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EDITORIAL

Rheuminations

Prashant Kaushik[1], Aarya A. Kaushik[2]

I'll be honest…it has been 35+ years since I started Medical School [MBBS]. And in the realm of Medicine at large, and Immunology/Rheumatology in specific, we are still struggling to find a 'cure' for chronic systemic inflammatory immune-mediated diseases also known as 'autoimmune rheumatic diseases (ARD)'. Rheumatology is still in its cradle having gotten the recognition as a subspecialty of Medicine only in 1972. I have seen the field evolve in terms of understanding the orchestrated 'play' of the immune cells along with cytokines etc. over the past 3 decades, all of which has led to the concept and birth of 'biologic' disease modifying anti-rheumatic drugs [b-DMARDs]. The first b-DMARD to get approved by the Food and Drugs Administration [FDA] was etanercept, a TNF-alpha receptor fusion protein in 1998. Infliximab, a chimeric monoclonal antibody against TNF soon followed in 1999. Ever since then, there has been a flurry of b-DMARDs including 3 more in the same family of TNF-antagonists, 2 in the Interleukin [IL]-6 antagonist class, 1 blocker of the second co-stimulatory T-cell signaling: CTLA-4Ig, 3 IL-1 antagonists, B-cell depleting chimeric monoclonal antibody directed against CD-20 etc. Also, 3 oral Janus-kinase inhibitors have joined the 'gang' and are called targeted synthetic DMARDs.

I still remember the pre-b-DMARD era when rip roaring rheumatoid arthritis was still around, and with my Ustaad Saheb (Mentor), all what we had to offer pharmaceutically were the conventional synthetic [cs] DMARDs including methotrexate, hydroxychloroquine, sulfasalazine, leflunomide and [the younger generation can hold their breath] cyclosporine, d-penicillamine, chlorambucil…GOLD injections and even cyclophosphamide! Corticosteroids have been around since 1950! The 1st and "*so far*" […well, I/You might be next one!] the only Nobel Prize winning revelation in the realm of Rheumatology.

The availability of the b-DMARDs has changed the entire paradigm of pharmaceutical treatment in Rheumatology. They are all quite effective yet extremely expensive making them literally unaffordable in the parts of the world, where health-insurance coverage is suboptimal/non-existent, more so, given the indefinite duration of therapy. Although the b-DMARDs tend to target a specific pathway in the immune system, they are still fraught with some rather challenging adverse drug effects (ADE) including infections: bacterial, mycobacterial [especially reactivation of tuberculosis, more so, in the parts of the world where this disease is endemic] fungal and from other pathogens; malignancies, increased incidence of cardiovascular and cerebrovascular events, thromboembolic events etc. All in all, b-DMARDs are a double-edged sword! They all come with 'a price to pay'!

Now, let's reflect upon the burden of ARD in the community. Rheumatoid arthritis, a potentially crippling and life-threatening disease affects at least 1% of the population, with more than 13 million patients in America itself! Axial and peripheral spondyloarthritis is now being recognized more and more. Various other autoimmune diseases including systemic lupus erythematosus, Sjogren's syndrome, scleroderma, autoimmune myopathy including dermatomyositis and polymyositis, vasculitides, and some more novel entities like IgG-4 related disease, checkpoint-inhibitor chemotherapy associated rheumatic diseases: the list continues to grow!

What can be done to prevent, slow, stop and reverse ARD? In fact, the answer is the other side of the question itself! Human body has a tremendous capacity of healing itself! Only, if we are willing to make healthy choices. Truth is Self-effulgent! It does

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not require a lab-proof! However, as 'scientists', we are always inclined to see/measure the outcomes. Well, it is out there now! SYSTEMIC INFLAMMATORY DISEASES CAN BE PREVENTED AND REVERSED!!! Here are the revelations about some of these ailments including coronary heart disease, diabetes mellitus and even prostate cancer from just a few extremely humbling articles published quite recently.

The Lifestyle Heart Trial showed that it is possible to significantly reduce coronary stenoses and risk of cardiac events using aggressive lifestyle changes, and without lipid-lowering medications. A strong dose-response relationship between self-reported adherence and angiographic changes was found, with excellent adherence during the study. Overall, self-reported adherence was highly correlated with percentage of stenosis.[1] It has also been shown that an intense lifestyle treatment can reduce the expenses on cardiac health/procedures drastically.[2] Interestingly, adherence to a whole food plant-based nutritional program was found to be more important than the type of diet consumed. More adherent subjects showed greater improvements in weight and cardiac parameters. Thus, the intensity of the intervention may be more important than the specific diet for weight loss.[3]

By limiting the daily caloric consumption to 600 Calories, decreased pancreatic and liver triacylglycerol stores, improved maximal insulin sensitivity.[4] It's very humbling! The DIETFITS, a 12-month randomized clinical trial demonstrated that epigenetics must be part of the measures assessed in lifestyle diet intervention studies. Diet determines the expression of many genes![5]

The Direct study was the first large rigorous trial to show such success in remission of diabetes in a clinical practice setting. Diabetes-remission was strongly associated with weight loss in a dose response relationship.[6,7]

A fasting-mimicking diet (FMD) demonstrated that the power of dietary interventions may include reprogramming of tissues to restore lost metabolic function, such as beta cells in the pancreas. Once confirmed in humans, this could elevate lifestyle medicine intervention as a 'primary' modality for type 2 diabetes mellitus treatment. Also, should this treatment lead to beta-cell neogenesis in humans, it could make type 1 diabetes mellitus reversible.[8]

From diabetes 'care' to diabetes 'cure': In a seminal article published about 5 years ago, creative ways to implement lifestyle interventions were reiterated. Those services would include coaching, information, and communications technology.[9]

Intensive nutrition and lifestyle changes can even modulate gene expression in the prostate cancer.[10]

So, in a nutshell, ALL chronic lifestyle mediated diseases have systemic inflammation, alteration in the gut microbiome, oxidative stress, allostatic load, and many other features in common! Well, then the answer becomes simple! It is possible to prevent, slow, stop the progression and even reverse all these diseases with 'the exact same' 4-pronged approach: eat well, move more, think right, and love ALL! The sage generational wisdom of Dadi/Nani (grandmothers) has no ADE!

It's work, yes, but 'its works'!

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ORIGINAL ARTICLE

Parental Iron Therapy to Treat Iron Deficiency Anemia in Malnourished Children

Saadia Khan[1], Imran Iqbal[2], Asad Abbas[3], Reema Arshad[4], Ibad Ali[5], Sabeeha Khan[6], Adan Ijaz[7]

ABSTRACT

Objective: To evaluate the safety and efficacy of parental iron therapy to treat iron deficiency anemia in malnourished children.

Study Design: Quasi experimental design.

Place and Duration of Study: Stabilization Centre, Children Hospital and the Institute of Child Health, Multan from 1st December 2014 to 31st December 2020.

Materials and Methods: A total of 250 malnourished children with iron deficiency were included in the study. The laboratory parameters i.e., Hemoglobin, Hematocrit, Red Blood Cells Count, mean corpuscular hemoglobin, mean corpuscular volume, and Serum ferritin of all patients were done. Using the iron deficit formula, all participants were given the measured iron sucrose complex. The iron sucrose complex was diluted with 0.9% normal saline and administered steadily for 3-4 hours. After 6 weeks of therapy, hemoglobin, RBC count , ferritin was measured. Comparison of mean ±SD of baseline laboratory parameters and after 6 weeks of iron supplementation was analyzed by using t-test.

Results: A total of 250 participants were registered, male patients (57.2%) were more than female patients (42.8 %). Most of the 92(36.8%) participants were 12-24 months old. The key cause of anemia among 102(40.8%) admitted patients was inadequate diet or excessive milk consumption. The mean ±SD value of the Hb level at admission was 7.5±1.9 and it increased to 11±1.15g/dL after 6 weeks of active supplementation which is statistically significant (P-value < 0.05). Six weeks after giving intravenous iron therapy mean serum Ferritin increased from 11.5ml to 21.61 ng/ml.

Conclusion: Current study concluded that controlled administration of IV iron sucrose for treatment of iron deficiency anemia among inpatients is efficacious and safe. IV iron sucrose should be considered for patient with severe IDA, those who are not compliant with oral formulations, and patients with malabsorption.

Key Words: *Hemoglobin, Intravenous Iron Sucrose, Iron Deficiency Anemia, Red Blood Cells, Severe Acute Malnutrition, Serum Ferritin.*

Introduction

Protein energy malnutrition is a prime concern of developing countries, and it is often linked with iron deficiency anemia (IDA) among children. Iron deficiency anemia is prevalent in children up to 63% in Pakistan. According to Pakistan National Nutritional Survey 2018, 17% children were wasted, 24% children were stunted and 31% were underweight.[1]

Anemia is interpreted as a low red blood cell concentration along with low hemoglobin, or hematocrit, in a routine blood test. The main causes of iron deficiency anemia are poor Infant and Young Child Feeding Practices (IYCF) practices, poor diet, and consumption of over diluted milk and worm infections. Poor serum iron concentration in blood can lead to growth failure, developmental delay, behavioral and cognitive issues, learning disabilities and immune dysfunction.[2-5]

Oral iron therapy is the global standard for the management of anemia.[6] It is mostly well tolerated by well-nourished children but in under-nourished children particularly Severe Acute Malnutrition (SAM) children body undergoes reductive

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adaptations, Gut absorptive abilities also compromised.[7,8] Previous studies suggested that iron supplementation by malnourished children mostly presents with complications of diarrhea and vomiting that leads to poor compliance of iron in children with severe acute malnutrition which may be especially due to GIT dysfunction.[6,8] Moreover, young children are non-compliant with the oral iron supplements, therefore, other alternatives such as the parenteral route of iron administration must be sought.

For decades parenteral iron has been used to treat iron deficiency unresponsive to oral iron therapy. Iron preparations, including low molecular weight (LMW) iron dextran, iron sucrose, ferric gluconate, and the newest formulation, ferumoxytol, have generally replaced HMW iron dextran for use in both adults and children with chronic kidney disease due to their more favorable safety profiles.[7] Intravenous (IV) iron sucrose was approved by the FDA in 2000 for patients. Iron sucrose has been reported to be safe and effective in adults with iron deficiency due various non-renal causes, including pregnancy or inflammatory bowel disease.[9] Blood transfusions is not a solution to overcome this problem in children particularly with mild and moderate anemia with low iron residues.[9] Previous studies documented that IV iron sucrose therapy can help in improving Hb level to a variable extent. Previous international as well as national studies documented that intravenous (IV) iron therapy is safe for the management of anemia in children.[10-14] A study conducted at Ben-Gurion University of the Negev, Israel showed Hemoglobin (Hb) rise to 9.27±1.23g/dl with intravenous (IV) iron sucrose therapy in children with Iron deficiency anemia IDA. Unfortunately, some adverse effects have limited its use in children.[15]

To this date, only a few studies from Pakistan have emerged evaluating the safety and efficacy of parental iron therapy in malnourished children. Hence, the current study will have significant clinical implications enhancing our understanding and our capability to tackle the malnourished children with iron deficiency anemia. So current study was planned to evaluate the safety and efficacy of parental iron therapy to treat iron deficiency anemia in malnourished children. This study will help establish the usefulness of intravenous iron sucrose in malnourished children with anemia in resource-constrained countries like Pakistan.

Materials and Methods

This was a quasi-experimental study conducted in preventive Pediatrics Department Children Hospital and the Institute of Child Health, Multan from 1st January 2014 to 31st December 2020. Registration of patients was started after taking approval from Institutional Ethical Committee (Ref. no. 794, dated: 16.12.2013). Simple convenient sampling technique was used. Informed consent was taken from parents and guardians after explaining risk and benefits of IV iron therapy. A total of 250 participants were registered in current study by fulfilling inclusion criteria i.e., all the children were included with age group 1 year to 5 years with primary Severe Acute Malnutrition (SAM) with Wt/Ht Z-score <-3SD or MUAC 11.5cm or presence of any bilateral pedal edema and/or primary Moderate acute Malnutrition (MAM) children Wt/Ht Z-score <-2SD or MUAC 11.5-12.5 cm with anemia categorized as: Serum Hb levels 6-10g/dl was classified as anemic, 6-8g/dl was classified as moderate anemic, 8-10g/dl was classified as mild anemic and <6g/dl was categorized as severely malnourished and Serum ferritin levels <20ng/ml.

Exclusion criteria was defined as critically ill children with anemia less than 6g/dl and any previous iron therapy during last 3 months, hemolytic anemia, those who refused consent, children with chronic illnesses or secondary malnutrition.

A planned questionnaire was designed by trained medical staff and required variables were noted. The laboratory parameters i.e., Hemoglobin, Hematocrit, Red Blood Cells Count, Serum ferritin, mean corpuscular hemoglobin, mean corpuscular volume of all patients were done once at admission and again 6 weeks after the intervention.

Injectable iron is available in 5ml ampule that contains 100mg of iron in it. Dose of IV iron was calculated by using following standard formula[10]

$$\frac{\text{Normal Hb levels for age-Initial Hb levels}}{100} \times \text{Body blood volume} \times 3.4 \times 1.5$$

Here:3.4 is converting factor for Hb in mg of iron,1.5 is constant to replenish iron stores and 80ml/kg blood volume.

Derived dose from formula was injected 2ml/day for

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consecutive two days but not more than 3ml/day was given. After proper available aseptic measures calculated dose diluted in 100ml normal saline in peds chamber with precautions and cannot co-mixed with other medications and TPN. Unlike other forms of injectable iron viable of anaphylactic reaction are minimum with iron sucrose but were not overloaded. So, test doze was given initially over 15 minutes for any reaction. Required calculated dose added to 100 ml normal saline with the help of infusion pump. 100 ml fluid was adjusted over 4 hours. After 15 minutes infusion stopped and assessed for any reaction for 30 minutes. If no anaphylactic reaction occurs in 15 minutes infusion was started again. Hypotension, anaphylaxis, nausea, vomiting, diarrhea, abdominal pain, headache, edema, muscle cramps, fatigue and dizziness were common side effects of IV iron that were monitored throughout the infusion. Post and parental iron sucrose therapy was started and changes in ferritin levels were accurately measured within 48 hours even. Data shows 18-68% IV iron dose incorporated into erythrocytes within 2 weeks.[2] After completion of initial dose over two consecutive days, MMS (multi micronutrient sachet) with iron content one per day was started. After 15 days repeat samples of CBC and Serum Ferritin was sent and compared with initial baseline levels. All the patients turned up for follow up and no lapse was noted. Comparison of mean ±SD of baseline laboratory parameters and after 6 weeks of iron supplementation was analyzed by using t-test.

After completion of study duration, this data was entered in SPSS version 21.0 for analysis. Frequency distribution of qualitative variables was done. Descriptive statistics was applied to analyze the significance of study. Mean comparison of quantitative variables was analyzed by using t-test and p-value less than 0.05 was considered as statistically significant.

Results

A total of 250 malnourished patients were enrolled in present study, from which 150(60%) patients were severely malnourished and 100(40%) were moderately malnourished. Male/female was 1.3:1. Male participants (57.2%) were more than female participants (42.8%). The majority of 92(36.8%) participants belonged to 12-24 months, followed by 72(28.8%) from age group 36-48 months and 47(18.8%) were from age group 36-48 months respectively (Table II).

Table I: Gender, Age and Nutritional Status Distribution of all Participants (N= 250)

Characteristics	Frequency	Percentage (%)
Gender		
Male	143	57.2
Female	107	42.8
Age(months)		
12-24	72	28.8
24-36	92	36.8
36-48	47	18.8
48-60	39	15.6
Nutritional stats		
MAM	100	40
SAM	150	60

MAM: Moderate Acute Malnutrition, SAM: Severe Acute Malnutrition

The feeding history and diagnosis of admitted patients was noted in Table II. Most of the participants were on mother feed along with formula feed after birth (39.2%) and only 23.2% admitted patients were exclusively on breast milk and 37.6% were on formula milk only. Poor diet or excessive milk intake was the major cause of anemia among 102(40.8%) admitted patients and another reason behind anemia was mal absorption in 58(23.2%).

Table II :Feeding history and Diagnosis at the time of admission

Variables	Frequency	Percentage (%)
Feeding history		
Exclusive B.F	58	23.2
B.F + Formula Feed	98	39.2
Only Formula Feeding	94	37.6
Etiology of IDA in SAM		
Excessive milk	89	35.6
Poor IYCF	102	40.8
Celiac disease	37	14.8
Worm infections	22	8.8

IYCF: Infant and young child feeding practices

Severe acute malnutrition with edema was present in 13.3% enrolled subjects and without edema was observed in 86.67% enrolled subjects. Anemic status (moderate and severe anemia) compared to nutritional status of admitted patients was statistically significant as P-values was <0.05 analyzed (Table III).

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Table III: Distribution of anemia according to nutritional status (n=250)

Anemic status	MAM N=100	Edematous SAM N=20	Non-Edematous SAM N=130	*P*-value
Mild Anemia (8-10 g/dl)	29	02	35	0.09
Moderate Anemia (6-8g/dl)	45	09	73	0.022

Mean ±SD value of Hb level was 7.5±1.9 at admission and it improved up to 11±1.15g/dL after successful supplementation of 6 weeks. Mean levels of Hb, RBCs count, MCH and ferritin levels was significantly correlated (Table IV).

Table IV: Comparison of Base line and after 6 weeks laboratory parameters (n=250)

Baseline	At admission		After 6 weeks		*P*-value
	SAM N=150	MAM N=100	SAM N=150	MAM N=100	
Mean Hb	7.5 ± 7.9	8.0 ± 0.05	10.03 ± 1.15	10.5±1.10	0.02
HCT	20.17 ± 6.13	20.13 ± 5.14	25.5 ± 1.55	26 ± 1.13	0.13
RBC count 10^{12}/L	3.928 ± 1.77	4.0 ± 1.5	4.2 ± 1.8	4.1 ± 1.5	0.04
MCV	42.7 ± 3.0	45.7 ±5.0	75.55 ± 3.55	72.35 ± 2.03	0.051
MCH	15.50 ± 1.50	15.30 ± 1.00	23 ± 5.00	22 ± 4.00	0.047
Ferritin	10 ± 3.37	12 ± 4.01	22 ± 3.00	21 ± 2.00	0.01

Common side effects were analyzed of all studied participants; fever was highly prevalent in 25(10%) patients (Table V)

Table V: Common Side Effects Observed in Studied Subjects

Side effects	Frequency	Percentage
Fever	25	10
Anaphylaxis	6	2.4
Nausea	2	0.8
Vomiting	2	0.8

Discussion

Iron deficiency anemia has a significant impact on health and survival of children under five years of age. It is the leading cause of global burden of disease.[1] According to UNICEF report 2020, over 149 million children less than 5 years of age in developing countries have significantly impaired growth.[11] Therefore, it is imperative that iron deficiency anemia should be treated promptly and effectively, more so in malnourished children. Some children with severe acute malnutrition may be intolerant, non-complaint or non-responsive to oral iron therapy. As blood transfusion carries some hazards, parenteral iron therapy was assessed for its safety as well as efficacy in malnourished iron deficient children. Current study reported that IV iron sucrose in pediatric patients with IDA leads to clinical meaningful and statistically significant increases in hemoglobin, RBCs, MCH, and serum ferritin. We carried out this study in malnourished children who were having iron deficiency anemia Current study reported children were 60% severely malnourished and 40% were moderately malnourished. Similar trends were also observed in another study, where 79% children were severely malnourished and were intolerant, non-compliant or unresponsive to oral iron therapy.[11] All these patients were treated for malnutrition according to WHO guidelines in addition to intravenous iron therapy.[13] Male were prominent participants of our study. Another study also shares the same results where male outnumbered than females.[12]

The significant cause of anemia among 40% admitted patients was poor IYCF practices, excessive milk intake 35.6% and celiac disease 14.8%. While similar findings suggested that most of the participants were on mother feed along with formula feed after birth (39.2%) and only 23.2% admitted patients were feeding exclusively mother milk and 37.6% were feeding only formula milk.[16]

This study revealed that serum Hb levels improved up to 11±1.15g/dL by intravenous iron sucrose therapy. Another national study documented that parenteral iron sucrose therapy improved mean Hb level from 6.65±0.65g/dl to 10.35±1.17g/dl in malnourished children with IDA.[14] A Pakistani study reported Hb rise to 9.21±1.13g/dl with IV iron sucrose therapy.[10] These findings were lower than current study however they also concluded that IV iron sucrose therapy in malnourished children with IDA is safe and efficient.[6,17] An international study conducted at Ben-Gurion University of the Negev, Israel showed Hemoglobin (Hb) rise to 9.27±1.23g/dl with intravenous (IV) iron sucrose therapy in children with IDA.[15] Current study reported that IV

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iron sucrose in pediatric patients with IDA leads to clinical meaningful and statistically significant increases in hemoglobin, RBCs, MCH, and serum ferritin. Similar findings were also reported by Kaneva et al., 2017 where significant association with hemoglobin, ferritin and iron therapy was documented.[16] A rise in posttreatment hemoglobin levels implies that erythropoietic recovery is achieved with intravenous iron sucrose which also strengthens the findings of our study.[16,18]

The most common side effect in our study is fever 10% whereas the study by Mantadakis et al. reported the most common adverse effect of parental iron to be injection site extravasation followed by a transient alteration in taste.[19] Papadopoulos et al. found that rash following infusion and the urticarial rash was a common adverse effect following therapy.[20] No side effects were noted in children during follow up and the objective of follow up was to analyze hematocrit profile only.

Iron sucrose complex therapy appears to be highly and rapidly effective without major side effects.[21] This makes it convenient and cost effective in iron deficient, malnourished children.

We followed-up patients till 6weeks for study purpose but we recommend further trials with prolonged follow-ups to rectify the IDA completely and achieve normal hemoglobin level. It should be emphasized that iron deficiency even without anemia should be prevented before its development. In other words, to treat patients when they become anemic is too late.

Conclusion

Current study concluded that controlled administration of IV iron sucrose for treatment of iron deficiency anemia among inpatients is efficacious and safe. IV iron sucrose should be considered for patient with severe IDA, those who are not compliant with oral formulations, and patients with malabsorption.

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Authors declared no conflicts of Interest.

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ORIGINAL ARTICLE

Types of Various Oral Mucosal Lesions with Respect to Trends of Chewable Tobacco and Their Subsequent Histopathological Findings

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ABSTRACT

Objective: To find out the pattern of tobacco use practices and the effects of chewable tobacco and other forms of tobacco use on oral mucosa.

Study Design: Retrospective observational study.

Place and Duration of Study: Study was started from 1st July 2018 to 31st December 2018 and was conducted at Maxillofacial surgery OPD, Isra Dental Hospital.

Materials and Methods: Samples of leukoplakia, erythroplakia or growth in oral cavity were collected from Maxillofacial surgery OPD. After taking detailed history including chewable tobacco habits, biopsy was taken and then results were analyzed by using SPSS version 22.0.The categorical data were expressed in terms of frequencies and percentages. The Chi square test was used to determine the association of different variables.

Results: Majority of the patients were found to have naswaar addiction followed by gutka, smoking, areca nut, mainpuri and paan. Most of the patients i.e., 59% with oral lesions were having basic education at primary level and belonged to middle class monthly income category 35(39.77%) followed by low monthly income 28(31.8%).We noted significant association between various oral habits of tobacco use and biopsy reports and oral squamous cell carcinoma was observed as the common findings among study population.

Conclusion: We have reached to the conclusion that in our region chewable tobacco is most common and significantly associated with risk of development of oral lesions and subsequent oral squamous cell carcinoma.

Key Words: *ChewableTobacco, Gutka, Mainpuri, Naswar, Oral Lesions, Squamous Cell Carcinoma*.

Introduction

In Southeast Asian countries including Pakistan tobacco is easily available in open market and our cultural norms are adding support to these habbits.[1] The habits of chewing tobacco are also popular in younger age groups and females due to attractive appearance and easy availability of these products at cheaper rates. Such habits are also supported by illiteracy and deficiency of knowledge about their devastating effects. The cultural norms and regional demographic variations are responsible for differences in the incidence of oral lesions.[2] Tobacco use is directly linked with higher incidence of oral cancer as large proportion of our population is consuming the various forms of tobacco. Tobacco is used in the form of cigarettes, pipe, bidi or chewable form such as naswar, ghutka and paan.[3] Various studies have reported the presence of nearly 28 or more carcinogenic agents in chewable tobacco such as tobacco-specific nitrosamines (TSNAs), polonium, formaldehyde, cadmium, lead and benzopyrene.The various forms of chewable tobacco have been reported to be linked with malignant tumors of head and neck.[4,5]

Most of the cases of oral lesionsinvolve prolonged usage of tobacco. Such lesions also have chances of malignant transformation at the rate of 3-5%.[6] The type of oral lesionboth malignant and nonmalignant varies with the type of tobacco being consumed and the way it is used.[7] Oral cancer is gaining attention as one of the most challenging dilemma for the world which is thought to be directly associated with prolong tobacco usage.[8] Despite of modern therapeutic modalities, Pakistan is still ultra-receptive to oral cancer. This can possibly be credited

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to the exposure to lower socioeconomic status, illiteracy, and various environmental factors.[9]

Looking at the co-morbidities associated with use of tobacco and its consequences, it is very sad to write here that at the country level no definitive measures are being taken. Thereforeit is a real need for public awareness to curtail such tobacco addiction to reduce the incidence of different oral lesions as well as oral squamouscell carcinoma.[2] Although we know that tobacco is linked with oral cancer but it is not clear in literature that which form of tobacco and tobacco chewing habits are more prone to cause which type of oral lesion; therefore the present study was designed with the objective to find out the patterns of tobacco use practices and the effects of chewable tobacco and other forms of tobacco use on oral mucosa.

Materials and Methods

This was a retrospective observational study done from 1st July 2018 to 31st December 2018.The study was approved by Ethics Review Committee (ERC), Board of Advanced studies and Research (BASR)Isra university Hyderabad. A total of 88 samples were collected from Maxillofacial surgery OPD, Isra Dental Hospital by non-probability purposive sampling technique. Samples from patients with leukoplakia, erythroplakia or growth in oral cavity were included in the study.Both the male and female patients, belonging to all age groups and ethnic groups without socioeconomic discrimination were included in this study. Medical records were studied for demographical data of the participants.

Samples with inadequate oral biopsy material were excluded from the study. Informed consent was taken from all the participantsand biopsy was performed by standard protocols by dental surgeon. Paraffin embedded blocks were prepared from all the biopsy samples and were cut into 5µ thin sections by microtome. Thin sections were processed further by using Haematoxylin and Eosin stains and were focused under light microscope by experienced pathologists for the histopathological diagnosis. The data was analyzed through SPSS version 22.0. The categorical data were expressed in terms of frequencies and percentages. The Chi square test was used to determine the association of different variables.

Results

In present study 88 patients with leukoplakia, erythroplakia or growth in oral cavity were studied. In our study most of the patients i.e., 59% with oral lesions fall under the category of basic education level according to proforma designed (Table-I). According to socioeconomic status patients were divided into four categories with respect to their monthly income as shown in table-I. Most of the patients with oral lesions belonged to middle class monthly income category 35(39.77%) followed by low monthly income 28(31.8%). The biopsy findings based on histopathological diagnosis revealed; oral squamous cell carcinoma (OSCC) being most common finding with 64(72.7%) cases (Table-II).According to the various addiction trends majority of the patients were found to have naswar addiction 21(23.9%) followed by gutka 15(17%), smoking 15(17%), areca nut 13(14.8%), mainpuri 6(6.8%) and paan6(6.8%). However about 12(13.6%) patients were found with no use of chewable tobacco. This shows that most patients with oral lesions 61(69.3%) were addicted to smokeless tobacco use (Table-III).The association between various oral habits of tobacco use and biopsy findings were found statistically significant with p-value=0.01, as is shown in table-III.

TableI: The Distribution of Patients according to Literacy Level and Economy Status

S.No	Education Status	No. Of Patients (88)	Percentage
1	Illiterate	24	27.27 %
2	Basic education (Up to Primary)	52	59%
3	High education (Up to Matriculation)	10	11.36 %
4	Graduation	02	2.27 %
	Socio-Economic Status	**No. of Patients (88)**	**Percentage**
01	Very Low monthly Income(<Rs.20,000/-)	15	17.04%
02	Low monthly Income(20,001 to 50,000/-)	28	31.8%
03	Middle monthly Income (50,001 to 100,000)	35	39.77%
04	High monthly income(>100,000/-)	10	11.36%

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TableII: TheDistribution of Patients According to Biopsy Findings (n=88)

Biopsy Diagnosis	Number of Patients (n=88)	Percentage
Squamous cell carcinoma	64	72.7%
Benign tumor (Pyogenic granuloma, Squamous cell papilloma)	15	17%
Inflammatory	06	6.8%
Material inadequate	03	3.4%

Table III: Association of Biopsy Findings with Various Chewable Tobacco Habits

Biopsy Findings	Habits							Total	p-value
	Naswaar	Gutka	Smoking	Areca nut	Mainpuri	Paan	None		
Oral squamous cell carcinoma	21	10	11	11	0	3	8	64	0.01
Benign tumor (Pyogenic granuloma, Squamous cell papilloma)	0	5	4	2	3	0	1	15	
Inflammatory	0	0	0	0	3	3	0	6	
Inadequate material	0	0	0	0	0	0	3	3	
Total	21	15	15	13	6	6	12	88	

P value significant at ≤ 0.05

Discussion

Tobacco induced oral mucosal lesions are result of damage to oral protective mechanism or presence of carcinogen in tobacco products.[10]In our study the most prevalent habit was naswaar chewing. Similar results with little variations were given by Saira et al in 2019.[11]Inpresent study the second most common habit was smoking and gutka chewing which is in consistent with the results of Behura SS in 2015.[12] However another study conducted in India by Rooban has reported alcohol as most seen habit for oral mucosal lesions.[13]These differences might be due to cultural variations and increase alcohol misuse among individuals in their population. In another study, the second mostly reported chewing habits was betel quid which is in similarity with our study showing 17% cases with gutka or quid chewers.[14]

According to our study most encountered oral lesions were oral squamous cell carcinoma which was in contrast with the results found by Mohiuddin S in 2016 and Priya MK in 2018 who found oral submucus fibrosis as most common tobacco induced oral lesions.[15,16]In present study majority of the patients i.e., 59% with oral lesions had primary education level. This finding is consistent with an Egyptian cohort study in which they classified patients according to education level in three groups i.e. No education, basic education, and high education and their most of the patients were of basic education (55.2%).[17] In another study in Iran has divided population in two groups i.e., illiterate and literate having 78.9% oral lesions in illiterate people. However, they did not define the term illiterate. As many people doesn't consider primary education as criteria of literacy; if it is that so then our study is also consistent with this study.[18]

In present study majority of the patients with oral lesions belonged to middle class monthly income category 35(39.77%) followed by low monthly income 28(31.8%).It may be also because most of the population in our country is comprised of middle class that is low monthly income and middle monthly income. It may also be due to their working environment and easy availability or affordability of chewing tobacco to these proportions of population. The comparable findings by some other studies have reported the low socioeconomic status in majority of the patients in other parts of the country.[19] Another national study conducted in Karachi reported higher 45% of the cases with OSCC with very low socioeconomic status which contrasts with the findings of present study.[20]

Our study revealed that most of the OSCC cases were smokeless tobacco addicts;in the form of naswaar and ghutka which was in similarity with the results of studies done by Younis S et al in 2016 and Muange P in 2014.[21,22] However Wang X has revealed that joint effect of tobacco and alcohol had a significant effect on occurrenceof OSCC.[23] Our study showed that second mostly seen risk factor for oral squamous cell carcinoma was smoking and areca nut which was in similarity with the results by Khan et alwho have reported both smoking and betel nut chewing as most common related factors for oral submucus

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fibrosis.[24] According to present study tobacco induced reactive inflammatory lesions were about 7% which is also supported by Kamble KA study, conducted in india.[25] But in contrast Cebeci AR in 2009 reported that mostly oral mucosal lesions are reactive in nature.[26] This difference might be due to less frequent usage of tobacco among study groups and some cultural variations.

Our study proved the indication that unfortunately prevalence of tobacco induced OSCC in our community is 17%. However other authors believed that tobacco induced OSCC is only 1% in their society.[27] This variation might be due to adequate screening programs of oral precancerous lesions by timely biopsies done by oral practitioners in their society. But in our society oral soft tissue biopsies are advised at very late stage.[28]

Conclusion

We reached to the conclusion that in our region chewable tobacco is most common and significant risk factor for development of oral lesions and subsequent oral squamous cell carcinoma.

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CONFLICT OF INTEREST

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ORIGINAL ARTICLE

Verbal Autopsy of Maternal Mortality in Rawalpindi District

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ABSTRACT

Objective: To identify the causes and risk factors leading to maternal mortality through verbal autopsy in the District of Rawalpindi, Pakistan.

Study Design: A retrospective, descriptive study.

Place and Duration of Study: The study was carried out in Community Department of Foundation University Medical College Islamabad from January 05, 2019, to December 25, 2019.

Materials and Methods: Data of 105 women died of causes related to death during pregnancy/ delivery between 01 April 2013 and 30 April 2018 was retrieved from the office of District Health Officer (DHO) Rawalpindi. A Verbal Autopsy was conducted to determine cause of death and the possible risk factors, through a structured questionnaire that was filled by close relatives of the deceased women. Analysis of data was done using SPSS version 25.0.

Results: The Mean age of the patients was 31 years, and it ranged from 15 to 49 years. In 26.7% of mothers cause of death could not be determined. Overall, the major and most obvious cause of maternal death was delivery related hemorrhage in 58% cases. Out of these, antepartum hemorrhage was the commonest cause occurring in 43.8% of the total cases. Postpartum hemorrhage occurred in 11.4% cases, while fatal hemorrhage during the delivery occurred in 2.8% mothers.

Eclampsia was the next common cause that occurred in 11.4% mothers. Difficult and prolonged labour was found to be cause of death in 2.8% cases, while 0.95% died of Sepsis.

Among the risk factors, lack of antenatal care emerged as the leading risk factor, present in 62% mothers, followed by anemia being present in 46.6% mothers. Multi-parity was found to be the next common risk factor being present in 26.6% mothers. Reduced interval in successive pregnancies was found in 21% cases. Systemic medical disorders like hypertension, renal disorders, Diabetes Mellitus, Pneumonia, hepatic failure, were found in 6.66% mothers. History of complications in previous pregnancies was present in 3.8% cases. History of lack of proper medical services in the hospital as possible factor leading to death was present in only 5 (4.8%) cases.

Conclusion: Hemorrhage related with delivery, especially the antepartum hemorrhage emerged as the commonest cause of maternal mortality, followed by eclampsia. At the same time, lack of antenatal care and anaemia emerged as the commonest risk factors in this regard.

Key Words: *Delivery related Hemorrhage, Maternal Mortality, Maternal Risk Factors, Unknown Maternal Deaths, Verbal Autopsy.*

Introduction

Pakistan, having a population of over 20 billion, is the sixth most populous country of the world as per the latest census conducted in the year 2017. The population growth rate recorded was 2.10 in 2016, and since then it has been increasing. This creates an overall burden on the economy of the country, where health indicators like maternal mortality remain a matter of great concern.

Most of the developing countries are facing Maternal Mortality as a major health issue. It is considered to be one of the top priority health issues in the formulation of health policies and research strategies in the developing world. It is a bitter reality that most of maternal deaths take place in the developing world and ironically, a vast majority of

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these are preventable.

According to WHO, any non-accidental maternal death, occurring during the pregnancy or childbirth or within 6 weeks of delivery, is considered as Maternal Mortality.[2] It depicts the health and development status of a country. Unfortunately, in Pakistan it figures around 30000 maternal deaths, which is a very high number like any other developing country.Thus the maternal mortality rate in Pakistan is calculated as 276 per 100,000 live births and it stand as 147th in the world for the year 2017. Pregnancy related hemorrhage is found to be the commonest cause of maternal mortality, being present in 47.7% deaths. Highest incidence of 35% was seen in 25–29-year age group.

Causes and risk factors leading to maternal mortality in developing countries vary greatly. According to WHO 75% of the causes of maternal mortality include hemorrhage, mostly post-partum, post-partum sepsis and eclampsia/ pre-eclampsia.

Though substantial decrease in maternal mortality in Pakistan has occurred since 1990, but is far lower than the targets set by the UN and also quite low as compared to other developing countries of the region. Pakistan has also been declared as the most risky place for a birth to take place. This lack of achievement of the target of low Maternal Mortality Rate is mostly due to many of the socioeconomic reasons like poverty, low female literacy rate, poor nutrition, and lack of access to the health facilities etc.

A decrease of 44% in the maternal mortality has been observed all over the world from 1990 to 2015. It has been observed that almost all of the maternal deaths occur in the low income countries. Even minimal modifications in the SOPs can lead to a decrease of 80% of maternal deaths even in the poor countries. UN SDGs of less than 70 per 100 000 maternal deaths is achievable by implementing a better accountability system. Many of the countries are moving towards achieving this goal by improving their accountability systems by introducing verbal autopsies and external enquiries to take measures to reduce maternal mortality.

It is an irony that most of the factors leading to maternal mortality can be prevented simply by proper registration of the patients so that information can be obtained about these mothers. Even in developed countries like UK, the actual number of maternal mortality is 60% higher than the reported figure. Hence it is not surprising that a lot of maternal deaths in Pakistan are not reported which makes it difficult to determine the exact numbers currently. This is mainly due to the lack of reporting of births and deaths to proper governing bodies. In order to fill the missing information, verbal autopsy is considered as an effective tool. Verbal Autopsy is defined by W H O as “a method to ascertain the cause of a death based on an interview with next of kin or other caregivers” and it is applicable on all those deaths where a death is not formally medically certified. Hence verbal autopsy provides an effective alternate tool to record causes of maternal deaths and has been implemented at various levels.

As many of the cases of maternal mortality are neither nor reported, it was felt that Verbal Autopsy can be carried out in such cases to determine the cause of maternal mortality. Hence a retrospective, descriptive study was carried to find out the causes and risk factors leading to maternal mortality, through verbal autopsy in the District of Rawalpindi, Pakistan.

Materials and Methods

A retrospective descriptive study was carried out in Community Medicine Department of Foundation University Medical College from January 05, 2019, to December 25, 2019. Data of 105 women died of the causes related to death during pregnancy/ delivery was retrieved from the office of District Health Officer (DHO) Rawalpindi, Pakistan by Convenient sampling technique and evaluated. Approval of the Institutional Ethical Committee for this study was obtained beforehand. Permission was obtained from DHO Office for this study. Informed consent of the next of kin was obtained and data confidentiality was assured.

Data of all the women, who died of the causes related to pregnancy or delivery, from April 2013 to April 2018 was included in the study. The data was collected by the team of authors along with a Senior Staff Nurse detailed by the DHO. Data of those subjects who could not be traced due to improper address entry or those women whose immediate family members did not cooperate during the study, were excluded. Through a modified version of questionnaire, developed by the National

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Committee for Maternal and Neonatal Health (NCMNH) and validated by National Institute of Population Studies Pakistan & UNICEF, a Verbal Autopsy was conducted to determine the cause of death and the risk factors. This questionnaire was translated in Urdu and was filled by a two-member team, comprising of a Medical Officer and a Staff nurse who were well versed in local language, while interviewing close relatives (Next of Kin or those who remained close to the deceased during her illness) of the deceased women at their homes/ villages in selected rural and urban areas of Rawalpindi District. In some cases, help of the local administration was also sought to convince the relatives for the interviews. Analysis of data was done using SPSS version 25.0 and was analyzed for frequencies and percentages.

Results

The Mean age of the patients was 31 years, and it ranged from 15 to 49 years. Regarding causes of maternal deaths as shown in Figure: 1, in 28 (26.7%) mothers, cause of death could not be determined even after Verbal Autopsy. Overall, the major and most obvious cause of maternal death was delivery related hemorrhage in 61 (58%) cases. Out of these, antepartum hemorrhage was the commonest cause occurring in 46 (43.8%) of the total cases. Postpartum hemorrhage occurred in 12 (11.4%) cases, while fatal hemorrhage during the delivery occurred in 3 (2.8%) mothers.

Delivery related hemorrhage was followed by eclampsia (fits) as the next common cause that occurred in 12 (11.4%) mothers. Difficult and prolonged labour was found to be cause of death in 3 (2.8%) cases. One (0.95%) mother died of Sepsis.

Among the risk factors, as shown in Figure: 2, lack of antenatal care emerged as the leading risk factor, as 62 mothers (59%) had only 1-4 antenatal visits, while 2 mothers (1.9%) never visited antenatal clinic. Anaemia followed it as the next commonest risk factor. It was present in 49 (46.6%) mothers. Multiparity (≥ 4 children) was found to be the next common risk factor being present in 28 (26.6%) mothers. Interval with previous pregnancy of 1 year or less was found in 22 (21%) cases. History of medical disorders like hypertension, renal disorders, Diabetes Mellitus, Pneumonia, hepatic failure, was found in 7 (6.66%) mothers. History of pregnancy related complications in previous pregnancies was found in 4 (3.8%) cases.

Regarding lack of proper medical services in the hospital as possible factor leading to death, the answer was affirmative in only 5 (4.8%) cases.

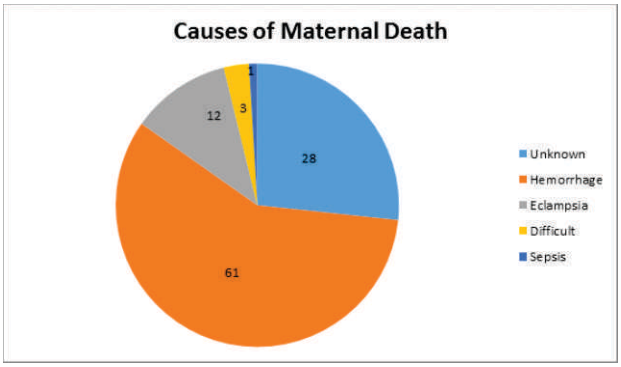

Figure 1: Causes of Maternal Mortality

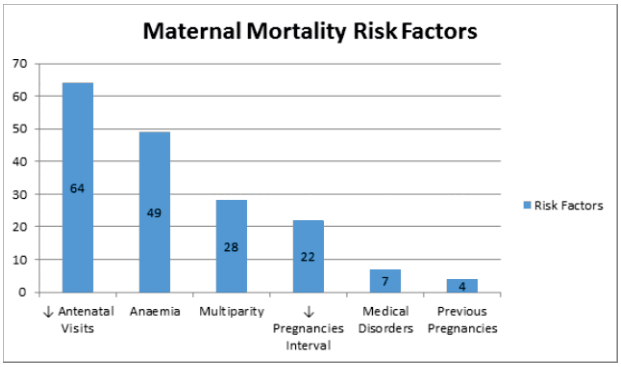

Figure: 2 Risk Factors for Maternal Mortality

Discussion

Maternal Mortality is one of the major health issues in the developing world, including Pakistan. Pakistan ranks 126 out of 149 on HDR-Gender Inequality Index due to the low women empowerment, limited contributions, and lack of maternal healthcare facilities. Data collection regarding Maternal Mortality serves to monitor and lower the rate. The purpose of our research was to identify the causes and risk factors leading to Maternal Mortality. Hemorrhage, related to delivery, emerged as the commonest direct cause of maternal mortality, followed by eclampsia. Among the risk factors, anaemia emerged as the biggest risk factor followed by multi-parity and reduced interval between successive pregnancies respectively. As shown by our findings, most of the causes of Maternal Mortality are modifiable and preventable. This information can help us elevate the health status of mothers in our country.

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Results of our study correspond to the study carried out by Sami & Baloch (2002) in which Maternal Mortality Ratio was calculated to be 560 out of 100000 live birds with delivery related hemorrhage accounting for 42% as the biggest cause of maternal deaths. Similarly in another study carried out in four districts of Afghanistan by Bartlett et al (2005), delivery related hemorrhage emerged as the leading cause of maternal mortality in three of the four districts, as found in our study. Yet in another study similar results showed hemorrhage to be the biggest cause of maternal mortality (36%) followed by eclampsia (17%). Similarly, Bhutta & Black (2013) showed hemorrhage (22.9%) as the biggest cause of maternal mortality. In a similar study by Perveen & Ilyas (2017), eclampsia was shown as the most common cause of maternal mortality, followed very closely by hemorrhage. Since this study was also carried out on a limited number of patients, such minor differences in data may not be considered very significant and the results are not much different than our study. In a study carried out in USA, after cardiac diseases, hemorrhage was still the most common cause of maternal mortality. Results of most of these studies show hemorrhage as the most common or one of the most common causes of maternal mortality as shown in our study.

A study conducted by Akseer et al (2018) showed that though the Millennium Development Goal (MDG) period saw immense achievements in health goals for improving child and maternal health, many of the Muslim countries had much higher maternal mortality rates as compared to the rest of the world, due to very similar factors as shown in our study.

A study carried out in Jharkhand, India by Khan & Pradhan (2013) showed similar causes of maternal deaths as shown in our study, but this study attributed these deaths to preventable factors like ignorance, illiteracy, and lack of nursing facilities.

According to yet another study by Austin et al (2014), multiple factors contribute to Maternal Mortality, including lack of medical facilities and lack of affordability of the available health facilities, and of course illiteracy further aggravating it.

As regards the risk factors, in our study, lack of antenatal care emerged as the biggest risk factor, followed by anaemia, multi-parity and reduced interval among successive pregnancies respectively. In a study by Mahmood et al (2018) multiparity was shown as the biggest risk factor for maternal mortality, although it was the third common risk factor in our study. Similar to our study, Astuti et al (2017) also show lack of antenatal care as one of the important risk factors in maternal mortality. Similar results regarding risk factors were shown in a study by Masturoh et al (2017) that showed lack of antenatal care and obstetric problems as the leading risk factors in maternal mortality. In yet another study, Bauserman et al (2015) showed lack of education, lack of antenatal care, obstetric causes and hypertension as the leading risk factors in maternal mortality. Yet another study by Diana et al (2020) showed anaemia and nutritional status, lack of antenatal care and obstetric complications as the leading risk factors for maternal mortality.

It is evident from these comparisons that results of our study also correspond to these studies regarding causes and factors leading to maternal mortality.

Our study has certain limitations too. A major setback of verbal autopsy is the lack of requisite resources needed to successfully conduct it on a large scale. Due to this shortcoming, we were compelled to keep the sample size limited to one district only. Hence inference from this study cannot be generalized.

Moreover, reaching out for data collection in rural communities is particularly difficult owing to unfavorable conditions brought on by the reluctance of the locals to associate with outsiders regarding such sensitive matters. Clearly, a general sentiment of mistrust towards outsiders prevails among these tightknit communities. This is reflected by the fact that family members or relatives of the deceased women were not very willing to give interviews.

Furthermore, at times, the volunteers were unable to recall events of the pregnancy that are pertinent to our research & many questions remained unanswered. In the light of our study following recommendations are made:

1. Employment of Trained Birth Attendants (TBA): Most of the deliveries in the developing countries like Pakistan are carried out at domestic set up, in the absence of any skilled attendant. Therefore, training of the traditional birth attendants should be ensured with adequate knowledge of midwifery skills along

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with emergency obstetric care so that the complications of labour are minimized.

2. Proper prenatal care should be ensured to minimize risks and complications. Conditions like hypertension, malnutrition, iron deficiency anemia should be addressed in prenatal assessments. Free, disposable and easily usable delivery kits should be made available to avoid any transmission of infection from mother or surroundings to the newborn.
3. Good antenatal care and obstetric care must be ensured.
4. Most importantly an awareness campaign should be launched at national level to improve quality of life especially in girls and women. They should be educated about health, family planning and hygiene. Moreover, community-based intervention packages may be introduced to reduce maternal mortality as shown in a study by Lassi & Bhutta (2015).

Conclusions

Hemorrhage related with delivery, especially the antepartum hemorrhage emerged as the commonest cause of maternal mortality, followed by eclampsia. At the same time, lack of antenatal care and anaemia emerged as the commonest risk factors in this regard. These are preventable and treatable causes.

This information can help us elevate the health status of mothers in our country. Although we could not establish cause of mortality in 28 patients even after the verbal autopsy, still this study establishes verbal autopsy as an effective tool in getting missing information about causes of maternal mortality.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

GRANT SUPPORT AND FINANCIAL DISCLOSURE

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Functional Outcome of Intramedullary Tibial Nail in Distal Femur Shaft Fractures

Raja Adnan Ashraf[1], Kamran Asghar[2], Saba Sohail[3], Zara Sohail[4], Waleed Bin Waris[5], Muhammad Imran Sohail[6], Qazi Muhammad Sibghatullah[7]

ABSTRACT

Objective: Assessment of the functionality in patients with supracondylar fracture of femur managed with intermedullary tibial nails.

Study Design: Case Series Study.

Place and Duration of Study: We conducted a prospective cohort study for 6 months, from September 2021 to February 2022.

Materials and Methods: 25 adult patients presented in the accidents and emergency department of Railway General Hospital, Rawalpindi. They were managed using tibial nail and their functionalities after the operations were managed using the Tegner-Lysholm Criteria measured at 2 weeks, 6 weeks, and 12 weeks till union achieved

Results: Five of our patients were females and twenty males. Average healing time was calculated at 15 weeks and 6 days approximately (2.646 SD) 24% (n=6) showed excellent healing, 48% (n=12) had good results and 28% (n=7) had fair results. We did not observe any complications.

Conclusion: Tibial nails are convenient and effective to manage the patients with supracondylar fracture of femur and show good functional outcomes.

Key Words: *Retrograde Femoral Nail, Supracondylar Femur Fractures, Tibial Nail.*

Introduction

Distal femur fractures are very commonly seen in patients suffering from high intensity trauma.[1] They contribute to 0.4% of all fractures.[2] A unanimous mode of management for the different types of distal femur fractures; transverse, oblique, spiral, and comminuted, is still debated by orthopedic surgeons.[3]

Renowned surgeons like Sir John Charnley, initially managed, supracondylar fractures conservatively using manipulation and casting, skeletal traction, external splints, and braces.[4] Unfortunately, these resulted in poorer outcomes and complications like non-union, mal-union and compartment syndrome causing significant disability.[5]

With the advancements in surgical techniques majority of femoral fractures now achieve good results.[6] Initially distal femur fractures were managed using dynamic condylar screws, condylar blade plates, distal femoral locking plates, and less invasive stabilization system plates.[7] The most significant disadvantages of these surgical options were deep tissue dissections, postoperative collection of hematomas, infection and a large surgical incision resulting in a scar on the lateral aspect of the thigh, except for less invasive stabilization system technique.[8] The application of blade plates requires great expertise and not many orthopedic surgeons are skilled in it.[9] Furthermore, blade plates and dynamic condylar screws mechanically pull the distal fragment of the femur laterally which can result in mal-rotation and consequently implant failure.[10]

Recently retrograde intramedullary nailing for the management of supracondylar fracture of femur is being accepted owing to minimal blood loss, smaller surgical incisions, lower risks for infection, early weight-bearing and decreased operative time.[11] However, retrograde femoral nails designed especially for the fixation of supracondylar femoral fractures are expensive and not cost effective for patients in developing countries.[12,13]

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Use of tibial plates for fixation of supracondylar fractures of femur is being employed by a few surgeons due to cost effectiveness and analogous success rates as specially designed distal femoral nails.[14] We evaluated the functional outcomes of tibial locking nails in the supracondylar fractures of the femur.

Materials And Methods

We conducted a prospective study for 6 months, from September 2021 to February 2022. 25 adult patients presented in the accident and emergency department of Railway General Hospital, Rawalpindi with supracondylar fracture of femur.

The inclusion criteria were distal one-third femur fractures, linear Type A extra-articular supracondylar femur fractures, and closed fractures. The exclusion criteria were all open fractures, B2, C2, B3, C3 fractures, and preoperative deformity. The study was commenced after getting approval from the Ethical review board of the Hospital. upon taking informed consents, all the patients were managed using tibial Nail by an experienced consultant orthopedic surgeon team.

A midline incision of 4cm was made from the inferior pole of the patella up to tibial tuberosity. The para-tenon over the patellar tendon was incised sharply and the patellar tendon was split in the midline along with the direction of its fibers. A straight bone awl was used and inserted into the knee joint through the split tendon and positioned against the femoral inter-condylar notch. The position of awl was confirmed using the image intensifier as antero-posterior and lateral. A guide wire was passed after making an entry point and the awl removed. The fracture fragments were aligned under image intensifier and guide wire passed in the proximal fragment. The distal fragment was then reamed with flexible reamers and the predetermined tibial nail of appropriate diameter and length was then loaded over the jig. The nail was finally inserted over the guide wire and its position confirmed with the help of image intensifier. Depending on the length of the nail, the proximal holes were locked. After inserting both proximal and distal locking screws, the jig was then disengaged, the joint washed thoroughly with normal saline to remove the debris, homeostasis achieved, and incision closed in layers. Particular attention was paid to repair para-tenon of patellar tendon.

Postoperative x-rays were obtained, and patients were discharged on the 2nd postoperative day after non-weight bearing mobilization. Follow-ups were done after 2 weeks, 6 weeks, and 12 weeks till union. The functional outcome was measured using Tegner-Lysholm criteria, which measures the functional outcome in terms of limping, pain, locking, stair climbing, support, instability, swelling and squatting. The follow up was ensured by taking phone numbers of the patients. SPSS 23 was used for statistical analysis. Frequencies and percentages were calculated for the categorical variables while mean and standard deviations were calculated for the numerical variables. Statistical significance was defined as a P value of 0.05. P value of 0.05 was considered statistically significant.

Results

Out of 25 patients 20(80%) were male and 5(20%) were female. The mean age in our study was 37. The average time of healing was between 12 and 21 weeks and mean time of healing was estimated near 15 weeks and 6 days with a standard deviation of 2.464 as shown in Table I

Functionality assessed using Tegner-Lysholm scoring system showed excellent scores for 24% (n=6), good scores for 48% (n=12) and 28% (n=7) showed fair scores after management through tibial nail for supracondylar fractures of femur as assessed at 12 weeks interval (Table II).

Discussion

In our study we treated 25 patients treated with tibial nail for supracondylar fracture of femur and documented 24% (n=6) showed excellent healing, 48% (n=12) had good results and 28% (n=7) had fair results. Average healing time was calculated at 15 weeks and 6 days approximately (2.646 SD)

Retrograde nails for the management of femur fractures are a widely accepted and convenient option for most of extra articular supracondylar fractures of the femur. They are considered a preferred option compared to conventional blade plates, condylar screws and newer locking plates in terms of stability, surgical exposure and healing time.[15] Nails have load sharing capability and provide better stability at the fracture site that promotes the

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use of closed technique more commonly.[16] Retrograde nails have low complication rates compared to other methods when used for the fixation of the supracondylar femur fractures.[17]

Our study was conducted on 25 patients, and 20 were male and 5 females. The mean time of healing was 15 weeks and 6 days compared to 25 weeks in a study by Gurkan et al. in which supracondylar femur fractures were fixed with standard retrograde femoral nails.[18] None of our patients had complications of nonunion or malunion. Our results were comparable to Gurkan et al. who reported excellent results in 29.4% (n=5), good in 35.3 (n=6), moderate in 31.2% (n=5), and poor results in 5.9% (n=1) of their patients.

Only 3 patients in our study developed coronal deformity. One patient developed valgus deformity and the other two patients developed varus deformity. This was also observed by Gurkan et al in which postoperative radiographic examination showed varus angulation of 10° in 23.5% (n=4) and posterior angulation of 10-20° in another 23.5% (n=4) patients.

7 patients developed flexion contractures of 5 degrees while one patient developed extension contracture. Contractures developed because of poor compliance of patients to physiotherapy. There were no nail ends protruding into the joint space.

All nails were kept up to the level of lesser trochanter of the femur, to reduce the chances of stress fracture, implant failure and rotational instability.[19]

All our cases were managed using a closed technique using a tibial nail compared to Rao et al. who converted 25% of the cases to open technique for reduction of the fracture fragment.[20] Rao et al. reported excellent results for 65% of their patients with the mean healing time of 16.2 weeks. Average knee flexion was 108 degrees with an extensor lag of 4.15 degrees.

Simil Sanders et al managed 18 patients of supracondylar femur fractures using AO Universal Tibial Nail, 92% fractures healed within 12 weeks with no complications like infection, loss of reduction, or nail failure[21] Knee flexion averaged at around 120 degrees, while only two knees had an extensor lag of more than 5 degrees. They reported the cost of retrograde Smith and Nephew femoral nails to be twice the price of Zimmer tibial interlocking nails making it a more cost-effective method of fixation.

our study had few limitations like in follow up of our study, we did not see postoperative complications like infection, nonunion, loss of reduction, stress fracture, or implant failure. further studies are recommended to confirm our results.

Conclusion

It is concluded that the retrograde tibial locking nails for stabilization of extra articular supracondylar fractures of femur are convenient and result in good functional outcome in most of the patients. we recommend tibial nail, an implant of choice to treat supra condylar fracture femur. Tibial nail has the added advantage of economic feasibility for the patients and easy learning curve for junior surgeons. However, more studies are required to support the evidence of our research.

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CONFLICT OF INTEREST

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DATA SHARING STATMENT

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ORIGINAL ARTICLE

Pattern of Impaction of Mandibular Third Molar and Its Relation with Caries in Mandibular Second Molar

Numra Mumtaz, Jawaria Bibi, Hawa Jabbar, Mohsin Fazal

ABSTRACT

Objective: To determine caries frequency in mandibular second molars in proportion to level of angulation and depth of impaction of mandibular third molars established on winters and Pell and Gregory classification system.

Study Design: This was a Cross-sectional study.

Place and Duration of Study: This study was regulated in Department of Oral and Maxillofacial Surgery at Islamic International Dental Hospital, Islamabad from 1st January 2018 to 30th June 2018.

Materials and Methods: An overall 100 cases of caries were investigated on clinical and radiographic basis in mandibular second molars. Each panoramic radiograph was studied for the presence of carious lesion in lower second molars. The depth and angulation of impacted third molars was being assessed using Pell and Gregory and winter's grouping respectively. Chi square test was applied for analysis of data.

Results: The participants in this study had age range from 18 to 60 years old. Mean age was 39.24 ±9.77 years. Majority of the patients 59 (59.0%) were between the ages 18 and 40. Among these patients, males were 83 (83.0%) and females 17 (17.0%) having a 4.9:1 male-to-female ratio. Caries at the distal aspect of mandibular second molars were seen in 39 percent of individuals with impacted lower third molars and mesioangularly impacted teeth most resulted in caries.

Conclusion: This study concluded that 39% of the patients with impacted mandibular third molars caused distal cervical caries in second molars, with mesioangular impaction being the most prominent type causing caries. So, an attentive follow up of impacted mandibular third molars should be considered as health of lower mandibular second molar is influenced by pattern of impaction.

Key Words: *Caries, Lower Second Molar Impaction, Lower Third Molar Impaction, Mesioangular, Preventive Removal.*

Introduction

An impacted tooth is defined as being partially or totally embedded in the soft tissue or bone, having an obstruction in its eruption pathway and is unlikely to erupt within the expected time frame.[1] Third molars are classified using Pell and Gregory (1933) and Winters (1926) grouping that describes depth and angle of an impaction respectively relative to the adjacent second molars.[2]

Third molars are related to various complications such as tooth decay, root resorption, periodontal problems, pericoronitis, infections, cysts, dental crowding, and neoplastic lesions. Distal caries on mandibular second molar are a frequently noted complication associated with impaction of mandibular third molar tooth. Extraction of third molar is a commonly performed surgical procedure due to various reasons but removal due to caries on distal surface of mandibular second molars ranges from 4.2 to 37.5%.[3]

The caries prevalence seems to be significantly influenced by the positioning of the impaction. There are numerous studies in literature regarding this subject highlighting the association of distal caries with mandibular third molar mostly related to mesioangular impaction.[4,5] Also a statistically important link was found between horizontally impacted third molar and caries along with mesioangular impaction.[6] So, to preclude the development of caries and early loss of second molar teeth, removal of third molars should be given consideration.[7]

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This study was conducted with an objective to determine the mandibular third molar impaction pattern and its consequences in causing carious lesions in mandibular second molars so a better practice can be formulated for early diagnosis to prevent caries in the adjacent tooth in our Centre.

Materials and Methods

This cross-sectional study was conducted over a duration of 6 months, in the department of Oral and Maxillofacial Surgery at Islamic International Dental Hospital, Islamabad commencing from 1st January to 30th June 2018.

Total 100 subjects satisfying the criteria for inclusion and exclusion were included in this study with Non-probability, Consecutive Sampling method. The World Health Organization sample size calculator was used to compute sample size. After selecting patient informed consent and demographic details were recorded in a study pro forma.

Participants who were included in this study were 18 to 60 years old, having both mandibular second and third molars with caries present in lower mandibular second molars being identified clinically and radiographically. Patients with already missing/extracted mandibular second molars and filled mandibular second molars were not involved in this study.

All the patients were approved from the OPD of Oral and Maxillofacial Surgery department in IIDH. After patient selection associated complaints like pain, caries and pericoronitis were also documented. Further, clinical examination was done to investigate the extent of caries clinically and then patient was subjected to standard preoperative OPG (orthopantomograms) and periapical radiographs to confirm carious lesion. Each radiograph was studied for presence of carious lesion in lower second molar and also depth and angulation of impacted third molar teeth was evaluated. The Pell and Gregory classification system was used to evaluate depth based on extent of tooth enclosed by anterior border of ramus (class I, II, and III), and when considering occlusal surface (Class A, B and C). Winter's classification was used to assess the angle by measurement of angle between second and third molar, intersecting longitudinal axes[8]. Angles measurements were done using a protractor (180º) with vertical impaction angle (10º-10º), mesioangular impaction(11º -79º), horizontal impaction(80º-100º) and distoangular impaction(-11º-79º).

Age, gender, impaction type, angulation and depth were study variables to assess carious lesions in lowers second molar teeth in relation with impaction pattern of third molar.

The statistical analysis of data was done by IBM SPSS software version 16 (Statistical Package for the Social Sciences). For qualitative factors such as gender, caries presence, depth of impaction and type of angulation, frequency and percentage were determined. For all quantitative data such as age, the mean and standard deviation were computed. Chi square test was applied to evaluate relation among caries in mandibular second molar to both depth and angle of impacted third molar. The effect modifiers like age and gender were measured by stratification. The post-stratification chi square test was used. Confidence level was 95%. Statistical significance was considered as P value ≤ 0.05.

Results

The participants in this study were in age from 18 to 60 years old, with mean age 39.24 ± 9.77 years. Majority of the patients 59 (59.0%) were between ages of 18 and 40.

Among these patients, males were 83 (83.0%) and females 17 (17.0%) having a 4.9:1 male-to-female ratio.

Table I shows the patient distribution according to angulation type and impaction depth.

Tables II and III indicate the relation between mandibular second molar caries and impaction depth and angulation type.

In this study, cervical caries at the distal side of second molars occurred in 39% of patients having impacted mandibular third molars, and mesioangular impaction was the most occurring as shown in figure I.

Table I: Distribution of Patients with Respect to Type of Angulation

		Frequency	%Age
Type of angulation	Vertical	22	22.0
	Mesioangular	31	31.0
	Horizontal	19	19.0
	Distoangular	15	15.0
	Others	13	13.0
Depth of impaction	Level A	21	21.0
	Level B	33	33.0
	Level C	46	46.0

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Table II: Relation Between the Mandibular Second Molar Caries to Depth of Impaction

Depth of impaction	Caries		p-value
	Present	Absent	
Level A	10	11	**0.151**
Level B	14	19	
Level C	12	34	

p value = 0.05*

Table III: Relation Between the Mandibular Second Molar Caries to Type of Angulation

Type of angulation	Caries		p-value
	Present	Absent	
Vertical	06	16	**0.183**
Mesioangular	13	18	
Horizontal	05	14	
Distoangular	04	11	
Others	08	05	

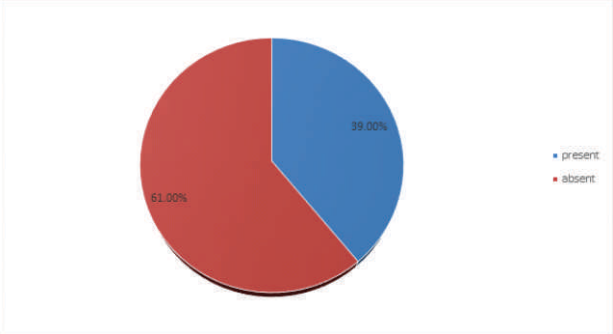

Figure 1: Percentage of Caries (n=100)

Discussion

Diverse patterns are seen in impacted third molars in relation to depth, position, and angle in comparison with mandible and plane of occlusion respectively. Understanding of these pattern forms is essential as some of these are linked to greater caries risk in next immediate tooth that is second molar[5], discomfort and pericoronitis[8] and early loss of second molar tooth[9]. According to a research distal caries was the highest stated pathology between the second and impacted third molars, second being the periodontal pocketing[10].

In light of the abovementioned issue, this study was conducted to determine frequency of caries in mandibular second molar in relation to level of angulation and depth of impaction, established on Winter's and Pell and Gregory's categorization system so a close follow-up of impacted molars should be considered to protect the second molar tooth.

In this study, of 100 patients, 83.0% were male gender and 17.0% female having a 4.9:1 male-to-female ratio. Majority of patients with impacted mandibular third molar showed in their second and third decade, that is, 59.0%. Distal cervical caries in second molars occurred in 39 percent of patients having impacted mandibular third molar teeth, and mesioangular impaction the most commonly occurring.

A study carried by Srivastava et al[5], supports the outcomes of our study, male predominance and majority of patients being in the second decade. Although, numerous former studies advocate a female predominance.[9]

A study shows consistent results reporting caries to be more common in those with mesioangular impaction, that is, 68.3%, then vertical with 25.4%, followed by horizontal being 4.2% and lastly distoangular impaction 2.1%[11]. Also, third molars above the level of cemento-enamel junction of adjacent second molar were related to causing distal cervical caries.[12] Several other studies show caries on the distal side of second molars occurred with unerupted mandibular third molars, and the mesioangular impaction was the common kind.[4,6,13]

According to pentapati et al[3] caries on the distal surface of mandibular second molars may not be related with all impacted mandibular third molars but teeth with mesioangular and horizontal angulations may lead to caries on the distal aspect of second molars.

Some studies have shown increased risk of caries associated with other types of impactions, vertical and horizontal mostlyx.[7,14]

Altan et al suggested that prophylactic removal of mandibular third molar between 51º to 71º can lead to avoidance of distal carious lesions.[15]

However, sample size and duration of our research work are the limitations of our study

In view of these studies prophylactic removal of third molar can be beneficial for the health of second molar tooth but in our region, it can also be an economic burden for the patient. So, consideration should be given to keep follow up of an impacted molar and attempting its removal when required. Further studies need to be carried out to devise a specific protocol for management and follow up of patients with impacted mandibular third molars to

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maintain long term health of mandibular second molar.

Conclusion

According to the findings, cervical caries is seen on the distal aspect of mandibular second molars in 39 percent of individuals and most common impaction was the mesioangular impaction.

To ensure the continuing health of mandibular second molars next to impacted third molars with mesial angulation between 30° and 70°, notably located at Level A and Class I, should be called for an attentive follow-up of impacted mandibular third molar.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATMENT

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ORIGINAL ARTICLE

Cardioprotective Effects of Nigella Sativa and Enalapril in Doxorubicin-induced Cardiotoxicity

Uzma Naeem[1], Salma Saleem[2], Rabia Iftikhar Malik[3], Alia Rehman[4], Nimra Ijaz[5], Aqsa Tazarat[6]

ABSTRACT

Objective: To determine the combined cardioprotective effects of *Nigella Sativa* and enalapril in doxorubicin-induced cardiotoxicity in rats.

Study Design: Experimental randomized control trials.

Place and Duration of Study: This research was carried out from September 2020 to August 2021, in the department of pharmacology, in collaboration with the National Institute of Health (NIH) Islamabad, Pakistan.

Materials and Methods: For this experiment, 4 groups of adult male rats were taken, each containing 10 rats. Group 1 rats acquired a normal diet without any medication throughout the experiment. On day 8 (after acclimatization) cardiotoxicity was induced in groups 2, 3, and 4 rats by administering doxorubicin 5mg/kg intraperitoneally for 3 consecutive days. After the confirmation of cardiotoxicity, Group 3 rats were administered only angiotensin-converting enzyme inhibitors (ACEI) enalapril 2mg/kg, while group 4 rats were given a combination of *Nigella sativa* 100mg/kg and Enalapril 2mg/kg orally for 14 days. Baseline blood samples were taken on day 0 to obtain normal values of Cardiac Troponin T (cTnT), Cardiac Troponin I (cTnT), and CK-MB enzyme. To confirm cardiotoxicity 2nd sampling was done on day 11, and the final sampling was done through cardiac puncture on day 26. Serum biochemical estimation was done and data were analyzed through SPSS 22 by using one-way ANOVA and paired t-test. A P-value < 0.05 was believed statistically considerable.

Results: Enalapril alone produced significant cardioprotective effects as shown by the marked reduction in cTnT, cTnI, and CKMB levels in group 3 ($p<0.05$), but combined administration of *Nigella sativa* and enalapril in group 4 mice produced a more significant reduction in Trop T, Trop I, and CK-MB levels ($P <0.05$).

Conclusion: *Nigella sativa* and enalapril in combination significantly lower cardiac enzyme in Doxorubicin-induced cardiotoxicity in rats.

Key Words: *Cardiotoxicity, Doxorubicin, Enalapril, Nigella Sativa.*

Introduction

Doxorubicin is an extensively used anthracycline for the treatment of several solid tumors and childhood malignancies for years. The main concern about the use of this drug is its cardiac adverse effects because about twenty percent of patients who receive doxorubicin can develop adverse cardiac effects.[1] Cardiomyocytes have a lesser capability to regenerate therefore, they are potentially more vulnerable to the long-term adverse effects of doxorubicin.[2] Its cardiotoxicity occurs because of its quinone group-based metabolites that produce reactive oxygen species and free radicals.[3] Cardiomyocytes are intrinsically more susceptible to oxidative stress, so these free radicals & reactive oxygen species impose mitochondrial and nuclear DNA lesions in cardiomyocytes. [4,5] Doxorubicin-mediated reactive oxygen species also stimulate mitogen-activated protein kinases, which induce the expression of several proapoptotic proteins. These processes lead to cardiomyocyte death either by necrosis or apoptosis and cause the release of

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cardio-specific contractile proteins; cardiac troponins I (cTnI), cardiac troponin T (cTnT), and creatinine kinase MB into the circulation.[6] Cardiotoxicity is more specifically expressed by cTnI and cTnT because they are exclusively expressed in the myocardium and are more abundant than CK-MB in the myocardium. Therefore, the quantitative approximation of these sensitive biomarkers is used for the presence of cardiotoxicity at the subclinical as well as clinical stages.[7,8] Several strategies have been recommended for the prevention of doxorubicin-induced cardiotoxicity. Still, the protection deliberated is not always effective and is expensive as well.[9] Several clinical studies and meta-analyses assessing the use of angiotensin-converting enzyme inhibitors (ACEIs) in anthracycline-induced cardiotoxicity have recently been revealed, and these studies suggested that ACEIs are effective as cardioprotective agents because of their antioxidant and anti-inflammatory properties.[10,11]

Nigella sativa has been used medicinally for decades because it is a marvel herb with a wide range of pharmacological properties and astonishing religious background.[12] This herb has proven antioxidant, anti-inflammatory, cardioprotective, hepatoprotective, antidiabetic, neuroprotective, and anticancer, effects among others.[13] The cardioprotective effects of both *Nigella sativa* and enalapril have been studied and proved separately, but according to the best of our knowledge, their combined effects are not yet explored. So, this study aimed to evaluate the extent of the protective role exerted by *Nigella sativa* in the prevention of cardiotoxic effects of doxorubicin in combination with an ACEI enalapril.

Materials and Methods

This experimental randomized controlled study was performed from September 2020 to August 2021 in the Department of Pharmacology, after getting approval from the institutional review committee. This study was initiated on a total of 40 healthy male albino rats weighing 200-250 g, 8 weeks of age, and with normal cTnI, cTnT, and CKMB levels. Rats were placed in well-aerated cages for acclimatization, a room temperature of 22 ± 2 ° C, and a 12-hour light-dark cycle was maintained.[14] Rats were randomly divided into 4 groups of 10 rats each. Group 1, the control group, consumed a normal diet and tap water throughout the experiment while group 2, 3, and 4 rats were given three intraperitoneal injections of doxorubicin at a dose of 5mg/kg for three consecutive days (cumulative dose 15 mg/kg).[15] After the confirmation of cardiotoxicity by measuring and analyzing cTnI, cTnT, and CK-MB levels; group 3 rats were given enalapril 2mg/kg/day[16] alone while group 4 rats were given *Nigella sativa* seed powder 100mg/kg/day[17] and enalapril 2mg/kg/day dissolved in distal water for 14 days.[16] Nigella sativa and enalapril powders were prepared at the Riphah Pharmaceutical Science Institute (RIPS) in Islamabad. On day 0, blood samples were taken for a baseline evaluation, and on day 11, a second sampling was done for the confirmation of cardiotoxicity in groups 2, 3, and 4. The final sampling happened on the 26th day of the experiment, all samplings were accomplished by cardiac puncture. The sample was centrifuged at 3000 rpm for 5 minutes, and the serum was separated and stored at -8 ºC in eppendorf tubes for further biochemical analysis. cTnT, cTnI, and CK-MB were assessed using the chemistry Analyzer, Micro lab 200 (Merck). These parametric data were statistically analyzed by using SPSS 22. The mean and standard error of the mean was calculated for all four groups. One Way ANOVAs were done for comparison among different groups while comparison between two groups was done by using the paired t-test. Results were considered significant at a p-value less than 0.05.

Results

Cardiac troponin I (cTnI) and cardiac troponin T (cTnT) were measured in ng/l ±SD while CK-MB activity was measured in U/l ±SD. On day 11 the confirmation of cardiotoxicity in groups 2, 3, & 4 was

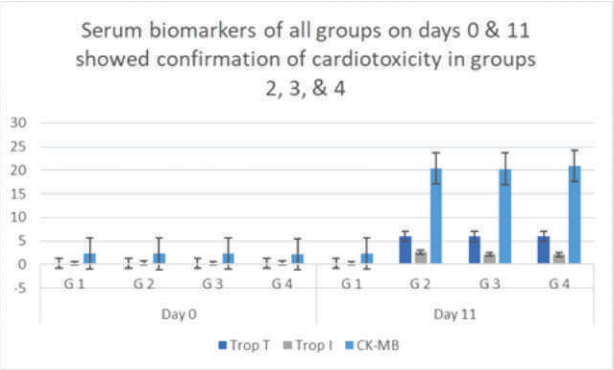

Figure 1: Comparison of Biomarkers Among Groups on Days 0 & 11.

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done by the results shown in figure 1. The p-values for cTnI, cTnT, and CKMB were 0.001, 0.003, and 0.000 respectively.

When we analyzed the 26th-day results of all groups, remarkably significant improvement was found in the cardiotoxic profiles of groups 3 & 4, their parameters were almost equal to normal control values and their day 0 levels (table 1).

Table I: Comparison Among Serum Biomarkers of all Groups on days 0 and 26.

Serum Tests	Day 0				Day 26				*p*-value
	G 1	G 2	G 3	G 4	G 1	G 2	G 3	G 4	
Trop T (ng/l) ±SD	0.17± 0.01	0.18± 0.03	0.17± 0.01	0.17± 0.05	0.17± 0.30	5.96± 0.37	0.22± 0.37	0.18± 0.37	0.001*
Trop I (ng/l) ±SD	0.26± 0.17	0.21± 0.33	0.22± 0.14	0.25± 0.08	0.25± 0.10	2.60± 0.21	0.32± 0.11	0.26± 0.17	0.000*
CK-MB (U/L) ±SD	2.35 ± 0.08	2.25 ± 0.07	2.32 ± 0.05	2.29 ± 0.07	2.35± 0.07	20.4 ± 1.31	2.79 ± 1.31	2.30 ± 1.31	0.000*

*Significant *p*-value

To confirm our hypothesis, we further compared the serum markers of group 3, & 4 and we observed *p*-values of 0.000, 0.023, and 0.000 respectively for trop T, trop I, & CKMB levels. These results showed that *Nigella sativa* increased the efficacy of enalapril.

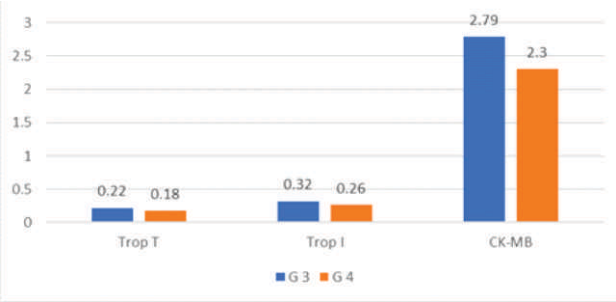

Figure 2: Comparison of Serum Markers of groups 3 & 4 on day 26.

Discussion

In the present study, we observed that *Nigella sativa* potentiates the cardioprotective effects of enalapril in doxorubicin-induced cardiotoxic rats as represented by the comparison of the cardiotoxicity indicating biomarkers. Enalapril alone also proved cardioprotective.

We artificially induced acute cardiotoxicity by a cumulative dose of doxorubicin 15 mg/kg/day in groups 2, 3, and 4 rats, this cardiotoxicity was confirmed by significant rises in serum biomarkers of cardiac injury including cTnI, cTnT, & CKMB. Doxorubicin's cardiotoxicity is a piece of evidence used by numerous researchers to induce cardiotoxicity in different animal models. Lin and his associates induce cardiotoxicity in rats with doxorubicin, they use an accumulative dose of 18mg/kg over 2 weeks.[18] Aziz and his colleagues observed similar changes in biomarkers following the use of doxorubicin as a single intraperitoneal injection in rats.[19] Sawyer and his colleagues observed such kinds of effects in their preclinical studies both in vitro and in vivo, while Georgakopoulos and coworkers observed the effects of doxorubicin in clinical studies on lymphoma patients and established that doxorubicin caused a significant and dose-dependent cardiomyocyte apoptosis and myocytes death.[20,21] Another study by Eisvand et al also supported the cardiac enzyme disruption after introducing a single dose of doxorubicin in rats.[22] In our study the rationale behind the measurement of CKMB was its historical value but our stress remained on cTnI & T as more specific and sensitive biomarkers, these markers are considered the gold standard biomarker of cardiac injury in all mammalian species.[23]

The second part of our study was a comparative analysis of the cardioprotection provided by enalapril alone and in combination with *Nigella Sativa*. The Group 3 animals were treated with enalapril for 14 days and they confer cardioprotection. The cardioprotective effects of enalapril and other ACEIs are well established. In a recent study, Ghasemi and his fellows comprehensively review the clinical trials performed on the prevention of doxorubicin-induced cardiotoxicity. They conclude that ACEIs plus doxorubicin are the best treatment for preventing cardiotoxicity in these patients.[24] Divergent effects of enalapril and eplerenone in primary prevention against doxorubicin-induced cardiotoxicity were studied by Hullin et al and they concluded that primary prevention with enalapril preserves left ventricular morphology and function in mice.[25] Georgakopoulos et al studied the cardioprotective effects of metoprolol and enalapril in lymphoma patients.[21]

Adıyaman used the same dose of *Nigella Sativa* seed powder for the prevention of doxorubicin-induced toxicity[17] while we use it for the treatment

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and in combination with enalapril to define their combined effects. A study conducted by El-Kerdasy also showed the beneficial effects of Nigella Sativa and ACEIs on myocardial fibrosis Induced by lipopolysaccharide.[26] Cardioprotective effects of the ethanolic extract of Nigella sativa (800mg/kg/day) were studied by Hassan and his colleagues, they observed improvement in different cardiac markers.[27]Extensive literature is present regarding the use of this herb in animals but very few studies have been done on humans and this is the need of time.

Conclusion

Nigella sativa and enalapril in combination significantly lower cardiac enzyme in Doxorubicin-induced cardiotoxicity in rats. So, Nigella sativa can be used as an adjunct with enalapril in the treatment of doxorubicin-induced cardiotoxicity.

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CONFLICT OF INTEREST

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ORIGINAL ARTICLE

Level of Stress Among Health Care Workers in COVID-19 Dedicated Setup

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ABSTRACT

Objective: To determine the co-relation between perceived social support and stress among nursing staff working in a COVID-19 dedicated hospital setup.

Study Design: Cross-sectional study.

Place and Duration of Study: Armed Forces Institute of Mental Health (AFIMH), Rawalpindi from 30 Aug 2020 to 02 March 2021.

Materials and Methods: We consecutively sampled 128 subjects. All participants were requested to complete a brief demographic sheet, Urdu version of the Depression, Anxiety and Stress Scale 21 (DASS-21) to assess the level of severity of stress among nursing staff and the Urdu version of the Multidimensional Scale of Perceived Social Support (MSPSS). Data analysis was done using SPSS version 23.0.

Results: The mean duration of stay of nursing staff in ward was 4.86 ± 2.28 weeks. Sixty-two (48.44%) nurses had duration of 2 to 4 weeks while 66 (51.56%) nurses had duration of more than 4 weeks of stay in the ward. The mean total stress score was 6.86 ± 5.80. The mean multidimensional scale of perceived social support (MSPSS) score was 47.29 ± 22.53. There was significant negative correlation between MSPSS score and stress score ($r = -0.396$, p-value < 0.05).

Conclusion: Results of this study highlighted that a significant negative co-relation is present between perceived social support and stress among nursing staff working in a COVID-19 dedicated hospital setup.

Key Words: *Anxiety, COVID-19, Depression, Nursing Staff, Stress.*

Introduction

Infectious disease caused by coronavirus (SARS-Cov-2) reached the scale of a pandemic on March 11, 2020.[1] COVID-19 brought unprecedented challenges and catastrophic burden on healthcare services particularly health care workers were affected. Nursing staff was at increased risk of getting infected with this virus, were continuously in danger of being infected while on duty and they also carried the same risk for their families.[2] Long working hours at hospitals kept them away from their families, which further added to their stress, they also had the duty of caring for their colleagues who were COVID-19 affected and they needed to work with Personal Protective Equipment (PPE), which made their routine tasks more arduous.[3] In addition Health care professionals had to make decision to selectively put certain patients on life support, while knowingly depriving other patients of these facilities due to lack of available resources[4]. To add to these issues, some staff required going themselves into quarantine while those who were pregnant or immune-compromised were not able to contribute as frontline workers and as a result feelings of guilt surfaced in some individuals.[5] In these difficult circumstances, having social support from colleagues, hospital administration (formal social support) and family (informal social support) may play a major role in deterring mental health challenges for the nursing staff. Nurses who have increased perceived social support have been documented to have decreased stress levels.[6,7] Social support can have four different characteristics in the form of emotional, instrumental, informational and evaluative support.[8] Every individual in his own way perceives his social network adequately supportive or not, is in simple terms "Perceived social support". Evidence has shown that Social support is correlated with mental health as it protects against mental

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health problems, thereby alleviating stress and anxiety issues.[9] In these circumstances, social support may be a highly effective factor in off-setting the effects of stressors for nursing staff, thereby protecting their mental health and ultimately contributing to their ability to provide an improved quality of patient care. Currently, there is a paucity of literature investigating relationship between perceived support and level of stress among nursing staff of Pakistan. Therefore, this study aimed at finding evidence that social support protects the nursing staff from development of stress while serving COVID-19 patients.

Materials and Methods

After approval of ethical committee vide ERC ref (019/20), this cross-sectional study was done at Armed Forces Institute of Mental Health (AFIMH), Rawalpindi from 30 Aug 2020 to 02 March 2021. A total sample size of 128 was estimated using statistical formula N= [(Zα+Zβ)/C]2+3 by Hulley[10] keeping results of study by Xiao et al as reference.[11] We consecutively sampled 128 subjects using convenience non probability sampling technique. Both genders, age range 20-60 years, Nurses working in COVID-19 dedicated wards, HDUs and ICUs at PEMH, Rawalpindi, Nurses who had worked at least for a duration of 2 weeks in above settings were included in this study after consent. Doctors and ancillary support staff, COVID-19 infected nurses, Nurses with pre-existing mental health problems were not included. Participants completed a brief demographic sheet, Depression, Anxiety and Stress Scale 21 (DASS-21) Urdu version[12] and Multidimensional Scale of Perceived Social Support (MSPSS) Urdu version.[13] MSPSS a 12-item scale has subscales for family, friends and significant other (each subscale having 4 items on the MSPSS).[14] The respondents answered each item on a 7-point Likert scale with the following responses, 1 for very strongly disagree, 2 for strongly disagree, 3 denoting I disagree, 4 representing neutral response, 5 meant I agree, 6 denoting I strongly agree while 7 meant I very strongly agree. Total sum of all twelve items were calculated for all respondents for obtaining the mean score for Perceived social support (range = 1 to 84). Mean and standard deviation for PSSS score was described. The DASS 21 has three sub scales for stress, anxiety, and depression with each subscale having seven items on the scale.[15] Each item on the scale is required to be responded from 0 to 3 on Likert scale where 0 denotes that it did not apply to me at all, 1 means it applied to me to some degree, or some of the time, 2 means it applied to me to a considerable degree or a good part of the time and 3 represents that it applied to me very much or most of the time. Seven items of stress subscale were added and then multiplied by 2 to obtain a Stress score representing 0 to 7 as normal, 8 to 9 as mild, 10 to 12 as moderate, 13 to 16 as severe while more than 17 as extremely severe.

SPSS version 23.0 was used to analyze data. For age, duration inward, PSSS and Stress score mean and standard deviation while frequency and percentages for categorical variables such as gender, and proportion of nurses in the various categories of perceived social support and stress were calculated. The Outcome variable for the study was the Perceived social support score (**PSSS**). The Dependent variables for the study was the Stress Score (**SS**). Pearson's correlation coefficient was calculated for the PSSS and SS. Effect modifiers such as age, gender duration of work/stay in ward were controlled by stratification and post-stratification correlation was applied. Post stratification chi squared test was used. Statistical significance level was set to maximum of 5% ($p<0.05$).

Results

The mean age of participants in this study was 30.81 ± 6.56 years (21 - 45 years), 80 (62.50%) were male and 48 (37.50%) female nurses with higher male to female ratio. The mean duration of stay of nursing staff in ward was 4.86 ± 2.28 with minimum and maximum duration in ward was from 2 to 8 weeks, 62 (48.44%) nurses had duration of 2 to 4 weeks while 66 (51.56%) nurses had duration of more than 4 weeks of stay in the ward. The mean total stress score was 6.86 ± 5.80, 72 (56.25%) nurses had normal scores, 19 (14.84%) had mild stress, 10 (7.81%) had moderate, 18 (14.06%) had severe while 9 (7.03%) had extremely severe stress. The mean MSPSS score was 47.29 ± 22.53 with significant negative correlation between MSPSS and stress scores r-0.396, ($p < 0.05$).

Discussion

Current study findings show a significant negative correlation between MSPSS score and stress scores

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Table I: Demographic Variables

S.no	Category	
1.	**Age** (Mean ± SD)	30.81 ± 6.65
2.	**Gender**	N (%)
	Male	80 (62.50)
	Female	48 (37.50)
3.	**Marital Status**	
	Married	100 (78.12)
	Unmarried	28 (21.87)
4.	**Education**	
	Matric or more	123 (79.35)
	Below matric	32 (20.62)
5.	**Stress**	
	Normal Level	72 (56.25)
	Mild Level	19 (14.84)
	Moderate Level	10 (7.8)
	Severe Level	18 (14.06)
	Extremely Severe	9 (7.03)
	Level	6.86 ± 5.80
	Mean ± SD	
6.	**Duration of time spent in wards**	62 (48.44)
	2-4 weeks	66 (51.56)
	> 4 weeks	4.86 ± 2.28
	Mean ± SD	
7.	**Perceived Social support**	47.29 ± 22.53
	Mean ± SD	

Table II: Comparison of Stress Score with Demographic Variables

S.no	Category	Variables		Stress Score	P value
1.	Age (years)	20-40	Pearson Correlation	-349	0.004
		> 40	Pearson Correlation	-437	<0.001
2.	Gender	Male	Pearson Correlation	-419	<0.001
		Female	Pearson Correlation	-375	0.009
3.	Duration	2-4 weeks	Pearson Correlation	-387	0.002
		> 4 weeks	Pearson Correlation	-409	<0.001

of nursing staff working in wards/ICUs of PEMH Rawalpindi, indicating psychological distress among nursing staff while dealing with COVID-19 patients. These findings are like those of various other studies which have described psychological adverse effects among medical staff working during COVID- 19 health crisis.[16,17,18]

This study has focused on co-relation of stress with

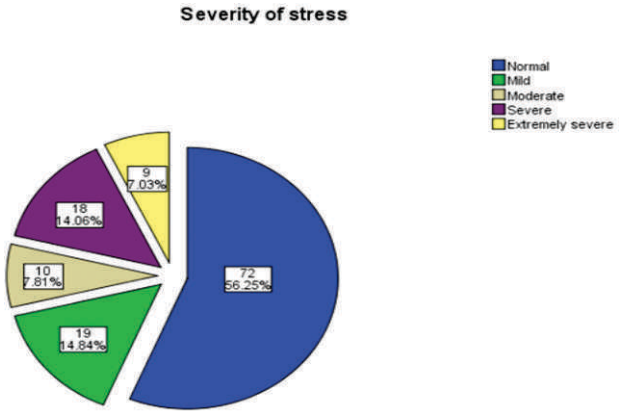

Fig. 1: Severity of Stress in Nurses

perceived from informal social support of friends, family and significant others, related to psychological health and quality of life which in turns improves the mental health and quality of life.[19] Our findings are almost in agreement to another published study, i.e., Xiao et al. which assessed the correlation between social support and stress of 180 health care workers involved in taking care of patients with COVID-19 in a hospital in Wuhan, China. Their investigation found that social support had a negative weak correlation with stress (Standardized coefficient = - 0.245).[11] In another study done during COVID pandemic by Turkish investigators it was observed that the level of social support perceived by the nurses was very good while perceived psychological resilience level was moderately good which increased as the perception of social support was increased.[20] Informal sources of social support have received less attention in research as compared to formal sources of support.[21] However, for most individuals, family and friends are the basic and foremost form of support and connection which they will turn to first in times of stress. They tend to utilize this resource before they turn to more formal sources of support i.e., superiors and organizations[22]. Williams et al state that structure of informal social support network is an indicator of good social support therefore larger support network is preferable.[23]

These results substantiate findings of other studies by uncovering the underlying mechanisms between social support and mental health. They have impact on mental health services for nurses working during the peak period of COVID-19. During pandemic there is need to focus on availability of informal sources of

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social support particularly for nursing staffs who serve in closer proximity to patients as compared to doctors. Health care administrators need to be sensitive to these issues to address them in a better way.

Conclusion

It is concluded that stress was seen in several staff nurses with significant negative co-relation between perceived social support and stress, whether formal or informal, has the capacity to impact the efficiency of nursing staff. Hence, social support must be enhanced to reduce the stress levels among the nurses who have important role as spearheads in the fight against COVID-19.

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ORIGINAL ARTICLE

Effects of Microwave and Light Emitting Diode as Disinfection Methods on the Dimensional Stability of Polymethyl Methacrylate and Polyamide Denture Base Resin

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ABSTRACT

Objective: To compare the effects of microwave and light emitting diode disinfection on the dimensional stability of two denture base materials; polymethyl methacrylate and polyamide.

Study Design: In-vitro study

Place and Duration of Study: Peshawar Dental College and Material Research Laboratories, University of Peshawar from 10th June 2021 to 8th December 2021.

Materials and Methods: Fifteen specimens each for polymethylmethacrylate and polyamide were divided into three groups, control, microwave & light emitting diode. The specimens for microwave group were irradiated at 1000W for 3 minutes, thrice a week. The specimens for light emitting diode group were disinfected in a device for 30 minutes, thrice a week. The control group specimens were placed in distilled water for 4 weeks. Dimensions were measured before disinfection, and four weeks after the assigned disinfection. The mean and the standard deviation of the differences between three groups were statistically analyzed using one-way ANOVA and after obtaining significant values, through post hoc Tukey HSD.

Results: For polymethylmethacrylate highest dimensional difference (-9.02mm) was noted for microwave disinfected group while the control group showed the lowest value (-6.99mm). For polyamide, the highest dimensional changes were recorded for light emitting diode group (8.66mm) and the lowest (-7mm) for the control group. Statistical analysis showed that the differences were significant for both polymethylmethacrylate and polyamide when compared with the control (p<0.05) but insignificant when microwave disinfected group was compared with light emitting diode group (p>0.05)

Conclusion: No significant difference in dimensional stability of both the denture base resins was observed after disinfection with microwave and light emitting diode.

Key Words: *Dimensional stability, Disinfection, Denture base resin, Light emitting diode, Microwave, Polymethyl methacrylate, Polyamide.*

Introduction

Polymethyl methacrylate (PMMA) is widely used for the fabrication of partial and complete dentures. Even though implant treatments are on the rise, but still there is a vast majority of cases that need removable dentures in developed as well as developing countries.[1] Therefore, the use of PMMA in prosthetic dentistry remains substantial as it shows adequate material properties and ease of application.[2] However, concern has been expressed with the adverse effects due to monomers present in acrylic materials among patients and medical staff.[3] In addition, the aesthetics of PMMA based removable partial denture can be impaired by the appearance of metallic components. A viable or possible alternative to PMMA can be polyamide.[4] Polyamides (PA) are preferred for persons allergic to methyl methacrylate, bone undercuts, in thin mucosa and excessive resorption of bone, in production of temporary dentures after implants placement surgeries.[5]

Due to poor oral and denture hygiene, removable prostheses provide a source for microbial growth[6], and thus causing denture related stomatitis.[7] Denture hygiene is achieved both through chemical and mechanical methods which affect the physicomechanical properties of materials used to make removable prosthesis.[8] To overcome the

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complications, microwave radiation has been advocated as an easy, safe, and effective way for denture disinfection.[10] In a recent review, microwave disinfection has been claimed as an efficient antifungal therapy for the treatment of denture stomatitis.[11] Microwave disinfection is mostly carried out in wet conditions[12] where the denture base is placed in water in the microwave oven, this may cause further polymerization of the resin.[13]

Despite the effectiveness of microwave as denture disinfectant, researchers have reached contradictory findings regarding its harmful effects on some properties. These detrimental effects may be due to the heating of material during irradiation, which could affect the structure of polymer.[14] The consequences of microwave disinfection of denture base materials have been vastly studied, but no consensus could be developed regarding the deleterious effects of microwave on prosthodontic materials[11]. Some of these studies showed notable dimensional changes of upto -1.12%[15], & 3%[16] after disinfection with microwave.

Blue LED light in the visible spectrum of wavelength (405nm), has been found to have bactericidal/ fungicidal effects.[18] Blue LED light of this wavelength inhibits the candida biofilm production on prosthesis and can also disinfect denture surfaces swiftly than conventional disinfection methods. Therefore, blue LED light can be a promising technique for denture disinfection. However, there is very limited information available for the effects of LED for disinfection of both PMMA and PA denture base resins on their dimensional stability. Similarly, no data is available to compare the effect of microwave and LED disinfection of two denture base materials on their dimensional stability. The aim of this study was to compare the effects of microwave and LED disinfection on the dimensional stability of polymethyl methacrylate and polyamide denture base resins.

Materials and Methods

This was an in-vitro, study conducted from 10th June 2021 to 8th December 2021, in Peshawar Dental College and Material Research Laboratories, University of Peshawar.

A total of thirty specimens were made, fifteen each for the two materials used; Polymethyl methacrylate (Engropolymer, Meadway, UK) and Polyamide (Vertex Dental B.V, Netherland). The specimens for each material were further subdivided into three groups: Group (A) Control (without treating either with MW or LED), group B microwave (MW) and group C light emitting diode (LED) disinfected containing five specimens each (n=5)[19] (Table I). Each specimen measuring 25×25×5mm was made in a stainless-steel split mold. Four holes, measuring 0.5mm in depth, were engraved in the metal mold as index marks.

After fabrication of specimens, wax patterns were invested in curing flask with dental stone type III. The flasks were put in boiling water for about 10 minutes. After removal of wax, sodium alginate was applied to the mold. Heat cure acrylic powder was mixed with its monomer in a ratio of 2.5:1 w/v[20] and was packed into the molds. The flasks were gradually heated to 100°C in a period of one and a half hour. This temperature was maintained for 30 minutes. The flasks were bench cooled overnight. The specimens were taken out and immersed in water for 48 hours. The specimens were then trimmed, using belt emery paper (400-800 grit). Further refined with grade 1200 and finished with grade 2400 emery paper. Final polishing was done with a motor driven revolving disc, with a velvet polishing cloth.

Wax patterns for PA specimens were made in stainless steel molds and invested in the flasks with dental stone (type III), following the procedure adopted for PMMA specimens. Wax sprues were then attached to the wax patterns. The investment was coated with petroleum jelly. The flasks were then filled with dental stone and placed in boiling water. After dewaxing, the flasks were placed in the hydraulic injector for flexible denture base resin. Molten polyamide was forced into the flask by using polyamide injection system at a pressure of 5 bars for 3 minutes. The flasks were bench cooled before deflasking[15]. Following deflasking, finishing was performed with 600 and 800 grit silicon carbide paper, and then polished with white cotton yam wheel polishing brush.

Measurements were recorded with a digital caliper (Mitutoyo, Mfg Co., Japan), using elevated indentations labeled by letters A, B, C & D. Six dimensions (distances AB, BC, CD, AD, AC and BD) were documented for each specimen. Five measurements were recorded for each of the six

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dimensions before calculating the mean. The algebraic norm was calculated by taking the square root of sum of squares of individual dimensions.[21]

Norm[22] = $[AB^2+BC^2+CD^2+AC^2+AD^2+BD^2]^{1/2}$

For control group (A) specimens, after initial measurement were kept in distilled water at room temperature and the water was changed corresponding to the water change for the interventional groups (B & C). For group B, after taking the initial measurements, individual specimens were placed in 200ml of distilled water at room temperature in a microwave oven (Dawlance, model: DW-162H, Korea) and then subjected to disinfection at 1000W for 3 minutes, thrice a week for 4 weeks. For group C (LED disinfection), after the initial measurements, the specimens were subjected to irradiation for 30 min, 3 times a week for 4 weeks.

Water for sample immersion was changed after conducting 2 disinfection protocols for groups B & C and after every 4th day for group A. After completing 12 disinfection cycles, specimens were measured for final measurement. The percent difference was determined as follow[21]:

Percent Difference = final measurement - initial measurement / initial measurement × 100

Mean and standard deviation values for the linear dimensions were determined. Data collected before and after disinfection with microwave and LED, were statistically analysed by one-way ANOVA and post hoc Tukey's test using SPSS version 26. P value less than 0.05 was considered as significant.

Results

The mean values of the initial, final measurements and their differences for all the groups of PMMA are given in Table I. Group B1 (disinfected using microwave) exhibited the highest change in dimensions (-9.02mm) while the control group (A1) displayed the lowest change in dimensions (-6.99mm) (Table I). One way ANOVA showed highly significant difference (p=0.002) among the groups after disinfection protocol (Table I). Post hoc Tukey's test for multiple comparison showed significant difference for both the groups B1&C1 when compared to control (A1) (p=0.004) &(p=0.006) respectively while the difference between group B1 & group C1 was insignificant (p=0.964) (Table II).

The mean values of the initial, final measurements and their differences in mm with standard deviations for each group of PA are given in Table III. It can be seen from the Table III that group C2 exhibited the highest (-8.66mm) while the control group, displayed the lowest change in dimensions (-7.0mm). One way ANOVA showed statistically significant difference among the three groups ((p=0.013). Post hoc Tukey's test showed statistically significant difference between group B2 and the group A2, similarly the difference between group C2 and group A2 was significant (p=0.042). The difference between the group B2 and group C2 was also statistically insignificant (p=0.835).

Table I: Comparison of Dimensional Changes In PMMA* Using One Way ANOVA

Group	Initial Measurements mm (Mean)	Final Measurements mm (Mean)	Difference mm (Mean) ± Std Dev	% Difference	F	*p*
A1 (control)	56.81	49.81	-6.99±0.64	-12.32	10.65	0.002
B1 (M/W)**	57.03	48.01	-9.02±1.03	-15.82		
C1 (LED)***	56.68	47.78	-8.89±0.56	-15.69		

* PMMA: Polymethylmethacrylate,
** M/W: Microwave,
*** LED: Light Emitting Diode.

Table II: Post Hoc Analysis (Tukey's HSD) of Dimensional Changes In PMMA

Multiple Comparison				
Tukey HSD				
Dependent Variable	Groups (I)	Groups (J)	Mean Difference (I-J)	Significance *(p)*
Dimension PMMA	Control (A1)	M/W	2.02	0.004
		LED	1.89	0.006
	M/W (B1)	Control	-2.02	0.004
		LED	-0.13	0.964
	LED (C1)	Control	-1.89	0.006
		M/W	-0.13	0.964

Table III: Comparison of Dimensional Changes in PA Using One Way ANOVA

Group	Initial Measurements mm (Mean)	Final Measurements mm (Mean)	Difference mm (Mean) ± Std Dev	% Differences	F	*P*
A2 (control)	57.04	50.04	-7.0±0.42	-12.27	6.39	0.013
B2 (M/W)	56.90	48.53	-8.37±1.08	-14.71		
C2 (LED)	57.02	48.37	-8.66±0.69	-15.17		

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Table IV: Post Hoc Analysis (Tukey HSD) of Dimensional Changes in PA

Multiple Comparison				
Tukey HSD				
Dependent Variable	Groups (I)	Groups (J)	Mean Difference (I-J)	Significance *(p)*
Dimension PA	Control (A2)	M/W	1.40	0.042
		LED	1.65	0.015
	M/W (B2)	Control	-1.37	0.042
		LED	0.28	0.835
	LED (C2)	Control	-1.65	0.015
		M/W	-0.28	0.835

*PA: Polyamide

Discussion

Dimensional stability of denture bases during service is of great importance as it helps in retention of the dentures and cuspal interdigitation.[23] Therefore, any effects of the adopted disinfection techniques on the dimensions of denture bases may pose problems. There are no standard specifications for measuring linear dimensions of denture bases. Wolfaardt et al[24] stated, that many factors affect the dimensional changes of denture bases such as size and shape etc. It has been recommended to test specimens of simple shapes for dimensional measurements.[21] Therefore, square shaped specimens were used in the present study.

Statistically significant difference was observed, when the interventional groups were compared with the control group whereas comparison of the MW with LED showed insignificant results. Therefore, the null hypothesis of this study was partially rejected as significant differences were observed for both the resins after disinfection with MW and LED when compared with control.

The contraction of resin for the control groups of this study could be attributed to the thermal contraction during storage and due to release of stresses that were induced during polymerization.[25] The storage of resin in water helps in residual monomer dispersion in PMMA.[26] This elution of monomer continues for a few days of storage in water.[27] Such loss of monomer from the polymerized specimens can be accredited for the shrinkage or decreased dimensions of specimens of control groups of PMMA, after storage in water for four weeks.[25]

The shrinkage in PA control group was recorded to be around 7mm. Dimensional accuracy of PA is technique sensitive and require more precise and careful processing. It has been reported in literature that storage of nylon (PA) in water has shown decrease in dimensions after about 24 hours.[28] However, an increase in dimensions of the same PA used in the present study after storage in water has also been reported by Chuchulska & Zlatev [29], which contrasts with the results of this study. This might be due to aging of the specimens for 5000 thermocycles.

The change in dimensions of both denture base resins can be explained by the fact that microwave irradiation causes increase in temperature of the specimens.[17] Despite all the precautions taken and careful processing of PMMA, some monomer content is left unreacted in the final product.[30] This increase in temperature can cause reaction of the unreacted monomer at reactive sites of the polymer and thus cause further shrinkage due to thiolymerization.[15] Resins can experience a plasticizing effect after their Tg is exceeded, which causes rearrangement of the polymer chains[31] and thus this change in dimensions could be due to the plasticizing effect of resins above their Tg.

The highly significant result for MW disinfected PMMA group in comparison with the control group of this study is in accordance with results reported by Wemken et al.[17] Polychronakis et al[15] reported shrinkage of 0.35mm for heat cure PMMA and 0.09mm for Valplast after wet microwaving at 450 W for 3 minutes. This can be considered in accordance with the present investigation, as they had measured only the length of the specimens, while in this study, means were calculated for the six measurements of each specimen and the algebraic norm was calculated.

Polyzois et al[32] contradicts the results of the present study as disinfection of acrylic base resin specimens with a 500W MW for 3 minutes and 15 minutes manifested linear shrinkage of - 0.005%. Although the changes were significant statistically but were of no clinical importance. It can be noted in the arguments presented so far that the microwaves

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used for disinfection of denture base resins specimens were of low powers. The power levels of MW ranged between 450W and 700W, with most studies conducted with 650W. This observation is consistent with a critical review by Brondani & Siqueira.[33] The microwave used in the present study had power of 1000W which is a normal domestic microwave device found in our part of the world. Due to unavailability of studies on LED disinfection in the literature, we were not able to compare the results of our study with other studies.

Conclusion

Within the limitations of this study, it is concluded that the dimensional stability of PMMA and PA can be affected by disinfection with MW and LED, and the dimensional changes observed for both materials are comparable, therefore, one disinfection procedure cannot be preferred over the other.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATMENT

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ORIGINAL ARTICLE

Challenges of Online Learning Environment Faced by Undergraduate Medical Students During Covid 19 Pandemic

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ABSTRACT

Objective: This study aimed to define the challenges faced by medical students rotating in the orthopedics department and their suggestions regarding improvement during covid-19 pandemic.

Study Design: A mixed method cross sectional study design.

Place and Duration of Study: It was conducted on 4th and 5th year MBBS students at Shifa college of Medicine with clerkship rotation in the department of orthopedics from 16th March 2020 to 23rd August 2021.

Materials and Methods: Students were enquired about their comfort levels while using the internet and computer for online sessions. Data was collected through an online questionnaire and analyzed using Google forms. Frequencies, percentages, and standard deviations were calculated for qualitative variables.

Results: Out of 147 study participants, 64(43.4%) students strongly agreed that they had no difficulty and were extremely comfortable using internet and computer during covid-19 pandemic. Eighty-five (58%) students used online available reading material shared on Google classrooms and what's app groups. While only 23(16%) agreed to concentrate during online sessions. One hundred and eighteen (80%) agreed with a lesser desire to study for online classes as compared to on campus. Major problems faced by the students during the pandemic included very limited patient centered learning, limited hands-on experience, less interactive sessions, problems with internet connections, technology handling and class timing issues due to time zone differences.

Conclusion: We conclude that our students faced lot of challenges during Covid-19 pandemic including internet issues, lack of awareness of technology, distractions because of family, siblings and homely environment and lack of conducive learning environment like learning at bedside. Flexible class timings, multiple breaks, recorded lectures and online interaction of real patients can improve online clinical learning.

Key Words: *Medical Education, Medical Students, Online Learning, Pandemic.*

Introduction

Online education is becoming increasingly common as the situation of the world progresses especially after recent COVID 19 pandemic.[1] Although there are quite a few benefits of online learning, like worldwide accessibility, convenience and cheaper education.[2] But developing countries face their own set of challenges when it comes to teaching students online, especially in the field of clinical medicine where patient interaction makes up a huge component of the education.[3] Many colleges have adapted virtual clinical experiences as a method for providing students with patient interaction.[4] Lack of prior experience in online learning and the competency of people using these online learning systems may also be a challenge to deal with in developing countries.[5, 6] The various factors that were found to be a barrier to online learning are (a) administrative issues, (b) social interaction, (c) academic skills, (d) technical skills, (e) learner motivation, (f) time and support for studies, (g) cost and access to the Internet, and (h) technical problems.[7] Increased need for self-discipline and lack of desire to compete with others are also problems encountered in online learning.[8] Increasing interaction, practice exercises and feedback is associated with improved outcomes. The attitudes and motivation of students towards online

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education is also important as studies have shown that some students do not view it as a formal means of education.[9] In literature, few studies have been done to understand the attitudes and experiences of students when exposed to online clinical learning during the lockdown from Pakistan.[6,10,11]

Our present study was planned to determine the challenges faced by medical students and their suggestions regarding that, in orthopedics surgery clerkship during the pandemic lockdown period.

Materials and Methods

We conducted this mixed method designed study (both qualitative and quantitative) at Shifa college of medicine from 16th March 2020 to 23rd August 2021. Total 160 students of 4th and 5th year MBBS rotating through orthopedics surgery clerkship were included in this research survey. At Shifa College of medicine medical students of 4th year MBBS have orthopedics clerkship of 2 weeks; during this time medical students have clinical encounters with orthopedics cases in out-patient clinics, in-patient wards, emergency room and operation rooms. Students also get experience of visualization of live orthopedics surgical procedures and have hands on sessions on mannequins as well. As during COVID-19 pandemic majority of these sessions were shifted to online teaching only. Hence, orthopedics clerkship was squeezed to online sessions only including lectures, demonstrating skills by the teachers on mannequins, sharing videos of surgeries; clinical methods and history taking, and interactive sessions of problem-based scenarios of orthopedics diseases. We analyzed the students prospective and suggestions regarding these online sessions using convenient sampling technique. Study was approved by the institutional review and ethical committee (IRB no: 4459-1279-2020) before commencement. Data collection was done through a self-constructed online questionnaire which was already piloted on a small group of students. The questionnaire was sent to the students via emails as Google forms. Only those students who did not fill the questionnaire or filled it incomplete were excluded from the study. Total 160 students rotated through orthopedics department during study period, out of which 147 responded to our questionnaire and gave consent to participate in the study. In first section of the questionnaire students were asked questions regarding different aspects of online learning and their responses were recorded on the Likert's scale. The participants of the study also had to give three problems they faced in online classes and three suggestions for what they felt could be improved upon. Similarly, the students were enquired about the level of comfort while using the internet and computer for the online classes. In the second part of the questionnaire open-ended questions were asked with questions regarding the three problems they faced during online sessions and their three suggestions for some improvements that could be made. Data was analyzed using SPSS version 21.0. Descriptive statistics (frequency and percentage) were used to analyze data for quantitative variables. Qualitative data was collected on Google forms and analyzed using thematic analysis.

Results

A total of 147 students participated in the study, out of which there were 47.3% males and 52.7% females. 65(44.5%) of the students believed the teacher has full control over the class during the online sessions while 29 (19.9%) disagreed this. 64(43.4%) students strongly agreed to the fact that they had no difficulty and were extremely comfortable while using the internet and the computer, 19.3% of the students were neutral and 15.9 % disagreed that the usage of computer and internet was a comfortable experience for them. 85(58%) of the students agreed that they used online available reading material shared on Google classrooms and what's app groups. 23(16%) agreed that they were able to concentrate during online sessions. Figure 1 and 2 shows the counts of student's agreement/disagreement on questioning about that subject is easier to understand online than on campus and motivation to study the subject online was the same as it would have been if classes were face to face on campus respectively.

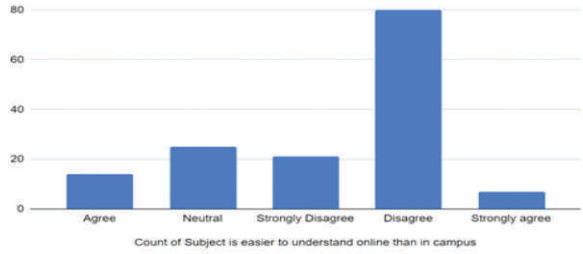

Figure 1: Subject Is Easier to Understand Online Than on Campus

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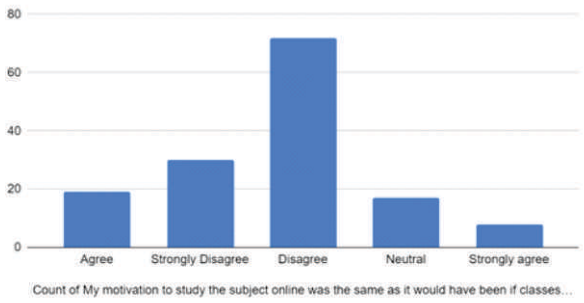

Figure 2: Count of My Motivation to Study the Subject Online was the Same as It would Have Been If Classes Were Face To Face On Campus

118(80%) agreed that they had a lesser desire to study for online classes as compared to on campus. Table I and II are reflecting the main problems and suggestions of the students regarding online sessions.

Table I: Main Problems Faced During Online Sessions of Orthopedics Clerkship.

S no	Main problems identified
1	I had far less motivation to learn and study
2	I felt lack of non-verbal communication with peers, teachers and patients
3	Missed my student-to-student interaction a lot
4	Faced lots of Internet issues and had lack of awareness of technology
5	Felt hypothetical scenarios were not so effective as compared to communicating patients directly
6	Missed actual patient-based learning; this modality of teaching should be reserved for non-clinical subjects only actually
7	Short attention spans because of monotony and too comfortable environment at home; sometimes even went to sleep in between sessions
8	Distractions because of family and siblings, many a times became too difficult to concentrate.
9	The environment was not conducive like learning at bedside and out-patient departments
10	I had stress of covid pandemic & was waiting when it would end, there was un-certainty
11	I had eye strain because of increased screen time
12	There was very limited hands-on experience as a result students felt very in-confident while performing in examinations
13	I had time management issues while at home

Table II: Main Suggestions for Improvement of Online Clinical Sessions of Orthopedics Clerkships

S. No	Suggestions of Students
1	More quizzes should be added
2	Practice questions/exercises between the sessions so that we can learn to apply that knowledge. Time allotment for questions and answer session.
3	Workshops for online teaching and learning
4	Shorter lectures because looking at screen for too long is causing headaches
5	Make it standardized, shorter class duration, multiple breaks for concentration to come back, and using cameras would be nice.
6	There should be no attendance for online sessions and this mode of teaching should be for basics and not for clinical learning.
7	Online sessions should not be mandatory to attend and especially for the clinical sessions and clerkships it's useless.
8	Discussion of questions and MCQs. Going through online videos with students step by step and explaining them. Focusing on clearing key concepts before moving onto advanced learning.
9	More flexibility in timings, access to lectures after classes, recording lectures for later re-viewing
10	Make attendance fluid or non-mandatory and add student presentations to encourage self-learning and participation
11	Provide some website/online platform which uses less data so easier for people with connection issues
12	Patient online appointment sitting with consultants
13	Classes should be in evening with more flexible timings in evening
14	Online learning is non preferred form of learning you cannot improve it so stop it
15	There should be online clinical tutorials, patient interaction online, recorded lectures
16	There should be more teacher student one to one interaction in online sessions rather than in groups

Discussion

Online learning being a relatively new concept came with a lot of pros and cons during Covid-19 pandemic.[5,10] We have identified the factors impacting medical students' ascension or slumps in proportion to concurred online learning. Some of the undergraduates in our research were stimulated by the fact that learning hours were less in time as contrary to studying on campus. They employed modernized techniques needed for students and promoted student-centered learning. Moreover, majority of undergraduates in our study found online learning more feasible as they had ample time dedicated to their families and were safe at homes during the pandemic that had caused havoc. The overall level of comfort with electronic learning and usage of modern technology was high in our group of students(43.4%). However, our students were of the view that usage of e-learning was more productive in preclinical years and basic medical science subjects. They pointed out that it was quite a challenge for clinical years as there was limited patient exposure, on basis of this we carried out the present study.

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Contrary to this, in 2008, Cardall S. conducted a study, concluding that pre-clinical years prefer live lectures when they were given an option.[12]

Our study participants highlighted an important factor lacking in e-learning was one to one patient interaction. According to them nothing is equivalent to seeing a real patient, hence patient interaction is extremely important for learning during clinical years. Distant and e-learning could serve as an efficient resource for clinical students by integrating modalities such as virtual simulated patients, online clinics, and live recordings of real-life processes. This opinion of our group is like many others reported in literature.[13,14] Our group of students identified many barriers to adapt online learning. The most common among these was technical issue, including poor internet connectivity and less familiarization with computer skills; these aspects are backed up by few previous studies as well (shown in table 1).[15,16]

The lack of gestures by preceptors /tutors during online learning was also identified as a significant drawback for the students participating in the study (20%) as reported by others as well that psychological closeness felt by student with teacher is based upon the nonlinguistic signs.[17,18] Body language and kinesics, such as one to one eye contact, gesticulations, and poses entail majority of communications and divulgence, which were certainly not provided by the online classes.[19] Thus, making it even more difficult for the students to cope up with the on line classes.

Our data found many suggestions for improvement of e-learning and making e-content more useful; more of student presentations should be encouraged and teachers delivering the lectures need to be well prepared, concept of formative multiple-choice questions incorporated at the end of learning sessions which added to interest and active engagement during the online session. They suggested that there should be some brainstorming questions and short quizzes in between the lecture to avoid monotony and maintain some level of interest during class. The suggestions highlighted by our study is also supported by the previous research that emphasizes flexible learning, a student-centered approach which provides students with various learning choices to make the learning less monotonous, exciting, and productive.[20] The pandemic taught us that its need of the hour to prolong and sustain online education. Traditional learning has more face-to-face interactions thus motivates one to learn better.[21] The feeling of solidarity in learning and sharing opinions makes it easier for the students to maintain the level of concentration.[22] This is one of the major aspects that is lacking in online learning. Our study also advocated, that if we teach the same topic and amount of content through both methods of teaching, students were more likely to prefer classroom learning. Our group of students preferred classroom learning because according to them self-discipline is better acquired through being physically present in the classroom. Studying while being in the comfort of the home makes it harder to focus on the class and the added distractions in the home are a major factor that makes the students prefer classroom learning over online learning.[23]

Another concern pointed out by our data was regarding excessive screen time, some of the students' experienced headaches, eye strains and blurring in visions. This was another factor that made online learning less suitable for them as they did not have any way to socialize physically with their peers.[24,25]

Our study has a big limitation that we only analyzed student's perspective in one small sub-clerkship of orthopedics. So, we cannot globalize our results for all clinical clerkships and e-learning. Further studies should be conducted to record student's views and challenges faced in other clinical disciplines/ clerkships as well.

Conclusion

We conclude that our students faced a lot of challenges during Covid-19 pandemic including internet issues, lack of awareness with modern technologies, distractions at homely environment because of family and siblings and lack of conducive learning environment like learning at bedside. Flexible class timings, multiple breaks, recorded lectures, workshops for online learning and online interaction of real patients can improve online clinical learning.

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CONFLICT OF INTEREST

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

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REVIEW ARTICLE

Ophthalmic Complications Associated with Atopic Dermatitis: A Review

Jamal Hussain[1], Shams Ul Haq[2], Adnan Ahmad[3], Javed Rasul[4]

ABSTRACT

Atopic dermatitis (AD) is a long-lasting dermatological disease that is associated with ophthalmic complications in the long run. Those having AD are more likely at risk of developing comorbidities in eye as compared to normal persons. This review encompasses the clinical manifestations, pathophysiology and treatment of common ophthalmic complications presented with AD i.e., blepharitis, kerato-conjunctivitis, corneal ectasias, glaucomatous eyes, lens opacification, detachment of retina, herpetic eye disease (HED) and dupilumab associated eye toxicities. It is necessary for dermatology colleagues to be vigilant enough not to miss ophthalmic problems associated with AD, as an early detection and management can save the vision.

Key Words: *Atopic Dermatitis, Atopic Keratoconjunctivitis, Blepharitis, Corneal Ectasias, Herpetic Eye Disease.*

Introduction

Atopic dermatitis (AD) is a long-standing dermatitis with a disease burden ranging from 12% to 22% in developed countries.[1] It typically affects the face (cheeks), neck, arms, and legs but usually spares the groin and axillary regions. AD usually starts in early infancy, but it also affects number of adults. AD is commonly associated with elevated levels of immunoglobulin E (Ig-E) resulting in allergic diathesis which may include food allergies, asthmatic events and atopic rhinitis in sequence referred as "atopic march" theory, which suggests that it is a part of progression that may lead to subsequent allergic disease at other epithelial barrier surfaces.[2,3] Any age group can be affected but it predominantly affects adults in their second and third decade manifested as dry skin patches with itching that remits and exacerbates. Primary physical findings include xerosis, lichenification and eczema.[2]

Recently, evidence have shown that AD can present with extra-cutaneous features. Epidemiological surveys have revealed that an enormous proportion of patients develop ocular comorbidities in the course of the disease as compared to normal people, with varying range of severities.[2,3] Notable ocular morbidities include blepharitis, kerato-conjunctivitis, corneal ectasias, glaucomatous eyes, lens opacification, retinal detachments, herpetic eye disease and dupilumab associated eye toxicities.[3]

The pathophysiological basis for these ocular morbidities is myriad and involves multiple mechanisms. Innate immunity dysfunction, excessive eye rubbing due to itching, steroid induced ocular toxicities and genetic susceptibility all have been implicated.[2] Some ocular conditions develop lately in the course of disease, while some presents acutely, however if not picked up early and managed appropriately can result in severe visual impairment. This review encompasses the clinical manifestations, pathophysiology and treatment of common ophthalmic problems associated with AD.

Blepharitis

This inflammatory/infective lid margin disease affects approximately more than 5% of people with AD as compared to normal people.[2] It is divided into an anterior and posterior types, based upon the anatomical landmark of meibomian gland orifices at the lid margins. Patient complains of ocular itching and irritation of the lids, watering of eyes, ocular grittiness or feeling of burning, lid crusts, and light sensitivity.[4] Anterior blepharitis is mostly caused by staphylococci, while posterior one is secondary to meibomian gland dysfunction (MGD).

Though pathophysiology is still unclear, tissue desiccation in atopic patients is accompanied by barrier disruption and trans-epidermal desiccation, causing eyelid dermatitis.[4,5]

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The conventional therapy of AD associated blepharitis consists of conventional lid-hygiene measures, such as warm compresses and gentle scrubbing of the lid margins to remove crust and debris, which can be done with non-prescription cleansers, lid-scrubs, and baby shampoos. Acute flare needs topical antibiotics, topical calcineurin inhibitors (i.e., cyclosporine 0.05%), or low-strength topical steroids.[5] Due to possible toxicities of medication especially topical steroids, ophthalmic consultation is mandatory for early diagnosis and treatment.

Kerato-conjunctivitis

Atopic kerato-conjunctivitis (AKC) is a non-infectious inflammatory condition involving the corneal and conjunctival tissues with a prevalence ranging from 23% to 43% of patients with AD.[6,7] Mostly present in the late teens and peaks from the third to fifth decade.[8] The symptoms of AKC include itching, red eyes, stringy mucous secretion, burning sensation, light sensitivity and decrease vision. Long standing disease can cause corneal vascularization, punctate epithelial erosions and secondary bacterial keratitis, repeated corneal trauma can lead to scarring and corneal blindness.[7]

Pathophysiology of kerato-conjunctivitis involves inflammatory involvement of the conjunctiva by eosinophil, mast cells and other inflammatory cells. It has been reported in studies that patients having peri-orbital AD is linked with the development of severe form of atopic kerato-conjunctivitis, which in the long run can turn into development of entropion if not properly mananged.[7] Eye consultation is very important in AKC for its proper management in order to avoid ocular complications ultimately leading to visual impairment.[7,8] Conservative measures include cool compresses and treatment with ophthalmic eye drops containing antihistamines (i.e., ketotifen 0.025%) and mast-cell inhibitors (i.e. olopatadine 0.2% drops).[8] Atopic kerato-conjunctivitis flare ups may require short-term use of topical steroids or calcineurin inhibitors, or systemic steroids/ immune-suppressants for refractory cases.[6] In the long run patients with AKC needs maintenance therapy with long acting anti-inflammatory agents in the form of calcineurin inhibitors which controls the inflammatory component of the disease without having steroid induced complications.[8] Corneal involvement resulting from chronic inflammation requires steroids, calcineurin inhibitors, amniotic membrane grafting and in severe cases may need limbal stem cell transplantation.[7]

Keratoconus

Keratoconus (KC) is a non-inflammatory ectatic corneal disease characterized by slowly advancing ectasia and cone-like bulging of the cornea. Corneal topography reveals changes in the thickness profile characteristic of KC along with irregular astigmatism depending upon the severity of condition clinically manifested as diminished vision with distorted images.[2,9] Numerous studies have shown positive link between KC and AKC.[10,11]

The exact mechanism of KC development in AKC is ambiguous and thought to be multi-factorial. Excessive eye rubbing from peri-ocular itch and irritation has been shown to be responsible for KC.[12] Furthermore, immune deregulation and altered synthesis of inflammatory mediators have also been implicated in the causation of KC.[13]

KC is dynamic in its course with significant effect on visual acuity, making it imperative to detect it earlier on before its lead to severe visual impairment. Certain risks predisposes the person to develop KC includes, AKC, AD involving the lids, excessive eye rubbing and familial KC. Any of these conditions make it prudent to seek ophthalmic consultation for screening and visual assessment.[10,11,12]

Early management of KC includes spectacles and rigid gas permeable (RGP) contact lenses for refractive correction. For severe KC, specially designed contact lenses are used. The RGP contacts are custom made lenses to vault over the ectatic corneal surface.[9]

For moderate cases of KC without apical corneal scarring, a technique developed to strengthen the bond between the corneal collagen fibers to prevent its progressive thinning by using riboflavin and UV-A irradiation to make firm bonds between collagens in the corneal tissue, this is known as corneal cross linking. Studies have shown its efficacy and safety in halting the progression of KC, especially if undertaken earlier in the disease, and has been given FDA approval in 2015.[9,10,11]

Glaucoma

Glaucoma development is common during the therapy of AD and can cause irreversible damage to

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the nerve fiber layer of the retina and optic discs. Steroids used in the treatment of AD is mainly responsible for its causation.[14]

Numerous case reports have attributed glaucomatous risk to chronic use of high potency topical steroids in the peri-ocular areas, which is mainly responsible for it to direct absorption by ocular tissues, as glaucoma seldom develops with topical steroid application anywhere else in the body.[15-17] Oral steroids (i.e. betamethasone) taken for more than 2 months is also associated with very high intra-ocular pressure (IOP).[18]

Predisposing factors for raised IOP, includes preexisting glaucoma, diabetes, connective tissue disorders, and high myopes.[15,19] Steroid responders and younger lot also shows hypersensitivity to steroids.[20]

As glaucoma progresses silently until advanced, earlier diagnosis is important from the management point of view. Patients who are showing exaggerated clinical response (raised IOP) to optimal dose of steroids as compared to normal individuals, patients on long standing steroids via different routes for their medical conditions and those having positive family history of glaucoma should be screened for glaucoma assessment.[17] In addition to that, individuals having simultaneous glaucoma and AD should seek consultation from both the Ophthalmologist and Dermatologist for their management, and preferably steroid sparing agents should be used in such cases to avoid steroid induced complications.[21,22,23]

Cataracts

Prevalence of cataract ranges from 6% to 23% with AD.[21,24] Pre-senile cataracts are quite common in patients of AD, which can be attributed to both steroids use and disease process itself. Cataract development can sometimes become abrupt and number of evidences from studies have shown it to be associated with flare ups of AD.[25,26]

Sub-capsular variants of cataract are quite common in AD, in contrast to nuclear and cortical ones, which mostly effect normal elderly population.[27,28] Anterior sub-capsular cataract is more specific to AD, whereas posterior sub-capsular ones are specific to long-standing steroids use in AD.[27] Younger age group are more prone to steroid induced cataract development with short duration of therapy and even less potent ones as compared to elderly people.[29]

The patho-physiology of cataract development in AD is multi-factorial. Evidence based scientific reports have shown that patients with AD have breached blood retinal barrier and high levels of free radicals in the lens suggestive of oxidative damage.[30,31] Steroids in any form can cause cataract formation but mostly the oral form are strongly associated with cataractous changes in the lens, however steroids in the form of inhalers and topical creams/ointments are also responsible for cataract development.[26,32]

Patients with early onset peri-orbital AD, long standing steroids use, and positive family history need to be reviewed periodically. Anterior and posterior sub-capsular lens opacities are detected with red-reflex assessment that can readily be performed by the optometrists or ophthalmologist.[33]

Retinal Detachment

Retinal detachment (RD) is a vision threatening ocular comorbidity of atopic dermatitis that hits younger people more than 5 years old. The prevalence of RD in patients with AD is in the range from 3% to 7%.[34] Patients with RD presents with loss of vision, photopsia, floaters and curtain like field defects.[35,36]

Many studies have reported that involvement of peri-orbital region by AD along with long standing history of eye rubbing is strongly associated with retinal detachment. RD is also accompanied with other ocular pathologies such as proliferative vitreo-retinopathy, ectopia lentis, and lens opacifications.[34-38] The underlying development of RD is thought to be due to ocular distortions from forceful ocular rubbings, also the morphological appearance of RD in AD-associated RD versus traumatic RD both are characterized by retinal breaks at vitreous base.[37]

Avoiding eye-rubbing and optimal therapy for peri-orbital AD can reduce the risk of developing RD. In addition to that, all patients with symptoms of RD should seek ophthalmic consultation.

Herpetic Eye Disease

Herpetic eye disease (HED) presents with potential ocular morbidity, as recurrent attacks can lead to corneal scarring and neo-vascularization. Individuals with atopic dermatitis are more prone to develop severe herpetic ocular infection and mostly of atypical variants with more complication and refractory to conventional therapy as compared to

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normal indivisuals.[38,39] Additionally, atopic disorders are associated with frequent herpetic recurrences leading to neurotropic keratitis .[38,39,40]

These observations suggests that Atopic dermatitis patients with a prior HED should be carefully observed and treated with anti-virals and topical steroids in case of dendritic keratitis or topical steroids only in disciform keratitis, while for recurrences prophylaxis with acyclovir is needed for few months.[39,40] Addionally, active HED warrants urgent ophthalmic consultation.

Dupilumab associated Ocular Complications

Dupilumab, is a monoclonal antibody that inhibits IL-6 and IL-12 transduction pathways. It is one of the first biologics given approval for treatment of moderate to severe AD. Some studies have reported a higher incidence of anterior conjunctivitis in dupilumab treated AD patients (6%–26%) compared to placebo (1%–9%).[41] Surprisingly, the incidence may go as high as 68%, reported in some literature.[42] However, in some other studies it has been found that dupilumab given in asthmatics, nasal polyposis and eosinophilic-granulomas didn't show any rise in the incidence of dupilumab associated conjunctivitis in dupilumab treated patients when compared with control group, emphasizing upon an AD-specific mechanism.[43]

Main findings of dupilumab associated conjunctivitis includes conjunctival congestion and limbal hyperemia, along with eye symptoms such as watering, itching and blurring of vision. Its use has been associated with reduced goblet cell density in conjunctiva on histological and spectroscopic specimens.[44] Blepharo-conjunctivitis is also reported in some literature due to dupilumab therapy.[45]

Standard treatment protocol for dupilumab associated ocular complications hasn't yet been established. It is noteworthy that anti-histamine eye-drops are ineffective in the treatment of dupilumab associated conjunctivitis.[42] But, topical less potent steroids and tacrolimus ointment 0.03% has shown some promising results in its management.[41] Lifitegrast, an immunosuppressant agent has been granted approval in the treatment of kerato-conjunctivitis sicca, in patients who are resistant to topical steroids.[45] As a last resort, stopping of the therapy is the only way to get rid of therapy induced ocular toxicities in AD patients.[43,44] Those taking dupilumab, who develop eye problems should seek ophthalmic consultation.

Recommendations

Dermatologists who are dealing with AD should be made aware of possible ocular comorbidities that develops in due course of time. They should be educated via conducting joint clinco-pathological sessions by increasing their knowledge with inputs from both the ophthalmologists and dermatologists, mutual clinical rotations of the postgraduate residents of both specialties, interdisciplinary and multidisciplinary approach towards managing such patients and making joint protocols/ guidelines for AD patients with liaison between both specialties.

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CASE REPORT

Parotid Gland Oncocytoma-A Case Report

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ABSTRACT

Tumors of parotid glands are majority benign and commonest of them is Pleomorphic adenoma. Patients commonly presents with a painless swelling in face. Parotid Oncocytoma is a rare parotid tumor with incidence of 0.1-1.5% (rarest of salivary tumor type) of all parotid tumors, and it occurs in 6-8th decade of life. In this case report we will present a case of 75 years old male with painless swelling in parotid gland and diagnosis of Oncocytoma was made.

Key Words: *Benign Tumors, Oncocytoma, Parotid Gland.*

CASE

A 75-year-old male presented to us in surgical OPD of Shifa International Hospital on Dec 06, 2020, with complaints of swelling left angle of mandible and preauricular region. He noticed this swelling 2 months ago as a small pea size nodule and it progressively increased in size. Swelling was painless and there was no associated fever, dry mouth or pain while chewing. He did not notice any change in salivation. Patient had no co-morbid and no prior exposure to radiations. There was no past surgical history, and he wasn't on any routine medications. Upon examination patient was vitally stable. There was a swelling in left preauricular region extending till the angle of mandible and had size of ~2x2cm. Swelling was soft, nontender, mobile and non-fluctuant. Surface of swelling was smooth and had regular margins. Bimanual palpation was done which showed no attachment to muscles and mobile mass. No lymph nodes were palpable. Facial nerve was intact.

His laboratory workup was normal. Ultrasonography of swelling showed a well-defined lesion with macro lobular margins and hypo echoic appearance in left parotid gland which measured approximately 17.4*13. 5mm. Swelling showed mild internal vascularity on Doppler Ultrasound. It was predominantly in superficial lobe with mild extensions into deep lobe, and possibility of Pleomorphic Adenoma was arisen.

We then proceeded for Fine Needle Aspiration Cytology (FNAC) which showed moderate cellular smear composed of cluster and sheets of oncocytic cells with bland central nuclei, no mitosis was seen. These features were favoring Oncocytic neoplasm. Patient was counselled in detail about surgery and possible complications, and he was admitted in the hospital for superficial parotidectomy. Nerve stimulator was used for the identification of facial nerve. We performed superficial parotidectomy and extension of tumor into deep lobe was also excised preserving facial nerve (shown in Figure 1). A drain was placed, and wound was closed. Postoperatively he had drooping of the angle of mandible, but there was no significant saliva leak. Patient was discharged on postoperative day 2. Currently he only has minimal droop which is not visible. His final histopathology report showed that superficial lobe had focal chronic inflammation and deep lobe was oncocytic neoplasm favoring oncocytoma was partially circumscribed, had monomorphic large polygonal cells, which had abundant eosinophilic granular cytoplasm, Nuclei were small, centrally placed, round to oval with prominent nucleoli, there was mild hyperchromasia but no nuclear atypia or pleomorphism and mitosis was present, Stroma was vascular. Immunohistochemistry showed p63 focal present CK5/6 was Patchy positive.

Introduction

Parotid gland is bilateral and one of the major salivary glands. Tumors of Salivary gland are uncommon and represent 1% of head and neck

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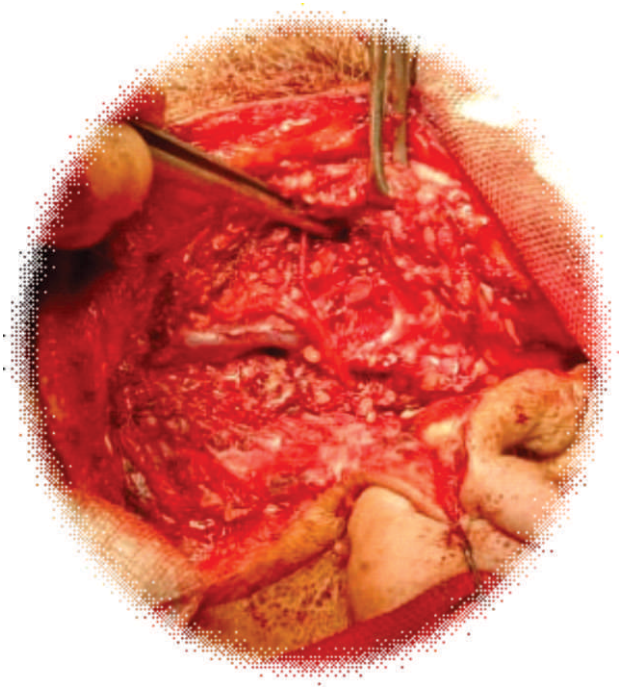

Figure 1

tumors[1]. Most common site of tumor in salivary gland is parotid gland which accounts for 85% of all. Out of this 85%, majority of it are benign and commonest benign tumor is Pleomorphic adenoma, whereas commonest malignant tumor is Mucoepidermoid[1]. Rarely an entity is parotid oncocytoma, as it occurs in less than 1 percent of all salivary tumor types. Its clinical presentation is often misdiagnosed as pleomorphic adenoma or other types.[2]

Majority tumors of parotid glands are benign whereas tumors of minor salivary glands are predominantly malignant. Salivary gland tumors are slow growing and are well circumscribed. Lesion which are rapidly growing, have pain, paresthesia, and facial nerve weakness have increase potential of being malignant and needs further workup and are managed aggresively.[2]

Recent publications showed that multiphase contrast enhanced CT is potentially helpful, as few of the parotid tumors are invisible on CT scan resulting in reducing effectiveness of the scan.3 However, cytological analysis (FNAB) is excellent tool to exactly diagnose the oncocytoma as an entity.[3]

MRI is an improved study showing enough information of soft tissues, providing characterized parotid masses.[4]

In this case report we are presenting a case of 75 years old male with painless swelling of left parotid gland, which on workup was diagnosed with Oncocytoma, a rare benign parotid gland tumor.

Discussion

Parotid gland is the most common site of tumor in all salivary glands, and majority of tumors in parotid gland are benign. Most common benign tumor in parotid gland is pleomorphic adenoma, whereas most common malignant tumor is mucoepidermoid tumor.[2]

Oncocytoma is a rare benign parotid tumor with incidence of 0.5-1.5% in salivary gland[5]. Commonest location of oncocytoma is parotid, however they can be found in other areas including but not limiting to Sublingual gland, soft palate, and hard Palate[5]. The word Oncocyte is derived from Greek word "*onkousthai*" meaning Enlarge/Swollen and this was first recognized in 1897 by Schaffer who observed presence of eosinophilic cells in salivary glands, later Hamperl in 1931 fully characterized the term Oncocyte.[12-13] Oncocytes are epithelial cells with abundant eosinophilic cytoplasm and mitochondria[7], due to characteristic eosinophilic cytoplasm oncocytes are also called oxyphilic cells.[11]

The term oncocytoma was first described by Jaffe in 1932 who called tumors of salivary glands with abundant oncocytes as Oncocytoma.[9,11]

Incidence of oncocytoma is most common in 6-8th decade of life with relative female predisposition.[8] In 2005 World Health Organization (WHO) classified Oncocytic neoplasm in three distinct types and these are Oncocytosis, Oncocytoma and Oncocytic Carcinoma. Oncocytosis has only Hyperplastic change and it present with generalized enlargement of salivary gland, Oncocytoma is a benign well-circumscribed and encapsulated lesion whereas Oncocytic carcinoma is Infiltrative with mitosis and pleomorphic cells.[10.13]

Oncocytes are normally present in limited number in normal tissue like in thyroid, parotid, pancreas, with advancing age their number increases and transformation into tumor occur which is thought to be because of exhaustion of cell and mitochondrial hyperplasia, this leads to metaplastic transformation of normal cells.[9]

Presentation of oncocytoma is as a painless swelling. Risk factors are unknown although in 20% of cases,

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prolonged radiation exposure is found to be the cause. MRI and CT are investigation of choice but diagnosis of oncocytoma is usually made by use of FNAC, with accurate diagnosis in 29% cases.[7] Histopathological, Oncocytoma has low mitotic rate and less pleomorphism as compared to oncocytic carcinoma which has high rate of mitotic activity and pleomorphism.[5]

Management involves surgical excision of tumor with preservation of facial nerve, final histopathology confirms the diagnosis. Recurrence is reported in 20-30% of patients, so follow-up is advised with MRI after 1 and 2 years.[12]

Conclusion

Oncocytoma of parotid gland is a rare benign tumor, with limited reporting. Definitive treatment so far is with surgical excision. Though rare but proper imaging includes CT and MRI followed by FNAB would help in proper surgical approach. Its recurrence has been documented so follow-up is advised in all patients with MRI.

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- Objective
- Study Design
- Place & Duration of Study
- Materials & Methods
- Results
- Conclusion

Four elements should be addressed: "why did you start?", "what did you do?", "what did you find?" and "what does it mean? “.” Why did you start?" is addressed in the objective. "What did you do?" constitutes the methodology and could include design, setting, patients or other participants, interventions, and outcome measures. "What did you find?" is the 'results', and "what does it mean?" would constitute the conclusions. Please label each section clearly with the appropriate sub-headings. Structured abstract for an original article, should not be more than 250 words. At least 3 key words should be written at the end of the abstract. Review articles, case reports and others require a short, unstructured abstract. Commentaries do not require an abstract.

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- Sampling technique
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- Inclusion and Exclusion Criteria
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- Type of data: parametric or nonparametric
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