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Editorial **Open Access**

Ethical Aspects of Studying Anatomy by Cadaveric Dissection

Quratulain Javaid

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Cadaveric dissection is being there for ages serving as an important tool for teaching anatomy and that's why it is an indispensable part of medical students' curriculum.[1,2] It is believed that dissection for the purpose of anatomy teaching was there since the period of Renaissance. Other than the anatomical core knowledge for medical students, cadavers serve many purposes including how death seems like and they are able to judge the importance of life seeing a dead body in front of them.[3] The basic purpose behind this is to establish a sense of empathy in the students along with sensitizing them with the feel, features and structures of a real body. Other than the knowledge of structures, dissection is an essential way to sensitize the future doctors with the core ethical values.[1] Development of ethical norms and their maintenance remains a cornerstone in the development of ethical values in the young learners.[2] It is a crucial part of medical education to nurture values of respect and ethics in the students.[2,4]

Nurturing the ethical aspects of the dead bodies can be initiated form the very beginning of the medical profession. Kundu et al in their study documented the role of cadaveric oath and cadaveric gratitude ceremonies by the medical students a needed aspect of developing core ethical values for the deceased. The importance of these activities in the hidden curriculum remain a cornerstone in teaching bioethics of dead bodies to the young medical learners and also to make them morally and ethically sound physician.[3] In China at Zhongshan School of Medicine, cadaveric gratitude ceremony by the name of 'Salute to *silent mentor'* is organized annually at the commencement of human anatomy course. Other than professionalism, the cadaveric gratitude ceremonies cultivate empathy for the dead ones.[5] The oath ceremonies at the start of the medical profession play an imperative role in developing values of dignity, respect and empathy for the dead bodies. The students realize that those who are in front of them as cadavers were once alive as they are. This contemplation make them virtuous and righteous medical personals.[6] There are various aspects which must be kept in mind while handling the cadavers. First and foremost, respect should be given to all the bodies as they are serving as teachers to all the medical students.[1,4]

The human dead bodies must be kept moist so that the body tissues could not get putrefied.[2,4] Also, only those body parts should be exposed which are being used for the educational purpose at a certain given time in a learning session. Other remaining parts of the cadaver must be covered with respect and dignity.[2] Other than the organs, small dissected parts which are not in use must be buried or cremated with respect and it's a duty not to throw the parts in the waste bins. All the students of the medical students must be facilitated by a teacher who could make sure that students are following the ethical guidelines and are not showing unethical behavior in the dissection hall. It is must to make sure that students are there only for the academic purpose and must not at any point be indulged in any other activities related to fun and leisure, like eating food or drinking, making videos or taking selfies. Additionally students are supposed not to make any derogatory remarks about the dead bodyies.[2] The bodies that serve as an educational tool to the medical students need to be dissected with great respect and paramount carefulness.[3] Lastly one should keep in mind that disrespecting a human body is equivalent to disrespecting the humanity. Once dead body is used for the purpose, funeral should be organized in which body should be buried with due respect in presence of the family members.[7]

The bodies that are used for the purpose of dissection are either donated or they are among the unclaimed bodies.[4] Kramer et al has mentioned in their research that in South Africa recent trend in dissection is to have more donated bodies as compared to unclaimed bodies and female gender was more in comparison to the male gender.8 Other than the unclaimed bodies, many donate their bodies for the purpose to be a source of imparting knowledge to the future healers of the society.[2,4] The donation of the human bodies for the purpose of education was started in the late 20th century. The selfless act of donation on the one hand was as brightening as a beam of light for the learners but on the other hand, the process also has ethical aspects associated with it. One important feature is getting informed consent from the donor.[2] It is also vital that the person giving the informed consent must be of sound mind so he could be able to rationalize his decision.[7] Also, other ethical aspect could be misuse of the human body for the commercial

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purpose. Other cardinal feature is that the donors of the bodies or their families should not get any sort of monetary benefit from donation. Another salient aspect is confidentiality of information of the donor or the family.[2] Proper legal documentation regarding the donation of the body and how the body will be handled by the organization has to be mentioned in the document. The legal procedure prevents commercialization of the body.[9] The act of altruism must be kept in mind while one explores the dead body.

The evolvement of Bioethics has made many realize that the use of unclaimed bodies for dissection is unethical. Since the deceased has not consented for the use of his/her body, that is why it is equivalent to showing contempt for the dead. As many unclaimed dead bodies belong to poor, there is a chance of exploitation of the vulnerable.[10] Keeping in mind, the possibility of exploitation and the ethical values, it is crucial that informed consent be received from the donor during his life. Informed consent regarding the donation of body makes the person exercise autonomy and also dignity is maintained. Creation of awareness among the public regarding donation is a must. Trust of people on those who carry the procedures of dissection is considered to be vital for public to donate.[11] Exploitation of bodies of donors can also come to a halt provided there is a regulatory body that ensures that bodies will not be exchanged for any sort of financial benefit. The finance for cremation should be the responsibility of the institutes receiving and using the bodies.[12]

It is highly advisable that every medical professional entering the field should be involved in certain important practices when they come across deceased. They include giving honor, staff should always be there with the students, gratitude ceremonies be held, use of attire should be appropriate, only required minimal exposure of bodies for purpose of teaching has to be ensured, human tissues should not be the part of general waste bins, drinking, eating, video making, photography should be banned, avoidance of irrelevant and funny chats, dissection region should only be for selective staff and students and after use bodies should be cremated or buried with utmost esteem.

Authors Contribution:
Quratulain Javaid: Substantial, (direct, intellectual) contribution to the conception, design, analysis and/or interpretation of data

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Original Article **Open Access**

Estimation of Oxidant and Antioxidant Levels in Hemodialysis Treated end Stage Renal Disease Patients and Comparison with Normal Population

Sadia Rehman, Santosh Kumar, Om Lal, Suniya Rehman, Hasan Ali, Fatima Rehman

ABSTRACT:

Objectives: To estimate the plasma oxidant and antioxidant levels in hemodialysis treated end stage renal disease patients and to match them with normal population.

Study Design and Setting: It was a comparative prospective study. This study was carried out at Jinnah Post Graduate Medical Center Karachi, from January 2018 till December 2018.

Methodology: The hemodialysis patients (group B) were selected from the Dialysis Center of JPMC Karachi whereas the controls (group A) were recruited from normal healthy population. Consecutive sampling technique was used. The cases taken were receiving maintenance hemodialysis thrice a week. Antioxidant levels were determined by estimating plasma superoxide dismutase (SOD) while oxidant levels were estimated by detection of serum malondialdehyde (MDA) and compared with the levels of control group.

Results: The mean superoxide dismutase level in control group was 108.53±19.44 while mean SOD levels in hemodialysis group was 46.20±19.18. . In control group mean MDA was 10.87±3.04, and in hemodialysis group mean MDA was 31.01±8.48.This results show the increased risk of oxidative stress resulting in complications in hemodialysis patients.

Conclusion: Antioxidant levels are reduced in hemodialysis patients as compared to the normal population while the oxidant levels are much increased in hemodialysis group. This imbalance contributes to the oxidative stress related complications taking place in these patients. This study will help the nephrologist to elaborate the protective role of antioxidant administration in oxidative stress that can improve the cardiovascular mortality rate in hemodialysis treated end stage renal disease.

Keywords: Antioxidants,End Stage Renal Disease, Hemodialysis, Oxidants, Oxidative Stress.

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INTRODUCTION:

Development of chronic renal failure has become serious problem all over the world. Chronic renal failure (CRF) is characterized by slow and progressive decline in the kidney function. Haemodialysis (HD) is the commonest renal replacement therapy in developing countries and has been reported to induce repetitive bouts of oxidative stress primarily through membrane bio-incompatibility. While CKD is a pro-oxidant state, HD may contribute significantly to oxidative stress in these patients.[1] Oxidative stress in chronic kidney disease (CKD) results from increased production of prooxidant molecules such as reactive oxygen species (ROS) and nitric oxide (NO), insufficient clearance of oxidative products, and deficient antioxidant defense mechanisms.[1]

Total antioxidant capacity is described as the sum total of all endogenous and exogenous antioxidants in a medium.[2] There exists an equilibrium among the free radicals and antioxidants in humans.[2] The imbalance between these systems is called oxidative stress. Oxidative stress occurs due to disturbance in the equilibrium between the pro-oxidant and antioxidants which results in the formation of reactive

oxygen species (ROS) and free radicals which cause damage to the body cells. Reactive oxygen species (ROS) are highly reactive molecules derived from molecular oxygen.[3] These ROS include hydrogen peroxide (H_2O_2) and superoxide anion (O_2^-).[4]

The half-life of free radicals is very short that is only a few seconds so the clinical evaluation of oxidative stress is done by estimating stable oxidized compounds or their derivatives.[5]

Malondialdehyde (MDA) is a low molecular weight, 3-carbon containing aldehyde with the $\hat{E}CH_2(CHO)_2$ and a byproduct of lipid metabolism in the body. MDA is commonly used as a biomarker of lipid peroxidation.[6] Reactive oxygen species causes the degradation of$\hat{E}$, causing lipid peroxidation and formation of MDA. This compound also forms mutagenic DNA adducts when it reacts with and in DNA. Thus the levels of production of MDA can be used as a biomarker to estimate the level of$\hat{E}$.[7]

Oxidative stress leads to over production of free radicals and hence more MDA is formed.[8] Certain theories explain this reduction in antioxidant levels; these include the uremic state itself, the impermeability of the dialyzer membrane to antioxidants and the bacterial contamination of the dialysate.[10] Superoxide dismutase (SOD) is one of the most important enzymatic antioxidants and a major defense system against oxidative damage. A recent study suggests that superoxide dismutase is a major antioxidant enzyme, involved in managing oxidative stress during progressive renal injury.[9] SOD is involved in prevention of atherogenesis by causing inhibition of oxidative damage caused by O_2^-, inhibition of O_2^- mediated removal of NO and therefore enhancing endothelium-dependent vasorelaxation,$\hat{E}$inhibiting the adhesion of leukocytes and altered vascular cellular responses.[10] Hence the deficiency of SOD acts as an important cause in the development of oxidative stress related complications in hemodialysis patients. When SOD levels were measured in patients with chronic inflammation, their enzyme activity was significantly lower when compared to healthy individuals. Researchers suggest new therapeutic possibilities that target SOD antioxidant pathways so that pro-inflammatory responses can be limited.[10]

New pharmacological antioxidant therapies and dialysis strategies can help in reducing the complications of oxidative stress in hemodialysis patients. The presence of oxidative stress even before the initiation of maintenance dialysis therapy suggests that therapeutic antioxidant strategies should preferably be developed very early in the course of renal failure.

Hence the current study is planned to estimate the levels of superoxide dismutase and malondialdehyde in hemodialysis patients in order to access their antioxidant and oxidant levels and to match these levels with the control group.

METHODOLOGY:

This comparative prospective, hospital based study was carried out in Nephrology Department Ward 22 of Jinnah Post Graduate Medical Centre, Karachi from January 2018 till December 2018 in collaboration with the Department of Biochemistry, Basic Medical Science Institute of JPMC Karachi. Ethical permission for the present study was taken by the Institutional Review Committee JPMC, Karachi dairy no: NO.F.2-81-IRB/2018-GENL/5173/JPMC. Informed consent was obtained from all study participants and the data obtained from the study subjects was kept confidential. Open epi website calculator was used for calculation of sample size by using a reference study carried out in Shanghai, China.[13] A sample size of 120 subjects was calculated which was further divided into two groups. Group A (control group) included 60 normal controls from healthy population and Group B (hemodialysis group) included 60 patients receiving maintenance hemodialysis for more than 2 years duration and were not on any supplementary antioxidant therapy.

The subjects' age, gender, duration of hemodialysis and drug history was noted. Height, weight, BMI, blood pressure (BP), pulse, temperature, respiratory rate and previous medical record were also noted. A written informed consent was taken from every subject. A pre formed proforma was used as a data collection tool.

The inclusion criteria included subjects both males and females with age between 18 to 50 years, and receiving hemodialysis therapy for more than 2 years and not taking any supplementary antioxidants.

The exclusion criteria were patients suffering from any other chronic inflammatory state like malignancy or tuberculosis and patients receiving hemodialysis due to acute renal failure and all subjects having history of any previous cardiovascular disease or event and all subjects not willing to participate in the study were excluded from the study.

Non probability consecutive sampling technique was used for the recruitment of study subjects. Biochemical parameters (serum malondialdehyde, plasma superoxide dismutase) were measured in both the study groups.

BMI was calculated by using the formula for BMI i.e weight (kg)/height (m^2)

Levels of SOD were measured by using reagent method (method of Kono, 1978)

The malonldialdehyde (MDA) was estimated in the form of thiobarbituric acid reacting substances (TBARS) by the method of Okhawa et al, 1979.

Data was analysed using SPSS 23. Descriptive statistics of categorical data were presented as frequencies and percentages.

RESULTS:

Results showed that mean age of control group samples (Group A) was 34.67±7.73, mean BMI was 23.47±3.26,

mean systolic blood pressure was 107.33±9.80 mmHg, mean diastolic blood pressure was 66.33±8.09 mm Hg, mean weight was 66.10±7.75 Kg, and mean height was 1.69±0.12 meters whereas hemodialysis group patients (group B) had mean age 43.20±4.66 years, mean BMI was 22.21±4.21, mean systolic blood pressure was 159.0±12.42 mmHg, mean diastolic blood pressure was 93.67±10.66 mmHg, mean weight was 64.67±6.13 Kg and mean height was 1.63±0.12 meters. The mean superoxide dismutase level in control group was 108.53±19.44 while mean SOD levels in hemodialysis group was 46.20±19.18. In control group mean MDA was 10.87±3.04, and in hemodialysis group samples mean MDA was 31.01±8.48. The mean difference in serum MDA concentration was found statistically significant with p-value less than 0.01.

Table 1: Comparison of Anthropometric Measurements among study groups

Characteristics	A (controls) (n=60)		B (hemodialysis group) (n=60)		p value
	Mean	**SD**	**Mean**	**SD**	
Age (years)	34.67	7.73	43.20	4.66	0.20
Body Mass Index (kg/m2)	23.47	3.26	20.21	4.21	<0.01*
Systolic Blood Pressure	107.33	9.80	159.00	12.42	<0.01*
Diastolic Blood Pressure	66.33	8.09	93.67	10.66	<0.01*
Weight (kg)	66.10	7.75	59.19	6.13	<0.01*
Height (m)	1.69	0.12	1.63	0.12	0.20

*p<0.05 was considered statistically significant using t-test

Figure 1: Comparison of mean plasma superoxide dismutase (SOD) levels between studied groups

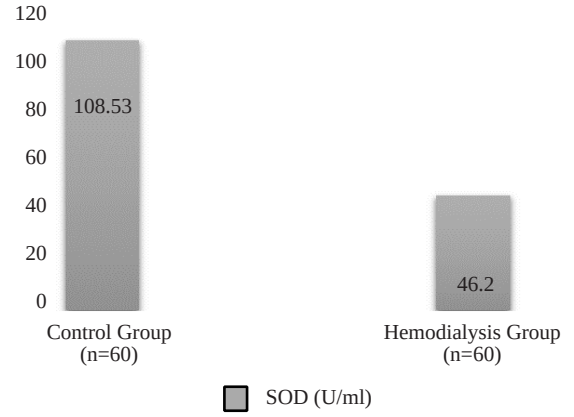
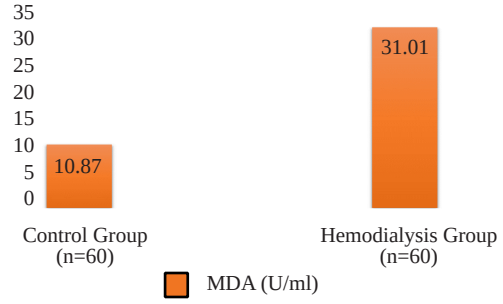


Figure 2: Mean comparison of serum malondialdehyde (MDA) levels among studied groups



DISCUSSION:

Oxidative stress is a major complication in patients treated with hemodialysis. The dialysis procedure itself leads to a decrease in the antioxidants and an increase in oxidative molecules, thus aggravating the already present oxidative stress.[22] Uremic state along with dialysis procedure is a major risk factor for oxidative stress related complications in these patients. The present study was designed to estimate oxidant and antioxidant levels in hemodialysis treated end stage renal disease patients. Significant results were seen during the comparison between the studied groups.

The aim of our study was to estimate the antioxidant and oxidant levels in hemodialysis treated end stage renal disease patients. For this purpose we estimated serum malondialdehyde and plasma superoxide dismutase levels. We found a significant increase in the mean systolic BP (159± 12.42mmHg) and diastolic BP (93.67±10.6mmHg) of the hemodialysis patients as compared to the control group (107.33±9.80mmHg) and (66.33±8.09mmHg) respectively. Our results are similar to the findings of Wang *et al* [14] who reported a mean SBP of 143.2 ± 32.7mmHg and mean DBP of 79.0 ± 15.9 mmHg among hemodialysis patients. This increase in blood pressure can be due to fluid overload, over-activity of renin angiotensin system, erythropoietin administration and enhanced stimulation of the sympathetic nervous system.[15] No significant difference in the mean ages among the two groups was found. A significant decrease in the weight and BMI was seen in the hemodialysis patients. This is similar to the findings of Rysz *et al.*[16] Li *et al* [17] who also reported a decrease in BMI in hemodialysis treated patients. The decreases in BMI may be due to protein energy wasting, chronic inflammation, repeated infections and restricted diet in hemodialysis patients.[18] Moreover the uremic state and chronic illness also contributes to anorexia, nausea and vomiting in these patients.[11,12,19]

We also explored the relationships between oxidants and antioxidants. Our study showed that very low levels of SOD were found in hemodialysis group (46.2U/ml) as compared to the control group (108.53U/ml). The possible mechanism behind this low level depends on several factors, such as age, creatinine clearance, the duration of dialysis, arteriosclerosis, imbalance of hemostasis and coagulation factors. Chronic inflammation and uremic state contributes to the formation if reactive oxygen species which causes an imbalance between oxidants and antioxidants. Moreover the selective permeability of the dialyzer membrane to antioxidants also significantly contributes to the decreased levels of antioxidants in these patients as the antioxidants are decreased after every cycle of dialysis. Our results are similar to the published work of Rysz *et al* [16] and Kundoor *et a.l*[20] Marjani *et al* [21] also reported a decrease in the

antioxidant levels in hemodialysis patients. These findings of our study and international studies show that hemodialysis patients are subjected to a constant reduction in antioxidant levels due to repeated infections, dietary restrictions, removal of antioxidants during dialysis procedure, impermeability of the dialyzer membrane to antioxidants and enhanced inflammatory cascade. Decreased SOD activity may also be due to a direct inactivation of the enzyme by its product hydrogen peroxide, or by superoxide anion itself. This reduction in antioxidants is a major factor that leads to oxidative stress in these patients. The morbidity and mortality can be much reduced if this imbalance is treated prior to development of complications.

Serum malondialdehyde was also significantly increased in hemodialysis group (31.01 U/ml) as compared to control group (10.87U/ml). Kundoor *et al* [20] and Barati *et al* [22] also described a significant increase in serum MDA in hemodialyzed patients as compared to controls. The possible mechanism which leads to an increase in MDA levels is that ROS activate phospholipase A2 causing peroxidation of many mediators by arachidonic acid which is finally metabolized to MDA. As MDA is a biomarker of oxidative stress hence elevated MDA levels indicate excessive reactive oxygen changes and oxidative changes in low density lipoprotein molecule and other lipid and protein molecules. This could be due to the fact that hemodialysis by the application of a modified circulation and forced passage of blood through a number of filters, activates, endogenous inflammatory mechanisms and induces chronic release of molecules resulting in an increased production of reactive oxygen species.[22] The enhanced oxidative stress in hemodialysis patients is caused due to poor intake of exogenous antioxidants in diet, formation of oxidative products and loss of antioxidants during hemodialysis. The levels of MDA rise with repeated cycles of dialysis. This relationship of repeated dialysis cycles and MDA concentration was shown by Hou *et al* [23] in his study.

These factors are linked to the development of atherosclerosis and chronic inflammation and lead to cardiovascular complications in these patients. Yeter *et al* [24] studied the effects of dialysis membranes on inflammation and oxidative stress. He concluded that increased oxidative stress in this patient population is multi-factorial and is affected by other factors other than inflammation which include the dialysis membranes also. Lestaringsih *et al* [25] studied the relationship of oxidative molecules with the development of atherosclerosis in hemodialysis treated patients and showed that increase in oxidative molecule lead to excessive formation of oxidized LDL which leads to development of atherosclerosis.

Our data led us to conclude that oxidative stress is enhanced in hemodialysis patients which may contribute to the development of dialysis-related complications such as cardiovascular disease, anemia etc. The administration of antioxidants plays a protective role against oxidative stress by neutralizing the harmful effects of oxidative molecules, however, it has still not been adopted as a regular treatment protocol in clinical practice. Antioxidant supplementation with vitamins A, C, and E; beta-carotene; or N-acetylcysteine (NAC) seems to be beneficial in decreasing cardiovascular risk in hemodialysis patents. Vitamin E is a powerful antioxidant exerting anti-inflammatory properties; it has been shown to interfere with cell membrane lipid peroxidation. Observational clinical studies have shown that the intake of vitamin E (more than 100 IU/day), which inhibits oxidized LDL formation by hindering lipid peroxidation, reduced the rate of coronary events in hemodialysis. Vitamin C plays a significant antioxidative role as it can reduce ROS levels, thus providing protection against kidney oxidative damage and helping to maintain vascular and endothelial function. Wang et al.[25] demonstrated that vitamin C (ascorbic acid) diminished oxidative damage, inflammation and renal injury in ischemia nephrotoxic acute kidney injury and rhabdomyolysis-induced renal injury. More prospective studies are required to elaborate the protective role of antioxidant administration in oxidative stress that can improve the cardiovascular mortality rate in hemodialysis treated end-stage renal disease. More over the oxidative stress parameters in these patients need to be monitored to avoid the possible outcomes of oxidative stress. Dietary guidelines should also be developed to ensure the intake of adequate vitamins and minerals in these patients. This study will help the nephrologists to elaborate the protective role of antioxidant administration in oxidative stress that can improve the cardiovascular mortality rate in hemodialysis treated end-stage renal disease. We recommend the addition of antioxidants in the treatment regimes of these patients.

The limitations of the study were small sample size and limitation to only one dialysis center. It was a self-funded study so the scope of study could not be extended beyond one study setting. Also, since non-probability sampling technique was used, it was difficult to make inference about the entire population. Other markers of oxidative stress like CRP, glutathione peroxidase and myeloperoxidase enzyme could not be included due to budget limitations. More studies with bigger sample size and multiple centers are required for further investigation of these findings. More markers of oxidative stress should be explored. Interventional studies using supplementary antioxidants should be carried out to further validate the protective role of antioxidants in hemodialysis patients.

CONCLUSION:

Antioxidant levels are reduced in hemodialysis patients resulting in elevated oxidant levels in hemodialysis patients as compared to control group. This decrease contributes to the oxidative stress related complications which are the major factors of mortality in these patients.

Authors Contribution:
Sadia Rehman: Principal researcher
Santosh Kumar: Research supervisor
Om Lal: Data collection and analysis
Suniya Rehman: Literature review and writeup
Hasan Ali: Approval of draft and literature review
Fatima Rehman: Statistical analysis

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Original Article **Open Access**

Efficacy of Sofosbuvir and Ribavirin in Children Presenting with Hepatitis C at Tertiary Care Hospital, Faisalabad

Naginal Shahzadi, Naureen Kanwal Satti, Huma Arshad, Nadeem Hashmat

ABSTRACT

Objectives: To assess efficacy, safety, and outcome of combination of Sofosbuvir and Ribavirin in various genotypes, in children with hepatitis C infection.

Study design and setting: It was a quasi-experimental study, conducted at the Gastroenterology and Hepatology Department, Children Hospital Faisalabad, from August 2017 to August 2021.

Methodology: 50 confirmed cases of HCV infection aged 5 to 18 years, were given an oral dose of Sofosbuvir and Ribavirin daily for 12 weeks. PCR was assessed at 4 weeks (for Rapid Viral Response (RVR)) and repeated at 8 weeks and 12 weeks (for Early Viral Response (EVR)) and again 12 weeks after the completion of therapy for Sustained Viral Response (SVR)). Primary outcome was the number who achieved an SVR at 12 weeks (SVR12) after completion of treatment with a viral load below quantitation level.

Results: Genotype 3 was found in 80% , type 1 in 6% , type 2 in 4% and 10% were untypeable. All children were PCR positive at presentation; 96% became PCR negative at 4 weeks (RVR), while 100 percent were negative at 8 weeks, 12 weeks (EVR), and SVR 12 weeks after completion of 12 week course was 100%.

Conclusion: Although majority of patients were Genotype 3, 12 week course of Sofosbuvir and Ribavirin of hepatitis C-infected children was highly effective, with 100 percent PCR-negative cases at 8 weeks and 12 weeks with only minor side effects, and, SVR of 100% twelve weeks after completion of therapy.

Keywords: Chronic Hepatitis C, Children, Antiviral, Sofosbuvir, Ribavirin

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INTRODUCTION:

Hepatitis C (Hep C) infection is a global health burden in children as well as adults. It is estimated that 70 million people, or 1% of the population, are infected with hepatitis C worldwide [1]. In Pakistan 6.5% population is afflicted with Hep C with prevalence in children of 1.6%.[2] Chronic Hep C virus infection is the most common cause of liver transplantation globally and its importance is signified by 2016 WHO strategy to reduce Hep C infection by 90% by 2030.[3]

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Hep C virus has 6 genotypes. The most common worldwide is type 1 with a prevalence rate of 49% globally, followed by genotypes 3, 4, and 2 with prevalence rates of 17.9%, 16.8%, and 11% respectively. The rest of the genotypes account for less than 5%.4 On the other hand, the most common genotypes prevalent in Pakistan are 3 and 3 b, followed by 1a, 2a, and untypeable.[5]

The routes of spread of hepatitis C in Pakistan include reuse of syringes, surgical procedures, dental extractions, blood transfusions, perinatal transmission, and reuse of instruments at barbershops. Chronic disorders requiring repeated blood component transfusions have an alarmingly high prevalence of Hep C; a meta-analysis done on 5789 beta-thalassemics revealed a prevalence of 36.21%6

Diagnosis of Hep C virus requires PCR to confirm on Serology Positive patients. Genotyping is done to further categorise into one of the 6 genotypes.

The importance of treating hepatitis C disease in childhood cannot be overemphasised due to its impact on halting progression to chronic liver disease in later years.

Until 2017, pegylated interferons and ribavirin were the only approved treatments for children with hepatitis-C. This

treatment regime has several drawbacks, including duration of treatment, compliance, and parenteral use for a longer duration than Direct Antiviral Agents (DDA). DAAs were approved for children above 12 years of age by the FDA in 2017.Recently, the FDA has approved the use of Sofosbuvir and Velpatasvir in children 6 years and older and weighing at least 17 kilograms with any of the genotypes of hepatitis C.[7] At the time of writing of this account, WHO has already recommended conditional use (due to very low certainty of evidence) of combination of DAAs from 3-5 years of age.8 Sofosbuvir and Ribavirin is the first combination approved for use in children. Limited local data is available regarding its efficacy and safety in children. A study done in The Children's Hospital Lahore showed excellent results of Sofosbuvir and Ribavirin combination in children in genotypes 1 and 3 with sustained virologic response of 97%.[9] Recent treatment recommendations in all children older than 03 years are use of interferon free directly acting antiviral regimens. First line combinations are Glecaprevir and pibrentasvir for 08 weeks in children 12 years and older and Sofosbuvir and Velpatasvir Ribavirin for 12 weeks in children 03 years and older. These combinations have good virological response across genotypes. All patients older than 03 years having positive HCV detection by PCR should be treated regardless of initial viral load, genotype and liver biochemistry.[10]

The introduction of DAAs has dramatically changed the treatment outcome of hepatitis C in children. In Pakistan Genotype 3 is the predominant genotype, seen in the large majority of patients. Data on the use of Sofosbuvir and Ribavirin in adults is available in Pakistan, but there is limited data on its use in children. The available studies, globally and locally, however have shown excellent results with a combination of Ribavirin and Sofosbuvir.?'[11] Both drugs are used in combination and are safe in children with fewer side effects. Standard recommendation for genotype 3 is a regimen of 24 weeks, but since RVR and EVR are excellent in genotype 3 patients in studies done to date, we assume that if we give a regimen of 12 weeks only, this effect will be maintained in SVR 12 as well. Therefore we planned to do a 12 week treatment study. This may increase confidence in retaining Ribavirin in regimens used to treat Hep C in children and increase its acceptability because of short duration.

METHODOLOGY:

A Quasi-experimental study was conducted from August 2017 to August 2021. The research was carried out in the Gastroenterology and Hepatology Department of the Children Hospital and Institute of Child Health, Faisalabad, to investigate the efficacy, safety, outcome, and complications profile of treatment with Sofosbuvir and Ribavirin for 12 weeks in Hepatitis-C confirmed cases.

The study was approved by the Ethical Review Board of The Children Hospital and Institute of Child Health, Faisalabad bearing ERC number "33" dated 10-11-2020. Informed written consent was taken from parents or guardians of all children prior to enrolment in this study. Eligibility criteria for patients to be enrolled for the study included; age above 6 years (> 5 completed years) to 15 years, the evidence of chronic HCV infection with any genotype (positive Qualitative PCR) and no prior treatment at any centre for HCV. Patients who had decompensated liver disease, co-infection with Hepatitis A, B or HIV, end stage renal disease or any history of psychiatric illness, were excluded from the study. Children who had previously received any treatment for HCV infection were also excluded from the study.

Patients were enrolled using the Consecutive Sampling technique. Openepi.com Sample Size Calculator was used to calculate the sample size keeping confidence interval 95%, absolute precision 5%, and anticipated efficacy (sustained virologic response at 12 weeks after completion of therapy) 97%.[11] Therefore Effect Size was 97. Total sample size thus calculated was 10 by Kelsy, 8 by Fleiss and 12 by Fleiss with CC. Our sample size however was 50 cases, well above the calculated numbers.

A detailed proforma was filled out, which recorded a detailed history, all clinical features of chronic liver disease, extrahepatic manifestations, disease severity, and the exclusion of other causes. Other causes of liver disease were ruled out using biochemical tests and imaging. To rule out concomitant infection, baseline tests including hepatic viral markers for HBV, HCV, HAV, and HIV were performed. Data on HCV transmission routes, risk factors, lab work, and previous treatment received by patients were collected.

All enrolled patients were followed up at 04 weekly intervals. The history of new symptoms and clinical signs, as well as any side effects related to the medication and the disease itself, were recorded at four-week intervals during the course of treatment. If advanced liver disease was suspected, CT scans, MRIs, and endoscopies were performed to rule out the disease and its complications.

Patients were given Sofosbuvir 400 mg once daily and Ribavirin at a dose of 10-15 mg per kg twice daily for 12 weeks irrespective of the genotype. All children were closely monitored, and a 4-week follow-up was performed, which included a detailed history of clinical signs and symptoms after treatment, as well as lab work. A CBC was performed weekly to assess low Hb levels, as well as LFTs, serum albumin, INR, PT, and APTT. PCR was assessed at 8 weeks and repeated at 12 weeks. Finally, PCR was done 12 weeks after the treatment finished. The primary outcome was efficacy, which was defined as the number of patients who achieved a sustained viral response 12 weeks after the medication stopped (SVR12), which was the treatment's end point and defined as a negative PCR or a viral load less

than the quantitation level. Safety was defined as no or minimal nonspecific side effects during a 12-week treatment period that did not necessitate drug discontinuation.

The data was analysed with SPSS 20.0, and the study's findings were subjected to qualitative and quantitative assessments. A statistically significant P-value was defined as less than 0.05. Demographics, disease presentations, reaction to therapies, changes in lab values, compliance, and complications of disease or treatment failure were all assessed quantitatively and qualitatively.

RESULTS:

In total, 50 children of both genders participated in the study. The group consisted of 38 males (76%) and 12 females (24 %). The male-to-female ratio was 3.2:1. The median age was 7.2 years. The most common genotype was type 3, which was found in 80% of patients, followed by type 1, which was found in 6% of patients and type 2 in 4% of patients. In 10% of patients, genotype could not be determined and were labelled untypable (Figure: 1).

At the time of the presentation, all of the children tested positive for PCR. 56 % cases were admitted from Outpatient Department and 44% were referred from Hematology and Oncology ward. Blood transfusion was the most common mode of Hep C transmission, accounting for the vast majority of cases. Children with thalassemia made up 74% of the cases. Bleeding and platelet function disorders accounted for 12% of all cases; 2% had previous abdominal surgery, and 2% had perinatal transmission, 4% of cases were in remission from leukaemia and the aetiology could not be determined in remaining 6% of cases.

A staggering 86% of cases had comorbidities. 80% had chronic blood transfusion requirements, including thalassemia, leukaemia, lymphomas, bleeding disorders and platelet disorders, which still speaks volumes about the importance of routine blood screening before transfusion.

ALT was raised in 97% of cases, and the mean ALT at the beginning of treatment was 67, while post treatment ALT became normal in all the cases. Mean ALT post treatment at 12 weeks was 17.6 and the difference after treatment was significant ($p < 0.001$). Another significant finding was a drop in haemoglobin from a mean of 11.6± 1.42 at the start of treatment to 10.10 ±1.45 ($p < 0.002$).

At 4 weeks, 96% of patients were PCR negative, and 100% were negative at 12 weeks of treatment. SVR (Negative PCR at 12 weeks after stopping treatment) was also 100% (Figure: 2). Poor appetite was observed in 76.6 percent of cases, weakness and lethargy in 64% of cases, vomiting in 16% of cases, and headache and abdominal pain in 56% and 66% of cases, respectively.

DISCUSSION:

The success of DAAs in adults with hepatitis C has opened up new possibilities for paediatric hepatitis C treatment. For

Figure 1: HCV Genotypes

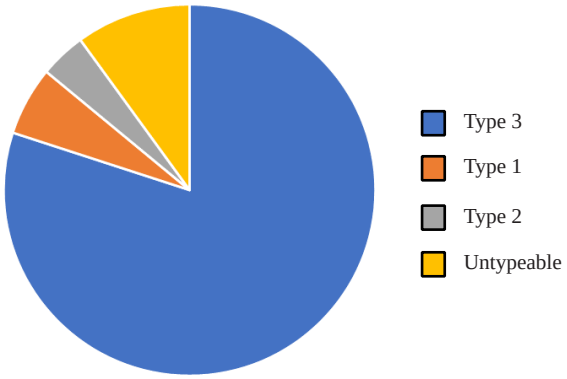
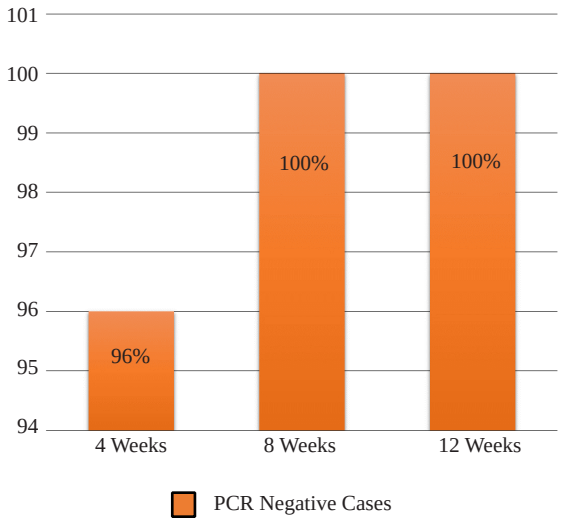


Figure:2 Percentage of PCR Negative cases at 4,8 and 12 weeks



children over age six, they are more powerful and safer than conventional therapy methods. In children, Ribavirin and Sofusbuvir have been used in a few trials, and have resulted in high SVR post therapy with minimal adverse effects since the introduction of DAAs. Trials have shown a 98% effectiveness rate as compared to 60 to 70% efficacy with interferons. The traditional interferon treatment regimen has a number of side effects, including effects on children's growth and low success rates in genotypes 1 and 4, which have been successfully treated with DAAs [12,13].

The average age in our sample was 7.2 ± 0.5 years, with a male to female ratio of nearly 3:1. According to a recent assessment of the literature, the average age reported in other studies was 9 and 10 years, respectively. [13] In our research, type 3b was the most prevalent genotype, but studies show that genotype 3 is more common in Asia and genotype 1 is more common in Europe and America.[14]

In our study, blood transfusion was identified as the leading cause of hepatitis C transmission, with perinatal transmission having the lowest frequency. In a study conducted in Lahore, Pakistan, 51% of childhood hepatitis B and Hepatitis C infection was associated with history of past blood

transfusion. Underlying pre-existing medical conditions were acute lymphoblastic leukaemia (15%) and thalassemia (9%).[15] These results closely concord with the results of current study and are indicative of use of less effective blood screening methods being used in our country. Contrarily, most of the industrialized countries that employ highly effective screening methods have largely eradicated blood borne transmission of viral hepatitis. As a result, perinatal transmission is the predominant mode of transmission industrialized nations .[14]

Based on our study, 96% of cases had a negative PCR test at 4 weeks, and 100% of cases had a negative PCR test at 12 weeks and SVR was maintained at 100% of EVR. On the other hand, sustained viral response (SVR) was achieved in 99% of cases at 4 weeks and 100% of cases at 12 weeks in a similar studies using Ledipasvir-Sofosbuvir without Ribavirin and with it [12-13]. In contrast to our findings, the use of interferon resulted in SVR of 79% in type 1 and 88% in genotypes 2 and 3. This demonstrates a significant difference in the outcomes of two different regimes.[16] The results of this study strongly favour use of interferon free regimens because of their high virologic response rate as well as markedly superior side effect profile.

In our study,76% of patients reported poor appetite, followed by fatigue and weakness in 64%, vomiting in 16%, and headaches and abdominal discomfort in 56% and 66%, respectively; all these resolved in a short duration. A similar study in children reported vomiting as the predominant side effect in 46% of cases below 6 years and 32% in children above 6 years, followed by diarrhoea and headache in 39% and 29% cases respectively. Other studies reported fatigue, headache, abdominal pain and nausea as main side effects of the combination therapy.[17-20]

The results of our study show that hepatitis C can be effectively treated in children between 5 to 18 years of age with a 12 week regimen of Sofosbuvir plus Ribavirin with minimal side effects. The limitation of our study was limited data based on single centre. There is a scarcity of data in the paediatric literature, indicating the need for larger multicentre studies in Pakistan and other countries. More studies should be done with 12 week therapy; these will help improve the quality of care for children infected with hepatitis C while also reducing the financial burden on families.

Another limitation of our study was duration of treatment of 12 weeks instead of the usual 24 weeks; this was due to time constraint and in engaging patients for a longer duration. However this same limitation seems to have emerged as the strong point in that a shorter duration of therapy may be as effective as the longer one. More studies need to be done to strengthen these findings.

CONCLUSION:

Twelve weeks Sofosbuvir and Ribavirin treatment of hepatitis C-infected children was highly effective, resulting in 100% sustained virologic response; and for genotype 3 (which was 80% of our patients), this shorter regimen was as good as 24 weeks regimen.

Authors Contribution:
Nagina Shahzadi: Acquisition of data, Case Management, Original Draft Preparation, Revising it critically for important intellectual content, Supervising, Final approval of the version to be submitted
Naureen Kanwal Satti: Conception and design, writing original draft, visualization, revision, final approval of the version to be submitted
Huma Arshad: Revising it critically for important intellectual content, final approval of the version to be submitted
Nadeem Hashmat: Review and editing, revising it critically for important intellectual content, conception and design, final approval of the version to be submitted

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Original Article **Open Access**

Acanthosis Nigricans in Adolescents versus Adults; Association with Obesity, Diabetes and Hypertension

Furquana Niaz, Nadia Shams, Naresh Kumar, Irfan Sheikh, Nayer-ul-Islam, Najia Ahmed

ABSTRACT:

Objectives: Acanthosis nigricans presents as black velvety plaques on flexural surfaces which is associated with obesity, T2DM and HTN. To study sites and types of AN (Acanthosis Nigricans) in adolescents Vs. adults and its associations.

Study design & setting: This cross sectional study was conducted from IstMar-31stAug 2021 at RIHS Islamabad after ethical approval.

Methodology: Adolescents and adult cases of both the genders with AN were *included* by convenience sampling. Critically ill cases, endocrine disorders, pregnancy and malignancy were *excluded*.57 adolescents and 57 gender matched adults were included. After the detailed clinical evaluation, BMI, waist circumference, sites and types of AN were documented. Blood sugars and workup for PCO's, suggested. Data was analyzed by SPSS 21. Chi-square test and Mann-Whitney-U test applied.

Results: Out of 114 cases,77(67.5%) were females. The mean age was 17.99+14.18 years and mean BMI was 31.63+6.92 kg/m^2.Obesity was observed in 75(65.8%); 44(77.2%) adolescents Vs. 31(54.4%) adults *(p=0.010).* Mean waist circumference was 37.03+3.74 inches.AN at Neck 113(99.1%) and benign AN 111(97.4 %) were the most frequent. The types of AN were associated with obesity, DM 31(27.2%) and HTN 27(23.7%) ($p<0.05$).

Conclusions: Benign and HAIR-AN were most frequent. Adolescents with AN have significantly higher obesity than adults. HTN was significantly higher in adults. DM in AN was observed regardless of age group. It is suggested to screen all AN cases regardless of age or gender for obesity, HTN and DM. Early diagnosis may contribute to improve quality of life, prevent morbidity of systemic diseases and improve outcome in AN cases.

Keywords: Acanthosis nigricans, BMI, HAIR-AN syndrome, Obesity, PCO

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INTRODUCTION:

Acanthosis nigricans (AN) is an asymptomatic skin condition which presents as brown/black rough velvet like thickening of skin that involves intertriginous areas and mucosal surfaces including oral mucosa, lips, conjunctiva and vulva.[1-3] Dr. Paul & Pollitzer documented the 1st case of AN[1,4], while Robinson & Tasker documented its relation with obesity. The prevalence of pediatric obesity from 2-19 years of age is 10.4%-15.5 and in male children is 26.7% and 34.6% in females which increases risk for DM.[1,5] The prevalence is 62% in children of any race with BMI>98th percentile and in adolescents 66% with gross weight of more than 200%.[1,4] The American Medical Association (AMA) declared obesity to be "A category disease".[5]

AN can present from birth to adolescence that impact on health of individuals[6] and causes psychological disturbance due to unsightly appearances.[5] Stuart et al proposed Acanthosis score in literature ranging from 0 to 4, based on degree of involvement while Hud et al provides severity of AN on the basis of texture. Burke et al proposed a visual scale for severity of AN on neck and its correlation with BMI. Kobaissi et al criteria was based on severity of AN.[5]

The three classifications of the types of AN include [2]Curth

classification (benign, malignant and syndromic AN), Hernandez-Perez (simple and paraneoplastic AN), Schwartz classification (Benign, associated with obesity, unilateral, syndromic, mixed, drug induced, acral and malignant AN).[2]

Benign AN is associated with IR.[1]Obesity associated AN is associated with obesity in prepubertal children. Among children and young child at risk for overweight if BMI > 85th percentile but < 95th percentile for that age but if BMI till 95th percentiles are consider as overweight.[7]This can be indicator of obesity, hyperinsulinemia, IR and T2DM and detected by increased WC .[6]AN may appear prior to obesity[5] Obesity in adolescence increases the risk of heart diseases.[8]Regarding pathogenesis of AN, hyperinsulinemia leads to activation of IGF that causes proliferation of dermal fibroblast and epidermal keratinocytes. Friction and sweating may also causes AN.[6]Obesity causes negative stereotypes on cognitive functions and intelligence .Weight bias, stigmatization and discrimination which leads to physical and psychological hazards.[5]

The type A insulin resistance syndrome (HAIR-AN syndrome).[1]is associated with PCO.[1,4,9]The type B insulin resistance syndrome presents as periocular AN.[1,4]Acral AN is associated with NFP and dermato-fibrosarcoma.[1]The Unilateral/Neavoid AN has no associations.[1]Facial AN could be manifestation of impaired glucose tolerance, increase waist hip ratio and BMI. Mixed type AN, if >1 type of lesions are present in one patient. Drug induced AN is caused by nicotinic acid, OCP, corticosteroids and fucidic acid.[1,4]The Malignant AN is associated with gastric carcinoma[4]presents with Tripe palms.[8]

Obesity can be associated with AN and MetS like IR, hyperinsulinemia, acne, T2DM, PCOs, HTN and dyslipidemia.[2,3,5,9,10] AN is a good clinical indicator for impaired glucose tolerance. American Academy of pediatrics suggested AN being the evidence of IR clinically while ADA recommended AN as a risk factor for cardio metabolic problems in asymptomatic overweight children.AN in the neck and axillae is non-invasive, valuable and simple screening tool to determine T2DM and other comorbidities.

Obesity leads to risk of high BP and BMI is a good indicator for obese and overweight.[7]So far, very few local studies are available regarding AN associated with obesity (increased BMI and WC) HTN and T2DM.In our study we determined the frequency of AN in obese adolescents Vs adults in accordance with BMI and WC. This study will help us to identify the cases of AN to be screened for obesity and its associations like T2DM, HTN on the basis of gender, age and types of AN. Also, this study may help us to develop a clinical approach to diagnose and manage obesity, DM and HTN that are the systemic associations via skin presentation.

METHODOLOGY:

This hospital based cross sectional study enrolled AN cases from outdoor clinic Department of Medicine Rawal institute of Health Sciences Islamabad after institutional review board approval (IRB letter number: RIHS-REC/059/21).Patients were selected by non-probability convenience sampling over five months duration (1st March to 31st Aug 2021).The sample size calculated to be 114 cases by WHO calculator(17.5% prevalence of acanthosis nigricans,5% precision and 95% CI).Cases referred to Medical Department from pediatrics OPD with clinical diagnosis of AN were included after informed consent (from patients and guardian).**Inclusion criteria:** Children & adolescents; both the genders of age group of 10-48 years. **Exclusion criteria:** Critically ill, underlying Addison's disease, pregnancy and malignancy. 57 adolescent AN cases were selected and 57 gender matched adults.

After the detailed history regarding onset, progression and duration of pigmentation and systemic co-morbidities like T2 DM, HTN and PCOS were documented. Dietary habits, drug history, personal, family history inquired. Menstrual and reproductive history were taken in females. General physical, systemic and detailed skin examination (neck, axillae, groin, sub mammary region, palms, soles and all mucous membranes checked) for AN. Weight in kg was measured by platform type digital electronic scale by keeping patients barefoot and height in meters measured by keeping patient upright with united foot. BMI calculated by CDC child and teen BMI calculator in which mentions age in years and months, gender, height in feet and inches/cm, weight in kg/lbs and calculated BMI by formula weigh in Kg/height (m^2). Waist circumference was measured by flexible measuring tape from narrowest part of torso, midway between the lowest rib and iliac crest and noted in inches for central obesity after expiration. Blood pressure was measured in the right arm, at the level of heart in a sitting and resting position. The patients were classified on the basis of BMI as overweight or obese according to their age and height via using criteria by CDC child and teen BMI calculator. Relevant investigations were suggested as per indication in individual cases and data recorded in specifically design proforma.

Data were analyzed by SPSS version 21. Frequency and percentages were calculated for qualitative variables (gender, obesity, co-morbid, type of AN); mean with standard deviation for quantitative variables (age, height, weight, BMI, waist circumference). Shapiro-Wilk test was performed to assess the normality of the distribution of the variables, this showed that our data was non-normal. Chi-square test was used to compare qualitative variables between adolescents and adults. Mann-Whitney-U test was used to compare non-normally distributed continuous variables between two groups. The p-value < 0.05 was considered to be significant.

RESULTS:

In our study total number of cases were 114 in which half

57 were adolescents and half (57) were gender matched adults. There were 77(67.5%) females and 37(32.5 %) males, both groups were comparable with respect to gender *(p=0.841)*. The mean age was 17.99+4.72 (10–48 years range); 14.44+1.80 years(adolescents) Vs. 21.54+3.9 years adults*)(p<0.0001)*. The mean height was 4.99+0.44 feet; 4.88+0.48 (adolescents) Vs. 5.09+0.39 (adults) *(p=0.026)*.The mean weight was 70.66+14.18kg; 66.39+13.02(adolescents) Vs. 74.93+14.12kg (adults) *(p=0.001)*. Mean waist circumference was 36+3.52(range 14-47 inches); 34.91+4.28 (adolescents) Vs. 37.10+2.07(adults) (*p<0.0001)*. As per WHO criteria for adolescents and adults; obesity was seen in 44(77.2%) adolescents with AN Vs. 31(54.4%) adults with AN *(p=0.010)*. Over all, among the 114 cases of AN, 75(65.8%) were obese and 39(34.2%) were non-obese *(fig 1)*

Table 1: The demographic variables, anthropometric measurements, site and types of acanthoses nigricans in adolescents Vs. Adults *(n=114*

VARIABLES	n (%) n=114	Adolescents n=57	Adults n=57	P-value
Age(10-48yrs)	17.99+4.72	14.44+1.80	21.54+3.9	**<0.0001**
Height (3.5-5.9 ft)	4.99+0.44	4.88+0.48	5.09+0.39	**0.026**
Weight (30-120 kg)	70.66+14.18	66.39+13.02	74.93+14.12	**0.001**
Waist circumference (14-47 inches)	36+3.52	34.91+4.28	37.10+2.07	**<0.0001**
Obesity				
Obese	75(65.8%)	44(77.2%)	31(54.4%)	**0.010**
Non-obese	39(34.2%)	13(22.8%)	26(45.6%)	
Gender				
Females	77(67.5%)	39(68.4%)	38(66.7%)	0.841
Males	37(32.5%)	18(31.6%)	19(33.3%)	
Site of AN				
Neck	113(99.1%)	57(100%)	56(98.2%)	0.315
Groin	88(77.2%)	43(75.4%)	45(78.9%)	0.655
Knuckles	61(53.5%)	28(49.1%)	33(57.9%)	0.338
Axilla	55(48.2%)	23(40.4%)	32(56.1%)	0.123
Sub-mammary	59(51.8%)	26(45.6%)	33(57.9%)	0.190
Types of AN*				
HAIR AN	61(53.5%)	32(56.1%)	29(50.9%)	0.573
Acral	14(12.3%)	05(8.8%)	09(15.8%)	0.302
Mixed AN	01(0.9%)	0(0%)	1(1.8%)	0.315
Unilateral AN	0(0%)	0(0%)	0(0%)	-
Syndromic	2(1.8%)	0(0%)	02(3.5%)	0.154
Benign AN	111(97.4%)	56(98.2%)	55(96.5%)	0.558
Diabetes mellitus				
Diabetic	31(27.2%)	14(24.6%)	17(29.8%)	0.528
Non-diabetic	83(72.8%)	43(75.4%)	40(70.2%)	
PCO (n=77 females)	62(80.5%)	30(76.9%)	32(84.2%)	0.707
Hypertension	27(23.7%)	6(10.5%)	21(36.8%)	**0.001**
Autoimmune	36(31.6%)	13(22.8%)	23(40.4%)	**0.044**
Drug induced	0(0%)	0(0%)	0(0%)	-
Familial	0(0%)	0(0%)	0(0%)	-

Regarding site of AN, neck was the most common site 113(99.1%). This was followed by groin 88(77.2%),knuckles 61(53.5%),sub-mammary region 59(51.8%) and axillae 55(48.2%)*(fig. 2)*. and Regarding types of AN, the benign type was most common i.e., found in 111(97.4%) in our study; 56(98.2%) in adolescents and 55 (96.5%) in adults *(p=0.558)*,followed by HAIR-AN syndrome 61(53.5%) and acral AN 14(12.3%).Only 2(1.8%)syndromic types and one case of mixed type were noted in our study. Not a single case reported of unilateral variety in our study. Regarding associated conditions and co-morbid, DM observed in 31(27.2%) AN cases and 83(72.8%) AN cases were non-diabetic. Diabetes was seen in 14(24.6%) adolescents Vs. 17(29.8%) adults *(p=0.528)*. PCOs seen in 62(80.5%) out of total 77 females with AN with no difference between adolescents and adults (p>0.05). Hypertension were seen in 27(23.7%)cases of AN, hypertension was much more common in adults with AN 21(36.8%)Vs. adolescents 6(10.5%) *(p=0.001)*.Autoimmune conditions were seen in 36(31.6%) AN cases and no case were found of drug induced and familial variety of AN.

Fig 1: Bar graph representing sites of Acanthosis Nigricans in Adolescents Vs. Adult cases (n=114)

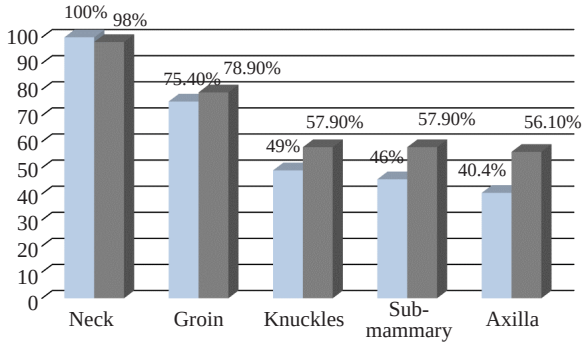
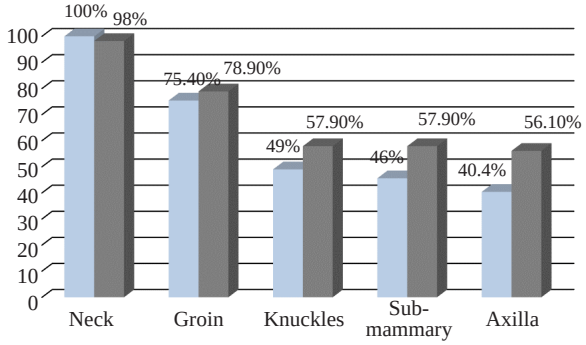


Fig 2: Bar graph presentation of various type of acanthosis nigricans in Adolescents Vs. Adults (*n=114*)



DISCUSSION:

AN is a skin condition that is featured by brown/black velvety plaques in skin folds and associated with syndromes, hereditary disorders, DM, Hypothyroidism, Addison's disease ,Cushing Syndrome and hypogonadal syndromes.[6,11] Prevalence of AN varies from 74% in Obese persons and 7% involves unselected population.[12] AN acts as skin marker for malignancy, IR and metabolic syndromes(Mets)in overweight/obese children and adolescents.[13,14] AN secondary to obesity is related to IR, increased insulin level in the blood.[15,16] The pediatric obesity is related to increased risk of prevalence and incidence of T2DM in childhood which is associated with higher risk of micro(nephropathy, retinopathy and neuropathy)and macrovascular complications (like myocardial infarction and stroke).[17]

In our study, we took 114 patients in which 57 were Adolescence and adults in each group. The age range was 10-48 years. Out of 114, 75 (65.8%) were obese in which 44 (77.2%) were adolescent and 31 (54.4%) were adults; obesity was more in adolescents than adults.

Regarding gender in our study, we had 77 (67.5%) females in which 39(68.4%) were adolescent females and 38(66.7%) were adult females. There were 37(32.5%) adolescent males and 18(31.6%) adult males, our study had more females than males presenting with AN. Study by Munise daye showed more obese females as compared to males in their study[15] Study conducted by Wolters Kluwer had same findings, i.e., more females than males. The ratio was 2:1.[2] In our study, the mean BMI was 31.63 ± 6.92 while more in adolescents 34.4 ± 6.92 than in adults 26.45±2.66 but the difference in BMI was not statistically significant *(p>0.05)*. In study by Ashraf, [11] the mean BMI was same as in our study i.e., 31.8 ± 3.9.

Regarding obesity, among 75(65.8%) obese cases as per criteria of BMI by WHO, we observed obesity in 44(77.2%) in adolescents and 31(54.4%) in adults (p=0.010) that is quite significant. While Prakash found 47% obesity in adults in his study that is slightly higher than our study.[2] Generally, obesity is a result from imbalance of energy when intake exceeds from requirement of body. However, it is a complex problem that results from genetic predisposition, environmental factors, human behavior and policy interventions but furthermore, gut flora, epigenetic modifications, viral infections and some psychological factors may also be involved in the pathogenesis of obesity in childhood and adolescents. Previous studies suggested that obesity in childhood exerts adverse effects on health throughout life if not tackled in childhood and cardiovascular risk can be minimized if obese adolescent becomes a nonobese adult.[5]

Regarding Waist circumference, we found this to be 37.03 ± 3 inches in our study. In adults it was 37.7±4.25 and in adolescents 35.769±1.93 inches. A study by Shiva Prakash[18] found mean WC 27(50%) in patients with AN. The WC shows the central obesity and cut off for Asian females is 80cm while in males is 85cm. There is an increased prevalence of AN if WC is 90cm or above. Similarly, decreased occurrence of AN if WC = 90 cm. Hence, if patients have BMI 30 kg/m2 or more than that with WC 90 cm or above he may have AN as a marker for IR. Obesity is a known risk factor for the T2DM & IR.[19,20]Waist circumference is a cost-effective measure, this is not only the good anthropometric measurement to detect abdominal obesity but also an independent guider for insulin resistance.

IDF suggests children of age group of six years, the 90th percentile as a waist circumference but hasn't explained the waist circumference cut off point for less than six years of age in children. Previous studies in the US suggested use of waist circumference for insulin resistance or metabolic syndrome or cardiovascular risk rather than BMI in clinical settings. Studies in the US on children and adolescents suggested cardiovascular risk for waist circumference cut off point at 94th percentile for boys and for girls at 84th percentile. A single measurement of waist circumference cut point in different genders and ethnic groups may be easy to apply but less sensitive to diagnose metabolic syndrome in children.[7]

Regarding the site of AN, out of 114 patients we found the commonest site of AN is neck in 113 (99.1%) cases in which 57(100%) in adolescence & 56(98.2%) in adults (P=0.315). Study by Hasan A Kobaissi found neck involvement in 131(73%) subjects with AN which showed more neck involvement in patients with AN than we found in our study.[20] Nisha[2] found more neck involvement which coincides with our results. Neck involvement was followed by groin 88 (77.2%), 43 (75.4%) in adolescence and 56 (98.2%) in adults (P=0.655), knuckles 61 (53.5%) and axilla in 55 (48.2%). Study by Rodriguez found knuckles, the commonest site of AN (21.6%). The results did not match with our study while Rodriguez found knuckles is a positive value for specificity of AN while detecting HOMA-IR levels more than 90th percentiles in their study.[21]

The neck involvement is the most common site in children and maximum involvement of neck and axillae is due to perspiration or friction and these two sites are the indicator of metabolic risk. Mechanical trauma may be important cause for proliferation of epidermal keratinocytes.[22] Helaisa Marcelina found neck, the most common site (93-99%) followed by axillae (73%).[6,]

Regarding types of AN, out of 114, Benign AN was found in 111(97.4%), the most common type in our study which is followed by HAIR–AN syndrome (includes high insulin resistance, obesity and hyperinsulinemia).[23] Benign type is the indicator for IR secondary to obesity.[24]We found HAIR-AN syndrome, the 2nd most common type 61(53.5%) in which 32(56.1%) were adolescents and 29(50.9%) adults

(p=0.573). HAIR-AN syndrome can be caused by adipose cell dysfunction.[22]

In our study, out of 114, 83(72.8%) were non diabetic and 31 (27.2%) were diabetic, more were non diabetic than diabetic (P=0.523), also more Diabetes in adults than in adolescents in our study. The previous pediatric obesity related studies showed increase incidence and prevalence of childhood T2DM which is not supported to our study. ADA classifies T2DM as a condition caused by progressive loss of beta cells by pancreas that secretes insulin in a person of IR. The ADA recommended for screening of the children and adolescents from 10 years old or above it who are overweight with BMI more than 85th percentiles for that age and sex or obese person with BMI more than 95th percentile for that age and sex. Childhood T2DM is usually developed during puberty and females are more commonly affected than males while age related type T2DM is more common in adult males than females. The cause of this difference is due to increased muscle mass and decreased fat mass in adolescent boys and increased physical exertion and increased sensitivity of insulin in boys than girls.[11]

Regarding PCO in our study, out of 114, 77 females in which 62(80.5%) had PCOs. Study published by Wolters Kluwer showed 30% AN found in patients with PCO.[3]

Hypertension was seen in 27(23.7%) patients in our study that was more prevalent in adults (p=0.001) that is quite significant. Munise Daye[15] in his study showed 10.8% had an increase systolic blood pressure and 12.1% with Diastolic blood pressure which is lower blood pressure than we found in our study. Persistent high insulin level leads to developing HTN. Thus, there is an association between AN and HTN which is a clinical sign for suspicion of early cardiovascular alterations.[6]

Sorof et al found increased prevalence of HTN if BMI percentiles increase from normal weight (2%) to over weight (11%) and Steinberg, Daniels et al found that HTN is a high-risk factor for common conditions so it should be track from childhood to adulthood.[7]

CONCLUSION:

Acanthosis nigricans is a common major cosmetic skin concern and important pathological problem among obese in our population. In our study, benign and HAIR-AN were most frequent types which is associated with obesity, increased BMI, raised waist circumference and increased hypertension in adolescents and adult groups. Hence, it is suggested to screen all adolescents and adults with acanthosis nigricans for obesity, DM, hypertension, PCO's, autoimmune conditions and IR regardless of age or gender. This may lead to identification of systemic disorders in dermatologically presenting acanthosis nigricans. Here, we may conclude that the early diagnosis of acanthosis in obese cases may improve quality of life of patients, prevent systemic complications and improved outcome.

Authors Contribution:
Furquana Niaz: Contributed to the conception, design, data collection, analysis and interpretation of data, Drafted the article and revising it critically for important intellectual content, final approval of the version to be published, submitted in the journal
Nadia Shams: Contributed to the conception, design, data collection, analysis and interpretation of data, Drafted the article and revising it critically for important intellectual content, final approval of the version to be published
Naresh Kumar: Contributed to the conception, design, data collection
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Original Article **Open Access**

Evaluation of Hematological, Coagulation and Inflammatory Parameters in COVID-19 in a Tertiary Care Setting of Sindh, Pakistan

Faiz us Saba, Zunera Sajjad, Ayesha Khan, Muhammad Iqbal, Muhammad Faisal Faheem, Nabeela Khan

ABSTRACT

Objective: COVID-19 is caused by SARS-CoV-2. Although pulmonary manifestations have been identified as the major symptoms, several hematological abnormalities play a vital role in disease treatment and monitoring. This study summarizes the hematological abnormalities (platelets, white blood cells, hemoglobin, coagulation alterations) as well as changes in inflammatory markers.

Study Design And Setting: A retrospective cross-sectional study was conducted among PCR positive COVID-19 patients. The study was conducted at pathology department of CMH Malir between Aug 2021 and Jan 2022.

Methodology: All the individuals with positive real-time reverse transcription-polymerase chain reaction (PCR) results were involved in the study. One hundred and twenty six COVID-19 patients were included using convenience sampling. Six ml venous blood was collected and analyzed. The data were entered and analyzed using SPSS version 23.

Results: Among 126 patients different hematological and inflammatory parameters were noted. Significantly raised CRP, ESR in 96.8% and 92.9 % were noted respectively. Other parameters like raised D-dimers was found in 60.3 %, leukocytosis 65.1%, neutrophilia in 62.7 %. Significantly elevated neutrophil lymphocyte ratio was seen in 62 % of patients. Parameters like anemia and prolonged PT / APTT were not significant.

Conclusion: The study concluded that CRP, ESR, leukocytosis, neutrophilia, elevated Neutrophil to lymphocyte ratio and D-dimers are significantly raised among serious patients with COVID-19 disease and can be used as monitoring, prognosis and severity index.

Keywords: COVID-19, hematological parameters, neutrophil to lymphocyte ratio.

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INTRODUCTION:

December 2019 was the beginning of a new era in the medical world, when the world was hit by an outbreak of cluster of pneumonia cases. The cause was found out to be a novel corona-virus. It was formally designated as COVID -19 by WHO in Feb 2020, and name of the virus was decided as severe acute respiratory syndrome corona-virus 2 (SARS-COV-2).

It was highly contagious among close contacts and in two months it was spread to the whole world affecting 213 countries. It was declared as the deadliest pandemic in the history affecting more than 253 million and causing 5 million deaths till Nov 2021.[3]

In Pakistan around 1.53 million confirmed cases of COVID-19 have been reported with 30,379 deaths so far.[4] COVID-19 is a multiorgan disease affecting pulmonary, cardiovascular, neurological, musculoskeletal, gastrointestinal and hematological system. It is a very diverse disease and shows a magnitude of symptoms of varying severity. Some patients remain asymptomatic while others develop severe life-threatening complications resulting in death.[5] Good patient management requires early diagnosis, isolation and

risk stratification of patients.[6]

COVID-19 significantly affects the hemostasis and the hematopoietic system. The PCR is the gold standard investigation for diagnosing covid but it is not widely available specially in villages and far flung areas of developing country like Pakistan. In this setting, one of the commonest and earliest investigation advised for the suspected COVID-19 patients is complete blood count (CBC). It is easiest, quickest, widely available and one of the most reliable tests which helps not only in the diagnosis but also in prognosis of the disease. The virus also causes cytopenia, neutrophilia, thrombocytopenia and coagulopathies.[7] Commonly affected parameters include platelet count, absolute lymphocyte count, neutrophil count, NLR ratio and D dimers.[8]

We carried out this study to determine hematological, coagulation and inflammatory markers in hospitalized PCR positive covid patients which can be used as a monitoring tool and give an idea about disease severity as well. Furthermore, these parameters can also give us an idea where PCR facility is not available so the suspected patients may be timely isolated, referred and managed at the desired facility.

METHODOLOGY:

This retrospective cross-sectional research was organized and managed at the Department of Pathology, in CMH Malir, a tertiary care hospital in Karachi. The study data was collected from the hospital records from 1st Aug 2021 to 31st Jan 2022. The study was conducted after approval from Hospital Ethical Review Committee (IRB no.70/2021/Trg / ERC). Sample size was calculated using WHO calculator.[8] Informed consent about the sampling and research was taken from patients or their families.

All cases which were confirmed positive after PCR testing were included in study. PCR positive patients managed outdoors were excluded from the study irrespective of their signs and symptoms.

Nasopharyngeal swabs were collected by using the recommended and standardized technique. The nasal swabs were then tested by PCR for corona virus. Further laboratory tests were performed on only those patients who turned out to be positive. Complete blood picture (Hb, WBC, platelet, neutrophil, lymphocyte), coagulation profile (PT/ APTT), D-dimer, ESR and CRP were performed.

For CBC, 3ml sample was collected in EDTA and run on haematology analyzer celtac-alpha by Nihon Kohden. For coagulation profile 2 ml venous sample was collected in Trisodium citrate bottle. PT/APTT was performed on ACL 7000 analyzer, whereas latex agglutination method detected D-Dimers with cut off value of 200ng/ml. 1 ml venous sample was taken and CRP was performed using a spectrophotometric assay. ESR was performed by westergrens methodology using automated roller 20 LC.

Following definitions were used during CBC interpretation:

Anemia : Hb <13 x g /dl in males and Hb < 11x g /dL in females.

Neutrophilia: Absolute neutrophil count > 8000/ul.

NLR ratio: The calculation of neutrophil-to-lymphocyte ratio was carried out by simple division method. In normal adults its value is 3.5.

Thrombocytopenia; Defined as platelet count of < 150 x 10^9/l.

CRP: More than 6ng/l is taken as positive.

ESR : > 15mmHg in males and > 10 mmHg in females is taken as increased.

The information was entered and interpreted using Statistical Package for Social Science (SPSS) version 23. Outcomes were framed as frequencies. To calculate P value, Chi square test was applied. A P-value of less than 0.05 was taken as significant.

RESULTS:

In this study, out of 126 admitted patients most of the presenting patients were male. The male comprised of 62 % of total while females were about 38.1 %. The age distribution is as under:

In this research, the extent of high white blood count, neutrophilia and lymphopenia is found to be 65.1%, 62.7% and 64.2% respectively. Anemia was present in 23.8 % cases. Abnormal neutrophil to lymphocyte ratio was relatively more common (62%). On the otherhand CRP and ESR, D-dimers were significantly raised which were 96.8%,92.95 and 60.3% respectively. Clotting factors PT and APTT were found to be normal in majority of patients, while inflammatory markers D-dimers and CRP were raised with a significant association P-value 0.00 and 0.028 respectively. The magnitude of raise ESR was found to be higher in most of cases i.e (92.9%).

DISCUSSION:

Anemia is one of the important clinical manifestation that has been observed with SARS-CoV-2 infection. Anemia occurs due to the changes in immune mediated system of

Table 1: Gender and age distribution of patients.

GENDER	Frequency (N=126)	Percent
Male	78	61.9
Female	48	38.1
Age	Frequency	Percent
17-35	46	36.5
36-55	41	32.5
>=56	39	31.0
Total	126	100.0

Table 2: Significance of haematological and inflammatory parameters in Covid 29 Patients

Test	Normal		Abnormal	
	Frequency	Percentage	Frequency	Percentage
D DIMERS	50	39.7	76	60.3
CRP	4	3.2	122	96.8
ESR	9	7.1	117	92.9
PT	116	92.1	10	7.9
APTT	120	95.2	06	4.8
Hb	96	76.2	30	23.8
WBC	44	35	82	65.1
NEUTROPHILS	47	37.3	79	62.7
LYMPHOCYTES	45	35	81	64.2
PLATELETS	101	80	25	19.8
NLR	48	38.1	78	62

Neutrophils to lymphocytic ratio was raised (62 %) with significant p value of 0.00

iron metabolism and homeostasis. It is quite commonly seen in elderly suffering from covid. Although it does not directly affect the mortality but it can have negative impact on the life quality of frail and elderly population. The extent of anemia in our study was found to be 23.8 %, which is comparable to a study conducted by Bellmann-Weiler et al where 24.7% of the patients were anemic and anemia was secondary to inflammation in majority of the cases.[9] However in another study, it was found to be much more common as compared our study. In this research conducted by Tao et al, it was reported to be 35.5%. This research concluded that anemia aggravates the disease and is an independent risk factor for increasing severity of disease.[10]

Center for Disease Control and Prevention (CDC) showed cases of leukopenia in (9–25%), leukocytosis in (24–30%), and lymphopenia in (63%) covid patients who reported in hospital with pneumonia.[11] In another research article by Guan et al of China which analyzed 1099 patients from 552 different hospitals and verified that 33.7%, 36.2% and 83.2%, of COVID-19 patients had leukopenia, low platelets and lymphopenias respectively. Lymphocytopenia was the most prominent finding in this research.[12] These abnormalities were more evident in severely ill patients as compared to non-severe patients. The parameters like neutrophilia, lymphopenia and raised neutrophil-to-lymphocyte ratio (NLR) have strong association with risk of acute respiratory distress syndrome (ARDS) development requiring ICU (intensive care unit) care. Similarly, some other studies demonstrated that there is association of leukocytosis, thrombocytopenia, lymphopenia and high neutrophil count with poor prognosis and critical care requirement.[12]

In our study neutrophilia and leukocytosis was found significantly increased similarly, in majority of studies conducted among acutely ill patients. However, the commonest finding was found to be neutrophilia and lymphopenia was not a significant finding in our case. One of the study by Qin et al among 138 indoor patients showed that neutrophilia was significantly higher in critically ill ICU patients (77.6%) which was comparable to our study.[13] In another research conducted by Gong et al also had similar results with (P<0.001).[14] Neutrophilia was associated with bad outcome which was also shown by Li et al.[15] Another study by Zhang et al among 82 dead COVID-19 patients also revealed that 74.3% of them had neutrophilia on admission and this increased to 100% in 24 hours before death.[16] There could be relationship of neutrophilia with the cytokine storm which is the characteristic of disease severity. One of the possibilities of high neutrophil count could be due to bacterial co-infection. One of study in China revealed that leukocytosis on admission of COVID-19 patients was associated with increased risk of death in hospital. In another research by Zhou et al[9] it is elaborated that non-survivors had more significant leukocytosis than the survivors (P<0.001).[17]

Neutrophil to lymphocyte ratio was high with significant value. Our study showed significant NLR ratio in 62 % of patients. According to a similar study conducted by Yang AP et al, some independent factors to indicate poor prognosis in COVID-19 patients include age and higher neutrophil to lymphocyte ratio.[18]

C-reactive protein is an acute phase reactant which rises in response to any inflammatory condition in body. Levels of CRP may increase with inflammation in respiratory diseases.[19] In these studies, critical covid patients in ICU revealed significantly raised CRP levels which is due to the aggressive inflammatory response described in association with severe disease and cytokine storm.[20]

We found significantly raised D-dimers levels among 60.1% patients. Coagulation parameters like prothrombin time (PT) and activated partial prothrombin time (APTT) do not reveal any significance. However, raised D-dimer levels are reported to be one of the significant prognostic factors in COVID-19 pneumonia.[21] Another research conducted in 2020 by Guo et al, revealed association of disease severity and poor outcome with raised levels of D-dimer.[22]

Most of the patients under study revealed normal platelets. Only mild decrease in platelet counts were noted in around 19.8 % of patients. Same findings were observed in a research by Chen N who reported mild thrombocytopenia in 20% of cases.[23] Similarly according to a French cohort, mild thrombocytopenia was reported in one fourth of COVID-19 admitted patients and it was reported to be an independent predictive risk factor for intensive care monitoring, ventilatory support or even death.[24]

The population under study was from similar demographic area and were the admitted patients who required monitoring and management therefore further verification is needed in different areas and in outdoor patients with mild symptoms. Outdoor patients were not included in the study.

CONCLUSION:

Our study showed that neutrophilia, leucocytosis, raised Neutrophil to lymphocyte ratio, CRP, ESR and D-dimers are important parameters among patients with COVID-19. COVID-19 disease directly affects the hematological, coagulation and inflammatory bio-markers so they should be used not only for prognosis but also to predict and intervene with effective management plan before the disease triggers to severe crisis, end organ failure or inflammatory storm.

Authors Contribution:
Faiz us Saba: Data analysis
Zunera Sajjad: Conception and design of article
Ayesha Khan: Data collection and design of article
Muhammad Iqbal: Design of article
Muhammad Faisal Faheem: Application of stats and data analysis
Nabeela Khan: Proof reading and reference writing

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Original Article **Open Access**

Injection Sclerotherapy vs Rubber Band Ligation in the Management of Patients with 2nd Degree Haemorrhoids

Zahid Raza, Muhammad Jalil, Waseem Ahmad Khan, Jehanzeb Rahman, Shahid Abbas, Shahid Mahmood

ABSTRACT:

Objective: To compare the efficacy of injection sclerotherapy and rubber band ligation in patients with 2nd degree haemorrhoids.

Study design & Setting: Prospective Observational study was conducted in PNS Shifa Karachi from 1st July 2018 to 31st March 2019.

Methodology: A total of 240 patients of both genders, known cases of 2nd degree haemorrhoids were included in the study. Patients with a known history of liver cirrhosis, previous history of haemorrhoidectomy, severe anaemia uncontrolled hypertension and patient requiring additional intervention post-procedure were excluded. Patients were randomized to either the injection sclerotherapy Group A or rubber band ligation Group B by lottery method. Final assessment was done at 6-months post-procedure regarding the effect of treatment on rectal bleeding.

Results: The age range in this study was from 18 to 65 years with a mean of 36.641±7.00 years in Group A while 35.700± 5.65 years in Group B. Mean BMI was 26.525±1.54 Kg/m2 in Group A and 26.316±1.48 Kg/m2 in Group B and duration of disease was 7.466±2. 15 months in Group A and 7.883±1.78 months in Group B. Efficacy was seen in 87.5% patients in Group A as compared to 98.3% in Group B (p=0.001).

Conclusion: Rubber band ligation is more efficacious in the management of 2nd-degree haemorrhoids in terms of per-rectal bleeding from 3rd-week to 6 months post-application.

Keywords: Prolapsed haemorrhoids, Rubber ligation, Injection Sclerotherapy

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INTRODUCTION:

Haemorrhoids are a frequently encountered condition in the surgical outpatient department. As symptomatic haemorrhoids cause a sufficient reduction in quality of life. It is estimated that about 5% of the total population experience haemorrhoids once in their lifetimes and half of the patients in the fifth decade of life receive some haemorrhoid treatment, and nearly 10-20% of the individuals will require surgery[1]. A poorly-developed healthcare system coupled with an unhealthy lifestyle and poor dietary habits put our population at an even higher risk for developing haemorrhoids, making it a significant problem[2]. Haemorrhoids are symptomatic enlargement and abnormally downward displacement of anal cushions causing venous dilatation. Other pathologies include degenerative changes in supportive tissue within the anal cushions, vascular hyperplasia, and hyper perfusion of hemorrhoidal plexus[3].

Patients present with complaints of itching, burning, protrusion of mass from the anus, bleeding, generalized weakness and constipation. Low-grade haemorrhoids are effectively treated with dietary and lifestyle modification, medical intervention[4]. Surgery is required high-grade or complicated haemorrhoids. Haemorrhoidectomy has been the mainstay of treatment, more recently other approaches have been employed including rubber band ligature (RBL), stapled haemorrhoidopexy, and Doppler-guided hemorrhoidal

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artery ligation[5]. Injection Sclerotherapy (IS) and rubber band ligation are the commonly performed procedures for 2nd-degree haemorrhoids.[6]

Jehan S. et.al in their randomized control study on 100 patients with 2nd-degree haemorrhoids concluded that in patients treated with injection sclerotherapy, 56% were symptoms free after 4 weeks, as compared to 88% after 4 weeks undergoing rubber band ligation. Whereas at 12-month follow-up, 92% remained symptom-free in the Injection sclerotherapy group, as compared to 100% in the rubber band ligation group[7].

In a setup like ours, where people are very apprehensive of surgery, it becomes imperative to adopt non-operative, outpatient and short methods of treatment for haemorrhoids because of cost, hospitalization and morbidity associated with surgery. This brings Injection sclerotherapy and rubber band ligation is the best-suited choice for outpatient treatment of haemorrhoids. The goal of this study was to compare the efficacy of injection sclerotherapy and rubber band ligation.

METHODOLOGY:

A total of 240 patients of both genders, suffering from 2nd degree haemorrhoids with no improvement after dietary and lifestyle modifications were included in the study after obtaining approval from hospital ethical committee. Informed written consent was obtained from all participants. Patients with a known history of liver cirrhosis, previous history of haemorrhoidectomy, severe anaemia and uncontrolled hypertension were excluded. Patients were randomized to either the Injection sclerotherapy group (Group A) or rubber band ligation group (Group B) by lottery method. All procedures were performed by the same surgeon to exclude bias.

Subjects fulfilling the inclusion criteria a detailed clinical history concerning bleeding per rectum, painful defecation and dietary habits was recorded. A focused general physical exam was done in all. Each patient was subjected to local examination, proctoscopy was performed by the same surgeon to exclude observer bias. All the patients were given an enema in the evening and the morning before the procedure. After the procedure, all the patients were advised to report emergency department in case of any complication in the form of bleeding per rectum or prolapse. All patients were advised tab diclofenac 50mg thrice daily for 5 days. Post-operative bleeding up to 3 weeks is usually common and will not render the procedure non-efficacious. A final assessment was done at 6 months post-procedure regarding the effect of treatment on rectal bleeding. Those patients requiring additional treatment due to post-operative pain were excluded from the study. The Performa was filled for record-keeping.

Data Analysis: Data were evaluated and analysed using Statistical Program for Social Sciences (SPSS) version 23. Mean and Standard deviation was reported for quantitative variables like age, BMI and duration of disease. Qualitative variables like gender and efficacy were measured in terms of frequency percentage. The results were presented using graphs and Pie charts. Categorical data were compared between the study groups using Chi-square and Quantitative data was compared by independent t-test. $P < 0.05$ was considered statistically significant.

RESULTS:

Out of the total 240 patients the age range in the study was from 18 to 65 years with a mean age of 36.641± 7.00 years in Group A while 35.700± 5.65 years in Group B. Mean BMI was 26.525±1.54 Kg/m^2 in Group A and 26.316±1.48 Kg/m^2 in Group B and duration of disease was 7.466±2.15 months in Group A and 7.883±1.78 months in Group B as shown in Table-I. Male gender was dominant in both groups as shown in Table II. Efficacy was seen in 87.5% of patients in Group A as compared to 98.3% in Group B (p=0.001) as shown in Table III. Stratification of efficacy in both groups concerning gender and duration of disease are shown in Table-IV, and V respectively.

Table 1: Means of patients according to age, BMI and duration of disease n=240

Demographics	Mean ±SD Group A (n=120)	Mean ±SD Group B (120)
Age (yrs.)	36.64 ± 7.0	35.7 ± 5.6
BMI kg/m^2	26.53 ± 1.54	26.3 ± 1.48
Duration of disease	7.4 ± 2.12	7.88 ± 1.78

Table 2: Frequency and percentage of genders in both groups

Gender	Group A (n=120)	Group B (120)
Male	90(75%)	86(71.7%)
Female	30(25%)	34(28.3%)
Total	120 (100%)	120(100%)

Table 3: Comparison of efficacy in both groups

Efficacy	Group A (n=120)	Group B (120)	P value
Yes	105 (87.5%)	118 (98.3%)	0.001
No	15 (12.5%)	2 (1.7%)	
Total	120 (100%)	120(100%)	

Table 4: Stratification of efficacy with respect to gender in both groups

For male gender			
Efficacy			
Group	Yes	No	P value
A	79 (87.8%)	11 (12.2%)	0.003
B	85 (98.8%)	1 (1.2%)	
For Age 41-65 years			
Group	Yes	No	
A	26 (86.7%)	5 (15.2%)	0.122
B	33 (97.1%)	1 (2.9%)	

Table 5: stratification of efficacy with respect to duration of disease in both groups

For duration < 6 months			
Efficacy			
Group	**Yes**	**No**	**P value**
A	37 (94.9%)	111 (12.2%)	**0.003**
B	27 (100%)	0 (0%)	
For duration > 6 months			
Group	**Yes**	**No**	
A	68 (84%)	13(16%)	**0.122**
B	91 (97.8%)	2 (2.2%)	

DISCUSSION:

The present study aimed to find out the frequency of complications in patients undergoing sclerotherapy or rubber band ligation of first or second-degree haemorrhoids. Patients undergoing rubber band ligation more frequently complained of post-procedure pain and bleeding as compared to patients who underwent injection sclerotherapy. Haemorrhoids can occur in all ages, gender and socioeconomic status. Our study showed a high male proportion. Shamim et al from Karachi also showed a male predominance of 74.88%. Various other authors in our population show male predominance in haemorrhoid patients[8-10]. However, western literature showed an equal or mixed male or female predominance pattern in haemorrhoid disease[11-17]. This could be due to different hospital setup, social, cultural values and eating habits. Haemorrhoids are a common problem in the general population with an estimated 5–30% of adults suffering from[18]. It is imperative that the early side-effect profile of the two most common outpatient procedures for the management of first and second-degree haemorrhoids injection sclerotherapy and rubber band ligation, be evaluated in a local cohort of patients. Studies on a direct quantitative comparison of the frequency of pain between patients undergoing sclerotherapy and band ligation of 2nd-degree haemorrhoids are rare. The present study compared the results of sclerotherapy with band ligation for which direct comparison was possible. The results of this study indicate that pain to some degree is experienced during the first postoperative hour by half of the patients undergoing rubber band ligation. In most of the patients experiencing pain in this group, the degree of discomfort varied from mild to moderate.

This observed frequency of pain is in conformation with the findings of Watson et al who observed that at 4 hours after banding, 55% of patients complained of some degree of pain[19]. Although the frequency is significantly higher than that seen in local series of patients undergoing banding which have noted 6–20% of patients complaining of pain, most of these studies, unlike this study, did not include discomfort felt by the patient while noting the frequency of pain[20]. Early postoperative per-rectal bleeding, within the first 24 hours following the procedure was noted in 56% of patients in the group which underwent rubber band ligation. This conforms to Watson et al who found that 65% of patients complained of per-rectal bleeding on the day following operation[15]. In the case series by Bhutta et al and Dilawaiz et al, only 6–12% of patients complained of per-rectal bleeding immediately following the procedure[16,17]. Those studies also carried out banding as an outpatient procedure, however, limitations in the follow-up of the patients probably accounted for the fewer patients who came back with complaints of per-rectal bleeding. As compared to the frequency of patients in the rubber band ligation group, significantly fewer patients undergoing sclerotherapy had complaints of early bleeding. Only 26% of patients, almost half of the patients in the RBL group experiencing per-rectal bleeding, complained of such a problem. Lesser instrumentation and damage to the mucosa of the upper anal canal during the submucosal injection of sclerosant[18] probably accounts for the lesser frequency of early bleeding seen in patients undergoing injection sclerotherapy. Efficacy was seen in 87.5% of patients in Group A as compared to 98.3% in Group B (p=0.001). Jehan S et al in their randomized control study on 100 patients with 2nd-degree haemorrhoids concluded that in patients treated with injection sclerotherapy, 56% were symptoms free after 4 weeks, as compared to 88% after 4 weeks undergoing rubber band ligation.

Also, at 12-month follow-up, 92% remained symptom-free in the Injection sclerotherapy group, as compared to 100% in the rubber band ligation group[7].

According to Chaleoykitti these patients would be better benefited by applications of multiple instead of the single band as this is known to influence the outcome in banding procedures 20. A recent study from Faisalabad 22 showed that 60% of patients developed mild to moderate bleeding in the first postoperative week. Bernal et al showed that 32% of the patients suffered pain after ligation and 13.81% of cases were operated on due to persistent rectal bleeding or hemorrhoidal prolapse[13]. Rubber band ligation procedure is preferred over sclerotherapy because it provides a more definitive and long-lasting treatment of haemorrhoids and without the risks of surgery such as Haemorrhoidectomy or stapled haemorrhoidopexy[14]. Greca et al showed that 15% of patients required retreatment following rubber band injection sclerotherapy as compared to only

5% of patients who underwent rubber band ligation[21]. Other authors have also concluded that despite a higher frequency of post-operative complications, but owing to its significantly better long-term results, rubber band ligation is preferred over injection sclerotherapy for outpatient treatment of first- and second-degree haemorrhoids.[22]

CONCLUSION:

In conclusion, rubber band ligation of second-degree haemorrhoids is associated with fewer complaints of per-rectal bleeding, from 03 weeks to 6 months

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Waseem Ahmad Khan: Intellectual supervision, design, proof reading.
Jehanzeb Rahman: data analysis, interpretation and supervision
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Original Article **Open Access**

Perception of Telemedicine in Health Care Workers of a Tertiary Care Hospital

Shehnaz khan, Tahseen Haider Kazmi, Noor Shahid, Shamaila Hassnain

ABSTRACT:

Objective: This investigation aimed to determine the feasibility of using telemedicine for screening and to observe healthcare provider's opinion about telemedicine. In addition to that, explore the barriers in use of telemedicine

Study Design and setting: A cross-sectional study was carried out at Central Park Medical College and Teaching Hospital.

Methodology: The study was conducted between November, 2020 to April,2021 from 176 doctors and nurses working at Central Park Teaching Hospital using a convenience sampling technique. Convenience sampling was used because there is always a high probability of non-response or unavailability of clinical doctors and nurses. The minimum sample size was calculated as 88 for the group of doctors. The minimum sample size was doubled to collect the data from two cadres. The questionnaire was based on demographic information, general opinion about telemedicine such as reliability, comparison with standard examination procedure, nature, popularity, knowledge requirement, cost-effectiveness, designed frame and barriers for telemedicine.

Results: Nearly, 80.1% of the participants were doctors with clinical experience while the remaining were nurses. Approximately 72.5% of the doctors and 58.5% of the sampled participants said that telemedicine does not fulfill the need for standard examination procedures.

Conclusion: The findings of our study showed that the general opinion of healthcare professionals about telemedicine was unfavorable. Doctors had negative views but the nursing staff was optimistic. There was a mixed response about convenience. The main barrier to telemedicine was the poor communication skills of patients and availability and knowledge for using infrastructure.

Keywords: challenges, digital health, healthcare, telemedicine.

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INTRODUCTION:

Advancements in communication and information technology have made the world a global village. This reflects as telemedicine in the health care system. Telemedicine is a new approach in technology that facilitates the treatment of patients from a distance and has led countries to accept the idea of opening their health systems to trade.[1]

Novel computer capabilities and improved telecommunication services will make telemedicine possible through laptop computers and multi-media notebooks for health care providers in developed countries in the coming future. However, the developing countries should not be denied this facility and arrangements should be made for its provision to the developing world in the coming decade. This will bring a complete change in health education and healthcare delivery.[2]

Telemedicine, defined by W.H.O in its 1997 Health Development Strategy Report states it as "the delivery of health care services, where distance is a critical factor, by all health care professionals using information and communication technologies for the exchange of valid information for the diagnosis, treatment, and prevention of disease and injuries, research and evaluation, and for the continuing education of health care providers, all in the interests of advancing the health of individuals and their communities".[3]

According to W.H.O statistics, more than one-fourth of countries all over the world have an acute paucity of healthcare force. This includes Pakistan as well. The shortage

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of resources coupled with poor medical services makes telemedicine an affordable and effective solution for providing health care results for populations living in remote areas. Telemedicine by providing reliable diagnosis, consultation, and training can be beneficial for people living in distant geographical areas.[4]

Telemedicine was introduced in Pakistan in 1998 and since then has expedited its activities due to improvement in the telecommunication industry. A high bandwidth favors its usability and productivity. Since Internet has become a popular medium for communication for many users in Pakistan, with more than three million telephone lines spread all over the country the feasibility and potential contribution of telemedicine has become complimentary for the citizens of Pakistan.[5]

Pakistan Space Organization (SUPARCO) established its first satellite-based telemedicine network in conjunction with the Ministry of IT. It intends to establish three satellite-based centers in big cities. The government also plans to build a telemedicine network country-wide.[6]

The Covid-19 pandemic made use of telemedicine as a front-line program for safe healthcare delivery. Being cost-effective, safe, and providing strategic medical care with clear guidelines has led to its promotion by many healthcare institutions. "Sehat Kahani" is a recent communication-technology- initiated project where virtual consultations are provided in Pakistan.[7]

A telemedicine survey done by W.H.O in 2016 in Pakistan reveals some of the challenges/ deficiencies faced by the country for the establishment of telemedicine. It highlights the lack of general rules and regulations as well as the absence of a framework for approval of launching programs and what permissions are required from which department.[8]

Lack of standard government regulations, absence of malpractice liability insurance policy, deficiency in medical services licensing, all pose risks for the security and confidentiality of personal data.[9]

Ethical and deontological issues related to confidentiality of data, protection of dignity, and private life of the patient are some other concerns of health care professionals worldwide.[10]

Keeping all the above possibilities in mind we plan to interview the healthcare staff to find out their perceptions about the ease of use of telemedicine, how willing they would be to use it, and if they have any reservations about its usage.

METHODOLOGY:

A cross-sectional study was carried out at Central Park Medical College and Teaching Hospital from 01-November 2020 to 30-April 2021. The data was collected from 176 doctors and nurses working at Central Park Teaching Hospital using a non-random convenience sampling technique. As the data was collected from clinical doctors and nurses, where there is always a high probability of non-response due to unavailability. That is why the convenient sampling technique was used. The minimum sample size was calculated as 88 by using 34.8% as the proportion of doctors' favored practice of telemedicine by introducing national standards,[11] 90% power of the test, and 5% level of significance. The sample size 88 was calculated for the group of doctors. The minimum sample size was doubled to collect the data from two cadres. The double sample was taken to ensure that it represents the population well. This can also be justified as when we calculate the sample size for the difference between two population proportions,[12] we get almost double the sample size. The inclusion criteria were doctors and nurses working at Central Park Medical College and Teaching Hospital.

A self-designed questionnaire was used to collect data. The questionnaire addressed demographic information such as gender, educational level, year of experience, profession, and graduating college or university. The questionnaire was also based on statements tailored under general opinion about telemedicine such as reliability, comparison from standard examination procedure, nature, popularity, knowledge requirement, cost-effectiveness, and designed frame for telemedicine. Some information on barriers against telemedicine was also gathered. The first part of the questionnaire addressed the demographic information about the graduating college, years of experience, age, and profession of participants. The second part of the questionnaire was based on general opinion about telemedicine and its reliability and the third part was based on barriers against telemedicine. The questionnaire was designed and administered in British English (BrE) language. The reliability of the questionnaire was observed using Cronbach alpha which came out to be approximately 70%.

Before data collection, written consent was taken from all the participants. Ethical approval of the study was taken from the Institutional Review Board (IRB) of Central Park Medical College and Teaching Hospital (CPMC/IRB-NO/1319). The data was analyzed using SPSS version 26. Chi-square test of association was performed to observe significant association of different variables with the opinion of the participants whether telemedicine meets the needs of standard examination procedure or not. Descriptive statistics were presented as mean and standard deviation. The general opinion about the reliability, adoption, requirements and barriers is given in the form of frequency and percentages.

RESULTS:

A cross-sectional study was carried out to collect data from 176 participants. The mean age of the participants was 33.11 ± 11.65 SD (in years). About 65.9% of the participants were female while 34.1% of the participants were male. The data were collected both from doctors and nurses. Nearly 80.1%

of the participants were doctors with clinical experience while the remaining were nurses.

Most of the participants whose educational level was post-graduation or above were of the opinion that telemedicine does not meet the need of standard examination procedure. The level of education was significantly associated with the opinion. Approximately 72.5% of the doctors and 58.5% of all the participants said that it does not fulfill the need for standard examination procedures. The opinion of nurses was quite different. Nearly 80.5% of the nurses favored telemedicine. The profession was also found as the significantly associated factor with the opinion. Working experience and graduating college or university were insignificantly related to telemedicine. Most of the participants, regardless of their graduating college or university did not favor telemedicine.

Two-thirds of the respondents found telemedicine expensive. About 33% of the respondents said that the cost of telemedicine is not high. Nearly 83.5% of the participasnts mentioned that knowledge is required for medical practitioners and nurses to be able to use technology. Approximately 80% of the participants mentioned that older people are least likely to use telemedicine. The general opinion of 34.7% of participants on the use of telemedicine was that its application was little likely, 35.8% of the participants found the use of telemedicine somewhat likely. Only 4% of the participants found it very likely to be used.

About half of the participants agreed that telemedicine is convenient for more patient appointments in a day and more than half agreed that it is reliable for more frequent contact (Table 1). However, approximately 66% of the participants were of the view that it is more reliable compared to physically visiting a doctor. Approximately 79% of the participants said that telemedicine is comparatively less adopted in rural areas and 72.7% mentioned that a full design framework is required for awareness about telemedicine. Major reasons for the lack of awareness about telemedicine in rural areas were lack of a fully designed structure for telemedicine followed by lack of availability and knowledge to use system and unavailability of internet facilities. Most of the participants mentioned that the communication skills of the patients were the biggest barrier followed by fear of incomplete information and infrastructure cost (Table 2). A chi-square test of association was performed to observe the significant association between opinions of the participants about telemedicine that it meets the needs of standard examination procedure with various factors (Table 3).

DISCUSSION:

Searching for prospects of telemedicine we took responses from both doctors and nurses working at a tertiary care hospital in Kahna. We found that 72.5% of doctors disapproved of telemedicine and thought it does not meet the needs of standard examination procedures; however, the response was different from nurses and 80.5% thought telemedicine was useful. In a study conducted in Korea, patient satisfaction with telemedicine was reported as 86%,

Table 1: Opinion about the reliability and requirements of telemedicine (Frequency (%))

Factor	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
Telemedicine is convenient for more patient appointments in a day.	14 (7.95%)	74 (42.05%)	56 (31.82%)	26 (14.77%)	06 (3.41%)
Do you think that telemedicine is reliable for more frequent contact?	20 (11.36%)	78 (44.32%)	48 (27.27%)	25 (14.20%)	05 (2.84%)
Telemedicine is more reliable as compared to physically visiting a doctor.	09 (5.11%)	21 (11.93%)	30 (17.05%)	70 (39.77%)	46 (26.14%)
Is it difficult at times to diagnose through telemedicine?	36 (20.45%)	86 (48.86%)	25 (14.20%)	22 (12.5%)	07 (3.98%)
Is it user-friendly for patients with less awareness of technology?	11 (6.25%)	43 (24.43%)	43 (24.43%)	58 (32.95%)	21 (11.93%)
Do you think that training is required for doctors, nurses, and physicians for telemedicine?	58 (32.95%)	80 (45.45%)	24 (13.64%)	10 (5.68%)	04 (2.27%)
Do you think that telemedicine is comparatively less adopted in rural areas?	55 (31.25%)	84 (47.73%)	26 (14.77%)	09 (5.11%)	02 (1.14%)
The lack of a fully designed framework is the main reason for low awareness of telemedicine in small towns/villages.	39 (22.16%)	89 (50.57%)	37 (21.02%)	07 (3.98%)	04 (2.27%)
Do you think that the current system promotes telemedicine?	09 (5.11%)	47 (26.70%)	63 (35.80%)	41 (23.30%)	16 (9.09%)

Table 2: Barriers against Telemedicine

Barriers	Not at all n (%)	Little bit n (%)	Somehow n (%)	Often n (%)	Always n (%)
Unsure about diagnosis	21 (11.93%)	44 (25%)	49 (27.84%)	24 (13.64%)	38 (21.59%)
Fear of incomplete information	09 (5.11%)	23 (13.07%)	57 (32.39%)	59 (33.52%)	28 (15.91%)
Communication skills of patient	12 (6.82%)	16 (9.09%)	65 (36.93%)	46 (26.14%)	37 (21.02%)
Infrastructure	15 (8.52%)	23 (13.07%)	39 (22.16%)	45 (25.57%)	54 (30.68%)
High cost of telemedicine infrastructure	19 (10.80%)	32 (18.18%)	58 (32.95%)	37 (21.02%)	30 (17.05%)

Table 3: Crosstab of opinion with various Social and Demographics Factors

Factors	Categories	Telemedicine meets the need of standard examination		Chi-square (p-value)
		Yes	No	
Gender	Male	17 (28.33%)	43 (71.67%)	4.08 (0.05*)
	Female	51 (43.97%)	65 (56.03%)	
Level of Education	Graduation or less	36 (48%)	39 (525)	4.83 (0.03*)
	Post-graduation or above	32 (31.68%)	69 (68.32%)	
Profession	Doctor	39 (27.46%)	103 (72.44%)	38.69 (0.00*)
	Nurse	29 (85.29%)	05 (14.71%)	
Working Experience	1-5 Years	43 (41.35%)	61 (58.65%)	1.29 (0.73)
	5-10 Years	10 (30.30%)	23 (69.70%)	
	10-20 Years	07 (38.89%)	11 (61.11%)	
	Above 20 Years	08 (38.10%)	13 (61.90%)	
Graduating College / University	Public Sector	23 (32.39%)	48 (67.61%)	1.96 (0.21)
	Private Sector	45 (42.86%)	60 (57.14%)	

**Significant at 5% level of significance*

but only 52.7% of doctors and 48.0% of nurses were satisfied with it.[13] A study conducted in Pakistan reported that there was slight disagreement between the practitioners in acceptance of telemedicine and considering it a proper way for medical consultation.[14]

In our study, 83.5% of the participants thought that knowledge is necessary to use technology. In another study conducted in India where 86 doctors were interviewed, 50% said that lack of knowledge prevented them from using telemedicine.[15] Among physicians working at Tabriz teaching hospital in Iran, 33.55% knew telemedicine. 45.3% had used telemedicine in the form of telephonic conversations.[16] Another study mentioned that telemedicine is the most effective way however the distance is large, experts are rare and technology is limited.[17]

Regarding the convenience of telemedicine for patient appointments, 50% of health staff in our study agreed, another 50% also thought that it is reliable. Nearly, 66% thought that telemedicine is unreliable. A study done in Korea during the Covid epidemic showed 80% patient satisfaction regarding convenience. About 38.2% of doctors and 30.0% of nurses also found it convenient.87.1% of patients found it equally reliable as in-patient visits but only 14.5% of doctors and 14.0% of nurses also found so.[13]

Clinical usefulness of telemedicine was perceived as 34.7% less likely usefulness, 35.8% as somewhat likely usefulness, and 4.0% very likely usefulness in our study. In a UK study, the usefulness of telemedicine was rated as 76%, 74%, and 74% respectively for clinical usefulness, functioning of equipment, and ease of use of equipment.[18]

About 33% of health professionals found telemedicine inexpensive but most thought it was expensive in our study. In contrast, in a study in rural India, 90.0% of the doctors found telemedicine cost-effective and 61.0% of doctors found an increase in patients' inflow apart from regular visits.[19] Telemedicine is not very popular and is now in Pakistan, but it does add benefits to the lives of people living in remote areas.[14]

The barriers to telemedicine reported in our study were poor communication skills of patients, fear of giving incomplete information about the disease, and the high infrastructure cost. In a study conducted in N. America and Europe through e-mails about barriers to telemedicine, no technological problems were reported and neither cultural issues were a problem.[20] In rural India, 47.0% of problems were related to technology and 39.0% in time scheduling.[19] In a study conducted in Lahore, Pakistan, most of the participants favored telemedicine if the health care provider is far away and they can save more than 60 minutes.[21] The important barriers in the UK were recorded as 55.0% as lack of suitable

training, 54.0% as high cost of purchasing telemedicine equipment, and 43.0% as an increase in GP and nurse workload.[17] The use of telemedicine is unpopular in Pakistan, however, only a few applications are introduced. A study concluded that active involvement is required to regulate and expand digital health, as it seems to have a future in Pakistan.[22]

CONCLUSION:

The findings of our study showed that the general opinion of healthcare professionals about telemedicine was unfavorable. Doctors had negative views but the nursing staff was optimistic. Despite it adds benefits to the healthcare system, it has many barriers. The hindrances were identified as lack of appropriate technological knowledge, high operating cost, and lack of reliability and clinical utility. There was a mixed response about convenience. However, the communication skills of patients and availability and knowledge for using infrastructure were the main obstacles to telemedicine. Clinical staff is not much adaptive to the use of technology. More efforts should be done to create awareness about the uses of telemedicine and to reduce the infrastructure and technology barriers. Workshops much be conducted on basic knowhow of modern IT devices and technology system.

Authors Contribution:
Shehnaz Khan: Data Collection, Write-up
Tahseen Haider Kazmi: Study design, Final Proof Reading
Noor Shahid: Data Collection, Data Analysis, write-up
Shamaila Hassnain: Drafting, Proof Reading

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Original Article **Open Access**

Effects of Myopia on Visual Evoked Potentials in Patients at Tertiary Care Hospital

Abdul Haleem Mirani, Amjad Ali, Ataullah Bukhari, Tehmina Imdad, Ateeq Ur Rehman Channa, Maqbool Ahmed Jamali

ABSTRACT

Objective: To determine the effects of myopia on Visual Evoked Potentials among the subjects attending the eye OPD.

Study design and setting: This was a cross-sectional study with non-probability convenience sampling technique carried out at Department of Ophthalmology, Peoples Medical College Hospital Nawabshah / GMMMC Sukkur from March 2021 to November 2021.

Methodology: Total sample size was derived to be 180. Diagnosed myopia irrespective of gender and aged 25 to 45 years were included. Optic atrophy, Extensive retinal disease, any neurological disorder like multiple sclerosis, stroke and Visual pathway disorders were excluded. SPSS version 25.0 was used for data analysis.

Results: The mean age of the patients was 39.14 ± 6.73 years. There were n=96 (53%) females and n=84 (47%) males. In myopic samples the mean pattern stimuli latency P100 in right eye was 92.07 ±5.1 in cases (without correction) and 82.09 ± 5.8 in controls (with correction) with significant P-value 0.023, while in left eye was 93.55 ± 6.7 in cases (without correction) and 83.6 ± 7.0 in controls (with correction) with significant P-value 0.028.

Conclusion: Greater the myopia; greater was the Visual Evoked Potential (VEP) changes with regards to latency and amplitude in pattern stimuli especially P100 being the most affected component in this regard. It is therefore necessary that every patient who goes for VEP test should be corrected for myopic refractive error.

Keywords: Amplitude, Latency, Myopia, Visual Evoked Potentials, Visual acuity

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INTRODUCTION:

Visual Evoked Potential (VEP) is an electrical potential resulting after Visual Stimulus and is recovered from person's scalp.[1] This is a noninvasive test and is used to assess the visual function. VEPs are affected by non-pathological factors such as age, sex, pupil, and diameter, type of stimulus, electrode position and refractive states of these, the refractive error by a blur in the retina. It is a better test to identify the visual pathway than the scanning such as MRI (magnetic resonance imagining).[2] Visual pathway and visual cortex abnormalities affects the VEP results. For example, cortical blindness, demyelination due to optic neuritis, optic atrophy, hydrocephalus and tumors of the brain which compress the optic pathway. In multiple sclerosis the myelin plaque slows the speed of VEP.[3] A study reported that poor dormancy was augmented and amplitude diminished devoid of modification of refractive fault.[4] There is decreased amplitude by 25% per diopter of defocus.[5] Refractive errors blur the stimulus causes de focusing of image. That stimulated de focused image show very significant changes in latency and amplitude of VEP. It is estimated globally that one to two billion people have refractive error.[6] These refractive errors are corrected by spectacles because it is the safest and easiest method of treatment. Visually intensive occupations are also at risk factor for the progress of this refractive erros. The diagnosis of refractive error is based on clinical examination of eye

by using a retinoscope and large number of lenses of different powers. Sometimes automated refract meters used to estimate the error.[7] In our community the prevalence of myopia is greater than hypermetropia. The estimated prevalence of myopia in Pakistan is 36.1%. While that of hypermetropia is 27.1%.[8]

The different components of VEP are disturbed in different disorders for example latency of VEP is prolonged in demyelinating diseases of the visual pathway and the amplitude is reduced in the axonal damage.[9,10]

The rationale of study is to prevent the misinterpretation of the VEP results for ocular pathologies in the more prevalent myopia individuals. Present study determine effects of myopia on Visual Evoked Potentials in subjects attending tertiary care eye hospital.

METHODOLOGY:

A prior ethical approval was taken from the Institute Review Board (IRB) of the institute protocol number given was RP/03-2021. This was a cross-sectional study with non-probability convenience sampling technique. It was carried out at Department of Ophthalmology Peoples Medical College Hospital Nawabshah tertiary care hospital of Sindh / GMMMC Sukkur from March 2021 to November 2021. Sample size calculation was calculated using statistical formula, $n=Z^2 \times Px\ q \times N/e^2\ (N-1)+Z^2\ P \times q$ where, Z = Standardized tabulated value=1.96 at 95% confidence interval, P = Prevalence (36.1%)

e = Margin of error 5% and required sample size was found to be n = 180

Inclusion criteria were any gender, age 25 to 45 years with diagnosed with myopia. (Below the age of 25-year myopia is progressive and refractive error becomes is not static. Above 45-year myopia is rare, so researcher took the peak age). A written consent were taken from all respondents. Exclusion criteria were optic atrophy, Extensive retinal disease, any neurological disorder like multiple sclerosis and stroke, and those who did not give consent.

Patients diagnosed to have myopia by doing retinoscopy / auto refractometer (objective refraction) and manually corrected with the trial lenses that is subjective refraction were sent to Shanza Neuro Center opposite PMC hospital Nawabshah for VEP test as routine protocol and findings were recorded. The amplitude and latency of VEP waves were recorded with and without correction of visual acuity. Any change in parameters of Amplitude and latency were tabulated in data form. The data statistics was there after analyzed. The trial box were provided to the concerned doctor of the Shanza Neuro Center (where this VEP testing facility is available) who performed the VEP without (Case) and with correcting lenses (Control) already prescribed by optometrist / doctor of eye OPD. Financial expenses were beard by researcher. Statistical Analysis was done using Statistical Package for Social Sciences (SPSS) version 25.0. Descriptive variables were used and presented as Mean, Standard deviation and frequency and percentages. Normality of data was checked prior to analysis. Variables were found to have symmetrically distributed. Inferential statistics were explored using one-way ANOVA test and Independent sample t-test. P-value = 0.05 was considered as statistically significant level.

RESULTS:

A total of 180 patients were included in this study. Mean age of the patients was 39.14 ± 6.73 years. There were 108 (60%) patients with =40 years of age and 72 (40%) patients with >40 years of age. Gender distribution showed that 96 (53%) females and 84 (47%) males. Best corrected visual acuity of right eye was found 6 /6 in 147 (81.66%) while left eye 162(90%) patients. Mild degree of myopia of right eye was found in 81 (45%) patients, moderate in 69 (38.33%), severe in 30 (16.67%) patients. Mild degree of myopia of left eye was found in 90 (50%) patients, moderate in 69 (38%), severe in 21 (12%) patients. (Table 1)

The mean pattern stimuli amplitude of right eye was 6.11 ± 0.7 in cases (without correction) and 6.14 ± 0.6 in controls (with correction) with not significant P-value 0.855, while in left eye was 6.13 ± 0.2 in cases (without correction) and 6.33 ± 0.8 in controls (with correction) with not significant P-value 0.766. The mean pattern stimuli latency N70 in right eye was 86.5 ± 8.1 in cases (without correction) and 83.62 ± 7.9 in controls (with correction) with not significant P-value 0.081, while in left eye was 88.62 ± 7.9 in cases (without correction) and 85.09 ± 7.0 in controls (with correction) with not significant P-value 0.087. The mean pattern stimuli latency P100 in right eye was 92.07 ±5.1 in cases (without correction) and 82.09 ± 5.8 in controls (with correction) with significant P-value 0.023, while in left eye was 93.55 ± 6.7 in cases (without correction) and 83.6 ± 7.0 in controls (with correction) with significant P-value 0.028. The mean pattern stimuli latency N155 in right eye was 85.90 ± 5.6 in cases (without correction) and 83.20 ± 6.3 in controls (with correction) with not significant P-value 0.078, while in left eye was 84.55 ± 6.6 in cases (without correction) and 82.05 ± 6.3 in controls (with correction) with not significant P-value 0.056. (Table 2)

In cases of Mild Myopia, mean pattern stimuli latency P100 in right eye was 85.68 ±7.5 and in left eye was 81.20 ± 7.9. In moderate myopia mean latency P100 in right eye was 94.21±8.1 and in left eye 93.46±6.4. Whereas in severe myopia mean latency P100 in right eye was 98.37±6.7 and in left eye was 99.28±7.35 with significant P-value < 0.001. Other parameters like amplitude, latency N 70 and Latency N 155 was found insignificant in different degree of myopia cases. (Table 3)

DISCUSSION

Visual evoked potential (VEP) is a tool to screen out the

Table 1: Demographic Characteristics of respondents

Age (years)	Frequency	Percentage
=40	108	60.00
>40	72	40.00
Gender		
Male	84	46.67
Female	96	53.33
Best corrected Visual Acuity (Right Eye)		
< 6/6	33	18.33
6/6	147	81.67
Best corrected Visual Acuity (Left Eye)		
< 6/6	18	10.00
6/6	162	90.00
Degree of Myopia (Right Eye)		
Mild	81	45.00
Moderate	69	38.33
Severe	30	16.67
Degree of Myopia (Left Eye)		
Mild	90	50.00
Moderate	69	38.33
Severe	21	11.67

Table 2: Mean Visual Evoked Potential (VEP) with and without correction of Lens versus study Parameters

FLASH STIMULI Amplitude	**Mean Visual Evoked Potential (VEP) without correction of Lens**	**Mean Visual Evoked Potential (VEP) with correction of Lens**	**P-value**
Right Eye	6.11±0.7	6.14±0.6	0.855
Left Eye	6.13±0.2	6.33±0.8	0.766
LATENCY N70			
Right Eye	86.5±8.1	83.62±7.9	0.081
Left Eye	88.6±7.9	85.09±7.0	0.087
LATENCY P100			
Right Eye	92.07±5.1	82.09±5.8	0.023
Left Eye	93.55±6.7	83.6±7.0	0.028
LATENCY N155			
Right Eye	85.90±5.6	83.20±6.3	0.078
Left Eye	84.55±9.6	82.05±6.3	0.056

*Independent Sample t test was applied to see the significance
*P-value = 0.05 considered to be statistically significant

Table 3: Comparative Analysis of Study Parameters versus Degree of Myopia

Parameters / Visual Status	Mild Myopia		Moderate Myopia		Severe Myopia		P value
	RIGHT EYE	LEFT EYE	RIGHT EYE	LEFT EYE	RIGHT EYE	LEFT EYE	
AMPLITUDE	5.62± 0.7	5.43± 0.5	5.07±0.6	5.21±0.6	4.90±0.8	5.01±0.6	0.124
LATENCYN70	83.80±6.4	85.63±6.7	85.6±7.20	89.06±6.5	91.4±6.2	92.3±5.8	0.07
LATENCY P100	85.68±7.5	81.20±7.9	94.21±8.1	93.64±6.4	98.37±6.7	99.28±7.3	< 0.001
LATENCY N155	82.89±6.3	83.11±5.2	86.51±7.1	86.20±8.9	90.20±6.9	89.95±7.2	0.11

*One Way ANOVA test was applied to see the significance
*P-value = 0.05 considered to be statistically significant

visual pathway defects it uses visual stimuli and measures the response in reaction to it. Myopia is a refractive error mostly prevalent in adulthood characterized by focusing of light rays behind the retina.[11] In this study we measured the changes in VEP with regard to amplitude and latencies in myopic individuals with and without correction (case/control) it was found that flash stimuli VEP do not show significant change in myopic with and without correction but N70, P100 and N155 showed noticeable change in the amplitude and latencies. A literature evaluated that the poor latency in myopia and found significant negative correlation between refractive error and poor latency and found that in high myopia the latency of uncorrected eyes was 107.99 mile seconds and after correction of high myopia 102.19 mille seconds.[12]

In present study the mean pattern stimuli latency P100 in right eye was 92.07 ±5.1 in cases (without correction) and 82.09 ± 5.8 in controls (with correction) with significant P-value 0.023, while in left eye was 93.55 ± 6.7 in cases (without correction) and 83.6 ± 7.0 in controls (with correction) with significant P-value 0.028.

Similar results showed by **Thabit MN** et al[13] with significant differences in amplitude of P100 latency increases among cases and controls. Mean value in case were presented as 132±2.2 and in control 107.7± 1.8. Another study[14] from Bhopal reported that no significant differences observed in latency P100 in the group without refractive error. However, it was highly significant found with refractive error. This is parallel to the study[15] carried out by **Agrawal A** et al who also deduced that P100 amplitude decreases and P100 latency increases with degree of myopia. The P100 being the most significant element of VEP that is effected by myopic change.

Evans AB[16] stated that it is of the same idea that P100 amplitude and latency changes are directly proportional to the refractive error.

Myopia effects on parameters like amplitude, latency N 70 and Latency N 155 was found insignificant in different degree of myopia cases. Similar results reported Hamilton R et al[17] blur in stimulus effects VEP. Another author **Zheng X** et al[18] in his study that Reduction of Visual acuity (VA) or of the contrast of the stimulus induces a prolongation of the pattern reversal visual evoked potential (PR-VEP) latencies. Literatures support that these conditions cause deterioration of the visual capacity to recognize objects and may preferentially activate the slower central retina channel.[19,20]

Present study showed that P100 amplitude decreased significantly and latency increased significantly with degree of refractive error and correction of the refractive error reduces these changes thus flash VEP is not much effected by refractive errors but pattern especially P100 significantly changes with refractive error. Henceforth it is suggested that prescribing investigation of VEP for any neuro-ophthalmic diseases the refractive error be corrected first in order to restrain from false positive results.

CONCLUSION:

Greater the myopia greater were the VEP changes with regards to latency and amplitude in pattern stimuli. P100 being the most affected component in this regard. It is therefore postulated that every patient sent for VEP investigation for any neuro ophthalmic disease should have refractive error myopia corrected first.

Authors Contribution:
Abdul Haleem Mirani: Conceived the study, Manuscript writing, Design of study, Literature review
Amjad Ali: Supervised the work and final review
Ataullah Bukhari: Study design & Methodology writing
Tehmina Imdad: Statistical Analysis and Results
Ateeq U Rehman Channa: Clinical work and data collection
Maqbool Ahmed Jamali: Help in discussion writing and Final Review

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Original Article **Open Access**

Assessment of Family planning services utilization among women of Union Council Bangoin (Rawalakot) Azad Jammu and Kashmir

Mehwish Fayaz, Qandeel Tahir, Tehmina Zafar, Muhammad Usman Tayyab Butt

ABSTRACT

Objectives: To determine the percentage of women in Union Council Bangoin (Rawalakot) Azad Jammu and Kashmir who use family planning services, and to determine the relationship between demographic characteristics and family planning service use (AJ&K).

Study design and setting: A cross-sectional study was conducted in UC Bangoin (Rawalakot) Azad Jammu and Kashmir over the duration of 6 months, from 5 January to 5 July 2021.

Methodology: A sample of 344 married women with the age range 18 to 45 was obtained. The study's assessment instrument was developed from an existing assessment tool (Reproductive health knowledge and services utilization among rural adolescence in Ethiopia 2014). It included 14 questions on demographics and 13 questions about the use of family planning services.

Results: High utilization was 52% (n=179) while low utilization was 48% (n=165). Most of them had fear of side effects of using contraception (n=170, 48.9%). Chi-square test showed significant association (p-val =0.05) between fear of side effects of using contraception, decision of using contraception, education level, distance from home to hospital, number of children, exposure to mass media and utilization of family planning services.

Conclusion: There was low family planning services utilization in that area. Study showed that there was a strong association between fear of side effects of using contraception, low education and low exposure to mass media with utilization of family planning services in Union Council Bangoin (Rawalakot) Azad Jammu and Kashmir (AJ&K).

Keywords: Contraception, Contraception behavior, Family Planning services, Family planning policy, Sex education.

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INTRODUCTION:

To control population and improve mother and child health, family planning is broadly acknowledged. Family planning has the potential to save 30% of maternal fatalities and 10% of infant deaths, making it one of the most health-promoting and cost-effective public health efforts. By decreasing the maternal mortality and morbidity and improving space between pregnancies, family planning assists in achieving the Millennium Development Goals (MDGs).[1]

The government of Pakistan has been striving to enhance access to family planning services. However, as in many nations across the globe, there is still a need for family planning that has not been fulfilled. In the last 60 years, Pakistan's population has grown. Pakistan has grown from 44 million to 221 million people since 1960, and it is estimated that by 2050, the country would have a population of over 330 million. The country's growth rate of 3.00 percent is quite generous. “Overall, 34% of the married women employed some form of family planning, with 25% using modern methods and 9% using traditional methods. The most common modern techniques are male condoms and female sterilization (each used 9 percent). The contraceptive prevalence rate (CPR) among married women varies by age, rising from 7% among women aged 15-19 to 48% among women aged 40-45 before dropping to 37% among women aged 45-49”.[2]

Women in urban areas are more likely to use a contraceptive method than women in rural areas (43 percent and 29 percent, respectively). With knowledge and money, the use of contraceptive treatments, both contemporary and traditional, rises.[3]

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For example, compared to 30 percent of married women with a secondary or higher level of education, 22 percent of married women with no education used modern contraception. Similarly, 7 percent of married women with no education used conventional practices, compared to 14 percent of married women with a higher level of education who did. The population of Azad Jammu and Kashmir (AJ&K) is growing at a pace of 2.41 percent each year, with an average family size of 6.7 members.4

A total of 57 Family Welfare Centers are currently providing family planning services in ten districts in the state. These include Family Welfare Centers (FWCs) in the districts of Neelum, Bagh, Haveli, Poonch and Muzaffarabad as well as RHSC-A Centers in the districts, RHSC-A Centers in the tehsils, and 120 Social Mobilizers. In AJ&K, the demographic pyramid also shows the usual youthful hump, and rising urbanization trends are providing an even larger difficulty for our policymakers. 5

As a non-industrialized state with a limited private sector, we will have a major challenge in the years to come when it comes to finding jobs for our people. 6

The unmet need for family planning services in AJ&K is reaching 46 percent, which is intolerable. 7

Because of the dispersed population over such a large hilly area, impoverished people's access to services is severely restricted. Women's mobility is restricted outside the home due to poor economic conditions and a lower social status".8

This study was conducted to find out the percentage of women utilizing family planning services, to find out the association between demographic factors and utilization of family planning services in the Union Council Bangoin (Rawalakot) Azad Jammu and Kashmir (AJ&K).

METHODOLOGY:

In Bangoin (Rawalakot), Azad Jammu and Kashmir, a cross-sectional research was undertaken (AJ&K), over a period of six months from 5 January to 5 July 2021. It consist of 21 village, having 9456 household with the population of 1509 (census 2017).A sample of 344 married women with the age range 18 to 45 was obtained. Nonprobability convenient sampling was used. Informed Consent was taken from participants taking part in study. Confidentiality of participants was ensured. Data was collected by using questionnaire from door to door 34% prevalence was taken from (PDHS 2017-2018).[20] By using formula $n=Z^2(pq)/e^2$

e is the margin of error and Z is the z-score of the number of the standard deviation. At Margin of error of 5%, 95% confidence interval and 34% prevalence the sample size was 344 and after summing up 10% possible non-response final sample size was 390.Data was collected using a semi-structured questionnaire derived from a prior research on the usage of family planning services (Reproductive health knowledge and services utilization among rural adolescence in Ethiopia 2014).

It consisted of two section A and B.

Section A (Demographic profile); Age of respondent, Education level of respondent, Respondent Profession, Husband education, Husband Profession, Family type, Total family income, Total family members, Distance from home to hospital, Number of children, Fear of side effects of using contraception, Exposure to mass media, which family member decide to use contraception, Birth interval between last two children.

Section B (Utilization of Family Planning Services); It consists of 13 questions to assess the utilization of family planning services.

Contraception use, use in last 12 months, Contraception method, heath worker service, health facility visit, health center, family planning poster, brochure, Discussion, Consultation, Doctor reviews, comfort, Availability.

Inclusion criteria was married women with one or more children. Women who were resident of Union council Bangoin (Rawalakot) AJ&K.

Exclusion criteria was women who were not willing to participate. Women who were not available at the time of data collection.

Reliability was tested by calculating Cronbach's alpha by using SPSS that was 17.0. Cronbach's alpha was 0.7. Statistical significance was set up to $p= 0.05$.

Questionnaire was translated into Urdu and a pilot study carried out to ensure its validity before the main study could begin.

SPSS version 17.0 was used to conduct the analysis. Through frequency generation and sorting, all the initial data was thoroughly cleaned. For categorical variables, frequency and percentage were used to conduct descriptive analysis. Statistical significance was established using a Chi-square test for independence and a 95% level of confidence was used to find the relationship between independent and dependent variables, respectively.

Research was approved by institutional review board of Al-Shifa School of public health Rawalpindi Pakistan IRB number was MSPH-IRB/10-27.

RESULTS:

Demographic Characteristics of Respondents: Total sample of 344 women of age 18-45 was included in the study. About age of respondent 8.9% were with the age of 18-24, 39.7% were with the age of 25-31, 32.5%were with the age of 32-38, 17.5% were with the age of 39-45.

Concerning respondent profession; 83% were housewife, 10% were teachers, 0.6% were health workers, 2% were Tailor, 3% were with other profession. Out of 344; 16% husbands were illiterate, 41% were with primary education, 17% were with Matric education, 10% were intermediate,

and 13% were graduates.11% husbands were unemployed, 8% were government employees, 34% were business man, 5% were private employees, 41% were with other profession. About 18% having 3 family members, 10% having 4 family members, 19% having 5 family members, 21% having 6 family members, 28% having more than 6 family members.

Out of 344; 11% with 10, 000 monthly income, 16% with 20,000 monthly income, 14% with 30,000 monthly income, 15% with 40,000 monthly income and 42% with more than 40,000 monthly income.44% women were living in nuclear family and 54%were from joint family.

10% having 1-2km, 26% having 3-4km, 21% having 5-6km, 31% having 7-8km, and 10% have more than 8km from home to hospital. 51% have no fear, 49% have fear of side effects of contraception. Out of total sample 45% have no exposure, 54% have exposure to mess media.

3% having 1 child, 32% having 2 children, 37% having 3 children, 18% having 4 children, 8% having more than 4 children.

44% had husband wife mutual decision, 43% respondent itself decide,6% only husband involve in decision, 4% mother in law involve,2% having other to decide.

Concerning birth interval between last two children; 23% have 1 year birth interval, 33% have 2 year birth interval, 21% have 3 year birth interval, 10% have 4 year birth interval, 11% have more than 4 year birth interval between last two children.

Utilization of Family Planning Services: Low utilization was 48%(n=165) while high utilization was 52%(n=176). Regarding utilization of family planning services 16% had never used any contraception to avoid pregnancy, 46% had rarely used, 14% occasionally used, 18% frequently used while 6% used very frequently. Concerning use of contraception in last 12 months; 41% had never used, 40% rarely used, 7% occasionally used, 6% used frequently while 5% used very frequently. About contraception methods; 33% had used natural method, 24% used condoms, 18% used oral contraceptive pills, 15% used injections, 8% used other methods. Concerning information and services by health workers; 43% never get any service or information, 39% were rarely served, 12% were occasionally served, 4% were frequently served while 0.6% were served very frequently. Regarding visit to health facility to get family planning information or services; 36% were never visited, 31% were rarely visited16% were occasionally visited, 7% were frequently visited, 9% were very frequently visited. About last visit; 32% were visited to government health centers, 39% had visited to private health center, 12% had visited to trust health centers, 16% had visited to other health centers. About Posters on family planning; 24% had never seen any poster, 41% had rarely seen any poster, 19% had occasionally seen any poster, 4% had frequently seen any poster, and 10% had very frequently seen posters on family planning. Concerning provision of brochure on family planning; 48% had never got any brochure, 28% had rarely got brochure, 10% occasionally got brochures, 12% frequently got brochures, and 1% very frequently got brochures on family planning. Regarding talk about contraception by doctor during consultation; 41% had never, 31% had rarely, 9% had occasionally, 14% had frequently while 5% had very frequently listen about contraception by doctor. Concerning comfort to ask questions about contraception; 15% were strongly disagreed, 27% were disagreed, 39% were undecided, and 17% were agree while 1% were strongly agreed. Regarding availability of Family planning services; 8% were strongly disagreed, 27% were disagreed, 32% were undecided, and 28% were agreed while 4% were strongly agreed for availability of their required services.

Association of various demographic factors to utilization of family planning services:

The association between demographic factors and the use of family planning services was examined using the Chi-square test. There are two categories of family planning service use: low utilization (18%) and high utilization (72 percent). A strong association between Education level of respondent and utilization of family planning services, 54% of respondents who were graduates had high family planning services utilization as compared to under graduates .898(2) ,p-value 0.001. x^2 (df) 18.898(4),p = 0.001.Cross tabs between income and utilization of family planning services showed a significant association 75% of respondents who had monthly income more than 40,000 had high family planning services utilization as compared to respondents who had monthly income less than 40 thousand x^2 (df) 12.038(4), p 0.017. Detailed results given in table.

DISCUSSION:

The purpose of this research was to determine how often family planning services were used. Contraception is the only tool that can stop this population growth that is

Figure 1: Utilization of Family Planning Services

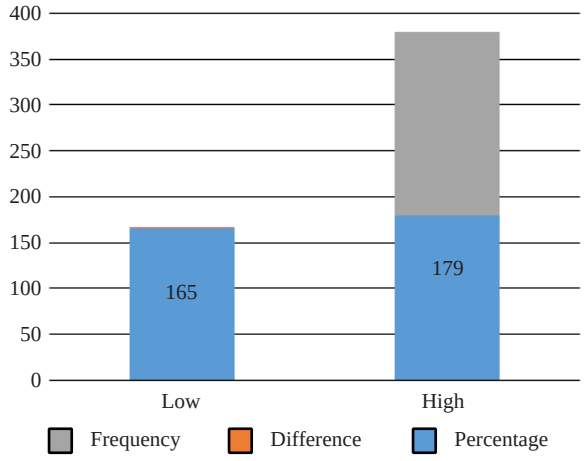

Table 1: Association of demographic factors to utilization of family planning services

Variables	High	Low	Df	x^2	P-value
Respondent education Illiterate Primary Matric Intermediate Graduation	31(48.4%) 83(61.0%) 20(29.0%) 20(48.8%) 16(54%)	33(51.6%) 53(39.0%) 49(71.0%) 21(51.2%) 17(51.5%)	18.898	4	0.001*
Income 10000 20000 30000 40000 More	26(63.4%) 35(60.3%) 15(31.9%) 24(46.2%) 70(48.3%)	15(36.6%) 23(39.7%) 32(68.1%) 28(53.8%) 75(51.7%)	12.038	4	0.017
Fear of side effects No Yes	86(49.7%) 84(49.4%)	87(50.3%) 86(50.6%)	0.003	1	0.001*
Number of children 1 2 3 4 More	9(75.0%) 69(62.7%) 59(45.7%) 23(36.5%) 10(34.5%)	3(25.0%) 41(37.3%) 70(54.3%) 40(63.5%) 19(65.5%)	18.421	4	0.001*
Decision Husband wife Mutual Respondent itself Husband Mother in law Other	78(51.3%) 84(56.0%) 3(13.6%) 5(35.7%) 0(0%)	74(48.7%) 66(44.0%) 19(86.4%) 9(64.3%) 5(100.0%)	20.02	4	0.001*

**Significant at 95 CI, alpha, or p-valve < 0.05*

exponential. Since it gives parents the freedom and responsibility to decide how many and how far apart to their children, family planning out space has long been seen as an effective tool for enhancing the health of both mother and child. In the district of Poonch in Azad Jammu and Kashmir, this research discovered that education, monthly income, fear of side effects, contraceptive usage, and the number of children are the most significant variables impacting women's use of family planning services (AJ&K).

According to a fertility and family planning study, just 24 percent of Pakistanis use contraception, despite the fact that 94 percent of Pakistanis are aware of at least one kind of family planning. According to this study's findings, 40% of women had never used family planning procedures but had stopped due to fear of adverse effects, and several women had also reported side effects, while the remaining 40% had never used contraception.[9] Husband dissatisfaction was expressed by about 43% of respondents. When it comes to using family planning services, man permission and decision-making are critical.[10]

The majority of decision makers in this study were husbands when it came to the number of children and contraceptive use. Research conducted in Bangladesh found that about 85 percent of women need their husband's permission to use contraception.[11] Fear of negative effects was noted by 68 percent of women in a cross-sectional survey in GAZA, with husbands' opposition accounting for 31% of those who didn't use family planning techniques. According to another survey conducted in Turkey, the top reason for married women not using any Family Planning (FP) methods was their husband's disapproval.[12]

In contrast, research conducted at a tertiary care hospital in Lahore indicated that roughly 74% of men had a favorable attitude toward contraception.[13] Education plays a vital role in the lives of women and helps them make decisions. Pakistan has a low literacy rate, with rural areas having a higher rate. According to the research, 15% of women were illiterate, while 39% had only received primary education.[14]

In a cross-sectional research was out in the Khairpur district, oral pills were found to be the most popular option, with 90 percent of respondents knowing about them, followed by female sterilization at 88.3 percent and injectable contraceptives at 87.6 percent.[15] Although it is believed that the media is a significant source of public information[16,17], only 6% of women in this study received family planning information from the media, with health care providers

remaining the most common source of information. While this is encouraging, the media must demonstrate its role in combating resistance to fertility decline in Pakistan[18]. In our country, increasing the use of family planning services is a major challenge.[19,20] Over half of presently married contraceptive users (53%) acquire their supplies from public hospitals, whereas 45 percent get their supplies from the private sector.

CONCLUSION:

Finding suggested that low utilization was 48% while high utilization was 52%. This study found association between family planning use and education, monthly income, fear of side effects, exposure to mass media, interval between last two children and distance from home to hospital. Fear of side effects for using contraceptives has been identified as the major cause of unmet need for family planning in Pakistan.

Authors Contribution:
Mehwish Fayaz: Conduct whole research, (including research design, data collection, data analysis), paper writing
Qandeel Tahir: Supervisor
Tehmina Zafar: Contribution in data collection
Muhammad Usman Tayyab Butt: Data collection & paper writing

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Original Article **Open Access**

Association Between Stress and Parafunctional Habits Among Undergraduate Healthcare Students of Pakistan

Rabia Masood, Afifa Ehsan, Naila Umer, Simra Khan, Mahgul Asif, Sabaiyna Sohail

ABSTRACT:

Objective: Stress is a feeling of mental pressure and tension which leads to parafunctional habits increasing the risk of developing temporomandibular disorders. The purpose of this study was to assess the association between parafunctional habits as well as stress in undergraduate medical and dental students.

Study Design And Setting: This cross-sectional study was carried out from April 01, 2020, to October 31, 2021, amongst the students of different medical and dental colleges, both in the private and public sectors in Punjab, Sindh, and the Federal areas in Pakistan.

Methodology: The study comprised 466 students between 18 to 25 years. A self-compiled and validated questionnaire was shared with students belonging to various years of different medical and dental colleges. Response from all the forms was analyzed using SPSS Version 20 and the relationship between stress and parafunctional habits was assessed.

Results: Results indicated that the stress of studies was the most common stress among students (75.1%, n = 350) while the most common parafunctional habit was lip biting (30%, n = 140). The association between different types of stresses and parafunctional habits was seen to be significantly related to one another.

Conclusion: A significant relationship between parafunctional habits and stress was seen in undergraduate medical and dental students.

Keywords: Bruxism, dental students, habits, medical students, nail-biting, parafunctional habits, stress, temporomandibular joint disorders, thumb sucking.

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INTRODUCTION:

The word "stress" was made up by Hans Selye in 1936, who described it as "*the non-specific response of the body to any demand for change.*". Hans Selye, also known as the father of stress observed that patients with different illnesses were found to be suffering from many similar symptoms that were commonly due to a stressful stimulus.[1] In psychological sciences, it is a feeling of mental pressure and tension. The predictable prevalence of emotional disruption seen in various studies on medical students is greater than that in the overall population.[2] Stress among healthcare students can be a substantial peril, ensuing corporeal or psychological illness, and can harm students' performance as well as professional practice.[3]

Stress can also lead to insomnia which causes hyperarousal leading to an imbalance between sleep and wakefulness. Less sleep duration furthermore results in negative neurophysical functioning causing voluntary and involuntary parafunctional habits.[4] It has also been reported that parafunctional habits such as bruxism are in response to emotional stress and are more commonly encountered in miserable, anxious individuals who are emotionally stressed. Stress has developed into a widespread phenomenon that has advanced extensively in recent years.[4]

Masticatory muscle movements can be natural or irregular and are characterized as functional (e.g., swallowing, chewing, and speaking) or parafunctional (e.g., tooth clenching, grinding, nail-biting, cheek biting, and various other oral habits).[5] Parafunctional behaviors are commonly witnessed in the overall population and can bring about impairment of the dentition, masticatory system, and joints when they surpass the individual's physical and structural forbearance of the masticatory system.[6] Parafunctional habits for instance bruxism and clenching of teeth may likewise intensify the possibility of resulting temporomandibular disorders.

Bruxism and clenching of teeth have occurrence equal to 90% of the overall population and are the most common parafunctional habits. The harmful results of parafunction bring about the collapse of vulnerable structures, which include the teeth, temporomandibular joint, periodontal tissues, and muscles. Whether normal or acute, bruxism and clenching of teeth can cause wear of teeth and can damage oral structures. It can also cause the collapse of periodontal tissues in the existence of muscular dysfunction, inflammation, and internal derangement. Consequently, a patient with such parafunctional habits can have tooth and joint pathology together.[7]

In addition to stress, parafunctional habits are also caused due to anxiety and depend on the personality type of the individual. Personality traits play an important role in an individual's ability to cope with different forms of stress such as those due to emotional reasons and others due as a consequence of depression.[8] Undergraduate learning is a fragile phase in the life of a learner in which they deal with academic pressure and apprehension. Undergraduate learners need to manage the educational and social difficulties which they encounter during their professional careers.[4] Therefore, it is imperative for undergraduate institutes to recognize the levels of stress among their students to present a stress-free learning environment to learners.[4] The current study aims to evaluate the association between these parafunctional habits and stress in undergraduate medical and dental students.

METHODOLOGY:

This cross-sectional study was carried out between April 01, 2020, to October 31, 2021, amongst 466 students of 19 different medical and dental colleges in Punjab, Sindh, and the Federal areas in Pakistan. The sample of the study was calculated through the WHO sample size calculator taking the proportion of stress and depression among medical and dental students equal to 50%, confidence level equal to 95%, and margin of error equal to 5%.[9-10] A random sampling technique was employed to collect the sample. Informed consent was sought from the research participants beforehand. A self-compiled and validated questionnaire was shared with the students belonging to various years of different medical and dental colleges, both in the private and public sectors. The value of Cronbach's alpha achieved was 0.76. The questionnaire comprised various questions regarding types of stress encountered along with different parafunctional habits.

Participants were well-versed regarding the purpose of the research and informed consent was sought beforehand. The study was permitted by the Ethical Review Committee of Islamic International Dental College (IIDC), Riphah International University, Islamabad, Pakistan vide letter no IIDC/IRC/2020/003/009.

The inclusion criteria comprised of:

- Subjects from both sexes, male and female were considered.
- Subjects ranging from 18 to 25 years of age were incorporated.

The exclusion criteria comprised of:

- Subjects who previously had orthodontic treatment were excluded.
- Subjects whose age was less than 18 years and more than 25 years were also excluded from the research.
- Subjects who had fresh trauma to the head, neck, or jaw were also excluded.

The data obtained as a result of the questionnaire was statistically evaluated using Statistical Package for Social Sciences SPSS® software for Windows® version 20. Descriptive analysis was generated to calculate frequencies and percentages and the association between the variables of stress and parafunctional habits was studied using the help of the Chi-square test. The significance level was kept at $P = 0.05$.

RESULTS:

Out of the total 466 respondents from different medical and dental colleges, both in the private and public sectors 65.2% (n = 304) were females and 34.8% (n = 162) were males. The age limit included in the investigation was from 18 years to 25 years. The majority of the respondents (87.1%; n = 406) reported that stressful situations (e.g., during exams, viva, and patient interactions) make them feel anxious while the rest 12.9 % (n = 60) stated that they don't feel nervous in such situations. The prevalence of different types of stress among the students is shown in Figure 1, highlighting stress of studies (n = 350; 75.1%) to be the most common stress among students followed by the stress of unclear concepts of the study material (n = 333; 71.5%), the stress of failing (n = 313; 67.2%) and meeting parents and teacher expectations (n = 267; 57.3%). A total of 385 respondents reported having some sort of parafunctional habits, among them most common was lip biting (30%; n = 140) followed by the clenching of teeth (13.3%; n = 62). Other parafunctional habits among the students were lip licking (11.4%; n = 53), nail biting (9%; n = 42), grinding of teeth (10.1%; n = 47), chewing of food on one side (4.7%; n =

22) and cheek biting (4.1%; n = 19). The association of parafunctional habits with gender was found to be insignificant (Table-1). A significant association was found between a few types of stress and parafunctional habits (Table-II). The stress of failure, future uncertainty, and stress of unemployment was found to be the most common reason resulting in maladaptive habits among the students. Lip biting, clenching, and grinding of teeth was commonly noted concerning this stress.

Figure 1: Prevalence Of Different Types Of Stress Amongst Medical and Dental Students

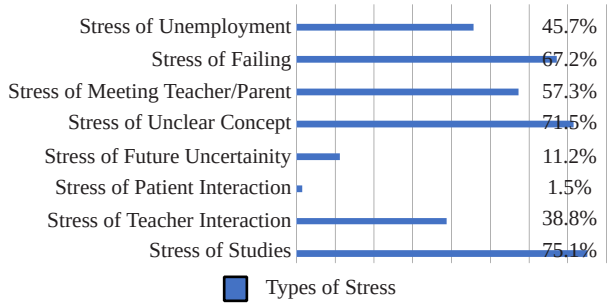
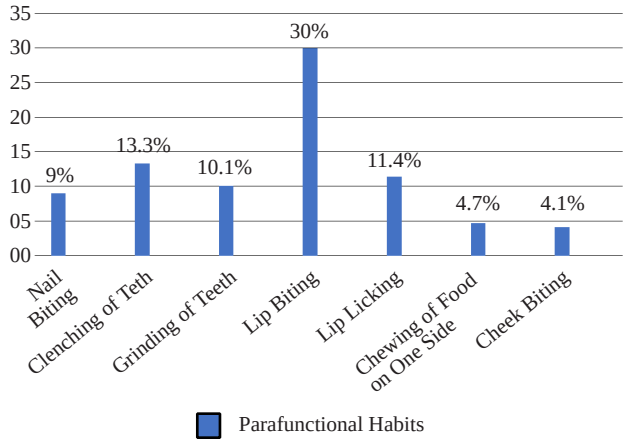


Figure 2: Prevalence Of Different Types Of Parafunctional Habits Among Medical and Dental Students



DISCUSSION:

Medical and dental school is often regarded as a demanding program. Fear and insecurity are rampant among the pupils, making their psychological and bodily health vulnerable. In this research, dental and medical students were recruited as study participants to accentuate the link between stress and parafunctional behaviors in undergraduate medical and dental students.[4] Bruxism, clenching, grinding of teeth, lip licking, lip biting, nail-biting, thumb sucking, and other oral behaviors not related to mastication, swallowing, or speaking are all examples of oral parafunctional habits. Parafunctional potencies surpass customary masticatory forces, with the subsequent force vector being predominantly horizontal. Keeping in view such circumstances, impairment is prospective to transpire to the teeth and the periodontal tissues.[4]

In the current study, the association between stress and parafunctional habits was assessed and the incidence of parafunctional habits in students was documented. According to the results, 75.1% of the students reported stress from their studies, 71.5% reported stress from unclear concepts of the study material, and 67.2% reported stress from failing. Respondents who reported the previously mentioned stresses also reported parafunctional habits like clenching and grinding of teeth, and lip and cheek biting, thereby showing a positive association between stress and para-functional behaviors.

Studies conducted by Butt et al. found no significant relation between nail-biting, teeth grinding, and clenching while Paulino et al. reported that parafunctional habits, stress, and anxiety had a significant relationship with the development of temporomandibular disorders which are in agreement with the results of the present study.[8,11] Various studies also reported a close association between females and parafunctional habits. Apprehension and dejection scores were found to be considerably greater in female participants. In the current study, 65.2% of the study participants were females and a majority of the respondents had stress which lead to the development of parafunctional habits progressing to temporomandibular disorders.[11-14,16-17]

The most widespread parafunctional habit seen in the present

Table-1: Association Of Gender With Parafunctional Habits

GENDER (%ages within gender)	PARAFUNCTIONAL HABITS								P-value
	Nail Biting	*Clenching Of Teeth*	*Grinding Of Teeth*	*Lip Biting*	*Lip Licking*	*Cheek Biting*	*Chewing Food On One Side*	*None Of Above*	
Male	16 (9.9%)	25 15.4%)	18 (11.1%)	36 (22.2%)	22 (13.6%)	9 (5.6%)	8 (4.9%)	28 (17.3%)	0.268
Female	26 (8.6%)	37 (12.2 %)	29 (9.5%)	104 (34.2%)	31 (10.2%)	10 (3.3%)	14 (4.6%)	53 (17.4%)	

P < 0.05 was considered a significant
*P is significant at the 0.05 level
Statistical analysis was performed by applying Chi-Square Test

Table-2: Association Of Stress With Different Parafunctional Habits

TYPES OF STRESS (%ages within stress)		PARAFUNCTIONAL HABITS								
		Nail Biting	*Clenching Of Teeth*	*Grinding Of Teeth*	*Lip Biting*	*Lip Licking*	*Cheek Biting*	*Chewing Food On One Side*	*None Of Above*	*P-Value*
Stress Of Studies	Yes	30 (8.6%)	50 (14.3%)	35 (10%)	100 (28.6%)	40 (11.4%)	15 (4.3%)	17 (4.9%)	63 (18%)	0.89
	No	12 (10.3%)	12 (10.3%)	12 (10.3%)	40 (34.5%)	13 (11.2%)	4 (3.4%)	5 (4.3%)	18 (15.5%)	
Stress Of Teacher Interaction	Yes	13 (7.2%)	27 (14.9%)	21 (11.6%)	58 (32%)	21 (11.6%)	11 (6.1%)	6 (3.3%)	24 (13.3%)	0.20
	No	29 (10.2%)	35 (12.3%)	26 (9.1%)	82 (28.8%)	32 (11.2%)	8 (2.8%)	16 (5.6%)	57 (20%)	
Stress Of Future Uncertainty	Yes	9 (17.3%)	0 (0%)	7 (13.5%)	19 (36.5%)	6 (11.5%)	1 (1.9%)	3 (5.8%)	7 (13.5%)	**0.03***
	No	33 (8%)	62 (15%)	40 (9.7%)	121 (29.2%)	47 (11.4%)	18 (4.3%)	19 (4.6%)	74 (17.9%)	
Stress Of Patient Interaction	Yes	1 (14.3%)	2 (28.6%)	1 (14.3%)	1 (14.3%)	0 (0%)	0 (0%)	1 (14.3%)	1 (14.3%)	0.69
	No	41 (8.9%)	60 (13.1%)	46 (10%)	139 (30.3%)	53 (11.5%)	19 (4.1%)	21 (4.6%)	80 (17.4%)	
Stress Of Unclear Concepts	Yes	30 (9%)	43 (12.9%)	33 (9.9%)	99 (29.7%)	40 (12%)	13 (3.9%)	17 (5.1%)	58 (17.4%)	0.99
	No	12 (9%)	19 (14.3%)	14 (10.5%)	41 (30.8%)	13 (9.8%)	6 (4.5%)	5 (3.8%)	23 (17.3%)	
Stress Of Meeting Parents/ Teacher Expectations	Yes	21 (7.9%)	41 (15.4%)	31 (11.6%)	81 (30.3%)	33 (12.4%)	12 (4.5%)	12 (4.5%)	36 (13.5%)	0.15
	No	21 (10.6%)	21 (10.6%)	16 (8%)	59 (29.6%)	20 (10.1%)	7 (3.5%)	10 (5%)	45 (22.6%)	
Stress Of Failure	Yes	24 (7.7%)	51 (16.3%)	34 (10.9%)	93 (29.7%)	39 (12.5%)	12 (3.8%)	10 (3.2%)	50 (16%)	**0.02***
	No	18 (11.8%)	11 (7.2%)	13 (8.5%)	47 (30.7%)	14 (9.2%)	7 (4.6%)	12 (7.8%)	31 (20.3%)	
Stress Of Unemployment	Yes	12 (5.6%)	36 (16.9%)	27 (12.7%)	69 (32.4%)	25 (11.7%)	8 (3.8%)	8 (3.8%)	28 (13.1%)	**0.01***
	No	30 (11.9%)	26 (10.3%)	20 (7.9%)	71 (28.1%)	28 (11.1%)	11 (4.3%)	14 (5.5%)	53 (20.9%)	

P < 0.05 was considered a significant
*P is significant at the 0.05 level
Statistical analysis was performed by applying Chi-Square Test

study was lip biting in 30% of the students which was in agreement with the results of Malik et al. whereas other studies observed chewing gums as the most common one.[16,18-19] Thumb sucking was found to be least prevalent which was in agreement with Malik et al. findings although the least prevailing parafunctional habit narrated by Butt et al. was chewing gums.[8,16] Prevalence of temporomandibular disorders as a consequence of oral parafunctional habits was found to be higher in dental students as reported by different studies.[13-15]

The stress experienced by students had a significant association with clenching and grinding of teeth and a close relationship between bruxism and anxiety was also reported by Homeida et al.[14] Bruxism is described as the clenching or grinding of teeth whether awake or sleeping. It's generally done unconsciously, and most individuals aren't aware of it.[6] In an investigation conducted by Atsü et al. there was a positive association between nail-biting and temporomandibular disorders whereas the present study showed no significant association between stress and nail-biting in medical and dental students.[6]

Within the scope of this study, it was determined that there

is a positive association between stress and parafunctional habits like clenching and grinding of teeth, lip biting, pen/pencil chewing, cheek biting, and chewing of food on one side of the oral cavity as seen in other studies as well.[21-22] Treatment planning should take oral parafunctional habits, and anxiety into account simultaneously, and a multidisciplinary methodology combining dentists and psychologists should be appointed for prosperous treatment. Further studies should be conducted with much larger sample sizes including a larger number and a wider spectrum of participants from different hospitals in various areas of the country.

CONCLUSION:

Based on the current investigation we concluded that stress and parafunctional habits are closely associated with one another. There is an increase in parafunctional habits when students encounter stressful situations. The stress of studies is the most commonly encountered among medical and dental students followed by the stress of future uncertainty. Lip biting, clenching and grinding of teeth, and cheek biting are the most common parafunctional habits reported.

Authors Contribution:
Rabia Masood: Contributed to the conceptualization of the study and is responsible for the integrity of the study
Afifa Ehsan: Helped in the acquisition, analysis, interpretation of data, and writing of the manuscript
Naila Umer: Contributed to the initial write-up in the introduction and discussion part
Simra Khan: Contributed to the initial write-up in the introduction and discussion part
Mahgul Asif: Helped in the acquisition, analysis, interpretation of data, and writing of the manuscript
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Original Article **Open Access**

Cytogenetic Analysis of Patients with Recurrent Miscarriages

Muhammad Umar, Hamid Saeed Malik, Hira Nadeem, Babar Zaman, Noor ul Huda Alhadi, Fauzia Khan

ABSTRACT

Objective: To evaluate the cytogenetic analysis of patients with recurrent miscarriages.

Study design and setting: Cross-sectional study, Department of Hematology, Armed Forces Institute of Pathology, Rawalpindi from February 2022 to August 2022.

Methodology: 196 patients (98 couples) of recurrent miscarriages within the reproductive age group were included. Cases with known anatomical or endocrinal causes of recurrent miscarriages were excluded. Couples with abnormal reproductive tract anatomy or abnormal endocrine functions were excluded. A standardized system for human cytogenetic nomenclature was used for identifying all chromosomal aberrations. Axioscope microscopes (MetaSystems, Germany) were used for visualizing the metaphases, and MetaSystems software (MetaSystems, Germany) was used to determine the karyotype of each metaphase. Data were analyzed using the student t-test and Chi-square test. A p-value =0.05 was considered significant.

Results: Of 98 couples, most of the couples experienced 3 miscarriages. The difference in ages between males and females was significant (p-value <0.001). Chromosomal abnormalities were found in 7 (7.2%) of females and 5 (5.2%) of males. Positive family history of RPL was noted in 27 (13.8%) of the participants. A total of 12/196 (6.1%) males and females experiencing RPL had chromosomal anomalies. Out of these 1 individual (0.5%) had structural aberration, 1(0.5%) numerical abnormality, and 10 (5.1%) were found to have Chromosome Polymorphism.

Conclusions: Translocations, numerical aberrations, and chromosomal polymorphism are common cytogenetic abnormalities noted in cases with RPL. Clinicians should refer such couples for karyotyping to rule out the possible genetic causes of recurrent miscarriages.

Keywords: Chromosomes, Cytogenetics, Recurrent Pregnancy Loss

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INTRODUCTION:

One of the most common clinical complications during pregnancy is miscarriage. In nature, miscarriages usually occur at 20–28 weeks of pregnancy as a way to select genetically normal offspring. As nature's quality control, miscarriages occur spontaneously.[1] It is estimated that 15–20% of clinically recognized pregnancies end in early pregnancy loss in the first trimester.[2]

The term recurrent pregnancy loss (RPL) refers to three or more consecutive losses of pregnancies before 20 to 22 weeks of pregnancy, but in recent years, even two consecutive miscarriages have been considered RPL. In clinically recognized pregnancies, approximately 15% will result in pregnancy failure, with occult abortion being an unrecognized subset of these cases.[3]

Only 50% of RPL cases have an identifiable etiology, while the rest remain undetermined.[4] A chromosomal aberration in the embryo is thought to be responsible for 60% of RMs.[5] Several factors have been proposed as contributing factors to RPL, making it difficult to determine its exact cause. Among these factors are genetics, advanced maternal and paternal ages, luteal phase defects during pregnancy, endocrine dysfunction, autoimmunity, infectious diseases,

environmental toxins, congenital anomalies, and uterine anomalies.[6]

Statistically, 25–50% more chances for miscarriage are present when one parent carries chromosome abnormalities than when the other does.[7] In fact, 50% of spontaneously aborted infants have abnormal chromosomes.[8] The abnormalities include structural chromosomal aberrations as well as numerical chromosomal anomalies.[9] Fetal genetic defects are usually responsible for repeated pregnancy losses during the first trimester.

Chromosome anomalies are also common in late pregnancies. Approximately 30% of pregnancies lost in the second trimester of pregnancy and 5% in the third trimester are affected by chromosomal anomalies.[10]

As a result of balanced chromosomal rearrangements, unbalanced gametes can cause RPL, stillbirths, and neonates with multiple congenital anomalies. Recurrent miscarriages can be caused by balanced structural chromosome abnormalities (such as inversions and translocations) in parents.[10] Couples, who are unable to create a viable pregnancy, may feel guilty and physically exhausted because of RPL. Chromosome analysis of both parents is recommended for the management of recurrent miscarriages.[10] Researchers have reported varying frequencies of balanced chromosomal rearrangements between 2% to 8% in couples that experience RPL. The rate is much higher than the 0.2% to 0.5% observed in the general population. Chromosome rearrangements were not accurately estimated in our population of couples with RPL.[3]

Currently, cytogenetic analysis of miscarriages is an uncommon practice, and couples with RM have been negatively affected by this unfortunate omission. Unfortunately, this omission has negatively impacted the management of couples with RM. The study aims to improve the knowledge of clinicians in the region regarding cytogenetic analysis of repeated miscarriages as well as generate baseline data regarding chromosomal aberrations among RM patients.

METHODOLOGY:

This cross-sectional study was conducted at the Department of Hematology, Armed Forces Institute of Pathology Rawalpindi for a duration of six months (February 2022 to August 2022). Ethical approval was obtained from the institutional review board (IRB) vide reference number (FC-HEM21-13/READ.IRB/22/1293). After a thorough literature search, we calculated the sample size using a WHO calculator, keeping a 5% margin of error,95% confidence level, and prevalence of recurrent pregnancy loss (RPL) of 15%.[3] Sample size of 196 was calculated. Sampling was done using the nonprobability convenient sampling technique.

Inclusion criteria: Affected couple (Husband & wife) within the reproductive age group with two or more consecutive pregnancy losses.

Exclusion Criteria: Abnormal reproductive tract anatomy, abnormal endocrine functions, positive TORCH screening, and positive antiphospholipid antibody screen were excluded from the study.

Before enrolling all patients, we obtained their written consent, and the confidentiality of the patients was ensured at all levels. Detailed history and complete physical examination were done. Following standard protocols for preparing metaphase chromosomes, they were G-banded using Trypsin-Giemsa banding preparations. During this process, at least 20 metaphases were studied; however, if abnormal findings were observed, the metaphases were studied by 50. A standardized system for human cytogenetic nomenclature was used for identifying all chromosomal aberrations. Axioscope microscopes (MetaSystems, Germany) were used for visualizing the metaphases, and MetaSystems software (MetaSystems, Germany) was used to determine the karyotype of each metaphase.

Data were entered in Microsoft excel and later analyzed using Statistical Package for Social Sciences (SPSS) 21.0. A Chi-square test and a student t-test was used. A p-value =0.05 was considered significant. Calculation of mean and SD was done for quantitative variables while frequency and percentage calculation was done for qualitative variables.

RESULTS:

A total of 98 couples (196 individuals) with a history of recurrent pregnancy loss (RPL) were included in this study. Of these, the number of miscarriages ranged from 2 to 5. Most of the couples experienced 3 miscarriages. The mean age of patients was 30.16±3.23 years. The mean age of females was 27.87±1.85 years with a mean of miscarriage 3.27±0.53 while the mean age of males was 32.45±2.64 years with a mean of miscarriage 3.27±0.53. The difference in ages between males and females was found by using a student t-test which is significant (<0.001). (Table 1) Among all participants, chromosomal abnormalities were found in 7 (7.2%) of females and 5 (5.2%) of males whereas 91 females (92.8%) and 93 males (94.8%) had a normal karyotype. This study also revealed a positive family history of RPL in 27 (13.8%) of all participants. In our study, only 12/196 (6.1%) males and females experiencing RPL had chromosomal anomalies. Out of these 1 individual (0.5%) had structural aberration, 1(0.5%) numerical abnormality, and 10 (5.1%) were found to have Chromosome Polymorphism. Detailed information on the frequency of chromosomal abnormalities is provided in Table 2. The structural Chromosomal Abnormality included Robertsonian translocation detected in 1 female at Chromosome 45XX t(14;21). The only numerical anomaly was 47, XYY. Chromosome Polymorphism comprises about 10/12 (83.3%) of total chromosomal abnormality observed. The most frequent polymorphisms observed was $1qh^+$ (3 male and 4 females), followed by $9qh^+$ (1 female and 1 male) then $16qh^+$ (1 female).

DISCUSSION:

The consequence of RM is both physical and psychological. Physical issues include bleeding and infections whereas psychological consequences increase the risk of anxiety, depression, post-traumatic stress disorders, and suicidal thoughts. A study done in the year 2021 by Prof Sibohan *et al*,[11] stated that the risk of miscarriages is 15.3% (95% CI; 12.5%-18.7%) in all pregnancies. They noted a prevalence of 1.9% for two miscarriages (1.8%-2.1%) , 0.7%(0.5-0.8%) for three or more miscarriages. We also noted 1% of our cases with two miscarriages but in our study, the highest number of cases were with three miscarriages n=73, 74.5% followed by four miscarriages, n= 21 (21.6%). In a local study done in Pakistan, the mean abortions in cases with RPL was 3.40± 1.23 which is similar to our mean miscarriage of 3.27±0.53.[12] A study done by Santjohanser *et al*,[13] documented the mean age of participants as 37.3 ± 4.4 years. The mean age of patients in our study was 30.16 ± 3.23 years. In another study, the mean maternal age at the time of pregnancy loss was 34.3 years.[14]

Our study revealed a positive family history of RPL in 13.8% of n=27 cases. A positive family history was also noted by FABIO *et al*,[15] in a case-control study (13 cases versus 8 controls, RR 3.2%, CI (1.3- 8.1%). In another study done by Silvana *et al*,[16] the family reproductive data showed that there is a two to three times high risk of RPL in couples with positive family history than that in the general population. Similar results were observed by Andrea *et al*,[17] in a meta-analysis, and a systematic review was done in the year 2020. They documented that women who reported recurrent miscarriages were more likely to report a family history of miscarriage (OR 1.90,95% CI 1.37-2.63). They also documented that all the recurrent miscarriages occurred in the first trimester as noted in our study(100%, 98 couples).

In our study 92.8% females n= 91 and 94.8% males n=93 had normal karyotype. In a study done by Silvana *et al*,[16] the majority of spouses had normal karyotypes (88.5% females and 91% males). Among the remaining cases, 65% of females and 76% of males expressed constitutional chromosomal variation most frequently pericentric inversion of chromosome 9 was noted. However, in our study, the only structural abnormality noted was Robertsonian translocation in a female 45 XX t (14;21). A study done by SUDHIR *et al*,[18] noted a chromosomal aberration frequency of 3.4%.In our study chromosomal abnormality was noted in 6.1% cases (n=12/196, 5.2% males , 7.2% females). Balanced translocations formed the largest group in the study of SUDHIR et al 19 with 60% anomalies. In our study, only Robertsonian translocation was noted. 45 XX t(14;21) noted in our study are carriers and at risk of having a child with translocation Down Syndrome.[19] In another study by Kochhar *et al*,[20] chromosomal rearrangements were noted in 6.8%(54/788) cases. These chromosomal rearrangements included 5.9% reciprocal translocations, 0.7% Robertsonian translocations and 0.1% inversions.

In our study numerical abnormality in chromosomes found was 47, XYY (1, 0.5%). Chromosomal polymorphism comprised the highest chromosomal abnormality noted in our study (10/12 . 83.3%). Feng, X. *et al*,[21] in a study on the Chinese population noted that chromosomal polymorphism occurred most frequently in the RPL group as compared to the control group. This finding is similar to that ours**.** The most statistically significant chromosomal polymorphism they observed was in the acrocentric chromosome (p<0.001). We observed the most frequent polymorphism of 1qh+, followed by 9qh+ and 16qh+. They also observed statistically significant Polymorphism of 9qh+, inv (9) and Yqh+ among both groups(p=0.01).[21]

Table 1: Mean age of couples with recurrent miscarriages

Parameter	Females (%)	Males (%)	p-value
Mean age	27.87±1.848	32.45±2.640	<0.001

Table 2: Frequency of chromosomal Abnormality

Parameter		Females (%)	Males (%)	Total (%)	p-value
Numerical Chromosomal Abnormality	Yes	0 (0.00)	1 (1.00)	1 (0.5)	0.316
	No	98 (100)	97 (99.0)	195 (99.5)	
Structural Chromosomal Abnormality	Yes	1 (1.00)	0 (0.00)	1 (0.5)	0.316
	No	97 (99.0)	98 (100)	195 (99.5)	
Chromosome Polymorphism	Yes	6 (6.1)	4 (4.1)	10 (5.1)	0.516
	No	92 (93.9)	94 (95.9)	186 (94.9)	
Consanguineous Marriage	Yes	19 (19.4)	18 (18.4)	37 (18.9)	0.855
	No	79 (80.6)	80 (81.6)	159 (81.1)	
Family History of Congenital Abnormality	Yes	0 (0.00)	0 (0.00)	0 (0.00)	
	No	98 (100.0)	98 (100.0)	196 (100.0)	
Family History of Miscarriages	Yes	16 (16.3)	11 (11.2)	27 (13.8)	0.300
	No	82 (83.7)	87 (88.8)	169 (86.2)	
Time of Pregnancy Loss (trimester Wise)	First	98 (100.0)	98 (100.0)	196 (100.0)	

CONCLUSIONS

RPL is a concerning reproductive health issue that needs further research for correct treatment. Translocations, numerical aberrations, and chromosomal polymorphism are the common cytogenetic abnormalities noted in cases with RPL. Clinicians should understand the significance of cytogenetic analysis in couples with RPL and should refer them for karyotyping at least after two miscarriages to rule out the possible genetic causes of recurrent miscarriages.

Authors Contribution:
Muhammad Umar: Principal Investigator
Hamid Saeed Malik: Supervisor, Study Objective
Hira Nadeem: Proof reading, limitations
Babar Zaman: Biostatistics
Noor ul Huda Alhadi: Discussion
Fauzia Khan: Compilation of Data

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Original Article **Open Access**

Spectrum of Biochemical Derangements in Patients with Covid-19 Infection

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ABSTRACT

Objectives: To evaluate the biochemical derangements in COVID-19 patients according to disease severity.

Place and Duration of Study: This Cross-Sectional Study was conducted at Chemical Pathology Department of Armed Forces Institute of Pathology, Rawalpindi from March to August 2021.

Methodology: A total of 996 patients of age between 20 to 75 years admitted at Pak Emirates Military Hospital Rawalpindi with COVID-19 were selected and further categorized into mild, moderate, and severe groups. Serum samples were collected and analyzed for various biochemical parameters. A mean comparison of the results of these biochemical markers amongst three groups was carried out by applying a one-way analysis of variance (ANOVA), p value = 0.05 was statistically significant.

Results: The values of total bilirubin, ALT, AST, CK, CK MB, troponin I, LDH, urea, creatinine, CRP, PCT, and ferritin increased with the severity of the disease. Whereas the values of albumin and total protein decreased with the severity of the disease. The difference in these parameters amongst all three groups was found to be statistically significant with p value <0.05. However, the values of GGT, total cholesterol, and TG were found non-significant amongst all three groups (p value>0.05).

Conclusion: Derangement of biochemical parameters increased proportionately with the severity of the disease. Hence these markers can provide significant assistance to categorize patients into different severity groups as well as monitoring and prognosis of the disease. In this way, earlier and more accurate medical interventions can be provided to patients for a better outcome from this pandemic.

Keywords: COVID-19, Biochemical markers, Severity groups

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INTRODUCTION:

Emerging pathogens have always been a threat to the whole world. In December 2019, an outbreak of pneumonia of unknown origin was reported in Wuhan, China. On further workup of pneumonia, it was found that the disease is caused by a new respiratory virus whose genome analysis revealed it to be a novel coronavirus related to SARS-CoV and was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] The outbreak then spreaded to many countries causing thousands of deaths worldwide. World Health Organization (WHO) declared coronavirus disease (COVID-19) a pandemic on 12 March 2020.[2] WHO statistical data reveals that 570 Million cases of COVID-19 along with 6.3 Million deaths have been reported worldwide till July 2022. Pakistan is also severely affected by this disease. According to the number of COVID-19 cases worldwide, Pakistan ranks in the 51st position with 1.5 Million confirmed cases and 30 thousand deaths.[3] Various treatment modalities and vaccines have been developed to curtail the spread of disease and to minimize the mortality rate from this outbreak.[4] So far 12.2 billion doses of vaccines have been administered globally.

The virus spreads from one individual to another through respiratory droplets which are produced during sneezing and coughing. The incubation period varies from 2 to 14 days with an average of 5 days. The laboratory plays a significant role in the clinical management of COVID-19, starting from screening to diagnosis, prognosis, and

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monitoring of the disease. The standard investigation to diagnose COVID-19 is by reverse transcription polymerase chain reaction (rRT-PCR) from a nasopharyngeal or throat swab. However, a combination of the history of disease exposure, clinical symptoms, and a chest CT scan showing features of pneumonia are also used to augment the diagnosis.[5]

COVID-19 patients can be identified and prognosticated by changes in their biochemical and haematological parameters. The liver, lungs, heart, kidneys, brain, striated muscles, and RBCs produce more lactic dehydrogenase (LDH). A variety of pathophysiological processes can be triggered by cytokine-mediated tissue damage. LDH is often used in COVID-19 as a non-specific indicator of cellular death. Inflammatory cytokines produce CRP, which increases in response to tissue destruction and the overproduction of inflammatory cytokines. The level of inflammation influences and correlates with CRP levels. An early marker of pneumonia can be used to diagnose the disease and predict its progression.[6]

COVID-19 has a broad spectrum of clinical manifestations, with various degrees of disease severity ranging from asymptomatic patients to acute respiratory distress syndrome (ARDS), multiple organ failure (MOF), and death.[7] The disease affects multiple organs of the body including the liver, kidneys, heart, and CNS, hence leading to various biochemical derangements. These biochemical findings may help the clinician to ensure adequate clinical monitoring, administration of supportive interventions, and assessment of disease severity, progression, and outcome.[8]

Despite abundant research regarding the number of patients and the death rates, there is a scarcity of data regarding biochemical derangements in COVID-19 patients. There has been limited data regarding the pattern of the outcome of disease in relation to biochemical derangements. Our study aims on quantifying the levels of biochemical parameter derangements in relation to the severity of disease which will help in distinguishing the survival and mortality rate of individuals.

METHODOLOGY:

A cross-sectional study was conducted at the Chemical Pathology Department of the Armed Forces Institute of Pathology, Rawalpindi over a period of six months from March to August 2021 after getting approval from the Institute Ethical Committee (FC-CHP19/17/READ-IRB/570). WHO sample size calculator was used to estimate the sample size with a 95% confidence interval and 5% margin of error taking 17.5% as the prevalence of COVID-19 in the Pakistani population.[9] A total of 996 patients who were admitted to the COVID ward of the Pak Emirates Military Hospital Rawalpindi (PEMH) were included in the study. Sampling was done using a nonprobability convenient sampling technique. Inclusion criteria for this research were patients of either gender aged between 20-75 years, diagnosed cases of COVID-19 by using rRT-PCR from a nasopharyngeal swab, and hospitalized in the COVID ward of PEMH Rawalpindi. Whereas, patients without proper medical history and incomplete investigations were excluded from the study. According to the severity of symptoms, patients were categorized into three groups i.e. mild (598), moderate (197), and severe (201). Those who had uncomplicated disease with mild clinical symptoms and without radiological evidence of pneumonia were categorized into a mild group, whereas those who had a fever, respiratory distress, and evident pneumonia on chest imaging were categorized into a moderate group. While, patients who had respiratory complications having a respiratory rate of more than 30 breaths per min, a saturation of oxygen less than 93% at rest, and an oxygenation index (PaO2/FiO2) less than 300 mm Hg were categorized into the severe group.[10]

The blood sample of the patients was collected in a gel tube. After separation of serum samples were analyzed for serum total bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyltransferase (GGT), albumin, creatinine kinase (CK), CK-MB, troponin I, lactate dehydrogenase (LDH), urea, creatinine, C-reactive protein (CRP), procalcitonin (PCT), ferritin, total protein, total cholesterol and triglycerides (TG). Analysis of all these biochemical markers was performed on an automated chemistry analyzer ADVIA 1800 (Siemens). Controls were run on the instrument and plotted on the LJ chart before analysis and were within normal limits.

Statistical analyses were performed using IBM SPSS 26. On applying the Shapiro-Wilk test of normality the data was found to be normally distributed. Percentage and frequencies were used for qualitative variables whereas quantitative variables were expressed as mean ± SD. One-way analysis of variance (ANOVA) was applied to compare means of biochemical markers amongst all three patient groups. p-value = 0.05 was considered to be statistically significant.

RESULTS:

A total of 996 patients were included in our study. Amongst those, 598(60%) had mild, 197(19.7%) had moderate and 201(20.3%) had severe disease. Out of total 996 patients, 739(74.2%) were male and 257(25.8%) were female. Amongst 739 male patients, 470(63.6%) had mild, 166(22.4%) had moderate and 103(14%) had severe disease. Whereas out of 257 females 128(49.9%) had mild, 31(12%) had moderate and 98(38.1%) had severe disease. The mean age of patients was 52.6±9.4 years. The patients with mild, moderate, and severe disease had a mean age of 38.79±9.79, 51.84±13.3, and 67.17±5.27 years respectively.

There have been asymptomatic patients who did not experience any symptoms during the whole duration of the disease but were Covid-19 positive. Table I shows the frequency and percentage of patients who suffered from the major clinical features of COVID-19 which included fever, cough, shortness of breath, and myalgia/ fatigue according

to their disease severity. The recovery and mortality data of the patients were also followed up. Out of 996 patients, 872(87.5%) recovered and were discharged, 93(9.3%) were under treatment and 31(3.2%) patients who were in the severe group died during our study. The patients who recovered and discharged were the highest in the mild group. All the patients who died were in the severe group. On comparing various biochemical markers amongst different severity groups it was found that the values of total bilirubin, ALT, AST, CK, CK MB, troponin I, LDH, urea, creatinine, CRP, PCT, and ferritin increased with the severity of the disease. Whereas, the values of albumin and total protein decreased with the severity of the disease. The difference in these parameters amongst all three groups was statistically significant with a p-value <0.05. However, the values of GGT, total cholesterol, and TG were found insignificant amongst all three groups (p value>0.05) as shown in Table II.

Table 1: Frequency Table of clinical symptoms according to disease severity

	Fever		Cough		Shortness of Breath		Myalgia / Fatigue	
	Yes	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**
Mild (n=598)	430 (72%)	168 (28%)	280 (46.8%)	318 (53.2%)	25 (4.1%)	573 (95.9%)	450 (75.2%)	148 (24.8%)
Moderate (n=197)	175 (89%)	22 (11%)	154 (78%)	43 (22%)	124 (63%)	73 (37%)	160 (81%)	37 (19%)
Severe (n=201)	189 (94%)	12 (6%)	193 (96%)	8 (4%)	201 (100%)	0 (0%)	197 (98%)	4 (2%)

Table 2: Comparison of biochemical markers amongst various severity groups

Parameters	**Mild** (Mean ± SD)	**Moderate** (Mean ± SD)	**Severe** (Mean ± SD)	**p-value***
Total Bilirubin (umol/L)	8.04 ±1.45	9.40 ±2.20	11.60 ±2.56	.001
ALT (U/L)	38.80 ±11.5	42 ±26.02	52.21 ±11.0	.004
AST (U/L)	26.21 ±5.50	30.25 ±7.67	49 ±13.60	<.001
GGT (U/L)	45.2±5.50	41.5±3.93	48.62±4.65	.584
Albumin (g/L)	45.46 ±3.93	36.82 ±9.89	29 ±4.24	<.001
CK (U/L)	71.57 ±17.19	101.08 ±23.28	149 ±15.1	<.001
CK.MB (U/L)	15.18 ±3.03	22.6 ±8.5	35 ±9.8	.001
Troponin I (ng/mL)	0.02±0.01	0.69±0.52	1.29±0.22	<.001
LDH (U/L)	233.2 ±28.27	289.38 ±43.83	338.8 ±34.6	.001
Urea (mmol/L)	5.33 ±1.37	6.14 ±2.29	8.5 ±2.19	.001
Creatinine (umol/L)	80.01 ±11.74	109.51 ±19.26	131.6 ±23.3	<.001
CRP (mg/L)	6.66 ±4.75	63.74 ±3.12	97.2 ±26.39	<.001
PCT (ug/L)	0.14±0.24	2.65±1.25	3.58±1.89	<.001
Ferritin (ng/mL)	128.2 ±54.96	384.88 ±26.36	529.5 ±201.4	<.001
Total Protein (g/L)	68.1 ±4.2	66.3 ±5.3	61.3 ±3.9	<.001
Total cholesterol (mmol/L)	4.19±1.27	4.26±2.96	4.24±1.90	.432
TG (mmol/L)	1.77±0.65	1.36±1.1	1.74±0.97	.587

*One-way ANOVA

DISCUSSION:

Coronaviruses comprises of four structural proteins; Spike (S), membrane (M), envelop (E), and (N). The surface of the virus contains Spike which is a major determinant factor for the diversity of coronaviruses. These proteins bind with Angiotensin-converting enzyme 2 (ACE2).[11] ACE2 receptors are found on lung epithelial cells, heart, ileum, kidney, and urinary. The presence of ACE2 expression on multiple organs, tissues, and cell types could allow virus entry, multiplication, spread, and pathogenesis which may lead to clinical symptoms like breathing difficulties, diarrhea, myocardial injury, and renal failure.[12] Effect of COVID-19 on multiple organs leads to the release of a wide spectrum of biochemical markers which can be used as an important predictor of disease progression and outcome.[13]

In our study, we found that levels of total bilirubin, ALT, AST, CK, CK MB, troponin I, LDH, urea, creatinine, CRP, PCT, and ferritin increased with the severity of the disease.

The values of all these biochemical parameters progressively increased with the severity of the disease. However, serum albumin and total protein were found to be lower in patients with severe disease. Whereas, GGT, total cholesterol, and TG had no role as a prognostic markers of disease severity. Similar results were seen in various studies.

Pourbagheri-Sigaroodi., et al[14] in a study concluded that increased levels of LDH, ALT, AST, CK, creatinine, total bilirubin, and hypoalbuminemia are the most common biochemical findings in COVID-19. Chen., et al[15] revealed that LDH, ALT, AST, bilirubin, and CK were found elevated in 76%, 28%, 35%, 18%, and 13% of patients respectively, whereas albumin level was found to decrease in 98% patients. Guan., et al[16] showed that ALT and AST levels were raised by 21.3% and 22.2% respectively in COVID-19 patients representing virus-induced liver injury. Another study carried out on 149 COVID-19 patients revealed that the serum creatinine levels were raised in 28.8% of patients indicating the ability of SARS-CoV-2 to induce kidney injury.[17] Li., et al[18] found that raised ferritin levels in 90.7% of COVID-19 patients. As an acute phase reactant, raised serum ferritin during inflammation, also its release from dying cells may indicate the extent of organ damage and can be used as a diagnostic tool in COVID-19.[19] Another study revealed that increased levels of PCT and CRP levels could be an important tool for the physician to differentiate between severe and non-severe COVID-19 cases.[20] Major limitation of this study was that it was conducted in a single hospital setting on admitted patients only and biochemical findings of patients were not followed up after they were discharged, secondly the data regarding the effect of treatment given during the course of illness on these markers was not obtained which could be added in subsequent studies. Therefore, a multicentric study with a large sample size involving more hospitals may give a good representation of the desired comparison of various biochemical markers amongst different COVID-19 severity groups.

CONCLUSION:

Diverse variation in the clinical symptoms which range from asymptomatic to severe disease necessitates the use of biochemical markers such as total bilirubin, ALT, AST, CK, CK MB, troponin I, LDH, urea, creatinine, CRP, PCT and ferritin for early and economical prediction of prognosis of COVID-19. Although the gold standard diagnostic test for COVID-19 is rRT-PCR however these biochemical parameters can also provide significant assistance to categorize patients into different severity groups. In this way, earlier and more accurate medical intervention can be provided to patients for a better outcome from this pandemic.

Authors Contribution:
Sajjad Ali Haider: Data collection, data analysis, results, discussion, and literature review
Zujaja Hina Haroon: Data Analysis, results, discussion, and literature review
Athar Iqbal Paracha: Results, discussion, and literature review
Muhammad Aamir: Discussion and literature review
Saima Bashir: Data Analysis and Results
Syed Raza Jaffar: Data collection, Discussion, and literature review

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Original Article **Open Access**

Effectiveness of Intracervical Foley's Catheter with PGE2 Versus PGE2 Alone for Induction of Labour at Term Pregnancy

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ABSTRACT

Objective: To compare the effectiveness of intracervical foley's catheter with prostaglandin E2(PGE2) and PGE2 alone in achieving vaginal delivery in a patient having full-term pregnancy and its impact on maternal and fetal outcome.

Study design and setting: This Comparative cross sectional study was conducted in the Department of Obs & Gynae, in January-December 2021.

Methodology: A detailed history of the patients was obtained, and a physical examination was performed. Patients were randomly allocated into two groups A (cervical Foleys and PGE2) and group B (PGE2 alone).

Results: In Group A, 176 (90.7%) patients showed effective results in achieving vaginal delivery out of which 68.0% were spontaneous and 22.7% instrumental, while in Group B, 172 (88.7%) patients delivered vaginally out of which 48.5% spontaneous and 40.2% instrumental with P<0.01.

Conclusion: This study demonstrated that intracervical foley's catheter with PGE2 yielded significantly better and more effective results in terms of improved maternal and fetal outcomes as compared to PGE2 alone in terms of achieving vaginal delivery and duration of active phase labour.

Keywords: Term Pregnancy, Induction of Labour, intracervical Foley's Catheter, PGE2

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INTRODUCTION:

A frequent obstetric procedure is labour induction. It's an iatrogenic initiation of labour pains. The cervical state at the time of induction determines whether or not labour induction is successful. It is usually expected that patients with low Bishop's scores (B3 or lower) may experience unacceptable greater rates of induction failure. Cervical ripening can be enhanced using prostaglandin E2 and an intracervical balloon catheter.[1] A study demonstrates that the pre-induction cervical ripening effects of the Foley's Catheter and PGE2 gel are comparable.[2] Cervical ripening by whatever means is the solution to reduce induction failure. A low Bishop's score has also been linked to a higher incidence of cesarean sections, maternal fever, and foetal hypoxia, according to research.[3] The great effectiveness of a three-component labour induction shows that PG2 has a significant impact on the cervix, even in the presence of resistance to the previously used PGE2 and followed by Foley catheter.[4] The intracervical Foley catheter balloon was as effective as the dinoprostone on the cesarean delivery rate. In terms of maternal or neonatal safety, there were again no notable differences between the two approaches.[5] For many years, cervical ripening and labour induction have been commonly treated with dinoprostone and misoprostol, prostaglandins. While the details of their mechanics are still being worked out.[6] Combining an intracervical Foley catheter with dinoprostone (PGE2, 0.5 mg) was more effective than using a Foley catheter alone for cervical ripening.[7] Two studies evaluating the use of Foley alone, PGE2, and combined Foley and PGs found that the combined use was not more effective than the separate approaches.[8,9] While maintaining maternal and fetal safety, labour induction seeks to reduce the time to vaginal birth. One study showed rate of vaginal delivery in using Foleys catheter and PGE2 gel simultaneously versus PGE2 was 60% nad 50% respectively.[10] It's crucial to explain to the patient why labour induction is necessary, the risks involved, and any potential alternatives. There are numerous techniques for inducing labour, such as mechanical and pharmacological ones that

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can be combined with one another or used separately. The most appropriate and efficient procedure for cervical ripening and labour induction can be difficult to choose for the proper patient because there is currently insufficient information available.

This study compares the combined mechanical (Foley catheter in combination with PGE2) and pharmacological (PGE2) alone approaches to cervical ripening in unfavourable cervix. Additionally compared between these two groups were the duration of active phase of labour, mother and foetal outcomes.

METHODOLOGY:

This Comparative cross sectional study was conducted in the Department of Obs & Gynae, Khyber Teaching Hospital and CMH, Peshawar from January-December 2021. The sample size for this trial was based on the previously reported outcome rates for Foleys catheter and prostaglandin E2 (PGE2) gel simultaneously versus PGE2, 60% & 50 % respectively[10], taking 95% confidence interval and power of 80% by using WHO sample size calculator. It is a total number of 388 patients, 194 patients in each group. Patients having age 18 Years to 38 Years with 37 weeks pregnant or more and having singleton cephalic fetus with intact membranes were included in this study, while patients who had previous cesarean section or other uterine surgery with fetal malpresentation and multiple gestations having spontaneous labor (3 contractions in 10 min) presented with fever and premature rupture of membranes, PROM and any contraindication for vaginal delivery, Vaginal bleeding, sensitivity to either latex or PGE2 and polyhydramnios were excluded from this study.

DATA COLLECTION PROCEDURE

This study was conducted in the Department of Gynecology, Khyber Teaching Hospital and CMH Peshawar after taking ethical review board with letter no: 173/DME/KMC. Patients fulfilling the study criteria was recruited for the study. Informed Consent was taken from all the included patients. A detailed history of the patients was obtained, and a physical examination performed. Patients were allocated into two

groups A (cervical Foleys and PGE2) and group B (PGE2 alone). In group A the patient lied in a lithotomy position and was covered by sterile sheets. The Foley was inserted through the internal cervical os, filled with 60 ml of normal saline, and taped to the patient's thigh with gentle traction. An hour after placing the Foley bulb, a monitor was performed. If less than 3 contractions per 10 min interval appear in the monitor the patient was transferred to the delivery room and PGE2 was administrated. If 3 contractions or more appear in 10 min intervals, a further intervention was personalized according to a medical decision. The Foley catheter was removed in case of expulsion, each systole, and spontaneous rupture of membranes. In Group B PGE2 alone was given. It was inserted in the posterior fornix using a small amount of water-soluble lubricant. An hour after placing PGE2 fetal monitoring was performed after every 6 hours. If less than 3 contractions per 10 min interval appear in the monitor the patient was transferred for observation and a monitor was performed every 6 hours. If 3 contractions or more appear in 10 min intervals the patient was examined and in dilatation of 3 cm or more was transferred to the delivery room. All the data was documented in proforma.

Data was analyzed in SPSS version 22.0. Mean and standard deviation was computed for numeric variables like age, APGAR score (at 1 minute and 5 minutes), Bishop score and gestational age. Frequencies and percentages were calculated for categorical variable like gravidity, and mode of delivery APGAR score. Chi-square test was used to statistically compare the two groups. Differences with a P-value of <0.05 was considered statistically significant. Effect modifiers like age, bishop score, and gravidity were controlled through stratification to see their effect on the outcome. All results were presented in the form of tables.

RESULTS:

In Group A, the mean age was 25.90+3.55 years. The mean gestational age was 38.51+0.853 weeks. Mean Apgar Score at 1 min was 6.65+1.66 score. Mean Apgar Score at 5 min was 7.65+1.66 score. The mean bishop score was 4.62+1.36 score.

In Group B, the mean age was 25.76+3.55 years. The mean gestational age was 38.50+0.835 years. The Mean Apgar score at 1 min was 6.64+1.67 years. The Mean Apgar score at 5 min was 7.64+1.67 score. Mean bishop score 4.69+1.342 score. In Group A, 110 (56.7%) patients were recorded in 18-25 years age group while 84 (43.3%) patients were recorded in 26-35 years age group. In Group B, 114 (58.8%) patients were recorded in 18-25 years age group while 80 (41.2%) patients were recorded in 26-35 years age group. P Value = 0.681. In Group A, 133 (68.6%) patients were primigravida while 61 (31.4%) patients were multigravida. In Group B, 154 (79.4%) patients were primigravida while 40 (20.6%) patients were multigravida. P Value = 0.015. In Group A, 132 (68.0%) patients had a normal vaginal delivery, 44 (22.7%) patients had instrumental deliveries and 18 (9.3%) patients had C Sections. In Group B, 94 (48.5%) patients had normal vaginal deliveries, 78 (40.2%) had instrumental deliveries, and 22 (11.3%). Patients had C Sections. P Value = 0.0002 (Table No. 1). In Group A, 145 (74.7%) neonates had normal Apgar score while in Group B, 143 (73.7%) neonates had normal Apgar score. P Value = 0.816. (Table No. 3). As per frequencies and percentages for effectiveness in both groups, 132 (68.0%) patients showed effective results while 94 (48.5%) patients in Group B showed effective results, p=0.000092.

DISCUSSION:

According to a study done in India there was no statistically

Table No.1: Mode of Delivery in both groups Frequency

Treatment Group		Frequency	Percent	P Value
Group A (n=194)	Normal Vaginal Delivery	132	68.0%	0.0002
	Instrumental Delivery	44	22.7%	
	C Section	18	9.3%	
	Total	194	100.0%	
Group B (n=194)	Normal Vaginal Delivery	94	48.5%	
	Instrumental Delivery	78	40.2%	
	C Section	22	11.3%	
	Total	194	100.0%	

Group A = Cervical Foleys and PGE2 Group B = PGE2 alone

Table No.2: Duration of an active phase of Labour

	Mean	**Standard Deviation**	**P value**
Group A	3.9	1.1	<0.01
Group B	4.9	1.03	

Group A = Cervical Foleys and PGE2 Group B = PGE2 alone

Table.3: Normal Apgar Score in both Groups

Treatment Group	Normal Apgar Score	Frequency	Percent	P Value
Group A (n=194)	Yes	145	74.7%	0.816
	No	49	25.3%	
	Total	194	100.0%	
Group B (n=194)	Yes	143	73.7%	
	No	51	26.3%	
	Total	194	100.0%	

Group A = Cervical Foleys and PGE2 Group B = PGE2 alone

significant difference between the two groups, however, both groups showed a substantial change in the Bishop's score for Foley's catheter (5.54 ± 1.89) and PGE2 gel(5.44 ± 1.82) with P<0.001. Both group's rates of cesarean sections and side effects were comparable. A comparison of the two groups Apgar scores, birth weights, and NICU admissions revealed no differences.[2]

According to Lixia Zhu's meta-analysis, for this trial, eight trials were used, with 1191 women receiving the dinoprostone insert and 1199 receiving the intracervical Foley catheter balloon. In a random effect model, there was no significant difference between the two groups in terms of the time from induction to delivery (mean difference, 0.71 hours). Regarding the incidence of cesarean deliveries (relative risk, 0.91; 95% CI, 0.78-1.07; P=0.24), the Apgar score, or side effects including the prevalence of maternal infection, postpartum hemorrhage, and hyperstimulation, there was no statistically significant difference between the 2 approaches.[5]

India's study was reported. The change in Bishop Score, the need for a cesarean section, any complications, and the neonatal outcome were the additional outcomes in addition to the Induction Delivery Interval (IDI), which was the primary outcome. Over 80% of the baseline Bishop were nulliparous, with a total of about <4. The combined group had a substantially lower Induction Delivery Interval(IDI) (16 hours and 16 minutes vs. 20 hours 44 minutes, p=0.002) and a significantly higher post-ripening Bishop (6.67 vs. 5.98; p=0.045). (29.1 vs. 25.5%; p=0.669) The CS rate was comparable. The newborn results were similar, and no mother experienced hyperstimulation or chorioamnionitis. As a result, co-administering a single dose of an intracervical PGE2 gel with Foley was more effective for cervical ripening and IOL than using Foley alone.[7] While in our study 68.0% of Group A patients had a normal delivery with 74.7% of neonates were having a good Apgar Score.

In the study, which was conducted in the USA, 71 patients were induced with Foley catheter and 69 with catheter-and-gel in combination. There were no differences between the groups in terms of delivery indications, ultrasound results, labour interventions, intrapartum time interval, mode of delivery, postpartum complications and newborn outcomes.[8]

In a study published in India, 50 women were of Group A received intracervical Foley catheters and PGE2 gel at the same time. Group B had intravaginal insertion of PGE2 gel only. The mean time from induction to the active phase was 5.8 hours for Group A and 6.23 hours for Group B in both groups. Additionally, the mean time from induction to delivery in Group A was 10.085.6 hours, compared to 14.66.9 hours in Group B. This difference is substantial, favoring Group A. Although there was a modest increase in the vaginal delivery rate in Group A, it was not statistically different from Group B (66% vs. 58%, respectively).[10] These results are consistent with our findings, which showed that 94 (48.5%) and 132 (68.0%) patients in Group A and Group B, respectively, had normal vaginal births. P Value = 0.0002.

In terms of better maternal and fetal outcomes, we can confirm that a comparison between the groups showed that one approach offers a statistically significant advantage over the other. However, theoretical concerns about the spread of infection with the use of a Foley's catheter exist, however in this study, 49 (25.3%) and 51 (26.3%) perinatal morbidities were documented in Groups A and B with P=0.816 respectively. These results support what Deshmukh VL and Yelikar KA[11] had seen.

In this study, the two group modes of delivery were compared. In Group A, 132 (68.0%) women delivered normally vaginally, 44 (22.7%) patients used instruments, and 18 (9.3%) patients underwent C Sections. For Group B, 94 (48.5%) patients underwent normal vaginal births, 78 (40.2%) underwent instrumental births, and 22 (11.3%) underwent C Sections. The P=0.0002. This indicates that using a foley's catheter in conjunction with PGE2 dramatically improved maternal outcomes, particularly in terms of fewer C sections when compared to PGE2 alone. These results were in line with what Patabendige M. and Jayawardane A[12] had noticed.

There are several ways to induce labour induction, including

mechanical and pharmacological approaches that can be employed separately or in combination. It is vital to inform the patient on the justification for labour induction, including the dangers involved and potential alternatives. There is currently inadequate knowledge regarding the most appropriate and efficient strategy for cervical ripening and labour induction, making it difficult to choose the proper method for the right patient.

Both the prostaglandin E2 gel and the foley catheter have been shown in numerous investigations to be equally efficacious in promoting pre-induction cervical softening.[8,13] For the mother, fetus, and infant, Foley's Catheter is a safe way to induce labour.[14] This is in contrast to our findings from this study, which showed that the use of an intracervical foley's catheter in combination with PGE2 on a patient's cervix during a full-term pregnancy produced significantly better and more effective results than PGE2 alone in terms of bettering maternal and fetal outcomes.

A total of 153 patients were enrolled in a different study156 (82 Foley; 71 PGE2). With the exception of the PGE2 group's lesser dilatation (16% vs. 38% 1cm dilated; P=0.05), baseline parameters were comparable. When parity, gestational age, initial dilatation, and administration of oxytocin were controlled for in the CPH model, there was no difference in time from insertion to delivery between the PGE2 and Foley catheter groups (median 27 vs. 33 hr; HR 1.13, 95% confidence interval 0.77- 1.68). Patients in the PGE2 group had a higher chance of developing uterine tachysystole (9% vs. 0%; P=0.01) and needing an additional form of CR (34% vs. 1%; P=0.001). Negative outcomes for mothers or newborns did not differ between groups. However, in one research, we noted 51 (26.3%) perinatal morbidities in Group B compared to 49 (25.3%) in Group A, p=0.816.[15] While in our study 68.0% of Group A patients had a normal delivery with 74.7% neonates were having good Apgar Score with p=0.0002 and 0.816.

In a study published in India, In one group, intracervical Foleys catheter instillation was followed by a single dose of dinoprostone gel if necessary, and solely dinoprostone gel for ripening in the other group. The length of the induction-delivery interval, birth method, and neonatal and maternal problems were evaluated. In comparison to the other group, which had a vaginal delivery rate of 64%, the first group had an 82% rate. The change was statistically significant (p=0.0426).[16] While in our study, 68.0% of patients in Group A had normal deliveries, and 74.7% of the newborns had good Apgar scores (p=0.0002 and 0.816).

In a research published in India, group A received a Foley's catheter and PGE2, while group B only received a Foley's catheter; all groups had equivalent maternal ages, gestational ages, and reasons for induction. The average pre-induction Bishop score between the two groups did not differ significantly. Following a 6-hour infusion, there was a noticeable Bishop score improvement in both groups. Though group B made more progress than group A.[17] According to a different study, 153 files were recovered from 168 attempted inductions of labour. Post-date cases made up 69.7% of all cases. The majority of patients (69.3%) were able to deliver naturally via vaginal birth, whereas one patient required assistance. As a result, 30.1% of inductions were unsuccessful and necessitated caesareans.[18] According to another study, the probability of mechanical ventilation was 0.54%, admission to a newborn ICU was 5.4%, and stillbirth was 0.15% among singleton-term deliveries. The rates of induction of labour (minimum 17.5%, maximum 40.7%) and emergency cesarean sections (minimum 5.6%, maximum 17.1%) varied widely between hospitals. Better perinatal outcomes were seen in women who gave birth in hospitals with greater rates of induction of labour. There was a 9% reduction in the likelihood of term stillbirth and a 14% reduction in the need for mechanical ventilation for every 5%-point increase in induction. Neonatal unit admission at term and hospital-level induction of labour rates did not significantly correlate (p>0.05).[19]

Foley's dinoprostone (n=75) groups, as demonstrated by another investigation. The intracervical Foley's injection was combined with a single dosage of 0.5 mg intracervical dinoprostone gel. The induction-delivery interval (IDI) was the main endpoint, with changes in Bishop's score, the need for oxytocin, the cesarean section (CS) rate, chorioamnionitis, and newborn outcome serving as secondary outcomes. Indications for IOL and the average parity and gestation were comparable. The neonatal outcome, IDI (19 hours and 20 minutes; p =.683), cervical ripening time, oxytocin demand, CS rate (25.4%; p =.322), and oxytocin requirement were also identical. 1.3% of people who used Foley's-dinoprostone had hyperstimulation (p=0.55). Not a single woman experienced chorioamnionitis.[20] There were certain limitations of this study which include its small sample size and being a two-centered study that does not generalize its results to the overall population of Khyber Pakhtunkhwa. Therefore, large multicentered randomized control trials shall be carried out across the province of Khyber Pukhtunkhwa for better and robust outcomes.

CONCLUSION:

This study demonstrated that intracervical foley's catheter with PGE2 application on the cervix of a patient with-term pregnancy yielded significantly improved maternal bishop score, mode of delivery, duration of labour and fetal outcomes as compared to PGE2 alone.

Authors Contribution:
Fauzia Afridi: Manuscript writing, data analysis and critical review
Romana Bibi: Manuscript writing, concept of study and data collection, data analysis
Maimoona Qadir: Result interpretation and discussion writing
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Original Article **Open Access**

Age Related Cytoarchitectural Comparison of Histopathological Changes in Thyroid Nodule

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ABSTRACT

Objective: To compare age related histomorphological changes through cytology (Bethesda category) and histopathology in thyroid nodules.

Study design and setting: This cross sectional study was conducted at the Department of Anatomy, BMSI, JPMC Karachi from 31-March-2021 to 31-August-2021.

Methodology: Total n=120 patients of all ages, genders and ethnicities that underwent surgery for thyroid nodules were included after taking duly signed consent. On the basis of cytological reports (FNAC) patients were grouped according to age and gender. Processed paraffin blocks were sectioned at a thickness of 5µm and then were stained with Haematoxylin and Eosin (H&E) for histological evaluation. Masson trichrome stain was used to observe fibrosis, that was measured through Image J Fiji software.

Results: We evaluated that out of 120 patients, male to female ratio was 1:5.67. Among various ethnic groups; Urdu speaking (40.8%) with mean age of 40.3% were commonly affected. Histopathological examination revealed that most common benign lesion was colloid nodular hyperplasia and papillary carcinoma was the most common malignant lesion. Highest percentage of fibrosis (36%) was seen in middle aged participants (p-0.045). Basement membrane thickness with lowest percentage (12%) was observed in younger age participants while highest (31%) was measured in older aged participants (p-0.001). Accuracy score of FNAC showed sensitivity 59%, specificity 96.6%, accuracy 86%, positive predictive value (PPV) 86% and negative predictive value (NPV) 87%.

Conclusion: With progression in age thyroid gland undergo histomorphological changes, early diagnosis will help in categorical nomenclature and its implications for subsequent management of patients with thyroid lesions.

Key words: Bethesda category, Cytoarchitecture, Thyroid gland, Thyroid lesion, Thyroid nodule.

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INTRODUCTION:

Thyroid nodules are one of the frequently presented endocrine disorders with prevalence range of 4% to 10%.[1] It remains a challenging task for clinicians to reach a clear diagnosis regarding the nature of the nodule and thereby, advocating precise and passable management. Various studies showed that 8% of population has palpable masses, most of them are benign and less than 5% are malicious.[2] Thyroid is a butterfly shaped bilobular gland joined by isthmus at center. It is situated in the neck anterior and inferior to the larynx at the level of C5-T1 vertebrae, surrounded by a thin capsule and pre-tracheal layer of deep fascia.[3]Microscopically, the

gland consists of thyroid follicles that are lined by follicular cells secreting thyroid hormone and parafollicular cells are interspersed between them producing calcitonin. Lymph from thyroid gland drains into pre-tracheal, para-tracheal, pre-laryngeal, retro-esophageal and retropharyngeal lymph nodes.[4] With increase in age the thyroid gland undergoes cytoarchitectural as well as functional characteristic changes. These variations vary from mild atrophy, decrease in weight, increase in basement membrane thickness and fibrosis to decreased peripheral formation of thyroid hormones.[5]

In Pakistan, due to different geographical distribution of population, the prevalence of thyroid nodule is quite common, increasing overall economic burden on the healthcare system.[2]With the introduction of iodine, prevalence of detectable goiter has been dropped in endemic areas of Pakistan[1]. Many clinicians and researchers have categorized thyroid nodules as benign and malignant through various clinical, biochemical and imaging techniques, however, minimally invasive fine-needle aspiration cytology (FNAC) is usually used for pre-operative analysis.[6]Yet FNAC is not without limitations; its accuracy is low in doubtful cytology and in specimen adequacy. About 20% of nodules with indeterminate cytological findings are found malignant, when excised surgically, therefore, histopathological assessment of surgically excised nodules has an utmost importance as it is gold standard method for diagnosis.[7] Studies have shown that FNAC yields both false positive and false negative results. In order to make definite diagnosis of thyroid nodule that whether it is benign or malignant by comparing it with findings of the excisional biopsy.[8]

In our region most of the studies have focused on malignant thyroid lesions.[9] In our work we tried to include both, benign and malignant thyroid nodules belonging to different age groups and genders to figure out prevalence of thyroid masses in our population. Previous studies have reported differences in incidence of thyroid nodules in relation to age and gender. Age has been said to have a crucial effect on patient's response to treatment. This study is proposed to compare histological differences in thyroid nodule based on FNAC and excisional biopsy in young and old subjects. Knowledge of age-related cytoarchitectural changes will help in categorical nomenclature and its implication on treatment and subsequent management of patients with thyroid lesions.

METHODOLOGY:

This cross sectional study was conducted at the Department of Anatomy in collaboration with Department of Histopathology, Basic Medical Sciences Institute (BMSI) and Surgical Units Jinnah Postgraduate Medical Centre (JPMC), Karachi, from 31-March-2021 to 31-August-2021 after getting ethical approval from Institutional Review Board (IRB) of JPMC (NO. F.2-81/2022-GENL/199/JPMC).

During the study period of five months, 120 patients of all ages, genders and ethnicities undergoing surgery for thyroid nodule were recruited after taking their consent on a duly signed consent form. Demographic and clinical data was also recorded. Patients with history of previous thyroid surgery for thyroid lesions were excluded from the study to avoid bias due to post-surgery structural changes.[10]

Sample size was calculated through OpenEpi, based on a prevalence rate of 8% mentioned by a recent study that studied incidence of thyroid lesions among different Asian ethnic populations, with confidence interval of 95%.[11] Non probability convenience sampling was used for the study.

On the basis of FNAC findings patients were stratified into different age groups and genders. Thyroidectomy specimen of same patients were collected and fixed in 10% formalin for 24 hours. After gross morphological examination specimens were dissected in midsagittal plane and three specimens from each thyroid gland were collected dehydrated, cleared and embedded in paraffin. The processed blocks sectioned at a thickness of 5µm were stained with Haematoxylin and Eosin (H&E) and masson trichrome stain for histological examination (basement membrane thickness and fibrosis respectively). These parameters were measured using image J Fiji software. Three slides per specimen and three areas per slide were studied thoroughly under light microscope (Nikon Eclipse 5oi; Japan) connected to video link digitalizing board system (DS Camera control unit- DS-L2). Results were obtained by comparing microscopic features in different age groups of FNAC findings based on Bethesda scoring with histopathological outcomes of Thyroid lesions. Statistical analysis was carried out through SPSS version 21 by applying chi square test. A p value of < 0.05 was considered statistically significant.

RESULTS:

Total one hundred and twenty (120) patients with thyroid nodules were enrolled during study period out of them most of patients (30%) were age ranged between 31 to 40 years. There were 15% males and 85% females representing male to female ratio 1: 5.67. In our study we found 40.83% patients were from Urdu speaking ethnicity. Neck swelling was the major presenting complaint as 85.83% patients were admitted with swelling; most commonly right side of lobe was affected (35.8%). Lobectomy was done in 70% of patients and 63.3% swelling had firm consistency (Table 1).

According to patient's FNAC reports there were 74.17% benign Bethesda category ? patients. Bethesda category ? includes 4.17% patients and 8.3% belonged to category ?. Bethesda category ? had 5.8% patients and 7.5% were included in malignant category ?. On histopathology of surgically removed thyroid gland we found 81.6 % were benign and 18.4% were malignant lesions (Table 2). It was observed that on FNAC out 74.17% benign lesions, there were 36% true positive colloid nodular hyperplasia, 31% were true positive benign lesion with cystic change lesions,

while 4.2% were false negative for follicular adenoma and 3.33%)were false negative for papillary carcinoma. Out of 10% follicular neoplasm there was 4.2% true positive follicular adenoma while 2.5% Colloid nodular hyperplasia and 3.33% were false negative for follicular carcinoma. The percentage of fibrosis was compared between age groups, lowest percentage of fibrosis (19%) was observed in age group ranged between 41 to 50 years and highest (36%) was seen in age group ranged between 31 to 40 years (p-0.045). out of 98 benign lesions, basement membrane with lowest percentage of thickness (12%) was perceived in age group ranged between 20 to 30 years while highest (31%) was measured in age group ranged between 51 to 60 years (p-0.001) (Table 3). Statistical analysis of thyroid nodules showed sensitivity 59%, specificity 97%, accuracy 86% positive predictive value (PPV) 86% and negative predictive value (NPV) 87%.

Table 1: Clinicopathological characteristics of Patients

Characteristics	Number of patients (n=120)	Percentage (%)
Gender		
Male	18	15
Female	102	85
Age		
20-30	34	28.33
31-40	36	30
41-50	19	15.83
51-60	31	25.83
Ethnicity		
Sindhi	30	25
Pathan	10	8.33
Balochi	2	1.67
Urdu	49	40.83
Punjabi	26	21.67
Bengali	4	3.33
Presenting complain		
Neck Swelling	103	85.83
Neck discomfort	17	14.17
Side		
Left	41	34.17
Bilateral	36	30
Right	43	35.83
Type of surgery		
Lobectomy	84	70
Total thyroidectomy	36	30
Consistency		
Soft	35	29.17
Firm	76	63.33
Hard	9	7.5

DISCUSSION

Thyroid gland is the most important endocrine gland of the body that controls metabolism, serum calcium levels, development and growth in mammals. Thyroid nodules are commonly presented lesions in outpatient departments; palpable lumps are observed in 4-7% of individuals and have chances to remain undetected in about 10 percent of subjects.[12] FNAC is performed to decrease the unnecessary load of surgical interventions for benign thyroid lesions.

In present study, the thyroid lesions were categorized according to Bethesda system and histopathological evaluation was performed to determine the diagnostic accuracy of FNAC with age related histomorphological changes. We found that females are most commonly affected by thyroid nodules with male to female ratio of 1:5.67, which is also reported by various other studies[13] this could be due to fluctuations in female hormones; like estrogen, that predispose females to develop thyroid diseases.[14]

It is believed that with increase in age, accumulated free oxidative radicals can damage thyroid cells and predispose to thyroid diseases, our results showed that most prevalent age group was from years 31-40, followed by 20-30, these findings were in accord to many other studies.[15] In terms of ethnicity majority of participants were from Urdu speaking ethnic population, similar results were observed in Pakistani study, this might be due to fact that the Urdu speaking residents being pioneers of Karachi constitutes main bulk of Urban population.[16] However, another local study found equal incidence of thyroid lesions in various ethnicities.[17] Majority of patient's complaint (85.8%) was neck swelling which is comparable to study done by Rout and coworkers.[18] According to Kumar and associates the consistency is subject dependent, but it doesn't exclude the presence of malignancy, in our study we found majority of nodules had firm consistency which is in accordance with above study.[10] In Rawalpindi a 20 years retrospective study done by Mehmood and colleagues,[19] showed that rate of total thyroidectomy was 27.37% and lobectomy was performed for 5.04% of all thyroid surgeries, whereas in our study lobectomy was done in 70% of thyroid nodules and total thyroidectomy was done in 30% of nodules these results are relatable to a five years study on thyroid malignancies done by Razzak *et al*.[20]

In our study FNAC showed 39.17% Colloid nodular hyperplasia and 35% were benign lesion with cystic changes, similar findings were also found by Gupta *et al*, [21] but histopathology confirms that 4.17% cases of follicular adenoma and 3.33% cases of papillary carcinoma were misdiagnosed as benign by FNAC. Out of 10% follicular neoplasms diagnosed by FNAC, biopsy confirmed that there were only 4.2% follicular adenoma, 2.5% Colloid nodular hyperplasia and 3.33% were follicular carcinomas. There were 5.8% cases of suspicious for malignancy on FNAC but on histopathology 5% patients had papillary carcinoma and 1% found to have medullary carcinoma, such drawbacks

Table 2: Comparison of Bethesda categories with histopathology of Thyroid Nodules

Bethesda Category N=no (%)	FNAC	No. of Patients (%)	Histopathology	No. of patients (%)
Non- diagnostic/ inadequate (I)	----------	----------	----------	----------
Benign (II) 89 (74.17%)	Colloid nodular hyperplasia	47 (39.17%)	Colloid nodular hyperplasia	43 (36%)
			Benign lesion with cystic changes	37 (31%)
	Benign lesion with cystic changes	42 (35%)	Follicular Adenoma	5 (4.2%)
			Papillary Ca	4 (3.33%)
Atypia/ follicular lesion of Undetermined significance (III) 5 (4.17%)	Atypia of undetermined significance	5 (4.17%)	Benign nodular hyperplasia	5(4.1%)
Follicular neoplasm / suspicious for FN (IV) 12 (10%)	Follicular neoplasm	12 (10%)	Follicular Adenoma	5(4.1%)
			Colloid nodular hyperplasia	3(2.5%)
			Follicular Ca	4 (3.33)
Suspicious for malignancy (V) 7 (5.83%)	Suspicious of malignancy	7 (5.83%)	Papillary Ca	6 (5%)
			Medullary Ca	1 (1%)
Malignant (VI) 7 (5.8%)	Papillary Ca	7 (5.8%)	Papillary Ca	7 (5.83%)

Table 3: Histopathological variables

Variables	Age Distribution (years)				p-value
	20-30	31-40	41-50	51-60	
Fibrosis (%) n= 120	**34**	**36**	**19**	**31**	**0.045**
B/M thickness (%) n=98	**12**	**29**	**26**	**31**	**0.001**

of FNAC were also observed in earlier studie.[22]

With the increase in age thyroid gland also undergo structural and functional changes, on microscopy increased basement membrane thickness and fibrosis was observed with increase in age by previous studies [23] that also effect the treatment of patients, such studies are in covenant to our study results. Literature review of FNAC findings showed that the study conducted by Agrawal and colleagues found sensitivity 88.8%, specificity 100%, PPV 100% and NPV 95.12% [24] while Jesrani *et al*, in their elastographic study of benign and malignant thyroid nodules perceived, sensitivity100%, specificity 80.2%, PPV 61.7%, NPV 100% and accuracy 85%.[25] These results are in favour of our study findings for FNAC of thyroid nodules except for the sensitivity which is at a little lower side in our observations.

The main limitation is that it was single centered study conducted on small group of population so results could not be generalized in relation to ethnicity. It is recommended that in future study should be done on different demographic zones involving large scale of population.

CONCLUSION

The current study determines that, age related histomorphological assessment of thyroid nodules in relation to fibrosis and basement membrane thickness might be helpful for clinicians to classify and modulate the treatment plans for patients of different age group with suspected thyroid lesions.

Authors Contribution:
Tanweer Fatima: Conception & design, interpretation of data and analysis
Sanum Ali: Literature search, manuscript drafting, data analysis and interpretation and critical review
Ghansham: Surgical expertise and relevance in write up
Surrendar Dawani: Surgical expertise and relevance in write up
Sehrish Hussain: Data analysis and interpretation, follow-up of patients
Sarah Zahid: Literature review, data acquisition, follow-up of patients
Aillah Baluch: Data analysis and computational graphics
Shahid Rasul: Surgical relevance in write up and critical review

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Original Article **Open Access**

Frequency of Post-Endoscopic Retrograde Cholangiopancreatography (ERCP) Complications

Asma Abdul Razzak, Muhammad Raza

ABSTRACT

Objective: Endoscopic Retrograde Cholangiopancreatography (ERCP) is a highly technical procedure that carries some risks associated with it. It consolidates the utilization of an endoscope with X-ray to look at the biliary and pancreatic channels with the ability to intervene when indicated to address problems identified during surgery. This study aimed to determine the frequency

Study Design & Setting: Cross-sectional study design at Dow Hospital Karachi.

Methodology: The patients with the age ranging from 18 to 60 years who had endoscopies were taken from July 2020 to February 2021. All the pregnant patients and those who were unwilling to participate in the study were excluded from the study. The data were collected from the patients and they were kept under observation for 4 – 6 hours after ERCP to monitor the development of an immediate complication. The findings were recorded only at 48 hours of the procedure.

Results: The age of the participants was 37±12 years on average. The complications were recorded with pancreatitis at 36% followed by 34.5% bleeding and 29% perforation. 92% of the procedures were successful.

Conclusions: In conclusion, while ERCP is generally considered a safe and effective procedure, it is not without risks. The most common complications of ERCP are pancreatitis, bleeding, and perforation.

Keywords: Endoscopic Retrograde Cholangiopancreatography, Pancreatitis, Endoscopy

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INTRODUCTION:

Endoscopic Retrograde Cholangiopancreatography or ERCP is a procedure that is commonly used by Gastroenterologists in a number of clinical scenarios to both diagnose and treat issues involving the upper gastrointestinal tract. As more non-invasive diagnostic modalities have emerged over the past few decades, the ERCP has become almost exclusively a therapeutic procedure and a less invasive non-surgical therapeutic procedure. ERCP has become the standard initial management for most pancreaticobiliary diseases. As with all invasive procedures, ERCPs have a number of side effects including bleeding, perforation, acute pancreatitis, and cholangitis.[1] Pancreatitis is the most common complication of ERCP, with an incidence ranging from 1% to 9% depending on the patient population and procedural factors.[2]

Endoscopic retrograde cholangiopancreatography is a medical procedure that combines endoscopy and fluoroscopy to diagnose and treat conditions of the bile ducts and pancreas. During the procedure, an endoscope (a thin, flexible tube with a camera and light at the end) is inserted through the mouth, down the esophagus, and into the stomach and duodenum. From there, the endoscope is advanced into the bile ducts and pancreatic ducts. A contrast dye is then injected into the ducts, and X-ray images are taken to help diagnose any abnormalities, such as gallstones, blockages, or tumors.[3] ERCP can also be used to perform certain treatments, such as removing gallstones or inserting stents to open blocked ducts.[4]

Patients who underwent general anesthesia with intubation had a 1.27 times increased risk of low blood pressure and hypoxia whereas those who underwent sedation without intended intubation had 1.51 times reduced risk. The reported incidence of such complications varies from study to study with Pancreatitis and Cholangitis having an incidence of 1-5% depending on the study, hemorrhage having an incidence of 1-4%, and perforation having an incidence of 1-2%.[5]

Bleeding post ERCP is a major concern for healthcare professionals despite its low incidence as it can lead to major complications in patients who often have prior comorbidities.[6] A number of risk factors can predispose a patient to bleeding after undergoing an ERCP including use of anticoagulants whether or not the physician performed a sphincterotomy,[7] presence of liver cirrhosis,[4] age[5] and a number of others. As such, it is the goal of all physicians performing the procedure

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to minimize the risk of hemorrhage in the often already at risk population undergoing the treatment.

Perforation is another possible complication that can cause major issues post ERCP. Perforations are classified using the Stapfer classification of duodenal perforations.

Stapfer I: Endoscopy related injuries to the wall of the duodenum

Stapfer II: Perforations associated with sphincterotomies

Stapfer III: Perforations of the actual ducts

Stapfer IV: Micro perforations

Perforations may require immediate surgical intervention depending on their size and location.[8] The physician performing the ERCP must be vigilant in preventing such complications from occurring. Perforation is a rare but serious complication of ERCP, with an incidence ranging from 0.1% to 1%.[9]

During an ERCP, the patient undergoes conscious sedation in which they are given intravenous medication which causes them to become relaxed and allowing them to tolerate the procedure. Occasionally, in more complex cases, the patient may undergo general anaesthesia and be completely sedated during which they require intubation.[10] Difficult intubation is a risk factor for poorer outcomes post ERCP.[11] The studies have shown that the use of artificial airways and prolonged intubation can lead to higher risk of post-procedural complications.[10] According to the studies, the ES incision's length is the most crucial element. Therefore, in order to avoid post-ES bleeding, endoscopists who do ERCP should try to keep the ES incision to the shortest possible length. Endoscopic hemostasis should be initially considered if post-ES bleeding develops since it is a sufficient and reliable method.[12]

METHODOLOGY:

This cross-sectional study was carried out at Dow Hospital Karachi with the agreement of the institute's ethical committee with Reference App # 0488-2020-DUHS-ERC. The participants who had endoscopy were taken from July 2020 to February 2021 by using non-probability consecutive sampling technique. The individuals with age range of 18 to 60 years were included in the study. All patients were kept under observation for 4-6 hours post ERCP to monitor development of immediate complications. Demographic data, lab reports indicating the findings of ERCP was collected. The patients were assessed 48 hours of ERCP to record any further complications. The outcome measures were the success rate of the procedure and the failure rate. The sample size calculated from open EPI version 3 estimated sample size 112 with the 99% confidence level and 5% margin level. Data was entered and analyzed using statistical package of social sciences (SPSS) version 20. Descriptive statistics were employed as mean and standard deviation for the numeric findings whereas frequency with percentages for the qualitative data.

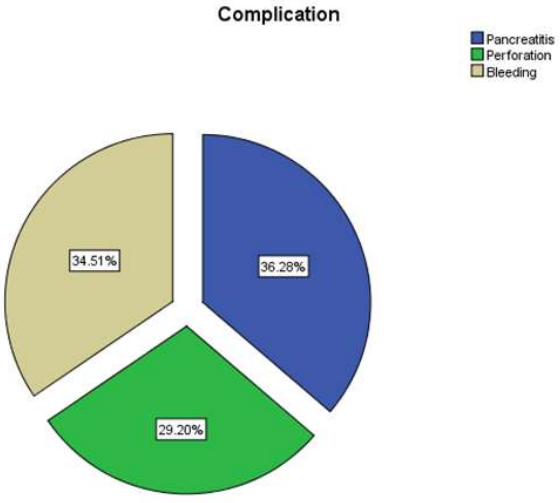
RESULTS:

Out of 113 patients who went through ERCP 58(51%) were males and 55(49%) were females. The mean age of the participants was 37±12 years. The common bile duct (CBD) cannulation was directly done in all patients. Sphincteroplasty needed for extraction of large stones. CBD stones were found in 17(15%) patients. 22 cases (19.5%) of large stones were observed that were unreachable by endoscopic extraction and as a result, a stent was inserted to ease obstruction in these patients. The details of all endoscopic findings are given in Table 1. The complications were recorded with 41(36%) pancreatitis followed by 39(34.5%) bleeding and 33(29%) perforation (Figure 1). Based on length of hospitalization, post-ERCP acute pancreatitis was rated as mild, moderate, or severe. There were 21 cases of acute pancreatitis (4.4%), 18 people had moderate pancreatitis, while 3 people had severe cases with fluid collections. After a brief hospital stay of a few days, they were discharged. Retroperitoneal perforation occurred in 3 cases (0.6%), of which 2 were treated conservatively and 1 had surgery. A severe post-procedure hemorrhage in 4 patients (0.8%) requiring a re-scope with an adrenal injection on the bleeding side and the hemostasis achieved. Most of the procedures were successful comprised of 104(92%) cases.

Table 1: Frequency of Findings and their percentages.

Endoscopic Findings	Number of cases	Percentages
Stone	17	15.0
Structure	22	19.5
Stone With Structure	13	11.5
Ampullary Growth	22	19.5
PD Stones	17	15.0
Large Stone	22	19.5

Figure 1: Percentages of complications



DISCUSSION:

After an endoscopic retrograde cholangiopancreatography (ERCP) procedure, patients are usually monitored in a recovery area until the sedative wears off and they are alert enough to be discharged. Depending on the type of sedation used, this can take several hours.[2] It is common to experience some mild side effects after the procedure, such as a sore throat, bloating, and cramping. These side effects usually resolve within a day or two. Patients may also experience some mild bleeding from the biopsy site or where an instrument was inserted during the procedure. More serious complications after ERCP, such as pancreatitis, bleeding, infection, or perforation of the gastrointestinal tract, can occur but are relatively rare. Patients should be advised of these potential complications before the procedure and instructed to seek medical attention if they experience symptoms such as severe abdominal pain, fever, or vomiting after the procedure.[11]

Malignancy at an age over 80 years old and sphincterotomy in the pancreatic duct were found to be important risk factors for death following ERCP-related perforations in a population-based investigation.[13] Since pancreatic duct sphincterotomy has been introduced as a useful adjuvant in challenging biliary cannulation, the high prevalence of sphincterotomy in the pancreatic duct among fatal perforations is a significant observation.[14] Numerous prospective and retrospective studies have presented data on ERCP-related problems in the elderly. These investigations revealed that both old and younger participants had a high success rate for selective biliary cannulation and PEP.[15]

According to various prospective studies, the total ERCP or sphincterotomy complication rate is between 5 and 10 percent.[16-18] ERCP-related problems can be divided into two categories: those that are particular to the surgery itself and those that are general, such sedation-related side effects.[19] Post-ERCP pancreatitis is one of the most dangerous ERCP-related consequences (PEP).[19] This study showed 39 patients with this complication which comprised of 38%.[15] The endoscopist's method affected the risk of pancreatitis and a large portion of the damage to the pancreas appeared to be caused by the procedure of cannulating the bile duct rather than by the sphincterotomy itself.[9] A score of 2 on the modified Observer's Assessment of Alertness/Sedation (OAA/S) scale was regarded as severe sedation by the researcher who examined how long it took the patient to achieve it following the initial sedative injection.[20] Throughout the surgery, they made an effort to keep patients at a modified OAA/S score of 2, and they also checked the total amount of sedatives used and the length of the treatment.[21]

CONCLUSION:

ERCP is generally considered a safe and effective procedure, it is not without risks. The most common complications of ERCP are pancreatitis, bleeding, and perforation. To minimize the risk of complications, careful patient selection, appropriate pre-procedural preparation, and attention to procedural technique are crucial. It is also important to promptly recognize and manage any complications that do occur.

Authors Contribution:
Asma Abdul Razzak: Data analysis
Muhammad Raza: Conception and design of article

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Case Report **Open Access**

Dumanian Technique for Repair of Complex Incisional Hernias

Sadia Lateef, Surrendar Dawani, Salman Jafferi, Nimra Aslam, Shahid Rasul

ABSTRACT:

Incisional hernia is protrusion of tissue at or near the site of an incision from a previous surgery. It is a challenging procedure to repair complex incisional hernias. Most of the numerous reconstructive techniques are unable to achieve goals of hernioplasty owing to various factors being planar mesh impose the risk of pain and infection whereas conventional suture repairs can fail due to suture pull through, rupture or slipping of knot. The open components separation technique (CST) creates large undermining skin flaps especially useful in patients with complex hernias who require judicial approximation of the midline fascia. Another novel technique for repair of such hernias is the Dumanian Technique : using mesh as a suture material and has been shown to improve the ultimate tensile strength (UTS) and thus prevent surgical failure. Both the techniques are implemented in our case to achieve successful abdominal closure.

Keywords: Component separation, Dumanian technique, Incisional hernia, Mesh repair.

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CASE PRESENTATION:

A 27 years old male with history of gunshot and burst abdomen 2 years back. He developed a large left diaphragmatic hernia and a huge incisional hernia. For this he underwent repair of diaphragmatic hernia prior to planning for incisional hernia repair. Then after 8 month of it he was planned for incisional hernia repair by Dumanian Technique for complex hernias with significant loss of domain which may not be treated even with component separation.

He presented to our clinic with huge incisional hernia extending from xiphisternum to pubic symphysis(Fig 1). CT scan revealed a large defect in anterior abdominal wall measuring approximately 20*18 cm with evidence of herniation of omental fat, bowel loops along with mesentery within the hernial sac.

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The patient was lying down supine with arms extended on arm rest on the operating table. Preparation and draping of the field was done from the nipple line extending up to the mid-thigh and laterally up to the edge of the table. The advantage of wide prep is to allow for wide mesh fixation points, if needed. We chose open approach considering hernia orifice being large and planned for its repair using Component Separation.

Technique, Transversus Abdominis release (TAR) and Dumanian Technique for complex hernias with significant loss of domain . Successful surgery was done on 22nd June, 2021. The patient developed wound dehiscence due to poor skin condition on follow-up, which was managed conservatively, and wound was healed on this conservative management. About 5 cm from the midline, skin flaps were raised, from one lateral border of rectus muscle , the linea semilunaris, to another. External oblique was divided vertically 2 cm lateral to linea semilunaris, separating it from the Internal Oblique muscle. This was medialization of Rectus. The separation was done till midline could be brought as close as possible. In addition, Transversus Abdominis release was also done to minimize the defect as much as possible. Release of Transverse Abdominis muscle fibers was attained, extending from xiphoid process above up to and along its entire insertion line at linea semilunaris level. Inferiorly separation extended to the point where deficiency of muscles is there and only peritoneum is present, the arcuate semilunaris. Laterally, release was extended up to the bilateral psoas muscles visualization. Superiorly, extension was taken up to the diaphragm central tendon. Though the posterior rectus sheath approximation in the midline was achieved, but there was still a defect of about

7 cm left with no further room for external oblique mobilization or transversus abdominis release.

This 7 cm defect was then repaired using Dumanian Technique. Macroporous, uncoated Polypropylene mesh of size 30*30 cm was used after cutting along blue lines and converting it into 2 cm wide strips this way it gave the tensile strength equivalent to ultimate tensile strength of a number 1 polypropylene. The abdominal wall already brought close together using CST, was pierced with a sharp hemostat.

Figure 1: Preoperative assessment (Anterior & lateral views)

Figure 2:

Figure 3: Postoperative assessment

These were then tied as simple interrupted sutures after passing the strips of mesh through the abdominal wall. Several strips were placed and tied in interrupted fashion to attain the tensile strength and midline closure was made (Fig 2). A subcutaneous suction drain was placed. Patient was again seen postoperatively after 1 week and followed regularly further. Patient has been well without recurrence for over 6 months since last operation (Fig 3)

DISCUSSION:

Incisional hernia is defined as abdominal wall hernia occurring at the site of a previous surgical incision. More common site for incisional hernias is midline and is a type of ventral hernia.[1] For incisional hernias, it is crucial to avoid their recurrence and minimize the spread of infection which makes their reconstruction a difficult procedure. Therefore, the primary goals of the restoration of the abdominal wall are securing the visceral organs and avoiding the recurrence.

10–25% of patients suffers from incisional hernia undergoing laparotomy and is a very common complication of abdominal surgeries.[2] The incidence of infection in ventral hernia repair is high being 8% .[3]

To achieve a reliable high-tension closure, many materials have been tried and implanted including silver wire[4] dermal autograft strips[5] and collagen ribbon.[6] Earlier, closure of large defects was done using procedures like free flaps or myofascial flaps with high recurrences and complications.[7] But the novel technique of usage of a mesh as a suture material and component separation techniques reduces the above mentioned risks. Furthermore, there is added benefit of reduction in recurrence rates.

Ramirez originally described Component separation technique (CST) in 1990.[8] Wide undermining of skin flaps causing wound-related complications was a major issue with this technique. Preserving peri-umbilical perforators reduced wound-related morbidity as evident in some recent works.[9]

This new reconstructive technique of TAR was introduced by Novitsky in 2012 and sdurable results were achieved using this technique. Another modification of the Rives-Stoppa technique, where anterior to posterior fascia, mesh is placed retromuscularly. Primary closure of the anterior fascia is then done. This new retro-rectus plane is bounded laterally by Psoas muscle, superolaterally by diaphragm central tendon, inferolaterally by the inguinal ligament and inferiorly by space of Retzius. Mesh reinforcement is aided by this plane as well as tension-free midline rectus closure is achieved.[10]

TAR, another new myofascial release technique in

complicated repair of ventral hernias, is a type of separation of posterior component. It facilitates significant advancement of fascia of Posterior Rectus, wide dissection laterally and neurovascular supply preservation. It also avoids subcutaneous tissue undermining with added advantage of provision of ample space for Sublay mesh. An immense retromuscular plane is created by TAR which also has benefit of bilaminar ingrowth of the mesh. Aiming low perioperative morbidity and a low recurrence rate is achieved by deploying this novel technique of posterior component separation. Overall, TAR seems to be an exquisite addition to the armamentarium of surgeons who wish for major abdominal wall reconstructions, especially those who have previously failed multiple attempts of other types of reconstruction.[11]

A new closure technique introduced by Dr Dumanian for abdominal defect in which macro porous polypropylene mesh strips were cut from a sheet of mesh and sutured for tissue approximation. Since its introduction, this sutured repairs from mesh strips is deployed successfully in various institutions naming: Northwestern, The Ohio State University, the University of Illinois Chicago and Walter Reed. Their safety can be assessed by comparing with both the abdominal wall sutured closures and planar mesh hernia repairs done in contaminated fields.[12]

We applied these techniques for repair of our patient's incisional hernia and there is no recurrence up to date

Authors Contribution:
Sadia Lateef: Writeup
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Salman Jafferi: Writeup
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Case Report Open Access

"Endocrown" A Major Paradigm Shift in Restorative Dentistry: A Case Report

Amir Hamza, Parivash Anwar, Nehal Sher Khan, Rana Saad Bin Sohail

ABSTRACT

Endocrowns are a conservative and aesthetic treatment option for restoration of extensively destructed posterior teeth. The main advantage is the fact that there is no need for imprudent preparation of the access cavity as done for post and core buildups. Moreover, the clinical visits are less time-consuming and less frequent unlike the ones for post and core buildups and subsequent crown preparation. This case report features the case of a coronally damaged maxillary first molar treated by zirconium endocrown following endodontic treatment.

Keywords: *Endocrown, Restorative Dentistry, Endodontic Treatment, Zirconia, Resin Cement*

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INTRODUCTION:

The advent of Endocrowns revolutionized restorative dentistry by providing a modernist means to restore an endodontically treated tooth. Theoretically, as a rule of thumb, every tooth with moderate to severe coronal breakdown is prescribed a post and cast core buildup followed by a crown.[1] The main goal of post and core buildup is to replace the missing tooth structure in order to provide stabilization to the tooth and an encirclement for the final restoration.[2]

The restoration of an endodontically treated tooth poses several concerns and controversies among dentists. An endodontically treated tooth, compared to a vital tooth, tends to lose its integrity and strength because of the extensive cavity preparation owing to caries, trauma etc.[3] Due to the loss of structural integrity, the endodontically treated tooth is prone to biomechanical failure.[4] This imposes a challenge for the dentist which requires them to conservatively prepare the access cavity, preserve as much anatomic form as possible and choose the ideal restorative material.

There are certain limitations to use of posts in endodontically treated teeth, including presence of calcified canals, narrow canals, cases with endodontic mishaps including instrument separation.[5] Such clinical situations lead to the advent of Endocrowns.

Endocrowns are blocks made of porcelain/metal that consist of a post/core component and a crown component. This saves dentist the time and effort of doing post and core buildups and even crown lengthening in many cases.[6] It also decreases the chances of hybrid layer degeneration by reducing the number of adhering surfaces. [6] This crown attaches to the inner access cavity margins to provide macro mechanical retention and the adhesive layer provides retention on a micromechanical level.[7]

The aim of this case report is to present a clinical case where a conservative endocrown restoration was cemented on the maxillary molar after endodontic treatment was done. Significant coronal destruction indicated the use of endocrown.

Case Report:

A 27-year-old male was referred to The Dental Lounge with pain on biting and food impaction in the upper right first molar which upon examination was grossly carious. The medical history was clear. Clinically, there was a substantial loss of natural tooth structure due to caries. The occlusocervical height of the remaining crown was approximately 4mm. The radiographic findings reported a radiolucency that involved the pulp chamber and periapical widening. After necessary investigations, the diagnosis was pulp necrosis with symptomatic apical periodontitis.

After explaining the treatment options to the patient and taking his consent, root canal treatment followed by an endocrown prosthesis was decided to be the treatment plan. Root canal treatment was carried out using the V Taper Gold

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rotary system with 2% NaOCl as an irrigant. (Figure 1) Calcium hydroxide was used as an intracanal medicament in between the visits. On the second visit, obturation was done using ProTaper gutta percha (GapaDent). (Figure 2)

Figure 1: Clinical view of the tooth demonstratingthe three orifices of maxillary first molar

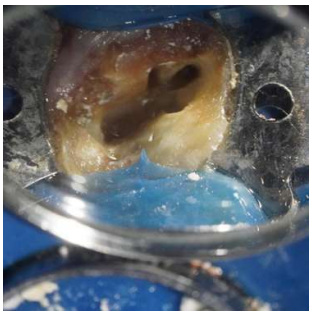

Figure 2: Radiograph of obturated molar

One week after obturation, the patient was recalled for the preparation of tooth for endocrown. It was aimed to receive butt-joint margins with no undercuts in the walls of the preparation. The internal undercuts were blocked using Flowable composite SDR plus. The cervical margins were prepared using a diamond tapered fissure bur and a taper of around 6 to 10 degrees was given in the tooth. (Figure 4) The interocclusal space was evaluated and clearance of 2mm was ensured An impression was made using dual impression technique. Prior to impression, a retraction cord was used to expose the prepared margins of the tooth. The tooth was air dried and isolated from saliva. Light body silicone was injected along the margins of the prepared tooth, while putty silicone was loaded in a stock tray and impression was made. The impression was then sent to the laboratory along with the shade information. The chosen restorative material was zirconia due to the added strength of the material with minimal preparation as compared to PFM (Porcelain Fused to Metal) crowns.

On the subsequent visit, the tooth was etched with 37% phosphoric acid for 15 seconds, starting from the margins and then moving towards the core of the tooth.

The tooth was washed and air dried. To cement the endocrown, single-step bonding system (Prime&Bond Universal, Dentsply Sirona) was used. The bonding agent was applied on the internal walls of the tooth and cured.

Dual-cure resin (Total C-RAM, ITENA Clinical) was used as an adhesive to cement the endocrown in place. The resin was spread along the walls of the tooth and the crown seated in place, the excess cement was removed using an explorer. The restoration was polymerized and checked for occlusal interferences and finished

DISCUSSION:

Dealing with molars with considerable coronal breakdown,

Figure4: Finished endocrown restoration

it is difficult to decide a treatment option that provides efficient function and clinical durability. The endocrown is an acceptable option for all kinds of molars, especially those with short clinical crowns and narrow canals.[8]

The advantages of endocrown includes preservation of the biologic width, increased surface area providing more bonding surfaces, decreased stress concentration due to less number of restorative interfaces[6] and ease of bonding due to a single block restoration.[9]

According to the literature, endocrowns should be limited to the monoblock restoration of molars only due to a more durable masticatory and clinical performance. The aim of an endocrown preparation is to achieve a broader and a steady surface that can resist compressive forces and is more easily achievable with molar teeth.[10]

Due to the advancement of bonding systems, micromechanical retention is more emphasized than macromechanical for endocrowns.[11]

According to Belleflamme et al.[12], it has been proven that the in vitro fracture strength of endocrowns are far more optimal than that of conventional treatment for endodontically treated teeth. Hence, they are indicated for all molars and would be more efficient in cases of calcified canals, short clinical crowns and also a good option for patients with unfavorable occlusal relationships and parafunctional habits e.g.: bruxism.[13]

Endocrowns serve to be a promising alternative for the restoration of endodontically treated molars. It is conservative of tooth structure and this type of restoration should be practiced more frequently after careful case selection.

Authors Contribution:
Amir Hamza: Case Documentation
Parivash Anwar: Writeup
Nehal Sher Khan: Case Documentation
Rana Saad Bin Sohail: Writeup

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Commentary **Open Access**

Personality Disorders among Medical Professionals

Henna Fatma

ABSTRACT:
There is an increase in the amount of conversation surrounding “toxic” environments within many workplaces today, and efforts to bring about a radical change in workplace policies that have let destructive and egotistic individuals survive and succeed in highly competitive posts. Individuals that are part of an environment contribute to its culture and toxicity is a result of an accumulation of negative behaviors dictated by negative personality traits. It is our observation that such traits are very common amongst our very own medical community. Doctors and nurses bear the same modicum of human folly as the rest of this world, though they are loath to admit their vulnerabilities to anyone, including themselves.

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Studies done previously on negative behaviors amongst physicians have made use of a broad term i.e. "disruptive behavior”. The American Medical Association describes this as “personal conduct, whether verbal or physical, that negatively affects or that potentially may negatively affect patient care,”[1] and the Joint Commission definition includes all “behaviors that undermine a culture of safety.”[2] A study of physicians reported for disruptive behavior within the workplace found that several of these physicians, in fact, met criteria for psychiatric diagnoses, such as mood disorders, adjustment disorders, personality disorders, and anxiety disorders.[3]

We have worked with plenty of physicians on whom we can juxtapose the textbook traits of narcissistic personality disorder. While this may be a big label to adorn someone with, we do encounter some of our colleagues entertaining discernably arrogant and entitled proclivities. They will always provide to anyone listening, an inflated account of their accomplishments, and carefully curate a self-congratulatory image of themselves in which they are impeccable and capable of absolutely no mishap or even an occasional misjudgment. If the situation demands it, they will throw a colleague under the bus without much empathy. However, a study done by Bucknall and colleagues shows that there is hope. The study compared 3 dark triad personality traits (narcissism, Machiavellianism, and primary psychopathy) in the general population to those in individuals from the healthcare systems through validated self-reported personality questionnaires. The results showed that the health care group had lower mean scores for dark triad traits than the general population.[4] However, a lack of insight among narcissistic individuals can undermine the validity of a questionnaire-based study.

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Another personality trait commonly noticed is obsessive-compulsive personality disorder. The WHO recognizes OCPD as a personality disorder with prominent anankastic features (anakastia) in the ICD, with symptoms reflecting an excessive conscientiousness, scrupulousness, and undue preoccupation with productivity to the exclusion of pleasure and interpersonal relationships.[5] They strive towards an uncompromising ideal of perfectionism and tend to micro-manage the smallest of tasks and have trouble delegating responsibility. They too, like narcissistic individuals, are unable to exercise empathy towards their co-workers and exhibit rigid thought patterns that translate into an inflexible attitude in the workplace. These individuals also may be relentlessly addicted to their work and thus are more prone to burn-out and its adverse consequences.[6] Similarly, traits indicative of paranoid personality disorder or avoidant personality disorder are also observed among medical professionals, which interfere with their thought patterns, behavior, and daily functioning.

Many models of personality traits exist, including Gordon Allport's list of 4,000 personality traits, Raymond Cattell's 16 personality factors, and Hans Eysenck's three-factor theory.[7] Psychoticism is a dimension of personality in Eysenck's dimensions characterized by aggression, impulsivity, aloofness, and antisocial behavior. Most contemporary psychology focuses on the five-factor model also known as the Big Five developed in 1949. The five broad personality traits this model is comprised of are extraversion, agreeableness, openness, conscientiousness, and neuroticism.[8] Neuroticism is characterized by sadness, moodiness, insecurity, anxiety and irritability.

Neuroticism and psychoticism could be associated with lower work performance among medical individuals. In studies on the general population, employees falling in the neuroticism group of the Big 5 personality traits, had lesser interactions in the workplace, compared to emotionally stable employees. They were also less attentive and had lower job

satisfaction.[9] A study observing national differences for thirty-seven nations in extraversion, neuroticism, psychoticism, and their correlation with per capita incomes and other variables (suicide, homicide, and alcoholism) revealed that neuroticism was significantly correlated with Hofstede anxiety scores ($r = 0.50$, $P < 0.05$). Hofstede anxiety was also significantly correlated with alcoholism ($r = 0.52$, $P < 0.05$). The study further showed that there was a significant negative correlation between psychoticism and work ethic ($r = - 0.48$, $P < 0.05$). Per capita income was significantly negatively correlated with competitiveness ($r = - 0.48$, $P < 0.05$).[10]

There is no robust data available on the exact prevalence of personality disorders within the medical community, and one may argue whether there is any need for detailed researches regarding the subject. After all personality is mostly shaped during childhood and there is little one can do about it once developed

To answer the above, awareness about maladaptive personality types could be used to help physicians and nurses become more self-aware regarding their personal characteristics. One can also better understand the impact personality traits have on other life indicators, such as success in social

Robinson OC. On the social malleability of traits: Variability and consistency in Big 5 trait expression across three interpersonal contexts. Journal of Individual Differences. 2009 Jan;30(4):201-8., and professional contexts[12]. Also while personality traits tend to be fairly consistent over short periods of time, they can be changed through deliberate effort. A study conducted on a personality change coaching program showed that there was a significant positive change in participant selected facets, with gains maintained three months later suggesting that a structured personality change coaching program may facilitate beneficial personality change in motivated individuals.[13]

There is a need for open and evidence-based discourse on the topic of difficult personality traits within our hospital environments as a hospital system thrives on mutual understanding, respect, and cooperation amongst individuals. Instead of expecting employees to adjust themselves around a toxic work culture, there is a greater reward to be reaped by changing the culture altogether and making it better and fairer for all.

Authors Contribution:
Henna Fatma: I state that I have made a (direct, intellectual) contribution to the conception, design, analysis and/or interpretation of data

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Artificial Intelligence and Telehealth as Diagnostic Approach to Middle Ear Disease- Advances in Otology

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As with other subspecialities, remote otoscopy commonly regarded as telehealth is being studied as a new approach for diagnosis of middle ear diseases. As in covid-19 pandemic, otolaryngologists were the most affected health care professionals as aerolized particles were a hurdle to conduct routine upper airway and ear canal examination, telehealth gain popularity, also to justify shortage of PPE. Beside this, reduction in post operative follow up visits, and cost savings in terms of greater access for rural populations were the major attractions to adopt remote otoscopy in ENT.[1]

In recent literature, telehealth in accordance with artificial intelligence has proven to have diagnostic accuracy of 78.7% of middle ear pathologies. The video otoscope tympanic membrane image is uploaded in android application, that process the image on smartphone. Connected server perform the task of feature extraction and ultimately, diagnosis of the disease. Broadly the disease is classified into four categories, namely, normal, abnormal, obstructed wax and chronic perforation. The abnormal division is actually the group of pathologies such as acute otitis media. Therefore, this system also, triage patients appropriately.[2] Two specialist comparative diagnosis by Livingstone et al, and cross checking of images by primary author from medical records was done in a study by cha et al. this learning via machine had high precision of images for otitis media.[3] Chen et al., formulated a smartphone-based edge artificial intelligence application that divided common middle ear diseases into ten known ear pathologies through transfer learning. This model was meticulously superior to previous experiments, as those used cloud computing techniques requiring access to internet and latency connections.[4]

Thirty-nine studies were systematically evaluated for artificial intelligence-based otoscopy processes. With the accuracy of 90.7%, AI was successful in discriminating between normal and abnormal images. Overall precision of 97.6% was reported. Equated against manual classification, human evaluators are outpaced by artificial intelligence in classifying otoscopy images (93.4% versus 73.2% accuracy respectively).[5]

In conclusion, the lack of Ent specialists in underdeveloped countries, general practitioners are forefront to treat medical issues related to ear, despite of the fact that they may not have enough training to make correct diagnoses in this field. Therefore, to discourse this issue, a computer-aided system based on machine models and image processing techniques, also known as artificial intelligence, or telemedicine acts as a support for a more exact diagnosis of ear disorders at primary care before specialist referral.

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Letter to Editor **Open Access**

Narcissism in Medical Students - A Matter of Concern

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The term, Narcissism derives from the tragic story of the Greek Folklore, about a young man, named, Narcissus. He fell in love with his own appearance, which he saw in a pool of water and started getting infatuated by it to the point that he eventually died, looking at it continuously for weeks and months. Presently, Narcissism is a terminology used in Personality Psychology.[1]Narcissism, is defined as a grand view of self and feeling of superiority of one's own talents and a desire for admiration, an extreme sense of entitlement, lack of empathy, and selfishness and egoism. The culture in our society of considering getting admission in medical college as one of the highest academic achievements, has somewhat made students feel superior in academic as well as their professional abilities. Hence, Narcissm is being observed as a prominent abnormality in personality among a lot of medical students.[2]

It has been quite concerning news that medical professionals display narcissistic personality characters which may harm their future patient dealing and further damage the already spoilt reputation of doctors in our society. This trait starts showing at student level. Students showing narcissistic traits are in lead among the medical students. Psycho-social methods should be implemented to help students overcome these insufficiencies.

Medical studies are physically and mentally demanding. The arduous workload and the exhaustive program as well as the pressure to do well on the assessments contributes to the stressful environment. Lack of moderation activities also contribute and plays a leading role in the development of the stress. So, undeniably, stress is a normal part of a medical student's routine.

The number of people having narcissistic personality traits has reached a 30% increase has been seen over the last four decades. In America, every 1 in 200 persons, have this disorder. There are major gender differences, almost of people with narcissistic personality disorder are male.[3]

According to a study in USA, narcissism occurs in 17% of first-year medical students.[4] However, data on narcissism in medical students are limited, more so in the local context. A study done in 2019 in Karachi University among 1145 students of the age group 18 to 25, showed high scores of narcissistic personality Inventory (NPI), male (47.44%) and females (43.63%) showed overt narcissism signs.[5]

It used to be a misconception, especially in the UK, that health professionals are more narcissistic than common people as they feel they are superior in their profession and abilities, especially Surgeons.[6] One study done among health care professional in UK, claims to refute the assumption that Medical professional are more Narcissistic than common public.[7]

People with narcissistic personality disorder often seen to be selfish, however this is because they're usually making up for a fragile sense of their weak self-esteem. Personalities high in narcissistic traits have an embellished feeling of selfimportance which impedes their decisions. This usually makes them think grand about themselves and they overestimate their abilities. However, sub-clinical narcissism is considered to possess a positive competitive side to it and not always considered as a negative trait. Some studies claim that it is related with academic success, possibly because of competitive desire in narcissistic students.

There are two sides of a narcissist. He/ She is someone who defends his/her ego and to control people and the environment. Also, who wishes to enhance ego, pursues achievement, acts independently and selects short-term goals that might lead to approval and validation from others. This might help them achieve their goals of the highly demanding medical profession if they use their good side of this personality trait in a controlled manner.

Medical institutes need to encourage student counselling and students should be taught to overcome such negative personality characteristics. Psychological interventions made for solving these problems should be incorporated into the framework of medical teaching. There is also urgent need to probe further into the matter and to study and document the overall mental health of medical students.

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