pISSN: 2220-7562
eISSN: 2617-9482
Recognized by PMDC

JBUMDC

Journal of Bahria University Medical & Dental College

Volume 10 Issue 2, April - June 2020

Bahria University Medical & Dental College Adjacent PNS SHIFA, DHA Phase II, Karachi

JBUMDC
Journal of Bahria University Medical & Dental College
Peer Reviewed Multidisciplinary Quarterly Published Journal
ISSN (print): 2220-7562, ISSN (online): 2617-9482
Recognized by PM&DC (IP/0072)
Online edition is available at URL: https://jbumdc.bahria.edu.pk,
Indexed with Index Medicus for the Eastern Mediterranean Region (IMEMR),
ROAD Directory of Open Access Scholarly Resources at https://portal.issn.org/
Pakmedinet at www.pakmedinet.com/jbumdc,
Google Scholar at https://scholar.google.com.pk/,
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Published by: Bahria University Medical & Dental College

JBUMDC

Journal of Bahria University Medical & Dental College

Journal of Bahria University Medical & Dental College
Volume-10, Issue-2. April - June 2020

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DOI: https://doi.org/10.51985/JBUMDC2020029

COVID-19: A Global Challenge and Its Remedy through Natural Foods

Kiran Fatima Mehboob Ali Bana, Kulsoom Fatima Rizvi, Shakeel Ahmed

COVID-19 is indeed the crisis of the century**.** Previously unidentified coronavirus, (SARS-Severe acute respiratory syndrome) in 2002-2003 and in the form of (MERS- CoV-2 Middle East Respiratory Syndrome coronavirus-2) in 2011 [1] now named as COVID-19 emerged from Wuhan, China in late December 2019. [1] This COVID-19 is exponentially expanded worldwide in 25 countries by (Feb-6-2020) and in 195 countries by (April-18-2020).[2]Globally, there are 2162408 cases: 543312 recovered, 144683 deaths and 56986 critically ill patients according to international statistics by(April-18-2020).[2] By January 30-2020, the WHO declared the Public Health Emergency of International concern.[1] On feb-11-2020, this disease was named as Coronavirus Disease 2019 (COVID-19) by WHO and is single stranded RNA virus. [3] COVID-19 is named as fifth category of communicable disease by Center of disease control, Taiwan and disease with severe pneumonia on January 15, 2020.[1]

In Pakistan, the first case of COVID-19 was reported in February 26-2020 from Karachi; there are 7,638 confirmed cases, 1832 (24%) recovered, 144(1.9%) deaths as by 18-april-2020. [2]

The confirmed cases of COVID-19 has similar clinical symptoms as of SARS and MERS such as fatigue, fever, dry cough, arthralgia, myalgia, respiratory symptoms, elevated C reactive protein, prolonged prothrombin time and elevated lactate dehydrogenase. [4] Majority of infected persons are asymptomatic or having mild symptoms, the infection can lead to pneumonia or death. The transmission in human to human during incubation period from asymptomatic individuals is troublesome which make it difficult to limit the spread of disease. [5] The average case fatality rate is 2.3% and it is increased as 8% between 70-79 years and 14.8% among aged 80 years and over which is of major concern. [6] In china, currently the case incidence rates are decreased due to the measure steps taken by them but case fatality rates are exponentially increased all over the world. [7] Worldwide, there are various measures underway to limit the transmission of disease such as closure of educational institutes, cancellation of large gatherings and conferences, travel curtailment etc. It will remain a formidable challenge to develop an anti COVID-treatment or vaccine. The precautionary measures includes washing hands for 20 seconds, wearing mask, social distancing, coughing and sneezing etiquettes are being practiced worldwide. In addition lock down is also observed in various countries of the world to inhibit the local transmission of COVID-19.

The extent of the adverse impacts of COVID-19 on economical, social, cultural, educational, scientific, health, commercial and various aspects, along with the burden on healthcare, anticipated rates of fatalities and predicted spread of the disease worldwide, it is significantly important to explore the preventive strategies to fight against COVID-19. Currently, there is no treatment or vaccine available for COVID-19 and only symptomatic treatment is provided to the patients.

There is an increased incidence of pneumonia among elders due to weakened immune response[8] and inflammatory process leads to case fatality among pneumonic patients.[9]

Therefore enhance the immune response is an effective way to reduce the pneumonia and inflammation and ultimately reduce the case fatality and incidence rate of COVID-19. Indeed there are various interventions to boost immunity such as exercise/physical activity, cold shower, dance , forest bathing trips, sauna , sunlight exposure, meditation, acupuncture, intermittent fasting, living at a high elevation, yoga ,tai chi, smoking cessation, avoid excessive alcohol, laughter, rhythmic breathing, calorie restriction, reduce red meat, yogurt, consumption of natural fruit-vegetable ,probiotic foods, vitamin D supplementation, whole grains, statins, deuterium-depleted water consumption, aspirin, statins, adequate sleep, massage, reducing light at night, exclusive breast feeding, psychological counseling, reducing circadian disruption, pleasurable experiences, exposure to short term radio frequency radiation, ozone therapy, ultraviolet blood irradiation, radon spa therapy, hyperbaric oxygen therapy, whole body vibration exercise, hyperthermia, low level radiation exposure, influenza and other vaccinations etc.[10]

Now it is time to learn the lesson from past. Here we would like to shade on light towards enhancing the immune system by using nutritional based foods in order to decrease the chances of infecting with COVID-19. It is well said that you are what you eat. To fight against COVID-19, it is a time to go back to nature and use natural foods to boost immune system. It is strongly urged by the International

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Received: 03-04-2020
Accepted: 21-04-2020

Society for Orthomolecular Medicine that the best method to prevent the antiviral infection is to take nutrient based diet. [11] It is evident from literature that strong immune response acted as first line of defence as observed in SARS and MERS-CoV-2. [5] The strong immune system is highly associated in pathological process against COVID-19.[5] Dysfunction immune system was reported in 452 confirmed cases of COVID-19 at Tongji hospital in China.[11]

To enhance the innate antiviral immune system refers to boost the immune response towards an antigen and keep the body more resistant towards viral infection or clean the body from infections. Antimicrobial peptides in plants can boost human innate immunity and have no side effects. It can keep the human disease free. There are many traditional medicinal plant reported having strong antiviral activity. Viral enzymes have a vital role to trigger disease. Viral replication is halted if viral enzymes are neutralized. The antiviral activity includes inhibit the formation or replication of viral RNA or DNA.[12] The natural plant products has proved as an anti-viral agents such as flavonoids, allicin, betacarotene, oleuropein and are anti RNA anti-oxidants.[13-15] An antioxidant is a material that quench a free radical and are widely found in fruits and vegetables such as carrot, raddish, spinach, citrus pulp, ginkgo biloba , olive leaf extract, garlic, tomato pomace , grape pomace , selenium, etc in dried form.[13,14] The freshly crushed garlic (allicin) is a plant medicine. It has strong antimicrobial effect because of the chemical reaction of allicin with thiol groups of various enzymes, e.g. alcohol dehydrogenase, thioredoxin reductase, and RNA polymerase.[13] They have various antioxidants effects against artherosclerosis, cancer, and Alzheimer's disease. Flavonoids have anti viral activity.[15] Against SARS-CoV, flavonoids showed antiviral activity.[4]

In 1970, Canadian researchers reported antiviral activity against polio type 1, herpes simplex virus (HSV), echovirus 7 and coxsackievirus B5 from straw berry, apple, carrot, grape fruit juices.[12]

It is recommended that instead of dying with fear and stress of COVID-19. It is the time to follow precautionary measures against COVID-19 and take food in natural form to strengthen the immune system and fight against COVID-19.

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Original Article DOI: https://doi.org/10.51985/JBUMDC2019133

BlaOXA-48 Genotypic Detection of Carbapenem Resistance in Isolates of *Pseudomonas Aeruginosa*

Shaista Bakhat, Yasmeen Taj, Faisal Hanif, Saman Nadeem

ABSTRACT

Objective: To determine the prevalence of carbapenem resistance in strains of *Pseudomonas aeruginosa* at a molecular level by detecting OXA-48 gene which transcribe for resistance to the antibiotic carbapenem among indoor patients of a tertiary care hospital Karachi.

Study Design and Setting: This observational cross-sectional study was conducted from September 2018 to May 2019 at PNS Shifa hospital of Karachi.

Methodology: Total 140 strains of *Pseudomonas aeruginosa* were received and cultured from pus samples. These samples were collected from different wards like medicine, surgery, burn unit, ICU, ENT, plastic surgery, paedriatic and family ward. Carbapenem resistance was screened phenotypically by AST (Antibiotic susceptibility test), MHT (Modified Hodge test) and mCIM (Modified Carbapenem Inactivation Method) in all samples. Only in resistant cases OXA-48 gene was detected by real time PCR (polymerase chain reaction). Data was analyzed by following the proper loading sequence on product specification sheet. Data was statistically analyzed by SPSS version 23.0. Results were expressed as frequencies (percentages).

Results: Out of 140, 17 (12%) were found to be resistant to carbapenem by AST, 20 (14%) by MHT, 25 (17.8%) by mCIM. Out of 25 resistant cases, 4 (16%) presence of OXA-48 gene by real time PCR were detected.

Conclusion: OXA-48 gene showed 16% carbapenem resistance in this study. *Pseudomonas aeruginosa* is an opportunistic organism which causes multidrug resistance especially in hospitalized patients. Carbapenem is the last resort for serious infections.

Keywords: carbapenem resistance, OXA-48 gene, *Pseudomonas aeruginosa*, real time PCR,

INTRODUCTION:

Antibiotic resistance in microorganisms is the major challenge to global health all over the world. Several factors are involved in the emergence of resistance in microorganisms like *Pseudomonas aeruginosa*, *Acinetobacter bauminnii* and *Enterobacteriaceae* group. The major one is the non-judicious use of antibiotics in human beings and animals. These microorganisms exhibit resistance towards multiple drugs. Initially, few antibiotics were ineffective but resistance towards multiple antibiotics is observed all over the world. For the last twenty years, resistance as a result of β-lactamase enzymes occurred towards cephamycins, cephalosporins, carabapenems and monobactum. New resistance mechanisms are evolving and disseminating all over the world and reduce physician's abilities to treat common infections. Bacteria elaborated new type of β-lactamase; extended spectrum β-lactamase (ESBL) that is a carbapenemase and pan-drug resistance is expected in near future.[1]

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Received: 13-Dec-2019
Accepted: 12-Mar-2020

Pseudomonas aeruginosa is an opportunistic and sturdy microorganism that can cause disease in those individuals suffering from debilitating conditions in hospital settings like infections in burn patients and ventilator associated pneumonia. According to CDC (Center for disease control), the elderly, young and sick people are more vulnerable to diseases which are resistant to antibiotics. *Pseudomonas aeruginosa* exhibits both intrinsic and acquired resistance. Intrinsic resistance is caused by over-expressed efflux pumps and reduction of the uptake of antimicrobial drugs. Genotypic resistance is acquired by mutation in genes encoding influx pumps, efflux pumps, penicillin-binding protein and β-lactamases. Bacteria can acquire extensive genetic diversity through acquisition and deletion of genetic elements and this converts non pathogenic form of microorganisms into pathogenic form and plays important role in further dissemination of resistant genes among bacterial population. Antibiotic resistance mediated by β-lactamase is caused by many plasmid borne genes (KPC, IMI, GES, NDM, VIM, GIM and OXA-48) which encode enzymes that inactivate carbapenem.[2]

GENEVA WHO has provided the list of resistant pathogens in 2017. These bacteria are genetically equipped with resistant genes. According to this list, *Pseudomonas aeruginosa*, *Acinetobacterbauminnii and Enterobacteriaceae* exhibited resistance towards carbapenem. Carbapenems like

(meropenem, imipenem, doripenem and ertapenem) are the last option in some debilitating infections caused by this group of bacteria.[3] This drug is capable of treating life threatening infections of extended spectrum β-lactamase producing isolates of *Pseudomonas aeruginosa*. Excessive use of carbapenem has led towards a pattern of resistance. These resistant genes are grouped into different classes.[4] According to Ambler's classification, these are categorized into class A serine beta-lactam (KPC), class B metallo beta lactemases that contain zinc at active site (VIM,IMP,NDM), and class D carbapenemase serine beta-lactam (OXA-48). OXA-48 has ability to hydrolyze carbapenems by breaking its beta-lactam ring.[5] Detection of OXA-48 was first time reported in isolates of Enterobacteriaceae in Turkey *in 2001*.[6] Isolates carrying these genes have been reported all over the world. It was further reported in Europe and Middle East. OXA-48 gene has now also reported in gram negative bacteria in neighboring countries like India, China, Iran and Bangladesh.[7-11] Different phenotypic and molecular methods have been employed to detect carbapenem resistance. Molecular methods are gold standard for detection genotypic resistance. At molecular level genes NDM, KPC, VIP and IMP have been reported in Pakistan, but OXA-48 has not been detected in strains of *Pseudomonas aeruginosa* in our country. This resistant gene was detected with help of real time PCR. It is quantitative test with high level of accuracy, high sensitivity and high specificity.[12]

In this study, we detected bla_{OXA-48} transcribing resistance towards carbapenem 16% in strains of *Pseudomonas aeruginosa* in a tertiary care hospital of Karachi within time period of one year.

METHODOLOGY:

This observational cross sectional, study was conducted at PNS Shifa (tertiary care hospital) Karachi. Sample size was calculated by WHO calculator with prevalence rate 10.2%.[7]140 specimens of *Pseudomonas aeruginosa* were received from different wards of hospital from Jan 2018-Jan2019. This study was approved by both Ethical Review Committee of Bahria University Medical and Dental College and from PNS Shifa. Written consent was obtained from hospitalized patients after briefing the purpose of research work.

The strains of *Pseudomonas aeruginosa* were collected from pus swab of infected site from different body parts. These pus swabs were received at microbiology laboratory from different wards. Repeat samples, out-door patients and patients already on antibiotics were excluded. Samples were collected from several wards like Intensive care unit, Burn unit, Plastic surgery, General surgery, ENT (ear, nose and throat) ward, Paedriatic ward, medicine and family ward. Microorganisms were considered as gram negative *Pseudomonas aeruginosa* on basis of gram staining, blood culture[13], MacConkey agar[14] and oxidase test (Scien cell). Carbapenem like meropenem 10**µ**g (oxoid) and imipenem 10µg (oxoid) susceptibility were checked by antibiotic susceptibility test (disc diffusion method) according to CLSI (clinical laboratory standard institute).[15] Screensing of carbamanimase producing *Pseudomonas aeruginosa* was done by MHT (Modified Hodge Test)[16] and mCIM (Modified carbapenemase inactivation method)[17].

Genotypic resistance of *Pseudomonas aeruginosa* was confirmed by detecting bla_{OXA-48} gene with help of real time PCR (polymerase chain reaction) as per Figure 1. Microbial DNA was extracted from culture of up to $2X10^9$ bacterial cells with help of Qiagen Medical DNA qPCR assay kit CATALOG NO 330033 BBXX-#####X (R/F) 330043: BBID-####Z (R/F)-3/4/5/6/7/America. Homogenous mixture was prepared by adding 400µl ATL buffer after vertexing at 14,000Xg speed. Mixture was lysed with 40µl proteinase K and vertexed for 10 seconds andIncubated at 56?C for 10 minutes. Buffer APL2 200ml was put into mixture, this mixture was vertexed for 30 seconds and incubated at 70?C for 10 minutes. Then it was spinned in order to remove the drops. Precipitation was done by adding 300µl ethanol and mixed by vertexing for 15-30 minutes. After passing through vacuum pump, the lysate was added into the tube extender of the QIA amp UCP Mini column. Whenever all lysate had been removed through the columns, its pressure was released to 0mbar by switching off the vacuum pump. 750µl Buffer APW2 was added to mini column of QIA amp UCP and pressure was released by switching off the vacuum pump. 2ml collection tube held the mini column and centrifuged at 20,000xg; 14,000 rpm for 3 minutes. Mini column was kept in into a new 2ml collection tube with open lid and incubated at 56?C for 3 minutes. Mini column was shifted from collection tube to 1.5ml elution tube. 20-100µl Buffer AVE was used at the center of mini membrane. After incubated at room temperature for a minute, it was centrifuged at 20,000xg; 14,000rpm for elution of DNA. Primers were available in Qiagen kit as per Table 1. OD (optical density) of extracted DNA was confirmed from Dow University of Health Sciences as per Table 2.

Real time PCR was performed for detection of resistant gene. Reaction mixture was arranged with DNA positive control (OXA-48), sample and negative template control .25µl reaction mixes were poured into PCR wells.20µl reaction mixes was added as per well only for Rotor-Gene. Data was analyzed by following the proper loading sequence on product specification sheet. The real time thermal cycler was used. Calculation of thermal cycle (C_T) was done for each cycle with help of cycler's software. Threshold 0.02 was considered as standard. The values of threshold cycles were shifted for each well to Excel spread sheet.

Data was statistically analyzed by SPSS version 23.0. Results were expressed as frequencies (percentages).

REULTS:

Among the total 140 samples of *Pseudomonas aeruginosa*, 17 cases (12%) exhibited resistance towards carbapenem by (AST method), 20 (14%) resistant cases by MHT and 25 (17.9%) cases by mCIM. These 25 resistant cases were further evaluated for detection of resistant gene OXA-48 as per Figure 2. We detected OXA-48(n=4) (16%) resistant genes, in strains of *Pseudomonas aeruginosa*.

Table 1: Primers for detection of OXA-48 in *Pseudomonas aeruginosa*

Targeted Gene	Kit Name	Primer Name	Sequence (5'-3' Direction)	Length Bases	Amplicon Size, bp	Tem in C?	Primer conc, pmol/µl
OXA-48	Qiagen Microbial DNA qPCR Assay Kit	Reverse	ACGACGGCATAGTCATTTGC	20	585 or 597	56	15pmo
		Forward	AACGGGCGAACCAAGCATTTT	21			

Table 2: Confirmation of extracted DNA (Optical density)

Samples	Yield
1	54.90g/µl
2	45.81g/µl
3	93.66g/µl
4	67.30g/µl
5	89.43g/µl
6	185.70g/µl
7	288.67g/µl
8	82.10g/µl

Figure 1: Cumulative result OXA-48 positive cases by real time PCR

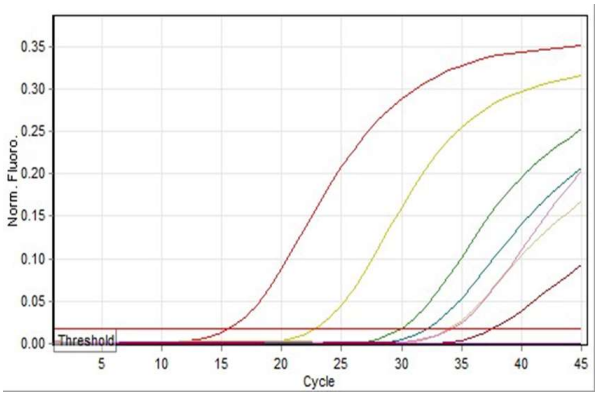
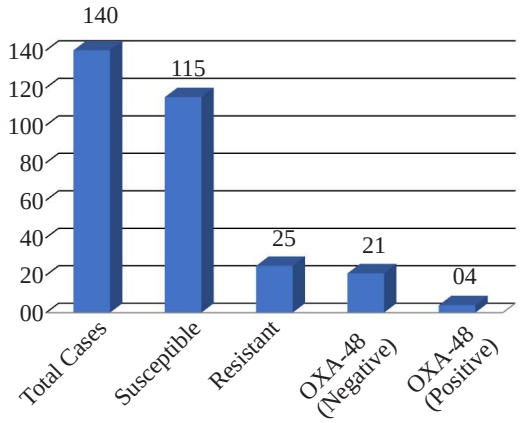


Fig 2 OXA-48 TRANSCRIBING RESISTANCE



DISCUSSION:

Pseudomonas aeruginosa is normal flora of human beings but whenever it gets opportunity it will become pathogenic and cause nosocomial infections. These infections are caused by imprudent utilization of antibiotics, surgical intervention and use of equipments. The resistance that is displayed by microorganisms towards multiple antibiotics can be both intrinsic and acquired or extrinsic. Resistant nosocomial infections do not respond to conventional antibiotics, and have for the last ten years inculcated a fear among health care facilitators.[18]

There are many phenotypic and genotypic methods for detection of carbapenamase producing *Pseudomonas aeruginosa*. Phenotypic methods are AST (Antibiotic sensitivity test), CDDT (combination disk diffusion test), MHT (Modified Hodge Test), mCIM (Modified carbapenem inactivation method), and genotypic methods are PCR amplification, MALDI TOFF (Matrix assisted laserdesorption / ionization-time of flight), real timePCR.[19] Carbapenem resistance towards *Pseudomonas aeruginosa*by phenotypic methods AST n=17 (12%) were detected according to CLSI (Clinical and laboratory standard institutes), MHT n=20 (14%) and mCIM n=25 (17.8%). Abbas et al exhibited carbapenem resistance 9.3% in isolates of *Pseudomonasaeruginosa* detected by AST which was higher as compared to our study.[20] Different studies described mCIM as a simple, accurate and reliable method for detection of carbapenemare in accordance with our study.[21-23] Phenotypic methods are screening methods. Genotypic methods are used for detection of multiple resistant genes. Multiple genes are involved in resistance like KPC, VIM, IMP, SIM, GES and NDM. In our study we only detected the presence of OXA-48 n=4 (16%) by using real time PCR. OXA-48 has been reported in different parts of the world. First OXA-48 gene was detected in Istanbul, Turkey. It has been found in African countries, Middle East, China, Afghanistan and India.[24] Our findings are in accordance with other studies like Bonnin et al recommended real time PCR as highly accurate and specific method.[25] This study focused on bla_{OXA-48} as it has not been found in strains of *Pseudomonas aeruginosa* in previous studies in Pakistan, while it is present in other neighbouring countries. Begum and Shamsuz zaman (2016) detected OXA-48 20% in Dhaka.[26] There is threat of

dissemination of this gene through horizontal gene transfer as Bangladesh is our neighboring country. According to study in Sudan Mohamed et al, OXA-48 exhibited resistance towards *Pseudomonas aeruginosa* was 22.4% which is quite close to our study.[27] Van der zee et al (2014) detected carbapenem resistant gene OXA-48 by real time PCR as accurate and reliable method in association with our study.[28]

Advances in diagnostic technologies have transformed the scenario of alleviating life threatening infections and have played pivotal role in contribution towards human health. It is the lack of motivation and interest of stake holders that now under minesserious problems such as nosocomial infections and antibiotic resistance by microorganisms like *Pseudomonasaeruginosa*. Although it is possible to overcome all these fatal infections through strict surveillance of resistant isolates economic problem in a resource poor country like ours hinders progress and allows dissemination of resistant genes. Hence Â-lactamases are transcribed by various genes like VIM, IMP, KPC, and so on. These genes are transferred from resistant strains to sensitive strains and have been reported in Pakistan. OXA-48 which transcribes class D was not previously reported in strains of *Pseudomonas aeruginosa* in Pakistan.

The foremost limitation of our study is that results cannot be generalized as we took data only from one Military set up where the subject population does not match the demograph of our country. OXA-48 gene showed 16% carbapenem resistance because of small sample size. Our study included only hospitalized patients. There are multiple carbapenemase genes and their allelic variants we looked for only OXA-48 gene using uniplex primers.

CONCLUSION:

Carbapenem resistance in strains of *Pseudomonas aeruginosa* due to the gene bla_{OXA-48} is accounted for 16% of tested cases, microorganisms can acquire extensive genetic diversity through acquisition of resistant genes and this converts a non pathogenic bacteria into pathogenic, which can disseminate at high rate, creating an antibiotic resistance crisis. Detection of these cases and establishing surveillance programs for control of antibiotic resistance will go a long way in resolving this problem.

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Original Article DOI: https://doi.org/10.51985/JBUMDC2019126

Superficial Surgical Site Infection after Primary Closure Versus Delayed Primary Closure of Wound in Perforated Appendicitis

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ABSTRACT

Objective: To assess the superficial surgical site infection after primary closure versus delayed primary closure of wound in perforated appendicitis.

Study Design and Setting: This was an observational study conducted at Darul Sehat Hospital & Civil Hospital Karachi during March 2019 to August 2019

Methodology: All patients of either gender between 18-50 years of age undergoing open Appendectomy through standard gridiron incision in emergency having consented for participation in the study prior to surgery and with per-operative finding of perforated appendix in emergency were included. Patients on steroids or immunosuppressive agents, smoker staking 5 or more cigarettes per day, patients with history of Diabetes Mellitus, chronic liver disease and chronic renal failure were excluded from the study. Patients with perforated appendix were randomly allocated into two Groups. Group A received delayed primary closure at 3rd post-operative day while in Group B primary closure was done immediately after appendectomy. All patients were examined for signs and symptoms of superficial surgical site infection at the 5th post-operative day before discharge from the hospital. SPSS version 13 was used for data analysis. Chi square test was applied to compare the outcome (superficial surgical site infection) in both groups. P-value <0.05 was considered as significant.

Results: A total sixty patients were allocated in each group. Wound infection was very high among patients with immediate closure (40%) as compared to group which received delayed primary closure (15%) (p=0.020).

Conclusion: The superficial surgical site infection was significantly higher after primary closure versus delayed primary closure of wound in perforated appendicitis.

Keywords: Perforated Appendicitis, Surgical Wound Infection, Wound Closure Techniques,

INTRODUCTION:

Appendicitis is one of the most common causes of acute abdominal pain; with an incidence of 110 / 100,000.[1] Wound infection at the surgical site is the most common complication after surgery. [2,3] The superficial surgical site is the actual incision site and is also called the surgical wound. They are often used interchangeably. Surgical wound infections can have serious consequences for patients and care facilities: surgical site infections (SSI) increase postoperative hospital stays, patient mortality, and the need for reoperations. The latest estimates indicated 15.7% of hospital-acquired infections were due to SSI and reported as third most prevalent form of healthcare-related infections. [4] Obesity is considered a risk factor for surgical site infection (SSI). A trend of increasing BMI from normal obesity may increase the risk for SSI risk morbidly has been observed in almost all types of surgery. [5]

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Received: 27-Nov-2019
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The wound infection rate is 4.7% for uncomplicated appendicitis but increases up to 34.1% in perforated appendicitis. [6] In perforated appendicitis; there is a contamination of the incision margins with colonic bacteria and results in surgical site infection during immediate post-operative day. To minimize this contamination and reducing the chances of infection, delayed primary closure of wound is advocated by some surgeons in perforated appendicitis. In this technique wound is left open, dressed daily for 3-5 days with anti-bacterial solution (Povidone-iodine) and then closed primarily.

Superficial surgical site infection (SSI) is common after appendectomy, especially in complicated appendicitis (i.e. gangrene and rupture); the incidence is 9% to 53%. It increases pain, length of stay and costs. The risk factors related to SSI are divided into patient-related factors, surgery-related factors and microbial-related factors. [7] A study by Siribumrungwong et al confirmed the results of previous systematic reviews and meta-analysis, which also indicate

that lower superficial SSI closure (PC) in primary wounds is better than delayed primary wound closure (DPC)) Group, 23% (12%, 33%) and 26% (10%, 42%). [8,9]

There is still controversy among surgeons about the appropriate method of wound closure in perforated appendicitis. Most surgeons favor primary closure as it is more satisfying for the patients, reduces length of hospital stay and treatment cost as no additional procedure has to be performed and infection rate comparable to delayed closure. [8,9]Several studies and randomized controlled trials (RCTs) have tried to answer this question in the past, with mixed results. [10,11]Meka et al. concluded that the risk of SSI in ruptured appendicitis showed no difference between PC and DPC techniques. In low-risk SSI patients, PC does not increase the risk of SSI. [12]

As one would expect, this difficulty is less common in today's era of laparoscopic appendectomy. However, open appendectomy is still standard practice in many parts of the world. In fact, even in the UK and Europe, one-third of appendectomy is still performed in an open way. [13] Wound infections is an extremely cumbersome morbidity for the patients. It not only increases hospital stay but also leads to poor scar and social burden on patients and their family. [14] As perforated appendicitis is an already known cause for post-operative wound infection in the selected cases (an intervention at the time of surgery) that reduces post-operative wound infection and results into better patient management and satisfaction. To assess the superficial surgical site infection after primary closure versus delayed primary closure of wound in perforated appendicitis.

This study aimed to investigate the effect of delayed primary closure on wound infection by comparing it to primary closure so that hospital stay and operative cost can be reduced and early discharge achieved.

METHODOLOGY:

This was the comparative observational study conducted at Darul Sehat Hospital &Civil Hospital Karachi during March 2019 to August 2019. All patients of either gender between 18-50 years of age undergoing open Appendectomy through standard gridiron incision in emergency having consented for participation in the study prior to surgery and with per-operative finding of perforated appendix in emergency were included.Patients on steroids or immunosuppressive agents, smokers taking 5 or more cigarettes per day, patients with history of Diabetes Mellitus, chronic liver disease and chronic renal failure were excluded from the study.The sample size was calculated using website open epi.com. Considering average infection rates of 2.9% and 38.9% in the study and control group respectively and taking 95% confidence interval and 95% power of the test, the sample size was 24 patients in each group.Total 60 patients in both groups were assessed for wound closure. Non-probability - consecutive sampling was used and patients were randomly allocated in Group A (Study group) and Group B (Control group) using random allocation software version 1.0.0.Group A was comprises of patients with delayed wound closure and Group B was comprises of primary wound closure. Initial resuscitation was done with intravenous fluids and analgesics. At induction, all patients were given 1gm of third generation cephalosporin and 500mg of Metronidazole for prophylaxis against infection. After that all patients underwent open Appendectomy via grid iron incision. In the group A, the skin and subcutaneous tissue was closed at 3rd post-operative day. However, in the group B, the wound was simply closed at the time of surgery. Similar post-operative antibiotics i.e. Cephalosporins and Metronidazole were given for 5 days in both groups.

All patients were examined for signs and symptoms of superficial surgical site infection at the 5th post-operative day before discharge from the hospital. Grading for examination of wound for infection on 5thpost-operative day was assessed as Grade 0 Normal healing, Grade 1 Normal healing with bruising, Grade 2 Erythema plus fever >380, Grade 3 Clear or hemoserous discharge, Grade 4 Purulent discharge, Wound infection was labeled to grade 2 and above. The study was executed after approval of Ethical Review Committee of Liaquat College of Medicine & Dentistry, Karachi. Confidentiality was protected by using password-protected files, encryption when sending information over the Internet, and even old-fashioned locked doors and drawers. Confidentiality of all record was maintained as per hospital policy. SPSS version 13 was used for data entry and analysis. Chi square test was applied post stratification to compare the outcome (superficial surgical site infection) in both groups. P-value > 0.05 was considered as statistically significant.

RESULTS:

Mean age of the patients was 23.31 ±10.06 years. Mean BMI of the patients was 19.11 ±2.99Kg/m^2.Duration of surgery of >30 minutes was higher in both groups with 29 (96.7%) in each group (Table – I). Among grading, grade 0 was found to be higher 11 (36.7%) in group A whereas grade 3 was found to be higher 9 (30%) in group B. Significant association was observed in between wound infection and group.

In group B; 24 patients (40%) suffered from wound infection as compared to group A in which 9(15%) patients got infected (Table – II). Wound infection was significantly higher among patients with group B as compared to group A (p-value 0.020). Post stratification analysis didn't show any significant difference in infection rate among the groups on the basis of gender, age, operative time and BMI.

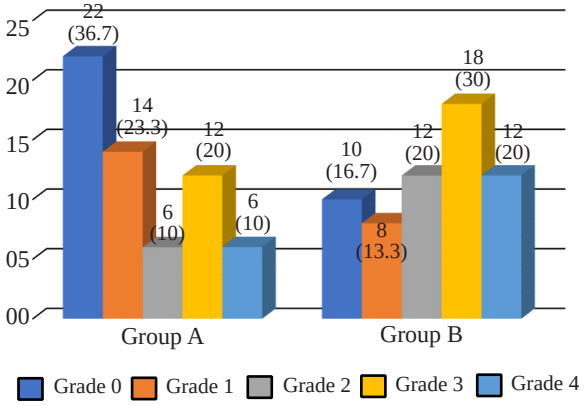
DISCUSSION:

In perforated appendicitis there is a contamination of the incision margins with colonic bacteria which leads to surgical site infection in the immediate post-operative day. There is

Table – I: Patient characteristics of the two groups

	Group A (n=60)	Group B (n=60)
Age of the patients (years)	23.5 ± 11.3	22.8 ± 13.4
Male : Female	35:25	37:23
BMI of the patients (Kg/m^2)	20.6 ± 4.1	19.8 ± 5.2
Operative time (minutes)	43.5 ± 12.3	41.8 ± 13.7

Figure I: Comparison of grading with respect to group



Southampton wound grading system: Grade 0 Normal healing, Grade 1 Normal healing with bruising, Grade 2 Erythema plus fever > 380, Grade 3 Clear or hemoserous discharge, Grade 4 Purulent discharge. Grade 2 and above was considered as wound infection.

Table – II: Comparison of wound infection between groups

Group	Wound Infection		Total	P-value*
	Yes	No		
A	9 (15%)	51 (85%)	60 (100%)	
B	24 (40%)	36 (60%)	60 (100%)	0.020
Total	33 (27.5%)	87 (72.5%)	120 (100%)	

* = Chi square test

still controversy among surgeons about the appropriate method of wound closure in perforated appendicitis. A lot of surgeons favor primary closure as it is difficult to brief patient that his/her wound would be left open after surgery and obviously it adds an additional procedure to all the patients and ultimately to the healthcare costs.[15-18]However, studies suggest that delayed primary closure is associated with a significantly lower wound infection rate thus reducing the length of hospital stay, operative cost and more patient satisfaction.[6, 19,20,21]

In our study, wound infection was significantly higher among patients with group B (40%) as compared to group A (15%) although the infection rate came out to be higher in both groups when compared to international literature. Chiang and colleagues have shown that in cases of perforated appendicitis wound infection rate in delayed primary closure group is 2.9% as compared to 38.9% in primary closure group.[20] A recent systematic review conducted by Hureibi et al. in 2019, they retrieved 471 studies; eight met the eligibility criteria and were included in the analysis. These trials included 1,263 patients, of whom 623 patients underwent delayed closure and 640 primary closures. Surgical Site Infections (SSI) rates were not significantly different between the DC and PC groups (16.25% & 12.68% respectively. OR=0.60, 95% CI: 0.23-1.54.[10]Wound infection is an extremely cumbersome morbidity for the patients. It not only increases hospital stay but also leads to poor scar and social burden on patients and their family. As perforated appendicitis is an already known cause for post-operative wound infection,[22] in theses selected cases an intervention at the time of surgery that reduces post-operative wound infection translates into better patient management and satisfaction.

The SSI rate was lower in the PC than the DPC group, with rates of 5% versus 9% respectively. Patients who received PC would be at an approximately 77.8% lower risk of SSI than patients who received DPC, but this was not significantly different.[11] Latif et al reported that delayed primary closure for different pathologies in appendicectomy is a safe approach associated with prolonged admission and adverse scar outcome while the primary closure is the most practiced approach which is associated with better patients satisfaction but morbidity rate being low can be grave and at times mortality is encountered.[23] SSI developed in 40.2 % of patients after closure of incisions. Primary closure group had a higher incidence of SSI and longer hospital stay.[24] Delayed primary closure employs a safe means of avoiding this morbidity and its associated cost issues and patient disappointment.

CONCLUSION:

The superficial surgical site infection was significantly higher after primary closure versus delayed primary closure of wound in perforated appendicitis.

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Original Article DOI: https://doi.org/10.51985/JBUMDC2019042

Association of Hyperuricemia With Hypertension In Pakistani Population

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ABSTRACT

Objective: To find an association between Hyperuricemia and Hypertension in patients presenting in outpatients department for regular check-up.

Study design and Setting: Case Control Study design conducted at Pak Emirates Military Hospital Rawalpindi (PEMH), Medical Outpatient department (OPD) from 4th Feb, 2017 to 4th Aug, 2017.

Methodology: A total of 200 patients, with 100 cases and 100 controls fulfilling the selection criteria were included in the study, which were selected from Medical OPD of PEMH. An informed written consent was taken. The Demographic such as age, gender were obtained. Veriable upon selection into study group, the blood samples were taken and two groups of patients were made on the basis of normal or raised uric acid levels. The Serum Uric Acid (SUA) was measured in the patients. Then blood pressure was measured by using sphygmomanometer by researchers themselves. If BP level was >140/90mmHg on 2 separate occasions, or patient is already a known case of hypertension, then hypertension was labeled.

Results: The mean age (years) in the study was 54.79 + 8.96. There were 136 (68%) male and 64 (32%) female patients. The frequency and percentage of hypertension in cases and control groups was (84%) and (41%) patients respectively which was statistically significant with a p-value of 0.000. The Odds ratio was found to be 7.55.

Conclusion: It was concluded that there was an association found between Hyperuricemia and Hypertension.

Key words: Hypertension, Hyperuricemia, Uric Acid.

INTRODUCTION:

The hypertension is very much prevalent and it affects approximately one-third of world population and is one of the common cause of death and disability.[1,2] Though the cause of hypertension is not known in most of the patients, SUA(serum uric acid) has been thought to activate the renin – angiotensin system, which results in damage to prerenal blood vessels.[3] Recently, a new study has shown that the mild hyperuricemia induces the arteriopathy and hypertension and this has brought renewed interest into this hypothesis.[4,5]

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Received: 10-Apr-2019
Accepted: 03-Mar-2020

The global prevalence of hypertension in adults is around 40%.[6] SUA is produced as result of a catabolism of normal purine, which is excreted mostly in urine but also through the gastrointestinal tract. Many studies have shown SUA concentrations >7 mg/dL is an independent and one of the other major risk factor associated with hypertension, a reduction in SUA is associated with lowering BP.[7,8] The mean uric acid levels and number of hyperuricemic subjects were found to be significantly higher in hypertensive cases than normotensive controls.[9,10] In a study conducted by Redon and colleagues on patients from European countries showed that 25% of population had hyperuricemia. It was associated with greater prevalence of metabolic syndrome, diabetes mellitus, rate of uncontrolled hypertension in these patients.[11] In a study conducted by Xiaoyun Lin et al in china concluded that, in males, hyperuricemia was an independent risk factor of hypertension with an adjusted OR of 1.131.[12] The hyperuricemia was also associated with post partum hypertension as concluded by Caraline C. Mars and colleagues with OR of 2.44.[13]

The younger individuals and women are at higher risk as compared to others.[14,15] In one of study in 2011, among cases of hyperuricemia, the frequency of hypertension was 36.6% and among patients of normal serum uric acid level was 18.8%. The difference was found to be significant (P<0.01).[16]

Similarly NHANES 2009-2012 study has found that among cases of hyperuricemia, the frequency of hypertension was 38% while among patients of normal serum uric acid level was 20%. The difference was found to be significant

(P<0.01).[17] In a study done in kenya by C.B. Mibey Sylvia and colleagues showed that prevalence of hyperuricemia was 44% in hypertensive patients; with 37.6% and 47.3% in males and females respectively.[18] In a study by Kuwabara M et al in Japan showed that the OR for association between hyperuricemia and hypertension were 1.79 in the total study population, 1.58 in men and 1.60 in women.[19] The regional studies in Pakistan revealed that hyperuricemia was found in 40.3% and 37.4% in hypertensive population.[20]

The rationale of this study was to assess the association between Hyperuricemia and Hypertension in patients presenting in outpatient department for regular check-up for other chronic illnesses in our populatin. It has been noticed in previous studies, that hyperuricemia may lead to increased cardiovascular events and accelerate the BP level. Therefor the study was aimed to find the association between Hyperuricemia and Hypertension in patients presenting in outpatients department for regular check-up.

METHODOLOGY:

This was a case control study done in Medical OPD of PEMH Rawalpindi, from 4th Feb, 2017 to 4th Aug, 2017 with a sample size of 200 cases: 100 cases and 100 controls. The sample size was calculated using 80% as power of test, with level of significance 5% and taking 18.8% as prevalence of hypertension in patients without hyperuricemia and 36.6% in those patients who were having hyperuricemia.[8] The cases were selected by non-probability, consecutive sampling technique. An Informed written consent was taken. The Patients with age between 35 to 70 years of either gender, presenting in OPD for regular checkup as follow up cases of various diseases (after applying exclusion criteria) were considered for selection. The patients taking drugs such as thiazide & loop diuretics, pyrazinamide, Cytotoxic drugs and those Patients with CKD, eclampsia, lymphoma, leukemia were excluded from the study. The demographic variables as age, gender were obtained.

From recruited patients, the blood samples were taken to determine the serum uric acid levels. After obtaining lab results patients were categorized as cases (those with hyperuricemia) and controls(those with normal serum uric acid levels), using the upper limit of normal range for both genders as cut off for hyperuricemia i.e > 7.4mg/dl for males and > 5.8mg/dl for females. Then blood pressure was measured by using sphygmomanometer by researchers themselves. If BP level was >140/90mmHg on 2 separate occasions, or patient is already diagnosed case of hypertension on anti hypertensive therapy, then hypertension was labeled.

The Data analyzed in SPSS version 20. The descriptive statistics was calculated for both qualitative and quantitative variables. The quantitative variables like age, blood pressure were analyzed as mean and standard deviation. The qualitative variables such as gender and hypertension were presented as frequency and percentage. The Chi square test was applied to compare hypertension between 2 groups and the Odd ratio was calculated. The effect modifiers such as gender, Diabetes, age, dyslipidemia, History of Ischemic heart disease were controlled by stratification. P-value < 0.05 was taken as statistically significant.

RESULTS:

A total of 200 patients were enrolled in of the study protocol applying the strict inclusion and exclusion criteria. The two groups of patients were made randomly. The cases consist of those patients who were found to have hyperuricemia whereas patients in control group were without hyperuricemia (normal serum uric acid level). There were 136 (68%) male and 64 (32%) female patients in our study, as shown in chart No. 01. The Mean age (years) in the study was 54.79+8.96 with ranges from 35 to 70 years.

The descriptive statistics blood pressure was measured twice time. The mean systolic Blood pressure in mmHg at 1st and 2nd reading was 136.75+16.20 and 136.17+16.02 respectively whereas mean diastolic Blood pressure in mmHg at 1st and 2nd reading was 86.32+9.71 and 85.50+8.73, as shown in Table No. 01.

The Frequency of hypertension in the study was 125 (62.5%) whereas 75 (37.5%) patient were without hypertension, as shown in Table No. 02

The objective was to find out the association between hyperuricemia and hypertension in patients presenting in outpatients department for regular check-up. The Frequency and Percentage of hypertension in both the groups was 84 (84%) and 41 (41%) patients respectively. The Chi Square test was used to compare hypertension in both the groups. The P value and odds ratio, as shown in Table No. 03

DISCUSSION:

The global prevalence of hypertensionin adults 25 years and above was around 26·4% and this figure is estimated to increase to about 60% to a total number 1.5 billion in year 2025.[6,21] In a study conducted in Japan, 43 million individuals were estimated to have high blood pressure with male and female prevalence of 60% and 45% respectively.

Figure 1: Gender Distribution

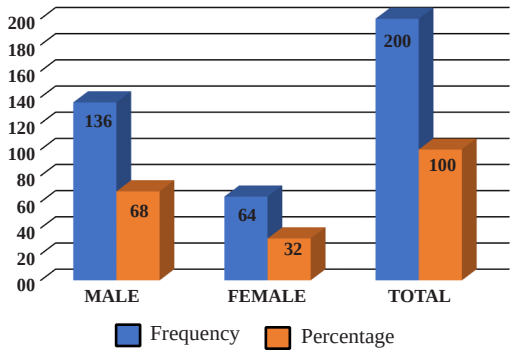

Table 1: Descriptive statistics of Blood Pressure (systolic & diastolic) 1st and 2nd reading

Reading		n	Mean (mmHg)	Std. Deviation
1st reading	Blood pressure (systolic)	200	136.75	16.20
	Blood pressure (diastolic)	200	86.32	9.71
2nd reading	Blood pressure (systolic)	200	136.17	16.02
	Blood pressure (diastolic)	200	85.50	8.73

Table 2: Frequency & Percentage of Hypertension

		Frequency	**Percentage**
Hypertension	No	75	37.5%
	Yes	125	62.5%
	Total	200	100%

Table. 3: Association of Hyperuricemia and Hypertension in both the groups

	Two groups			P-value	Odd Ratio
	Cases (hyperuricemia)		Control (without hyperuricemia)		
Hypertension	Yes	84	41	0.000	7.55
		84%	41%		
	No	16	59		
		16%	59%		
Total	100		100		
	100%		100%		

In developing countries one of the most common cause of death is Coronary artery disease. The cardio-vascular diseases has been the cause of more than 17.5million deaths in year 2012 globally.[22] The one of a major risk factor for cardiovascular death and morbidity is hypertension.[23]

The Hyperuricemia also results in an increased risk for cardiovascular disease. It is also associated with gout, renal dysfunction and the metabolic syndrome. The association between hypertension and hyperuricemia is being studied worldwide in recent years. The hyperuricemia plays a vital role in the development of hypertension, and association between the two, has been studies previous in many studies. The association between hyperuricemia and CV diseases in patients with hypertension is also being reported.[24] Many studies have shown that drugs that reduce serum uric acid levels ,also reduce BP in patients with hyperuricemia.[25,26] There are various mechanisms involved by which increased blood pressure occurs in patients with elevated uric acid.[27] Our study result showed that there were 84% of patients with hyperyricemia, which were hypertensive while only 41% without hyperuricemia had increased blood pressure. There was a strong association between hypeuricemia and hypertension with Odds ratio of 7.55. In a study done by Yokokawa et al, Hyperuricemia was 1.79 times more common in men with hypertension in comparison with those without than hypertension and almost 6 times more prevalent in hypertensive women with odds ratio of 5.92, while odds ratio in our study population was 7.55.[8]

In research done by Poudel et al, the mean SUA levels and number of patients with hyperuricemia was, significantly higher in hypertensive group, than those without hypertension (28.8% vs 13.7%) with Odds ratio of 2.55.[28] Shrivastav et al showed that the mean SUA levels and hyperuricemiac patients were significantly higher in newly diagnosed cases of essential hypertension as compared to prehypertensive or normotensive controls (37.33% vs 14%). In our study, percentage of hypertension in patients with hyperuricemia was 84% and without hyperuricemia, it was 41% respectively. In a study in Pakistan, that the SUA levels were significantly increased in patients with hypertension (6.51 ± 1.45 mg/dl) than those without hypertension (4.72 ± 1.83 mg/dl).[29] In another study by Bâ Hamidou Oumar et al, the prevalence of hyperuricemia was found to about 66% in hypertensive patients, while it was 84% in our study.[30] Therefore, blood pressure should be monitored regularly in patients with hyperuricemia or gout. Patients with Hypertension should be monitored for increased serum uric acid levels. This will help us treat raised uric acid levels to reduce the burden of patients with hypertension as well reduce the risk of other cardiovascular diseases.

CONCLUSION:

It was concluded that the association was found between Hyperuricemia and Hypertension.

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Original Article DOI: https://doi.org/10.51985/JBUMDC2019075

Comparison Of Periodontal Health Of Orthodontic And Non-Orthodontic Patients

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Objective: To compare the periodontal health status among orthodontic and non-orthodontic groups aged between 14-30 years of both genders.

Study design And Setting: This comparative cross sectional study was conducted at Department of Orthodontics and Periodontics from January 2019-till June 2019 at dental Hospital of Bahria Dental College Karachi.

Methodology: Those patients aged 14-30 under orthodontics treatment for about 3 months and were able to give consent were included in the study. Periodontal status among both groups (65 orthodontics and 65 non orthodontic) patients was evaluated with the help of CPITN probe on index teeth. To assess the oral hygiene status; the questionnaire was formulated regarding the use and frequency of toothbrush; use of interdental cleaners such as interdental brush, use of mouthwash, use of tongue cleaners and dental appointments. A single observer from periodontics department was appointed for observation and record data of patients coming to orthodontic department and to carry out a clinical examination. The data was scrutinized using SPSS 23, and using the chi-square test various other comparisons were performed.

Results: Statistically significant association was observed in CPITN scores between the orthodontic and non-orthodontic patients ($p < 0.05$). Patients who underwent orthodontic treatment had increased plaque accumulation and probing depth which resulted in periodontal tissue destruction.

Conclusion: It was concluded that the periodontal condition of ortho patients was deteriorating as compare to non ortho patient. There was no noticeable attachment loss found that could lead to mobility of the tooth and its loss.

Key words: calculus, non-orthodontics, orthodontics, periodontal status, plaque.

INTRODUCTION:

Orthodontic treatment has extensive effect on dentofacial complex. It helps in proper alignment of dentition by orthodontic treatment modalities; improving occlusion, enhancing esthetics and maintaining oral hygiene. Oral hygiene can be affected by different abnormalities in teeth alignment. Plaque retention is one of the causative factor leads to imbalance in micro biota of oral cavity; further accumulation of plaque results in malocclusion which is more often seen in crowded dentition; commonly a feature of lower anterior. Open bite, spacing, cross bite impacted teeth, crowding, narrow arches and rotation of teeth are the atypical features of malocclusion.[1]

The initial inflammation of gingival tissue occurring around the gums, surrounding the teeth is known as gingivitis, when left untreated progresses into periodontal disease. On the other hand; the fixed orthodontic appliances; when horn in the gingival sulcus rendered plaque accumulation; results in food deposition. This cementation of ortho appliance and the food accumulation results while brushing and at times it is difficult to clean that debris further deteriorating the oral health.[2] Since patient fails to maintain appropriate oral hygiene, they are likely to develop gingivitis as it progresses within 21 days of its occurrence.[1]

Fixed orthodontic appliances increases the growth of microbial flora due to deposition of plaque and calculus and results in bleeding gums.[3-7] and other periodontal associated problems such as gingival recession, gingival hypertrophy, alveolar bone hammering, pocketing.[8,9] The predominant initiators of plaque are gram positive organisms which later get replaced by gram negative and then the anaerobes.[1]

Oral hygiene preservation during orthodontic treatment is only possible by proper teaching to the patient, their enthusiasm, collaboration and their approach towards their treatment played an active role to maintain oral hygiene.[10] A lot of researches proved that patients either lack knowledge of proper hygiene maintenance or show carelessness in maintaining it. Despite having the knowledge some patients still fail to follow proper oral hygiene instruction.[11, 12]

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Received: 12-Jul- 2019
Accepted: 17-Feb-2020

In order to overcome caries and periodontal problems during orthodontic treatment; there is a need to educate patients regarding maintenance of oral hygiene and how to control the calculus deposition[13] and indeed it was the rationale of the study to assess the periodontal health among orthodontic patients and further to educate them accordingly. It is important to guide orthodontic patients about oral hygiene maintenance before starting the treatment.[14] To address this; it is essential to practice proper brushing technique regularly. Awareness regarding different types of orthodontic appliances and brushes should be provided to the patients especially the interdental brushes.[15] Therefore this study was aimed to compare the periodontal health status of orthodontic and non orthodontic patients.

METHODOLOGY:

All those patients who were aged between 14-30 years of age and visited to orthodontic and periodontics department for regular dental check-up in the Dental Hospital of BUMDC from January 2019 to June 2019 were examined for this study. This study was conducted after the approval obtained from Ethical Review Committee of BUMDC. Those patients aged 14-30 under orthodontics treatment for about 3 months and were able to give consent were included in the study; while those patients having pathological or congenital condition such as craniofacial anomalies because of the compromised periodontal tissue condition and those who were seeking prosthesis treatment specially removable prosthetic appliances were excluded from the study. The Sample size was calculated by considering the prevelance of 10%[1]. The calculated sample size was 139 subjects .Total 65 patients from each respective department were taken into consideration were divided into test group (orthodontic patients) and control groups (non-orthodontic patients). Gender distribution details filled in figure 1. A single observer from periodontics department was appointed for observation and record data of patients coming to orthodontic department and to carry out a clinical examination. To obtain intra-examiner reliability, ten patients were examined on two occasions at a 1-week interval using the Community Periodontal Index and kappa test value of 0.95 was obtained.

Periodontal status among both groups was evaluated with the help of CPITN probe on index teeth.[2] To assess the oral hygiene status; the questionnaire was formulated and included questionnaire were regarding the use and frequency of toothbrush; use of interdental cleaners such as interdental brush, use of mouthwash, use of tongue cleaners and dental appointments.

The periodontal condition of all the patients was assessed conferring to WHO protocol, by the use of an axenic CPITN probe on the index teeth and a mouth mirror under a favorable light source. A tooth was examined to obtain the pocket depth, spot calculus and to check any bleeding response. The areas chosen for examination were the distal, midline and mesial aspects of the facial and palatal/lingual areas. The measure of the depth of gingival sulcus or pocket was carefully examined with the tip of the probe. The probing depth was measured by introducing the probe alongside the long axis of the tooth, between the tooth and gingiva starting at the distobuccal area of the index tooth. The corresponding maximum score for each sextant was calculated and noted down in the appropriate box. The dentition was classified into 6 sextants. The CPITN code noted on the index teeth according to their status were 0,1,2,3,4, denoting healthy gums, bleeding gums on the use of probe, presence of calculus on the gingival surfaces, existence of a low pocket of about 4 to 6 mm or a profound pocket measuring about 6mm or more. While x decoded a sextant with less than 2 teeth (excluded sextant).

The collected data was analyzed using the Statistical Package for Social Sciences (SPSS) version 23 and comparisons of CPITN codes were performed using the chi-square test, with a value of $P < 0.05$ regarded as significant.

RESULTS:

There were total 130 patients evaluated and comprised of 35 males and 95 females within 14-30 years of age. The periodontal pockets score was compared among both groups. It was revealed CPITN score was 57% in ortho group having periodontal pockets scoring of 3 and 4 on CPITN probe; and (17%) in non-orthodontic group pocket depth with same score (3 and 4 score) on CPTIN probe. The elevation in periodontal disease was found to be statistically significant between ortho and non-ortho groups ($p < 0.05$) (Table-1).

A CPITN score of 3 and 4 indicated the presence of a pocket in 4(6%) patients of orthodontic group who were interdental brushers. At the same time the same CPITN score of 3 and 4 was also found in about 34 (52%) patients who were not using the interdental brushes-Graph-2.

According to the results; from the total 130 patients, 4 of 40 interdental brush users that was about 10% had 3 and 4 CPITN score along with the periodontal pockets. Periodontal pockets were present in 46 (51%) of the 90 patients who were not using any sort of interdental assistance and CPTIN score was 3 and 4. (Graph-3). Table 3-depicted the progression of periodontal disease ($p < 0.05$) among patients who are not using dental aids to the ones using it.

According to the responses revealed: both groups were brushing their teeth with a tooth brush ranging 66% of them doing it once every day while 30% did it twice daily and only 1% doing it thrice daily. Whilst when it came to the use of interdental cleaners, in the ortho group 47% were interdental brush users, and in the non-ortho group, only 15% patients used dental floss. Volunteered tongue cleaners were 12% from orthodontic group and 5% from non-orthodontic. At the same time use of mouth wash was practiced by 10% orthodontic patients and 38% normal patients not undergoing ortho treatment. Total 20% patients

of orthodontic follow up and 10% were routine diagnostic patients.

Figure 1: Gender Distribution among Ortho and Non-Ortho patients

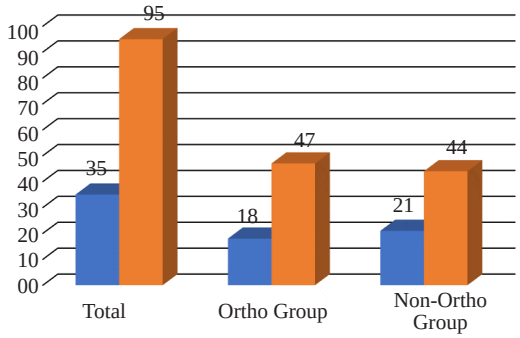

Figure- 2. Comparing the CPITN scores among Interdental and non-Interdental brush users among Orthodontic patients

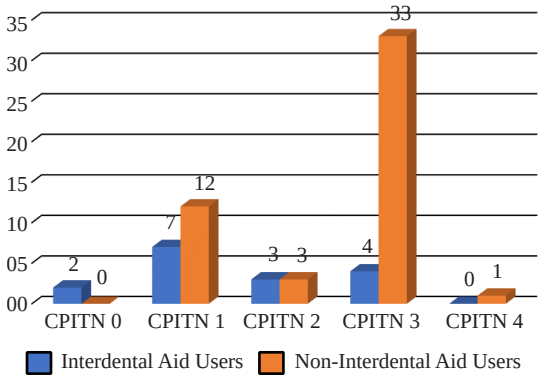

Figure 3: Relationship of CPITN Scores between Interdental and non-interdental Brush users

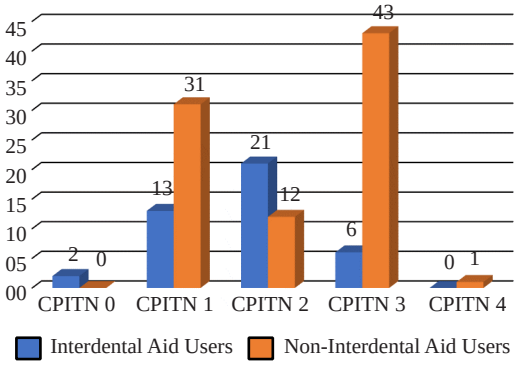

Table 1: Comparison of CPITN Score among Ortho and Non-Ortho groups

CPITN Score	Ortho group N=65	Non-Ortho group N=65	P-Value
0	2	13	0.000*
1	20	31	
2	6	10	
3	36	11	
4	1	0	

Table 2: Comparison of CPITN Score between interdental and non-interdental aid users among all patients

CPITN	Score 0,1,2	Score 3,4	p-value
Interdental aid users (N=40)	36(90%)	4(10%)	0.000
Non-interdental aid users (N=90)	44(48%)	46(51%)	

DISCUSSION:

The purpose of the study was to compare the periodontal health among patients seeking orthodontic help to the ones not undergoing orthodontic care. In this study; the CPITN score was increased among orthodontic treatment receiving patients. Momina et al.[16] revealed that the arrangement of brackets provides retentive sites and bionomic surroundings for accumulation of biofilm, furthermore the CPITN scores observed in this study harmonize with those fallouts. Excessive bleeding and inflammation worsen the periodontal health resulting in surveillance of noticeable raise in plaque and gingival index of test group. Three months after placement of fixed appliances there was foremost augment in clinical and microbial characteristics, comparable outcomes shown by Marda et al.[17]

Undoubtedly, the CPITN score of orthodontic and non orthodontic groups were contradicting, admitting the fact that score for group using interdental brush were lower as compared to the ones not using brushing. Since orthodontic appliances placement hinder maintenance of proper oral hygiene causing deposition of plaque leading to increase in pocket depth, which directly contributes to increase in CPITN score and the same observation reported by Nasir et al.[18]

As reported by Angelina et al,[19] the most affected area periodontally in orthodontic patient is the interdental area which agrees with the observation of this study. This truly confirms that orthodontic appliances are prone to plaque accumulation, eventually initiating periodontal problems. These results were in agreement with other studies.[20] A clinically healthy gingiva has ascertained depth which depicted by different methods as 1.5 mm and 1.8mm.[21]

Radiographic analysis indicated the areas of bone loss presuming the formation of pockets.[22]This study agrees with Fatemah et al[23]who reported orthodontic patients bearing fixed appliances have slight attachment loss with increase in pocket depth.

The primary etiological and commencing factor for any gingival or periodontal regression is plaque and its cleanliness becomes a challenge by fixed appliances placement. Earlier colonies initiating plaque are gram positive rods and cocci, transforming into gram negative and anaerobic organisms introducing periodontal defects.[24] Orthodontic treatments render the patient to achieve appropriate oral hygiene during the treatment period. This in turn causes plaque accumulation

which can trigger pathological conditions, since orthodontic appliances serve as mechanical trappers for plaque. Henceforth periodontal conditions in orthodontic patients can be bypassed by enduring plaque control therapy.

Encouraging the adolescents into proper oral hygiene maintenance can reduce the burden of dental distress.[25,26] Oral hygiene tools for orthodontic patients such as floss threaders, interdental brushes are available to control the plaque accumulation.[27]

The limitation of the study was the effects of orthodontic treatment upon periodontal health. Further studies can be conducted to assess the periodontal health after the exclusion of orthodontic appliances. Therefore; in a nutshell, proper oral hygiene measures along with interdental brushes can reduce the plaque accumulation.

CONCLUSION:

It was concluded that the periodontal condition of ortho patients was deteriorating as compare to non ortho patient There was no noticeable attachment loss found that could lead to mobility of the tooth and its loss.

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Original Article DOI: https://doi.org/10.51985/JBUMDC2019087

Clinical Profile Of Hepatocellular Carcinoma-Experience At A Tertiary Care Hospital

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ABSTRACT

Objective: To determine the characteristics of Hepatocellular carcinoma (HCC) in patients visiting PEMH Rawalpindi.

Study Design and Setting: Cross-sectional Study conducted at Department of Gastroenterology/hepatology in Pak Emirates Military Hospital Rawalpindi (PEMH) from Oct 2015 to Jan 2018.

Methodology: In this study total 100 patients, with HCC of both genders were included. All the cases were discussed in multidisciplinary team (MDT) meetings which were held once every week. A decision on the best possible management for the given case was arrived at in the MDT meeting. All the relevant features of each case were recorded in the Performa. Descriptive statistics were used to calculate mean, standard deviation and frequencies for gender, various presenting features, co-morbidities and clinical features. Data was analyzed on SPSS version 21. P value <0.05 was considered as statistically significant.

Results: Sixty seven men and 33 women with HCC were included in this study with a mean age of 58.23 years. The abdominal pain was the most common symptom present in 66 (66%) patients. Edema was seen in 30 (30%) and palpable splenomegaly in 26(26%). Diabetes mellitus was the most common co-morbidity found in 20(20%) patients. HCV was the commonest cause of HCC present in 79(79%) patients. Vascular involvement was seen in 15 (15%) patients. Most (62%) patients had a single HCC lesion and most belonged to Child –Pugh class A (68%) and BCLC stage B (42%). ECOG performance status was good in most patients with 49% patients scoring 0. The AFP levels were raised in 58 (58%) of the patients.

Conclusion: HCV was the most common underlying etiology. Most of the patients were asymptomatic at the time of diagnosis. Majority of subjects reported with the complaint of abdominal pain and had no underlying co morbidity. The metastasis was negative in majority of cases.

Key Words: Hepatocellular Carcinoma, Hepatitis C, Splenomegaly.

INTRODUCTION:

The Primary liver cancer is the 6th most common cancer world wide.[1] Hepatocellular carcinoma is one of the most common tumors involving the liver while it is the 2nd leading cause of cancer related death.[2] In year 2018; total of 841,000 (4.7%) new cases of liver cancers were reported and further incidences are increasing.[3,4] There are various risk factors associated with development of HCC including hepatitis B, hepatitis C, toxins exposure such as aflatoxins, lifestyle risk factors such as obesity, smoking and alcohol consumption. While 44% of HCC cases were attributable to chronic hepatitis B infection; Hepatitis C was responsible for 21% of cases.[5] Certain diseases such as hemochromatosis, Wilson and Alpha -1 anti trpysin deficiency are also associated with increased risk of HCC.[5]

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Received: 31-Jul-2019
Accepted: 11-Dec-2019

The etiological factors are different in different populations. HCC is one of the commonly occurring tumors in Pakistan with age-standardized rate 7.64/100000 for men and 2.8/100000 for women.[5] The majority of cases occurred having the background of liver cirrhosis.[6,7] The etiology during last few decades has changed from a majority of HCC cases previously being positive for HBV to a clear majority now being positive positive for HCV infection. Though the incidence of HCC are on rise and the overall associated mortality is decreasing.[8]

Majority of HCC cases are identified in patients who are already diagnosed with Chronic liver disease secondary to any other cause. The patients may be asymptomatic at the time of diagnosis or they may present with worsening of their disease. Increased surveillance of patients with liver disease with Ultrasonography for HCC, has led to increased number of patients identified at an asymptomatic stage.

Patients may present with variety of symptoms including abdominal pain, abdominal distension, appearance of or worsening of jaundice, weight loss, anorexia, sarcopenia, fatigue, vomiting. The treatment as well as prognosis of HCC depends on size, number of lesions, local as well systemic and extra hepatic spread and over all wellbeing of patient. The prognosis of untreated HCC is poor; overall median survival is 9 months. The main cause behind death was progression of tumor in these untreated patients.[9] As the Barcelona Clinic Liver Cancer (BCLC) stage worsened it resulted in progressive and significant decrease in median survival of the patients.[10]

Despite being a common tumor in our population, clinical features of this tumor have not been adequately described in local literature.[11] In Pakistan there is dearth of central cancer registries framework and data primarily comes from single center experiences. Several studies have been published describing one or more aspects of HCC but detailed clinical profile studies are limited.[5,8,11] Due to a paucity of published literature on HCC patients' profile, a need was felt to document the common clinical and laboratory features of HCC in Pakistani population for future use as a reference. Therefore; the aim of the study was to determine the characteristics of Hepatocellular carcinoma (HCC) among patients visiting to PEMH Rawalpindi.

METHODOLOGY:

It was a cross sectional study carried out from Oct 2015 to Jan 2018 at department of Gastroenterology, Pak Emirates Military Hospital (PEMH) Rawalpindi. The sample size was calculated using a prevalence of 5.2/100000 (7.6/100000 for males and 2.8/100000 for females) and keeping the confidence level at 95% and margin of error at 5%.[12] All patients diagnosed with HCC in PEMH and those coming with the diagnosis of HCC were enrolled in the study with non-probability convenience sampling. After taking consent and providing the rationale of the study; the history and clinical examination was performed; followed by investigations. Functional status of patients was recorded according to the ECOG scoring system. Investigation carried out for all cases included complete blood counts, Liver function tests including albumin, Prothrombin time and INR, renal function tests, hepatitis serology, Alfa fetoprotein (AFP) levels, ultrasonography and contrast enhanced CT scan of abdomen. Few investigations were only performed where indicated such as Upper GI endoscopy, PCR for HBV and/or HCV, MRI abdomen, liver biopsy, Doppler sonography for vascular involvement, tumor markers (CA-19-9, CEA). Patients were categorized according to BCLC and Child-Pugh classification systems. Data was analyzed in SPSS version 21. The descriptive statistics for gender and etiological factors for HCC such as frequency, percentage was calculated along with mean and SD for age. The frequency and percentages for various presenting features, associated co-morbid conditions were calculated. The descriptive statistics were used to calculate frequencies, means and standard deviation for various clinical, radiological and biochemical features of HCC. P value <0.05 was considered as statistically significant.

RESULTS:

Total one hundred patients were enrolled in the study. The gender distribution is shown in figure-1. The clinical presentation was varied as shown in table 1. Twenty seven (27%) patients were asymptomatic at presentation and were diagnosed as a result of screening or imaging for an unrelated problem. In symptomatic patients, abdominal pain was the most common symptom which was present in 66(66%) whereas haematemesis was the least common presenting symptom seen in only 5(5%) patients. Sixty three (63%) patients reported 2 or more symptoms at the time of diagnosis. Presenting features are tabulated in Table -1. Most patients (69%) had no other co-morbidities whereas diabetes mellitus was found in 20(20%) patients as shown in Table No 2. Other co-morbidities included hypertension and ischemic heart disease. HCV was the most common underlying etiology and was found positive in 79(79%) patients. Distribution of etiology of cirrhosis is given in figure-2. The Clinical profiling of the patients with HCC presenting to PEMH is shown in the Table No. 3. In an overwhelming majority (90%), no extra-hepatic metastatic deposits were identified. Vascular involvement was found at the time of diagnosis in 15(15%) patients with tumor most commonly involving a branch of portal vein. In most patients size of the tumor was more than 5 cm at the time of diagnosis. Most patients (62%) presented with a single tumor nodule and the size of largest lesion in most patients (60%) was more than 5 cm. Most patients (68%) were in Child-Pugh class A at the time of diagnosis and in majority (42%) BCLC tumor stage was found to be "B". Functional status of most patients (49%) was unimpaired at the time of diagnosis of HCC. The AFP levels were normal in 42% of patients while out of remaining 58% it was overwhelmingly raised to more than 1000 ng/ml in 19% of patients.

DISCUSSION:

The incidence and prevalence of HCC was high due to high prevalence of chronic viral hepatitis in our study sample. HCC more commonly affects men than women and this was reflected in the gender distribution of cases in this study with two thirds of patients being men.[13] The difference in the incidence of HCC in both genders has led to the hypothesis of a protective role of estrogens in female population.[13,14] As many as 27% patients were asymptomatic at the time of diagnosis which is a significantly high figure as other studies like Kumar et al[15] reported that 91.6% of patients with HCC were symptomatic at the time of diagnosis. The performance status as depicted by ECOG performance score 0 or 1 was seen in 87% of the patients. Studies have shown that those patients having better performance status had better survival rates.[16]

Table 1: Presentation of HCC

S NO	Parameter	Number of Patients (%)
1	Asymptomatic	27(27%)
2	Abdominal Pain	66(66%)
3	Ascites	15(15%)
4	Weight Loss	55(55%)
5	Haematemesis	5(5%)
6	Anorexia	43(43%)
7	Jaundice	9(9%)
8	Multiple symptoms	63(63%)
9	Palpable splenomegaly	26(26%)
10	Edema	30(30%)
11	Anemia(Hb<10g/dl)	24(24%)
12	Thrombocytopenia	21(21%)
13	Renal dysfunction	5(5%)

Figure 1: Gender Distribution

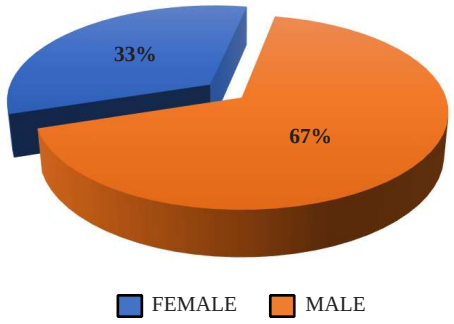
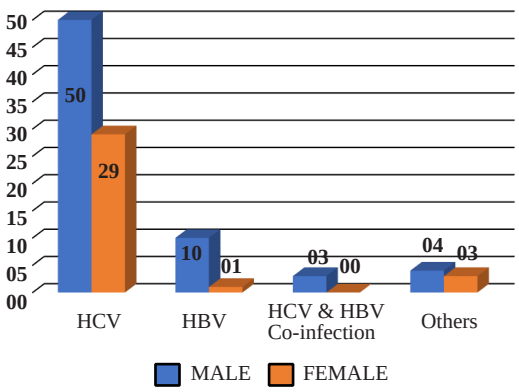


Table 2: Associated Co-morbidities

S NO	Condition	Number Of Patients(%)
1	No co-morbid illness	69(69%)
2	Diabetes mellitus	20(20%)
3	Hypertension	3(3%)
4	Ischemic heart disease	2(2%)
5	Diabetes mellitus & Hypertension	5(5%)

Figure 2: Distribution of Etiology



The effects of tumor size in HCC on clinical presentation and its role as a prognostic factor remain unclear .The 5-year mortality was higher in patients with tumor sizes more than 5 cm in comparison with those with sizes less than 5 cm,[18] Similarly, regardless of the tumor size in patients, the absence of vascular invasion or fibrosis was associated with better survival rates[19, 20, 21]. The AFP levels were normal in 42% of patients. The previous studies found that elevated AFP levels are associated with higher pathological grade, more advanced BCLC stage, and larger tumors.[22,23,24]

The vascular involvement was seen in only 15% of patients as compared to 35% in a study done in china.[25] Vascular involvement adversely affects the survival in HCCpatients independent of treatment modality being used. Patients with vascular involvement represent a distinct tumor phenotype of HCC. It is associated with younger age, aggressive tumor and poor performance status.[26] The majority of patients in our study had BCLC stage A or B tumor with a single tumor nodule with preserved functional status and few patients were asymptomatic as well at the time of presentation.[27] One possible explanation for high percentage of patients diagnosed before the development of symptoms and at an early stage may be the fact that majority of patients were known to have chronic liver disease due to chronic viral hepatitis and were also entitled to free medical treatment and hence were more likely to keep their appointments for surveillance of HCC. This could have led to an increasing number of patients being diagnosed at an earlier stage. Another possible reason for majority of patients falling in earlier tumor stages may be the referral bias; since PEMH is a tertiary care hospital and patients are referred to this center after being worked up at other hospitals in the country. It is possible that HCC patients with advanced stages of tumor were never referred to PEMH. Thus a referral bias cannot be excluded.

On the other hand, the size of tumor nodule in majority of patients was more than 5 cm which argues against the assumption that sticking to a surveillance program might have picked up patients at an earlier stage. It is therefore more likely that patients with more advanced disease did not report to this hospital.

The limitation of our study was possible referral bias. Another limitation was data being from a single center which might not necessarily be generalizable to the rest of country. It is recommended that future researches on HCC be carried out at multiple centers and referral bias be minimized. It is of critical importance for all the healthcare professionals involved in care of patients with HCC, to make themselves familiar with the common clinical features of this important tumor. Regular surveillance should be done in all at risk patients as per recommended guidelines to diagnose the HCC at an early stage, where the patients can be offered a treatment modality with favorable outcomes. If we are able to diagnose HCC at an early stage, outlook can be favorable

Table 3: Clinical Profiling of HCC Patients

		Number of patients(%)
Metastases	Nil	90(90%)
	Yes	10(10%)
Vascular involvement	Nil	85(85%)
	Main portal vein	4(4%)
	Branch of portal vein	9(%)
	Portal & Mesenteric veins	1(1%)
	Inferior vena cava & Portal vein	1(1%)
Tumor size (cm)	< 3	17(17%)
	3-5	23(23%)
	>5	60(60%)
Number of HCC lesions	1	62(62%)
	2	11(11%)
	3 or more	27(27%)
Child-Pugh Class	A	68(68%)
	B	30(30%)
	C	1(1%)
BCLC Stage	0	1(1%)
	A	34(34%)
	B	42(42%)
	C	18(18%)
	D	5(5%)
ECOG Score	0	49(49%)
	1	38(38%)
	2	7(7%)
	3	6(6%)
Alfa Fetoprotein Level (ng/ml)	<8.5	42(2%)
	8.6 – 100	24(24%)
	100.1 - 1000	15(15%)
	>1000	19(19%)

for these patients with potentially curative treatments now available

CONCLUSION:

HCV was the most common underlying etiology. Significant number of the patients were asymptomatic at the time of diagnosis. Majority of subjects reported with the complaint of abdominal pain and had no underlying co morbidity. No metastases were found in majority of cases.

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Original Article DOI: https://doi.org/10.51985/JBUMDC2019093

Hepatitis B and C Infection in Gujrat, Pakistan: A Cross Sectional Study

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ABSTRACT

Objective: This study was aimed to investigate the prevalence of Hep B and C, gender distribution, route of transmission, family history of Hepatitis and treatment options.

Study Design and Setting: This was a cross sectional study conducted at Dr Mujahid's Lab Bhimber road Gujrat, Pakistan.

Methodology: A total of 1181 individuals were included in this study. Among these 1181 individuals, 528 individuals were screened for hepatitis B and C by immuno chromatographic test (ICT) at Dr. Mujahid's Lab, Bhimber road, Gujrat while rest of the 653 individuals were asked about the hepatitis status by using a well-structured questionnaire. Other related questions were also included like age, sex, marital status, mode of transmission, and about treatment to evaluate the risk factors associated with disease. Data was analyzed by using SPSS 17.

Results: Prevalence of hepatitis B and C was 1.37% and 8.26% in surveyed while 1.5% and 9.1% in screened population of district Gujrat respectively. In surveyed hepatitis C patients, 72% were females and 28% were males. Among these, 91% patients were married and only 9% were unmarried. In case of hepatitis C, 9% stated polluted water, 9% medicines, 5.5% family history, 3.7% barber, 2% endemic, 2% dental surgery, 2% unhygienic food and 2% typhoid fever as a cause of infection while for hepatitis B, 33% individual's stated low standard hoteling as a cause of infection. Overall, incidence of hepatitis was higher in screened individuals as compared to surveyed.

Conclusion: This study concluded that hepatitis prevalence is high in district Gujarat. Moreover, Hepatitis C is more frequent than hepatitis B in this area.

Key Words: Hepatitis B, Hepatitis C, Prevalence

INTRODUCTION:

Hepatitis B and C infections appeared as a major health issues globally including Pakistan.[1] These viruses are one of the major causes of severe liver disorder, counting cirrhosis-related end stage liver disease and hepatocellular carcinoma (HCC).[2] Hepatitis B virus is infectious and spread chiefly by blood, body-fluid contact, and vertical transmission.[3] HBsAg in serum is the primary sero indicator of active HBV infection, whichever acute or chronic.[4] HCV infection is also widespread worldwide. It is transmitted in similar way to HBV and it is expected that approx 3% of the world's inhabitants carry HCV, with 3 to 4 million new infections every year.[5] Lack of information and health knowledge regarding safe dental treatments and general surgeries are the main threats for both hepatitis B and C transmission in Pakistan. There is a need to arrange awareness campaigns for health care professionals and general population to reduce this burden in our country.[6]

Both hepatitis B and C are prevalent in Pakistan. On the whole, prevalence varies between 2.6% and 5.3% for HBsAg and anti-HCV antibodies in Pakistan.[7] The estimated risk of HCV in Pakistan is 2.4-6.5%.[8] In case of hepatitis C, initially there are no symptoms but its infection can result in chronic liver disease which may cause liver fibrosis and result cirrhosis. The end result in some cases is hepatocellular carcinoma which appears several years later.[9]

Transmission of HBV is usually from contact with infected blood or blood products. It such, reuse of contaminated syringes and needles, vertical transmission, sexual contact and blood transfusion.[10] Hepatitis C also spreads via direct contact with the blood of an infected person. Earlier studies of clinical investigations had identified that transfusion of blood products is the main risk factor in the conduction of HCV infection.[11] Therefore, this study was aimed to investigate the prevalence of Hep B and C, gender distribution, route of transmission, family history of Hepatitis and treatment options.

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Received: 02-Sep-2019
Accepted: 12-Mar-2020

METHODOLOGY:

This study was consisted of two parts, 1st part was a survey with questionnaire Performa for patients. A total of 653 Performa's were filled randomly by individuals from district Gujrat, Pakistan. Informed consent of individuals including name, sex, age, address, contact number, NIC number along with hepatitis B and C related patient history such as route of infection, duration of disease, transfusion history, family hepatitis history, diabetes, obesity, injected drug users, surgery, vaccination status in case of hepatitis B, treatment type, treatment duration and different diagnostic tests related hepatitis were collected.

The 2nd part was consisted of screening 528 individuals randomly for hepatitis B and C by ICT (Acu-check) for further evaluation of hepatitis prevalence in district Gujrat. Three ml of blood was collected from each individual by disposable syringe and placed for clotting. Blood was centrifuged for three minutes at 5000 rpm to separate serum. Serum was collected in new apondrofs for qualitative detection of hepatitis B virus surface antigens and hepatitis C virus antibodies by immuno chromatographic assay. The data was enetered on SPSS version 17 and P value <0.05 was considered as statistically significant.

RESULTS:

A total of 653 individuals were recruited for part 1 of this study from Gujrat city and territories to estimate the prevalence of hepatitis in district Gujrat. Out of 653 surveyed individuals 371 were females and 282 were males. All the individuals were categorized in two age groups (Group 1: =40 years, Group 2: >40 years). Only 63 individuals were positive for hepatitis with 9 (1.37%) individuals positive for hepatitis B and 54 (8.26%) for hepatitis C.

Another 528 healthy individuals were screened for hepatitis by ICT to estimate its frequency in general population. There were 57% males and 43% females of screened individuals. A total of 10.6% individuals were positive for hepatitis including 9.1% positive for hepatitis C and 1.5% positive for hepatitis B.

In case of surveyed individuals 442 were married and 211 were unmarried. Out of 442 married individuals, 51 (11.53%) were positive for hepatitis including 49 (11%) positive for hepatitis C and 2 (0.45%) positive for hepatitis B. In unmarried individuals, 12 (5.6%) were positive for hepatitis with 5 (2.3%) positive for hepatitis C and 7 (3.3%) positive for hepatitis B. The risk of getting hepatitis seems to be four times higher in married people (Table 2).

Liver enzymes were elevated in both gender for hepatitis B and C. In hepatitis B patients, 55% individuals had elevated ALT while 41% individuals with hepatitis C showed elevated ALT levels. Elevated AST levels were same for both hepatitis B and C. In both types of hepatitis patients, up to 15% individuals were diabetic while 22% were obese with higher percentage in case of hepatitis C for both cases. Injected drug users were only 11% and 4% for hepatitis B and C respectively. Blood transfusion rate was very low in both hepatitis B and C cases (Figure 1).

Mostly patients did not know how they infected as only 33% and 35% individuals provide supposed information about their route of infection of hepatitis B and C respectively while rest of the patients have no idea about their infection route. In both hepatitis B and C, 33% patients had family history of hepatitis. The household hepatitis contact was 11% and 22% for hepatitis B and C respectively. Only few patients had their spouse infected with hepatitis (Figure 2).

Mostly patients preferred allopathic medicine for hepatitis treatment. As in case of surveyed individuals, more than 75% individuals provide information about allopathic medicine. Only few individuals were using homeopathic medicine hepatitis treatment.

About 11% and 9% patients used both homeopathic and allopathic medicines for hepatitis B and hepatitis C treatment respectively. Some individuals were not familiar with type

Table-1a: Prevalence of hepatitis in screened individuals

Age (Years)	Total positive (%)	HBV positive (%)	HCV positive (%)
Males			
≤40	16(2.45)	6(0.91)	10(1.52)
>40	5(0.76)	0(0)	5(0.76)
Females			
≤40	13(1.99)	1(0.15)	12(1.83)
>40	29(4.44)	2(0.3)	27(4.13)

Table 1b: Prevalence of hepatitis in surveyed individuals

Age (Years)	Total positive (%)	Hepatitis B (%)	Hepatitis C (%)
Males			
≤40	12(2.27)	7(1.32)	5(0.94)
>40	10(1.89)	1(0.18)	9(1.7)
Females			
≤40	13(2.46)	0(0)	13(2.46)
>40	21(3.97)	0(0)	21(3.97)

Table 2: Prevalence of hepatitis B and C in married and unmarried individuals

Marital Status	No. of individuals	Positive	HCV Positive	HBV Positive
Married	442	51 (11.53%)	49 (11%)	2 (0.45%)
Unmarried	211	12 (5.6%)	5 (2.3%)	7 (3.3%)
Total	653	63 (9.6%)	54 (8.2%)	9 (1.3%)

Figure 1- Relationship of hepatitis with Biochemical parameters.

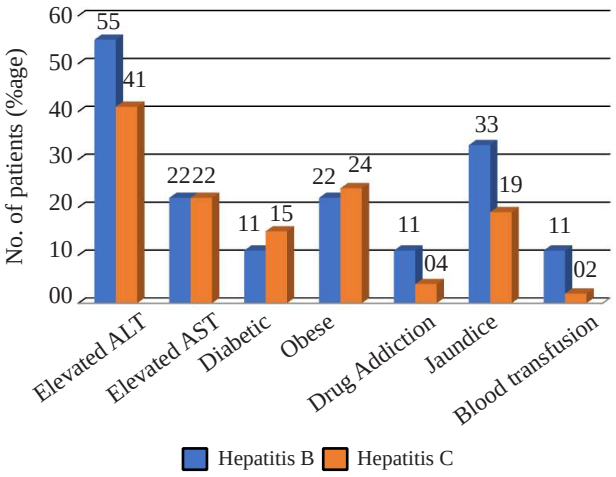


Figure 2- Relationship between hepatitis types with family status

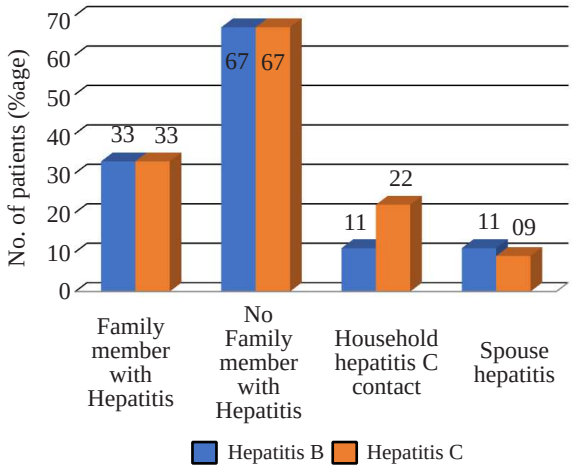
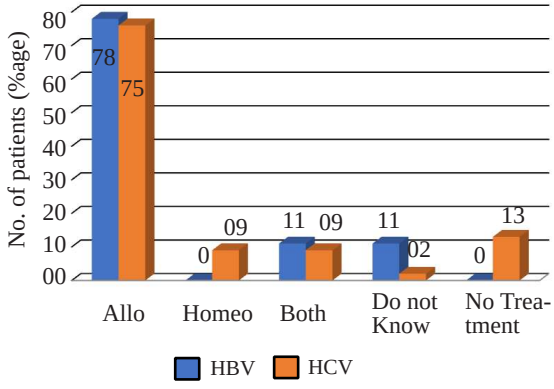


Figure 3- Types of treatment.



of medicine which they used. Surprisingly, 13% patients were not using any medicine for HCV. Only 33% and 31% of surveyed patients were cured in case of hepatitis B and C respectively (Figure 3).

DISCUSSION:

In Pakistan, mostly people are ignorant to health-related issues counting hepatitis B and C infections due to low literacy rate. Most of the HBV and HCV infected patient's diagnosed hepatitis when they visited doctor for other health issue such as dental treatment and surgeries. Similarly, in our survey, mostly patients were unaware of disease and they diagnosed when they came to doctor for some other health problems.

In present study, 1.37% and 1.5% of surveyed and screening individuals had hepatitis B respectively. For hepatitis C, we founded 8.26% and 9% of surveyed and screening individuals correspondingly. These are almost similar to other studies including Khan et al [12] and Basit et al.[13] Basit et al established that 1.3%, 8.4% and 3% for HBV, HCV and co infection of hepatitis B and C respectively. The gender wise hepatitis B distribution was also nearly similar to Basit et al, as he founded 6.3% and 3.7% for males and females while in this study the distribution was 6.7% and 3.3% for males and females respectively. We founded 2.8% and 7.2% hepatitis C male and female patients while Mushtaq et al stated 3.7% and 6.3% hepatitis C male and female's patients respectively[14], indicating an increasing trend of hepatitis C in females.

In present study, males had higher prevalence of hepatitis B which was also established by Wasfi and Sadek, 2011[15] while in case of hepatitis C females had higher prevalence supported by Mushtaq et al. [14] Mushtaq et al also conducted the study in district Gujrat. Individuals >40 years of age had high frequency of hepatitis C than younger individuals. It was reported by many studies that prevalence of hepatitis C rises after 40 years of age.[16,17] We founded similar results for hepatitis C with 61% and 62.5% individuals aged greater than 40 years of surveyed and screening population while hepatitis B contradicted this with 78% and 87.5% individuals aged less than 40 years of surveyed and screening individuals respectively. The prevalence of hepatitis C was higher in married individuals than in unmarried. It was supported by different studies including Adekeye et al and Ayele and Solomon.[18,19] In present study, 91% hepatitis C patients were married while for hepatitis B the result was again contradicted. It might be due to the reason of high number (59%) of individuals with age less than 40 years. The higher prevalence in married people can be due to the pre-exposure of hepatitis which later can be transmitted to spouse or elderly people had less information and knowledge about infectious diseases and their prevention. To reduce the incidence of hepatitis, general screening of blood, awareness about hepatitis B and C transmission and risk factors should be addressed to general population by campaigns.

CONCLUSION:

It was concluded that hepatitis C was more prevalent than hepatitis B in district Gujrat. High prevalence was found for females in case of hepatitis C while for hepatitis B it was vice versa.

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Original Article DOI: https://doi.org/10.51985/JBUMDC2020011

Frequency of Electrolyte Disorders and Its Effect On Mortality Among Children Admitted In Pediatric Intensive Care Unit

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ABSTRACT

Objective: To determine the frequency of electrolyte disorders, i.e., serum sodium and potassium and to evaluate its effect on mortality rate among children admitted at the pediatric intensive care unit.

Study Design and Setting: This was a descriptive cross sectional study conducted at Pediatric Intensive care unit of Civil Hospital Karachi from April to December 2017

Methodology: Informed consent was obtained from 150 parents of the children who fulfill the inclusion criteria. Laboratory data (serum sodium and serum potassium) were recorded during the stay in the pediatric intensive care unit. Data was analyzed using SPSS version 20. Mean ± S.D was calculated for quantitative variables. Frequency and percentage were calculated for gender, electrolyte disorders and mortality. Effect modifiers were controlled by stratification of age, gender and electrolyte disorders (Hypernatremia, Hyponatremia, Hyperkalemia, and Hypokalemia). Post-stratification, Chi-squared test was applied. P-value = 0.05 was taken as significant.

Results: Out of 150 patients, electrolyte disorders in terms of serum sodium and potassium, were found in 86(57.3%) children. Mortality in children with electrolyte disorders was found to be 46(53.5%) which was significantly higher (P<0.001) than patients without electrolyte disorders 40(46.5%). Hypernatremia was found in 48(32%), hyponatremia 24(16%), hyperkalemia 21(14%) and hypokalemia in 42(28%) patients.In comparison; of electrolyte disorders with mortality; significant association was found in hypernatremia (P<0.001), and hyperkalemia (P<0.001).

Conclusion: The most common electrolyte abnormalities were hypernatremia and hypokalemia. Mortality was significantly higher in subjects with electrolyte disorders, especially hypernatremia and hyperkalemia.

Keywords: Electrolyte Disorders, Intensive care unit (ICU), Mortality, Potassium, Sodium

INTRODUCTION:

Electrolytes such as sodium and potassium play a vital role in maintaining cellular structure and function, generating energy and controlling the potential for action across cell membranes, especially those of muscles and nerve cells, which play an important role in critically ill patient's outcome.[1,2]Any disruption in the serum level of these electrolytes may lead to a variety of clinical disorders including neuromuscular dysfunction and life-threatening cardiac arrhythmias, particularly where more than one electrolyte is deficient.[3,4] The most severe complications of hypokalemia are cardiac arrhythmia and acute respiratory failures due to respiratory muscles paralysis while other adverse effects include muscle weakness, fatigue, rhabdomyolysis, nausea and constipation.[5,6]Although hyperkalemia is associated with neuromuscular symptoms such as extreme muscle weakness or ascending muscle paralysis, it can also cause paresthesiaas, palpitation, and cardiac conduction that can lead to adverse outcome in patients in intensive care unit patients.[7] Hyponatremia is also a frequent electrolyte abnormality observed in critically ill patients.[8,9] Severe acute decline in serum sodium concentration may cause neurologic dysfunction such as seizures and coma. The most severe complication of hyponatremia is cerebral edema that may lead to catastrophic conditions like brain stem herniation and cardiac arrest[10]. On the other hand; hypernatremia can cause brain hemorrhage like subdural and subarachnoid hemorrhages due to the rupture of bridging veins because of a decrease in brain volume. The clinical symptoms are progressive that might commence with irritability, agitation, lethargy, and irritability and can progress to twitching, seizures, and coma[11]. Thus, maintaining the levels of potassium and sodium within acceptable limits is therefore well understood in most

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Received: 06-Feb-2020
Accepted: 22-Apr-2020

intensive care units. They are known as prognostic predictors and their disruption can be avoided by considering the appropriate intravenous fluids and nutrition[12].

Ample literature on electrolyte imbalance have concentrated on the occurrence and prevalence of such electrolyte disorders in patients in the intensive care unit but there is scarce literature on the impact of such disorders on mortality rate. Pakistan has a greater number of children with electrolyte disorders admitted every day to pediatric intensive care unit. Despite of this, the research on the prevalence of electrolyte disorders and its effect on mortality rates are lacking within our population. In fact, due to a lack of resources and clinical expertise about the treatment of electrolyte disorders, mortality in our population is estimated to be higher than in the western world.[13, 14] Therefore, the aim of this study was not only to assess the frequency of serum sodium and potassium disorders but also to assess their effects on mortality rate in children admitted to the pediatric intensive care unit in Civil Hospital Karachi. The outcome of this study would be beneficial to take aggressive measures against electrolyte imbalances to reduce the mortality.

METHODOLOGY:

All children between the ages of 2 months to 12 years who were admitted in Pediatric Intensive Care Unit, Civil Hospital Karachi from April to December 2017 with duration of at least 48 hours of PICU stay, were included in the study. Patients undergoing emergency or elective surgical procedures, patients on diuretic therapy and patients with documented chronic or co-morbid illness were excluded such as endocrinopathy, cerebral palsy, chronic liver disease, congenital heart disease. Patients were enrolled through non-probability consecutive sampling. The demographic data of all the participants regarding age, sex and admitting diagnosis was noted on a predesigned proforma. Blood samples were drawn on admission to find out the initial serum levels of sodium, potassium. Then, the levels were repeated 24 hourly or earlier (if needed). Determination of electrolytes was the standard examination in all patients admitted to the pediatric intensive care unit at Civil Hospital, Karachi. No personal identity revelation was made on the questionnaires and confidentiality of all data was maintained during the study phases. There is no conflict of interest or funding source to declare.The normal serum levels of sodium and potassium are given below[15].

Normal serum sodium level 135mEq/L-145 mEq/L.

Normal serum potassium level 3.4mEq/L-5.3 mEq/L.

Any value below or above the following cut-off values was considered to be anomalous suggesting an electrolyte imbalance.

For this study, Mortality was recorded for those patients, who died after at least 48 hours of admission in Pediatric Intensive care unit. Sample size of the study (n=142) was calculated by taking prevalence of hypernatremia i.e. 6.3%.[16] Confidence Interval of 95% and margin of error 4%. For convenience, a total of 150 patients were enrolled. Data was analyzed using SPSS version 20. Mean ± S.D was calculated for quantitative variables. Frequency and percentage were calculated for gender, diagnosis at admission, electrolyte disorders and mortality. Effect modifiers were controlled by stratification of age, gender and electrolyte disorders (Hypernatremia, Hyponatremia, Hyperkalemia, and Hypokalemia). Post-stratification, Chi-squared test was applied. P-value = 0.05 was taken as significant.

RESULTS:

A total number of 150 patients were included in this analysis with a mean age of 50.33 months ±46.46 (Table.1) with Confidence Interval (42.84-57.83). Out of these 150 patients, 93 (62%) were male and 57 (38%) were female.Regarding the admitting diagnosis, majority i.e. 52 (34.66%) had respiratory illness, 36(24%) had neurological illness, 28 (18.66%) had sepsis/infection, 12 (8%) had cardiovascular problem, 10 (6.66%) had gastrointestinal ailment and 12(8%) were categorized in miscellaneous group including endocrine diseases.

Mixed electrolyte disorders (serum sodium and potassium abnormality) were found in 86(57.33%) children. Hypernatremia was found in 48(32%), Hyponatremia 24(16%), Hyperkalemia 21(14%) and Hypokalemia was found in 42(28%) children. Hypernatremia and Hyperkalemia were significantly more common in patients who expired (62.5%) (P=0.0001), and (28.8%) (P=0.0001) respectively (Figure2 & 3).

Overall, mortality was found to be 34.66% (52 out of 150 patients). Mortality in children with electrolyte disorders was found to be 46(53.5%) which was significantly higher (P=0.0001) than children without electrolyte disorders 40(46.5%)(Figure1).

DISCUSSION:

This comprehensive case study was carried out at Civil Hospital Karachi to assess the prevalence of electrolyte disorders and their impact on mortality in children admitted in pediatric intensive care unit.

Fluids and electrolyte disturbances are one of the most common clinical problems encountered in the intensive care unit. Disturbances in fluid and electrolyte homeostasis can occur in critical conditions such as severe burns, sepsis, trauma, heart failure and brain damage. In most cases, electrolyte disturbances may remain subtle and may lead to higher mortality and morbidity.[17]

In our study, mixed electrolyte disorders were found in 86(57.33%) children. Since the four electrolyte disorders (Hypo/Hypernatremia, Hypo/Hyperkalemia) were considered together and imbalance among any of them was noted, this might be the reason for the high incidence. Cummings BM

Table 1. Demographic characteristics and main clinical variables (n=150)

Parameter	Frequency	Percentage%
Mean Age(in months)	55.33±46.46	
Gender		
Boy	93	62
Girls	57	38
Admitting diagnosis		
Respiratory	52	34.66
CNS	36	24
Sepsis/infection	28	18.66
CVS	12	8
GIT	10	6.66
Miscellaneous	12	8
Electrolyte Disorders		
Yes	86	57.33
No	64	42.77
Hypernatremia		
Yes	48	32
No	102	68
Hyponatremia		
Yes	24	16
No	126	84
Hyperkalemia		
Yes	21	14
No	129	86
Hypokalemia		
Yes	42	28
No	108	72
Patients Survived		
Yes	98	65.34
No	52	34.66

Figure 1. Comparison Of Overall Mortality With Mixed Electrolyte Disorders (N=150)

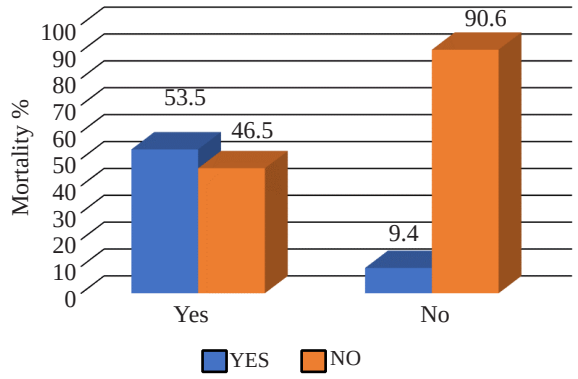


Figure 2. Comparison of mortality with serum sodium levels (n= 150)

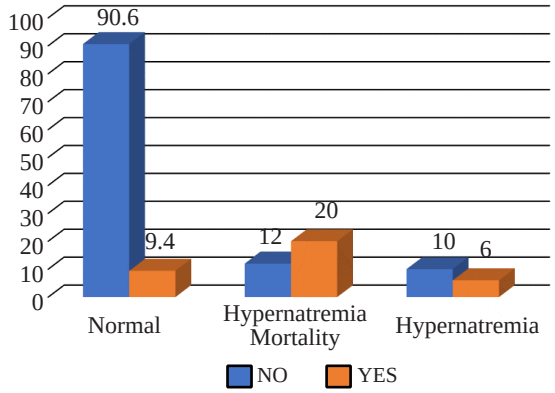
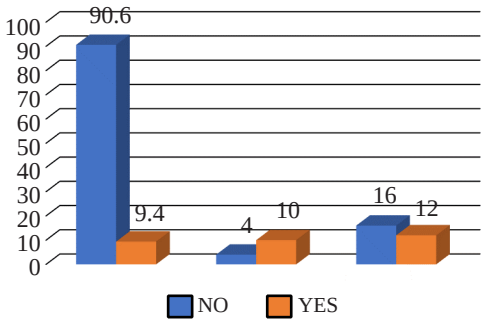


Figure 3. Comparison of mortality with serum potassium levels (n= 150)



found potassium abnormalities alone to be around 40%.[18] Another study focused at all five electrolytes showed 60% incidence.[2] This proves the statement that electrolyte abnormalities are very common in critically ill children.

Majority had respiratory (34.66%), neurological (24%) and infective/sepsis (18.66%) etiology as noted in previous studies.[2, 19, 20] The reason for less number of gastrointestinal cases (3.96%) could be the initial stabilization in ER and later shifting to ward upon improvement thus bypassing the PICU stay. This is important because gastroenteritis in children is the major source of electrolyte imbalance, but prompt and proper treatment may avoid PICU admission.

A study conducted in Kathmandu identified hyponatremiato be 56%, followed by hypokalemia 46%**.** Almost 37% of patients had mixed electrolyte imbalances[21]. However, our study showed hyponatremia (16%), hypokalemia (28%) and mixed electrolyte disorders (57.33%)

In another study, published in India, mixed electrolyte imbalances were observed in 33% of children. The most frequent electrolyte imbalance was Hyperkalemia which was found in 14.4% similar to our study in which hyperkalemia was found in 14% patients. Hyponatremia was found to be 6.9% compared to 16% of hyponatremia in our study[22].

Another prospective study showed that severe hyponatremia was associated with three fold increase risk of morbidity and mortality[23].

Most of the literature has reported hyponatremia to be more prevalent than hypernatremia i.e. 23.2% vs. 16.7%[15], 27.43% vs. 3.5%[6], 50.5% vs. 9.4%[2]. Sachdev A noted hyponatremia to be 19.3%[20]. However, hypernatremia was found in 48% of cases and hyponatremia in 16% cases. This might be due to the institutional policy of using 0.9% dextrose saline as maintenance intravenous fluid rather than half strength or other hypotonic solutions in children above one month of age.

One research concluded that potassium imbalance is frequent among children admitted in PICU. Hyperkalemia was observed in 5.4% of 727 children enrolled in this study, while in our study hyperkalemia was reported in 14%. This variation in prevalence could be due to the fact that in this study hyperkalemia was defined as a serum potassium value > 6 mEq / L. However, in this study serum potassium levels > 5.3 mEq / L are considered to be hyperkalemia. [24]

In a study conducted by Kathryn Maitland, it was found that extreme hyperkalemia wasassociated with falciparum malaria in 9 children (16%), of whom 7 (78%) died shortly after admission[25].

Overall mortality in this study was 34.66% (52/150). However, mortality documented by Panda I was 23.73%[6] and by Jan M et al as 22.8%[26].

In one local study, results showed that out of 101 children enrolled, electrolyte imbalances were present in 85 (84.15%) children. Among these patients, the most frequent abnormality noted was hypocalcemia which was seen in 49 (57.64%) patients, followed by hypernatremia in 32 (37.64%) cases and hypophosphatemia in 30 (35.29%) patients. Hypokalemia was observed in 26 (30.58%) and hypermagnesemia in 18 (21.17%) children. The study found that electrolyte imbalances in critically ill children are associated with a higher risk of mortality. Early mortality, i.e. within 48 hours of admission, was reported in 14 cases of which 12 had electrolyte disturbances.[27].

In another study carried out at a hospital in India in PICU, results revealed that out of132 children enrolled in the study, 71 (53.79%) had an electrolyte abnormalities. Among these patients, 29 (40.85%) had hyponatremia, 9 (12.68%) had hypernatremia, 13 (18.31%) had hyperkalemia, 8 (11.27%) had hypokalemia. They also found that patients with electrolyte abnormalities had relatively longer hospital stays.[28] The limitation of this study was the smaller sample size; a study with large sample size with multiple centers in Pakistan to validate the results of should be conducted in future. Electrolyte disturbances in children become obvious during illness and early detection and management of these derangements is essential to avoid serious life-threatening situation. They are considered as significant and reliable indicator of mortality as shown by this study. Another limitation as this study was that the mortality might be primarily due to underlying clinical disorder and not the electrolyte disturbances. For this purpose, children with documented chronic or co-morbid illnesses should have been excluded and mortality was recorded only in those patients with duration of PICU stay of at least 48 hours. Serial serum electrolytes tests are helpful in preventing severe life-threatening circumstances. Thus, the need for early interventions to correct these imbalances is imperative in reducing the mortality.

CONCLUSION:

The results of this study showed higher mortality in children with electrolyte disorders especially hypernatremia and hyperkalemia, thus, concluding that electrolyte imbalance was a significant predictor of prognosis in seriously ill patients.

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Original Article DOI: https://doi.org/10.51985/JBUMDC2019116

Correlation Between Clinical Oral Dryness Score and Salivary Flow Rates in Active and Passive Smokers

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ABSTRACT

Objective: To evaluate the mean clinical oral dryness score (CODs) and salivary flow rate (SFR) in subjects exposed to active and passive smoking. The secondary aim was to determine the correlation between CODs and SFR and potential factors associated with CODs and SFR in our subjects.

Study Design and Setting: The clinical observational study was conducted at the Outpatient department of oral diagnosis at Altamash Institute of Dental Medicine, Karachi from Jan 2019-Jul 2019.

Methodology: A total of 217 participants of ages 15 – 80years coming for routine dental checkup of either gender were included. A thorough oral examination was performed for all the subjects. A non-stimulated saliva sample was collected from the oral cavity of subjects in a graduated container. The salivary flow rate was noted in ml/min for 5 minutes. Assessment of oral dryness/hypo-salivation was examined through CODs (clinical oral dryness score).The data were analyzed using SPSS software version 23.

Results: The mean COD score and SFR were calculated as 1 and 0.42 ml/5min respectively. The Pearson's correlation between COD score and SFR level was calculated as -0.281 (negative correlation) such as the SFR significantly decreased when the COD score increased ($p<0.05$). The age, gender, smoking status, betel quid and areca nut consumption showed statistically significant difference in mean COD score and SFR levels ($p<0.05$).

Conclusion: Salivary flow rate was significantly decreased with increase in COD score thus having an implication on oral dryness feeling in these participants.

Keywords: Areca nut, Betel quid, Mouth dryness, Hypo-salivation, Smoking.

INTRODUCTION:

The oral tissues are continuously bathed with saliva in healthy individuals. The continuous flow of saliva helps to maintain oral hemostasis and helps in defense against microorganisms.[1-3] The salivary flow rate shows great variation from 0.3 - 0.65ml/min level to 1.5-6 ml/min when stimulated by chewing or by mild strength citric acid.[4] The salivary glands have secretions which plays vital role in the protection of mucosa from feeling of dryness. The feeling of dry mouth is a subjective and complex condition and affects approximately 46% of the population.[5] Clinically, mouth dryness may differ from a small decrease in salivary flow with temporary inconvenience to severe deterioration of oral health and concomitant psychosomatic indisposition. The hypofunction of saliva has mainly been associated with decrease in salivary flow rate (SFR) and estimated as below 3 ìL/cm^3/min.[1,2,6] Hence, the most appropriate technique for the diagnosis salivary gland disorder is to measure SFR and it can be used as easily available, safe and non-invasive diagnostic modality to diagnose different systematic and oral conditions.[7,8]

Clinical oral dryness score (CODS) is a new tool designed to assess oral dryness by clinical and visual inspection of the oral cavity based on several signs of oral dryness such as the presence of frothy saliva, the dryness of the oral mucosa and stickiness of the dental mirror to the tongue or the buccal fold. CODS closely determines both the unstimulated salivary flow and the thickness of mucin layer over the epithelium (mucosal wetness) suggesting a physiological basis to the feeling of dryness.[9] Osailan et al. also suggested CODS as a reliable tool for the estimation of hyposalivation severity.[3]

Hence, literature has shown varying results such as weak to no correlation between mouth dryness and SFR.[5,10-12] In Pakistan, there is lack of baseline data, and international data isn't applicable in our population due to variation in genetic and personal habits. Therefore, the aim of current study was to evaluate the mean CODS and SFR among

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Received: 22-Oct-2019
Accepted: 07-Apr-2020

patients exposed to active & passive smoking. The secondary aim was to determine the degree of correlation between CODS and SFR in these patients. The potential factors associated with changes in SFR and CODS were also determined in this study.

METHODOLOGY:

The clinical observational study was conducted at the department of oral pathology at Altamash Institute of Dental Medicine, Karachi from January 2019-July 2019. The sample size was estimated using WHO sample size calculator, by taking statistics for mean salivary flow rate as 1.93±0.65[13], keeping margin of error as 8.65% and confidence level as 95%. The non-probability consecutive sampling technique was employed which gave a sample size of 217 patients in total. All the patients of 15-80 years coming for routine dental checkup of either gender were included in the study. Patients who were taking systemic medications such as beta-blockers or steroids, patients with severe head or neck injury, undergoing radiotherapy, wearing dentures, patients with learning disability or pregnant women were excluded from the study.

Approval from ethical review committee was obtained prior to the commencement of study. All the participants were informed about the nature of the study and written informed consent was taken. A pre-designed proforma was used to collect the demographic information, along with the data regarding smoking habit of each individual (frequency and duration). An individual who had smoked >100 cigarettes (including hand-rolled cigarettes, cigarillos, cigars) in their lifetime and had smoked at least one cigarette in the past month or 28 days were labelled as *active smokers*. The data regarding the consumption of betel quid (pan) and areca nut (chalia) was also obtained. An individual who had consumed betel quid or areca nut more than 100 times in their lifetime and had consumed at least five times in the past month or 28 days were labelled as *consumers*. A thorough oral examination was performed for all the subjects. Each subject was advised not to eat, drink, smoke or perform any oral hygiene methods for a minimum of 60 minutes before and during the collection of the saliva sample. The subject was seated upon the dental chair. A non-stimulated saliva sample was collected from the oral cavity of each subject who were asked to drool in a graduated cup every 1 minute for 5 minutes, in a ventilated and well illuminated room. The saliva collection was performed within the working hours of the OPD at Altamash Institute of Dental Medicine, Karachi. SFR was measured in ml/5min. Assessment of oral dryness/ hypo-salivation was examined through CODS (clinical oral dryness score)[14]. The data were analyzed using SPSS computer software version 22. Quantitative variables such as age, COD score and salivary flow rate (SFR) were reported as mean and standard deviation. Qualitative variables like gender, ethnicity, smoking status and consumption of betel quid and areca nut were reported as frequency and percentage. Effect modifiers like age, gender, ethnicity, smoking status, consumption of betel quid and areca nut were addressed through stratification. Post-stratification independent t-test was applied. P-value of <0.05 was taken as statistically significant.

RESULTS:

In this study, a total of 217 participants attending for routine dental checkups were evaluated. The mean age of the study participants was reported as 32.86±6.30 years ranging from 22- 55 years. Out of 217 participants, 145 were males (66.8%) whereas 72 were females (33.2%). More than half of the participants were Urdu speaking (58.5%) and 19.8% spoke in Sindhi. About 24.9% of the participants were active smokers and average number of cigarettes smoked by them per day was reported as 5.09 ranging from 1-11 cigarettes per day. Out of 217 participants, 16.6% were betel quid and areca nut consumers. (Table 1)

Figure 1 shows the average COD score to be 1 within the range of 0-4. Whereas, Figure 2 shows that the mean SFR was 0.42 ml/5min ranging from 0.2-1 ml/5min. The Pearson's correlation between COD score and SFR level was calculated as -0.281 (negative correlation). It was inferred from our results that CODS was a significant predictor of SFR, as the value of SFR significantly decreased with an increase in the COD score ($p<0.05$).

Stratification of mean COD score and SFR ml/5min was done with respect to potential effect modifiers. The age, gender, smokers, betel quid and areca nut consumers showed statistically significant difference in mean COD score and SFR level ($p<0.05$). (Table 2)

DISCUSSION:

In last few decades,multiple researches have reported different aspects of mouth dryness and salivary flow rate. Yet, there is a big gap in the evidence for relation between salivary flow rate and oral dryness. In the present study, the mean CODS was estimated as 1±1.12 in patients coming for routine dental check up and mild dryness (COD score 1-3) was present in majority of them. A study conducted by et al. also demonstrated similar results in healthy controls i.e. mean CODS of 1.0 ± 0.9 whereas SFR value in our study were estimated at 0.42±0.10 ml/5min.[3] Hijjaw O et al. in their research found the mean stimulated whole saliva flow rate as 0.46 (±0.44) mL/5min which is slightly higher than that seen in present study.[10] In the present study, a negative weak correlation was observed between CODS and SFR (r=-0.281). Hence the results suggest that flow of saliva significantly decreased when the COD score increased ($p<0.05$). In line with our findings, Correia et al. found moderate negative correlation between CODS and SFR (r=-0.515, $p<0.05$). Patients with no oral dryness (CODs 0-1) had high rate of unsimulated SFR>0.5ml/5min whereas patients with moderate dryness had decreased rate of unsimulated SFR>0.1ml/5min ($p<0.01$).[15] In a study by

Table 1: Descriptive Characteristics of Study Population

Quantitative variables	**Mean**	**SD**
Age in years	32.86	6.304
Qualitative variables	**n**	**%**
Gender		
Female	72	33.2
Male	145	66.8
Ethnicity		
Sindhi	43	19.8
Balochi	20	9.2
Pathan	15	6.9
Punjabi	12	5.5
Urdu	127	58.5
Smokers		
Active	54	24.9
Passive	163	75.1
Betel quid (Pan)		
Yes	36	16.6
No	181	83.4
Areca nut (Chalia)		
Yes	36	16.6
No	181	83.4

Figure 1: Descriptive Statistics of Salivary Flow Rate

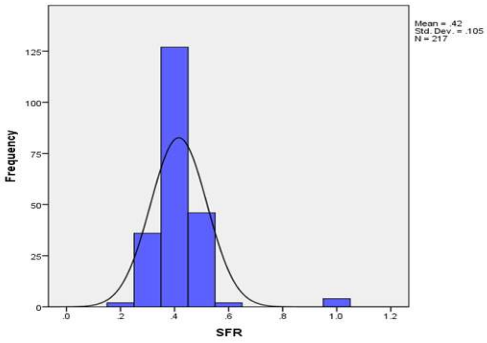
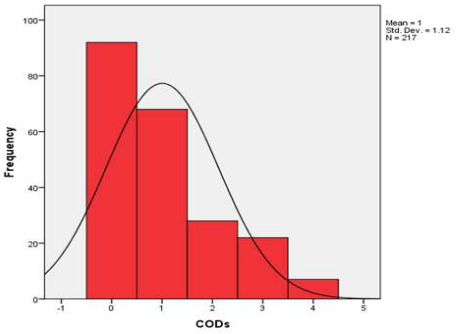


Figure 2: Descriptive Statistics of Clinical Oral Dryness Score



Farsi, it was seen that participants who complained of mouth dryness had significantly lower salivary flow rate as compared to non-complainers.[4] Osailan et al. also found negative correlation between CODS and SFR(p<0.01) in their research.[3] In the study by Jager et al., the relationship between

Table 2: Stratification of Cod Score And Salivary Flow Rate

	CODs			**SFR**		
Variables	**Mean**	**SD**	**P-value**	**Mean**	**SD**	**P-value**
Age groups						
</=35 years	0.87	0.99	0.001	0.42	0.10	0.01
>35 years	2.59	1.27		0.35	0.07	
Gender						
Male	1.14	1.11	0.009	0.38	0.06	0.001
Female	0.72	1.07		0.46	0.14	
Ethnicity						
Sindhi	1.00	1.17	0.509	0.41	0.10	0.631
Balochi	0.80	0.76		0.44	0.14	
Pathan	0.60	0.82		0.40	0.08	
Punjabi	1.17	1.03		0.39	0.05	
Urdu	1.07	1.18		0.41	0.10	
Smokers						
Passive	0.87	1.05	0.001	0.43	0.09	0.001
Active	1.43	1.22		0.37	0.14	
Betel Quid						
No	0.92	1.07	0.01	0.42	0.11	0.001
Yes	1.44	1.22		0.35	0.08	
Areca nut						
No	0.88	1.04	0.001	0.43	0.11	0.001
Yes	1.61	1.29		0.34	0.06	

CODS and SFR was evaluated and a weak negative correlation between CODS and hyposalivation group (r=-0.33, p<0.01), moderate correlation between CODS and normal & high salivation groups was observed respectively (r=-0.56, p<0.01 &*r* = - 0.55, p<0.01).[14] Hence CODS, being a sensitive tool, can be utilized in general oral examination and for distinguishing patients with normal salivation from those with hyposalivation.

In the current study, the average age of the participants was estimated as 32.86 years. Majority of our selected patients were males (66.8%) and less than and equal to thirty five years of age (92.1%). Mouth dryness significantly increased with increase in age (p<0.05) whereas SFR significantly decreased (p<0.05). Furthermore, males showed significantly high values of CODS and lower values of SFR as compared to females (p<0.05). Dissimilar findings were witnessed in the study by Farsi in which no statistically significant difference was found in dry oral cavity with respect to age and gender (p>0.05).[4] Ship et al. and Osterberg et al. also showed no change in SFR with increase in age but Nederfors et al. found higher prevalence of oral dryness with increase in age.[16-18] This might be due to increase in medication intake among elderly patients.

In the present study, the mean SFR of active smokers, betel quid and areca nut consumers was significantly low whereas CODS wassignificantly high as compared to passive smokers

and non-consumers of betel quid and areca nut($p<0.05$). In the studies by Alaee et al., Singh et al. and Rad M et al. significantly low mean SFR was reported in smokers as compared to non-smokers ($p<0.05$).[13,19,20] Whereas, the studies by Khan GJ et al. and Rehan et al. found no statistically significant relationship between smokers and SFR ($p>0.05$).[8,21] Furthermore Rehan et al. also concluded in their study that tobacco consumption had no effect on resting mouth SFR . Patil et al. in their study showed that consumers of cigarettes or chewable tobacco or both had significant effect on progression of oral abrasions.[22] In the study by Abdul et al. significantly high ratio of SFR among areca nut consumers (35.7 mm) was reported when compared to SFR of healthy individuals at 3rd min (30.7mm), but with increasing frequency, duration and exposure of areca nut consumption the SFR significantly decreased.[23] The personal habits such as smoking, consumption of areca nut and betel quid influence the individual's oral health in the long term. Previously, it has been demonstrated that the presence of nicotine in the smoke and alkaloids in areca nut directly affect the SFR as well as oral and dental health.[24,25] Initially with the consumption of these products the flow of saliva improves, but salivary secretion is usually decreased with long-term use. Among the limitation, it was the single centered study and there was an equal distribution of active and passive smokers, which may affect the correlation. It is recommended that COD score is a useful, simple and adequate tool for the routine investigation for evaluating patients complaining of mouth dryness.

CONCLUSION: Salivary flow rate was significantly decreased with increase in COD score thus having an implication on oral dryness feeling in these participants.

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Original Article DOI: https://doi.org/10.51985/JBUMDC2019140

Diabetes Self-Management Education and Practices among Type 2 Diabetic Patients

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ABSTRACT

Objective: To compare the knowledge and practices of diabetes self- care management among type 2 diabetic patients in two hospitals of Karachi.

Study Design and Setting: A cross sectional study was carried out at two Tertiary Care Hospital of Karachi from March 2018 to August 2018.

Methodology: A total of 120 subjects of type 2 diabetes were included in the study. Data was collected through structured questionnaire. Knowledge regarding diabetes includes normal blood sugar level, symptoms of low and high blood sugar and management of these symptoms. Structured questionnaire was used to collect information of sociodemographic characteristics, knowledge and attitude of diabetes and self-care management practices. Data was analyzed by SPSS version 21. P value less than 0.05 considered as significant

Results: Majority of the participants were females (55%) and males were (45%).The duration of diabetes in majority of participants, (43.3%) was less than 5 years. From total 53.3% of our study participants were aware about the knowledge of diabetic complications. Approximately ,59.6% participants thought visit to eye specialist is important and about 44.16% thought that monthly visit to hospital for general health is important for diabetic patients. When asked about early signs of development of complications 48.3% participants thought that development of foot ulcers ,83% thought diabetes was strongly associated with obesity. Total, 76.6% participants thought that plan of meal is important. Total, 30.83% participants were in agreement with this thought that diabetes was strongly associated with obesity.

Conclusion: The knowledge of self-care practices in diabetic patients was average in this study.

KEY WORDS: Diabetes Complications, Diabetes mellitus, Diabetes self-management education (DSME).

INTRODUCTION:

Diabetes mellitus (DM) is a medical condition characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. This may lead to long-term complications microvascular or macrovascular which includes damage, dysfunction and failure of various organs, in particular the eyes, kidneys, nerves, heart and blood vessels. Type 2 diabetes occur most commonly due to inability of the body to use insulin properly, resulting in increased blood glucose levels.[1]

Diabetes self-management education (DSME) is defined as "the process of facilitating the knowledge, skill, and ability necessary for diabetes self-care"[1].Diabetes self-management education (DSME), the process of teaching individuals to manage their diabetes, has been considered an important part of the clinical management of individuals with diabetes.[2] DSME provides informed support, self-care and self-management instructions in order to improve quality of life and decreases the probability of diabetes complications.

It was estimated that in 2017 there were 451 million (age 18-99 years) people with diabetes worldwide. These figures were expected to increase to 639 million by 2045.[3] In Pakistan approximately 7.89% populations is affecting with diabetes mellitus per annum. In this context, Pakistan is ranked seventh in diabetes prevalence.[4] Diabetes prevalence has been rising more rapidly in middle and low-income countries. According to WHO, the global prevalence of diabetes is 8.5% in 2014 and the burden of diabetes has doubled from 1980 to 2014.Several studies revealed that lifestyle modification in obese patient has been effective in achieving a very good glycemic control.[5]A study in Malaysia shows that public hospitals having specialist diabetologist were more inclined towards treating the complication of diabetes while in public health clinics having general practitioners for the treatment of diabetes, only focused on controlled blood pressure and HbA1c under normal ranges.[6] The mortality risk of Type 2 can be reduced by DSME among type 2 DM patients.[7] In a review including 118 unique interventions reported significant changes (61.9%) in A1C. Overall mean reduction in A1C was observed from 0.74 and 0.17 in intervention and control groups; as average absolute reduction in A1C of 0.57.[8]

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Received: 18-Dec-2019
Accepted: 15-Apr-2020

In a study of DSME programs among older adults revealed an absolute reduction in HbA(1c), lipid profile and blood pressure.[9] The study by Sherifali D[9] depicted that DSME programs improves the clinical outcomes by maintaining the blood pressure and lipid profile, and eventually improves the health status and quality of life of an individual.[10] DSME programs required proper assessment, interactive teaching methods and multidisciplinary approach.[11] The coordinated model of care can be helpful to meet the growing demand of proper accessibility and utility of DSME programs.[11] Some studies reflected that there was marked effect of DSME on diabetes distress ,despite of limited participation in DSME programs.[12`]

Therefore, this study was aimed to assess the knowledge of DSME among diabetic patient. The outcome of this study would assist to evaluate the awareness of DSME among diabetic patients which has an important role to prevent the diabetes progression and to reduce the seious threat to the life of diabetic patients worldwide.

METHODOLOGY:

A cross sectional study was carried out in PNS Shifa and National Medical Centre Karachi from March 2018 to August 2018 after obtaining approval from IRB BUMDC (No: 56-2018). The sample size calculated was 120 through open epi at 95% confidence interval with a significance level of 5 % at global prevalence of 8.5%.[04] Non-probability purposive sampling was used to collect data. Verbal consent was obtained after explaining the rationale of the study. Inclusion criteria consisted of Patients with Type 2 diabetes having diabetes for more than 6 months; sociodemographic variables used were age, gender, occupation, weight and BMI. Knowledge regarding diabetes includes normal blood sugar level, symptoms of low and high blood sugar and management of these symptoms. Structured questionnaire was used to collect information of sociodemographic characteristics, knowledge and attitude of diabetes and self-care management practices. Data was analyzed by SPSS version 21. Frequencies and percentages were used to express categorical variables. For quantitative variables mean and standard deviation was used. Chi square test was used and p value less than 0.05 was considered as statistically significant.

RESULTS:

Total 120 participants fulfilled the inclusion criteria from which (55%) were females and (45%) were males. Equal number of participants were taken from PNS Shifa hospital n=60 and National medical center (NMC) n=60 .The included age stratification groups were from 37 to above 70 years. Total 14% were from age group 37-47 years (PNS Shifa=15% NMC=13.3%), age 48-57 were 49.1% (PNS Shifa=45% NMC=53.3%), 30% were from age group 58-67 (PNS Shifa=36.7%, NMC=23.3%) and 6.6% were from age above 70 years (PNS Shifa= 3.3% NMC=10%).

The duration of diabetes in majority of participants was less than 5 years as (43.3%) , (25.8%) had 5-10 years of duration, (20%) had the duration of 10-15 years, (10.8%) had duration of 15-20 years. Out of these 120 participants almost half (50.8%) were diagnosed incidentally as type 2 DM whereas (39.2%) participants went to the hospital upon appearance of symptoms other (3.3%) were diagnosed with oral glucose tolerance test and (6.7%) did not exactly remember. Treatment taken by majority of participants was insulin n=26, n=72 on oral hypoglycemic, n=17 on both and n=5 took no treatment. When they were asked about insulin storage 81% from NMC and 92% from PNS Shifa hospital were aware to keep insulin in refrigerator. (Table-1).

About 53.3% participants were aware of symptoms and complications of diabetes and about 35% of participants were not aware of complications others didn't know neither thought it is important to know about complications. 59.6% participants thought visit to eye specialist is important and about 44.16% thought that monthly visit to hospital for general health is important for diabetic patients. When asked about early signs of development of complications 48.3% participants thought that development of foot ulcers and infections is the early sign and 14.16% thought recurrent urinary tract infection is the early sign and 24.16% were in agreement with both important signs of development of complications. When asked about care of feet 61.6% thought that care of feet is important and 38.3% participants were dis agree with importance of foot care. n our study about 76.6% participants thought that plan of meal is important. Total, 30.83% participants were in agreement with this thought that diabetes was strongly associated with obesity. Practice of DSME program was shown in table-2.

DISCUSSION:

Diabetes mellitus is considered as an emerging public health issue due to the global increase in the case incidence of diabetes. In our study majority of participants were female making 55% of the total participants in both health care systems. In our study, the duration of diabetes in majority of participants was less than 5 years as (43.3%) , (25.8%) had 5-10 years of duration, (20%) had the duration of 10-15 years, (10.8%) had duration of 15-20 years and these results are are consistent with the results of a study conducted by Muhammad Umar Ahmad et al.[13]

An important finding in our study was that the respondents have a good knowledge about diabetes and its self-management practices, which was opposite to the study done by Muhammad Umar Ahmed et al [13] according to which participants have poor knowledge of DSME.

In our study about 76.6% participants thought that plan of meal is important which is important to have a good glycemic control which was shown in a study conducted by Xuelian Jiang et al. in which participants were divided in control and intervention group after a period of 12 month intervention

Table:1- Knowledge of Diabetes regarding DSME among two different Health Care Systems.

	Responses	Place of Study		P-value
		NMC (n=60) %	PNS SHIFA (n=60)	
Normal blood sugar level.	**Yes**	43 (71.7%)	44 (73.3%)	0.988
	No	17 (28.3%)	16 (26.7%)	
Do you know symptoms of low sugar?	**Yes**	55 (91.7%)	53 (88.3%)	0.762
	No	5 (8.3%)	7 (11.7%)	
Symptoms of low blood sugar.	**Lethargy**	34 (56.7%)	44 (73.3%)	0.071
	Confusion	15 (25.0%)	5 (8.3%)	
	Palpitation	6 (10.0%)	4 (6.7%)	
	Sweating	5 (8.3%)	7 (11.7%)	
Manage of low blood sugar.	**Take sweets**	37 (61.7%)	48 (80.0%)	0.081
	Drink juices	12 (20.0%)	9 (15.0%)	
	Eats bread	8 (13.3%)	2 (3.3%)	
	Eat fruits	3 (5.0%)	1 (1.7%)	
Do you know symptoms of high blood sugar?	**Yes**	57 (95.0%)	55 (91.7%)	0.717
	No	3 (5.0%)	5 (8.3%)	
Symptoms of high blood sugar level.	**Increased thirst**	12 (20.0%)	14 (23.3%)	0.493
	Visual blurring	14 (23.3%)	9 (15.0%)	
	Leg pain	11 (18.3%)	8 (13.3%)	
	Increased urination	23 (38.3%)	29 (48.3%)	

Table: 2- Practices of DSME among Diabetes patients of two different Health Care Systems

	Responses	NMC (n=60)	PNS SHIFA (n=60)	P-value
Control of sugar by only diet or along with medicine	**Yes**	42 (70.0%)	43 (71.7%)	0.936
	No	18 (29.7%)	17 (26.3%)	
Plan of meal	**Yes**	42 (70.0%)	50 (83.3%)	0.130
	No	18 (30.0%)	10 (16.7%)	
Proportion of meal	**Vegetables/fruits**	46 (76.7%)	48 (80.0%)	0.841
	Oils	8 (13.3%)	9 (15.0%)	
	Only sea food and nuts	1 (1.7%)	0 (0.0%)	
	Only poultry	5 (8.3%)	3 (5.0%)	
Association with obesity	**Strong association**	18 (30.0%)	19 (31.7%)	0.795
	Weak association	13 21.7%	16 (26.7%)	
	No association	8 (13.3%)	9 (15.0%)	
	Don't know	21 (35.0%)	16 (26.7%)	
Engage in physical activity	**daily**	27 (45.0%)	31 (51.7%)	0.075
	Alternate days	7 (11.7%)	11 (18.3%)	
	Weekly	3 (5.0%)	7 (11.7%)	
	Monthly	23 (38.3%)	11 (18.3%)	
Mode of physical activity	**Gym workout**	6 (10.0%)	2 (3.3%)	0.044
	Brisk walking	53 (88.3%)	51 (85.0%)	
	Cycling	0 (0.0%)	5 (8.3%)	
	Swimming	1 (1.7%)	2 (3.3%)	

group had good glycemic control.[5]

Proper storage of insulin is very necessary for its efficacy according to a research conducted by Chakraborty P et al[14] which evidenced that errors in insulin therapy can result in failure of insulin efficacy and improper storage can result in expiration of insulin before time. In our study 21.6% participants were on only insulin therapy and 14.1% were on both oral and insulin and 97.6% were having knowledge that insulin should be stored in refrigerator which shows that participants have enough knowledge that proper storage of drug is important.[14]

In our study, 30.83% thought diabetes was strongly associated with obesity which depicted that people are less aware of association of diabetes with obesity. These results were comparable with the study conducted in India[15] which showed that occurrence of type 2 diabetes is very much common in people who are obese and is less common in those who are non-obese.

In our study, 48.3% thought that engaging in physical activities plays a significant role in a good control of diabetes which is beneficial for maintaining proper health in a diabetic person and these results are consistent with a study which showed that physical activity is critically focus for blood glucose management in individuals with diabetes and pre-diabetes. [16]

It is well known that foot care is important for a diabetic patient.[17] In our study, 53.3% participants agreed that foot protection can prevent from diabetic foot and non-healing infections and these results were higher than reported in a study which showed that 36.6% participants practiced self-foot care.[17]

The knowledge of participants about the importance of eye screening in a diabetic person was observed in our study and 59.16% participants responded positively and thought that eye checkup is very important this result was very similar to the study of Kazi Rumana Ahmed conducted in Bangladesh and showed that almost 50% of participants were aware of importance of eye screening. [18]

In our study, 53.3% of participants were aware about the knowledge of diabetic complications which was good enough when compared to a study in Ghana which revealed that 60% of participants had no knowledge about complications of diabetes mellitus. [19-20] However, the small sample size was the limitation of our study and further multi centered and case control studies are recommended. While the rising burden of diabetes, there is a dire need to address the awareness of Diabetes self-management education (DSME) in the health care systems and also focused on community level hence the major goal is to educate the population regarding the complications of diabetes to prevent the disabilities.

CONCLUSION:

The knowledge of self-care practices in diabetic patients was average in this study.With the increasing burden of diabetes in Pakistan the knowledge and attitude of people is augmenting towards diabetes.

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Original Article DOI: https://doi.org/10.51985/JBUMDC2019049

Dyslipidemia in Newly Diagnosed Diabetic Patients With or Without Micro Albuminuria

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ABSTRACT

Objective: To assess the dyslipidemia in newly diagnosed diabetic patients and compare it with or without micro albuminuria.

Study Design and Setting: Cross-sectional study at Department of Medicine, Military Hospital Rawalpindi from 01 March 2015 to 31 August 2015.

Methodology: A total of 150 patients who fulfilled the inclusion criteria were included after taking informed consent and approval from hospital ethical committee. Blood sample was obtained from each patient and samples were sent to hospital laboratory and reports were assessed by pathologist. Presence or absence of microalbuminuria, trigiyceridemia (200-499 mg/dl), raised LDL-C (>160 mg/dl) and decreased HDL-C (<40 mg/dl) were noted by researcher himself on a pre-designed performa. The collected data was analyzed statistically by using SPSS version 12.Quantitative variables like age, TG, LDL HDL levels were presented in form of mean ± S.D. Qualitative variables like gender, diabetes mellitus, micro albuminuria and dyslipidemia were presented as frequencies and percentages. Chi-square test was applied to find association between dyslipidemia and micro albuminuria. P value = 0.05 was considered as statistically significant.

Results: Mean ± SD of age was 47.97±7.08 years. Out of 150 patients 60% were male and 40% were female. Dyslipidemia was found in 42% patients. Highly significant association was found between dyslipidemia and micro albuminuria, i.e. (P=0.0001).

Conclusion: The frequency of dyslipidemia among newly diagnosed diabetic patients with micro albuminuria was significantly higher than in subjects without micro albuminuria.

Keywords: Dyslipidemia, Micro albuminuria, Newly diagnosed diabetic patients.

INTRODUCTION:

Over the last two decades Diabetes Mellitus (DM) has emerged as one of the challenging epidemics worldwide.[1] Initially DM was considered to be prevalent among developing countries, disease of privileged and senior citizens. It has now become common in developing nation irrespective of age, culture and socioeconomic status. South Asia owing to its demography, lifestyle and dietary habits of its population is emerging as epicenter of this global epidemic.[1] DM is affecting more than 150 million people worldwide. It is estimated that the number of people with DM is expected to rise to 552 million by 2030, with a 69% increase from 2010 to 2030 for developing countries, compared to 20% for developed countries.[2, 3] In Pakistan DM is rising at startling rate. According to World Health Organization report, about 12.9 million individuals are suffering from DM and this count accounts for about 10% of total population. [4] According to a survey Pakistan stood among top ten countries in the world with most cases of type 2 Diabetes Mellitus (T2DM).[5]

DM is known from ancient times. However, Aulus Cornelius Celsus (30 BC-50 AD) was the first one to describe the symptoms of this disease .[6] Over time the disease has been extensively studied with regards to its genetics, pathophysiology and treatment options. Today it is considered a complex heterogeneous entity requiring multidisciplinary approach. It progresses slowly over time leading to secondary complications or some time may present suddenly as coma. It is a multifactorial disease usually resulting from interplay between genetic and environmental factors. Genome-Wide Association Studies has shown that individuals with certain genetic variations are more likely to develop this disease [7]. Main pathophysiology leading to this metabolic syndrome is hyperglycemia resulting from either decreased insulin secretion or impaired insulin action on target tissues. This hyperglycemia along with poor circulation in Diabetes Mellitus can harm various organs including kidneys and heart.[8] Presence of high levels of protein (albumin) in the urine is an early sign of kidney damage. Micro albuminuria is defined as albumin excretion rate of 30-300 mg/day. Frequency of micro albuminuria in newly diagnosed diabetics

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Received: 26-Apr-2019
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was 50%.[9] Dyslipidemia is characterized by the elevation of plasma total cholesterol (TC), triglycerides (TG), reduced high- density lipoprotein cholesterol (HDL-C), and increased low-density lipoprotein cholesterol (LDL-C). It contributes significantly to the excess risk of cardiovascular disease.[10] The prevalence of hypercholesterolemia, hypertriglyceridemia, low HDL cholesterol and high LDL cholesterol in subjects with newly diagnosed Diabetes Mellitus are 67.7%,54.9%, 36.8% and 91.7% respectively.[11] Results of some studies show association between micro albuminuria and dyslipidemia. ln one study, in diabetic patients with and without albuminuria, hypertriglyceridemia was 93.7 vs. 67.3%, decreased HDL-C was 91.3% vs. 81.4% and raised LDL-C was 93.2% vs. 69.5%. However there is a contradiction, as albuminuria was found to be associated with low HDL-C not with TC, TG, and LDL-C. But some researchers have found significant differences in TC, TG and HDL-C between those with or without albuminuria respectively[12]. Despite all this there is increasing evidence of relationship between dyslipidemias and albuminuria. Several mechanism have been hypothesized to explain this association. According to one TG rich lipoprotein activates transforming growth factor â pathway (TGF- â) which promotes production of reactive oxygen species (ROS). ROS can cause glomerular damage [13].

Although the relationship between dyslipidemias, renal disease and DM has been investigated extensively. There is still a need to study these associations in our population which will not only improve our health care delivery system and protocols but also improve patients holistic health. Keeping this in mind we conducted this study at our clinical setup so as to improve our clinical practice and bring it up to international benchmarks. Therefore the aim of this study was to determine the frequency of dyslipidemia in newly diagnosed diabetic patients and compare it with or without micro albuminuria.

As diabetic patients with micro albuminuria are at more risk of developing cardiac and renal problems but often remain undiagnosed for presence of dyslipidemia. This study would be helpful to manage the cases accordingly and to prevent mortalities and morbidities.

METHODOLOGY:

After taking approval from Hospital ethical committee, I50 patients (sample size was calculated using WHO sample size calculator) who fulfilled the inclusion criteria, i.e. patients having age range 20-70 years of either gender and patients with newly diagnosed type 2 diabetes mellitus (diagnosed within 1 year), were enrolled in the study from OPD. Patients with history of smoking, pregnancy, long standing diabetes, elevated creatinine, overt proteinuria, patients on lipid lowering drugs, ACE inhibitors or angiotensin receptor blockers, hypertensive patients, patients with non-diabetic renal disease and heart failure, were excluded from the study. The purpose of the study was explained to each patient and informed consent was obtained. All basic demographic information of each patient (name, gender, address and contact number) was noted. Blood samples were obtained from each patient and samples were sent to hospital laboratory and reports were assessed by pathologist. Presence or absence of microalbummuria, triglyceridemia (200-499 mg/dl), raised LDL-C(>160 mg/dl) and decreased HDL-C (<40 mg/dl) were noted. Deranged lipid profile was assessed by spectrophotometric absorption.

The collected data was analyzed statistically by using SPSS version 12.Quantitative variables like age, TG, LDL HDL levels were presented in form of mean ± S.D. Qualitative variables like gender, diabetes mellitus, micro albuminuria and dyslipidemia were presented as frequency and percentage. Chi-square test was applied to find association between dyslipidemia and micro albuminuria. Effect modifiers were controlled through stratification of age, gender, duration and type of diabetes mellitus to see the effect of these on outcome variables. Post stratification, Chi-square was applied considering P= 0.05 as significant.

RESULTS:

In this study 150 newly diagnosed type 2 diabetic patients were included to assess the dyslipidemia with and without micro albuminuria and results were analyzed as follows:

Mean ± SD of age was 47.97±7.08 years. Mean ± SD of LDL, TG and HDL were 113.67±19.50, 160.68±19.30 and 41.32±7.77 mg/dl respectively. Out of 150 patients 90 (60%) were male and 60 (40%) were female. Dyslipidemia was found in 63(42%) patients. Micro albuminuria was found in 18(12%) patients. In comparison of dyslipidemia with and without micro albuminuria, 12% patients had dyslipedimia with micro albuminuria and highly significant association was found (P=0.0001).

Stratification of dyslipidemia with respect to age, gender, type and duration of diabetes mellitus, LDL, HDL and TG was done, as shown in Table 1 while comparison of dyslipidemias with microalbuminuria is shown in Table 2.

DISCUSSION:

The prevalence of Type II DM is on the increase according to age in spite of awareness programs that have been done in high risk population about DM. The proportion of Type II DM is higher than that of Type I DM and the difference is almost doubled[14]. The clinical characteristics which consist of BMI, waist circumference, total cholesterol level, triglyceride level, HDL cholesterol level and LDL cholesterol level among subjects with newly diagnosed DM are similar to those of subjects with diagnosed DM[15]. The most common pattern of dyslipidemia in DM are hypertriglyceridemia and low HDL cholesterol level[16]. In this study the proportion of dyslipidemia is significantly higher in patients with micro albuminuria as compared to that without micro albuminuria.

Table 1. Stratification of Dyslipidemia according toAge groups, Gender, Type and Duration of DM,LDL, HDL and TG

Clinicopathological variable	Cases (n=150)	Percentage (%)	Dyslipidemia		*P* Value
			Yes	No	
Age Groups (years)					
27-47	68	45	11	57	0.0001
>47	82	55	52	30	
Gender					
Male	90	60	38	52	0.0001
Female	60	40	25	35	
Type of DM					
Type II	150	100	63	87	NA
Duration (months)					
0-6	68	45	30	38	0.632
7-12	82	55	33	49	
LDL (mg/dl)					
89-113	87	58	01	86	0.0001
>113	63	42	62	1	
HDL (mg/dl)					
25-41	77	51	61	16	0.0001
>41	73	49	02	71	
TG (mg/dl)					
134-160	93	62	06	87	0.0001
>160	57	38	57	00	

Table 2. Comparison of Dyslipidemia With Micro Albumunria

DYSLIPIDEMIA	MICRO ALBUMINURIA		P-VALUE
	POSITIVE	NEGATIVE	
YES	15	48	0.0001
NO	3	84	

The mean LDL, HDL and TG levels among subjects with newly diagnosed DM with micro albuminuria is significantly different from that in those individuals who do not have micro albuminuria. Unfortunately, this study did not perform qualitative changes in LDL cholesterol, which in particular, theoretically the subjects with DM tend to have higher proportion of small dense LDL particles[17]. The mean ± SD of LDL, TG and HDL was 113.67±19.50, 160.68±19.30 and 41.32±7.77 respectively. As compared with the study of Goff DC et al[18] who reported mean ± SD of LDL,TG and HDL as 125.84±13.56, 165.28±17.48 and 44.69±9.34 respectively, which is comparable with our study. In this study, the proportion of dyslipidemia is higher in male population. In our population the largest proportion is in the range of 30-40 and 40-50 years old and more than half of them have central obesity. The prevalence of hypertension, obesity and central obesity are significantly higher among subjects with dyslipidemia and Type II DM than those with only dyslipidemia. The occurrence of both dyslipidemia and newly diagnosed DM will increase CVD risk components several folds and most of those subjects do not realize the risks[19,20]. In our study, majority of patients had age group > 47 years (55%) followed by age group 27-47 years (45%). This finding supported by the study conducted by Haffner SM[21] and Bays HE et al[22], which shows that the commonest age of newly diagnosed diabetes between 35 to 70 years with mean age of 50 years. From this data, it can be concluded that aggressive screening and education among high risk population and in general as well are still needed. Since the newly diagnosed DM occurs two fold in the fourth and fifth decade, it is better to start screening population in the third decade and maybe in the second decade among high risk population[23]. Unfortunately, this study did not collect history of the family, so the importance of genetic factor cannot be concluded. Among subjects without normal micro albuminuria, there is significant relationship between central obesity and all types of dyslipidemia. But, among subjects with newly diagnosed diabetes mellitus, the relationship between central obesity and dyslipidemia are not significant anymore. Thus, it may show that prevention should be started before glucose intolerance emerges. The occurrence of dyslipidemia among subjects with glucose intolerance will double the risk of CVD[24]. Screening among high risk population is the best way to detect metabolic changes prior to the occurrence of metabolic diseases. Besides that, earlier life style modification among general population may postpone or prevent CVD especially in high risk population[25]. Strength of the study was use of consecutive sampling best suited for our study design and sample selection, as our inclusion and exclusion criteria were stringent. The use of objective definitions for predictor and outcome variable also minimizes the source of bias in our study. The main limitations of our study were use of a weak study design that is cross-sectional analysis. Also limited outcomes selected in our study affects the worth of our study. There were many variables and factors that have association with our predictor and outcome variables that could have been included in our study. The use of non-probability sampling also limits generalizability; however we had a small number of patients and no follow up. This study was hospital-based study; hence the figure does not reflect true frequency and severity of the disease. Moreover, the study was conducted in one unit in single hospital which further confined its generalization. It is important for healthcare providers and policy makers to plan preventive strategies for micro albuminuria spread as well as diabetes prevention programs among high risk population. Effective preventive measures are the need of the hour and Pakistan may be considered as one of the areas of highest diabetes prevalence around the globe.

CONCLUSION:

The characteristics of newly diagnosed diabetes mellitus were similar to diagnosed diabetes mellitus. The frequency of dyslipidemia among newly diagnosed diabetic patients with micro albuminuria was significantly higher than that in subjects without micro albuminuria.

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Original Article DOI: https://doi.org/10.51985/JBUMDC2020008

Frequency and Location of Supernumerary Teeth in a Private Hospital of Karachi City

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ABSTRACT:

Objective: To investigate frequency of supernumerary tooth in relation to gender, age and location.

Study Design and Setting: Cross-sectional Study was conducted at Mamji Hospital, Karachi from June 2017 to June 2019.

Methodology: A total of 2160 patients seen and out of which 45 clinically diagnosed patients of supernumerary teeth were participated in this study. Supernumerary teeth were classified on the basis of location. Descriptive statistics were checked by means of percentages and frequency of all variables. Chi-Square test was applied, P-value < 0.05was considered significant.

Results: The total patients were 45 which comprised of 26 male and 19 females with ages ranging from 15 to 60 years. The prevalence of ST was 1.59%, the higher predilection of supernumerary teeth was seen in males than females. The male to female's ratio was 1.36:1. On the basis of location ST were further classified on Mesiodens, Paramolars and Distomolars category. Of the 45 supernumerary teeth, 36 were had Mesiodens (m= 62.1%, f=37.8%), 5 were Paramolars (m=60%, f=40%) and 3 were Distomolars (m=0, f= 100%).

Conclusion: The present study findings showed high prevalence of ST was dominant in males. Present study emphasizes the timely diagnosis and appropriate management of supernumerary teeth to avoid unwanted complications.

Key Words: anomaly, prevalence, Supernumerary tooth, teeth,

INTRODUCTION:

Supernumerary teeth (ST) are developmental anomaly of number of teeth characterized by presence of extra tooth/teeth in the dental arch.1 It is also known as hyperdontia.[2] ST may develop in any tooth bearing areas of the jaw in oral cavity. Clinically, ST may appear as a single tooth or multiple teeth in the oral cavity. It may also present unilaterally or bilaterally, erupted or impacted and in mandibular or maxillary arch.[3] The prevalence of supernumerary teeth varies may range from 0.1% to 3.8% in the jaw, and it is most commonly reported in permanent dentition. The higher prevalence of ST were reported in Mongoloid groups than in other racial groups. [3,4] The incidence of ST has greatly seen in the maxilla, about 93.3% were located in anterior maxilla while 2.2% present in anterior region of mandible and posterior mandible accounted for 4.4% of supernumerary teeth.[2] The ST was more commonly seen in males as compared to females[5,6] The ST are classified on the basis of location (Mesiodens, Paramolars, Distomolars) and morphology (conical, tuberculate, supplemental) The conical type of supernumerary teeth is most common.[7,8]

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Received: 27-Jan-2020
Accepted: 16-Apr-2020

The etiology of ST exactly unknown, but several theories such as phylogenetic, dichotomy theory and occurrence of hyperactive dental lamina plays an important role in the etiology of Supernumerary teeth.[9] One theory suggests that the supernumerary tooth is created as a result of a dichotomy of the tooth bud. Another theory, well supported in the literature, is the hyperactivity theory, which suggests that supernumeraries are formed as a result of local, independent, conditioned hyperactivity of the dental lamina. Heredity may also play a role in the occurrence of this anomaly, the ST are more common in the relatives of affected children than in the general population.[6]

They are usually discovered incidentally by the dentist on routine radiographic examination and this may sometimes causes displacement of adjacent tooth, interference with orthodontic appliance and aesthetic issues for patients.[10] The presence of a supernumerary tooth is the most common cause for the failure of eruption of a maxillary central incisor. It may also cause retention of the primary incisor teeth. The problem is usually reported with the eruption of the maxillary lateral incisors together with the failure of eruption of one or both central incisors. Supernumerary teeth in other

locations may also cause failure of eruption of adjacent teeth.[6] The supernumerary teeth can be transmitted as an autosomal dominant or autosomal recessive trait with incomplete penetrance, or may be associated with the X chromosome. Although there are some reports of multiple or bilaterally ST without any systemic conditions or associated syndromes, in most cases, ST are associated with other conditions or defects such as cleft lip/palate, cleidocranial dysostosis (CCD) and Gardner's syndrome, gardener syndrome,[11] Ehlers-Danlos syndrome, Crouzon syndrome.[12] craniosynostosis[13] and Enamel-Renal-Gingival syndrome. Less common syndromes that related with ST are; Fabry disease, Ellis-van Creveld (EvC) syndrome, Trico – Rhino – Phalangeal syndrome (TRPS), Nance-Horan syndrome, Rubinstein-Taybi syndrome.[13,14]

The supernumerary teeth are usually asymptomatic, and may diagnose during oral clinical examination. History and detailed examination and radiographic evaluation are mandatory.[3] The present study data was gathered in a District Central Hospital to investigate the frequency of Supernumerary teeth according to site and morphology. This study also elucidates supernumerary teeth correlation with gender.

METHODOLOGY:

This cross-sectional study was carried out at Mamji hospital Karachi from June 2017 to June 2019, the ethical approval was obtained from Hospital ethical committee. A non-probability convenient sampling technique was used. The sample size was calculated by using software OpenEpi.com by using prevalence of supernumerary teeth 3.8% and 95% Confidence interval. The required sample size was found to be 45.

Out of 2160 patients seen in dental OPD over a period of 3 years. A total of 45 patients diagnosed with supernumerary tooth participated in the study. Informed consent was taken prior to examination of each patient. The study included both male and female patients of any age group. The ST was classified on the basis of location and morphology. The location was mesiodens, Paramolars and distomolars. Morphologically, ST was further divided into Conical, Tuberculate, Supplemental and Odontomes. The diagnosis of ST was made on clinical and radiological grounds. The patients suffering from any type of syndrome or craniofacial anomalies[5] was also investigated. The exclusion criteria include patient refused to give consent, history of early age extractions and accidents.

The data was recorded on a proforma and analyzed by Statistical Package for the Social Sciences (SPSS) version 23. Frequency and percentages presented for categorical variables. To know the significance between gender and location of ST analysis was made using Chi-square test. P-value < 0.05 was considered significant.

RESULTS:

Out of 2160 patient sample size collected over an estimated period of three years, 45 patients were clinically diagnosed with supernumerary teeth in this study. Out of which 26 were male (57.8%) and 19 were females (42.4%) having a 1.36:1 male to female ratio. The mean age, median and standard deviation was found to be 30.67, 30.00, ± 9.686 respectively. The overall prevalence of supernumerary reported in the present study was 1.59%. Table 1 shows the highest number of ST was present in 32 years of age 4 (8.89%).

On the basis of morphological characteristics, the correlation of supernumerary teeth with gender was also investigated which revealed that all the ST were detected in maxilla. In maxilla, the most common ST present in males were mesiodens 23(62.1%) followed by Paramolars 3(60%) and Distomolars 0(%). In females, highest number of ST were mesiodens 14(37.8%) followed by Paramolars 2 (40%) and Distomolar 3 (100%). This showed insignificant findings with a p-value of 0.76. Table 2

In the current study, we also tried to find an association of supernumerary teeth with syndrome or other craniofacial anomalies. However, no syndrome or other anomalies were detected in ST patients.

DISCUSSION:

Supernumerary teeth are the notable dental anomaly of shape of teeth mostly seen in maxillary quadrant, however, it may also present in mandibular region. These may reveal in routine oral and radiographic examinations teeth.[14] Researches has shown that ST has been reported in both the primary and permanent dentition. Increased incidence of this anomaly has been reported permanent teeth.[15] The prevalence of supernumerary teeth was found to be 1.59% in permanent dentition in present study, while in Japanese reported 0.04%.[16] Study conducted by Shilpa in South Indian Children showed the overall prevalence rate of ST was 0.21% in primary dentition.[17]

The etiology of supernumerary teeth remains unclear. However, various theories have been suggested regarding the presence of supernumerary teeth. The widely accepted theory for splitting of the dental follicle (Dichotomy theory), some factors such as trauma or evolutionary mutations, can cause accidental follicle division into two or more fragments.[18] The hyperactivity of the dental lamina and the combination of genetic and environmental factors may be considered as the most acceptable etiologic factors in the development of mesiodens.[19,20,21.] Familial occurrence of mesiodens (ST developing between two central incisors) is reported to involve more than one sibling, or one generation.[22,23]

Supernumerary teeth have been classified primarily on the basis of location and morphology as shown in Table 3. Studies have shown that ST has been reported in patients

Fig No 1: Distribution of supernumerary teeth (ST) according to age

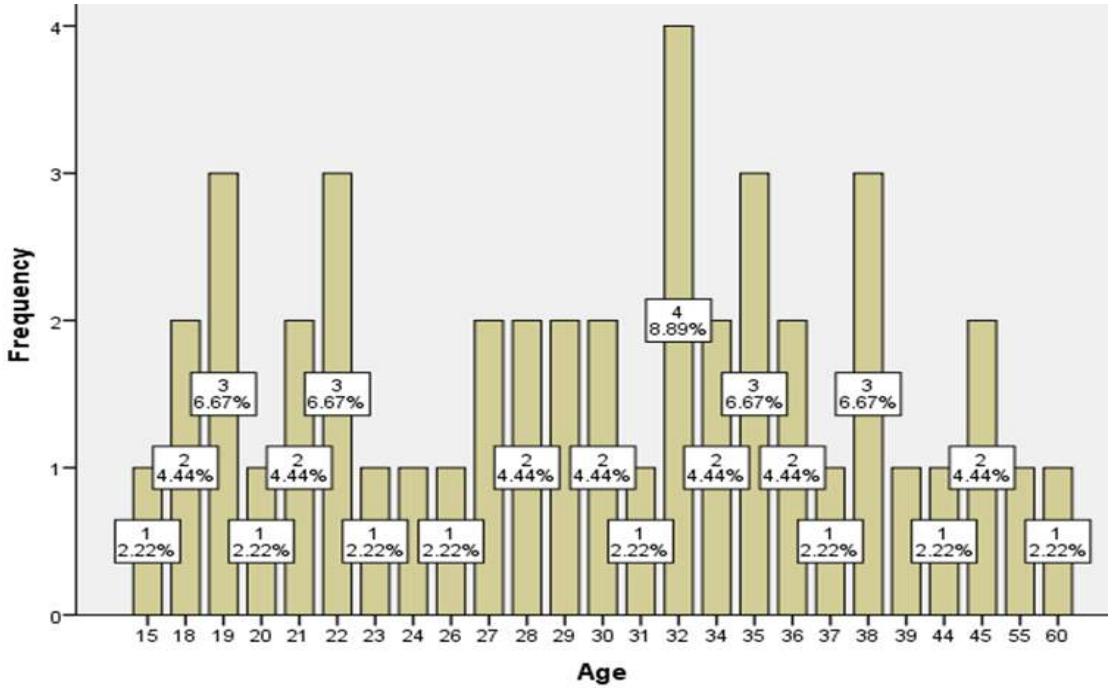

Table No 2: Distribution of Supernumerary teeth according to gender and location

Supernumerary Teeth Present Based on Location	Gender (n=45)		*P-Value*
	Male	**Female**	
Mesiodens	23(62.1%)	14(37.8%)	*.076*
Paramolars	3(60%)	2(40%)	
Distomolars	0(0%)	3(100%)	
Total	26	19	

*Chi-square test was applied to see the significance level.
*P-value < 0.05 considered to be statistically significant.

Table No 3: Classification of Supernumerary Teeth

Based on location	Based on Morphology
Mesiodens	Conical
Paramolars	Tuberculate
Distomolar	Supplemental
	Odontome

having syndromes and other craniofacial anomalies such as cleft lip and palate, Gardner's syndrome, Down syndrome and cleidocranial dysostosis.[24] The ST has shown a strong association with Ehlers-Danlos syndrome, Fabry Anderson's syndrome, chondroectodermal dysplasia, incontinentia pigmenti and tricho rhino-phalangeal syndrome.[17,18,] Evidences also revealed that ST is also seen in non syndromic patients[7,12]. In present study we also investigated the association of ST with syndromes. The current study findings did not observe any case of ST in syndromic patient. However, all were detected in non-syndromic patients. Clinically, ST can appear in any region of the jaws. The most commonly involve site is the premaxilla.[,21,22,23] Based on location the mesiodens is the supernumerary tooth present between two maxillary central incisors. In present study, the mesiodens was higher in proportion followed by Paramolars and distomolars. Higher predilection was seen in males as compared to females. Leco and colleagues discovered that the mesiodens was the most frequent supernumerary teeth found in the maxilla.[24] The Ferres-Padro conducted study on patient age ranging from between 5 to 19 years of age showed mesiodens were the most frequently found supernumerary teeth (53.16%). Similar results were also observed in Sharma and Singh study and found that 81.2% of the ST were located in the central incisor region (mesiodens 30.0%)[21,25].

The supernumerary teeth are usually asymptomatic and it may detect as an incidental finding during clinical and radiographic examination. For the proper diagnosis of ST the detailed history, clinical examination, radiographic investigation is mandatory for definitive diagnosis[26,27,28]. Evidences have shown that unerupted supernumerary tooth may be found by chance during radiographic examination. It is recommended that anterior occlusal or periapical radiograph, paralleling technique and orthopantomogram are the most useful investigations to visualize supernumerary teeth. Recently, computed tomography has also been used to detect the presence of supernumerary teeth.[29,30]

CONCLUSION:

The present study findings showed high prevalence of ST was dominant in males. Present study emphasizes the timely

diagnosis and appropriate management of supernumerary teeth to avoid unwanted complications.

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Original Article DOI: https://doi.org/10.51985/JBUMDC2020001

Low Dose Theophylline and Tiotropium Rotacap as Add on Therapy in COPD Patients-Clinical Trial

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ABSTRACT:

Objectives: To compare the role of low dose Theophylline and Tiotropium rotacap in improving the lung functions and day to day life of patients suffering from COPD.

Study Design and Setting: A Clinical trial study was conducted at Department of Pharmacology and Therapeutics, BMSI in association with Department of Chest Medicine, JPMC.

Methodology: This study was planned as an open label and parallel clinical trial study. A total of 168 patients of COPD were selected for this study and only 161 patients completed the 3 months duration of the study. The enrolled patients were grouped into 2, namely A and B. Tab. Theophylline 350 mg was given to Group A in two divided doses while Tiotropium rotacap18µg through rotahaler was given to group B once a day.

Results: Mean FEV1 ± SD was improved by 0.04 ± 0.02 in Theophylline therapy group while by 0.07 ± 0.01 in the Tiotropium therapy treated group and a significant difference between the changes in the two treatment groups was evident. There was a percentage improvement in PEFR of 8.9 ± 5.8 in the Theophylline therapy treated group and of 13.2 ± 4.7 in Tiotropium therapy treated group. When Tiotropium group was compared with Theophylline group for improvement in percentage change in PEFR from day 0, a significant difference was evident between the two groups. There was a significant improvement from day 0 in CAT score in Tiotropium treated groups versus Theophylline group after 3 months of therapy.

Conclusion: Tiotropium rotacap was more effective as compared to low dose Theophylline in improving pulmonary functions and CAT score in patients with COPD.

Keywords: COPD, CAT score, FEV1, FVC, Health related quality of life, PEFR, Theophylline, Tiotropium.

INTRODUCTION:

COPD (Chronic Obstructive Pulmonary Disease) is an alarming issue being the third highest mortality reason worldwide by the year 2030.[1] In Pakistan, it has an estimated death rate of 71 per 100,000. This problem needs to be addressed efficiently for being the fourth highest among the 25 most populated countries on the globe. It has been a great problem to provide medical access to patients of low socioeconomic status.[3] Risk for COPD is related to age, genetic make-up, decrease in maximally achieved pulmonary functions, previous pulmonary tract infections, chronic asthma, exposure to air pollutants and smoking.[4] Patient presents with chronic and progressive complain of shortness of breath, cough, phlegm production plus chest tightness.[5] The occurrence of COPD needs to be established by carrying out spirometry.[6] The criterion for labelling a patient with COPD is post-bronchodilator Forced expiratory volume (FEV1), forced vital capacity (FVC) less than 0.7.[7] Treatment with bronchodilators shows a principal effect by successfully decreasing airflow limitation and symptoms, hereby, improving health condition. They also lessen the number of exacerbations.[8] Inhaled long acting β2-agonists as well as anticholinergics are the most commonly prescribed drugs for relieving symptoms of COPD patients.[9, 10,11] In Triple therapy long acting muscarinic antagonist (LAMS) is added to patients already on long acting â agonist/Inhaled corticosteroid (LABA/ICS) to improve their health related quality of life.[12]

Symptoms of COPD can mainly be reversed by decreasing the parasympathetic tone of airway smooth muscles. This target is achieved by parasympatholytic drugs that bind to muscarinic receptors, reverses bronchoconstriction and improves airflow to lungs.[13] The extract from cigarette smoke causes release of interleukin-8 from airway myocytes. The cholinergic receptors regulate this secretion as well.[14] Tiotropium selectivity binds to M3 receptors. These muscarinic receptors are present on airway smooth myocytes and submucosal glands. Tiotropium, by binding to M3 receptors, causes decreased contraction of airway myocytes

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Received: 02-Jan-2020
Accepted: 07-Apr-2020

along with reduced mucus secretion and then a bronchodilator effect is achieved.[15]

Theophylline acts by nonselective inhibition of phosphodiesterase, thereby, producing bronchodilation. It moreover exhibits non-bronchodilator properties. When it is given at low plasma levels of 10 mg/l, it only acts as a mild nonselective inhibitor of phosphodiesterase and, thereby, clinically significant bronchodilation is not achieved[16]. Low doses of theophylline activate histone deacetylases (HDACs).[17] Therefore, at this low dose, significant anti-inflammatory effect and reversal of steroid resistance has been evident.[18] In this background, there is a strong need of studying the efficacy of Theophylline in reversing steroid resistance and its effect on health of a patient as an add on therapy as compared to addition of a bronchodilator, Tiotropium.

METHODOLOGY:

This study was planned as an open label and parallel group clinical trial study. It was conducted in the Department of Pharmacology and Therapeutics, BMSI in association with Department of Chest Medicine, JPMC; after taking approval from the ethical committee of JPMC.

Diagnosed patients with moderate to severe COPD disease (FEV1 30% to 80% of normal according to GOLD classification of COPD) [19] of both sex and ages >35yrs were included in this study. Patients with history of exacerbation of COPD or else pulmonary tract infection in preceding 1 month, asthma, tuberculosis, pneumoconiosis, bronchiectasis, old interstitial pneumonia, history of lung cancers or resection, administration of supplemental oxygen for >12 hours a day, moderate to severe BPH, deranged hepatic and renal functions, arrhythmias or cardiac failure were excluded from this study. Each patient gave written permission before being enrolled in the study. The study was conducted for 3 months with follow up appointments every fortnightly. Patients continued taking their Budesonide and Formoterol combination inhaler. Inhaler method was checked in each patient before commencing the study. We selected 168 COPD patients for this study but only 161 patients completed the 3 months duration of study. We randomly divided the enrolled patients into 2 groups in 1:1 ratio. Tab. Theophylline 350mg was prescribed to COPD patients in group A in two divided doses while Tiotropiumrotacap18µg through rotahaler to group B once a day. Patients were taught to place Tiotropiumrota capsule in a hole in the rotahaler with its clear end upside. Twisting the barrel of rotahaler resulted in splitting of capsule. The patients inspired deeply and quickly while placing lips around the mouthpiece and then held their breath for 10 seconds after removing the mouthpiece.

Forced expiratory volume in 1 sec (FEV1), forced vital capacity (FVC), Peak expiratory flow rate (PEFR) and chronic obstructive pulmonary disease assessment test (CAT) score were observed at day 0 and at day 91 of the study.[21]CAT score is based on eight different COPD related symptoms of patients. It uses a range from 0-40 to assess improvement in patient's quality of life. A decrease in score indicates improvement in symptoms and condition of patient.[22]

Computer program open epi version 2 was used to calculate sample size for our study. SPSS version 17 was used for data compilation and analysis. Chi-square test was to compare qualitative variables (gender, grading of disease, smoking history) and ANOVA to quantitative ones (Age, FEV1, FVC, PEFR and CAT score).

RESULTS:

Both groups were statistically comparable at baseline as shown in table 1. When the change from day 0 in mean ± SD of FEV1 in the Theophylline treated group (0.04 ± 0.02) and that of Tiotropium treated group (0.07 ± 0.01) were compared, a significant difference was observed between the two treated groups indicating that Tiotropium more effectively improved FEV1 in patients with COPD.

Mean improvement in FVC in Tiotropium treated group (0.12 ± 0.03) in comparison with Theophylline treated group (0.06 ± 0.03) was also significant, P value was 0.001 as shown in table 2.

Improvement in percentage of PEFR (l/min) from day 0 was 8.9 ± 5.8 in the Theophylline therapy treated group and was 13.2 ± 4.7 in Tiotropium group. Percentage change in PEFR from baseline in Tiotropium group in comparison with Theophylline group was statistically significant. Tiotropium was more effective than Theophylline in improving PEFR.

When improvement in CAT score was compared in Theophylline group and Tiotropium group, a significant difference was evident between the two treated groups, Tiotropium showed more efficacy in improving the health status of patients. Change in mean ±SD of CAT score in Theophylline treated group was found to be 1.8 ± 1.14 while in Tiotropium therapy treated group was found as 2.7 ± 0.82 on the completion of study.

DISCUSSION:

According to author's information, this was the first study in which the effectiveness of Theophylline was studied in comparison to Tiotropium as an add on therapy in terms of improving symptoms of patients with COPD. We find studies in which efficacy of low dose theophylline and Tiotropiumas add on therapies were studied [21,22] but we could not find any study in which their efficacy as an add on therapy is compared.

According to studies of Barnes et al, Histone deacetylase 2 (HDAC2) is activated because of oxidative stress in COPD patients. HDAC 2 has a role in suppressing expression of inflammatory genes. Moreover, glucocorticoid treatment deactivates the activated inflammatory genes through HDAC

Table No 1: Comparison of baseline characteristics between theophylline and tiotropium

	Theophylline group (n=80)	**Tiotropium group (n=81)**	**P value**
Age in years (Mean±S.D)	59.1 ± 8.07	58.8 ± 8.40	0.804
Gender			
Male	78 (97.5%)	78 (96.3%)	0.66
Female	2(2.5%)	3(3.7%)	
Smokers	78 (97.5%)	78 (96.3%)	0.66
Moderate COPD	43 (53.8%)	44 (54.3%)	0.942
Female	2 (2.5%)	3 (3.7%)	0.942
CAT score	17.7 ± 3.91	17.9 ± 3.34	0.812
FEV1	1.14 ± 0.24	1.17 ± 0.25	0.480
FVC	2.27 ± 0.29	2.29 ± 0.35	0.674
PEFR	184 ± 40.2	188 ± 39.3	0.586

Table No 2: Comparison of FEV1, FVC and PEFR between theophylline and tiotropium therapy treated COPD patients

Sr. No.		**Theophylline group (n=80)**	**Tiotropium group (n=81)**	**P-value**
1.	FEV1 (L)			
a)	Day 0	1.14 ± 0.24	1.17 ± 0.25	0.477
b)	Day 91	1.18 ± 0.24	1.24 ± 0.27	0.125
c)	Change from baseline	0.04 ± 0.02	0.07 ± 001	0.001
2.	FVC (L)			
a)	Day 0	2.27 ± 0.29	2.29 ± 0.35	0.681
b)	Day 91	2.32 ± 0.29	2.41 ± 0.35	0.098
c)	Change from baseline	0.06 ± 0.03	0.12 ± 0.03	0.001
3.	PEFR (L/min)			
a)	Day 0	185 ± 40.2	188 ± 39.3	0.582
b)	Day 91	201 ± 42.4	212 ± 40.6	0.085
c)	%age change from baseline	8.9 ± 5.8	13.2 ± 4.7	0.001
4.	CAT Score (Mean ± SD)			
a)	Day 0	17.7 ± 3.91	17.9 ± 3.34	0.808
b)	Day 91	16.0 ± 3.85	15.2 ± 3.72	0.202
c)	Change from baseline	1.8 ± 1.14	2.7 ± 0.82	0.001

2. Low dose Theophylline restores HDAC2 at molecular level through selective inhibition of phosphoinositide 3-kinase-ä.[23-24] This mechanism may explain improvement in FEV1, FVC and FEV1/FVC.

BREATH Trial by Bella et al. supports results of our study. In this randomized and multicenter study, effectiveness of oxitropium bromide was analyzed in comparison with theophylline and its combination with theophylline in patients with COPD. FEV1 and FVC were improved in all groups[25]. This supports the improvement in FEV1 and FVC seen in Theophylline treated group in our study.

Effect of Theophylline on health related quality of life was evaluated in terms of improvement in CAT score in comparison to earlier studies in which other different questionnaire were used to analyze health related quality of life (HRQoL) in COPD patients. A decrease of minimum 2 scores in CAT score is the criteria to be labelled as clinically significant improvement. In our study Theophylline did not cause any clinically significant improvement in CAT score.[23] This result is supported by the study of Devereux who used low-dose theophylline in comparison with placebo and the number of COPD exacerbations was not decreased during 1-year period.[26]

An increase in mean FEV1 of 0.07 ± 001 was evident in Tiotropium therapy treated patients. This result was in accordance with that of a 12 week SPRuCE study. In this multi-center, randomized study, effectiveness of Tiotropium was compared with placebo. Capsule Tiotropium 18µg through handihaler device was given as an additional therapy to COPD patients. Mean FEV1 was improved by 0.06 in Tiotropium treated group as compared to placebo on completion of the study. An increase in mean FVC was also

significant in our study and was in accordance with the results of SPRUCE study.[27]

In UPLIFT trial, efficacy of Tiotropium was studied in terms of SGRQ score. In this trial, a same dose of Tiotropium that is 18µg was given through handihaler device in higher proportion of Tiotropium therapy treated patients. An improvement of 4 scores was seen in the treated patients. This is a clinically meaningful improvement in health related quality of life.[28] This supports the results of our study in which a clinically significant decrease of 2.7 ± 0.82 in mean CAT score was evident at the end of study.

A study by Ford et al contradicts the results of our study. The results of his study showed that there was a significant decrease in the number of exacerbations in COPD patients when low dose Theophylline was given with inhaled corticosteroids as compared to when given alone.[29] Therefore, more research is needed to establish the significance of adding low dose Theophylline in COPD patients to improve their quality of life. The limitations of the study were the nature of the study from only one center which represented limited population. This study followed patient for only 3 months that was a very short period to comment on number of exacerbations and adverse effects.

CONCLUSION:

Tiotropium rotacap was more effective in terms of improving pulmonary functions as well as health related quality of life in COPD patients when compared with low dose Theophylline.

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Original Article DOI: https://doi.org/10.51985/JBUMDC2019092

Role of Myo-Inositol in Treatment of Young Females Affected By Polycystic Ovarian Syndrome: Quasi Experimental Study

Haniyah Qamar, Rozina Mustafa

ABSTRACT

Objective: To determine the effects of Myo- inositol in young females with polycystic ovarian syndrome.

Study Design and Setting: This was a quasi-experimental study and was conducted in United Medical and Dental College and Creek General Hospital from January 2017 to January 2018.

Methodology: Total 100 patients were recruited based on the specific inclusion criteria of PCO diagnosed by symptoms (body mass index, menstrual irregularity, hirsutism, acne) biochemical markers (fasting insulin, random blood sugar) and ultrasound findings. Each subject in the study group was given sachet (Myo- inositol 2000mg and folic acid 400ug) once a day dissolved in glass of water for duration of 6 months. Improvement in symptoms, biochemical markers and ultrasound findings were reassessed after the completion of 6 months duration. The SPSS version 21 was used for data analysis. The paired T test was used to assess the effects of Myo-Inositol before treatment and after six months of treatment.

Result: The significant relation (0.001) was observed between the intervention and PCO and its related symptoms. An evident effect was noticed in each individual after the intervention was provided to them. The relatable symptoms such as irregularities in menses, hirsutism,weight and insulin resistance were reduced by significant ratio.

Conclusion: Myo – inositol has proven to be effective in reducing the PCO and its relatable symptoms in young females. Despite the limitations, enough evidence was collected that indicated a significant effect of the intervention.

Key words: Polycystic Ovarian Syndrome, young females, myo-inositol

INTRODUCTION:

Polycystic ovary syndrome is a common hyperandrogenic disorder, resulting from escalating androgen hormone production. It is observed that 20 % of the reproductive age women suffer from this disorder.[1]

Guidelines from the Endocrine Society recommend using the Rotterdam criteria for diagnosis, which mandate the presence of two of the following three findings-hyperandrogenism, ovulatory dysfunction, and polycystic ovaries-plus the exclusion of other diagnoses that could result in hyperandrogenism or ovulatory dysfunction.[2]

The mechanisms leading to insulin resistance consist of a defect in insulin binding to its receptor or to changes in insulin signal transmission. However, the ovaries of these women maintain approximately a normal response to insulin. A partial elucidation of this mechanism is explained by the action of insulin on the ovary through the IGF-1 receptor. This binding occurs when insulin reaches high concentrations, as compensatory hyperinsulinemia. Moreover, the action of insulin on the ovary uses the inositol glycan system as a signal mediator, a different mechanism from the system activated by phosphorylation of the receptor at tyrosine level in other tissues. An increase was observed in urinary clearance of inositol in some American and Greek women with PCOS. It reduces tissue availability of inositol. This mechanism could contribute to insulin resistance present in PCOS women.[3]

Due to the key role of insulin in the syndrome, insulin sensitizers such as metformin have been considered as possible therapeutic option in the management of these problems. Metformin has been used on patients with a hyperinsulinemic status for the improvement of ovarian dysfunction with consecutive anovulation, irregular menstrual cycles, and infertility problems.[4] Nevertheless, metformin, when used in the therapeutic dose range, was shown to have several side effects such as flatulence, diarrhea, and nausea, so that many patients are unable to use this treatment option in gynecology for a longer period of time.[5,]Therefore, in parallel to the common use of metformin and other insulin sensitizer agents for the treatment of PCOS, in the recent years, other therapeutic alternatives have been investigated.[6]

Inositol is a member of vitamin B family; among nine forms of inositol, myo (MYO) and d-chiro-inositol (DCI) are the types, which have provided a beneficial result for treating the PCOS in current researches. The reason being that there is a defect in the secondary messenger of the women suffering from PCOs. Therefore, MYO-inositol in this situation acts as a secondary messenger to reduce the disturbance in the signalling pathway.[7]

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Received: 28-Aug-2019
Accepted: 12-Mar-2020

Based on the published results, both MI and DCI represent potential valid therapeutic approaches for the treatment of insulin resistance and its associated metabolic and reproductive disorders.. Furthermore, the combination MI/DCI seems also effective and might be even superior to either inositol species alone.[8] The use of 2×2000 mg Myo-inositol 2×200µg folic acid per day is a safe and promising tool in the effective improvement of symptoms and infertility for patients with polycystic ovary syndrome.[9]

The intervention of Myo - inositol have also shown effective result in other trials with an increase in HDL levels, resulting in weight loss. Myo inositol intervention resulted in lowering of insulin levels, triglycerides, testosterone, and blood pressure in women with PCOS.[10]

D-chiroinositol functions as an intracellular messenger in this process, which supports ovulation and improve fertility while Myo is responsible for increasing the insulin sensitivity.[11] Therefore; this study was aimed to evaluate the effects of myo- inositol in the treatment of young females affected by polycystic ovarian syndrome.

METHODOLOGY:

This was a quasi-experimental study design; to determine the effects of myo inositol in young females suffering from polycystic ovarian syndrome. This study was conducted in United Medical and Dental College and Creek General Hospital from January 2017 to January 2018. The inclusion criteria was women from aged 18 to 30 years and diagnosed with PCO on the basis of currently accepted criteria which include hyperandrogenism, anovulation and/ or polycystic ovaries as observed on ultrasonography.[12] PCOS is also accompanied by a number of metabolic disorders, such as insulin resistance, hyperinsulinemia, and obesity so women having BMI > 18kg/m^2, fasting insulin > 12mIU/L were also included in study. Other causes of hyperandrogenism (such as congenital adrenal hyperplasia or androgen-secretory tumours) and ovarian dysfunction (such as hyperprolactinaemia or thyroid gland impairment) were excluded.

Based on the inclusion criteria 100 subjects were enrolled in the study by non-randomization sampling technique. A single page leaflet was used to explain the study to the patients and the students in order to enrol them in the study. The subjects who were ready to participate in the study were given an informed consent to sign and fill a questionnaire. This study was executed by the approval obtained from Institutional Review Board. The women started with the intake of Myoinositol and folic acid at a dosage of 2000 mg Myoinositol and 400 µg folic acid/day and used it for 6 months. The primary outcome of the study was to determine the restoration of normal menstrual cycles, improvement in acne, reduction in hirsutism and weight loss. The data was collected through performa. The variables, which were assessed in the study include hirsutism, acne, ultrasound findings, BMI, random sugar level and fasting insulin levels. The paired t Test was used to analyse the data before and after 6 months of treatment with Myoinositol and folic acid at a dosage of 2000 mg Myoinositol and 400 µg folic acid/day and used it for 6 months. After data collection, the results were analysed using SPSS version 21. The final results were displayed in the form of a bar chart and pie chart that displayed the difference between the variables evidently. P value > 0.05 was considered as statistically significant.

RESULT:

The data of 100 patients with PCO was evaluated. Table 1 shows BMI reduced to 25.59 in treated subjects from pre-treatment level of 27.03, lower level of random blood sugar were observed from pre-treatment value of 115.25 to 112.76 and fasting insulin levels reduced from 17.62 to 16.29 after the treatment.

Figure 1: According to the record menstrual cycle abnormalities improved significantly after the treatment. Oligomenorrhea reduced from 39% to 23 % in total number of subjects evaluated.57% had regular cycles before starting treatment which increased to 73% after the treatment.

73% presented with hirsutism out of which 37 % showed significant reduction in hair growth. While only in 10% improvement in facial acne was observed.

Figure 2: In the studied subjects, 97% had ultrasound features of PCO. Out of these 57% patients had improvement while 43% subjects showed no change. It was also noticed that 81% subject had Myoinositol as 1st line treatment for PCO while 1% had already used oral contraceptive pills, 4% used anti androgenic hormonal therapy, 13 % used Glucophage in dose of 500mgTDS while 1% subjects used 250 mg Glucophage tds before this therapy. The evaluation of role of Myo inositol was not done in each group separately. All of these treatments were stopped before starting Myo inositol.

Regarding effect of diet control and exercise ,26% subjects had diet control along with treatment while 14% did exercise.

DISCUSSION:

As compared to a study conducted by Naz MSG et.al.[13] published in Sep 2019 the prevalence of polycystic ovarian syndrome in adolescents based on the Rotterdam criteria was 11.04% (95% CI: 6.84-16.09%)[13]. According to their result there is a variation in the prevalence of PCOS in adolescents based on different criteria. In our study the age group of 20 – 24 years occupied majority of the sample size.

Table 1 Paired t Test

	Pre	Post	P-Value
BMI	27.03 ± 3.19	25.59 ± 2.66	0.000**
RBS	115.25 ± 16.09	112.76 ± 13.9	0.000**
Fasting Insulin	17.62 ± 5.15	16.29 ± 4.07	0.000**

*Note: * Significant at 0.05: ** significant at 0.01*

Table 2: Proportion Testing

		Pre	Post	P-Value
Menstrual Cycle	Regular	57%	73%	0.02*
	Polymenorrhea	2%	2%	1.00
	Secondary Amenorra	2%	2%	1.00
	Oligomenorrhea	39%	23%	0.01*
Hirsutism	Yes	73%	36%	0.00**
	No	27%	27%	1.00
	Improved	0%	37%	0.00**
Facial Acne	Yes	94%	84%	0.02*
	No	6%	6%	1.00
	Improved	0%	10%	0.00**
Ultrasound Pelvis	PCO	97%	43%	0.00**
	Normal	3%	57%	0.00**

*Note: *Significant at 0.05: **significant at 0.01*

Figure 1: Menstrual Cycle

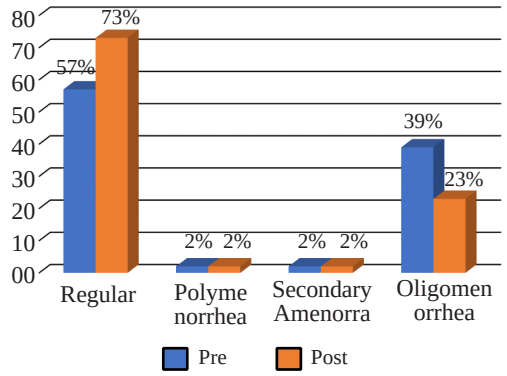
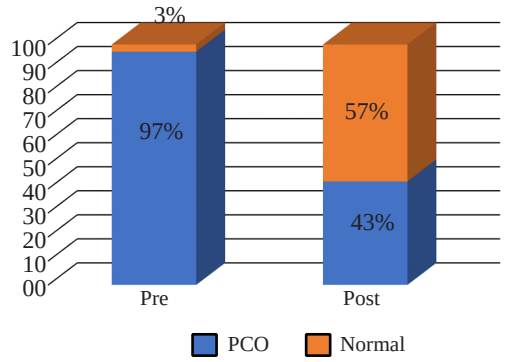


Figure 2: PCOs



This validated our study, which aimed to identify the effects of our treatment in young females.

The data collected showed a significant relation of the PCO with BMI as compared to a study done by Wang FF et al[14], 42% of the PCOS had normal BMI, but clinical and hormonal profile was similar to PCOS patients with elevated BMI (overweight/obese).In our study the mean BMI was 27.03 ± 3.19 which improved to 25.59 ± 2.66. Similarly significant association was seen between the random blood sugar level and fasting insulin levels with PCO in young females.

Our results are comparable to the study conducted by Unfer V[15], which showed Myo-inositol (MI) and D-chiro-inositol, two inositol stereoisomers, have been proven to be effective in PCOS treatment. However, in our study only MI has been shown to have beneficial effects on androgenic symptoms, whereas the administration of MI/D-chiro-inositol, in the physiological plasma ratio (i.e., 40:1) ensures better clinical results, such as the reduction of insulin resistance, androgens' blood levels, cardiovascular risk.

By Nordio M, Proietti E[16] the combined administration of MI and DCI in physiological plasma ratio (40:1) should be considered as the first line approach in PCOS overweight patients, being able to reduce the metabolic and clinical alteration of PCOS and, therefore, reduce the risk of metabolic syndrome ,as compared to our study which showed significant weight loss by improving patient's BMI with myoinositol alone and folic acid without D-chiro.

Bevilacqua A, Bizzarri M[17] clinical data support the beneficial effects exerted by inositol by reducing glycaemia levels and hyperinsulinemia and buffering negative effects of sustained insulin stimulation upon the adipose tissue and the endocrine system. Due to these multiple effects, Myoinositols has become a reliable treatment option, as opposed to hormonal stimulation, for insulin-resistant PCOS patients. Viewing the frequency table of fasting insulin level, it can be observed that though majority of the insulin levels were 17.62 ± 5.15, indicates these young females are at risk of increase in insulin resistance.

Nas K, Tûû L.[18] All the groups showed significant improvement ($p<0.05$) in prolactin and progesterone level after the treatment. Furthermore, the treated groups reported a significant improvement in the menstrual cycle disorders, while only life-style group showed an increase which was not statistically significant ($p>0.05$). After 6 months follow up, data was collected, to compare the results after the use of myo – inositol. The outcome displayed a significant effect (0.01) of myo-inositol in regulating the irregularities of the menses. Conclusion can be driven that females undergoing irregularities in menses can take this intervention.

Furthermore, the other symptoms hirsutism and acne, both showed different outcomes. Myo-inositol was successful in reducing the condition of hirsutism from 73% to 36.6 % while acne incidence reduced from 94.3 % to 84%. Therefore, it can be said that hirsutism is related to the hormonal imbalance while acne is associated with several factors; hence, does not portrait a definite relation with hormonal imbalance.[19]

Further after overviewing the entire result, it can be noted that Myo – inositol was not successful in treating entire sample of the young females, The reason for this can be deduced from the other studies that defect in the secondary

messenger is not the only reason for the disturbance in hormonal imbalance. Other reasons such as genetics or associated disorders can be responsible for irregular menses which eventually could lead to development of PCO; hence, this is supported by the results computed which displays a significant relation between the menstrual cycle and PCO[20].

Advani K et al conducted a study to evaluate the efficacy and safety of the supplementation. They have suggested that combination therapy can be used for the comprehensive management of PCOS. Monotherapy of insulin sensitising agents, antioxidants and vitamins is beneficial in the treatment of PCOS. Combined use of insulin sensitising agents (myo-inositol, D-chiro-inositol and chromium picolinate), antioxidants (N-acetylcysteine and lycopene), and vitamins (vitamin D, biotin and folic acid) is safe and effective in obese and non-obese women with PCOS[21].

As per a study by McBreairty LE,[22] diet control and exercise are considered as an additive factor, which supports the efficacy of the myo-inositol in playing an integral role as a secondary messenger in increasing the insulin sensitivity; thus, reduces any disruption in hormonal balance that can lead to obesity.[22] Hence, it can be stated that the role of the lifestyle balance is responsible in increasing the insulin sensitivity and lowering the BMI that maintains harmony in the body functions. The study holds some limitations, which leaves a gap in the literature to be further assessed. The blood sugar level taken was random rather than fasting, which would have given a more clear idea of high sugar level. The use of metformin, diet, exercise and other therapies was not evaluated as integrated treatment with Myo inositol. Myo-inositol used over last decade has been successful in treating insulin sensitivity. Use of Myo inositol in the PCO has displayed an evident result in our study conducted. The outcome displayed that Myo - inositol was successful in improving androgenic and metabolic effects of PCO syndrome. This improves compliance of the use resulting in better outcomes in the management of menstrual irregularities, hyperandrogenism, and metabolic parameters.

CONCLUSION:

This concludes that Myoinositol is an effective alternative in the treatment of PCOS. It's a safe option in young females with no side effects in the standard dosage.

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Student Corner OriginalArticle DOI: https://doi.org/10.51985/JBUMDC2019085

Correlation of Hand Hygiene Knowledge and Hand Decontamination Practices of Medical Students

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ABSTRACT

Objectives: To determine the knowledge of MBBS students of a public sector medical university regarding hand hygiene and to assess the practical implication of their knowledge regarding hand hygiene during the clinical postings.

Study Design and Setting: A cross sectional study was conducted in Sindh Medical College, Jinnah Sindh Medical University (SMC-JSMU) Karachi, from July to November 2018.

Methodology: A total of 316 M.B.B.S students from first year to final year were included in the study. Students were equally divided into preclinical and clinical groups. Hence, the knowledge of preclinical and clinical students were compared in the present study. Age range of participants was 18 to 24 years and both male and female participants were involved. Data was analyzed by SPSS 22.0. P value < 0.05 was considered as statistically significant.

Results: Approximately 249 (78.8%) students agreed that hands of health care workers are a source of nosocomial infections. Nearly 293 (92.7%) students admitted that hand decontamination and gloving is necessary before bedside procedures. Only 61 (38.6%) students performed it routinely. Chief restricting factor in performance of hand hygiene was inadequate supply of hand hygiene resources as reported by 122 (77.2%) students.

Conclusions: Majority of medical students in both preclinical and clinical groups were well aware of HH practices and its significant role in infection control. However, only a limited number of students routinely performed HH. The difference between knowledge and practice of students was mainly due to the inadequate facilities of hand washing in public sector hospitals.

Keywords: Hand hygiene (HH), Hand decontamination practices, Health care associated infections (HCI), Knowledge, Medical students.

INTRODUCTION:

According to World Health Organization (WHO), hand hygiene (HH) means cleansing of hands by any procedure of hand decontamination.[1] Practices of HH involve use of only water, soap, antimicrobial soap with water, antiseptic with water and an alcohol-based hand rub. Use of alcohol-based hand rub is more effective, consumes less time and depletes pathogens promptly than hand washing. Healthcare-associated infections (HCAIs) contribute significantly to infectious disease (ID) burden worldwide. A considerable number of patients suffer from HCAIs annually. Particularly in developing countries proportion of HCAIs is significantly increasing.[2] According to WHO 1.4 million people globally are affected from HCAIs. Contaminated hands of health care workers (HCWs) are the main source for transmission of HCAIs.[3] These constitute mainly skin, digestive system and respiratory system infections which become a source of major ID burden.[4] Pathogenic organisms transmitted from contaminated hands includes Staphylococcus aureus, Pseudomonas, Klebesilla and Rhinovirus.[5]

HH is considered as one of the best methods in prevention of HCAIs. Although the recommended process of HH is relatively a simple method yet its compliance is reported to be 40% among HCWs.[6] Globally hand washing practices were followed properly by minority of HCWs (2 to 10 %).[7] Efforts are being made worldwide to design effective strategies for implementation of HH practices. One such strategy is the presentation of theory of "My five moments for hand hygiene" by WHO.[8] According to this concept these are the critical moments when the intrusion in spreading of HCAIs may prove significant. These include the moment before touching a patient, before execution of aseptic and clean techniques, after contact with body fluids, after patient contact and after exposure to patient's surroundings. This theory has been used to promote knowledge and HH practices among HCWs.[6,8]

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Received: 31-Jul-2019
Accepted: 04-Mar-2020

Common factors associated with poor hand decontamination practices include irritation of skin, inadequate provision of hand-washing materials and towels, heavy work load, decreased manpower, lack of basic knowledge and awareness of HH also account for poor compliance. A positive attitude towards HH practices may contribute as an influential factor towards the attitude development of the fellow medical practitioners.[3, 9]

Study conducted in Pakistan revealed that only 17% doctors were familiar to the WHO instructions on HH. The less provision of sink, soap, water and disposable towel are notable factors associated with poor hand decontamination practices locally. Generally, adherence to HH was 38.8% but it indicates variation in different health care units.[3,10] Another study conducted in Ghana revealed that poor HH practices was due to inaccurate knowledge and insufficient facilities to perform HH.[11] A survey from Karnataka, India reported limited knowledge of HH among medical students.[12]

It is of utmost significance to identify the knowledge of HH and hand decontamination practices of medical students to develop a positive attitude of HH among them. It may also help the medical educationist to update the medical curriculum in light of the results of such studies. Therefore, the current study was designed to determine the knowledge and attitude of HH and hand decontamination practices in preclinical and clinical medical students of a public sector university of Karachi and to assess the practical implication of their knowledge regarding hand hygiene during their clinical postings.

METHODOLOGY:

A cross sectional study was conducted in Sindh Medical College, Jinnah Sindh Medical University (SMC-JSMU) Karachi, from July to November 2018. Our research protocol was approved by the Institutional Review Board of SMC, JSMU. A total of 316 M.B.B.S students from first year to final year were included in the study. Students were divided into preclinical and clinical groups. Although preclinical students have no patient interaction, however, they are being provided basic knowledge of HH during class lectures. Hence, the knowledge of preclinical and clinical students was compared in the present study. Age range of participants was 18 to 24 years and both male and female participants were involved. Students enrolled in non-medical faculties were excluded.

Non probability convenient sampling technique was used. Sample size was calculated using open EPI software. Considering population size = 1750, anticipated % frequency = 50 (assuming 50% as no specific similar study could be found), Confidence level = 95 %, confidence level as +/- percent of 100 = 5, design effect = 1. The sample size obtained was 316. Medical students were divided into two equal groups, preclinical students of first year and second year M.B.B.S (n= 158), clinical students of third year, fourth year and final year M.B.B.S. (n=158). The participants were selected based on their consent to be included in the study.

A structured questionnaire was designed after going through extensive literature review to be filled by participants. The content areas of questionnaire included socio-demographic characteristics, knowledge and attitude of medical students regarding HH and hand decontamination practices. Data was collected by investigators. After obtaining written informed consent and detailed rationale of the study; the questionnaire was filled by the participants within university premises in their free time.

Data was analyzed using Statistical Package for the Social Sciences (SPSS) version 22.0. Descriptive statistics were expressed as mean and standard deviation for numerical variables. Categorical variables were expressed in frequency and percentages. Chi-square test was applied to assess the difference between the knowledge of HH and practical application of this knowledge during the clinical rotations among the clinical group. P value of < 0.05 was considered significant.

RESULTS:

From total of 316 medical students who were interviewed in this study, 241 (76.3%) were females and 75 (23.7%) were males. Distribution of medical students in preclinical and clinical years was equal i.e. 50% in each group. Medical students included in the study were 108 from first year, 50 from second year, 74 from third year, 41 from fourth year, and 43 from final year.

Majority of the participants 293 (92.7%) were well aware that hand decontamination and gloving is necessary before any bedside procedure (Table 1). My five-moment concept of HH was known by 171 (44.9%) of medical students. Variables of my five-moment concept were answered accurately by most of the student as displayed in table 1. Methods of HH were known unsatisfactorily. Lack of accurate knowledge with respect to hand washing and rubbing methods is illustrated in table 1.

As recommended by WHO, alcohol-based hand rubbing is the gold standard method of HH.[1] Awareness among participants about WHO recommendations regarding preparations of HH was very low. In contrast to alcohol-based hand rubs, most of the participants (30%) 95/316 preferred water and antimicrobial soap as a hand hygiene preparation tool.

Approximately 190/316 (60.1%) students received information on HH from class lectures and 39/316 (12.3%) from clinical rotations. (Table 1)

Difference in knowledge and practical implementation of HH in clinical group is demonstrated in table 2. Significant number of clinical students 155/158 (98.1%) agreed that HH and gloving is necessary before any bedside procedure. However, 61/158 (38.6%) clinical students performed HH

Table 1: Frequency distribution of Knowledge of HH among preclinical and clinical medical students. (n=316)

Knowledge of hand hygiene	Preclinical students n (%)	Clinical students n (%)	Total n (%)
HH is practiced to prevent HCAIs of patients, HCWs and microbial contamination of health care environment	109 (34.49%)	129 (40.82%)	238 (75.3%)
Hands of HCWs are source of nosocomial infections	124 (39.24%)	125 (39.55%)	249 (78.8%)
Hand decontamination and gloving is necessary before any bedside procedure	143 (45.25%)	150 (47.46%)	293 (92.7%)
Hand rubbing is more effective against germs than hand washing	32 (10.2%)	100 (31.6%)	132 (41.8%)
Time needed to apply alcohol-based hand rubs	30 (9.53%)	35 (11.07%)	65 (20.6%)
Steps are in proper hand washing technique	137 (43.35%)	140 (44.30%)	277 (87.7%)
Washing hand with soap and water is recommended when soiled with blood, body fluids and visibly dirty	124 (39.24%)	124 (39.24%)	248 (78.5%)
Five moments concept			
Do you know about my five moments concept of hand hygiene?	81 (25.63%)	90 (19.27%)	171 (44.9%)
Hand washing prevents transmission of germs before touching patients	260 (82.3%)	130 (41.13%)	130 (41.13%)
Hand washing prevents transmission of germs after touching patients	145 (45.88%)	146 (46.20%)	291 (92.1%)
Hand washing prevents transmission of germs after exposure to surroundings of patients	113 (35.7%)	158 (50.0%)	271 (85.8%)
Hand washing prevents transmission of germs after exposure to body fluids patients	142 (44.93%)	142 (44.93)	284 (89.9%)
Hand hygiene techniques			
Method of HH is required before palpation of abdomen	9 (2.84%)	150 (47.46%)	159 (50.3%)
Method of HH is required before giving injections	64 (20.34%)	65 (20.56%)	129 (40.9%)
Method of HH is required after removing examination gloves	53 (16.77%)	60 (18.98%)	113 (35.8%)
Method of HH is required after visible exposure to blood	9 (2.84%)	89 (28.16%)	98 (31%)
Hand hygiene preparations			
Which preparation of HH product is most preferable?			
Alcohol based hand rubs	42 (13.29%)	43 (13.61%)	85 (26.9%)
Water and antimicrobial soap	15 (4.69%)	80 (25.31%)	95 (30%)
Water and plain soap	35 (11.07%)	30 (9.49%)	65 (20.6%)
Water and antiseptics	38 (12.02%)	15 (4.69%)	53 (16.8%)
Only water	9 (2.84%)	9 (2.84)	18 (5.7%)
Source of HH information and training			
Class lectures	100 (31.6%)	90 (28.5%)	190 (60.1%)
Clinical rotations	0 (0.0%)	39 (12.3%)	39 (12.3%)

Table 2: Comparative analysis of knowledge of HH and hand decontamination practices among clinical students. (n=158)

Knowledge of hand hygiene:	N (%)	Practice of hand hygiene protocols:	N (%)	P value
Do you agree that Hand hygiene and gloving is necessary before any bedside procedures?	155 (98.1%)	Do you routinely perform hand hygiene before any bedside procedure?	61 (38.6%)	0.007
Correct knowledge of steps of proper hand washing technique?	147 (93%)	Do you perform all steps of hand washing during clinical postings?	34 (21.5%)	0.109

Table 3: Frequency of distribution of Restricting factors in performance of HH in health care units as reported by clinical students. (n=158)

Restriction factors in performance of HH among clinical group	Frequency n (%)
Shortage of hand washing resources	122 (77.2%)
Inadequate provision of gloves	120 (75.9%)
Forgetfulness to perform HH	90 (56.9%)
Lack of knowledge on HH	59 (37.3%)
Irritation of skin by hand rubs and antiseptics	39 (24.6%)

during clinical rotations (P= 0.007). Similarly, knowledge of students regarding steps of hand washing technique was better 147/158 (93%) as compared to its practical implication 34/158 (21.5%). (P=0.107).

DISCUSSION:

Contaminated hands of HCWs are the main source for transmission of nosocomial infections. Nosocomial infections are effectively decreased by complying with HH. In the recent years there is a mushroom growth of medical institutes across Pakistan. These institutes are producing a good number of medical graduates each year. HH practices of undergraduate medical students have not been studied comprehensively in Pakistan. The Current study was aimed to assess knowledge and practical implications of HH among medical students.

In the present study 249 (78.8%) medical students agreed that hands of HCWs are source of nosocomial infections. In comparison, addressing the similar question, a figure of 46.4% was reported by a study conducted in Mumbai, India. [13] This low frequency in their study probably reflects lack of involvement of students in primary patient care and deficiency of class room teaching regarding significance of HH in undergraduate curricula.[13]

Hand rubbing is more effective method of HH in accordance with WHO recommendations. However, in the current study only 132 (41.8%) students responded that hand rubbing is most effective method of hand cleansing than hand washing. In the current study medical students had less satisfactory knowledge regarding effectiveness of hand rubbing method. Our finding was in contrast with a study conducted by Ariyaratne *et al*. which reported a much higher 72.9% frequency.[1,2,14] Time duration required by alcohol-based hand rubs to kill most of germs on hands was known correctly by only 65 (20.6%) of participants in the present study. This finding was consistent with a study conducted in India which reported a frequency of 28%.[15]

Importance of alcohol-based hand rubs was mentioned in previous studies.[2,16] However, only 85 (26.9%) participants in present study preferred to use alcohol-based hand rubs over various other products of HH. Study conducted by Immanuel *et al.* is in agreement with our findings as they reported 22.9% of HCWs who used alcohol-based hand rubs. This infrequent practice was probably due to lack of appropriate knowledge among HCWs, inadequate supply of alcohol-based hand rubs as well as work overload in government sector hospitals. Another important finding of the current study was that 129 (40.9%) of participants were aware of hand hygiene method needed before giving injections. Immanuel *et al.* reported a similar result in which 39.4% participants were aware of similar variable. This slight difference in results was may be due to inclusion of all HCWs in their study. This also signifies that professional status of HCWs is significantly associated with HH knowledge.[17]

In the current study 190 (60.1%) participants believed to obtain effective knowledge of HH from class room lectures. Similarly, Thea *et al*. in a 2010 survey recorded that 57.1 % students considered class lectures as a highly effective method of learning HH.[18] Study conducted by Ali *et al* reported that only 31.6% students were found to follow all steps of hand washing technique. This finding is consistent with a low frequency 21.5% of medical students in our study who reported to perform hand washing techniques accurately. (P=0.109). This reduction in practice was may be due to poor compliance and increase work load.[19]

Curriculum of undergraduate medical students should emphasize on HH. We suggest that HH practices of students should be evaluated during hospitals postings and exams. It will be helpful in training best medical practitioners who will not become a source of HCAIs.

The limitations-single centered study and cross sectional nature of the study. Moreover, HH practices of participants were purely self-reported and reporting bias may be encountered in this study. Due to the single centered study: the result of this study cannot be generalized for the entire public sector healthcare facilities for hand hygiene.

CONCLUSION:

Majority of medical students in both preclinical and clinical groups were well aware of HH practices and its significant role in infection control. However, only a limited number of students routinely performed HH. The difference between knowledge and practice of students was mainly due to the inadequate facilities of hand washing in public sector hospital.

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Review Article DOI: https://doi.org/10.51985/JBUMDC2019138

Clinically Significant Variation of Paranasal Sinuses on CT-Scan

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ABSTRACT:

Anatomical variations are not diseases and can be found in every individual. Due to the anatomical variations, the structural changes occur in nearby anatomical relations. By keeping in mind, the vast range of anatomical variations in nasal cavity and paranasal sinuses (PNS), every case of sinusitis must be planned carefully to avoid dreadful complications of surgical procedures. Sinus anatomical variations have been associated with the etiology of sinusitis. In this regard computed tomography (CT) imaging has become an important diagnostic tool. CT Scan imaging of nose and para nasal sinuses is mandatory in patients with history of sinusitis in order to evaluate the detailed anatomy which includes normal anatomy, anatomical variations, bony details and the extent of the disease pathology. Certain anatomical variants are supposed to be a causative factor for development of sinus pathology and hence it becomes compulsory for the radiologist to be aware of the anatomical variants of nasal cavity and PNS especially if the subject is considered for surgical intervention.

Key words: Anatomical Variations, Paranasal Sinuses (PNS), Nasal cavity, CT Scan, Functional Endoscopic Sinus Surgery (FESS).

INTRODUCTION:

Paranasal sinuses (PNS) are air-filled spaces present in specific bones of the skull. There are 4 pairs of paranasal sinuses which are named according to their location in which they are situated in the skull bones, which includes frontal sinus, maxillary sinus, ethmoid sinus, sphenoid sinus. Clinically, PNS are divided into 2 groups, the anterior group and the posterior group. Anterior group includes maxillary, frontal, and anterior ethmoidal, they all open together in the middle meatus and their ostia lie anterior to basal lamella of middle turbinate. Posterior group includes posterior ethmoidal sinuses which open in the superior meatus and the sphenoid sinus which open in the spheno-ethmoidal recess [1].

Research show that the anatomy of PNS is variable and complex. CT PNS is choice of investigation in evaluating PNS anatomy, pathology and the anatomical variations. The anatomical variations disturbing osteomeatal complex (OMC) includes Deviated nasal septum (DNS), concha bullosa (CB) bent middle turbinate, agger nasi cells and haller cells. These OMC anatomical variants can cause meatal narrowing and even obstruction of sinus. Knowledge of the anatomical variations does reduce the surgical complication rates during Functional Endoscopic Sinus Surgery (FESS), and helps explain recurrence of disease. It also allows one to change the operative technique for the benefit of patient. CT PNS has vital role in presurgical evaluation of minimally invasive FESS [2,3,4,5,6,7,8,9].

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Received: 17-Dec-2019
Accepted: 26-Feb-2020

It is necessary to identify the clinical and surgical importance of anatomical variants of PNS, certain anatomical variants are supposed to be causative factor for development of sinus pathology and hence it becomes compulsory for the radiologist to be alert of the anatomical variants of PNS especially if the subject is candidate for FESS[3,4,6,10,11].

The important ethmoid air cells which are included in anterior group are: agger nasi cells, ethmoid bulla, supraorbital cells, frontoethmoidal cells, haller cells[1]. The ethmoid air sinuses play a crucial role in FESS. The posterior ethmoids and the sphenoid sinuses can be accessed via the anterior ethmoid cells. Anterior ethmoidectomy helps improve frontal air sinus drainage hence minimizing the need for opening the frontal sinus during surgery[12,13]. Variations in the pneumatization of ethmoid sinuses may result in the disturbance of sinus ventilation and sinus drainage pathway. These can be the etiological factor for sinusitis and spread of infection to adjacent structures [13,14].

The coronal views of CT scan are best for the sphenoid and the ethmoid cell variants such as the onodi cells or sphenoethmoidal cells. The modification and advancement of computed tomography has granted extensive assessment of patient's paranasal sinuses thus providing a guide map for FESS surgeons to operate effectively [15,5,13]. In a study conducted in Egypt it was reported that the frequency of agger nasi cells and CB were equally frequent (30.6%), and Haller cells were detected in 11.2%. Variations of uncinate process were detected in 18.1%, and the large ethmoid bulla was detected in 10% [16].

Whatever may be the diagnosis, but for understanding of anatomical relations of paranasal sinuses, CT Scan of Para nasal sinus is mandatory before performing sinus surgery. This is to avoid chance of complications while performing the procedure. Patients having history of chronic sinusitis and who are not responding to medical therapy, computed tomography should be performed for the possible

identification of anatomical variants. In order to prevent harmful complications such as cerebrospinal fluid (CSF) leak, meningitis, or blindness, this prevention will decrease the burden of disease, patient disability and patient morbidity, so a detailed knowledge of the possible anatomical variations is essential [17]. Pneumatization (formation of air cells) of turbinate referred as concha bullosa (CB) is a normal anatomical variant of PNS. CB is classified into extensive CB, bulbous CB, lamellar (CB) and out of these middle turbinate CB has been identified as a possible causative factor in sinusitis [18,7].

As a number of lateral nasal wall diseases cannot be recognized and identified by endoscope, so with this regard computed tomography must be performed even when the diagnostic nasal endoscopic finding is insignificant, provided that the history and clinical findings suggest the presence of some disease [19]. The anatomical variations of lateral nasal wall and PNS are surgically and patho-physiologically important because they narrow the drainage pathway, impair the mucociliary function of the para nasal sinuses, which in turn leads on to stagnation of secretions, then infection and inflammation of the mucosa lining the sinuses occurs. Diseases in severely pneumatized sinuses direct on to exposure of important structures like Optic nerve, Internal Carotid artery, and anterior cranial fossa of the brain, to infection and inflammation, and also increases risk of injury during surgical procedure. Hence, CT Scan imaging of nose and PNS is mandatory in patients with history of sinusitis, to evaluate the detailed anatomy (normal anatomy, anatomical variations, bony details and the extent of the disease pathology) that are commonly encountered in the osteomeatal complex (OMC), and lateral nasal wall[20,3,4,21,7,8]. Frequent and extensive application of functional endoscopic sinus surgery (FESS) with experience makes it essential to know the complex anatomy and the pathology of PNS very well and thoroughly before surgery. The importance of paranasal sinus computed tomography in terms of identifying and determining anatomical variations of PNS before FESS, helps in predicting the complications that can occur during surgery has been highlighted [22,3,4,6].

METHODOLOGY:

The overall methodology was commenced by the following steps mentioned below;

1. Review of various articles related with the topic
2. Extraction of articles
3. Data gathered
4. Analysis and comparison of findings
5. Conclusion

After following above mentioned steps, a comprehensive literature search was done using Google Scholar, Medline, PubMed, and Pakmedinet from the year 2009 onwards using keywords like anatomical variations, CT-scan, FESS, nasal cavity and paranasal sinuses. For Ancient literature books and other clinical guidelines of international organizations were also reviewed for relevant references. The analysis of the data was done by regional analysis technique, and narrative synthesis methodology was used to synthesize overall review findings.

Literature Review:

The paranasal sinuses (PNS) form a complex variable unit of 4 paired air-filled spaces at the opening of the proximal airway. The development of PNS starts from furrows and ridges in the lateral wall of nasal cavity during 8th week of development, and sinuses continue their formation as air cells within the cavities until early adulthood from the age of 20 to 25 years. Each sinus is named according to the skull bone in which they are located[1,23].

Paranasal sinuses include frontal sinus, maxillary sinus, ethmoid sinus and the sphenoid sinus, maxillary sinus is largest of all[1]. Radiologic evidence of various sinuses appears by the age of 4-5 months after birth (maxillary sinus), 1 year of age (ethmoid sinus), 6 years of age (frontal), and 4 years of age (sphenoid). These 4 pairs of paranasal sinuses perform various important functions which are, air conditioning of the inspired air, improves the voice, provides quality and resonance to voice, act as thermal insulators to provide protection to the delicate structures which are present in the orbit and cranium from variable changes of intranasal temperature. It also, lightens the skull bones, provide extended surface for olfaction, offers immunologic defense against microbes, act as buffers against trauma and thus protect brain against any kind of injury[1,24,11].

Hippocrates in 5th century B.C. stated “In a person having a painful spot in head, with intense headaches, pus or fluid running from the nose removes the disease" which may be referred as sinusitis. Sinusitis is the inflammation or swelling of mucosal lining of PNS, and the spaces that secretes mucus which is necessary for the nasal passages to work effectively[25]. Sinusitis occurs when there is impaired mucociliary apparatus function with meatal narrowing or even obstruction, excessive mucus production or excessive mucus build up, stagnant mucous collection results in the sinuses becoming inflamed. Sinusitis can be acute or chronic, it can occur due to various reasons, such as viral, bacterial, fungal infection, allergic reactions, or even it can occur due autoimmune reactions[1,6,7].

Frontal sinuses are mostly paired and lobulated in shape. They are commonly symmetrical in shape, with presence of septum between the pair of frontal sinuses. Sometimes one or both of the sinuses may be missing. Frontal sinuses are not present at the time of birth, their development starts at the age of two years and reaches full size early adulthood. The frontal sinuses are located in the posterior most part of supercilliary arches, between the external and internal tables of frontal bone. Presence of bilateral frontal sinus was reported in (78.6%) subjects and presence of unilateral

frontal sinus was found to be present in (17.9%) subjects[23].

The most common anatomical variations of maxillary sinus were reported as pneumatization of the sinus and sinus septa. The prevalence of disease process in maxillary sinus was ranged from 7.5% to 66%[15]. The most frequent pathological findings of the maxillary sinus were sinus opacification, sinusitis, and mucosal thickening[26,13].

A study conducted in Philippines reported that most of the patients with sinusitis were males between age group of 31 to 40 years[16]. Most common anatomical variants were DNS, CB, agger nasi cells, and haller cells. Significant prevalence of anatomical variants of PNS was found among patients with sinus infection[27,3,5,8,24,9].

The study reported that the prevalence of bilaterally present agger nasi cells was found to be 100%[28]. The success rate of FESS is completely related to the knowledge of complex sinus anatomy[28]. Surgeon should be concerned about the anatomical variants of PNS for every patient before going for FESS[28,3,4,6].

The roof of ethmoid sinus is of great importance having close relationship with anterior cranial fossa. The anterior ethmoidal artery lies in the rostrum of ethmoid sinus, it is an anatomical reference point that goes from orbital region to anterior cranial fossa. Its location is of great importance during FESS. Adequate presurgical evaluation with CT scan imaging technique is important to assess the ethmoidal roof and its nearby structures[29,30].

Altered nasal septum occludes most of the nasal cavity considered as DNS. It is of three types osseous DNS, cartilaginous DNS and osteocartilaginous DNS type. DNS may result in compression of turbinate causing blockage of sinus drainage pathway and increases chances of infection and inflammation of the sinuses[31,5]. Deviated nasal septum was found in 62% of cases. The close proximity of PNS to important structures and neurovascular bundle such as optic nerve, orbit, skull base, and internal carotid artery stresses on the need of identification of anatomical variations of PNS in order to avoid the serious complications of surgical procedure[31,30,24].

Usman studied anatomical variations of PNS and nasal cavity in which DNS was found in 31% of cases, CB was present in 18.9% of cases whereas variation in uncinate process was reported in 12% of cases. Haller cells and aggernasi cells were found in 3.7% and 6.8% of patients respectively. Pneumatization of nasal septum was observed in only one patient with prevalence of 0.7%. Pneumatized turbinates were not reported in any patient, although pneumatization of uncinate process was observed in 2.2% of cases. Paradoxical middle turbinate was present in 9% of cases. Septal spur was seen in 3% of cases. Fifteen patients observed had more than single anatomical variants. In 2.2% of cases CB and haller cell both were present. Variation in uncinate process with paradoxical medial turbinate were seen in 2.2%. In 5.3% of cases DNS was present along with bony spur and in 1.5% of cases pneumatized nasal septum with pneumatized uncinate process was reported[32].

The structural morphology of paranasal sinuses shows vast diversity. They all vary in size, shape, morphology and count of the septa present, as in sphenoid sinus the MS which is main septum, and AS which is additional septum. The sphenoid sinus is related with important anatomical structures with respect to their walls, including both vascular and nervous relations, in addition to the anatomical organization of the sphenoid sinuses which is of great significance in the various surgical procedures such as FESS. CT imaging technique is one of the most accurate methods for imaging of the paranasal sinuses to visualize various structures along with their extent and depth. This method allows doctors to distinguish the variations in the anatomical relations of the PNS, due to the obvious clear-cut illustration of the bony structures[33,3,4,21,6].

Sphenoidal sinus variation is broadly used in skull base surgeries in a common surgical procedure called functional endoscopic sinus surgery. FESS is one of the best choices in a variety of surgeries such as endoscopic orbital surgery, sinonasal tumors. Various nerves and vessels are present near sphenoid sinus which are at danger during surgical procedure. These structures will be at risk of injury during surgery because of anatomical variations which includes protrusion, dehiscence, and pneumatization. CT scan imaging is a useful technique for the detection of PNS anatomical variants. Besides diagnostic value, CT scan imaging is valuable for risk assessment factors produced by anatomical variations of PNS[34,3,4,13].

In 1904 the posterior ethmoidal air cells called onodi cells were first reported by Adolf Onodi. The reported incidence was 10% in Indian population. It lies superior to sphenoid sinus. Its close proximity to optic nerve, internal carotid artery makes its diagnosis imperative prior to FESS. Variants of optic nerve in relation to sphenoidal sinus are classified as type 1: optic nerve is near to sphenoid sinus without indentation, type 2: nerve is near to sphenoid sinus indenting the wall, type 3: nerve courses through sphenoid sinus and type 4: nerve is near to sphenoid sinus and posterior ethmoidal cell[10,35].

Coronal plane computerized tomographic (CT) scanning has markedly improved the imaging of complex PNS anatomy as compared to sinus radiographs. Increasingly subtle bony anatomical variations and mucosal abnormalities of this region are being detected. Computerized tomography (CT) offers the gold standard in terms of imaging the extent of disease pathology and the fine detailed anatomy of paranasal sinus [35,3,4,21,5,6,13,24]. Neither plain X-rays nor Magnetic Resonance Imaging (MRI) offer optimal information in this respect[35,3].

The height of lateral cribriform plate lamella determines the

depth of the olfactory fossa. In 1962 Kero classified this height as: Type 1: 1-3mm, type 2: 4-7 mm, and type 3: 8 – 16mm. The increased depth of olfactory fossa produces a way for an increased chance of accidental injury to anterior cranial fossa during FESS, trauma and also in tumor erosion[10,36].

CT imaging is important to evaluate various pathologies of nasal cavity and PNS. It also helps to assess the fine bony details related to PNS, anatomical variants of PNS, and disease progress of PNS. Coronal high-resolution CT of the sinuses has become widely accepted as a necessary part of the preoperative evaluation of patients scheduled for FESS. CT scanning is better in identifying anatomical landmarks of PNS preoperatively and thereby reduces the complications of FESS. CT imaging technique is now established as the overall best method for evaluation of patients who are suspected of having a complex anatomy and any aggressive lesion of the paranasal sinuses (PNS)[3,4,5,6,37,38].

Literature has revealed that the conventional radiographs are of limited diagnostic use in evaluation of PNS diseases and modern imaging techniques like CT and MRI provide greater detail about the exact location, the extent of PNS disease and also helps in better understanding of complex anatomy, diagnosis and treatment plan of sinus diseases. It is also stated that CT is better than MRI in knowing the finer bony details, anatomical variations and fibro osseous lesions of PNS[4,39].

Literature search has also reported that the CT imaging proves to be a necessary tool in case of nasal pathologies as it provides a guide to the ENT surgeon and it also illustrates the whole pathway along with the anatomical variations of the individual and warns one of any existing or threatening complication of FESS[4,6,40,41].

It was concluded that use of CT scan is the most accurate approach in understanding the anatomical variations and diagnosing the diseases of PNS[3,4,5,6,13,21,24]. Surgeon must keep in mind that, remove only as much as required and preserve as much as possible, this has been the most important instruction of FESS. The anatomy of the nasal cavity and PNS is variable in every individual so in order to prevent various surgical or iatrogenic complications such as CSF leak, surgeon must have good idea about anatomical variants of the subject. CT is the investigation of choice particularly for the patients who are scheduled for FESS, assisting the ENT surgeon to understand the complex and variable anatomy affecting the paranasal sinus region. Thus, it is termed as ''ROAD MAP OF FESS''[4,42,43,44,45,46,]. The contribution of anatomical variants has been questioned as the variants are

Comparison:

Country	Year	Author name	Study type	Outcome
Poland	2009	Rysz M, Bakoñ L[52]	Retrospective	Haller cells: 13%, Bony septa per sinus:26%
Malaysia	2010	Vincent TE, Gendeh BS[51]	Retrospective	DNS: 46.7%, CB:62.9% (unilateral), CB:37.1% (bilateral)
Nigeria	2011	Amusa YB, Eziyi JA, et al.[54]	Cadaveric	Haller cells: 4%, Onodi cells:4%, Frontal cells:8%, Supra orbital cells:4%
Italy	2012	Fadda GL, Rosso S, et al.[49]	Prospective	DNS: 58.5%, Agger nasi cell: 24.3%, CB: 49.3%, Halle cells: 22.8%, Onodi clls: 8.5%
Pakistan	2013	Adeel M, Rajput MS et al.[55]	Retrospective	DNS: 26%, CB: 18.2%
Oman	2014	Al-Abri R, Bhargava D et al.[53]	Prospective	DNS: 80%, Agger nasi cells:49%, Haller cells:24%, Onodi cells:7.5%, CB: 49%, Olfactory fossa: Type 1-30%, Type 2-34%, Type 3-36%
India	2015	Tiwari R, Goyal R[50]	Prospective	DNS: 88.2%, CB: 76.4%, Agger nasi cells: 7%, Haller cells: 3.5%, Onodi cells: 1.6%
Turkey	2016	Dasar U, Gokce E[19]	Prospective	Agger nasi cells: 74.8%, CB: 67.5%, DNS: 59.5%
South India	2017	Gouripur K, et al.[16]	Prospective	Agger nasi cells: 96%, CB: 67.5%, DNS: 70%, Onodi cells: 6%, Haller cells: 14%
Egypt	2017	Alsowey AM, Abdulmonaem G et al[15]	Prospective	DNS:48.8%, Agger nasi cells: 30.6%, CB :30.6%, Haller cells: 11.2% , Uncinate process variations: 18.1%, Large ethmoid bulla:10%
India	2018	Kalaiarasi R, Ramakrishnan V et al[17]	Retrospective	CB: 54.7% bilateral, CB: 45.3% unilateral
Philippines	2018	Espinosa W, Genito R et al.[26]	Retrospective	Agger nasi cells: 78.3%, Haller cells 41.6%, DNS: 20.0%, CB: 11.7%
Turkey	2019	Yazici D.[47]	Retrospective	Haller cells: 19.3%, Onodi cells: 19%, DNS: 48.7% (right), DNS: 51.7% (left), Agger nasi cells: 82%, CB: 45.3%
Nepal	2019	Shrestha KK, Acharya K et al.[48]	Prospective	DNS: 64.5%, CB: 19.7%, Agger nasi: 18.4%, Septal pneumatization:6.5%, Onodi cell: 3.9%, Haller cell: 2.6%

equally prevalent in asymptomatic patients and in symptomatic patients of sinusitis. CT-scan can play an important role in formal preoperative assessment of normal anatomy along with variations of paranasal sinuses and nasal cavity that can have great impact over surgical planning and decreasing the ratio of surgical complications.

CONCLUSION:

Anatomic structural variations of nasal cavity and PNS have a practical importance during surgical procedures led on the sinuses by otolaryngologists.

The importance of this review is to identify the anatomical variations of PNS and nasal cavity on imaging techniques and their effective utilization while performing the minimal invasive FESS. CT-scan plays a fundamental role in the diagnosis of anatomical variations as well as of various diseases, for a better understanding in the decision making about clinical therapeutic and surgical approaches, acting as an indispensable aid for a better performance and success rate of less invasive operative techniques such as FESS.

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Review Article DOI: https://doi.org/10.51985/JBUMDC2019123

Local Drug Delivery to Treat Chronic Periodontitis

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ABSTRACT:

Periodontal disease is a chronic inflammatory disease of periodontium characterized by increased pocket depth, clinical attachment loss, sulcular bleeding, and bone loss. Bacterial plaque bio-film stimulates host derived enzymes and cytokines like TNFα, IL-1 and matrix metalloproteases that lead to destruction of periodontium, collagenolytic activity, decreased bone mineral density, intra-bony defects and ultimately bone loss. Chronic periodontitis is managed by conventional and systemic approach, where conventional therapy comprises of scaling and root planning. Mechanical debridement of plaque also requires an adjunct to eradicate the root cause of progressing disease. Hence, worldwide paradigm has shifted towards novel therapies; therefore, local delivery of drug is now preferred due to direct access to target sites with considerably less adverse effects and a better approach to deal with chronic periodontitis. The nano-particle technology to treat periodontitis is still an emerging and promising strategy for the management of disease with the provision of minimal dose, less invasive procedure and clinical efficacy.

Keywords: Conventional therapy, Chronic periodontitis, local drug delivery, plaque, scaling and root planning.

INTRODUCTION:

Periodontitis is a gradual inflammation of the periodontal apparatus, comprising of gingiva, periodontal ligament and alveolar bone in response to microbial plaque, resulting in annihilation of the periodontium.[1]

The worldwide prevalence of chronic periodontitis among the general adult population is reported to be 30–35 % [2] whereas according to National Health and Examination Survey III (NHANES III, 1988-1994), 50% of the adult population in United States, 42% in Britain,15.3% in Portuguese population has been reported in a study.[3] In 2003; Pakistan estimated 93% for periodontal disease among 65 year old with higher incidence in the rural population.[4,5]

The alveolar bone, gingiva, periodontal ligament and cementum are the closely related structures that collectively form the periodontium. The periodontal ligament is a fibrous, vascularised connective tissue that traverses the lamina dura, anchors the tooth to the alveolar bone, with the other half attached to the cementum.[6] The periodontium provides anchorage of tooth to the alveolar bone; provision of a barrier for the underlying structures from the oral microflora and distributed the forces of mastication.[7]

Antoni van Leeuwenhoek, a Dutch researcher, introduced the name of "microbial biofilm" as an adherent layer of microorganisms embedded in extracellular polymeric bacterial matrix.[8] Amongst pathogens, Treponemadenticola, Porphyromonas gingivalis and L. acidophilus are considered to be responsible for periodontitis.[9] The disease is initiated by chemotaxis of polymorphonuclear leukocytes (PMN) owing to bacterial lipopolysaccharide (LPS) antigen leading to release of cytokines TNFα and IL1 responsible for the resorption of bone and Matrix metalloproteinases (MMPs) released from fibroblasts that cause destruction of collagen. TNFα and IL-1 played a vital role in the formation of osteoclasts leading to bone resorption, rapid detachment of gingiva from the tooth surface and ultimately pocket formation.[10]

Evidences are present to demonstrate two-way relation between periodontal and systemic diseases, where both conditions could aggravate each other; such as acute myocardial infarction, infective endocarditis, bacteremia, respiratory diseases, diabetes, alzheimers' disease, pancreatic cancer, cerebral infarction and obesity. Lertpimonchai and colleagues concluded improper tooth brushing techniques and irregular dental visits may lead to the evolution of chronic periodontitis associated with bone loss.[11, 12]

Clinical features of chronic periodontitis exhibits morphological changes in gingival tissue like edema, redness, reduced consistency, bleeding on probing, halitosis, loss of clinical gingival attachment, pocket formation, furcation involvement, tooth mobility and alveolar bone loss.[13, 14]

According to the severity of the disease, the American Dental Association /American Academy of Periodontology 1999

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Received: 13-Nov-2019
Accepted: 05-Mar-2020

guidelines has classified Chronic periodontitis as mild=>3 - <5mm periodontal pocket depth (PPD),1 - 2 mm clinical attachment loss (CAL) ; moderate = = 5- <7 mm PD, 3 - 4 mm CAL and severe = >7mm PD, = 5 CAL.[15,16]

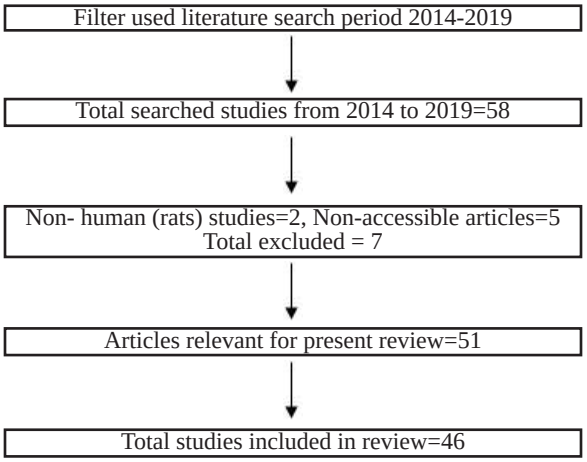
Conventional therapy is the most suggested approach to manage chronic periodontitis, also termed as "Initial therapy" comprising of supra and sub-gingival scaling root planning (SRP) with "adjunctive use of chemical agents."[17]However, conventional mechanical debridement procedures do not remove all pathogenic bacteria successfully from the sub-gingival sites, especially the ones found in non-accessible sites namely furcations, grooves, concavities, and deep pockets. Though systemic antibiotics produce beneficial effects in controlling the disease but they have the potential to produce adverse reactions and must be considered equally as their expected benefits. The world has shifted the treatment paradigm from conventional to local delivery system to treat chronic periodontitis. Therefore; this study aimed to assess the various local drug delivery strategies (intra-pocket) in order to provide more potent control of the disease and to avoid systemic adverse effects.

METHODOLOGY:

The search engines of google, google scholar and pubmed were used for literature search. Keywords and phrases used were chronic periodontitis, intra-pocket administration of drugs, gels, nanoparticles, periodontal fibres, periodontal strips, local delivery systems, adjunctive therapy to scaling and root planning, nanoparticles incorporated with drugs, and administration of drugs sub-gingivally.

The history tracking was from 2014 to 2019. A total of 58 articles were searched and selected for writing the review. Out of these, 2 studies were on non human (rats) and 5 articles had accessibility to abstracts only. 51 articles were relevant to this review. Therefore, 46 articles were selected for writing the review. (Flow Chart).

FLOW CHART



LOCAL DRUG DELIVERY STRATEGIES INTO THE PERIODONTAL POCKET:

Local drug delivery systems have been found beneficial due to direct access to target site which is usually non-responsive to conventional therapy. It also provides good patient compliance, bypasses first-pass metabolism in liver, have longer duration of action, cost effectiveness and safer route of administration. A still better approach is to introduce drug into the periodontal pockets where it actually stays confined, disseminates and is believed to produce better results than the systemic and other local strategies.[18]

Therefore, recommended drug delivery strategies through intrapocket administration are now available for the treatment of periodontitis and administered directly into the periodontal pocket directly. Such as; fibres, periodontal strip, films, gel, microspheres, nano particles, liposomes , nano-fibers, ointments etc.

1: Periodontal Fibers: The Periodontal fibers are the thread-like drug reservoirs that owe to drug delivery systems. They are inserted circumferentially within the periodontal pockets through an applicator. Then, fastened in-situ using an adhesive such as Cyanoacrylate with the provision of sustained release of the drug within the periodontal pocket.[19] Abeer AK acknowledged that the hollow fibers of cellulose- acetate, infused with tetracycline hydrochloride through which the drug basically disperses out from the reservoir system into the periodontal pockets and helped in eradicating spirochetes effectively from the gingival sulcus. A polymeric fiber device had been manufactured by Johnston & Co-Workers comprised of alginate with glycerol fibers, cross-linked with positively charged ions of barium incorporated with Ciprofloxacin and Diclofenac Sodium. This drug was pH dependent and functioned by the process of diffusion at pH 4.0, hence, provides zero-order kinetics.[20]

2: Periodontal Strips: A periodontal strip is an elongated thin, matrix band comprising of a flexible polymerinfused with the drugs dispersed evenly throughout its length with the virtue of securing interproximal space. The periodontal strips presented with noteworthy progress in different clinical parameters by eradicating microbes from the infected periodontal pockets. Since these are non-bio absorbable and removal after therapy is required as it may hamper tissue regeneration at the site.[21]

3: Films: Intra-pocket films are one of the most commonly used local delivery devices for periodontal pockets. The drug incorporated within the matrix of periodontal film spreads evenly throughout the polymer and is released in the infected sites by the process of diffusion or matrix dissolution.[22] The merits are easy insertion, suitable accommodation within the pockets and patient compliance. Periodontal films comprised of water-insoluble, non-degradable polymersare facilitating the release of drugs by the process of diffusion only whereas others; formed by

biodegradable soluble polymers release the drugs by the process of diffusion as well as matrix lattices or suspension [23].Presently,ethylated cellulose films comprising a number of anti-microbials and anti-septics such as Chlorhexidine, Metronidazole, Tetracycline and Minocycline have also been developed so far to produce encouraging results. However; non-biodegradable films have been replaced by biodegradable polymers due to several demerits.[24]

4: Gels: The Gels are semi-solid drug delivery mode and have gained awareness for delivering antimicrobials and other drugs to target the infected sites.This method offers several advantages like easy preparation; management; muco-adhesiveness to non-accessible sites and patient comfort.[25] While administering gels, the risk of irritation as well as allergies to host at the space of application is comparatively less due to the property of quick eliminating via simple catabolic pathways. Favorable results have also been achieved with the use of a number of organo gels and hydrocolloidal gels for delivery of antimicrobials like Tetracyclines (2.5%), Metronidazole (25%), Metronidazole benzoate (40%), along with the combination of tetracycline and metronidazole benzoate. [26] The Hydrogels are the hydrophilic polymers comprising of 3D structures in a meshwork of cross-linked structures of hydrogen bonding and ionic bonding.[27] These type of gels provide structural strength ,easy management at a cellular level and a source of bio-adhesiveness of drug.[28] Several polymers by the name of poloxamers, PLGA, collagen, D-glucosamine, Acrylic acid, Carbomer are incorporated to formulate a gel to provide an access of drug to the sites where conventional therapy alone cannot achieve desirable results. Gellan gum and lutrol with Ornidazole offered a muco-adhesive gel with the aim of drug release property.The gel used for this purpose is regarded as pseudo plastic, that is liquid at room temperature and less viscous at 34–37^0 C. The melting point of the gel is less than the body temperature, permits it to flow without obstruction all the way through the syringe into the periodontal pocket where it turns more viscous.[29]. The Sol-gel transition along with its transformation into semisolid state appears on interaction with GCF due to monoglyceride and triglyceride. The glycerides possess the property of forming liquid crystals, which provides more appropriate controlled release peculiarities when comes into interaction with water.[30]

5: Micro-sphere particles: Microspheres are solid spherical polymeric structures of size ranging from 1–1000 mm and comprised of a drug which is dispersed throughout the polymeric matrix.These are available in the forms of effusive powders that provides sustained and controlled drug discharge at the specified space.[31] Presently, there are several non-biodegradable and bio-degradable materials including polymers from natural and synthetic origin.[32] Protection of an unstable drug from getting degraded, before and after administration; sustained drug release; patient compliance, controlled therapeutic effects, increased bioavailability and decreased recurrence and intensity of adverse effects are significant benefits of employing micro sphere strategy.[33] The tetracycline infused micro-sphere particles provided extended release of drug and the antimicrobial activity was observed for more than 30 days against Staphylococcus aureus.[34] A Xanthan polymer infused with rosuvastatin and metformin showed decline in periodontal depth pockets , enhanced the clinical attachment levels by improvisation of gingival attachment as well as promote osteoblasto-genesis.[35]

6: Nano particles: The modern era of dentistry have been using so far microparticle-based hydrogels with the property of drug dispersion, which later on found to be affected by their structure . Several factors make the nanoparticles more beneficial over the microspheres, micro particles and emulsion-based delivery systems [36]. These are either dispersed particles or solid particles having size ranging from10–1000nm. The drug is suspended, incorporated and encapsulated to a nano particle matrix.[37] These are dispersible extensively in an aqueous medium, there by offers a controlled release rate and increased stability. The polymer-based nanoparticles are impregnated through micelles polymerization with particle size ranging from 50–180 nm. By virtue of its small size, the nanoparticles can access non-reachable sites like the sub-gingival periodontal spaces and provides an efficient mode of delivery for antimicrobials that can hardly gain access to host cells .[38]

7: Liposomes: Liposomes are the microscopic vesicles of lipids that are categorized as uni lamellar or multilamellar, derived from sphingo lipids, glycolipids, nontoxic surfactants, long-chain fatty acids, cholesterol and even membrane proteins.[39] They have the advantages of being bio-degradable, biocompatible,non-hazardous, non- immunogenic and highly stable.Simultaneously,few demerits like high cost production, short half-life, micro-leakage have been highlighted. Magnetite nano particles have been recently introduced within the newly developed liposomes like PEG-ylated liposomes and PEG-ylatedmagnetic liposomesranging from anaverage size of 204.3 nm to 286 nm, respectively,along with an iron component of 4.2 mg/ml.[40]

8: Nano-fibres: Polymeric fibers having diameters in sub-microns are known asNano-fibres.[41] The Nano fibers provide many peculiarities like quite extensive surface area to volume ratio, advanced mechanical performance such as tensile strength, stiffness and rigidity and the flexibility in surface functionalities . In a recent study by Bottino and Co-workers, the effects of Metronidazole and Ciprofloxacin on periodontal pathogens have been assessed by using polydioxanone (PDS) which possesses degradable nano-fibersmatrices. The growth of pathogens like Fusobacteriumnucleatum and Aggregati bacteractinomycetemcomitans was inhibited after utilizing nanofibers comprising of ciprofloxacin while commensals remained unaffected.[42] In a study of High Performance

Liquid Chromatography (HPLC), it was revealed that the higher amounts of drug in formulations demonstrated more release over time than those with the minimal amounts, with least dispersion.[43]

9: Ointment: The Minocycline ointment is an absorbableand prolonged drug delivery mode that comprises of 2% Minocycline HCl embedded in a matrix ofthe polymers Hydroxyethyl-cellulose, Aminoalkyl-methacrylate and Triacetine.[44]According to a study, 1300ìg/ml of minocycline has been reported to be available in the pocket spaces for almost an hour, soon after the topical deliverance of 0.05 ml ointment (1mgof minocycline) which later onreduces to 90ìg/ml after 7 hrs.[45] Another study has concluded with the results that scaling and root planning in adjunct with ointment application was significantly better than scaling and root planning alone in severe chronic periodontitis owing to periodontal pockets greater than 7mm. [46]

The world has shifted the treatment paradigm from the non-resorbable to a varying range of resorbable biodegradable polymers in order to achieve biocompatibility for sustained drug release, reduced frequency of dosing and less risks of developing bacterial resistance. Such strategies augment the effects of scaling and root planning therapy, thereby providing clinical efficacy to treat chronic periodontitis. Advanced clinical knowledge and better understanding of the periodontal disease has led to the introduction of novel drug administration methods which resulted in the innovative designing of targeted delivery systems for the minimization of the systemic adverse effects of anti-microbials and other drugs. These include the periodontal fibers, periodontal strips, periodontal films, chip, micro-particles, nano-particles and nano-fibers.

CONCLUSION: The nano-particle technology to treat periodontitis is still an emerging and promising strategy for the management of disease with the provision of minimal dose, less invasive procedure and clinical efficacy.

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Case Report DOI: https://doi.org/10.51985/JBUMDC2020019

Polycythemia Vera Complicated by Portal Vein Thrombosis and Budd-Chiari Syndrome:

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ABSTRACT:

Polycythemia vera is a medical condition characterized by raised hematocrit. Owing to increased viscosity, the blood flow in the vessels become sluggish leading to the clinical features of polycythemia such as headache, blurring of vision, red skin, dizziness, raised blood pressure, itching and more serious medical events like vaso occlusion, thrombosis and strokes. In this case report, polycythemia vera presenting unusually with heamatemesis, melena and abdominal distension. Physical examination of this case revealed massive ascites with dilated veins around the umbilicus. The diagnosis of polycythemia vera complicated by Budd Chiari Syndrome and Portal Vein Thrombosis was made. Patients with polycythemia vera are at risk of vaso occlusive sequelea like portal vein thrombosis and Budd chiari syndrome.

Key words: Budd chiari syndrome, Polycythemia Vera, Portal vein thrombosis.

INTRODUCTION:

Polycythemia vera is a disorder which is characterized by excessive production of red blood cells by the bone marrow. It may also lead to over production of white blood cells and platelets.[1] The WHO criteria for the diagnosis of polycythemia vera is as follows:

Major Criteria:

1) Heamoglobin >18.5 g/dl in men, Heamoglobin >16.5 g/dl in women
2) JAK 2 MUTATION or other functionally similar mutations

Minor Criteria:

1. Bone marrow biopsy revealing trilineage growth , hyper proliferation of erthrocytic, granulocytic and megakaryocytic precursors.

2. Serum erythropoietin levels below the lower limit of normal range.

3. Endogenous erythroid colony formation in vitro.

Diagnosis of polycythemia vera requires two major criteria plus one minor criterion OR 1st major criterion plus two minor.[2]

Patients with polycythemia vera are at on higher risk of thrombus formation and vaso occlusive crises attributable to the blood being thicker and sluggish to flow. The clinical course of the disease is characterized not only by thrombotic complications but also by transformation to leukemias and myelofibrosis, thus causing increased mortality and morbidity. Increasing age, previous history of thrombotic events and marked leukocytosis are the major risk factors for thrombotic complications in polycythemia vera. Portal vein thrombosis (PVT) and Budd-Chiari syndrome both are splanchnic vein thrombosis. Despite of features suggesting PVT ,the cell counts are not markedly raised due to iron deficiency, spleenomegaly and heamodilution thus rarely fulfilling the diagnostic criteria of polycythemia vera with these complications. BCS is characterized by hepatic vein outflow obstruction. It can be primary when the source is endo luminal i.e. pro thrombotic states and its secondary when the cause is extra vascular i.e. any tumor compressing from outside or any invasion. The etiology of primary BCS includes pro thrombotic disorders like myeloproliferative neoplasms, anti-phospholipid antibody syndrome, protein C, protein S deficiency, factor V Laiden mutation.[3] Polycythemia vera is the most frequent cause of BCS and is seen in around 40% of the diagnosed cases.[4] Portal vein thrombosis in the absence of liver cirrhosis and local malignancy is less frequently encountered and shows an etiological overlap with primary BCS. Acute portal vein thrombosis with associated portal hypertension presenting with massive hematemesis could be the initial presentation of polycythemia vera in previously asymptomatic patient. The strong relationship between Myeloproliferative neoplasms and splanchnic vein thrombosis would help the clinicians to screen the patients with MPN for SVT and vice versa. Hence the purpose of reporting this case was to highlight the clinical and molecular basis of MPN associated splanchnic vein thrombosis. [5]

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Received: 24-Feb-2020
Accepted: 06-04-2020

CASE REPORT:

A 50 years old man presented to medical ward of Sandeman Provincial Hospital Quetta on 13th February 2020 with abdominal distension since two months, hematemesis and melena since 3 days. Abdominal distension was gradual and

was associated with dull aching pain. He was afebrile and had no history of dark urine, head ache, seizures, loss of consciousness or itching. The family history revealed chronic myeloid leukemia in one of his brothers and was taking treatment for it. On examination the patient had congested lower conjunctiva without plethora. There was no evidence of jaundice. Patient had massive ascites with caput medusae and was mildly edematous.

Initial labs of the patient revealed the following; Hb 13.3g/dl, HCT 36.4%, MCV 70.2 fL, WBCs 19350/cmm, platelets 870000/cmm, ESR 09 mm/hr. Serum erythropoietin level was 3.75 IU/L i.e. i.e. around the lower limit of normal range. The liver function tests revealed ALT of 161 U/L, normal albumin and prolonged PT of 28 sec. His renal function tests and serum electrolytes were within the normal range. Viral marker were negative and an ultrasound of the abdomen showed massive ascites with cirrhotic liver, mild splenomegaly, dilated portal vein measured 1.8 cm, there was a thrombus in the portal vein. Moreover a Doppler ultrasound was performed which revealed absence of blood flow in the hepatic veins with partial thrombi in the inferior vena cava in addition to above mentioned USG findings. The ascitic fluid cyto chemical analysis showed a transudative picture with high SAAG ratio suggestive of portal hypertension. Upper GI endoscopy was performed which revealed grade III esophageal varices for which band ligation was done and the patients was started beta blockers too. Bone marrow biopsy was done and showed erhthroid hyperplasia, hyper proliferation of granulocytes precursors and megakaryocytes precursors. JAK 2 mutation test was ordered which came out to be positive and highly suggestive of myeloproliferative neoplasm with negative bcr-abl by FISH . A diagnosis of polycythemia vera complicated by Budd-chiari syndrome and portal vein thrombosis was finally made.

The patient was treated on the line of chronic liver disease. Later on when he became stabilized clinically, he was kept on low molecular weight heparin followed by oral anti-coagulants. His phlebotomy sessions were done in order to keep his hematocrit with the normal range. Low dose aspirin was added to the treatment in order to prevent pro thrombotic complications after routine phlebotomy and routine anti-coagulant therapy. JAK 2 inhibitor therapy Ruxolitinib was started for the underlying MPN i.e. polycythemia vera.

DISCUSSION:

The patient's normal Hb and HCT with low MCV could be attributed to hematemesis due to underlying portal hypertension induced variceal bleeding. Polycythemia is a stem cell disorder characterized by pan hyperplastic, malignant and neoplastic bone marrow. It's most prominent feature is increased red cell mass due to uncontrolled red blood cells production along with increased white blood cells and platelets production due to abnormal hematopoietic stem cells[6]. The JAK2 V617F mutation being present in 90-95% of polycythemia vera patients and in around 50% of ET essential thrombocytosis and myelofibrosis patients is used as a non-invasive diagnostic tool[7]. The mutation enhances the proliferative capacity of all erythropoietin independent erythroid colonies. Polycythemia vera is thus characterized by panmyelosis with significant quantitative and qualitative defects affecting all three cells lineages.

MPNs with negative Philadelphia are the most frequent pro thrombotic factor in splanchnic vein thrombosis. Hyper viscosity rendered by increased red cell mass in polycythemia vera is not the only factor leading vaso occlusive events, JAK 2 mutations also causes hyper sensitivity to cytokines which leads to production of pro thrombotic factors and adhesion molecules in the vessel walls.[7] The strong association between MPNs and portal vein thrombosis and Budd-Chiari syndrome was confirmed by the high frequency of JAK2V617F amongst these patients , present in 17-35% and 30-45% respectively. JAK2 Mutation not only defines the molecular basis of the disease but also responsible for its raised hematocrit, thrombotic events, pruritus and response to hydroxyurea[8, 9]. JAK2 mutations have frequently seen in patients with splanchnic vein thrombosis thus JAK2 mutation screening has become a part of diagnostic work up in SVT[8]. Anti-coagulants along with diuretics are the main stay in the treatment of BCS in the absence of hepatic insult. However balloon angioplasty with stent placement also have roles. Interventions are done in patients with inferior vena cava involvement. The current recommendation for the treatment of acute portal vein thrombosis is anti-coagulation for at least 3 months aiming a target INR 2.0-3.0[10]. For polycythemia vera phlebotomy being the mainstay in the management, low dose aspirin is recommended to prevent the thrombotic complications like acute myocardial infarction, stroke and major thromboembolic events. However myelosuppressive therapy, hydroxyurea and JAK2 inhibitor Ruxolitinib are also used.[10, 11]

CONCLUSION:

The risk factors for occurrence of SVT in MPN includes JAK2V 617F mutation, young age, female gender and concomitant other hypercoaguable states. Our case highlights a clear cut relationship between myeloproliferative neoplasms and incidence of splanchnic vein thrombosis. Understanding this association has significant implications on disease management and prognosis. The treatment of MPN should be started immediately as any delay could end up taking patient's life. Hence identifying the patients at risk of SVT and managing accordingly can considerably decrease the mortality and morbidity.

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Commentary DOI: https://doi.org/10.51985/JBUMDC2020005

Emergence of Chikungunya Virus in Pakistan: What should be done?

Abbas Ali Hussain, Rabia Sarwar

BACKGROUND:

Since 10 years, Chikungunya – a virus spread through *Aedes* spp mosquitoes – has reemerged in Africa, southern and southeastern Asia, and the Indian Ocean Islands.[1] In South-East Asia, epidemics have been documented in India, Malaysia, Sri Lanka, Myanmar, Thailand, Indonesia, the Philippines, Cambodia, Vietnam, Hong Kong, and Pakistan.[2] In September 2016, despite the warning of National Institute of Health (NIH) about the possible danger of chikungunya after its outbreak in India, Pakistan suffered its initial chikungunya outbreak in Karachi, megacity of the province Sindh infecting over 3000 people. [3]The very first case of Chikungunya outbreak in Pakistan was reported at a government facility in Malir, Karachi.[4] According to recent studies conducted by WHO, Pakistan shares the highest burden of major vector-borne diseases such as chikungunya.[5]

Chikungunya virus (CHIKV) is an alpha virus belonging to family *togaviridea*. It exists in three genotypes, the Asian, West African and East Central South African that are responsible for outbreaks in the respective areas. Chikungunya fever is spread by the bite of mosquitoes of the genus *Aedes, Aedes aegypti* being the principal vector.[2,6,7] *A. aegypti* mainly multiplies in fresh water storages such as desert coolers, water-tanks etc and around human habituation (pots, bins, cans etc) in urban and semi urban environments. The virus is postulated to exist in a human-mosquito-human circuit, and the bite of the female mosquito accounts to infection because it requires blood meal for the formation of eggs.[2]

INTRODUCTION:

Chikungunya fever is a disease of debilitating nature associated with a variety of symptoms. Since the Indian Ocean outbreak, information related to clinical picture of patients infected with CHIKV has increased substantially.[7] According to some studies, CHIKV fever affects all age groups and both sexes equally.[2,8] However males and individuals with blood Rhesus-positive were found more sensitive to get the disease in a single study.[7] The abrupt onset of high grade fever with rash, arthralgia in small joints of hands and toes, back pain and headache are the characteristic clinical signs of CHIKV fever.[1,2,6,7,9,10] The disease is now described in two clinical stages: Acute stage and the late stage of illness, with long-lasting arthropathy.

The initial 10 days after the start of the disease is characterized as the acute stage of illness.[6] The most usual symptoms during this stage are sudden high grade fever which responds poorly to anti-pyretics, myalgias, headache, fatigue and polyarthralgias.[1,2,6,7] Joint pain associated with the fever is found in majority of the cases and is mostly polyarticular, bilateral and symmetrical involving mainly small peripheral joints (hands, wrist, and ankles) and some large joints including knee and shoulder.[2.6.7] The chronic stage is characterized by unpredicted relapses and persistence of symptoms.[2,7] The affected patients may experience prolonged rheumatism with stiffness which can cause serious discomfort in walking and handling objects resulting in deterioration in the quality of life.[2,6,7] The disease may also cause neurologic, ocular or hemorrhagic symptoms atypically.[2,6-8]

Laboratory diagnosis is essential for a physician to diagnose Chikungunya fever and to distinguish it from diseases with similar clinical patterns like dengue virus infection. For this purpose samples collected early i.e. within a week after the infection are useful for virus detection and isolation due to high levels of viremia.[11] RT-PCR and real-time loop-mediated isothermal amplification (RT-LAMP) seems to be useful in early detection of viral DNA.[2,6,11] Viral culture by using vero cells, mosquitos or mouse models may take a week to grow and requires a laboratory with biosafety level 3 facilities, yet it remains the gold standard test for diagnosing Chikungunya fever. Serological tests for the detection of specific anti-CHIKV IgM and IgG are more frequently used. Anti-CHIKV IgM is detectable after 3-5 days of infection and remains elevated for 3-6 months. Anti-CHIKV IgG is detectable after 14 days of infection and may persist in the blood for years. Techniques like ELISA, immunofluorescence, complement binding and haemagglutination offers limited specificity and sensitivity but can be used as alternative tools for detection.

Emergence and reemergence of infectious diseases is closely associated with climatic changes, Mosquito-borne diseases are among the most sensitive to it.[12] Pakistan, along with many other countries in Asia is undergoing a serious climate change which has nurtured a variety of arboviral illnesses including chikungunya fever[3] In addition, wretched sanitary conditions, mountains of filth, open gutters and pools of stagnant water have contributed greatly to the outbreak.[3] Each individual in Pakistan generates around 0.612 kg of waste per day which is increasing at a rate of 2.4%. It is estimated that Karachi alone produces over 20,000 tons of

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Received: 19-Jan-2020
Accepted: 06-Apr-2020

waste per day, major share of which doesn't reach the junk sites. Moreover, overflowing gutters and stagnant water also provides a perfect habitat for arthropod vectors to grow.

RECOMMENDATIONS:

Currently, no authorized vaccine is commercially available for chikungunya fever however several vaccines have been tested with variable success rate.[6-9] Moreover, treatment for chikungunya fever is highly symptomatic which includes the use of analgesics and antipyretics.[2,6-9,11] Adequate oral rehydration and NSAIDs are the pillars of the treatment. For a country like Pakistan with debilitating sanitary conditions, Vector control and public awareness is crucial for the prevention of CHIKV.[2,6,8,11] Public awareness should be encouraged via campaigns and seminars to eradicate CHIKV transmission. Different campaigns were conducted since the outbreak however these only educated the literate population of the community while the underprivileged people remained untaught. Educating the underprivileged will have a pivotal role in controlling the virus as it constitutes the majority in Pakistan. Limiting practice of covering only lower half of the body in hot weather and the use of mosquito repellents, bed nets and wearing long sleeves is highly recommended.

Efficient government and health ministry also plays a significant role in preventing outbreaks in a state. Despite the warnings issued by the National Institute of Health (NIH) after the outbreak in India, no precautionary measures were taken by the Pakistani Government. Airports and railway stations remained unchecked, sanitary conditions were not optimized and no productive strategies were implemented in the hospitals.[3] Prevention of emerging infectious diseases are the responsibility of national governments and this cannot be delegated to any other agency. Strong political determination, educated ministers and adequate funding for preventive program management can help curtail the infection.

Early detection and accurate diagnosis is vital in controlling an infection.[9] Unfortunately, due to deficiency of proper diagnosing resources in Pakistan, samples were sent to United States for detection. [3]This diagnostic delay can lead to use of drugs which are contraindicated in chikungunya fever like aspirin which is an easily available over the counter drug in Pakistan and is generally self-prescribed for body aches (one of the symptoms of chikungunya fever).[6,11] This can potentially increase in the misery of the patient therefore appropriate detection is important to prevent devastating outcomes of the disease. Overall, preventing an emerging infectious disease is a collaborative effort and a well-educated community with potent public health machinery can help a state to establish solid grounds in terms of health.

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Letter to Editor DOI: https://doi.org/10.51985/JBUMDC2020027

Is Invasive Mucinous Breast Carcinoma A Rare Variant With Neuroendocrine Differentiation?

Ayesha Asghar, Aresha Masood Shah

We want to bring your attention towards the rare variant of breast cancer hence promoting its early detection and screening. The main advantage of early diagnosis is reduced tumor size without distant dissemination at the initial treatment.

Neuroendocrine malignancies are heterogenous with neuronal and endocrinal properties. Neuroendocrine cells are present throughout the body and hence neuroendocrine tumors (NETS) can arise from any anatomic region. Although breast cancer is the most frequently diagnosed cancer in women, breast NETS are very rare. With a prevalence of 1-2 cases per 10,000 women, breast NETS make up only 0.1% of all breast cancers and less than 1% of all NETS[1]. In other histopathological subtypes of breast carcinomas, invasive ductal carcinoma is the most common breast tumor reported worldwide of which mucinous (colloid) variant is the rare histological subtype, accounts for 1-7% of all invasive carcinomas [2]. However, 30% of invasive breast tumor are seen with nneuroendocrine differentiation, and is most commonly associated with mucinous and solid papillary carcinomas and therefore treated similar to another invasive carcinoma of breast[3].

Mucinous carcinoma is well circumcised and have soft gelatinous consistency. It has two subtypes, pure mucinous or mixed type. Pure mucinous carcinoma is a rare cancer which most commonly occur in older women and less than 1% occurs in younger than 35 years of age[4]. Pure type is composed of entirely mucinous carcinoma with two further subtypes, hypocellular and hypercellular variants. Axillary lymph node involvement is commonly rare. In a study of Kashiwagi, demographical data of 71 patients with mucinous carcinoma of the breast have suggests tumor size ranged from 0.5cm-12.3cm with mean tumor diameter-3.1cm[6]. Mucinous carcinoma with neuroendocrine differentiation shows good prognosis but tumors which are expressed of HER 2 neu shows negative prognosis and has increased risk of recurrence and metastasis. Primary neuroendocrine tumors of breast have worst prognosis due to lack of long-term survival data hence it's difficult to make a prognosis for this carcinoma[5].

Diagnosis of mucinous carcinoma depends upon tumor or lump detection on self-examination or through mammogram or MRI apart from that Ultrasound guided percutaneous core biopsy should also be ordered. Other signs include painful retracted nipples with discharge that isn't breast milk, unusual changes in the appearance of breast and milk.

Treatment plan include mastectomy or lumpectomy which do not differ from primary protocol treatment of all breast carcinoma. Adjuvant therapy such as chemotherapy, extra cranial stereotactic radiation therapy followed by endocrine hormonal therapy such as tamoxifen or an aromatase inhibitor which block the effect of estrogen. As mucinous carcinomas are estrogen and progesterone receptor positive hence it is likely to be effective[2]. Apart from this most mucinous are also negative for HER 2 neu so they should not be treated with Herceptin. Neuroendocrine tumors of the breast have a significantly higher rate of local and distant recurrence and lower overall survival than Invasive ductal carcinoma[2]. However, in the NCCN guidelines Mucinous Breast Carcinoma is regarded as the "a histological type with a favorable prognosis"[5].

Mucinous carcinoma of breast being the rarest form of invasive carcinoma which is mostly associated with neuroendocrine differentiation should be kept into consideration while diagnosing the cancers of breast in old age women particularly postmenopausal women. Management plan for invasive carcinoma with Neuroendocrine differentiation is a challenge particularly the diagnosis owing to the variably present and cytological features of NTE[4]. Due to its rarity, data on molecular characteristics is limited hence more research should be done on this carcinoma to enhance the diagnostic and treatment modalities for upcoming doctors.

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Received: 09-Mar-2020
Accepted: 16-Apr-2020

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Journal of Bahria University Medical & Dental College
Peer Reviewed Multidisciplinary Quarterly Published Journal
ISSN (print): 2220-7562, ISSN (online): 2617-9482
Recognized by PM&DC (IP/0072)
Online edition is available at URL: https://jbumdc.bahria.edu.pk,
Indexed with Index Medicus for the Eastern Mediterranean Region (IMEMR),
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