated. The contraceptives use was higher among educated women.

In our study duration of usage of current contraceptive was 1-2 years (45%), 3-4 year was (33.5%), less than 1 year was (6.6%) more than 5 years (4.1%) and more than 10 years was (0.6 %). In our study, the factors such as women and husband education, monthly income and source of knowledge have significant association with current contraceptive use. Another study was conducted in area of Punjab in Pakistan in 2020 also showed same association with currently contraceptive usage.[8]

Conclusion

The study about concern topic is to "assess different contraceptives and determinants among eligible couples attending the gynaecology and obstetrics out patients department of Hayat Memorial Hospital Lahore" that showed that the majority of contraceptive users are in middle age (26-30 years). The majority 95.9% were having the knowledge of different methods of contraception. Whereas the 89.8% couples were using different contraceptive methods. It was depicted that practices regarding barrier method were found highest. The male condom was preferred by majority of couples (53.9%). The least used method was emergency contraceptive pills (0.6%). As for as decision to choose types of contraceptive was concerned, majority used contraceptives according to advice by their doctors (28.5%). The most common reasons regarding avoiding contraception were pressure from husband (3.3%) and 3% were not using due to insufficient knowledge about contraception. The factors such as education, monthly income, number of children and source of knowledge had significant association with contraceptive methods. Overall results indicate that accessibility and obtainability of different types of contraceptives choices that can result in stronger family planning and in improvement of the society.

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Authors Contribution

MN: Conceptualization of Project

AUT: Data Collection

AUT: Literature Search

AUT: Statistical Analysis

MN: Drafting, Revision

AUT: Writing of Manuscript

Maternal Knowledge, Belief, And Practice Towards Dehydration Management in Children Under 5 Years

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Abstract

Objective: To assess the mothers' ethnomedical models of diarrheal disease, concepts of appropriate treatment of diarrhea, and the role of the primary health care system in shaping their knowledge about diarrheal management in young children in rural areas of Pakistan.

Methods: A cross-sectional study is conducted by using a pre-tested and pre-structured interview schedule. Prior to the interview, Informed verbal consent is taken from 1000 volunteer rural mothers of children with acute diarrheal episodes. This study is based on children under 5 years who presented at the diarrheal section of a pediatric medical emergency, Children Hospital, Faisalabad. from September2019 to February 2020.

Results: The use of ORS in the treatment of diarrhea by rural mothers is less than 50%. ORS is easily accessible to the people but there is disuse by masses due to lack of awareness and knowledge regarding diarrheal management. In the majority of the cases, the attitude and practice of caregivers determine the fate of children with acute diarrhea.

Conclusion: In this study, 100% of the rural mothers have had access to ORS but only about 30% showed compliance with the treatment. The rural mothers believe that IVT is more effective than ORS regardless of the severity of dehydration. Unnecessary IVT can potentially cause a number of complications. Failure to effectively give ORS leads to severe dehydration. As a result, lack of public awareness in managing simple diseases like diarrhea, is causing deaths more than HIV, dengue, and measles collectively.

Keywords: dehydration, gastroenteritis, ORS, rehydration, pediatrics, diarrhea.

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Introduction

With all the advancements in the medical field and treatment coverage, the mortality caused by diarrhea reduced to 87.4% from 1980 to 2017.[1] Despite this remarkable success, diarrhea is still having a significant impact, being the second most common cause of mortality in children under 5 years.[2] Globally, 1.7 billion children under 5 years are affected by diarrhea per year, and 5,25,000 die with it.[3] Among all the other poor and developing countries, Pakistan is contributing the most in under 5 mortalities, ranked third in maternal, fetal, and child mortalities, worldwide.[4] Pakistan has a mortality rate of 89 per 1000 which translates into 183,000 deaths per year of children under five years. Out of these 183,000, 30% (or 54,900 children) deaths/ year occur due to pneumonia and diarrhea collectively. It accounts for 53,000 deaths with diarrhea per year.[4,5] The primary cause of mortality with diarrhea is dehydration. Among secondary causes, are malnutrition, impaired immunity resulting in sepsis, and death with septic shock or hypovolemic shock, if left untreated.[6,7] Dehydration is the loss of the body's water content to the level where it starts to interfere with the normal functioning of the body, causing dizziness, confusion, loss of skin turgor, dry skin, dry tongue, sunken eyes,

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oliguria or anuria. It is categorizedas mild, moderate, and severe, depending upon the severity of these signs and symptoms. Gastroenteritis is an illness of acute onset that refers to the passage of 3 or more watery stools per day, lasting for 14 days or less, may or may not be accompanied by nausea, vomiting, abdominal pain, and fever.[8] Mostly, acute diarrhea is viral and self-limiting, causing mild dehydration to start with, which can be treated or prevented with continuous oral feed and adequate oral fluids intake.[14] Children with large volumes of fluid loss without adequate fluid replacement, having any co-morbidity i.e. malnutrition, are prone to deteriorate quickly, develop severe dehydration at a relatively rapid pace and need emergency treatment as early as possible. Low Osmolar Oral Rehydration Salt (Low Osmolar ORS) is a WHO-recommended solution for diarrhea as an effective and inexpensive method to treat mild to moderate dehydration, since 1970.[8] It is used for enteral rehydration can be given orally or via nasogastric tube and can be given at home. Antibiotics are not recommended for acute diarrhea but can be considered, depending upon regional epidemiology of diarrhea and clinical assessment of physician.[13,15] ORS is the treatment of choice in acute diarrhea with mild to moderate dehydration if the patient is able to tolerate Enteral Rehydration Therapy (via Oral or Nasogastric tube). While intravenous therapy (IVT) is expensive, a traumatic way of rehydration can only be given by trained physicians and staff.[16] Rehydration therapy is not the same for all children. Different fluids with different measurements are given to children with specific requirements. IVT has a great risk of miscalculation of required fluid, poor choice of fluid, rapid correction of electrolyte imbalances, leaking of fluid into surrounding tissues, the transmission of infection/s to the blood via an IV line, inflammation at the site (phlebitis).[8] IVT is only recommended in specific conditions like paralytic ileus, glucose malabsorption, or when ORT fails to treat dehydration i.e. in moderate to severe dehydration or rapidly progressing dehydration despite of proper ORT. (WHO 1995). This study aims to highlight the significance of Low Osmolar ORS for the treatment of acute gastroentritis in children under five years. Although, Low Osmolar ORS is widely available in health facilities yet rural mothers lack the knowledge regarding preparation and use of oral rehydration therapy. IVT is coupled with a number of complications and sometimes, adds unnecessary burden to the hospitals. This burden can be greatly reduced merely by public awareness, especially in rural mothers. The results of this research can be used by health policymakers to identify the weak link and initiate awareness programs via the primary health sector to decrease mortality, improve quality of life, and reserve financial and human resources by remarkably decreasing the burden of diarrhea, merely with the public health education.

For the data collection of this research, the subjects are selected by considering the following inclusion and exclusion criteria.

Methods

Ethical clearance and approval were obtained from the Ethical Committee of Children Hospital, Faisalabad. The pre-structured, questionnaire-based interview was scheduled. The data was collected from 1000 volunteered caregivers of selected children. To ensure the authenticity of the collected data, only those children were included in the study where attendants were the caregivers of the children. In the majority of the cases, the caregivers were rural mothers. Verbal consent was taken by explaining the purpose and procedure of this study, then all respondents were asked for their willingness. For those who were not willing to participate, their right was respected and was not included in the study. The caregivers were asked questions about sociodemographic aspects, their practices, and belief regarding the management of dehydration in diarrhea. IVT was only given to the patients with severe dehydration. The classification of dehydration (mild, moderate, and severe) was based on history, signs and symptoms.

- **Mild:** No hemodynamic changes, increased thirst, able to drink water adequately, normal skin turgor, normal peripheral perfusion.
- **Moderate:** Tachycardia, restlessness, irritable behaviour, skin pinch goes back slowly, eagerly drinks water in large amounts.
- **Severe:** Hypotension with impaired perfusion, drowsy/unconsciousness, sunken eyes, unable tp drink water, oliguria, skin pinch goes back very slowly in 2 seconds or more. Sometimes it does not go back if patient is malnourished as well.[20]

Multiple patients were received in Children Hospital Faisalabad with complications of IVT given in private clinics or hospitals. All responses and identities of the patients were kept confidential. The study did not adversely affect the rights and welfare of the subjects.

Inclusion Criteria

- Abrupt onset of loose stools with 3 or more episodes per day, in an otherwise healthy or stable child.
- Diarrheal episode lasting for 2 weeks or less.
- Paediatric age group of 5 years or less.
- Only those cases are included in the study where the attendant of the child is the caregiver, to ensure the authenticity of data collection.

Exclusion Criteria:

- Mothers, those were not willing to participate.
- Diarrhea lasting for more than 2 weeks.
- Diarrhea associated with any other disease like coeliac disease, hepatitis, inflammatory bowel disease, and dysentery is excluded.

Results

According to data collected, the male to female ratio is 1.0. The most affected age group is of children under 1 year, n=324 children (32.4%) accounting for one-third of total subjects. Children presented with various degrees of dehydration, mild n=378 (37.8%), moderate n=334 (33.4%), severe n=288 (28.8%) with mean duration of diarrhea of 2 days (Table 1). Out of total, n=291 (29.1%) children were having co-morbidities i.e. Iron deficiency anaemia n=116 (11.6%), 3rd degree malnutrition n=106 (10.6%), asthma n=52 (5.2%), congestive cardiac failure n=10 (1%), nephrotic syndrome n=6 (0.6%), are likely to develop complications with IVT or rapid fluid and electrolyte correction (Table 2),194 of them (66.9%) actually developed complications and presented in ER with facial puffiness n=90 (9%), generalized body swelling n=74 (7.4%) and respiratory distress due to pulmonary edema n=30 (3%). Otherwise healthy n= 33 (3.3%) children without any co-morbidity also developed complications of IVT i.e. generalized body rash with ringer lactate infusion n=6 (0.6%), phlebitis n=26 (2.6%) (Table 3). Availability of ORS to these subjects was 100%, while only 30% of mothers were fully compliant with ORS, 45% were non-compliant and 25% did not use ORS at all. Among 1000 mothers, n=60 (6%) preferred oral treatment and n= 940 (94%) were not satisfied with ORT, from which

Table 2: *Frequency Table showing co-morbidities, susceptible to develop over-hydration quickly and prone to develop complications by miscalculation of fluid, unnecessary infusion or the wrong choice of fluid administered for IVT.*

Sr. No.	Documented Co-morbidities intolerant to over hydration	Number of Children Affected	Valid Percent (%)	Cumulative Percent (%)
1.	3rd Degree Malnutrition	106	10.6	10.6
2.	Asthma	52	5.2	15.9
3.	Nephrotic Syndrome	60	0.6	16.5
4.	Iron Deficiency Anemia	116	11.6	28.1
5.	Congestive Cardiac Failure	10	01	29.1

Table 3: *Frequency table showing children presented to the pediatric medical emergency with complications developed immediately or shortly after intra-venous rehydration therapy.*

Sr. No.	Complications Developed with IVT	Frequency (n)	Valid Percent (%)	Cumulative Percent (%)
1.	Facial Puffiness	90	09	09
2.	Generalized Body Swelling	74	7.4	16.4
3.	Respiratory Distress (Pulmonary Edema)	30	03	19.4
4.	Skin Allergy with Ringer Lactate Infusion	06	0.6	20
5.	Phlebitis	26	2.6	22.6

Table 1: *Frequency table showing degree of dehydration and age distribution in different age groups.*

Age Groups	Gender				Degree of Dehydration		
	Male	Female	Frequency (n)	Valid Percent %	Mild	Moderate	Severe
1 month - 6 months	86	64	150	16	38	42	80
6 months - 1 year	84	80	164	16.4	54	48	62
1 year – 1.5 years	74	72	146	14.6	42	68	36
1.5 years – 2 years	76	82	158	15.8	66	54	38
2 years – 3 years	70	100	170	17	80	56	34
3 years – 4 years	40	52	92	9.2	40	34	18
4 years – 5 years	46	64	110	11	58	32	20
TOTAL	476	524	990	100	378	334	288

n=716 (71.6%) insisted on intravenous rehydration, irrespective of the degree of dehydration. Only 6% of mothers had a belief that ORS is effective in treating dehydration, 35% were not sure and 59% consider ORS as a placebo but not a treatment. None of them were ever educated about ORT by any health visitor via the primary healthcare system (Table 4).

Table 4: *Multivariable Analysis of Attitude and Practice of Mothers during an Acute Diarrheal Episode of their Children*

Sr. No.	Variables	Response	Frequency (n)	Valid Percent %
1.	Access to ORS	Yes	1000	100
		No	0	0
2.	Belief on ORS Effectiveness	Yes	60	6
		No	590	59
		May be	350	35
3.	Patient prescribed with ORS in the recent diarrheal episode	Yes	716	71.6
		No	284	28.4
4.	Use of ORS to treat dehydration	Compliant	300	30
		Non-compliant	450	45
		Never used	250	25
5.	Treatment preferences of mothers	Prefer ORT	60	6
		Not satisfied with ORT but agreed to use ORS	940	94
		Not satisfied with ORT and Insisted for IVT	716	71.6
6.	Ever educated by health visitor(s) about ORS use	Yes	0	0
		No	1000	100

Discussion

Regardless of substantial ameliorations in the medical field so far, the simple and apparently harmless looking disease is killing more than 2195 children per day.[3] Acute Diarrhea is most commonly viral in origin. Rotavirus is responsible for 90% of cases of acute diarrhea.[18] The acute episode is self-limiting, takes 5-7 days to resolve, and does not need any medication or special care, but the deleterious effects are caused by the dehydration accompanied bydiarrhea. With early management, the duration and severity of dehydration and diarrhea can be minimized.

The irony is, despite having all the essential tools of diarrheal management in hands, the rural mothers, here in Pakistan, are losing their children with it. WHO (World Health Organisation) is striving to provide ORS and zinc supplements to all the under-developed and developing countries to decrease the global mortality rate and improve the health condition of young children. According to the results of this research, ORS coverage was optimal. Almost everyone had the access to ORS and was prescribed with it earlier. Even with the full availability and proven efficacy of ORS, non-compliance of mothers or caregivers regarding ORT use in dehydrated children is the consequence of their lack of knowledge, impatience regarding oral treatment, myths and taboos associated with ORT, and personal beliefs that ORS cannot help in dehydration at all or maybe as effective as IVT can. The myths and taboos result in harmful practices i.e. restriction of oral intake of food and fluids including breast milk feed, during diarrheal episode.[10] This attitude results in increasing severity of dehydration as mothers or caregivers completely rely on IVT. Lack of initial management steps with ORT causes increased frequency of hospital visits, increase in disease load and burden on hospital, in terms of both financial as well as human resources.

The problem lies at the root level of the healthcare system, the basic health units, which are aimed to interact with the public directly and educate them by going door to door, about hygiene, health maintenance, and home remedies for the commonly occurring diseases of infants and children under 5. The results of the data collected show, no mother or caregiver is ever encountered or educated by any health visitor. The masses are directed to the tertiary care hospitals, skipping the steps of primary and secondary healthcare management, as a result of which, we are facing high mortality rates of children with severe diarrhea under age of 1 year with the late presentation in Paediatric Emergency.

With proper education, lives can be saved. ORS can be bought or can be made at home, either way, it is the best solution to manage dehydration and balance the water intake with ongoing water loss. The introduction of modern medicine misled people to take unjustified antibiotics and intravenous treatments. The satisfaction of mothers is bound with the IV drips and the belief system plays a role to decide the fate of the child. If the physicians do not recommend IVT, caregivers go to the quacks for it, followed by the presentation in ER (Emergency Room) with volume overload and other complications associated with it. Children with co-

morbidities are at high risk to deteriorate in such conditions, i.e. in severe anemia or cardiac failure, dehydration and overhydration both can prove to be fatal for them. Out of 500 patients, 97 presented to ER with complications of IVT (Intravenous Therapy), with a history of co-morbidities and acute onset of diarrhea with mild dehydration. Those children were treated symptomatically; some were critical but all survived.

The investment at the public awareness programs can save the health system from high infant mortality rate, the expense of unnecessary overzealous IV hydration, patient load at tertiary care hospitals, and it will enable the prompt management of dehydration, deceleration of dehydration during the course of an acute episode and prevent diarrhea at the first place with the proper diet and nutrition to combat the acute infections, effectively. This requires the education of mothers or caregivers about the normal course of the disease, how to pick up the symptoms and manage them accordingly, to maintain the child's health and up going growth and development curve.

Conclusion

The use of inexpensive and readily available low osmolar ORS (Oral Rehydration Salt) to treat dehydration is less than 50% in rural areas. In this study, only about 30% rural mothers showed compliance with oral rehydration treatment. 70% mothers insisted for IVT because they were not satisfied by ORS. Rural mothers believed that IVT is the most effective treatment for dehydration regardless of its severity whereas IVT is only recommended in severe dehydration, exceptions included.[17] In most of the cases, diarrhea is self-limiting and needs no intensive care, saving the child from dehydration can be enough. Low Osmolar ORS can effectively fulfill the purpose. Almost all of the rural mothers have had access to the ORS but lack of knowledge and awareness kept them from effectively using Oral Rehydration Salt as treatment. It is unfortunate that a remarkable number of children die every year with a preventable disease like diarrhea. If we could only educate the rural mothers about the efficacy of Oral Rehydration Salt, a considerable decrease in mortality rate in children under 5 is possible.

Conflict of interest *None*

Abbreviations:

ORT: Oral Rehydration Therapy

IVT: Intravenous Therapy

ORS: Oral Rehydration Salt

WHO: World Health Organisation

ER: Emergency Room

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Authors Contribution

HSK: Conceptualization of Project
MA: Data Collection
MS: Literature Search
SJ: Statistical Analysis
MS: Drafting, Revision
MA: Writing of Manuscript

Quality of Life of Caregivers of Epileptic Children, Using Zarit Burden Scale

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Abstract

Objective: To assess the subjective quality of life of caregivers of epileptic children and to figure out recommendations to improve it.

Methods: This descriptive study was conducted at The Children's Hospital and Institute of Child Health Lahore in collaboration with Institute of Public Health (IPH), from January 2018 to March 2018. Convenient purposive sampling was done to obtain a sample size of 85. Data collection tool employed was a predesigned questionnaire. Data were analyzed using SPSS version 20.0. Frequency tables were generated for all possible variables. Chi square test was used to compare categorical variables. Ethical considerations were born in mind including confidentiality and consent.

Results: Results of the study show that majority of caregivers had mild to moderate and moderate to severe burden. The mean age of caregivers was 34.69 years and all were females. Analysis of data showed that age and gender of children had no significant effect on level of stress on caregivers. However, frequency of seizures, duration since last episode of seizures, type of drug therapy, compliance with treatment and associated co-morbidities had statistically significant (p value < 0.05) effect on degree of burden on caregivers.

Conclusion: Epilepsy imparts remarkable stress on caregivers. It is recommended that increased awareness about dealing with epileptic children and physiological and psychological rehabilitation of caregivers must be established.

Keywords: Caregiver burden, epilepsy, quality of life.

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Introduction

Epilepsy is one of the commonly occurring neurological disorders with a prevalence of 0.5- 1%. It affects people of all nations, and races.[1] It is one of the most prevalent non-communicable diseases which evolves spontaneously and gives rise to a lot of neurologic and psychosocial implications affecting people of all age groups.[2] Children are more vulnerable to epilepsy and its complications.[3] Epilepsy has adverse implications not only for the patients but also for the caregivers as many are prone to an increased risk of spontaneous un-predicted fatality linked to epilepsy.[4] The clinical hallmark of epilepsy is termed as seizures resulting from abnormal excessive or synchronous neuronal brain activity. Epilepsy can be diagnosed if at least two reflex seizures happen in excess of twenty-four hours apart and confirmed on electroencephalogram.[5] Epileptic seizures occur spontaneously or triggered by fatigue, fever, stress or a specific recognizable precipitant such as flashing light, a sudden noise or cognitive activity. Epilepsy can result from various underlying brain disorders. Genetics is involved in a substantial part of cases of epilepsy.[6] In many cases, the

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underlying cause of epilepsy is unknown or poorly known.[7]

In Pakistan about more than two million people suffer from epilepsy and social stigma related to epilepsy and treatment gaps are very high.[8] The implications in epilepsy for a person's life depend on physiological repercussions of the epileptic episodes, their impacts on social status and their mental impact. Epilepsy is also linked to a greater risk of co-morbid conditions.[9]

In children, normal development and school performance may decline and parents may become very protective, which interferes with normal social functioning, self-esteem and independency. Early life epilepsy inevitably will also affect the future. People having seizures have to struggle with all these medical, social and psychological aspects of their condition in daily life, usually resulting in a reduced quality of life.[10] Childhood epilepsy is an elevated hazard for poor psychological outcomes and impacts on quality of life of children but also has a great effect on family functioning. Care provision is a tough experience which can drastically ruin the physiological & the psychological health of caregivers. Caregivers of epileptic children have been labeled as forgotten-patients & it was asserted that care provider's signs like mood swings, fatigability, headaches, arthralgia & myalgia, marital and family rivalries, and monetary issues can be indicators of care provider's strain in taking care of epilepsy subjects. Zarit-Burden score interview is a famous care-giver self-report tool employed by numerous geriatric organizations. Every question in the Zarit's is a problem-statement which the care-giver is required to answer. It consists of twenty-two questions regarding how the care givers feel about themselves, their concerned sick relative and whether their relation with the concerned relative negatively affects their life and he caregiver is asked to rate the burden they feel regarding the care of the concerned relative employing a five-point scale. Every question is rated from 0 (never) to 5 (almost always). Total score is interpreted as follows.

a. No or minimal burden: 0- 20
b. Mild to moderate burden: 21- 40
c. Moderate to severe burden: 41- 60
d. Severe burden: 61-88.11

The merits of Zarit Burden Scale include it being a relatively quick measure that is easy to administer and can be completed less than 10 minutes. The demerits include the self-checklist format which can be limiting, positive aspects of caregiving that might reduce feelings of burden being not explored. There is paucity of literature on the quality of life of caregivers, as in Pakistan most of studies include measurement of the quality of life of care providers and epileptic patients only. The study is an attempt to identify the magnitude of physical, psychological, social and economic effect on the quality of life of the caregivers of epileptic children because very less work has been done on caregivers in developing countries like Pakistan. This study will help patients, caregivers, healthcare providers and policy makers to take measures to improve the quality of life of caregivers.

Methods

Descriptive cross-sectional study was conducted in The Children's Hospital and Institute of Child Health Lahore in collaboration with Institute of Public Health (IPH), after approval by internal review board of Institute of Public Health and The Children Hospital, Lahore. We recruited 85 caregivers of epileptic patients from outpatient department of Paediatric Neurology by convenient purposive sampling technique. Caregivers with psychological and psychiatric health problems were excluded. Data were collected with the help of predesigned questionnaire after informed consent maintaining privacy and confidentiality. Study variables for caregivers were identified including age, gender, religion, education, marital status, occupation, family type, place of residence and monthly income were recorded. Study variables for epileptic children were also recognized including age, sex, schooling, type of seizures, frequency of seizures, drug therapy, comorbidities, compliance and duration of treatment. Zarit Caregiver Burden Scale (CBS) was used to assess the burden of caregivers of epileptic children. Data were analyzed using SPSS version 20.0. Frequency tables were generated for all possible variables. Means and other parameters of central tendency were calculated for continuous data and categorical data was analyzed by chi square test.

Results

Mean age of caregivers was 34.69 years and all were females. About 54.1% caregivers were literate while 45.9% were illiterate. Among 85 caregivers, 1.2% had little or no burden (group 1), 51.8% mild to moderate burden (group 2), 32.9% had moderate to severe burden (group 3) while14.1% had severe burden (group 4) as shown in Fig-1.

Group 1: little or no burden

Group 2: mild to moderate burden

Group 3: moderate to severe burden

Group 4: severe burden

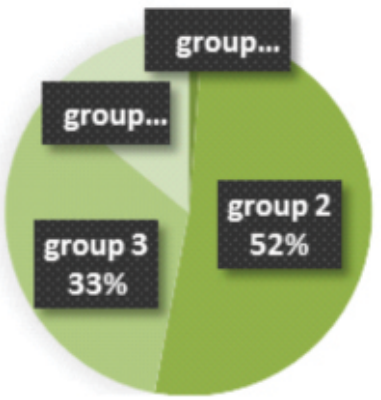

Fig-1: *Frequency Distribution of Caregivers According to Classes of CBS*

Table 1 shows that as far as sociodemographic and medical history of epileptic children in relation to burden on caregivers is concerned, age and gender of children and duration of epilepsy has no significant effect on level of stress on caregivers. While schooling, frequency of seizures in last four weeks, epilepsy control, associated comorbidities, compliance with treatment, duration since last episode of seizures and type of drug therapy had statistically significant (p value < 0.05) effect on degree of burden on caregivers.

Discussion

Epilepsy is a chronic illness where caregivers are an integral part of the treatment and rehabilitation of epileptic patients. Caregivers take the toll and burden of the intensive, rigorous and time-consuming duty of these patients. Present study was carried out to access the quality of life of caregivers of epileptic children presenting at a tertiary care hospital in Pakistan, using Zarit Burden Scale.

In our study, an analysis of the Caregiver Burden Scale shows that in majority (51.8%) of the cases, caregiver burden was mild to moderate followed by moderate to severe burden (32.9%), severe and little or no burden. An international study[12] had similar results, identifying caregiver burden to be on mild to moderate levels in majority of the cases. Another study of 231 caregivers of patients attending an outpatient clinic in Nigeria identified similar Zarit burden scores.[13]

Current study found that caregivers were between 26-44 years of age with a mean age of 34.69 years and all were females. Another study[14] to assess caregiver burden at Massachusetts General Hospital, in 2011 on the children with epilepsy found the mean age of caregivers to be 36.52 years which was quite similar to the results of the current study.

In our study 54.1% caregivers were literate while 45.9% were illiterate. This was in line with the work of Mohamed and coworkers where all caregivers were females and more than one third were literate.[16]

Table 3: *Comparison of Predictive Values (Bishop Score vs. Cervical Length)*

Characteristics	Category	Group1 count	Group2 count	Group3 count	Group4 count	X^2	*p value*
Schooling of children	No	0	10	10	11	19.94	0.000*
	Yes	1	34	18	1		
Seizure frequency past 4 weeks	<5	1	43	15	3	33.36	0.000*
	⩾5	0	1	13	9		
Epilepsy control	Poor	0	0	18	12	56.85	0.000*
	Good	1	44	10	0		
	Yes	1	28	5	1	22.22	0.000*
Comorbidities	No	0	16	23	11		
	Good	1	44	19	7	19.40	0.000*
Compliance	Poor	0	0	9	5		
Duration since last seizures	<1 week	0	3	19	12	47.90	
	⩾1 week	1	41	9	0		0.000*
	Monotherapy	1	40	18	3		
Drug therapy	Polytherapy	0	4	10	9	22.60	0.000*

*Statistically significant.

In current study, only 12.3 % of caregivers in severe burden group were married while 50 % were divorced or widowed. These results are in line with work of Samia and coworkers in 2019.[17] Severity of stress may be contributed by support of spouse and social pressures in divorced or widowed.

In our study, age and gender of children has no significant effect on level of stress on caregivers. While frequency of seizures 4 weeks prior to interview, epilepsy control, associated comorbidities, compliance with treatment, duration since last episode of seizures and type of drug therapy had statistically significant (p value <0.05) effect on degree of burden on caregivers. These findings are in line with the work of Samia and coworkers[17] as well as Riechmann and coworkers.[18] It may be due to the possibility that deterioration of health of child and prolonged treatment is tedious work and creates a significant burden for the caregivers. Westphal and coauthors, however stated that burden on caregivers is not dependent on severity or duration of illness.

Conclusion

An analysis of the results shows that most of the caregivers of children with epilepsy experienced remarkable burden associated with demographic and clinical characteristics of caregivers and patients.

Recommendations

An increase in awareness and health education about managing family life with epilepsy is highly recommended. Psychological and physiological rehabilitation cell for caregivers should be established at hospitals as most of the caregivers visit regularly for the follow-up of their epileptic children.

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Authors Contribution

AR: Conceptualization of Project
MS: Data Collection
SA: Literature Search
AR: Statistical Analysis
TM: Drafting, Revision
MS: Writing of Manuscript

Correlation Between Arm Span Length And Height

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Abstract

Height is one of the most important helping criteria to establish identity. Different body parts have positive correlation with height. Arm span length has very strong and positive correlation with standing height.

Objective: Aim of this study was to find out correlation between arm span length and height. The regression equation obtained will be used to estimate height from arm span length.

Methods: Study design: cross sectional study. Study sample: 108 male students of Sialkot medical college. Sampling Technique: Non probability purposive sampling technique was used to select the samples. Selection criteria: Male students of Sialkot medical college having no deformity of limbs and vertebral column were selected. Collection of data: Standing height was measured in inches. Arm span length was measured by extending arms. Statistical analysis: SPSS version 25 was used to perform statistical analysis. Correlation coefficient and regression equation was obtained. Tables and graphs were made.

Results: The value of Pearson correlation coefficient was 0.846. A statistically positive very strong and significant correlation was found between height and arm span length.

Conclusion: The results of this study indicate that arm span length can be used to estimate standing height. The regression equation can be used to predict standing height in a person who can not stand up.

Key Words: Arm span length, height, Pearson correlation coefficient.

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Introduction

Since centuries length or width of various human body parts has been used for many purposes. One of them was to indicate and differentiate the slaves. In Forensic, routine utilization of different measurements of human body for establishing uniqueness was started in France by Alphonse Bertillon in 1883.[1,2]

Human height is one of the most studied attribute. The reason is that it can be calculated with an ease without using sophisticated instruments. It can be recorded without wasting much time.[3] Human height provides very important data about health and socioeconomic conditions of humans separately and collectively as a community. Human height shows a lot of variety not only within family but also within country.[4]

When it becomes practically difficult to take measurement of height then other body part measurement can be used to estimate height.[5,6]

Almost all body parts have been studied to estimate standing height including foot length, foot breadth, hand length, hand breadth, index finger length, head circumference, head length, arm length, arm span length etc.[7,8] The extended arms length was found to be the most dependable attribute among all other body measurements in establishing identity through estimation of standing height.[9]

As height varies among different communities so a single statistical formula cannot be applied universally.[9]

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Acceptance Date: 00-00-0000

Methods

Study design: It was a cross sectional study.

Sample size: 108 male students of Sialkot medical college.

Sampling technique: Samples were selected by non probability purposive sampling method.

Selection criteria: Only male students who were free from any deformity of vertebral column, upper and lower limb.

Collection of data: Standing height was measured by stadiometer in inches. Every student was asked to stand still against wall in erect position. Every student was asked to put off shoes as well as socks. Head piece of stadiometer was lowered on the head turn by turn and standing height was noted in inches. Then each student extended his both arms laterally. The distance between the most extended part of finger was measured by measuring tape in inches. Every pupil was asked to spread both arms laterally. Both arms were at right angle to the body. Their palmer surface of hands was anteriorly placed. A measuring tape was taken and via between terminal parts of both middle fingers in extended form was measured. Both measurements were taken in inches.

Statistical analysis:

Statistical analysis was done by using SPSS Version 25. In addition to descriptive data Pearson correlation coefficient was calculated. Regression analysis was done. Arm span length was independent variable and height was dependent variable. Regression equation was obtained. Graphs and tables were made to show the data.

Objective

The purpose of this study was to find correlation and linear regression between arms span length and standing height of students of Sialkot medical college Sialkot. So that regression equation could be used to estimate the standing height in those patients who can not stand for the purpose of proper medication and nutrition.

Results

Descriptive data regarding standing height and arm span length including minimum and maximum values along with standard deviation has been depicted in table no 1.

Table 1: *Descriptive Data of Height and Arm span ength*

Descriptive Statistics					
	N	Min.	Max.	Mean	Std. Deviation
ARMSPAN_ LENGTH	108	67.00	76.50	72.4676	3.40167
HEIGHT	108	65.00	75.00	70.7269	2.92379
Valid N (listwise)	108				

Table 2: *Correlation Coefficient between Arm Span Length and Standing Height*

Correlations			
		ARMSPAN _LENGTH	HEIGHT
ARMSPAN_ LENGTH	Pearson Correlation	1	.846**
	Sig. (2-tailed)		.000
	N	108	108
HEIGHT	Pearson Correlation	.846**	1
	Sig. (2-tailed)	.000	
	N	108	108
**. Correlation is significant at the 0.01 level (2-tailed).			

Value of correlation coefficient is shown in table no 2.

Table 3: *Value of F.*

ANOVA[a]						
Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	655.364	1	655.364	267.879	.000[b]
	Residual	259.328	106	2.446		
	Total	914.692	107			
a. Dependent Variable: HEIGHT						
b. Predictors: (Constant), ARMSPAN_LENGTH						

Value of F along with significance value is shown in table no 3.

Table 4: *Value of t of Arm Span length(independent variable)*

Coefficients[a]					
Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
1 (Constant)	18.004	3.225		5.583	.000
ARMSPAN _LENGTH	.728	.044	.846	16.367	.000
a. Dependent Variable: HEIGHT					

Value of t of independent variable along with its significance value is shown in table no 4.

Table 5: *Value of R Square*

Model Summary[b]				
Model	**R**	**R Square**	**Adjusted R Square**	**Std. Error of the Estimate**
1	.846[a]	.716	.714	1.56413
a. Predictors: (Constant), ARMSPAN_LENGTH				
b. Dependent Variable: HEIGHT				

Value of coefficient of determination is shown in table no 5.

Regression Equation

Regression equation is depicted in figure no 1.

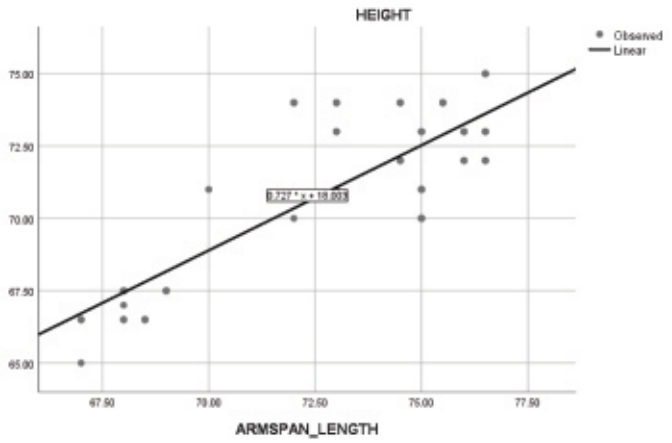

Figure No 1: *Regression Line Along with Regression Equation*

$$Y = 0.727 *X + 18.00$$

Discussion

The results of this study indicate that minimum height was 65 inches and 67 inches was minimum arm span length. Maximum height and arm span length was 75 and 76.50 inches respectively. The value of Pearson correlation coefficient was 0.846 with a p value far less than 0.01. This indicates that correlation between height and arm span length is strongly positive and statistically significant. A study conducted in India indicates almost same value of Pearson correlation coefficient i.e., 0.856.[11] Similarly another study indicates a value of 0.98 between arm span length and height.[12] In India a study carried out indicated that value of r was 0.908.[13] A study done in Montenegro University showed that the value of r between arm span length and height for males was 0.861.[14] A study carried out in Serbia also show similar value of r as 0.814 as in above mentioned studies.[15] A very strong positive correlation has been seen in the results of another study. In that study value of r was 0.98.[15] A study carried out in Bosnia also indicate positive and statistically significant values of r (0.876)[16]. A research carried out in Kosovo showed that there was positive and significant correlation between arm span length and height with a value of r 0.794[17]. Almost similar results have been seen in another study conducted in Kosovo with a r value of 0.776[18]. 0.806 value of r was calculated in a study brought out in India.

A study carried out in South Africa showed value of r as 0.76[19] in boys from 15 to 18 years of age. Another study carried out on medical students in India value of r for boys was 0.702.[20]

Value of t of independent variable 16.367 with significant value of p indicating that arm span length can be used to predict the standing height. Value of F is 267.87 with p value less than 0.01 .Value of F in this study also indicates that this model can be used for prediction purposes as the value of p indicates that the model is significant.

Conclusion

The results of this study indicate that arm span length can be used to estimate standing height.

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Authors Contribution

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

Protective Effect of Ajwa Fruit Extract on Weight of Liver of Albino Rats Against Hepatotoxicity Induced by Nicotine

Faeza Rauf,[1] Alvia Batool,[2] Attya Zaheer,[3] Hafiza Sadia Ahmed,[4] Ashiq Hussain,[5] Hafsa Nazeer[6]

Abstract

Objective: To reveal the protective effect of ajwa fruit extract on weight of liver after nicotine toxicity in adult albino rats.

Methods: It was an experimental study conducted in the Anatomy Department of Shaikh Zayed Postgraduate Medical Institute, Lahore.

Study was done on three groups each containing 10 female albino rats. Rats of group A were given 1ml distilled water by gastric intubation, experimental group B received 0.1mg/kg body weight intraperitoneal nicotine injection for 30 days. The rats of experimental group C were given 0.1mg/kg body weight intraperitoneal nicotine injection plus 1000mg/kg body weight ajwa fruit extract by gastric intubation for 30 days.

Conclusions: Nicotine administration in the female albino rats significantly reduces their weight of liver which was improved by the use of ajwa fruit extract.

Key words: nicotine, ajwa fruit extract, Rats.

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Introduction

A study from a university of Karachi described that regular users of shisha were 43% male and 11% female students.[1] More than 4000 lethal organic compounds are present in cigarettes, including nicotine ($C_{10}H_{14}N_2$), an alkaloid,[2] which contributes to smoking's addictive properties.[3] 1 mg nicotine is absorbed by a smoker from a cigarette that contains 7 to 22 mg of nicotine. Nicotine present in 20 cigarettes is equal to that present in an average hookah/shisha bowl.[4] Nicotine go through several paths of chemical transformation and breakdown.[5] Nicotine is metabolized mainly by the liver and to a lesser extent by lung and brain. Its metabolism occurs in two steps. First oxidation of the nicotine produce cotinine and nornicotine.[6,7] Secondly there is glucuronidation of the metabolites and elimination.[8]

Smoking seems to effect liver by 3 distinct mechanisms: poisonous, immunologic, and carcinogenic.[9] Nicotine causes oxidative tissue injuries in rat by increasing lipid peroxidation and superoxide dismutase (SOD) activity in liver while it decreases catalase (CAT) activity in liver.[10] Smoking in women lowers progesterone and estrogen and raises follicle stimulating hormone.[11] Maternal smoking increases incidence of intrauterine growth restriction, low birth weight in new born,[12] retarded fetal growth, still birth, miscarriage and mental retardation.[13]

Ajwa date fruits (Phoenix dactylifera L) is a prophetic medicine testified to exert tissue-protective effects against many poisons. It is the fruit of the female tree date palm (Phoenix dactylifera L.). An extensive variety of

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phenolic compounds existing in dates include flavonoids, procyanidins, p-coumaric, sinapic and ferulic acids.[14] Aqueous extract of dates significantly inhibits protein oxidation and lipid peroxidation and has a radical scavenging activity for hydroxyl and superoxide.[15,16] Antioxidants act together and neutralize free radicals and stop them from producing damage. A study of comparison of fresh and dried phoenix dactylifera shows that on drying at higher temperature phenolic contents increase due to maturation of degradative enzymes and degradation of tannins.[17]

Methods

This experimental study was conducted in the animal house of Department of Anatomy of PGMI, Lahore in association with the Anatomy Department of FPGMI, Lahore. Thirty female albino rats, weighing 200-250 gm, of 3-4 months age were divided into 3 groups as A, B and C. Rats were kept at 28±2ºC and a 12 hour light and dark cycle was maintained. They were fed on rat food and given water ad libitum. Before the experiment, rats were familiarized for one week. Ajwa Dates were purchased from Madinah and their extract was prepared by separating date fruit from pits and adding 1 liter distilled water to 3000 gram of crudely crushed date fruit (3:1).[18] This was kept for 2 days at 4°C with rare stirring.

1.752 mg Gallic Acid Equivalent /g of extract and 0.1239 mg Quercetin equivalent/g of extract) were enumerated by PCSIR, Lahore. Nicotine synthesis grade (99% pure) was purchased from Sigma-Aldrich (USA). After acclimatization for one week, 30 female albino rats were divided through simple random sampling into 3 equal groups A, B and C (n=10) and weighed. Group A (healthy control), received distilled water by gastric intubation (1ml/day), group B received (0.1 mg/kg body weight/day) intraperitoneal nicotine injection, group C was given (0.1mg/kg body weight/day) intraperitoneal nicotine injection plus (1gm/kg body weight/day) ajwa fruit extract by gastric intubation. The whole treatment continued for 30 days. On 32nd day, 48 hours after giving last dose, these rats were weighed properly. Rats were sacrificed and the liver was dissected out, weighed. It was fixed with 10 % formalin for 48 hours. Data was analyzed by SPSS 20. The data for liver weight was reported as mean ± S.D. ANOVA was used for comparison among groups (one way). For post hoc analysis, Tukey's test was used. P-value ≤ 0.05 was considered significant.

Results

The Liver weight of rats during experiment ranged between 7.186-7.973g for healthy control group A and that of group B, and group C were 4.753-5.755g and 6.772-7.908g respectively. (Table-1) The mean weight of liver was 7.671±0.301, 5.309±0.309 and 7.572± 0.384 in groups A, B and C respectively. (Table-1)

One way ANOVA test was applied to compare liver weight among groups. It showed statistically significant difference between mean weight of liver when compared between control and experimental groups (.000**) (Table-2)

Post hoc tukey test showed that mean liver weight in group B was significantly less than A and C groups. Difference in mean liver weight in groups A and C was not statistically significant, p-value = 0.736. (Table-3) There is noteworthy statistical difference in mean weight of liver in groups B and C, p-value = 0.000**. (Table-3)

Table 1: *Mean Liver Weights (g) of Female Albino Rats of A, B and C Groups*

GROUP	Mean	SD	Minimum	Maximum
A	7.671	0.301	7.186	7.973
B	5.309	0.309	4.753	5.755
C	7.572	0.384	6.772	7.908

Table 2: *Effect of Nicotine on Liver Weights (g) of Female Albino Rats of Experimental Hroups Based on One Way ANOVA*

Source	Sum of squares	Df	Mean Square	F	P-Value
Group	35.687	2	17.844	160.129	.000**
Error	3.009	27	.111		
Total	1446.823	30			

Table 3: *Multiple Comparison Among Control and Experimental Groups Based on One-Way ANOVA*

Group (I)	Group (J)	Mean Difference (I-J)	Std. Error	P- Value
A	C	0.0986	0.14929	0.736
B	C	-2.2628	0.14929	0.000**

Discussion

Intraperitoneal injection of nicotine to rats resulted in decreased weight of liver in group B. Nicotine suppresses appetite, modifies energy expenses, increases metabolic rate and reduces weight of body, and an average

4 kg weight increases on its stoppage.[19] So nicotine increases lipolysis as well as fat utilization.[20] Activation of arcuate nucleus of hypothalamic nicotinic acetylcholine receptors cause activation of pro-opiomelanocortin neurons, which later stimulate melanocortin 4 receptors, responsible for nicotinic-induced decreased food intake in mice.[21]

Nicotine produces free radicals which affects the regulation of biological processes. When free radicals increase, there is oxidative stress which favour various disease processes.[22] Liver weight is reduced due to metabolic dysfunction and liver damage in the rat as is seen in study performed by Jalili C[22] where nicotine significantly reduced liver weight of mice.

These results coincide with study performed by Rauf F, where paired ovarian weight was reduced in nicotine treated rats. [23]

Weight of liver among group A, and group C were comparable, with no significant difference. Aqueus extract of ajwa fruit is superior to alcoholic extract due to its polyphenols such as proanthocyaindins.[24] These results coincide with increase in weight in ajwa plus nicotine treated group by Rauf F[23] where appetite decreasing effects of nicotine is overcome by appetizing property and tissue protective effect of ajwa. Similar results are observed by Ali and Abdu[18] where antioxidant effect of ajwa fruit extract ameliorated the toxicity. Ajwa (Phoenix dactylifera L) has an antioxidant action as it hunts free radical, prevent iron-induced lipid peroxidation and protein oxidation.[25]

Conclusion

Ajwa fruit extract has significant protective effect against nicotine induced hepatotoxicity.

Conflict of Interest *None*

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Authors Contribution

FR: Conceptualization of Project
AB: Data Collection
AZ: Literature Search
HSA: Statistical Analysis
AH: Drafting, Revision
HN: Writing of Manuscript

Proximal Fibular Osteotomy (PFO) in Medial Compartment Osteoarthritis Knee Joint

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Abstract

Objective: To assess the effectiveness in our patients of proximal fibular osteotomy (PFO), a new surgical intervention which claims to provide substantial relief in medial compartment osteoarthritis (OA) of knee.

Method: A prospective analytical study was performed in DHQ Hospital, Rawalpindi on 25 consenting patients. A length of fibular segment 1.5 to 2 cm was resected at a distance of 6 to 9 cm from fibular head under local anesthesia, wound closed in layers and patient mobilized as soon as tolerated within few hours. Pre-operative and post-operative x-rays of knee were obtained. Pre-operative and post-operative VAS score for pain was recorded on each visit up to 6 months. Any complications and complaints were recorded.

Results: All opting patients were female with mean age of 47±4.2 years. The average pre-operative VAS score was 7.4±0.6, post-operative score was 4.4±1.1. Average improvement in VAS score was 3±1.2. The paired difference between pre and post-operative VAS scores was highly significant (8.1818E-12). Post treatment, 2 patients reported near complete relief, 3 very little reliefs and 80% of patients reported moderate relief. Post-operative complications included reversible temporary foot drop in all, one case of non-recovering common peroneal nerve injury, and mild ankle pain complaint in all patients. All patients expressed dislike of sawing procedure under local anesthesia although none complained of pain during operation. No patient opted for similar intervention in other limb.

Conclusion: Thus we conclude that the present protocol was not favored by the patients in our group, in spite of the fact that moderate alleviation of knee pain was reported by nearly all.

Keywords: medial compartment osteoarthritis, proximal fibular osteotomy, high tibial osteotomy, unicondylar arthroplasty.

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Introduction

Osteoarthritis (OA) of knee joint is a major cause of disability with worldwide prevalence of disease of approximately 36% in people aged more than 65 years.[1] It is anticipated that the prevalence will further increase substantially owing to increasing life expectancy. The need of the hour is not only to find new modalities of treatment of OA but also to apply fresh approaches to delay the progression of the debilitating effects of the disease. The management of OA of knee varies with stage of disease, with the socio-economic condition of individual patient and additionally with the health facility.[2] Whereas multiple non-surgical and surgical treatment procedures are available, total knee replacement has become the fastest growing orthopedic surgery in the world. This pursuit is being driven not only by genuine indications but also by patient demand

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for quick relief, encouraged by self-serving industry.[3] In this race of surgeries what has been lost is the knee preservation methods that delay or even abolish the need of arthroplasty, including drugs, platelet rich plasma and stem cell therapies, braces, physiotherapy and realignment osteotomies. Among the three compartments of knee the medial compartment shows early and predominant involvement as it bears approximately 70% of body weight the mechanical axis being more frequently medial to the center of the knee joint.[4,5] This leads to a stress concentration in the medial compartment and degeneration of the cartilage and meniscus, increasing varus deformity and decreasing medial joint space which are the major pathological manifestations of knee OA.[6,7] By shifting the load transmission from medial to lateral compartment the medial compartment can be unloaded, which can be facilitated by bracing, lateral wedge in-soles (nonsurgical), by osteotomy (surgical) or by joint distraction. This biomechanical approach has been used to reduce disease progression in osteoarthritis.[8,9] It has been observed that symptomatic pain relief and cartilage regeneration are possible in OA if joints are distracted for prolonged periods of time. However, the mechanism by which cartilage growth might occur in the distracted joint space is not well known.[10] It has been reported that cartilage regeneration is possible in OA joints that has been surgically pulled apart for a prolonged period of time.[9] High tibial osteotomy or HTO is the gold standard for medial compartment OA with varus, and is known to correct the deformity producing remarkable results lasting even 15 years or longer. However, it has gradually fallen out of favour because not only is it technically more demanding than total knee replacement but certain disadvantages have been reported, including delayed time to full weight bearing and risks of non-union or delayed union, peroneal nerve paralysis and wound infection.[11] Another good alternative for isolated medial compartment osteoarthritis is Uni-compartmental knee arthroplasty UKA. Although the procedure is less invasive but UKA has got even more high revision rate then TKA.[12] High tibial osteotomy (HTO) revision rate is less than UKA and is more suitable for younger patient and delays requirement for TKA or UKA.[12-14]

Recently a new concept of proximal fibular osteotomy PFO has been proposed for medial compartment OA of knee. The medial articular surface of proximal tibia is supported by single medial tibial cortex while lateral tibial articular surface is supported by 3 cortices; one lateral tibial & two fibular cortices. By resecting a small segment of fibula PFO redistributes the load on the tibia plateaus[15]. This alteration in the kinematics of knee may increase valgus, femoral external rotation, and distal translation of the knee and thus help reduce knee pain and improve early functional recovery.[16] This can be alternative treatment option for medial compartment OA which may delay or even abolish the need for TKA.[17] Hence we conducted a preliminary study to investigate the above hypothesis as it has been reported to be simple, safe, fast and affordable surgery that does not require insertion of additional implants. Such a procedure can prove to be of immense benefit for our population.

Materials and Methods

The study was performed in DHQ Hospital, Rawalpindi as prospective interventional study between Jan. 2017 and July 2019. Patients for this surgery were selected by the following criteria:

- Medial compartment arthritis with significant compromise in daily life activities
- Candidates who would, otherwise, be suitable for HTO or uni-compartmental knee arthroplasty.
- Those patients who gave consent for this procedure. A special consent was taken after explaining the experimental nature of this surgery to the patient.

A total of 25 patients were included in the study. All patients were females (as male patients refused to participate).

Surgical technique: The surgery was performed under local anesthesia without a tourniquet. The tip of fibular head was marked with a skin marking pen and the appropriate distance (6 to 9 cm) measured. Skin, and subcutaneous tissue were cut. The incision was a little more than twice the length of the resected segment. The fibular periosteum was well anesthetized and was exposed by separating the peroneus and soleus muscles. The periosteum was incised in line of skin incision, and a 1.5 to 2 cm piece of fibula resected with a narrow blade oscillating saw.

The length of fibular segment resected was 1.5 to 2cm, and the distance from fibular head to the proximal cut was 6 to 9 cm. The concept was to remove the two fibular cortices, converting the knee to a more balanced joint, with unicortical support on either side, allowing correction of mechanical axis. The size of the resected segment and its distance from fibular head depends on the patient's height. Shorter patients had a 1.5cm segment

resected 6 cm below fibular head, tall patients had a 2 cm resection, some 8 to 9 cm below the fibular head. The wound was washed, closed in layers and a light compression bandage given. The patient was mobilized as soon as tolerated which in most cases was within a few hours. All cases were performed as a day care surgery. Patients were followed up on day 15 (suture removal) and two, six months from the date of surgery.

Criteria of evaluation of results

1. Pain relief measured by VAS.[18]
2. Satisfaction of patient was to be taken as the criteria of success of the treatment. Only left knees were operated initially. We hypothesized that if patient was satisfied with the treatment she would agree for the operation of right counter knee. After checking the data for normality Statistical analysis was performed using SPSS version 23.0. Student's paired t-test was applied to determine the difference in the pre and post operative VAS. scores

Results

25 patients were included in the study. All were females, 38 to 55 years, mean age of 47 ± 4.2 years. The pre-operative VAS score ranged between 6 and 8, average of 7.4±0.6. The post operative average score was 4.4 ± 1.1. The paired difference between pre and post operative VAS scores was highly significant ($p \leq 0.05$). Average improvement in VAS score was 3±1.2. 80% of patients reported postoperative pain at VAS score of 4 and 5(10 patients each), 2 patients recorded 1 and 2 as post treatment VAS, 3 patients reported a little improvement at VAS-6. (Fig-1)

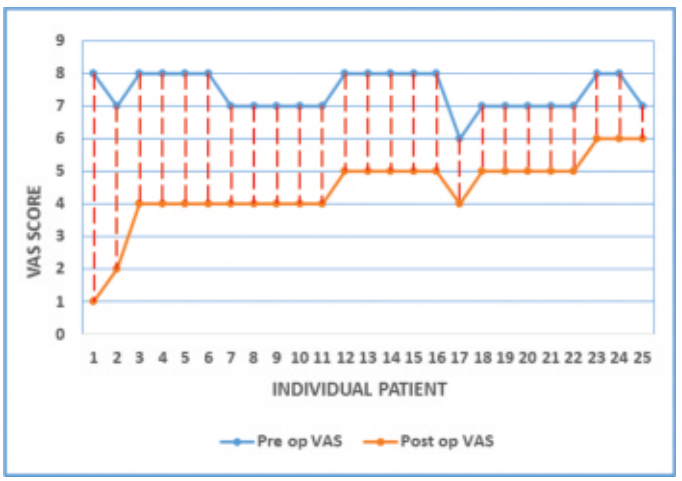

Fig-1: *Changes in Patient Vas Scores following Proximal Fibular Osteotomy*

Intra-operative and post-operative delayed complications

1. In all patients PFO procedure was performed under local anesthesia. No pain at operation site was reported but there was apprehension among patients due to constant vibration of oscillating saw. 15 patients reported mild ankle pain during the procedure.
2. In 4 patients there was a moderate hemorrhage (200-300ml) that was controlled with packing.
3. Post operatively all the patients had foot drop and paresthesia. Foot drop continued for 2-4 months and then dorsiflexion was regained. However, paresthesia persisted in patients for up to 6 months.
4. Among the foot dorsiflexors, extensor hallucis longus function was last one to recover. In four patients it was never regained but they were able to extend the ankle.
5. One patient had complete common peroneal nerve injury that did not improve. NCS showed level of injury at the neck of fibula, above the surgical procedure site.
6. Post-operative swelling in operated leg and ankle persisted for 2-4 months.
7. All patients reported ankle pain of mild intensity in operated limb during follow up period. Thus knee pain was reduced in intensity but ankle pain became the concern of patients.
8. 8: Postoperatively none of patient showed improvement in joint space as was expected before operation.

However, none of the patient showed willingness for second procedure in the contralateral limb, even that patient also refused who had shown complete recovery.

Discussion

The purpose of this study was to find an alternative way to treat OA of knee joint which would be relatively easily available to our patient population. Total knee arthroplasty, unicondylar arthoplasty, high tibial osteotomy undoubtedly have good results but they are expensive procedures available in only limited hospitals in a few larger cities of Pakistan. Moreover, the gold standard teaching is that TKR should be reserved as a last resort in management of knee OA, after exhausting all other methods of management. Unicondylar arthroplasty and HTO for various reasons are less frequently procedures offered to patients demanding operative intervention for disabling disease. Similarly, platelet rich plasma therapy and stem cell regeneration seem

to be very fascinating new procedures.[19] Both have shown early promising results and seem to delay the need of total knee replacement. However, their long term results are yet to come. They are costly and require special equipment and facilities.

In the above scenario PFO seemed to be an attractive option which is simple and can be readily done even in a remote area with the use of routinely used gadgets of orthopedic surgery.

This is a relatively recently introduced technique being performed in some Orthopedic centers in China, India, Indonesia which face somewhat similar limitations regarding nationwide health care facilities.[15-17] They have reported promising results on the basis of which we were encouraged to try this option in our patients. Our initial experience however fell short of expectations. We have tried to analyze factors which could have contributed to these unsatisfactory results.

We observed that patients in our study were generally younger (47±) than those who were reported from other groups undergoing PFO, e.g. 63.9±7.5, 61.47± 8.34 and 59.2.17,20 Also patients undergoing TKR in our own local hospitals were also significantly older. Thus Rahman et al and Amin et al reported mean age of the patients as 62±10 and 67.3±8.2 years in their studies of TKR performed in our region.[21-22] It is possible that expectation of these younger patients with shorter period of disease was for quick and complete cure which did not materialize. The hypothesis was to arrest the disease process, allow for regeneration and provide longer period of relief. Our relatively naïve patients perhaps did not comprehend this scenario and were looking forward to total reversal of disease. Better communication and counselling may have better outcome. Older patients with severe disability suffering for longer periods may be satisfied with the relatively less dramatic relief. Follow-up time was also shorter in our study. We could only follow our patients for 6 months, whereas Yang et al after 2 years follow-up reported VAS score decreasing from 7 to 2. Wang et al following up patients for 12-18 months (mean 13.38 months) reported VAS improving from 8.02±1.50 - 2.74±2.34. A longer follow up might have documented further improvement in patient wellbeing in our study group.

A major cause of concern expressed by nearly all of our patients was distressful, although not painful, vibration they experienced during use of oscillation saw on bone. We operated under local anesthesia as described in detail by Chen et al working in Sichuan University who did not mention such feedback from their patients.[23] Other groups such as Wang et al in Shanxi university operated under epidural or spinal anaesthesia.[17] We realize now that spinal anesthesia would definitely improve patient comfort and subsequent compliance. Spinal anesthesia was not opted for in this study as it was not possible for us to spare the heavy trauma list for an experimental procedure. Although the original reported case series were done under spinal anesthesia they themselves encouraged to do it under local anesthesia. Thus an important cause of reluctance of patients to participate in the second procedure of PFO on contralateral limb was the apprehension of oscillating saw vibration perceived under local anesthesia.

Transient neuropraxia that lead to foot drop and cumbersome paresthesia were also the cause of reluctance in patients. The ankle joint pain though reported as mild also served to be a major source of misgiving in many patients. It may be because of shifting in alignment and changing musculoskeletal stresses in the lower limb. These phenomena may well have cleared up over time but we did not follow up after 6 months. We recommend future studies with larger sample size and longitudinal follow-up.

Conclusion

PFO procedure needs further evaluation and should better be performed under spinal anesthesia. At present we have abandoned this procedure because the desired results were not obtained. Also it is very difficult to pursue local population for an experimental procedure, as it is evident from non-participation of males in this study.

But our results were not in favor of this hypothesis. Still we think that this concept needs large multicentric trials.

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Authors Contribution

SR, OUR: Conceptualization of Project
SR: Data Collection
AIB: Literature Search
OUR: Statistical Analysis
AMM, MH, NQ: Drafting, Revision
OUR, SA: Writing of Manuscript

Comparison of Postoperative Pain in Children After Closure of Peritoneal Layer Versus Leaving it Open in Open Appendectomy

Abdul Rehman Yousaf,[1] Muhammad Javaid Iqbal Khan,[2] Sajid Hameed Dar[3]

Abstract

Objectives: To compare pain scores and analgesia requirements in children after closure of peritoneal layer versus leaving it open in open appendectomy.

Methods: We performed this study in Department of Pediatric Surgery, Services Hospital/ SMIS, Lahore from 1st April 2016 to 30th September 2016. There were total 100 patients (50 in each group); Group A: leave peritoneal layer open. Group B: Close peritoneal layer. We assessed patients for pain score using visual analogue scale. Intravenous Ketorolac 0.5mg/kg 8hourly used for pain control. All the data was recorded on the proforma and analysed using SPSS version 21. For comparison of mean pain score we utilized Student t test with P-value ⩽ 0.05 as significant.

Results: In both groups, age, weight and obesity data were similar. Post operative results were significant in terms that we seen good pain control 90 % in group A whereas 76 % in group B (p=0.028). We found out that the pain score in group A was 19.86±4.18 mm which was significantly less as compared to 34.36±4.61 in group B (P value <0.05).

Conclusion: We concluded that in patient whom peritoneal layer is left open has significantly less Pain scores after open appendectomy. Our study supports leaving peritoneal layer as such after open appendectomy.

Keywords; Open appendectomy, VAS score, leave open, Peritoneal layer

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Introduction

Acute appendicitis is a frequent surgical emergency in children.[1] Appendectomy, either open or laparoscopic is the most accepted treatment method of appendicitis in children. Most pediatric surgeons during open appendicectomy, open abdomen layers, do appendectomy and then close layer by layer including peritoneal layer. There are divided opinions over the closure of peritoneal layer after open appendectomy and uniform accepted approach is not available in literature in children. There is a number of published data available in literature in gynaecology and obstetrics that prove the usefulness of repair of peritoneal layer after surgical procedure.[2-10] However, compelling figures of advantages of closing peritoneal layer vs leaving as such after open appendicectomy in children are not reported.

In the results reported by Suresh et al[11] 35.54 ± 4.92 mm was mean visual analogue score in peritoneal layer closure group but 28.21 ± 5.04 mm in peritoneal layer open group. Also, we noted that the result reported by Farooq et al[12] show few breakthrough pain episodes in peritoneal layer open group in comparison with peritoneal layer close group (<0.05 p value).

The rationale of our study was to compare the outcome of leaving the peritoneal layer open after open appendectomy versus closing it on post-operative pain and analgesic requirement. This study is one of very few on this subject, that highlights its importance.

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Methods

We performed this study in Pediatric Surgery department of Services Hospital/SIMS, Lahore from 1st April 2016 to 30th September 2016. It was a randomized controlled study having 100 patients in total (50 in each group) who met the inclusion and exclusion criteria. We included 6-12 years old children who were to undergo appendectomy for acute appendicitis and excluded patients with perforated appendix, appendicular mass and appendicular abscess (assessed on clinical examination and ultrasound abdomen).

We calculated sample size by Epi-info Software of the CDC, USA considering mean VAS score in peritoneal layer close group 32.54 ± 4.92 mm and 28.21 ± 5.04 mm in peritoneal layer open group.[11] After approval of hospital Ethical committee, patients who met the criteria to include in the study were admitted through the emergency services hospital Lahore. Informed consent for inclusion in the study was taken from parents. We divided the patients into two groups by random sampling via lottery method. Group A: leave peritoneal layer open. Group B: Close peritoneal layer. We did open appendectomy through the same steps in both groups as follows; opened abdomen via lanz incision, cut external oblique muscles, retracted internal oblique and transversus abdominus and opened peritoneal layer, did appendectomy and closed the abdominal wall layers in reverse order with one difference. In Group A, we did not close peritoneal layer as we did in group B. Postoperatively, we assessed patients for pain intensity with the help of visual Analogue scale at zero, 1st and 2nd post op day. Most of the patient were discharged on afternoon 1st post-op day, a few on 2nd post-op day. We made a record of pain episodes and analgesia administered on a predesigned proforma. For pain control we used Intravenous Ketorolac 0.5mg/kg 8hourly (max 03 doses) as regular medication and acetaminophen 10-15mg/kg every 06 hours and tramadol 1-2mg/kg (one dose only) in case of breakthrough pain. We monitored patients till discharge. All data was recorded on the the predesigned proforma. This study was single blinded to eliminate the bias.

We analyzed the assembled data through SPSS version 21. Numeric data such as age, weight and pain score were presented as mean and standard deviation. Qualitative variables such as gender and age groups were presented in frequency and percentage. Student t test was utilised to compare mean pain score in both groups. P-value ≤ 0.05 was considered as significant.

Results

Total 100 cases, 55 (55%) were males while 45 (45%) were females. In both groups gender, age and weight and obesity data were comparable (Table-1). Post operative we found out good pain control in 83 (83%) of our study cases. We seen it in 45 children (90 %) in group A whereas in 38 children (76 %) in group B (p= 0.028). (Table-2). Mean visual analogue score was 19.86 ± 4.18 in Group A and it was 34.36± 4.61 in Group B (Table-3). P-value was ≤ 0.05. Post-stratification Visual analogue score in children with post operative

Table 1: *Distribution of Gender, Age, Weight and Obesity in Group A& B(n=100)*

Parameter		Group A	Group B
Gender			
Males		29(58%)	26(52%)
Females		21(42%)	24(48%)
Age	6-9 yrs	24(48%)	25(50%)
	>09 yrs	26(52%)	25(50%)
Weight	upto 20kg	21(42%)	21(42%)
	>20 kg	29(58%)	29(58%)
Obesity	yes	07(14%)	05(10%)
	No	43(86%)	45(90%)

Table 2: *Distribution of Post Operative Pain Among Study Cases*

Pain (n=100)	Group A		Group B	
	Frequency	Percentage	Frequency	Percentage
Controlled n=83(83%)	45	90%	38	76%
Un-Controlled (needs additional analgesia) n= 17 (17%)	05	10%	12	24%
Total	**50**	**100%**	**50**	**100%**

Table 3: *Distribution of Visual Analogue Score Among Study Cases*

Visual analogue score (mm)	Group A		Group B		P value
	Mean	SD	Mean	SD	
	19.86	4.18	34.36	4.61	0.000
Total	**27.11 ± 8.50 mm**				

Table 4: *Stratification of Mean Visual Analogue Score with Regards to Pain Control in both Groups. (n = 100)*

Pain control	Groups	VAS		P value
		Mean	SD	
Yes (n=83)	Group A (n=45)	20.02	4.33	**0.000**
	Group B (n=38)	33.95	3.69	
No (n=17)	Group A (n=05)	22.00	0.00	**0.001**
	Group B (n=12)	35.82	7.04	

pain control in Group A was 20.02±4.33 and 33.95± 3.69 in Group B and with uncontrolled group A 22.00 ±0.00 and group B 35.82±7.4. (Table-4).

Discussion

This study was randomized controlled trial and both groups were comparable in terms of demography and symptomatology. Of these 100 cases of appendicitis, we had 55 (55%) male and 45 (45%) female patients. This observation that appendicitis is common in male is also seen by Hussain et al[13] who reported 63.33% male patients in their study while Rehman et al[14] 75% which is quite high incidence in males. Latif et al[15] described 10.5 years mean age in their study population which is comparable to our study patients. 12(12%) of our study cases were obese. None of the studies on the subject reported obesity incidence in children and it challenges especially pain control. Closure of peritoneal layer during open appendectomy has been a standard practice. However, the available literature on the subject supports that if peritoneal layer is left as such it has several advantages in terms of reduced post-operative pain, reduced analgesic requirements and less days spent in the hospital which in turn will reduce the cost in resource limited country. Post operatively, we noted good pain control 90 % in group A while 76 % in group B (p= 0.028). In 17 cases, additional doses of analgesia required to relieve pain (05 patients in group A needed additional 1-2 doses of analgesia as paracetamol while 7 patients in group B required 2-3 additional doses of acetaminophen and 5(of 12) patients needed tramadol 1-2 mg/kg to relieve pain). Pain control was especially challenging in the obese patients in both groups (09 out of 12 obese patients in both groups needed additional 1-2 doses of analgesia) In our study VAS were significantly less in group A than group B. In the results reported by Suresh et al[11] 35.54±4.92 mm was mean visual analogue score in peritoneal layer close group but 28.21±5.04 mm in peritoneal layer open group. Our study results are comparable to these. Also we noted that the result reported by Farooq et al[12] show few breakthrough pain episodes in peritoneal layer open group in comparison with peritoneal layer close group (<0.05 p value).

Conclusion

To conclude from our study, we found out that if we leave the peritoneal layer open during open appendectomy pain score and number of pain episodes decreases significantly. This could reduce operative time and cost in a resource limited environment. So, our study results support leaving peritoneal layer as such after open appendectomy.

Conflict of interest: *None*

Conflict of Interest *None*

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Authors Contribution

ARY, MJIK, SHD: Conceptualization of Project

ARY: Data Collection

ARY, MJIK: Literature Search

ARY, MJIK: Statistical Analysis

ARY, MJIK, SHD: Drafting, Revision

MJIK: Writing of Manuscript

Efficacy of Sistrunk's Operation for Thyroglossal Cyst and Sinus; My Experience

Ghulam Murtaza,[1] Sarwat Hassan Syed,[2] Faisal Rafiq, Sana Nadeem,[3] Faisal Rafiq,[4] Muhammad Awais Samee,[5] Mazhar Iftikhar[6]

Abstract

Objective: To study efficacy of Sistrunk's operation for excision of thyroglossal cyst and sinus in reducing the recurrence rate.

Methods: This study was carried out at the department of ENT and HEAD and NECK Surgery, Services Institute of Medical Sciences/Services Hospital Lahore from June 2008 to December 2019. All confirmed cases of thyroglossal duct cyst and sinus, both male and female belonging to all age groups were included in the study and operated under G/A.

Results: Twenty-five cases were included in the study, 16 females (64%) and 9 males (36%). Male to female ratio is 1:1.78. Out of 25 cases eighteen were thyroglossal cysts (72%), and seven were of thyroglossal sinus (28%). Among cysts, five were suprahyoid (27.77%), eleven were infrahyoid (61%) and two were pre-hyoid 11%. All cases were operated under G/A by Sistrunk technique. Follow-up was done for 02 years. No case was reported for recurrence.

Conclusion: Sistrunk operation is a very effective and reliable technique for excision of thyroglossal cyst and sinus.

Keywords: thyroglossal duct cyst, thyroglossal sinus, congenital anomaly, sistrunk operation

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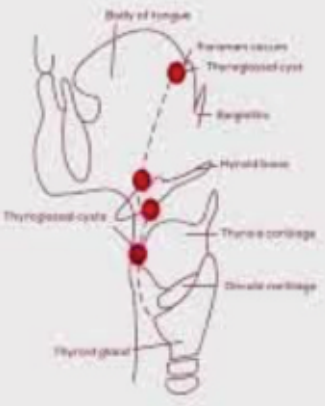
Introduction

Thyroglossal cyst is the most common non-neoplastic neck mass. This is the most common form of congenital neck cyst, among developmental, inflammatory and vascular lesions. 90% of Thyroglossal cysts lie in the midline and 10% on one side of the midline. Out of those on one side of the midline, 95% occur on the left side and 5% on the right side1. During the 4th week of development, thyroid primordium develops from floor of the earliest pharynx between tuberculum impar and posterior one third of tongue at the "foramen caecum". It enlarges caudally, following descent of the heart and great vessels into the loose pre-pharyngeal soft tissue in the midline. Following migration of the thyroid cells, the thyroglossal tract undergoes regression at around 10th week of gestation. However, in some individuals, this tract does not undergo complete regression and persists partially or completely, leading to the development of a thyroglossal cyst.[2] During this migration, the thyroglossal tract passes anterior to the hyoid bone, thyrohyoid membrane and thyroid cartilage. However, part of the tract goes posteriorly to the inner surface of the body of the hyoid bone as a result of growth



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and anterior rotation of the hyoid bone. So, the following are the courses of the thyroglossal tract: pre hyoid, trans-hyoid and retro hyoid.[3]

Two types of abnormal patterns of development of the thyroglossal duct exist. One is thyroglossal duct, which presents in three ways, true duct, fibrous cord or separate islands starting from supra hyoid to infra hyoid part upto pyramidal lobe of thyroid gland but the duct remains tightly adherent to the periosteum of the hyoid bone. In second variety, thyroglossal cyst, may form in isolation or in association with a patent duct or fibrous cord. The cyst is single, uniloculated, round or oval in shape; its walls are clearly defined in relation to surrounding structures, except when it is infected.

Sinus openings are always secondary to spontaneous or surgical drainage of the infected cysts. It may also be secondary to simple cyst removal when the hyoid bone and part of the tract are left behind. The epithelial lining of the tract is pseudo stratified ciliated columnar, but may be squamous. The discharge from the sinus is mucus and not saliva. Thyroid tissue is present in wall of the cyst in approximately 2/3rd of the patients due to its origin from the thyroid tissue[4]. Most common presentation of Thyroglossal cyst is as a discrete palpable neck mass in midline above, at or below the level of the hyoid bone, painless if not infected, mobile on swallowing and tongue protrusion. If infected, patients present with pain in throat, pain on swallowing (odynophagia), dyspnea, fever and variable spectrum of symptoms.[5]

Intralingual cysts can present with dysphagia and dyspnea. Approximately 1/3rd of the cysts present with coincident or previous infection, more commonly in adults. 25% of patients present with a discharging sinus resulting from spontaneous rupture of an infected abscess.[6]

Diagnosis is made by history, clinical examination and investigations. In all cases thyroid function tests, radioisotope scanning to avoid ectopic thyroid, ultrasonography and FNAC to confirm the diagnosis should be done. If infected, then get specimen for culture and sensitivity. In thyroglossal sinus, sinogram should be done. The differential diagnosis is dermoid cyst, infected lymph node, sebaceous cyst, lipoma, minor salivary glands tumor, hypertrophic pyramidal lobe of thyroid, tumor of the thyroid cartilage, synovial cyst and choristoma, (mass of normal tissue found in abnormal location). The treatment of thyroglossal duct cyst is complete excision of the tract with central part of body of the hyoid bone to avoid recurrence. Thyroglossal sinus also requires complete excision of the tract with central core of hyoid bone to avoid recurrence. This is called Sistrunk's operation.

Techniques of Sistrunk's operation: The patient is anesthetized preferably with a nasal endotracheal tube, positioned in supine position; a pillow is placed under the shoulders and head is stabilized with a ring. The neck is prepared and oral cavity is left exposed, as guidance with a finger is needed during operation. A 4-5 cm horizontal incision is made at the midpoint between thyroid cartilage and hyoid bone in infra hyoid cyst and encircling the sinus, if sinus is present. Flap is elevated in sub-platysmal plane, while staying clear of the lesion to avoid rupture of the cyst. Infra hyoid strap muscles are exposed. The cyst usually lies underneath the raphe of sternohyoid muscles. The cyst tract is freed from the surrounding muscles and tissues up to the level of hyoid bone. At the hyoid bone level, the muscles which are attached to the center of the hyoid body are resected and separated and the body of hyoid bone between the lesser horns is divided with Mayo scissor or bone cutting forceps. Bleeding from cut ends of the hyoid bone should be controlled with bipolar cautery to avoid damage to the hypoglossal nerve. From the upper aspect of hyoid bone, a part of the genioglossus, mylohyoid and geniohyoid muscles are removed up to the foramen ceacum, depending upon the location of the cyst and path of tract. If tract extends up to the base of tongue, then a finger is placed in the oral cavity at the site of foramen cecum and the tract is excised. Before excision of the tract, a purse string suture is applied at the base of tongue and tightened after excision of the tract. Hemostasis is secured, wound washed with normal saline, muscles are sutured with absorbable sutures, drain is inserted and wound is closed in layers. Drain is removed after 2-3 days. Patient is put on injectable antibiotics for 3 days and then orally for 5 days. Stitches are removed after one week. Follow up after every three months is recommended for two years.

Methods

The study was carried at the department of ENT and HEAD and NECK Surgery Services Institute of Medical Sciences/Services Hospital Lahore from June 2008 to December 2019. The mode of study was retrospective. All confirmed cases were admitted two days before surgery. Detailed history and physical examination were carried out in each patient. Each swelling was examined for site of location in relation with hyoid bone, mobility with swallowing and tongue protrusion along with consistency, fluctuation, Transillumination and relation with surrounding structures. Thyroid Function

Test, Thyroid scanning, Ultrasonography of neck and FNAC was done in all cases along with routine blood and urine tests. Those with infected cyst were given antibiotics according to culture and sensitivity. These cases were operated under G/A after complete resolution of infection.

Results

Twenty-five cases were included in the study, 16 females (64%) and 9 males (36%). Male to female ratio is 1:1.78. Out of 25 cases eighteen were thyroglossal cysts (72%), and seven were of thyroglossal sinus (28%). Among cysts, five were suprahyoid (27.77%), eleven were infrahyoid (61%) and two were pre-hyoid 11%.

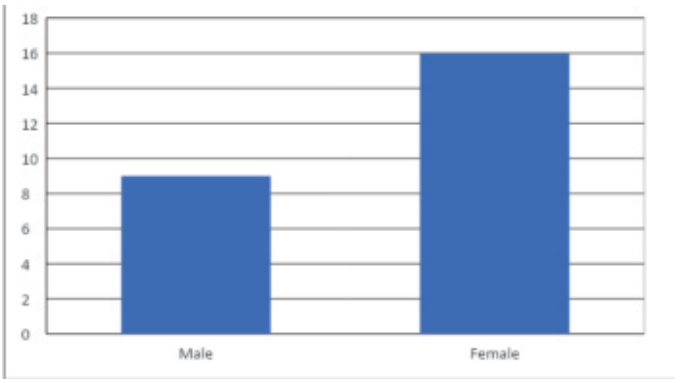

Fig-1: *Distribution of Patients according to Gender*

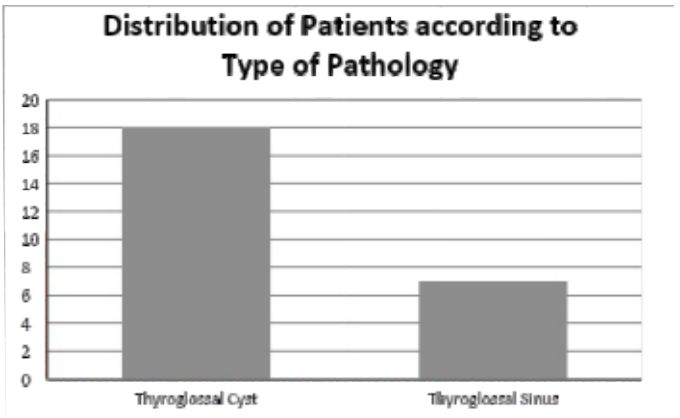

Fig-2: *Distribution of Patients According to Type of Pathology.*

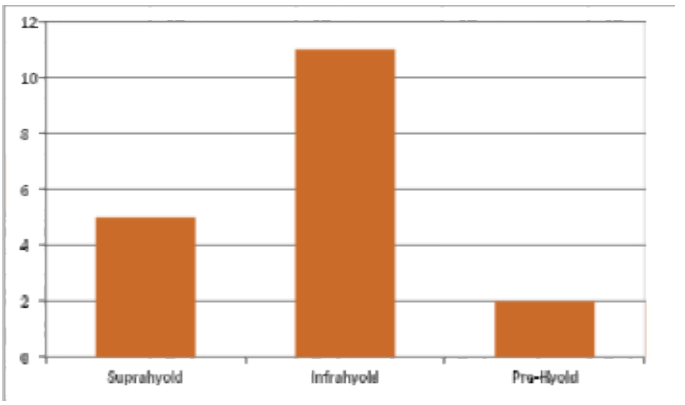

Fig-3: *Distribution of Patients according to Site of Pathology*

Discussion

Thyroglossal duct remnants are the commonest mid line neck masses in children as well as in adults. Sistrunk's operation, with dissection of the tract along with cyst or sinus and removal of the central part of the hyoid bone body is accepted as the operation of choice. WENGLOWSKI in 1912 performed much of the embryological study on neck cysts. He first suggested removal of body of hyoid bone with central core of tissue between this and foramen cecum. SCHLANGE 1893 was first to remove the body of hyoid. Sistrunk, adopted Wenglowski's suggestion and removed a central core of tissue between hyoid bone and foramen cecum.[7] A better understanding of the embryology and developmental anatomy of the thyroid gland is important for The successful management of thyroglossal duct cyst.[8] Sistrunk after original work, later concluded that foramen cecum and mucosa of tongue should be left undisturbed and the core of tissue removed from supra hyoid region should be 10 millimeters in diameter. The infected cyst must not be incised or excised. First aspiration of the cyst should be done with a wide bore needle to improve antibiotic penetration and allow resolution to be followed by removal later on.

The cysts are usually infected with H Influenza, Staphylococcus aureus and staphylococcus epidermidis.[6] Antibiotics effective against these organisms should be given.

The recurrence after Sistrunk procedure is 1.5-10%.[9] Risk factors for recurrence are: surgery performed on infected cyst, rupture of cyst during removal, multiple thyroglossal ducts and technical errors especially insufficient removal of base of tongue or fragmentation of the duct. Schlang's technique which is more rapid and

easier to perform, consists of removing the cyst and body of hyoid, associated with recurrence rate of 30% while simple cyst removal is associated with 100% recurrence rate.[10]

Conclusion

Sistrunk's operation is very effective procedure for treating thyroglossal cyst and sinus with comparatively low risk of recurrence. Cyst rupture during dissection and multiple off shoots of the tract lead to recurrence and meticulous surgical technique can low the risk of recurrence.

Conflict of Interest: *None*

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Authors Contribution

GM: Conceptualization of Project
SHS: Data Collection
SN: Literature Search
FR: Statistical Analysis
MAS: Drafting, Revision
MI: Writing of Manuscript

Diclofenac Induced Histological Changes on Proximal Renal Tubules in Kidneys of Albino Rats

Abdur Rehman Rajput,[1] Maria Mohiuddin,[2] Amatul Sughra,[3] Syeda Bushra Ahmed,[4] M. Nadeem Siddiqui,[5] Hemant Kumar[6]

Abstract

Objectives: Diclofenac sodium is commonly used worldwide. It is a potent analgesic, antipyretic and anti-inflammatory drug. The aim of this study is to determine histological changes in kidney due to nephrotoxic effects of Diclofenac sodium.

Methods: This was an Experimental study conducted in the Institute of Bio Medical Sciences (IBMS) with the cooperation of Dow Diagnostic Research and Reference Laboratory, Ojha campus, Karachi from December, 2013 to December, 2014.

Forty adult albino rats weighing 200 ± 20gms were included in this study. The rats were divided into control group A and treated group B. In group A, one cc of physiologic saline was given intramuscularly and in group B, diclofenac sodium 2 mg/kg body weight was given intra-muscular. Gross and histological changes were observed in kidneys and proximal convoluted tubules (PCT) of albino rats, after administering diclofenac treatment.

Results: Diclofenac sodium in a single daily dose of 2mg/kg given intra muscular, produces significant ($p < 0.001$) changes in weight of the kidney, diameter of proximal convoluted tubules, epithelial height of proximal convoluted tubules and tubular epithelial cell count. The morphological findings are correlated with other parameters like general health of animals, differences in the body weight, absolute and relative kidney weights.

Conclusion: It can be concluded that Diclofenac sodium induces nephrotoxicity and produces histological changes in proximal convoluted tubules in kidneys of albino rats.

Keywords: Diclofenac sodium, proximal tubules, kidney.

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Introduction

Kidney has a vital role in renal clearance, maintenance of blood pressure, elimination of toxic products and formation of prostaglandins. Certain medications are known to cause renal injury on its frequent usage. Among these medicine, one group which is commonly prescribed and used for different clinical conditions is, Non-steroidal anti-inflammatory drugs (NSAIDS).[1]

Non-steroidal anti-inflammatory drugs are widely used in clinical practice especially to manage soft tissue and orthopedic pain.[2] Due to the efficacy in reducing pain and inflammation, non-steroidal anti-inflammatory drugs (NSAIDs) are amongst the most popularly used medicines confirming their position in the WHO's Model List of Essential Medicines.[3] All drugs within this class work to reduce inflammation, pain, and fever through inhibition of cyclooxygenase (COX) enzymes. Both cyclooxygenase isoenzymes, COX-1 and COX-2,

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convert arachidonic acid into its endoperoxide metabolites, which include prostacyclin, prostaglandins, and thromboxane. COX-1 is constitutively expressed and is considered to be the primary source of prostanoids needed for physiologic homeostasis, such as protection of gastric epithelium. However, COX-2 is inducible, and its production of prostanoids is significantly up regulated during conditions of stress and inflammation.[4]

Diclofenac sodium, an analgesic, anti-inflammatory and antipyretic compound. Nowadays, it is one of the commonest used non-steroidal anti-inflammatory drugs (NSAID).[5] The remarkable acceptance of diclofenac is attributable to being a potent COX-2 inhibitor while retaining similar activity as some of other popular non-selective NSAIDs.[6,7] However, data from multiple placebo-controlled trials and meta-analyses studies alarmingly signify the adverse effects of NSAIDs in gastrointestinal, cardiovascular, hepatic, renal, cerebral and pulmonary complications.[3] Diclofenac sodium as an over-the counter drug may lead to its abuse resulting in threatening deleterious effects on the liver, kidney, and gastrointestinal tract.[8] It is postulated that inhibition of prostaglandin in kidneys causes decreased renal blood stream, glomerular filtration and mal-electrolyte regulation. Also oxidative stress and mitochondrial damage are the main elements collaborating in diclofenac sodium renal toxicity.[9,10] Therefore, this study is conducted to determine deleterious effects of diclofenac sodium on kidneys. The effects were studied on absolute kidney weight, relative kidney weight and epithelium of proximal tubules.

Method

An experimental study was conducted in the Institute of Bio Medical Sciences (IBMS) with the cooperation of Dow Diagnostic Research and Reference Laboratory (DDRRL). Approval was taken from institutional review board (IRB). The experiment was accomplished in Dow University of Health Sciences (DUHS), Ojha campus in December, 2013 to January, 2014. Non probability, purposive, sampling technique was used. Adult albino rats of both sexes, looking energetic and fit, were included in the study. They were weighing 180-200 grams, and taking food and water normally. Sample size was forty albino rats of 180-200 grams of both sexes.

In the experimental room of animal house, well labeled cages were used to accommodate the animals and were kept on well-adjusted food and water ad libitum (as ones desire) with 12 hours day and night cycle. Before the experimental procedure, they were kept under observation for one week, in order to look their level of health and weight. All rats were divided into two groups, A and B. The animals of this group (n=20) received normal saline 1 cc intra-muscular for 2 weeks.

The animals of this group (n=20), Diclofenac sodium 2mg/kg body weight given intramuscularly daily was given for 2 weeks. Each animal was placed in a glass container in which small quantity of ether was already poured, to anaesthetize the animal before sacrificing it. The animal was taken from the jar and was fixed on the board with paper pins for sacrifice. A magnifying glass was used to recognized and examine the kidneys, for any noticeable variations in size, shape, color, outline and uniformity. The kidneys were isolated and "Sartorius balance" (Sartorius Precision Balance, Model No. MSE 1203S, Sartorius Lab Instruments, GmbH & Co. KG) was used to measure the absolute weight of each kidney and the relative weight was considered by using the formula:

$$\frac{\text{Kidney's mean weight (gm)}}{\text{Animal's final weight (gm)}} \times 100$$

The tissues from each group were sectioned on a rotary microtome of "Bright instrument Co. model OTF 5000, UK" longitudinal sections of 5µm thick were cut, floated on a hot water bath of "Thermo- Fisher Scientific, USA" on a 37°C, fixed on gelatinized glass slides and a diamond pencil was used for numbering. A plate was used for slides, to fix the sections for 24 hours. Kidney tissues fixed in 10% formalin and stained for H&E. General morphology and architecture of the kidneys was observed under low power (10X ocular 4X &10X objective), cell count were done under high power (10X ocular & 40X objective) and after screening ten observations per animal were recorded; only those cells showing nucleus in their tubules were counted. Micrometry was done by using, 3B Scientific Binocular course Microscope Model 300, Hamburg, Germany. The right eye was used for ocular micro meter and left eye for reticule. Each division of micro meter measured 10µm, was conducted by stage micrometer. There were 100 divisions of ocular micro meter used in this procedure. Three divisions of stage micro meter were matched with ten divisions of ocular micro meter which was equivalent to 30µm. So, 3µm was equivalent to one division of the ocular micro meter. Each and every

observation and measurement was verified by the supervisor. Parameters used were absolute and relative weight of kidneys, diameter of proximal tubules, epithelial height and cell count of proximal convoluted tubules. Five observations were recorded for each parameter. Diameter of proximal convoluted tubules and epithelial height were calculated along their long and short axis, with the aid of counting reticule in randomly chosen five spots within the juxtamedullary regions in all animals. Tabulated data was put to statistical analysis using SPSS 16. The outcomes were stated as mean ± standard deviation and $p < 0.05$ was measured statistically significant at confidence interval of 95%. To assess the significance between various groups studied, one-way analysis of variance (ANOVA) was applied.

Results

Mean final body weight were considered as the weight alteration. Mean weight of Group (A) was 214.10 ± 5.44gm, while in diclofenac treated Group (B) was 153.60±19.14 gm. The absolute weight of kidneys in control group A with mean±S.D (Standard deviation) was 0.579±0.02gm and in group B was 0.504 ± 0.00 gm. On comparing mean absolute weight of kidneys of group-A with Group-B, there was a significant decline in absolute kidney weight with P – value 0.001 at C.I of 95 %. However, on comparing relative weight of kidney (0.270 ± 0.01gm) of the control group- A and the treated group- B 0.333 ± 0.04gm, the increase was significant P-value is 0.001 at C.I of 95 %. (Table:1)

The diameter of proximal convoluted tubules of kidneys

Table 1: *Comparison of Mean difference of Relative Weight of Kidneys in between Groups:*

Relative weight of Kidneys	Group	Mean Differences	SD	F-Statistic	P-value
Group A	Control Group	0.2708	0.01215	40.473	0.001
Group B:	Treated Group	0.3330	0.04343		

are found to be, in control group A, 50.68 ± 11.86 µm and in group B was 113.52 ±25.68 µm. On comparing diameter of proximal convoluted tubules of kidneys between the control (group-A) and treated group (Group-B), a significant increase P - value at C.I of 95 % was found shown in Table. No.2.

Epithelial height in proximal convoluted tubules of kidney with mean ± S.D (Standard deviation) was found

Table 2: *Comparison of mean difference of diameter of proximal convoluted tubules of Kidneys.*

Groups	Mean Differences	SD	F-Statistic	P-value
Group A: Control Group	50.68	11.867		
Group B: Diclofenac Na Group	113.52	25.689	32.331	0.001

to be 1.116 ± 0.06µm in Group- A and was 0.816 ± 0.16 µm in Group-B. However, when mean epithelial height of proximal tubules compared with group B, a significant decline was observed < 0.001 with P- value at C.I of 95 %. As shown in Fig-1 and Fig-2.

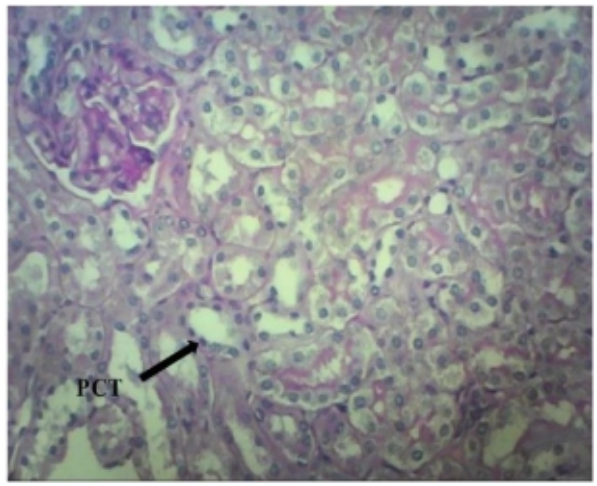

Fig-1: *H & E stained, 5 µm thick longitudinal thickness section of kidney from group A, showing proximal convoluted tubule normal epithelial height with brush border 10 × 10*

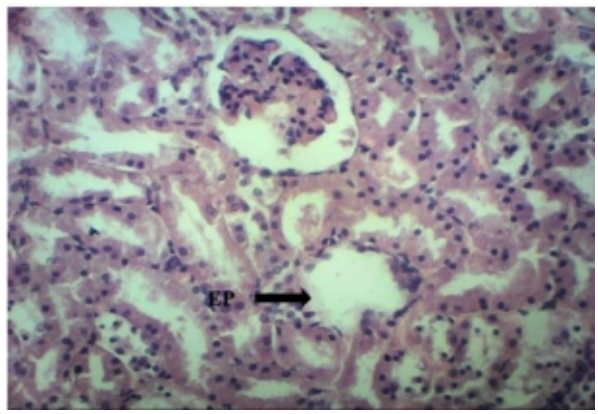

Fig-2: *H & E stained, 5 µm thick longitudinal thickness section of kidney from group B, proximal convoluted tubule showing decline in epithelial height 10 × 10*

Discussion

Appropriate NSAID prescription assumes that the patient has normal renal function at commencement, with ongoing monitoring recommended. In conclusion, appropriate NSAID use requires consideration of all risk.[11,12,13]

In this study, final weight of animals after two weeks of treatment with diclofenac sodium was found to be decreased significantly, P-value was 0.001 at C.I of 95%. However, absolute kidney weight was also found to be decreased significantly. These findings are supported with other studies conducted by Nadeem yaqoob etal and Suang N.T. Ngo. They reported decline in body weight and absolute weight of kidney.[14,15] Decrease in weight mainly occurs due to decreased appetite as a result of gastrointestinal toxicity induced by diclofenac sodium. Our findings are also in agreement with another study, which stated loss of weigh in rats primarily occurs due to NSAID-induced gastrointestinal toxicity, associated with non-selective inhibition of cyclooxygenase (COX)-mediated synthesis of prostaglandins.[16]

In this study, relative kidney weight in treated group B increases significantly, it could be due to mild edema and congestion of blood vessels in renal medulla. Our observations are in conformity with Farag et al., who observed in rats treated with NSAIDs, there was increase in kidney weight.[17,18] A study conducted by Soloman. E. Owumi et al, reported decrease in body weight and a significant increase ($p<0.05$) in relative kidney weight, probably due to release of highly reactive benzoquinone imines during oxidative stress during tissue damage.[11]

In our study, diameter of proximal convoluted tubule was found to be significantly increased. Our results are in accordance with study conducted by Xiaokui Huo et al., who also reported significant increase in diameter of proximal tubules. Probably, this because diclofenac sodium mostly is mainly eliminated unchanged through kidney in humans. This resulted in high exposure to renal tubules and consequently induction of nephrotoxicity.[19]

However, height of proximal tubular epithelium was found to be significantly decreased. This is congruent with findings that are reported by Muhammad Abubaker et al. In that study, they reported significant reduction and desquamation of proximal tubular epithelium Most likely oxidative stress is known to occur and generated reactive oxygen species, ROS (superoxide anion, O_2^-, hydrogen peroxide, H_2O_2; and hydroxyl radical, OH^-) overrides the cellular antioxidant competence.[20] Another study conducted in Academy of Hungkuang University, Taiwan, reported diclofenac renal toxicity effecting proximal tubules. Mainly due to increase in ROS, which results in increased levels of oxidized proteins, which in turn may alter key intracellular signaling pathways, among which apoptosis plays the key role and causes cell death of tubular cells.[21]

Conclusion

This study conclude that diclofenac sodium produces decrease in body weight, damage of proximal convoluted tubules in young albino rats. There were changes in diameter of proximal convoluted tubule and epithelial height of proximal convoluted tubule.

Conflict of Interest: *None*

Funding Source: *None*

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Authors Contribution

ARR: Conceptualization of Project
MM, ARR: Data Collection
AS, SBA: Literature Search
SBA: Statistical Analysis
MNS, SBA: Drafting, Revision
HK, MM: Writing of Manuscript

Nephroprotective Evaluation of Citrullus Lanatus (Water Melon) Seeds in Aminoglycosides Induced Nephrotoxicity in Albino Rats

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Abstract

Objectives: To induce nephrotoxicity by aminoglycosides in albino rats, to prepare Citrallus lanatus seeds (ethanolic) extract (CLSE) and to estimate dose dependant effect of CLSE on biochemical parameters of aminoglycoside induced nephrotoxicity.

Methods: The study was conducted from 14-10-2017 to 27-10-2017 at the Department of Pharmacology, King Edward Medical University Lahore and UVAS, Lahore after approval from IRB committee vide no. 165/RC/KEMU. The 'Animal Experimental Study' was carried out of 14 days duration. A sample size of 32 healthy albino wistar rats was taken and divided into four equal groups. Group A was normal control group and given normal saline once a day orally. Group B was disease control group and was injected Gentamicin 80mg/kg/day intraperitoneal (IP) in two equally divided doses with an interval of 12 hours for 14 days. Whereas, rats in group C and D received CLSE in oral doses of 400 mg/kg and 600 mg/kg/day once daily concurrently with the gentamicin 80mg/kg/day IP in two equally divided doses for 14 days. Renal function tests (Rfts) such as blood urea nitrogen (BUN), serum and urine creatinine, creatinine clearance were evaluated.

Results: BUN was decreased with significant p- value <0.001 in groups C and D in comparison to group B. Although serum and urine creatinine were also decreased in Groups C and D but did not reverted to normal. Whereas, creatinine clearance was significantly increased with p-value < 0.001 in groups C and D in comparison to group B.

Conclusion: The concurrent use of CLSE in aminoglycoside induced nephrotoxicity in Albino rats significantly reversed the nephrotoxicity by decreasing the raised levels of blood urea nitrogen and serum creatinine.

Keywords: nephrotoxicity, aminoglycosides, citrullus lanatus seeds, renal functions tests

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Introduction

Drug exposure often leads to toxicity resulting in acute or chronic renal failure (ARF/ CRF), irrespective of its duration and dose. About 20% of nephrotoxicity is due to medications, but in elderly patients, drugs raise the rate of nephrotoxicity by up to 66%.[1] Aminoglycosides are bactericidal drugs used to treat severe infections caused by aerobic gram-negative bacilli and demonstrate synergism against gram-positive species with other penicillin/antibiotics. Aminoglycosides includes the drugs amikacin, gentamicin, tobramycin and streptomycin. Nephrotoxicity, ototoxicity, neuromuscular paralysis and allergic reactions are the main side-effects of aminoglycosides. Nephrotoxicity with aminoglycosides occurs in 10-25 percent of all ARF cases.[2] Genta-

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micin is one of this group's most nephrotoxic agents. Higher patient mortality is usually correlated with the incidence of nephrotoxicity. Functionally, gentamicin induced nephrotoxicity is characterized by increased serum creatinine, BUN reduced glomerular filtration rate. Despite undesirable nephrotoxicity caused by gentamicin, the drug remains the key treatment against microorganisms that do not react to other antibiotics, such as pseudomonas, proteus and serratia. Unfortunately, there is no single drug available that can precisely treat or prevent gentamicin-induced acute kidney injury, so there is a need to determine or discover a drug/ substance that can actually help to prevent or reverse the harmful effects of gentamicin to kidneys to some extent. In many cases, the role of herbal medicines for the treatment of various diseases is highly appreciated. In recent years, traditional medicines and products have been selected by a number of people to improvise their health issues; alone and in combination with other herbal and allopathic treatments. Nephroprotective role of different herbs is being studied to reduce oxidative stress caused by aminoglycosides enlisted as Aloe vera, silymarin, Kabab chini, curcumin, rosemary, ginger, propolis, black seeds and turmeric but still there is lack of definitive treatment for the gentamicin induced nephrotoxicity. Citrullus lanatus is a fruit belonging to the Cucurbitaceae family whose various parts are used therapeutically for different diseases.[3]

Since oxidative insult is supposed to be the mechanism of aminoglycoside-induced nephrotoxicity[4] and Citrullus lanatus seeds have anti-oxidants and nephroprotective components, the effect of Citrullus lanatus seeds on aminoglycoside-induced nephrotoxicity has been studied. It would be effective as a nephroprotective agent when co-administered along with the main stay treatments involving aminoglycosides. In terms of cost-effective, safe and effective nephroprotective agents, this study will help to develop a new drug.

Methods

The study was conducted from 14-10-2017 to 27-10-2017 at the Pharmacology Department of Pharmacology, King Edward Medical University Lahore and UVAS, Lahore after approval from IRB committee vide no. 165/RC/KEMU. Citrullus lanatus fruit was acquired from the local fruit market, Lahore. It was properly sliced to separate seeds and identification was performed by authorized staff from Government College University, Lahore. CLSE was prepared in PCSIR, Lahore. The dried concentrated extract (28gms) was collected, mixed in 5ml of distilled water in a tightly closed bottle protected from sunlight and kept at 4°C[5] to be used throughout the experiment. A dose was calculated for individual rats, I.e. 400 mg/kg and 600 mg/kg respectively; administered through feeding gauge of no. 16. In rats, nephrotoxicity was induced by the administration of Gentamicin sulfate 80mg/kg[6] IP in two equally divided doses for 14 days at intervals of 12 hours. 32 male adult healthy albino rats were purchased from the local market. Their weight was 150-200 grams. Rats were randomly divided into four groups; eight in each. Group A (Healthy control group) was given 0.5 ml of distilled water orally once daily with 16 guage feeding tube. Group B was disease control group and Gentamicin 80mg/kg/day was injected IP in two equally divided doses with an interval of 12 hours for 14 days. Group C of rats received 400 mg/kg body weight 7 CLSE orally once daily concurrently with the gentamicin 80mg/kg/day IP in two equally divided doses for 14 days. Similarly, Group D of rats received 600mg/kg body weight CLSE orally once daily concurrently with the gentamicin 80 mg/kg/ day IP in two equally divided doses for 14 days. Blood and urine samples of rats were collected at day 0 and 14. Urine was collected in a clean glass container, and stored in serum cups at -20°C and was later analysed for urine creatinine. Approximately 1-1.5 milliliters of blood were drawn by cardiac puncture.[8] and centrifuged at 3000 rev/min for 15 mins[7]. The serum was then stored in serum cups at -20°C and later analysed for RFTs. The semi-automatic clinical chemistry analyzer, micro lab 300, was used for all the tests. As provided by the producer, methods were followed. The frozen samples were warmed to 37°C before analysis. The data was entered on the graph pad prism version 8 for statistical analysis and was evaluated by one-way analysis of variance followed by Tukey's multiple comparison tests. P value < 0.05 was considered significant. T test was used to see changes over a period of time in each group.

Results

Rfts:

BUN:

An insignificant difference was observed in BUN among the groups at day 0 with p-value 0.41 but on day 14 difference was significant among all the groups with p-value <0.0001. (Table 1, Fig-1)

Table 1: *Comparison of Mean Blood Urea Nitrogen (mg/dl) among Groups A, B, C, and D (ANOVA) and within the Groups (t- test).*

Blood urea nitrogen (mg/dl)	Group-A (n=8)	Group-B (n=8)	Group-C (n=8)	Group-D (n=8)	P-value
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
Day-0	12.08±2.67	12.39±1.40	13.29±2.97	12.18±1.35	0.41
Day14	12.43±0.75	47.31±8.10	29.49±3.22	30.40±4.35	<0.001

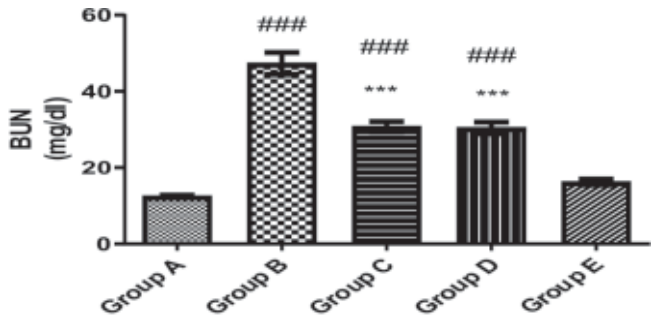

Fig-1: *Comparison of Mean Blood Urea Nitrogen (mg/dl) of Groups A, B, C and D Day 14*

*Group A=normal control, Group B = disease control, Group C = low dose, Group D = high dose, *** p. value < 0.001 versus group B*

Serum Creatinine

There was significant difference among the groups at day 14 with p-value <0.001. (Table 2, Fig-2)

Table 2: *Comparison of Mean Serum Creatinine (mg/dl) among Groups A, B, C, D, and E (ANOVA) and within the Groups (t- test).*

Serum creatinine (mg/dl)	Group-A (n=8)	Group-B (n=8)	Group-C (n=8)	Group-D (n=8)	P-value
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
Day-0	0.47±0.08	0.59±0.05	0.50±0.07	0.51±0.10	0.18
Day14	0.35±0.08	6.86±0.64	3.73±0.43	3.15±0.68	<0.001

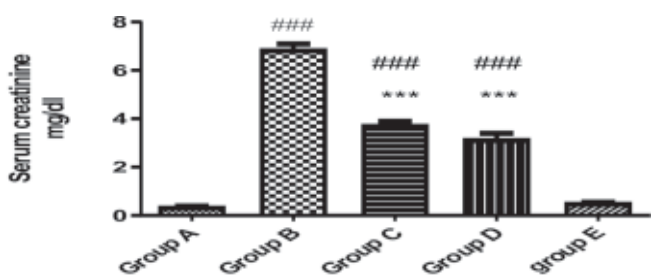

Fig-2: *Comparison of mean Serum Creatinine (mg/dl) of Groups A, B, C and D at day 14.*

*Group A=normal control, Group B = disease control, Group C=low dose, Group D = high dose, *** p. value < 0.001 versus group B*

Urine Creatinine:

No significant difference was observed among the groups at day 0 with p-value 0.61 but significant difference at day 14 with p-value <0.001. (Table 3)

Creatinine Clearance:

Table 3: *Comparison of Mean Urine Creatinine among groups A, B, C and D (ANOVA) and within the Groups (t- test).*

Urine Creatinine	Group-A (n=8)	Group-B (n=8)	Group-C (n=8)	Group-D (n=8)	P-value
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
Day-0	104.00 ± 28.10	118.12± 15.70	119.38± 30.54	112.50± 18.18	0.61
Day14	82.06 ± 21.13	684.00± 95.67	319.00± 50.90	298.50± 38.09	<0.001

Group A = normal control, Group B = disease control, Group C = low dose, Group D = high dose

No significant difference was observed among the groups at day 0 with p-value 0.31 but significant difference was observed at day 14 with p-value <0.001. (Table 4)

Discussion:

Table 4: *Comparison of Mean Creatinine Clearance (ml/min) among Groups A, B, C and D (ANOVA) and within the Groups (t- test).*

Creatinine clearance	Group-A (n=8)	Group-B (n=8)	Group-C (n=8)	Group-D (n=8)	P-value
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
Day-0	2.78±1.06	2.73±0.42	3.12±0.93	2.68±0.30	0.31
Day14	3.80 +1.06	1.99±0.37	1.60±0.32	2.09±0.78	<0.001

Group A = normal control, Group B = disease control, Group C = low dose, Group D = high dose

Our first objective of the study was to induce nephrotoxicity in albino rats which was induced using gentamicin because it is one of the most nephrotoxic drug among aminoglycosides. BUN, serum and urine creatinine levels were raised and creatinine clearance was decreased in rats of group B in comparison to normal control.

At the end of study, BUN was increased significantly in group B in comparison to group A. Whereas the results of groups C and D which were given CLSE along with gentamicin showed reduced levels of BUN in comparison to disease control group B. This decrease was significant and is in accordance to a previous study which also showed improvement in the levels BUN

after using CLSE.[9] Similarly, at day 14, serum creatinine and urine creatinine levels were increased in disease control group B with p-value < 0.001. This result is statistically significant in comparison to normal control group A. In groups C and D significant decrease in serum creatinine and urine creatinine was observed on day 14 with p-value <0.001 which was similar to the results of previous studies.[9,10] Although the decrease in serum creatinine level is significant as compared to the disease control group, but it did not revert to normal even after treatment. This implies that probably we have to use a dose greater than 600mg to normalize serum creatinine levels.

At day 14, there was significant decrease in creatinine clearance of disease control group B in comparison to normal control group A. Whereas in groups C and D after giving CLSE with gentamicin, creatinine clearance was increased. This shows that using CLSE in gentamicin induce nephrotoxicity alleviated the decrease in creatinine clearance. These results can be compared with a previous study in which CLSE is retaining the creatinine clearance within the normal range.[10]

Hence, CLSE alleviated the raised levels of BUN, serum and urine creatinine and decreased creatinine clearance due to aminoglycosides induced nephrotoxicity. This effect is probably due to the presence of antioxidants such as flavonides, lycopene, citrulline, vitamin E and catechins in Citrullus lanatus seeds as described in a previous study in which RFTs were corrected after using Citrullus lanatus seed extract in nephrotoxic rats due to its anti-oxidant activity.[9]

Conclusion

The concurrent use of CLSE in aminoglycoside induced nephrotoxicity in Albino rats significantly reversed the nephrotoxicity by decreasing the raised levels of BUN and serum creatinine. This beneficial effect of Citrullus lanatus seeds might be due to their anti-oxidant potential.

Conflict of Interest: *None*

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NY: Conceptualization of Project
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Correlation of Vitamin D levels and Inflammatory Markers with Hospital Stay and Disease Outcome in Hospitalized Covid-19 Patients

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Abstract

Objective: To determine correlation of vitamin D levels with CRP, Ferritin, D-Dimers, Procalcitonin, hospital stay and disease outcome in COVID-19 patients of corona unit.

Methods: This observational study was carried out at Corona Unit of Farooq Hospital Westwood branch Lahore. All prerequisites of Ethical committee and written consent were completed. All patients enrolled in study were RT-PCR positive for Covid-19. Parameters like age, sex, history of contact, symptomatic/ asymptomatic, duration of hospital stay and outcome of patient illness were documented. Serum 25 (OH)D, CRP, ferritin, D-dimer and procalcitonin were performed on automated chemiluminescence based immunoassay anlyser, Maglumi 800, analyzer.

Results: Mean age of COVID-19 patients was 58.7 ± 11.9 years and 65 were males and 35 were females. The mean duration of stay at the hospital was 8.47 ± 4.26 days. The mean levels of vitamin D, C-Reactive Protein, Ferritin, D-Dimer, and Procalcitonin were 31.9 ± 26.5 ng/ml, 56.4 ± 43.7 mg/L, 653.8 ± 661.1 ng/ml, 1.10 ± 1.7 mcg/ml, and 2.10 ± 12.3 ng/ml, respectively. Out of 100 patients admitted for treatment, 87% survived and 13% died.

Median differences of Procalcitonin levels in patients who survived or expired was statistically significant, $\chi 2(2) = -3.09$, $P<0.01$, which shows that patients who survived had lower procalcitonin levels as compared to those who died. The median differences of remaining characteristics in patients who survived or expired were not statistically significant. We found no significant correlation of low Vit.D levels with inflammatory markers, hospital stay and disease severity.

Conclusion: Our study found significant correlation between Procalcitonin levels and duration of hospital stay in COVID -19 patients. Our study has highlighted no significant correlation between low Vit.D levels and other inflammatory markers, with duration of hospital stay and disease severity. Controlled randomized trials and large scale studies are needed to test this hypothesis. (this green can be omitted)

Key Words: Vitamin D in Covid -19 Patients, inflammatory markers, Duration of hospital stay

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Introduction

COVID-19 is a disease of respiratory system that turned out to be a pandemic. It was an upsurge influencing heavily populated areas of various countries.

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A new virus "SARS-CoV-2"emerged as a catastrophic disease. This virus was an example of a zoonotic transfer to humans.[1]

COVID-19 disease became major health issue and a big burden on world economics.[2] Corona virus is affecting our routine life and future challenges as well.[3] It has been assumed that better immune status in Covid patients may help in cure of disease, so possible approach to limit the severity of COVID-19 cases and death rate must be enlightened.[4]

The fundamental role of Vitamin D in body is to maintain bone health and metabolism of calcium and phosphorus but it has been reported that it plays key role in different

viral infections and autoimmunity by varying immune response.[5] Vit D is involved in reducing the cytokine storm and boosting the immune levels.[6] Decreased Vit-D level increases vulnerability to viral infections.[7] It is assumed that levels of Vit D should be sufficient to protect against different viral infections like respiratory syncytial virus and influenza.[8]

Capacity of Vit-D to suppress cytokine production initiate our focus on insufficient Vit D levels and its link with severity of COVID-19 infection.[9] With reference to this COVID-19 pandemic, evaluation of vitamin D levels in blood may be helpful to assess severity of COVID-19 infection and course of this disease because it may help to prevent or treat this infection.[10]

It has been hypothesized on the basis of some epidemiological and clinical studies that there is a relationship of COVID-19 infection with Vit-D. It has been reported that COVID-19 is also linked with increased production of some pro-inflammatory cytokines, C-reactive protein and acute respiratory distress syndrome.[11] Other studies have also suggested role of inflammatory markers like CRP, Ferritin and D-Dimers in covid-19 patients.[12]

The Vitamin D deficiency among all age groups in Pakistan has been reported to be deficient in 53.5%, insufficient in 31.2% and normal in only 15.3%. In view of above sited literature and deficient status of Vitamin D levels in our population, a study was planned to measure the levels of Vit.D among hospitalized COVID-19 patients at Corona Unit of Farooq Hospital Lahore. The levels of Vitamin D, and its correlation was assessed with C-reactive protein (CRP), Ferritin, D-Dimers, Procalcitonin and duration of hospital stay.

Methods

This study was carried out as observational study at Corona Unit of Farooq Hospital Westwood branch Lahore. An informed and written consent was obtained either from the patient himself or first degree relative. All prerequisites of Ethical committee were completed and it was approved by Ethical & Review Committee of Farooq Hospital Westwood branch Lahore.

A total of 100 patients were included in study who were admitted in Corona unit of Farooq Hospital from 15th October 2020 to 15th November 2020. All patients enrolled in study were RT-PCR positive for Covid-19. The patients admitted in Corona Unit after 15th October were followed for their period of stay in hospital. Other parameters like age, sex, history of contact, symptomatic/asymptomatic, duration of hospital stay and outcome of patient illness were documented. 5 cc clotted blood was taken for determining serum 25(OH)D, CRP, ferritin, D-dimer and procalcitonin. These were analyzed at Farooq hospital lab westwood branch. All investigations were carried out in accordance with relevant lab protocols and quality control guidelines. Serum 25 (OH)D and ferritin levels were estimated by automated immunoassays on Architecti1000sr. CRP and D-Dimer were performed on automated immunoassay, Maglumi 800, analyzer. The data was analyzed using SPSS (v. 22.0). Mean, standard deviation, median, and interquartile range were generated for continuous variables and frequencies and percentages were calculated for categorical variables to present data descriptively (see Table 1). The assumption of normality in age, duration of stay at the hospital, and vitamin D, CRP, Ferritin, D-Dimer, and PCT levels, respectively. Outcome of patients (survived/expired) was assessed through Shapiro-Wilk test and presence of outliers was inspected through boxplots. As the p-values were less than 0.05 and outliers were present in all cases, non-parametric statistical tests were used. To see whether there were significant median differences in duration of stay, and levels of vitamin D, CRP, Ferritin, D-Dimer, and PCT, respectively, with regard to outcome (survived/expired), independent samples Mann-Whitney U Test was used. The results are summarized in Table 2. Further, Pearson's Point Bi-serial Correlation was conducted to see correlations between clinical characteristics and outcome (survived/expired) in COVID-19 patients (Table 3).

Results

The results presented in Table 1 show that the mean age of COVID-19 patients in this study was 58.7 ± 11.9 years. Out of 100 patients, 65 were males and 35 were females. The mean duration of stay at the hospital was 8.47 ± 4.26 days. The levels of Vit.D in 44% of the patients included in this study was deficient (<20ng/ml), 14% was insufficient (20-30ng/ml) and 42% had normal levels (>30ng/ml). The mean levels of vitamin D, C-Reactive Protein, Ferritin, D-Dimer, and Procalcitonin were 31.9 ± 26.5 ng/ml, 56.4 ± 43.7 mg/L, 653.8 ± 661.1 ng/ml, 1.10 ± 1.7 mcg/ml, and 2.10 ± 12.3 ng/ml, respectively. Out of 100 patients admitted for treatment, 87% survived and 13% died.

This has to be read carefully for final.

The comparisons of clinical characteristics in patients

with COVID-19 with respect to outcome (survived/expired) are presented in Table 2. The results show that the median difference of duration of stay at the hospital with respect to outcome was statistically significant,

Table 1: *Descriptive Statistics of Socio-Demographic and Clinical Characteristics in Coronavirus Disease 2019 (COVID-19) Patients (n = 100)*

Variables	*Mean (Standard Deviation)*	*Median (Interquartile Range)*
Age	58.7 (11.9) years	60 (50 – 68.8) years
Gender[1]		
Male	65 (65%)	
Female	35 (35%)	
Duration of Stay	8.47 (4.26) days	8 (6 – 10) days
Vitamin D	31.98 (26.51) ng/ml	23.15 (12.8 – 43.8) ng/ml
C-Reactive Protein	56.44 (43.71) mg/L	60.55 (33.6 – 74.3) mg/L
Ferritin	653.75 (661.08) ng/ml	438 (229.5 – 871.4) ng/ml
D-Dimer	1.10 (1.71) mcg/ml	0.59 (0.33 – 1.00) mcg/ml
Procalcitonin	2.10 (12.29) ng/ml	0.07 (0.03 – 0.23) ng/ml
Outcome[1]		
Survived	87 (87%)	
Expired	13 (13%)	

Results are displayed as frequency and percentage (within brackets); For remaining variables, results are displayed as Mean (standard deviation between brackets) and Median (Interquartile range between brackets).

$\chi^2(2) = -3.09$, P<0.01. This shows that patients who died had spent more days at the hospital as compared to those who survived. Likewise, the median differences of Procalcitonin levels in patients who survived or expired was statistically significant, $\chi^2(2) = -3.09$, $P < 0.01$, which shows that patients who survived had lower procalcitonin levels as compared to those who died. The median differences of remaining characteristics in patients who survived or expired were not statistically significant (see Table 2).

The results of point bi-serial correlation showed that there was a statistically significant correlation between duration of stay and outcome in COVID-19 patients, $r_{pb}(98) = .43$, $p < .001$, with those who survived having lower duration of hospitalization as compared to those who expired, $M = 7.76$ ($SD = 3.14$) vs. $M = 13.23$ ($SD = 7.12$). There was also a statistically significant

Table 2: *Median Comparisons of Clinical Characteristics in Coronavirus disease 2019 (COVID-19) patients who survived and expired (n = 100)*

Clinical Characteristics	Survived (n = 87)	Expired (n = 13)	p-value
Duration of Stay	8 (5 – 10) days	12 (7.50 – 19.5) days	***.002***
Vitamin D	23.8 (12.9 – 45.4) ng/ml	17.2 (9.95 – 40.45) ng/ml	.464
C-Reactive Protein	60.6 (30.3 – 74.5) mg/L	57.8 (44.1 – 69.4) mg/L	.587
Ferritin	419 (208.8 – 997) ng/ml	502 (310 – 694.7) ng/ml	.747
D-Dimer	0.59 (0.33 – 1) mcg/ml	0.68 (0.29 – 1.16) mcg/ml	.935
Procalcitonin	0.07 (0.03 – 0.20) ng/ml	0.16 (0.10 – 1.32) ng/ml	***.024***

Results are shown as Median and Interquartile Range (between brackets)

correlation between Procalcitonin levels and outcome in COVID-19 patients, $r_{pb}(98) = .37$, $p < .001$, with those who survived having lower Procalcitonin levels as compared to those who expired, $M = 0.35$ ($SD = 1.00$) vs. $M = 13.75$ ($SD = 32.70$). There was no statistically significant correlation found between Vit.D levels and C-Reactive protein, D-Dimer, Ferritin and Procalcitonin. The correlations of remaining clinical characteristics with outcome were statistically insignificant (see Table 3).

Discussion

With the emergence of COVID-19, it was speculated by the researchers that severity of the infection can be linked to vitamin D sufficiency or defeciency.[13] Vitamin D deficiency has been associated with increased susceptibility to respiratory infections and dietary supplementation has shown a reduced risk of developing severe infections.[14] The outbreak of COVID-19 occurred in winters and had a quick spread in the northern hemisphere when vitamin D levels are at their lowest due

Table 3: *Point Bi-serial Correlations of Clinical Characteristics with Outcome in Coronavirus Disease 2019 (COVID-19) Patients (n = 100)*

Clinical Characteristics	*R*	p-value
Duration of Stay	.43	***<.001***
Vitamin D	- .04	.685
C-Reactive Protein	- .03	.778
Ferritin	- .05	.559
D-Dimer	- .06	.547
Procalcitonin	.37	***<.001***

to seasonal changes.[15] Many studies have revealed that there is almost 4.4% increase in mortality in COVID-19 patients with low Vitamin D status.[16]

Patients who were habitual users of Vitamin D supplements had lower infection rates, depicting that vitamin D had a protective role in disease course.[17] Relative risk of positive infection rate is 1.8% higher in vitamin D deficient patients however decision should always be made keeping in mind all clinical variables including age, race and co morbid factors.[18,19]

In our study, inflammatory disease markers like CRP, ferritin and procalcitonin were higher in COVID-19 patients. Our study showed that there was a statistically significant correlation between duration of stay and outcome in COVID-19 patients highlighting that those who survived had short duration of hospitalization as compared to those who expired. There was also a statistically significant correlation between Procalcitonin levels and outcome in COVID-19 patients. It has been reported that as compared to moderate patients, values of mean serum procalcitonin were raised four times in severe patients and over eight times in critical patients[20]. It is evident clinically that vitamin D regulates immune function so it can play strong role as modulator of immune system in COVID infection.[21]

Low vitamin D levels lead to increased inflammatory response, cytokine storm and increased CRP levels.[9] Many clinical studies have demonstrated an inverse relationship between CRP and vitamin D status in COVID-19 patients.[22,23] Findings of our study highlighted that although Vit.D levels were low in 58% of patients but it had no significant correlation with inflammatory markers and disease severity. This finding is in contrast to an Indian study which has reported that patients with higher levels of vitamin D, had low disease fatality rate as compared to patients having deficiency of vitamin D. Moreover, vitamin D deficient patients in this study had significantly higher inflammatory markers like ferritin, TNF-alpha and Interleukin-6.[5]

Conclusion

Our study demonstrated no significant correlation between low Vit.D and disease severity and outcome. There is insufficient data on the association between Vit D levels and COVID-19 severity and mortality in our population. So, controlled randomized trials and large scale studies are needed to test this hypothesis.

Conclusion

Our study found significant correlation between Procalcitonin levels and duration of hospital stay in COVID -19 patients. Our study has highlighted no significant correlation between low Vit.D levels and other inflammatory markers, with duration of hospital stay and disease severity. Controlled randomized trials and large scale studies are needed to further explore this in our population.

Conflict of Interest: *None*

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AA: Data Collection
AM: Literature Search
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FF: Drafting, Revision
MU: Writing of Manuscript

Awareness, Attitudes And Practices About Menstruation Among School Girls

Baseera Imran,[1] Muneeza Taseer,[2] Shazo Sana[3]

Abstract

Objectives: To assess the knowledge and practices of adolescent girls about menstrual hygiene. To estimate the prevalence of medical and academic problems associated with menstruation.

Methods: It was a descriptive cross sectional study done in 199 school girls of age 10-19 years. A predesigned, pre-tested structured self- administered questionnaire was used for data collection. After taking permission from the school authority, school girls were explained the purpose of the study and verbal consents were obtained.

Data analysis was done by using SPSS-16. Descriptive statistics like frequency, percentage and mean ± standard deviation were applied.

Results: Fifty one percent of the girls were aware of menarche (having cycle for the 1st time) and major source of information were mother (36%) followed by friends (24%), sister (19%) and school (12%). 59.7% girls considered menarche as a physiological process and 22.6 % girls thought it as a disease process ,77.8% knew that poor hygiene causes several infections.

Conclusion: School girls are not fully aware of hygienic practices regarding menstruation and there is a need to educate them. Healthy reproductive life is impacted by menstrual cycle and measures taken for menstrual sanitation.

Key words: menstrual hygiene, menarche, school girls

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Introduction

Adolescence is the transitional phase b/w girlhood to woman hood.[1] WHO has defined adolescence as the age group of 10-19 years. It comprises 1/5 of the World's population of 1.2 billion. Adolescent girls constitute a vulnerable group not only with respect to their social status but also regarding their health that is why it is considered as a time frame that requires special attention.[2] In girls it has been recognized as a period which includes the transition from girlhood to womanhood. Menstruation is generally taken as filthy in the Indian society. The menstruating girls are isolated and restrictions are imposed on them in the family. This reinforces a negative attitude towards menstrual cycle. Several studies have reported restrictions during the daily activities.[1] Apart from these, they believe in specified taboos at menarche and menstruation [Menarche i-e the onset of menstruation is the most important happening in this transitional phase. Menstruation is the monthly flow of blood from vagina due to the shedding of the uterine mucosa[2]. The Curse'-he named menstruation, is very unhygienic asit may foster fecal contamination of vagina and also acts continuously as arousal rubbing the vulva during each walk. The different menstrual flow catching materials are: Rag made, Pad, Tampon, Cups and disposable or reusable, Panty liner and reusable pan.[16] Although menstruation is the most important event for womanhood yet most of the studies highlight negative attitudes towards menstruation. So, it is considered as a taboo and girls are not allowed to talk about it openly.[3] Since adolescence is the time of physical, intellectual and social development. So several socio cultural restrictions and barriers, make many girls afraid of or ashamed of menstruation. Consequently, many females have to suffer several gynecological

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problems because of poor personal hygiene and unhealthy cleanliness conditions.[4] Females having enough knowledge and healthy practices about menstrual hygiene are less liable to get genital tract infections, thus adequate knowledge about menstruation may result in safe practices and decrease the sufferings of a lot of future mothers.[5] Menstrual hygiene, is a very significant risk factor for reproductive tract infections. Educational television programmes, trained school nurses/health personnel, motivated school teachers and knowledgeable parents can play a very important role in transmitting the message of right menstrual hygiene to the adolescent girls of today.[5]

Methods

It was a school based, Descriptive cross sectional study. Two months time was taken for the purpose (from 1st Dec 2013- 31st Jan 2014) in a school in Lahore. 199 school girls of age group 10 to 19 years (age taken for adolescence) and those who already had menarche were included in the study. Data was collected from students who were present at the time of data collection.

A predesigned, pre-tested structured self- administered questionnaire was used for data collection.

After taking permission from the school authority, school girls were explained the purpose of the study, the hygienic methods, and informed verbal consents were obtained. Confidentiality was maintained. All the girls who have attained menarche and who were willing to participate were included. Girls who had not attained menarche and were not willing to participate in the study due to any reason or those who were absent on study days were excluded.

After collection of the filled questionnaires, health education regarding the physiology of menstruation and the role of hygiene plus the myths prevailing in the society concerning the same was imparted to the girls through lectures with the help of audio visual aids. This was followed by question answers sessions to clarify their doubts. Data analysis was done by using SPSS-16. Descriptive statistics like frequency, percentage and mean ± standard deviation were applied.

Results

A total of 199 secondary school girls were included in the study. Mean age of the participants of study was 15± 4.5 years. Mean age at the onset of menarche was 12.4±3.78 years. Majority of the girls have their menstrual cycle length of 25-30 days with 5-7 days bleeding and experience mild dysmenorrhea as given in (Table-1). Table 2 described that about 51 % of the girls were aware of menarche and major source of information was mother (36%) followed by friends (24%), sister (19%) and school (12%). 59.7% girls considered menarche as a physiological process and 22.6 % girls thought it as a disease process. Only 28.6% girls could understand that blood was coming from uterus. 33% of the females were afraid at the start of 1st menses and 64.8% of the girls shared this information with their mother followed by the sister. 75.8% girls give the suggestion that girls should be educated about menarche before hand. 77.3% of the girls used disposable sanitary pads during menstruation while15.1% of the girls use new cloth and 7.5% use old rag cloth. 55.2% took bath at the end of menstrual cycle. Majority of the girls clean the genitalia each time they go to toilet and change the sanitary pad twice a day. 77.8% of the girls know that poor hygiene predisposes to infection (Table-3). 78.9% of the females have to face religious restrictions, 15.43% of the girls are not allowed to enter the kitchen and 8.65% girls don't take sour food, 6.76% don't drink cold water and 14.20% can't attend family functions during menstrual days as shown in (Fig-1).

The median menstrual cycle lasts 28 days, beginning with the first day of menstrual bleeding and ending just before the subsequent menstrual period. The variable first half of this cycle is termed the follicular phase and is characterized by increasing follicle-stimulating hormone (FSH) production, leading to the selection of a dominant follicle that is primed for release from the ovary. (Shannon, 2018).

Table 1: *General Characteristics of Study Participants*

Variable	Responses	No.	%
age	10-14 yrs	90	45.2%
	15-19 yrs	110	54.8%
Age at menarche	10-12	97	48.7%
	13-15	102	51.3%
Length of menstrual cycle	<25 days	32	16%
	25-30 days	122	61.3%
	>30 days	45	22.6%
Duration of bleeding	3-5 days	48	24%
	5-7 days	129	64.8%
	>7 days	22	11%
Dysmenorrhea	Absent	19	9.5%
	Mild	86	43.2%
	Moderate	40	20.1%
	severe	54	27.1%

Table 2: *Knowledge and Attitude about Menstruation*

Variable	Responses	%
Awareness of menstruation before Menarche	Yes No	49% 51%
Multiple resources of information regarding menarche	Mother Sister Friend School Media	36.5% 18.9% 24.45% 12.7% 9.36%
Know the cause of menstruation	Physiological Disease Don't know	59.7% 22.6% 17.5%
Menstruation Is from???	Uterus Urinary tract Stomach Any part of abdomen	28.6% 44.7% 8.5% 8.4%
Reaction to 1st menstruation	Afraid Anxious Guilty Embarrassed No reaction	32.8% 30.8% 16.2% 12.5% 8.34%
Sharing of first menstruation	Mother Sister Friend	64.8% 26.1% 9.1%
Opinion - about educating girls About menarche	Yes No	75.8% 24.1%

Table 3: *Practices Regarding Menstruation*

Variable	Reponses	No.	%
Materials used as absorbent	Sanitary pads New cloth Old rag cloth	153 30 16	77.3% 15.1% 7.5%
Frequency of bathing during the cycle	Daily After 1-2 days At the end of menses	34 55 110	17.1% 27.6% 55.2%
Cleaning of external genitalia	Every time going to toilet No washing	121 78	60.8% 39.1%
Frequency of changing the pad	1 2 3 or more	55 101 43	27.6% 50.7% 21.6%
Know that poor hygiene predispose to infections	Yes No	155 44	77.8% 22.1%

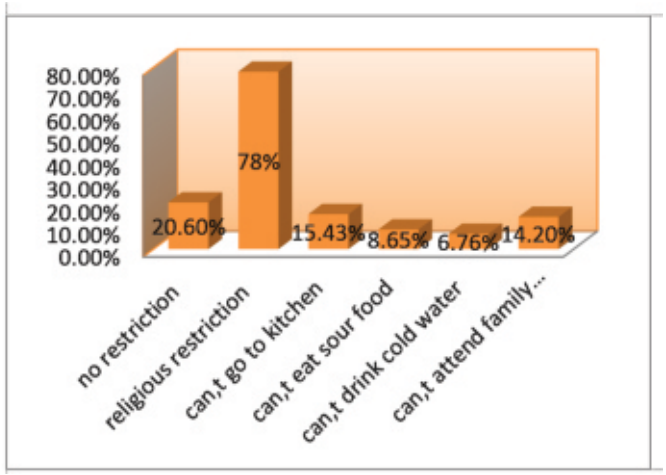

Fig-4: *Restrictions followed by Study Population during Menstruation*

Discussion

The current study showed the mean age of the girls at menarche was12.4± 3.78 years with a range of 10 -15 years and majority had a range of 13-15 years (51.3%). This is in line with the work done by Ali and Rizvi[6] in Karachi, Pakistan. In our study, 51% of the girls had prior knowledge about menarche before attaining it; similar results have been found by other studies[1,5] but Kamath R. et. al.[7] 2013 have shown that only 33.27% of urban and 35.82% of rural population were aware of menarcheand interestingly another study showed 72.1% of urban population and 39.1% of rural population has previous knowledge of menarche.[8] Similar to other studies,[5,7,9] mother was a major source of information about menarche for our girls. But one study showed that friends were the first informant in majority of girls[10] and one more study showed that mass media was the major source of knowledge for girls.[11] Fifty-nine percent of our study population thought of menses as a natural process while 22.6% perceived it as a disease process. This is similar to the study conducted by Dusguptathat 86.25% of the girls considered menstruation, a physiological process where as khannaet al have shown that nearly 70% of the girls considered menstruation as a disease process[5,12]. In the current study, only 28.6% of the girls knew that source of bleeding is uterus. This is similar to the work done by Ali et. al., 2009.[6,10] 33 % of our school girls were afraid at the time of 1st menstruation and 31% were anxious. The reaction to menarche depends on the prior knowledge and awareness, many other studies also show presence of anxiety and fear in the girls attaining menarche.[5,6,7]

Moreover, there were many girls who used menstruation

as a disguise against attending sport (physical education) class during physical exercises. However, the school officials didn't deny the real difficulty girls were facing during menses. The absence of clinics or health personnel or trained counselors in most of the schools made it not possible to help girls who really had problems so that they might be able stay in school and not miss classes. The other big issue raised by some of them especially female officials was the absence of menstrual hygiene material. This was considered as one of the important factors for most girls who had irregular menstrual cycles and for not ready ones. They, female officials also condemn the school environment for it is not suitablefor menstruating girls.[16]

Most of them believed to menstruate was healthy and a natural phenomenon. However, at times they even didn't know what was bad about it. There was mixture of mixed reactions towards it, its normality as well as there was nothing to be afraid of. They were asked of unpleasantness and distressing side of cycle. Mothers and family members didn't talk freely. They just told them that it was normal, no more no less. So, girls took the event as something not a matter to talk of with any one, but to keep silent. They just forgot it consciously.[16]

Seventy-seven percent of our girls are using sanitary pad. A similar work has been done by Ali and Rizwi, in Karachi that majority of our Pakistani girls use sanitary pads[6]. Although majority of the girls (77.8%) know that poor hygiene may predispose to infections but still majority (55.2%) don't take bath during menstruation rather they take bath at the end of the menstruation. Similarly, a study conducted in Saudi Arabia shows that only 8.3% of girls took bath daily during menstruation and 71.7% took bath only after 2-3 days.[13] Majority of girls (60.8%) wash their genitalia after urination in line with the study conducted by Sharma et. al., in North India[14] while Thakre et. al. has shown that girls don't even wash their genitalia after urination.[1]

In the current study, girls have to face certain restrictions during menstrual cycle. As Muslims, we know that there is religious restriction in menstruation, not to touch Holy Quran, not[15] to pray and enter in the mosque so in the current study, (78.9%) girls have to face religious restriction (praying, reading Quran). This is in line to other studies conducted in non-Muslim communities that menstruating girls are not allowed to enter temple and warship.[1,5] In present study, 15.43% are not allowed to enter the kitchen, 8.65% are not allowed to eat sour food, 6.76% can't drink cold water and 14.20% can't attend family functions. Similar restrictions have been reported in many different studies from different parts of the world.[1,10,11,13]

Conclusion

Our school girls are not fully aware of the safe and healthy practices regarding menstruation. So, it is essential to educate those regarding safe and hygienic practices during menstruation. It will help them to lead a healthy reproductive life.

Conflict of interest *None*

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Authors Contribution

BI: Conceptualization of Project

BI, SS: Data Collection

MT: Statistical Analysis

MT: Drafting, Revision

BI: Writing of Manuscript

Atypical Features of COVID-19 Patients Presenting At Mayo Hospital Lahore

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Abstract

Objective: To determine the atypical features of Covid-19 patients presenting at Mayo Hospital Lahore.

Methods: This was a cross sectional study conducted in Corona isolation wards of Mayo Hospital, Lahore, Pakistan from 1st June to 30th August 2020.After ethical approval, 185 Patients of all age groups with either gender & COVID-19 PCR positive were included in this study. Patients with other active systemic diseases were excluded from the study & symptoms of every patient at presentation or during admission were noted in a pre-designed proforma.

Results: Out of 185 patients, it was found that 131 COVID-19 positive patients had atypical features. Out of 131 patients, 49 patients were asymptomatic, 35 patients presented with musculoskeletal features, 29 with gastrointestinal features, 16 patients presented with neurological features,09 had cardiac,03 had renal,04 had cutaneous, 02 had eye symptoms and only 01 had endocrine features. 122 patients had only respiratory symptoms, out of which only 1 patient had hemoptysis.

Conclusion: Atypical features of COVID-19 can be the only symptoms of the disease. If these are not recognized by the physicians, it may delay the diagnosis, isolation & treatment of these patients.

Key Words: Atypical Features, Covid-19, Pandemic, SARS CoV-II

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Introduction

Corona virus disease (COVID-19) was first seen in Wuhan, China in December 2019, which has subsequently affected 215 countries so far.[1] It has affected over 20 million people globally, with over 400,000 cases in the United States alone.[2] In Pakistan it has infected over 260,000 people with over 5000 deaths till now. It has been strongly postulated that the outbreak was associated with a seafood market in Wuhan.[3]

COVID-19 is an acute self-limiting disease but it can also be deadly at the same time. Severe disease onset might result in death due to massive alveolar damage and progressive respiratory failure.[4] Although most coronavirus infections are mild, the epidemics of two beta coronaviruses, severe acute respiratory syndrome (SARS-COV) and Middle East respiratory syndrome (MERS-COV) have caused more than 10,000 cases in past 20 years with mortality rates of 10% and 37% respectively.[5] The COVID-19 belongs to the family of enveloped, positive sense RNA viruses, characterized by club shaped spikes that project from their surface.[4]

The presentation of the disease is either asymptomatic or with mild to moderate symptoms leading to acute respiratory distress syndrome (ARDS). As the disease has continued to spread, increasing information is becoming available about the involvement of other organ systems & presence of atypical symptoms. Although COVID-19 presents with respiratory symptoms, but recent studies take it as a systemic disease involving almost every system.[6] The other several clinical features of this systemic disease that include fever, dry or productive cough, flu, sore throat, dyspnea fatigue, myalgia, headache and joint pains.[7,8,9]

The atypical symptoms are unexplained fatigue, malaise, vertigo, acute functional decline, chills, headache,

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croup, itching, urticarial, conjunctivitis, anosmia, anorexia, dysgeusia, malaise, abdominal pain, nausea, vomiting and diarrhea. Others atypical signs are unexplained tachycardia, hypotension, hypoxia, fatigue, jaundice and difficulty in feeding infants[10].

However, data is lacking in our local Pakistani population. The mortality & morbidity of this disease puts significant strain on healthcare infrastructure and resources than any other respiratory illness. Hence, it is necessary to urgently identify atypical presentations of the disease that can be missed while diagnosing the disease. Therefore, we would like to identify atypical presentations of COVID-19 at our hospital.

Methods

It was a cross sectional study conducted in Corona isolation wards of Mayo Hospital, Lahore, Pakistan during the first wave of COVID-19 from 1st June to 30th August 2020. 185 patients of all age groups with either gender & COVID-19 PCR positive presenting at Mayo Hospital were selected for the study. Patients of active systemic diseases like inflammatory bowel disease, Hepatitis, coronary artery disease, obstructive airway disease and heart failure were excluded from the study. Informed consent was taken before enrolling. Demographic details including name, age, sex, address and clinical features including signs & symptoms of every patient at presentation or during admission were noted in a pre-designed proforma.

Results

Out of 185 COVID-19 PCR positive patients, it was found that 131 patients had atypical features. Out of 131 patients, 49 patients were asymptomatic, 35 patients presented with musculoskeletal features, 29 with gastrointestinal features, 16 patients presented with neurological features, 09 had cardiac, 03 had renal, 04 had cutaneous, 02 had eye symptoms and only 01 had endocrine features. Remaining 122 patients had only respiratory symptoms, with only 1 patient having hemoptysis.

The most common atypical presentation was asymptomatic in 49 patients of this study, thereby showing the major burden on the hospital was just for isolation purpose. Among musculoskeletal 30 had unexplained fatigue and 05 had body aches or myalgia. 17 patients had diarrhea, 04 had nausea & vomiting, abdominal pain each, 03 had malaise and anorexia was seen in 01 patient each. Neurological symptoms included headache in 07, anosmia in 05, dysgeusia in 02 and dizziness and impaired consciousness in 01 patient each. Cardiac features included chest pain, palpitations or tachycardia in 03, unilateral leg swelling in 02, and hypotension in 01 patient. Skin manifestations included itching, erythematous rash, vesicles and urticaria in 01 patient each. Endocrine features included testicular pain in 01 patient. Renal showed hematuria in 02 and oliguria in 01 patient. Eye features showed conjunctivitis & watering of eye in 01 patient each. Out of respiratory symptoms, only

Table 1: *Atypical Features of COVID-19*

Sr no	SYSTEM	FEATURES	N	%AGE
1.	**Asymptomatic**	**No Clinical Symptom**	49	26.5
2.	**Neurological**	Headache	07	3.8
		Dizziness	01	0.5
		Impaired Consciousness	01	0.5
		Anosmia	05	2.7
		Dysgeusia	02	1.1
3.	**Eye**	Conjactivitis/Redness	01	0.5
		Watering of eyes	01	0.5
4.	**Respiratory**	Haemoptysis	01	0.5
		Fever	38	20.5
		Sore throat	23	12.4
		Cough	29	15.7
		Dyspnea	10	5.4
		Flu	09	4.9
5.	**Cardiac**	Palpitations/Tachycardia	03	1.6
		Hypotension	01	0.5
		Chest Pain	03	1.6
		Unilateral Leg Swelling	02	1.1
6.	**GIT**	Nausea, Vomiting	04	2.2
		Anorexia	01	0.5
		Malaise	03	1.6
		Abdominal Pain	04	2.2
		Diarrhoea	17	9.2
7.	**Renal**	Oliguria	01	0.5
		Hematuria	02	1.1
8.	**Skin**	Erythmatus Rash	01	0.5
		Urticaria	01	0.5
		Chicken pox like vesicles/blisters	01	0.5
		Itching	01	0.5
9.	**Musculoskeletal**	Unexplained Fatigue	30	16.2
		Bodyaches/Myalgias	05	2.7
10.	**Endocrine**	Testicular pain	01	0.5

1 atypical presenting feature was hemoptysis.

Discussion

In our study we found that out of 185 patients presenting with COVID-19,131 patients had atypical multi-

Table 2: *Prevalence Of Multisystem Features Of Covid-19 Patients*

SYSTEM/FEATURES	N	%AGE
Asymptomatic	49	26.5
Neurological	16	8.6
Eye	02	1.1
Respiratory	122	65.9
Cardiac	09	4.9
GIT	29	15.7
Renal	03	1.6
Skin	04	2.2
Endocrine	01	0.5
Musculoskeletal	35	18.9

system features including diarrhea, dysgeusia, anosmia, palpitations, hemoptysis, hematuria, itching, blisters, conjunctivitis, and aches and pains etc. The purpose of our study was to detect these atypical extra-pulmonary symptoms so that earlier treatment can be initiated to avoid any further complication in our population. By reviewing the literature, it was found that several mechanisms are present by which SARS-COV-2 cause's multisystem manifestations. It binds to ACE-2 receptors present on enterocytes, hepatocytes & cholangiocytes.[11] It also damages digestive system directly by cytopathic process or indirectly by an inflammatory process.[12] There are several studies that favor our results. A meta-analysis consisting of 4243 patients from 6 countries done by Cheung et al. concluded that 17.6% patients had gastrointestinal symptoms with 12.5 % having diarrhea.[13] Similarly in a second meta-analysis of 59254 patients from 11 countries done by Borges et al. it was concluded that GI symptoms were present in 9% of the COVID-19 patients.[14] Similarly, like our study, anosmia & dysgeusia was noted as an atypical feature of COVID-19 by Redd et al. in their study.[15] These symptoms are probably due to entry of the virus through oral & nasal routes & subsequent damage to olfactory and gustatory receptors[16]. In another larger study by Guan et al. on 1099 COVID-19 patients' hemoptysis was found in only few patients.[17] Pleuritic chest pain was seen in our study as seen in previous studies as a possible atypical symptom of COVID-19 suspecting pulmonary embolism with raised levels of d. dimers & fibrinogen.[18,19] A case report of acute COVID-19 myopericarditis showed cardiac involvement and symptoms of tachycardia, hypotension as in our study.[20] The neurological manifestations of COVID-19 reported so far were few, including headache, dizziness, body weakness like Gullian-Barre syndrome, viral encephalitis, toxic encephalopathy etc as in our study.[21] Conjunctivitis has been shown in one third of the patients (16.7%) in a case series study with conjunctival swabs even positive for COVID-19.[22] Skin changes were shown by a number of case reports as diffuse erythematous urticarial rash two days before the onset of COVID-19 symptoms.[23] Similarly a study of 81 male patients noted testicular pain as in our study.[24] There were certain limitations of our study. Firstly, it was a cross sectional single centered study with limited sample size that can affect reliability as well as generalizability. Secondly, we didn't check stool or other body fluids RNA & other specific tests of COVID-19. So, it is difficult to correlate the results exactly but majority of the results were in line with the international researches.

Conclusion

It is concluded that atypical features of COVID-19 can be the only symptoms of the disease. If these are not identified by the physicians, it may delay diagnosis isolation & treatment of these patients. Hence by adequate knowledge of these atypical symptoms we can limit admissions and spread of the disease and can emphasize the proper protective equipment during patients' checkup.

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Authors Contribution

SUM, SI: Conceptualization of Project
SUM, TK, SI, AA: Data Collection
AA: Literature Search
AA,SA: Statistical Analysis
SM, SA: Drafting, Revision
SUM, TK, SM: Writing of Manuscript

Alvarado Modified CRP Scoring for the Diagnosis of Acute Appendicitis, with Histopathology Serving as the Gold Standard of Diagnostic Accuracy

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Abstract

Objectives: We aimed to determine diagnostic accuracy of combination of Modified Alvarado Scoring (MAS) of > 7 plus a positive CRP in diagnosis of acute appendicitis comparing it with the gold standard histology

Methods: This Cross-sectional study was done at the Surgery Department, Nescom Hospital from Dec 2018 to Dec 2020. Our study included 230 Patients who were consecutively recruited between the ages of 25 and 60, of either gender, who had appendicectomies based on the surgeon's clinical judgement and the results of blood tests (TLC > 10,500), ultrasounds, and urine (which came back negative for a urinary tract infection). Patients having infectious or inflammatory conditions were excluded from the study. For data entry and analysis, SPSS 22.0 was utilized.

Results: The participants' mean age was 34.6 9.3 years. Males made up 57.4 % of the population, while females made up 42.6 %. There were 108 (84.38%) true positive and 20 (15.62%) were false positive cases. 73 (71.57%) were true negative and 29(28.43%) were false negative cases.

The positive predictive value of MAS (Modified Alvarado Score > 7 plus a positive CRP was 84.37%, the negative predictive value was 71.56%, sensitivity was 78.83%, specificity was 78.49%, and diagnostic accuracy was 78.69%.

Conclusion: Modified Alvarado scoring (with score ⩾ 7) in combination with CRP greatly enhances the diagnostic accuracy for diagnosing acute appendicitis.

Keywords: Appendicitis, sensitivity, specificity, CRP protein, Appendectomy.

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Introduction:

Because the appendix is chronically infected, surgery is required for acute appendicitis.[1-3] Acute appendicitis is still best treated surgically,[4,5] despite recent advances in treatment.[6] The risk of developing chronic appendicitis is significantly higher than the risk of developing acute appendicitis. Appendicitis strikes girls and boys equally, with females accounting for 23.1% of all cases and males accounting for 13.1%.[5,7]

Surgery to remove the appendix reduces the risk of life-threatening complications, such as perforation and infection, which can be fatal. It is common for laparotomies to be performed when appendicitis is incorrectly diagnosed.[8] Removing an appendix that isn't inflamed comes with its own set of risks, and a failed appendectomy is no laughing matter.[9] When it comes to diagnosing acute appendicitis, abdominal ultrasonography is accurate and specific.[10] Because of the potential for surgical

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complications, negative appendectomy should be avoided whenever possible. For surgical decision making, a 7 MAS cut-off value has an 82% specificity and 82% sensitivity. For example, the Alvarado score was created to improve diagnostic accuracy.[11]

It was also discovered that the Alvarado scoring system had 93.5 per cent sensitivity and 80.3 per cent specificity and an accuracy of 89.5 percent in a local analysis by Memon and colleagues.[9] A significant number of patients with acute appendicitis on histology are missed by the Alvarado score. With the addition of CRP, the diagnostic accuracy of the MAS test for acute appendicitis can be improved.[12] In patients with appendicitis, the Alvarado score was 90% sensitive, 80% specific, and had a positive predictive value of 87%. People who had surgery had significantly higher levels of CRP than those who had not been diagnosed.[13] MAS and a positive CRP have not been studied locally to determine if they can be used to diagnose acute appendicitis. According to Thirumallai,[14] Alvarado scores predicted 84.5 percent accuracy in group I (scoring 7-10) and 50.7 percent accuracy in group II (scoring 11 and up) (scoring 4-6). In the evaluation of people with a score of 7-9, the sensitivity and specificity of MAS were increased to 98% and 54%, respectively, when CRP was added.[14] An important part of this study was determining how well MAS and the CRP work together to discover if the diagnostic accuracy of MAS can be enhanced by adding the findings of a positive CRP to it.

Methods

This Cross-sectional study was done at the Surgery Department, Nescom Hospital from Dec 2018 to Dec 2020. Using data from a study published in 2021[15] and the WHO calculator, a sample size of 230 people was calculated with a 95% confidence interval and an error margin of 5%. consecutive non-probability sampling was used. Our study included patients aged 25-60, of either gender, who underwent appendicectomies based on the surgeon's clinical judgement and the results of blood tests (TLC > 10,500), ultrasounds, and urine (negative for a UTI). We excluded patients with evidence of an infective or inflammatory disorder like acute infections like sore throat, urinary tract infection on history, patients with chronic infections like tuberculosis on history; patients with inflammatory disorders like rheumatoid arthritis and SLE on history.

Data was collected after taking permission from Nescom Hospital Ethical Committee, wide letter no NESCOM-44(33)/2018-IMC. The study was explained to the patient, and signed agreement was obtained only after the patient had been fully informed of the risks and benefits of participating in the research. Patients were recruited through the utilization of emergency, indoor, outdoor, and outdoor departmental methods of patient collection. The results of the patient's medical history, physical examination, and any subsequent tests or investigations were recorded on a Performa. Before the choice to perform an appendectomy was made, all patients were in this condition. C-Reactive protein (CRP) was detected in a sample of blood obtained before to surgery.

SPSS 22.0 was used for data entry and analysis. For quantitative data like age, descriptive statistics were employed to compute the mean and standard deviation. Qualitative variables like CRP levels, genuine positive and negative, were provided in frequency and percentages.

Alvarado scores of 7-9 and elevated CRP (more than 1 mg/dL) were used for comparing with the histology as gold standards.

The following standard formulae were used to calculate the sensitivity, specificity, positive predictive value, negative predictive value, and total diagnostic accuracy.

- *Sensitivity = TP / (TP/ FN) × 100*
- *Specificity = TN / (FP = TN) ×100*
- *PPV (Positive Predictive Value) = TP / (TP + FP) × 100*
- *NPV (Negative Predictive Value) = TN / (FN + TN) × 100*
- *Diagnostic accuracy = TP + TN/TP+TN + FP + FN× 100*

Results

The mean age of the participants was 34.6 ± S.D 9.3 years, with an age range of 25- 60 years.

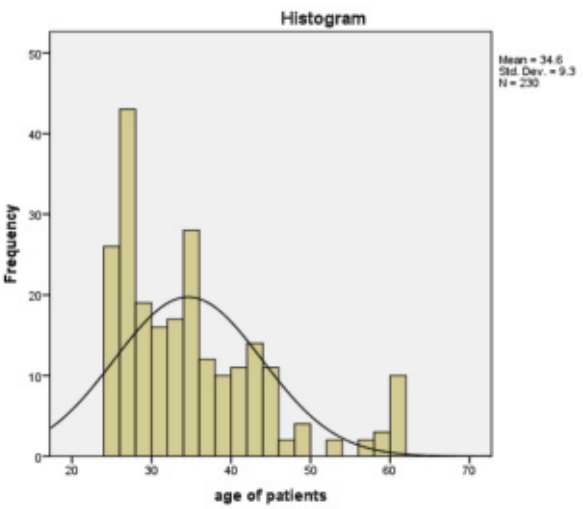

Figure 1: *Showing the Age Distribution of the Participants*

Regarding the gender distribution, there were 132 (57.4%) males and 98 (42.6%) females amongst the participants, as shown in Table I.

Table 1: *Showing the Gender Distribution of the Participants*

GENDER	FREQUENCY	PERCENTAGE
Male	132	57.4%
Female	98	42.6%

There were 108 (84.38%) true positive and 20 (15.62%) were false positive cases. 73 (71.57%) were true negative and 29(28.43%) were false negative cases, as shown in Table II.

Table 2: *Single Table Analysis for Acute Appendicitis: Histology Vs Modified Alvarado Scoring & CRP*

	Appendicitis on Modified Alvarado Scoring & CRP	
	Yes/Positive	No/Negative
Appendicitis on Histology		
Yes/Positive	108 (84.38%)	20 (15.62%)
No/Negative	29 (28.43%)	73 (71.57%)

The positive predictive value of MAS (Modified Alvarado Score > 7 plus a positive CRP was 84.37%, the negative predictive value was 71.56%, sensitivity was 78.83%, specificity was 78.49%, and diagnostic accuracy was 78.69%, as shown in Table III.

Table 3: *Showing the Diagnostic Parameters of Acute Appendicitis: Histology Vs Modified Alvarado Scoring & CRP*

Diagnostic Parameters Of USG detecting Renal Calculi	Values
Sensitivity = True Positive/ (True Positive +False Negative)	78.83%
Specificity = True Negative/ (True Negative +False Positive)	78.49%
Positive Predictive Value = True Positive/ (True Positive+ False Positive)	84.37%
Negative Predictive Value = True Negative/ (True Negative +False Negative)	71.56%
Diagnostic Accuracy = (True Positive +True Negative)/All Patients	78.69%

199 patients (86.5%) had a positive CRP whereas 31 (13.5%) had a negative CRP, as shown in Table IV.

Table 4: *Showing the Status of C Reactive Protein (n=230)*

C-Reactive Protein	Frequency	Percentage
POSITIVE	199	86.5%
NEGATIVE	31	13.5%

Discussion

Research shows that the Modified Alvarado Scoring and C-reactive protein are useful diagnostic tools for acute appendicitis. A combination of CRP and histology can be used to detect MAS in its early stages. According to previous research, this is consistent with findings. When it comes to making the decision to go through with surgery, researchers found that the cutoff value of 7 MAS had an 82% positive predictive value and 81% negative predictive value. Acute appendicitis is still being missed by the Alvarado scoring system, despite the fact that histology has proved it. The MAS test's ability to detect acute appendicitis can be improved with the addition of the CRP test. Accuracy scores of 93.5 percent and 80.3% for sensitivity and specificity are also excellent.[9]

Kostic[13] discovered that the Alvarado ratings varied considerably across groups based on histology results (group I acute appendicitis: 4.9±1.21; group II normal appendix: 8.55 ± 1.32) Between groups, there was a significant difference in CRP levels in the operating room (group I: 8.17±or- 4.7 mg/L, group II: 38 + or- 26 mg/L) Validity criteria for the Alvarado score included the following: The CRP had a sensitivity of 95 percent, a specificity of 75 percent, and an 87 percent positive predictive value. In group I, Thirumallai[14] predicted that scores 7-10 would be 84.5 percent accurate; scores 4-6 would be 50.7 percent accurate; and scores 4-6 would be 25 percent accurate in group III (score4-6). There was an 88% positive predictive value (PPV) for high CRP levels in group I, while group II had 63% positive predictive value (NPV) for normal CRP and group III had 86% positive predictive value (NPV) (PPV). The Alvarado score and CRP can be used together to accurately diagnose acute appendicitis. Patients with a MAS score of 7-9 had a 98 percent and 54 percent sensitivity and specificity increase, respectively, when CRP was added to MAS.[11] In Tanzanian research, a modified Alvarado scoring system was found to be very accurate in the diagnosis of acute appendicitis.[16] According to this research, MASS had an overall sensitivity and specificity of 94.1 percent (men 95.8 percent, women 86.3 percent) and 90.4 percent, respectively (92.9 percent for men, and 90.7 percent for women). The positive predictive value was 95.5 percent for men, whereas the negative predictive value was 88.1 percent for women. Ninety-two percent of the MASS measurements were accurate (91.5% for men and 87.5 % for women). Our investigation indicated that this high level

of diagnostic accuracy was the outcome. According to a Tunisian study, patients with clinically suspected acute appendicitis may benefit from an early adjustment in CRP. CRP and MAS data were not shown to increase diagnosis accuracy, according to a study.[17] Additionally, a KRL Hospital research found clinical and ultrasound concerns of acute appendicitis, but their TLC results were normal, which is significant because missed cases might lead to complications in the later stages of a disease state. If a normal TLC count is neglected, it's possible that appendicitis will be missed, resulting in poor surgical outcomes.[18] Failure of an appendectomy may be the result of an MRI or CT scan that is too positive. The likelihood that a patient may develop appendicitis can be accurately assessed using AAS. Appendicitis cases dropped considerably as soon as the score was used in clinical settings.[19] According to a Turkish study published in 2019, more diagnostic tests and clinical approaches are required to better understand the diagnosis process. AA diagnosis cannot be made solely on the basis of CRP, PCT, and NP levels. Increased diagnostic value comes from the AS' ability to distinguish more complex AA instances.[20] Researchers at the University of Cumbria found that combining WCC and CRP for diagnosis was more effective than doing it separately in 2018. Lactate levels can also be used to detect abdominal surgery. Accurate measurements of lactate levels are critical indicators of anaerobic glycogenesis and measures of tissue oxygen deprivation.[21] According to Dell Children's Medical Center criteria, a clinical H&P examination is sufficient to diagnose appendicitis in children with a high or low index of suspicion. The PAS is a diagnostic and therapeutic tool for appendicitis. There is no need to employ WBC and CRP unless there is a substantial degree of doubt. An infectious disease can be diagnosed using WBC and CRP after surgery. Ultrasound and CT can be used to diagnose appendicitis in children, despite ultrasound's lesser sensitivity compared to CT.[22]

CRP analysis aids in the clinical diagnosis of acute appendicitis, according to a prospective study conducted at the Federal Government Polyclinic Hospital in Islamabad. High sensitivity but low specificity are the main drawbacks of this method.[15] According to a study from Lahore, Pakistan, a serum C-reactive protein level can be used to diagnose acute appendicitis in areas where USG and CT scans are not readily available.[23] For the early detection of acute appendicitis in adults, another study from Pakistan published in 2017 found that the Modified alvarado score is an extremely sensitive test with a fair degree of specificity. It's especially useful for new doctors and those working in rural areas where more advanced tests aren't readily available.[24]

Another study obtained comparable results in our favour, suggesting that the Modified Alvarado Score is extremely useful in the diagnosis of acute appendicitis. The frequency of negative appendicectomies dropped after patients were evaluated using this grading method, as opposed to a basic clinical examination. As a result, this scoring system may be used frequently to aid in the diagnosis of acute appendicitis.[25]

Conclusion

Histopathology is still the gold standard for diagnosing acute appendicitis, however the modified Alvarado scoring (scores 7) and CRP are substantially more accurate. The Modified Alvarado scoring technique for acute appendicitis detection can save patients money by avoiding the need for more expensive testing that the majority of them cannot afford.

Limitations

Due to the small sample size, we cannot generalize our findings to a broader population. We also failed to account for the patients' period of presentation since the onset of their symptoms, which could have skewed our results and led to false negatives.

Conflict of Interest: None

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Authors Contribution

NA: Conceptualization of Project
SA: Data Collection
RHS: Literature Search
NM: Statistical Analysis
HM: Drafting, Revision
AJ: Writing of Manuscript

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