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Genetic Impact of Second Hand Cigarette Smoke

Dr. Zil-e-Rubab¹

Second hand smoke is a complex mixture of more than 4000 chemical compounds that are generated during the burning of tobacco products and affects all those who are exposed to smokers in a closed environment either at home or work place. This mixture contains numerous irritants and toxicants which leave severe as well as carcinogenic health effects in humans¹.

Short as well as long-term effects of tobacco exposure can lead to multiple health implications. It has been estimated that secondhand smoke is responsible each year for 22,000 hospitalizations, between 150,000 and 300,000 cases of bronchitis and pneumonia, and between 8000 and 26,000 cases of asthma. The SHS exhibits hazardous particles and gases. The particulate phase contains more than 4000 substances, most of them toxic or otherwise noxious while the gaseous phase contains about 500 substances. Non-smokers exposed to second hand smoke absorb significant amounts of these harmful substances. The blood levels of carbon monoxide, nicotine and other toxic substances rise in passive smokers. In the long run, non-smokers exposed to ETS could find their respiratory function decreased to the same level as that of a moderate smoker.²

Second hand smoke plays a pivotal role in etiology of lung cancer. A large number of models of carcinogenesis provide an outline for considering the associations of lung cancer incidence with smoking intensity, duration, and smoking cessation. These models suggest that carcinogens derived from chemical components in tobacco smoke react with the DNA of respiratory epithelial cells. Some of the carcinogens instigate mutagenic changes while others support the growth of these mutated cells or disable genes that restrain tumor growth. Mutagenesis, growth promotion, and inhibition of tumor suppression may all be compulsory for clinically evident cases of lung cancer. Procarcinogens in tobacco smoke must be metabolically altered in order to exhibit their carcinogenic outcome. Various enzymes are involved in

detoxification of these chemicals into inactive compounds. Genetic polymorphisms generate slightly different forms of the enzyme, resulting in variations in enzyme kinetics. These inherited differences in the transformation rate are source of variability in risk of cancers. In this regard, the enzyme CYP2D6 can transform polycyclic aromatic hydrocarbons and acrylamines into reactive chemical species that can bind covalently to DNA and induce mutations. The people who have CYP2D6 enzymes are extensive or intermediate metabolizers, as measured by the speed with which they metabolize the compounds present in second hand tobacco smoke. Extensive and intermediate metabolizers would be expected to have higher concentrations of these carcinogens in the lung than would slow metabolizers. The extensive metabolizing phenotype is associated with more than double the risk of lung cancer.³

Second hand smoke has an obvious role in the development of oxidative stress. Free radicals production due to oxidative stress modifies cardiac autonomic control resulting in heart rate variability (HRV). A positive association is found between polymorphisms in oxidant-scavenging glutathione S-transferase (GST) genes and their interactions with second hand smoke. The modifying effect of GSTM1 for the association of second hand smoke with heart rate variability suggests that these exposures cause systemic oxidative stress. This oxidative stress is scavenged by GSTM1 in the liver. The GSTM1 is responsible for the association between second hand smoke, GST polymorphisms, and lung cancer in passive smokers.⁴

Compared to adults, children may be more susceptible to secondhand smoke. This susceptibility may be exacerbated by alterations in inherited genetic variants of innate immunity genes. A genetic polymorphism in the mannose binding lectin-2 (MBL2) gene is found in the children with lung cancer exposed to second hand smoke. Functional MBL2 haplotype associated with high circulating levels of MBL and increased MBL2 activity was associated with increased lung cancer risk among those exposed to childhood.⁵ It has long been suspected that cytogenetic deletions and/or loss of heterozygosity on the short arm of chromosome

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Zinc and Copper Levels Fluctuate with Altered Glucose Homeostasis

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ABSTRACT

Background: Type 2 diabetes mellitus is becoming one of the major health problems worldwide. Especially in South East Asia, type 2 diabetes has gained critical significance. As pre-diabetes prevalence is increasing worldwide, it has become an important concern to prevent diabetes at an early stage. Trace elements have been gaining attention in improving the glucometabolic conditions like pre-diabetes and diabetes. Zinc and copper are the major trace elements present in the human body and they play a significant role in the pathogenesis of diabetes mellitus and pre-diabetes.

Objectives: The purpose of this study was to compare serum zinc and copper levels in type 2 diabetes and pre-diabetes.

Methods: This study was conducted in department of Biochemistry BMSI, JPMC Karachi. Total 90 subjects were taken out of which 30 were type 2 diabetics, 30 were pre-diabetics and 30 were normal healthy individuals. Serum fasting glucose was measured by glucose oxidase method. Serum zinc and copper were measured by colorimetric method. Statistical analysis was done using SPSS version 16.

Results: Serum zinc levels were significantly lower in type 2 diabetics as compared to pre-diabetics and normal individuals (mean differences were $45.17 \pm 15.63 \mu\text{g/dl}$, $59.97 \pm 13 \mu\text{g/dl}$ and $86.57 \pm 14.34 \mu\text{g/dl}$ respectively). Serum copper was significantly increased in type 2 diabetics compared to pre-diabetes and control samples (mean differences were $325.55 \pm 88.34 \mu\text{g/dl}$, $175.53 \pm 47.45 \mu\text{g/dl}$ and $126.87 \pm 21.57 \mu\text{g/dl}$ respectively).

Conclusion: It was concluded that serum zinc was significantly lower in type 2 diabetics and pre-diabetics and is inversely related to serum fasting glucose while serum copper is significantly higher and positively related with fasting blood glucose.

KEY WORDS: *Type 2 Diabetes, Pre-Diabetes, Zinc, Copper.*

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3 may be involved. The chromosomally fragile site, FRA3B, has been linked to lung cancers and more recently has been explored in cervical carcinomas. A large number of smokers and passive smokers showed fragility at FRA3B. FRA3B maps within the fragile histidine triad gene (FHIT), which is a tumor suppressor gene involved in tumorigenesis, including cervical neoplasia.⁶

Health professionals are also target of passive exposure to cigarette smoke which makes them also a focal group essential for creating awareness regarding hazards of passive smoking.⁷ In

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our environment, bidi and huqqa smokers is another addiction that needs to be studied from genetic aspect to find out the multi-factorial polymorphism. With new technology enabling scientists to analyze the interactions between genomic structure and environmental stimuli, researchers should be able to make efforts in clarifying the role that SHS exposure plays in different types of cancers. There should be valid methods for describing the interactions between environmental exposures, pathogens, and genetic composition in the trail to understand the mechanism of all cancers.

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INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by chronic hyperglycemia causing disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both.¹ The prevalence of diabetes and pre-diabetes is increasing globally and becoming a threat to the world population especially South East Asia.² In Pakistan the diabetes prevalence is 11.1% while prevalence rate of impaired fasting glucose is 4.2% in males and 2.3% in females.³

The role of trace elements for improvement of disturbed metabolic conditions like pre-diabetes and diabetes has been gaining attention.^{4,5} Zinc is the second most common trace element profusely distributed in the body after iron.⁶ Several studies on humans as well as on animals established that zinc plays a major role in the synthesis and release of insulin. Zinc serves as an effective antioxidant by lowering the oxidative stress and decreasing the insulin resistance and ultimately the progression of diabetes mellitus.^{7,8}

Copper is the third most abundant mineral in the human body. Copper is present in the body combined with various enzymes to form metallo-enzymes such as ceruloplasmin, SOD.⁹ These enzymes play a major role in redox reactions, such as superoxide dismutase which plays key role in antioxidant defense.¹⁰ Copper is associated with altered glucose metabolism through the stimulation of glycation and release of copper ion enhancing the oxidative damage.¹¹ Various studies on human subjects demonstrate that diabetic patients have abnormal circulation of copper.¹² Copper and zinc are the major components of antioxidant enzyme SOD.¹³ This enzyme inhibits oxidative stress which results from the accumulation of free radicals oxidative stress and plays an important role in the pathological processes ongoing in the diabetic patients.¹⁴ The objective of this study was to determine the serum zinc and copper levels in type 2 diabetics and pre-diabetics and their association with glycemic status.

METHODOLOGY

This is a prospective, cross sectional and comparative study. A total of 90 subjects were selected out of which 30 were pre-diabetics (17 females and 13 male), 30 were diagnosed patients of type 2 diabetes (14 females and 16 males) and 30 were normal healthy individuals (16 females and 14 males) aged 40-65 years. The study was conducted at a diabetes management tertiary care center of Karachi after taking ethical approval from committee of BMSI, JPMC. The required samples were collected from the diabetic patients and normal healthy individuals over a period of three months.

The subjects were selected after procuring written consent, detailed history and examination of the subjects. Patients suffering from endocrinal disorders, hepatic disease, renal diseases, alcoholism or other drug abuse were excluded. For female patients, those having pregnancy, on lactation and using oral contraceptive pills were excluded. Both patients and normal healthy individuals were requested to come with 8-10 hours of fasting for sample collection. Samples were collected for blood glucose level, serum copper and zinc level. 7 ml of blood was taken aseptically in 10cc disposable syringes. Out of 7ml, 3ml was placed in sodium citrate tube for FBS estimation; 4 ml of blood was placed in a second test tube and allowed to clot for determination of copper and zinc. Clotted blood in the test tube was centrifuged at 508 Xg for three minutes and serum was separated and stored at -20°C until analysis.

Considering the laboratory fasting blood glucose measurements, participants were categorized into three groups using American Diabetic Association (ADA) guidelines:

Normal (normoglycemic): Where fasting blood glucose level was < 100 mg/dl.

Pre-diabetics: Where fasting blood glucose level was 100-125 mg/dl, and

Diabetics: Where fasting blood glucose level was \geq 125 mg/dl.

Plasma glucose level was estimated by using glucose oxidase method. The colorimetric randox kit procedure was used for estimating serum copper and zinc estimation. All experimental data were expressed in mean and

standard deviation. Data obtained in the study and control group were compared through two-tailed t-tests by using SPSS (Statistical Package for Social Science) version 16. Pearson's correlation coefficient (r) was used to identify trace elements association with glycemic status. P-value <0.05 was considered as significant.

RESULTS

The age, sex, body mass index (BMI) and medication is shown in Table 1. The mean age of the healthy control group was 47.23 \pm 6.37, pre-diabetics was 47.40 \pm 6.06 and 48.97 \pm 6.9 for diabetic patients. There were 49% males and 51% were females in the sample. The BMI of diabetic group was significantly increased (27 \pm 3.5) as compared to impaired (25.2 \pm 3.03) and control (24.5 \pm 4.6). 72% of the patients in diabetic group were taking different hypoglycemic drugs.

Table 2 presents the fasting blood sugar (FBS), copper (Cu) and zinc (Zn) level among study groups. FBS was significantly increased in diabetic group (141 \pm 20.53) as compared to control (86.03 \pm 8.24) and pre-diabetic group (112 \pm 6.7), which is highly significant (p value <0.001). Copper was significantly increased in the diabetic group (325.55 \pm 88.34) compared to control (126.87 \pm 21.57) and pre-diabetic group (175.53 \pm 47.45), which is highly significant (p value <0.001). Zinc was significantly decreased in diabetic group (45.17 \pm 15.63) compared to control (86.57 \pm 14.34) and pre-diabetic group (59.97 \pm 13), which is highly significant (p value <0.001). The serum copper levels were positively correlated with fasting blood sugar, (Fig.1) while the serum zinc levels were negatively correlated with fasting blood sugar (Fig.2).

Table 1: Characteristics of Study Subjects

INDICATORS	CONTROL (N=30)	PRE-DIABETICS (N=30)	TYPE 2 DIABETICS (N=30)
Age (years)	47.23 \pm 6.37	47.40 \pm 6.06	48.97 \pm 6.9
Sex (n, %)			
Male	47	43	57
Female	53	57	43
BMI (kg/m ²)	24.5 \pm 4.6	25.2 \pm 3.03	27 \pm 3.5
Taking hypoglycemic Drugs (n, %)			

Yes	0	0	21(72.4)
No	30(100)	30(100)	9(27.6)

Table 2: Comparison of Fasting Blood Glucose and Other Biochemical Variables within Study Groups

	CONTROLS	PRE-DIABETICS	TYPE-2 DIABETICS	P-VALUE
FBS (mg/dl)	86.03 \pm 8.24	112 \pm 6.7	141 \pm 20.53	0.001*
Zinc (μ g/dl)	86.57 \pm 14.34	59.97 \pm 13	45.17 \pm 15.63	0.001*
Copper (μ g/dl)	126.87 \pm 21.57	175.53 \pm 47.45	325.55 \pm 88.34	0.001*

Values are expressed as mean \pm SD, values < 0.05 are considered as significant

Figure 1: Correlation between Fasting Blood Glucose and Serum Copper in Complete Study Population (n=90)

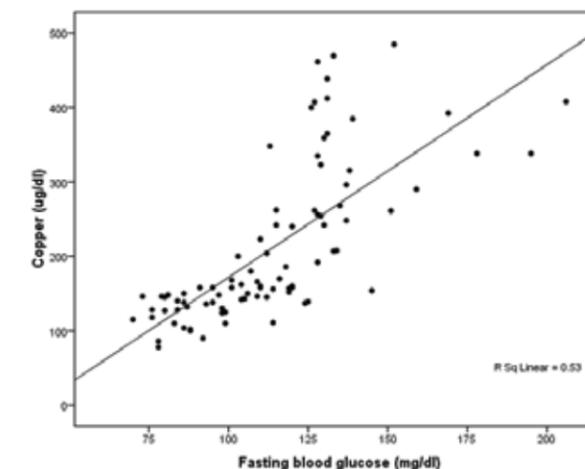
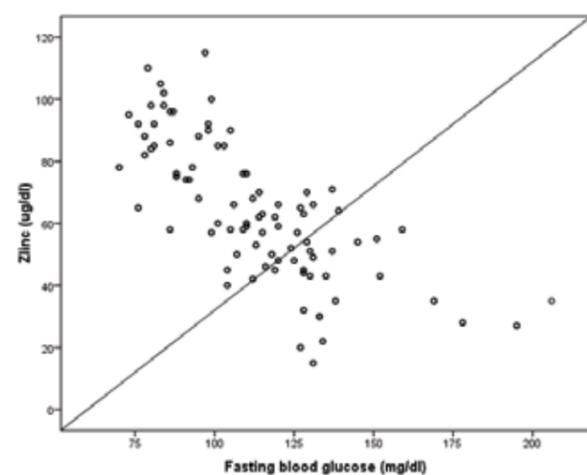


Figure 2: Correlation between Fasting Blood Glucose and Serum Zinc in Complete Study Population (n=90)



DISCUSSION

Trace elements have been investigated as potential preventive and therapeutic agents for type 2 diabetes and for common complications of diabetes. In particular, diabetes is shown to be associated with abnormalities in the metabolism of zinc, chromium, copper, magnesium and manganese.¹⁵ The present study was designed to evaluate serum zinc and copper levels in type 2 diabetes and impaired fasting glycemic individuals while evaluating against a healthy control group.

In the study, it was observed that mean serum zinc level was significantly low in diabetics as compared to the control subjects. Similarly Al-Marroof also reported significantly lower serum zinc level in diabetics than in control subjects.¹⁶

Lower levels of zinc were observed in impaired fasting glycemic group respectively. Some studies have reported zinc deficiency along with alterations in zinc metabolism in patients with diabetes. Zinc is useful in the synthesis, storage, and secretion of insulin.¹⁷ It effects antigenic properties of insulin which leads to hyperglycemia. Increase in the copper ion levels in patients with diabetes mellitus (DM) may be attributed to hyperglycemia that may stimulate glycation and release of copper ion and this accelerates the oxidative stress.^{18,19} The results have shown that copper levels are increased in

diabetic patients as well as in impaired fasting glycemic group as compared to control. The increased level of copper in the diabetic patients agrees with other studies.²⁰

Copper acts as a pro-oxidant and may participate in metal catalyzed formation of free radicals. The increased production of free radicals is likely to be associated with development of type 2 DM.²¹ A decrease in zinc concentrations and an increase in copper concentrations can be additional factors of atherogenicity.²² Serum copper levels were positively correlated with fasting blood sugar while serum zinc levels were negatively correlated with fasting blood sugar, depicting that both of these trace elements have marked effect on glucose metabolism.

Copper and zinc are the major components of antioxidant enzyme SOD. This enzyme inhibits oxidative stress which results from the accumulation of free radicals oxidative stress and plays an important role in the pathological processes ongoing in the diabetic patient. Excessive oxidative stress has adverse effects on islet survival and function, and accelerates complications in target organs and tissues.^{23,24}

Our study has a number of potential limitations as other trace elements such as iron are not considered even though they may influence zinc status. The sample size was also relatively small, therefore the numbers of individuals in each group were limited to reach definite conclusion for comparison among groups.

CONCLUSION

From the present study, it was concluded that type 2 diabetics and pre-diabetics have significantly lower level of serum zinc as compared to control group and significantly higher level of serum copper. It was determined that zinc deficiency plays an important role in the development of impaired glucose homeostasis. It prospectively might serve as a protective agent against the development of type 2 diabetes. However, in order to better understand the role of these trace elements on diabetes larger clinical trials are required.

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In-vitro Susceptibility of Levofloxacin against Different Clinical Isolates

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ABSTRACT

Background: Levofloxacin is a broad spectrum quinolone, widely used to treat infections caused by gram negative and gram positive bacteria. Development of resistance by pathogens against different broad-spectrum antibiotics is increasing and now becoming a global issue.

Objectives: The aim of the study is to evaluate the current sensitivity pattern of levofloxacin against various common clinical isolates like *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Klebsiellapneumoniae*.

Methods: A total of one hundred and ten samples were collected from different pathological laboratories of Karachi, Pakistan. The above mentioned pathogens were isolated from blood, stool/urine, sputum, skin samples.

Results: Results show least resistance of levofloxacin against *E.coli* (27.5%), and *P.aeruginosa* (27%), while *S.aureus* possessed highest resistance (45%).

Conclusion: Study concluded levofloxacin still possesses excellent anti-microbial activity against common pathogens. Routine monitoring and surveillance is further required to ensure effective treatment regimens to community.

KEY WORDS: Levofloxacin, Resistance, Susceptibility, Clinical Isolates, Pathogens.

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INTRODUCTION

In early 1960s the development of quinolones was initiated. Nalidixic acid, was granted a license to be used in the treatment of urinary tract infections (UTIS), mainly caused by gram negative bacteria, in 1967. In the initial days of the usgae, Quinolones were resisted by gram negative bacteria.¹ The first monofluoroquinolone, flumequine, exhibited improved sensitivity against gram positive pathogens in comparison to nalidixic acid due to structural modifications.² Off late, quinolones have been widely used to treat bacterial infections, with ciprofloxacin as an effective member of the class, having excellent bioavailability and active drug efflux.³

Levofloxacin, a broad spectrum antibiotic quinolones, is found to be effective against a variety of the clinical isolates, especially *Enterococcus spp.* and *S. pneumonia*. Among all quinolones levofloxacin is strongly active against both gram positive and gram negative bacteria. It is two times more effective than ofloxacin against *Enterobacteriaceae* and *Pseudomonas aeruginosa*.^{4,5} Additionally it also bears potential therapeutic response over *Pasteurella species*, *Eikenella*, *Corrodens*, *Legonella*, *Pneumophilia* and *BactoridesFragilis*.⁶ The minimum inhibitory concentration (MIC) of levofloxacin is 4-8 ug/ml against *Pseudomonas aeruginosa* while for *Heamophilus influenza*, *Neisseria gonorrhoeae* and *Moraxella catarrhalis*, MIC is around 0.015-0.06 ug/ml.^{7,8,9} The effectiveness of levofloxacin against *S.pneumoniae* infections was also reported.^{10,11,12} The antibiotic has been utilized in the treatment of ear infections in children.¹³

The objective of the study was to determine the in-vitro susceptibility of levofloxacin against common pathogens like *Escherichia coli*, *Staphylococusaureus*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae* using Baur-Kirby method.

METHODOLOGY

Clinical isolates were collected from different pathological laboratories of Karachi, Pakistan from January 2013 to May 2013. Pathogens were isolated from pus, sputum, stool, urine and blood samples. Susceptibility of levofloxacin was determined using disk diffusion method in laboratory to produce consistent results with bacterial isolates. Commercially prepared disc of levofloxacin (5µg) was purchased from the local market (Oxoid Ltd., England). Muller Hinton Agar (Oxoid, England) and broth were prepared according to standard guidelines provided by CLSI (Clinical and Laboratory Standard Institute).¹⁴ McFarland standard 0.5 was used and prepared.¹⁵ Commercial discs of levofloxacin were placed on dry inoculated streaked plates using sterile forceps, and incubated at 37°C for 18-24 hours. After incubation, the zones of inhibition appeared around the discs were measured using scale. The zones of inhibition for *E.coli*, *K.pneumoniae*, and *P.aeruginosa*, were set as resistant (≤13), intermediate resistant (14-16mm), and sensitive (≥17mm). While the zones for *S.aureus* were resistant (≤15mm), intermediate resistant (16-18mm), and sensitive (≥19mm).^{14, 15}

RESULTS

Pathogens were isolated by blood, stool, urine, pus and sputum. The detail of sources is given in Table 1. Percent susceptibility of *E.coli* (72.5%), *S.aureus* (55%), *P.aeruginosa* (73%), and *K.pneumoniae* (66%) showed *P.aeruginosa* to be more susceptible towards levofloxacin as compared to other tested pathogens. Table 2 presents the number of pathogens resistant (isolates not inhibited by normal dose of the anti-microbial agent or lack of insignificant zone around experimental disc), intermediately resistant (lower than susceptible response of isolates with smaller diameter zones around the experimental discs; clinically disregarded as higher doses can be used to treat infections and susceptible (isolates inhibited by normal concentration of drug and significant zones are appeared around the experimental disc).¹⁴

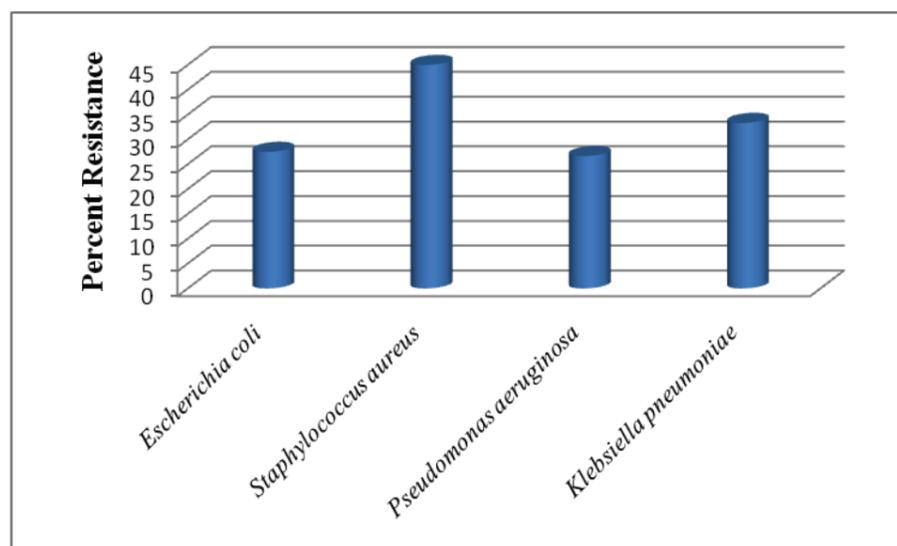
Table 1: Sources of Clinical Isolates

S. No.	Pathogens	Sources				
		Blood	Stool/Urine	Skin Pus	Sputum	Sample Size
1	<i>Escherichia coli</i>	14	23	3	-	40
2	<i>Staphylococcus aureus</i>	12	20	8	-	40
3	<i>Pseudomonas aeruginosa</i>	3	5	3	4	15
4	<i>Klebsiellapneumonia</i>	3	3	2	7	15

Table 2: Sensitivity of Levofloxacin against Clinical Isolates

S. No.	Pathogens	Resistant (R)	Intermediate Resistant (IR)	Sensitive (S)
1	<i>Escherichia coli</i>	08	03	29
2	<i>Staphylococcus aureus</i>	10	08	22
3	<i>Pseudomonas aeruginosa</i>	02	02	11
4	<i>Klebsiellapneumoniae</i>	02	03	10

Figure 1: Percentile Resistance of Levofloxacin against Clinical Isolates



DISCUSSION

Resistance to a variety of antimicrobial drugs is rising throughout the world.¹⁶ The emergence of antibiotic resistance is mainly due to needless use of antibiotics in humans and animals. Risk factors for the increase of resistant bacteria in hospitals and the community can be summarized as over-crowding, lapses in hygiene or poor infection control practices.¹⁷ In present study sensitivity pattern of levofloxacin was determined against 40 samples of *Escherichia coli*, 40 of *Staphylococcus aureus*, 15 of *Klebsiellapneumoniae* and 15 of *Pseudomonas aeruginosa*. In a previous study,

200 clinical isolates were tested including the species *Escherichia coli*, *Klebsiellapneumoniae*, *Proteus mirabilis*, *Proteus vulgaris*, *Providenciarettgeri*, *Pseudomonas aeruginosa*, *Enterococcus faecalis*, *Staphylococcus aureus* and *Staphylococcus epidermidis*.¹⁸ Findings indicated all isolates of *E.coli* were susceptible to levofloxacin with similar results.^{17,19} The sensitivity of levofloxacin against *S. aureus* was 55%. While past studies have shown good activity of Levofloxacin and ofloxacin against staphylococcal strains²⁰ compared with the majority of other antibiotics. Researchers reported 60.43% susceptibility of *S.aureus* to levofloxacin.²¹ The comparatively lower

susceptibility shows resistance has emergence against this fluoro-quinolone possibly due to irrational use of antibiotic, incomplete course of therapy and the self-medication.

The present study revealed only 2 pathogens of *K.pneumoniae* resistant to levofloxacin while reports depict *K.pneumoniae* to be 100% susceptible to levofloxacin.²² Another study showed 98% sensitivity of *K.pneumonia* towards levofloxacin²³ using CLSI disk diffusion technique.

Current susceptibility of *Pseudomonas aeruginosa* was 66% with a previous finding depicting greater anti-bacterial response than ciprofloxacin.²⁴ Comparable results of levofloxacin and ciprofloxacin against 300 *Pseudomonas aeruginosa* isolated from hospitalized patients are also available.²⁵ These results showed that the newer quinolones possessed good antimicrobial activity against various strains of gram positive and gram negative bacteria, however, rational and correct monitoring programs for its sensitivity should be conducted regularly in order to control the emergence of its resistance.

CONCLUSION

The present study shows that levofloxacin is still considered as a good choice for the treatment of infections caused by *E.coli*, *P.aeruginosa* and *K.pneumonia*. However, more investigations are required for *S.aureus*. Authors also suggested that the surveillance against such widely prescribed antibiotics must be done periodically to evaluate the current status of resistance against microbes

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Risk Factors for Nutritional Rickets in Children under 36 months: A Civil Hospital Case Study

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ABSTRACT

Background: Nutritional rickets is a common problem in Pakistan especially in Karachi with majority of the population living in enclosed housing and slums having limited or no sun exposure. There is a dearth of significant data regarding rickets in Pakistan especially in Sindh which emphasizes the need for further research. This study can be a foundation for other studies regarding strategies for prevention and early diagnosis of rickets.

Objectives: To determine the clinical presentation and identify risk factors for nutritional rickets in children less than three years of age.

Methods: A cross sectional study conducted in the department of pediatrics DUHS/CHK from June 11, 2007 to December 10, 2007. Fifty patients aged two months to thirty six months presenting with the clinical manifestation of rickets were included in the study. Information recorded included symptoms, socioeconomic status, feeding patterns, sun exposure, clothing, housing and malnutrition. Diagnosis was based on clinical signs, serum levels of alkaline phosphatase, calcium, phosphorus and radiological changes in X-ray wrist joint.

Results: Approximately 60% reported a weight for height less than ISD criteria set by WHO. Of the total assessed 58% percent were exclusively breast fed, 30% partial breast fed and 12% on formula milk. Weaning age was not reached in 20% of the children. Complementary feeding initiated late for 40% of the children with 78% percent exposed to sunlight less than 30 minutes per day and. Gross motor delay existed in 30% of children and hypocalcaemia convulsions in 14%. Past H/O repeated was in 32% had 22% had persistent/recurrent diarrhea.

Conclusion: Exclusivity breast feeding to complementary feed, inadequate exposure to sunlight and delayed introduction of complementary foods are the main risk factors for the development of nutritional rickets which can manifest itself in the form of ARI and diarrhea.

KEY WORDS: *Rickets, Vit-D Deficiency, Biochemical Abnormalities.*

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INTRODUCTION

Rickets is a term signifying failure of mineralization of growing bone or osteoid tissue with characteristic changes of growth plate cartilage among children before closure of growth plate. There are many causes of rickets; among them nutritional vitamin D deficiency remains the most common cause globally.¹ Independent research conducted in Lahore², Abbotabad³, and Peshawar^{4,5} also found nutritional deficiency of vitamin D as the most often cited cause of rickets.

Among ethnic minorities in the UK, 1.6% (77% of them of Southeast Asian descent) showed prevalence of rickets. The Center for Disease Control and Prevention places prevalence of nutritional rickets at 5 cases per 1 million children of six months to five years of age.⁶ Multiple studies highlight most black children to be the most effected.⁷

Review of studies conducted between 1986 and 2003 highlighted 166 pediatric cases of rickets USA. Among the effected children, majority were less than 30 months old at presentation, of which 83% were black and 96% were breast-fed.⁸

Nutritional rickets is a common problem in Pakistan as highlighted in different studies. In Peshawar rickets was observed in 2.25% children.⁵ There is dearth of significant data regarding rickets in Pakistan especially in Sindh which emphasizes the need for further research on this preventable disease. This study was undertaken to further evaluate the clinical presentation and risk factors of rickets. This can provide baseline data for other studies targeting early diagnosis and prevention of rickets.

METHODOLOGY

This cross-sectional study was conducted in the department of Pediatrics, CHK from June 2007 to December 2007. Clinical examination and laboratory investigations were used to assess the condition. Keeping the prevalence of rickets 2.25% with a CI of 95% and precision required 0.05 the sample size estimated was 39 using WHO sample size software. The study however

involved 50 children as subjects. The sampling technique used was non-probability, convenience based. Children under three years of age, presenting symptoms of rickets and biochemical abnormalities regardless of gender were included. Those having chronic illness like hepatic or renal disease, on anticonvulsant medicines for more than six months, having evidence of skeletal dysplasia and pre-term children with hypocalcemia were excluded from the study.

Written permission was sought from the ERC of CHK and informed consent was acquired from parents or attendants of the patients. Their anonymity, autonomy, confidentiality and beneficence were given top priority. The respondents were provided complete liberty not to answer any question or leave the study at any time.

A thorough history including, socioeconomic status, feeding pattern, weaning practices, sun exposure, type of clothing and housing condition were taken followed by a complete examination. Nutritional assessment of children was done using WHO Classification of normal, mild, moderate and severe malnutrition. Intake of vitamin D rich food was assessed in children by inquiring about the average intake of vitamin D rich food. Sun exposure in children was estimated approximately on average weekly exposure. The following investigations were done to confirm rickets, 1) serum calcium 2) serum phosphorus 3) Serum alkaline phosphatase 4) x-ray wrist joint.

Data was entered into SPSS version 16. Mean and SD were calculated for continuous variables. Frequencies were calculated for categorical variables and were exhibited through graphs

RESULTS

Out of the total 50 children with the rickets, 29 (58%) were male and 21 (42%) were female. Mean age was 15.13±9.6 months with mean age of male children at 13.3±9.1 months female at 17.6±10 months. The number of children in the age group 0-12 months were 25 (50%), with those belonging to the groups of 13-24 months and 25-36 months being 18 (36%) and 7 (14%) respectively. The Low socioeconomic group

constituted of 32 (64%) cases, while 17 (34%) belonged to middle and 1 (1%) to the high socioeconomic group. Children who were malnourished were 30 (60%) depicting levels of mild in 10 (20%), moderate in 13 (26%) and severity in 7(14%) cases having weight for height below 3SD. Exclusive breast feeding was noted in 29 (58%) cases whereas 15 (30%) got supplemented with top feeding out of which 5 (10%) with formula feed, 10 (20%) with fresh milk and 6 (12%) were never been breast fed. Weaning age not reached in 10 (20%) children (Table 1). Vitamin D rich food was not being taken by 60% (24) children who had started weaning while 40% (16) partook egg or fish. In majority of the cases (78%) children had sunlight exposure less than 30 min/week and only 11 (22%) had the required proper sun exposure. Rickets was more prevalent in families residing in apartments with limited or no sun exposure. Main clinical presentation revealed gross motor delay for 15 (30%) cases, hypocalcemic convulsions in 7 (14%), acute gastroenteritis in 6(12%) and pneumonia in 4 (8%) (Table 2). The most common clinical signs were wide wrist and wide anterior fontanelle (Table 3). The children who had low serum calcium levels were 33 (66%). Hypophosphatemia was observed in 23 but alkaline phosphatase was markedly elevated in all.

Table 1: Complementary Feeding (n=50)

S. No	Complementary Feeding	n	%
1	Children below weaning age (<6 months)	10	20
2	Appropriate Onset	17	34
3	Inappropriate Onset	23	46
	Not Started	3	6
	Started Late	20	40
Total		50	100

Figure 1: Factor Relating Sun Light Exposure i.e. Housing (n=50)

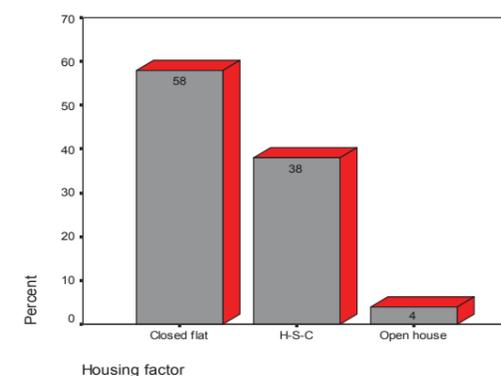


Table 2: Clinical Presentation (n=50)

S. No	Clinical Presentation	n	%
1	Delayed motor development	15	30
2	Hypocalcaemic seizure	7	14
3	Skeletal deformity	1	2
4	Acute gastroenteritis	6	12
5	Pneumonia	4	8
6	Co-morbid	8	16
7	Incidental finding	9	18
Total		50	100

Table 3: Clinical Presentation (n=50)

S. No	Clinical Sign	n	%
1	Wide wrists	38	76
2	Wide anterior fontanel	34	68
3	Frontal bossing of skull	18	36
4	Rachitrosary	10	20
5	Bowing of legs	5	8
6	Kyphosis	4	8
7	Crainotables	3	6
8	Caput Qaudratum	3	6
9	Harrison's grove	1	2

DISCUSSION

Presentation of rickets in the present study seems to be the tip of the iceberg as 50 cases with apparent signs of rickets were documented in a 6 month period at single tertiary care teaching hospital.

In the present study majority of the cases (50%) involved children less than one year of age. Kreiter in USA¹⁰ reported high prevalence of rickets in 5-25 month age. In Pakistan Khan et al² reported that 74% of rachitic children were aged below 12 months. The reason for increased incidence in this age group is the

increased metabolic demand due to rapid growth.

In the present study there was a male preponderance with a male to female ratio of 1.3. A male predominance has been reported in previous studies conducted in Australia, Ethiopia, and Sydney.^{11,12,13} Comparatively a Copenhagen based study depicted a large female predominance¹⁴, whereas a 1:1 ratio was reported from Saudi Arabia¹⁵. The reason of high incidence of nutritional rickets in female sex is not clearly understood, this may reflect preferential treatment given to male children in some societies and cultures. Additional research is required to identify the reasons for the disparity.

In the present study, rickets was associated with children suffering from malnutrition. In Ethiopia most of the patients with rickets were also malnourished.¹¹ The positive association of malnutrition with rickets is based on the prevalence of nutrient deficiencies and presence of other risk factors in their families. Lack of exposure to sunlight was found as a major contributing factor for rickets in children (78%). A study based in Saudi Arabia also cited lack of sunlight exposure as a major cause of nutritional rickets.¹² Nutritional rickets was strongly associated with families living in apartments. In a study conducted in slum areas of Karachi most of the effected children resided in apartments.¹³

Nutritional rickets was more associated with exclusively breast fed children in this study. This finding is consistent with other studies in Pakistan, in which Hatun et al observed that 83% infants who had vitamin D deficiency were exclusively breast-fed.¹⁴ Fresh milk, because of its high phosphorus content, can also lead to hypocalcemia.¹⁵ Other factors that play significant a role include cultural beliefs and religious orientation, where conservative clothing is donned by those observing pardah which limits sun exposure of sunlight.

In this study prevalence of nutritional rickets was observed in children who had not yet been weaned, or were weaned at a delayed stage. This finding is consistent with research conducted in Kuwait¹⁶ that cited delayed weaning as a factor for rickets in children.

Children with delayed weaning miss the opportunity of obtaining vitamin D from solid foods.

The study revealed intake of vitamin D rich food in children to be low (40%) which is consistent with previous studies^{17,18} that cite vitamin D poor foods as one of the cause of nutritional rickets. Majority of children suffering from nutritional rickets were from low and middle socioeconomic classes. Contrary to the findings, research conducted in India¹⁹ and Pakistan²⁰ showed high prevalence of vitamin D deficiency in infants and nursing mothers belonging to upper socioeconomic class as well.

Hypocalcemic fits were present in 7 (14%) cases. Findings by Ladhani et al attribute symptomatic hypocalcemia in almost half of children to nutritional vitamin D deficiency.²¹ In the present study all children presenting with fits were aged less than 6 months. Pal reported 9 cases of symptomatic hypocalcemia in young infants, more than half of whom were under 5 months of age.²² Thirty two percent of these children had history of recurrent respiratory tract infections. 1,25(OH)2D acts as an immune system modulator. Yener et al have reported more episodes of bacterial infections in children with vitamin D deficiency as compared to healthy children.²³ Recurrent diarrhea was present in 11 (22%) cases which is congruent with previous studies^{3,13,5} reporting positive association of rickets with recurrent and chronic diarrhea.

Present study identified 39 (78%) children having radiological findings of rickets, while these findings were detected as 73.84%²¹, 38.09%¹², and 100%¹⁰ in different studies. Elevated levels of serum alkaline phosphatase were a consistent finding in all rachitic children. Joiner et al²⁴ suggested a more cost effective approach of targeted screening of high-risk groups with alkaline phosphatase levels to detect asymptomatic affected infants.

CONCLUSION

Infants under 2 years of age are liable to have vitamin D deficiency rickets if they are exclusively breast fed and having inadequate exposure to sunlight. Delayed introduction of complementary foods and malnutrition are also

important contributing factors in nutritional rickets. Vitamin D deficiency can present with variety of symptoms other than musculoskeletal symptoms like recurrent ARI, diarrhea and seizures. These are under recognized features of vitamin D deficiency. It is therefore recommended that rickets should be investigated for patients reporting these complaints. It is also possible for clinical signs and symptoms to be present with no radiographic evidence of rickets.

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ORIGINAL ARTICLE

Comparing Attitudes of Medical and Engineering Students in Karachi Towards Smoking

Nadia Jajja¹, Farah Ahmad² and Syed Hasan Danish³

ABSTRACT

In Pakistan, tobacco consumption is at an all-time high with the tobacco industry witnessing a boom. According to the Pakistan Tobacco Company, production and sale has taken a sharp leap from Rs.1,000 million rupees to Rs.1,750 million in 2008. The youth remain particularly vulnerable as massive anti-smoking ad campaigns have failed to drill in the health hazards. The aim of this study is to assess the attitude, perception and practices of youth regarding cigarette smoking. Comparative cross-sectional study was conducted in Ziauddin University and Bahria University. Sample was taken from all years of teaching. Data was collected through self-administered structured questionnaire that was developed in English. It comprised of questions pertaining to their year of study, smoking history, and perception and practices regarding smoking. A total of 450 students were surveyed, medicine (n=260) and engineering (n=190). One-fourth of the survey sample admitted to have tried to smoke at least once in their lifetime (p=0.001), and at least 20% medical students (n=53) and 35% of engineering students (n=66) surveyed had smoked a cigarette (p=0.001). While students studying medicine were better aware of the risks associated with smoking and tobacco consumption, however compared to engineering students their overall knowledge of the health risks was unsatisfactory. A significant number of medical students were unable to list and hence effectively counsel about long and short term health benefits. Peer pressure and media played a large role in students picking up the habit.

KEY WORDS: *Pakistan/Epidemiology, Smoking, Karachi, Mechanism Medical Students.*

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INTRODUCTION

Fifty years have passed since the first report on health hazards from tobacco was released by the Committee of the Royal College of Physicians, United Kingdom, in 1962,¹ but scientists and epidemiologists continue to struggle to find a method to completely deter its use. The latest tobacco consumption report released on March 8, 2012 by the US Surgeon-General Office revealed that while there had been an overall decline in the rate of smoking across the US, the struggle to contain the epidemic of tobacco smoking is far from over.² According to 2012 US Surgeon-General report young people are most vulnerable to this perilous game, majority of them start by 18 years of age with progression to daily smoking and after age 26 initiation of smoking is infrequent.²

In Pakistan, tobacco consumption is at an all-time high with the tobacco industry witnessing a boom in its production. According to the Pakistan Tobacco Company, production and sale has taken a sharp leap from 1000 million rupees to 1750 million rupees in 2008.³ On the other hand, the youth remain particularly vulnerable as massive anti-smoking advertising campaigns have failed to drill in the health hazards. Of the total 1680 students who responded to the Global Youth Tobacco Survey (GYTS) conducted in Islamabad, 11.2% admitted using a tobacco product. Between 30% and 38% were exposed to second-hand smoke at home and outside, but only 0.4% perceived smoke from others as deleterious to health.⁴

Over the years, studies have been undertaken to assess the knowledge of various student groups to smoking in order to better understand the lacunae that promote smoking. In this study, the researchers chose students from the fields of medicine and engineering to compare and evaluate their attitudes to smoking. Internationally, studies have specifically focused on medical students and the impact their training has on them becoming good anti-smoking counselors. In 1998, Australian researchers found that medical student do not receive adequate training to negate smoking among their patients. Another worldwide survey

revealed that only 11% medical schools devote reasonable time to tobacco and smoking cessation.⁵ Similar findings were presented from two research conducted at European medical schools in London (UK) and Gottingen (Germany) in 2009. the authors concluded that current curricula about tobacco dependence and control in medical schools needs to be improved.⁶ Mortality related to smoking is underestimated by students as they lack relevant information on consequences of smoking and smoking cessation methods.⁶

The aims of this study were to evaluate and compare the behaviors of students enrolled in engineering and medical colleges for awareness about long and short term health consequences of smoking; factors that influenced initiation of smoking; smoking behavior and its frequency; attitude and motive behind sustaining the habit.

METHODOLOGY

This was a comparative cross sectional study design carried on medical students studying in Ziauddin Medical University and engineering students studying in Bahria University. Sample was taken from all years of teaching. The actual sample size was 384 students which was calculated by using the standard formula for calculating sample size on the basis of prevalence.

$$N = \frac{[(Z)^2 \times P(1-P)]}{d^2}$$

Prevalence was taken at 50% because no relevant data was available. The bound of error was taken at 5% with 95% confidence interval. The sample size was inflated to 450 to exclude non-response and poorly filled questionnaires. Fifty students were selected through random sampling technique from each year. Therefore 250 initially were selected from Ziauddin Medical University and 200 from Bahria University. But due to non-availability of required sample size from Bahria University, sample was completed from medical students of Ziauddin Medical University.

Students (of MBBS) who were present on the day of data collection were included in the study (Undergraduate students from all years were taken as participants). After explaining the purpose of the study students who refuse to be

part of the study were excluded or those who were absent at the time of data collection.

Data was collected through self-administered structured questionnaire that was developed in English. It comprised of questions pertaining to their year of study, smoking history, perception and practices regarding smoking and Fagerstrom questionnaire for nicotine dependence.

Data was entered on Epi Info. Before analysis, data was cleaned for possible data entry errors. Frequencies and Percentages were taken out for categorical variables. Association between medical and engineering students and smoking habits, perception and practices was done by application of χ^2 . P value less than 0.05 was taken as significant.

Before administering the questionnaires, students were briefed about the objectives of the study and consent was taken. The study was cleared through the ERB of Ziauddin University.

RESULTS

A total of 450 students were surveyed, medicine(n=260) and engineering (n=190). One-fourth of the survey sample admitted to have tried to smoke at least once in their lifetime (p=0.001), and at least 20% medical students (n=53) and 35% of engineering students (n=66) surveyed had smoked a cigarette (p=0.001) (Table 1).

That peer pressure impacted smoking behavior was obvious as 15% medical students (n=40, p=0.001) agreed that those who smoked looked cool, 16% of them (n=41, p=0.001) thought that people who smoked had more friends, and 15% (n=39) agreed that girls were more attracted to boys who smoked.

In engineering students, peer pressure influenced smoking more: 40% (n=74, p=0.001) engineering students agreed that people who smoked looked cool, 41% (n=77, p=0.001) thought that people who smoked had more friends and 40% (n=75, p=0.001) thought that girls were more attracted to boys who smoked.

70.5% medical students (n=183) and 69% engineering students (n=130) admitted that

media coverage did have a role in initiation of smoking. However, 28% of engineering students (n=53, p=0.001) were impressed by sportsmen and actors smoking versus 9% (n=22) medical students.

Table 1: Perceptions on Smoking Effecting Disease Occurrence

Query	Likert	Med (%)	Engr (%)	p-value
Do you think cigarettes are addictive	Agree	78.8	66.8	0.004
	Disagree	13.1	19.5	0.066
	Not sure	8.1	13.7	0.055
Smokers tend to die at a younger age than non-smokers	Agree	61.5	43.2	0.001
	Disagree	20.4	31.6	0.006
	Not sure	18.1	25.3	0.065
The majority of people with lung cancer are or have been smokers	Agree	81.9	60.5	0.001
	Disagree	7.7	18.4	0.001
	Not sure	10.4	21.1	0.002
Some cigarettes are less dangerous than others	Agree	40.4	52.6	0.010
	Disagree	38.1	28.4	0.033
	Not sure	21.5	18.9	0.501
Damage caused by smoking is reversible	Agree	25	34.7	0.025
	Disagree	53.1	39.5	0.004
	Not sure	21.9	25.8	0.339
Passive smoking is a health risk	Agree	86.9	61.6	0.001
	Disagree	3.5	19.5	0.001
	Not sure	9.6	18.9	0.004

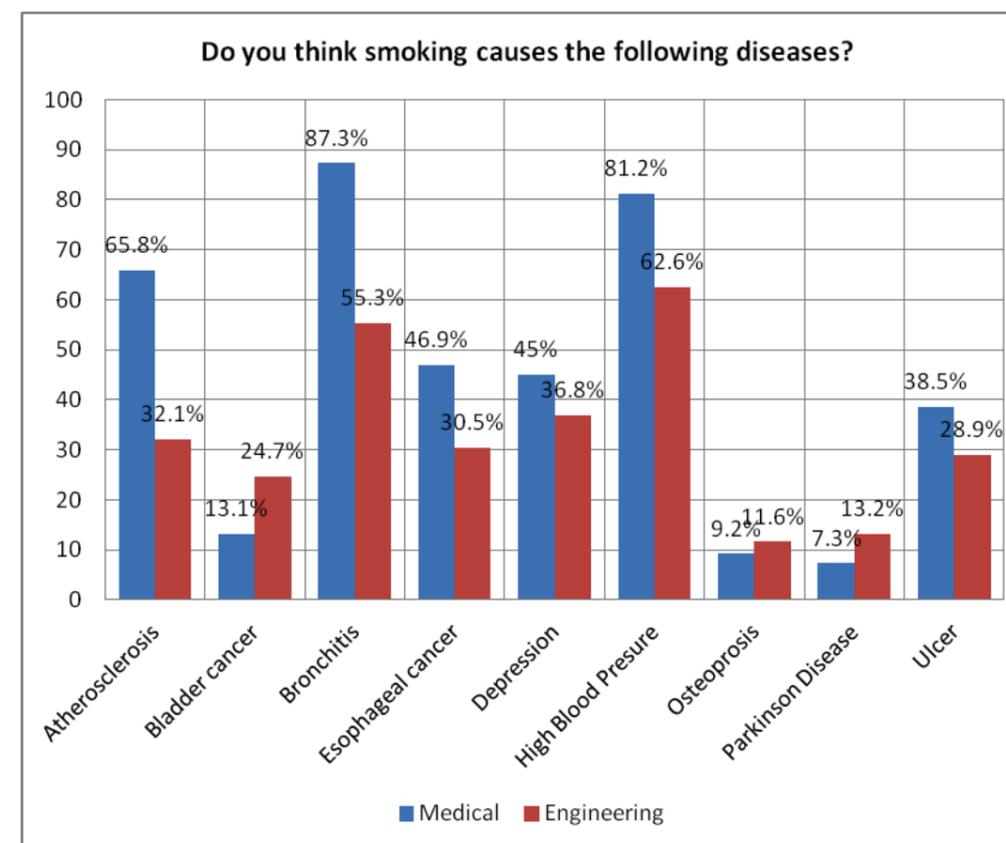
That the tobacco companies have marketed lighter versions of cigarettes well is reflected in the response to the question whether some cigarettes were less dangerous than the others: 40% medical students (n=105, p=0.010) agreed that some were less dangerous whole 53% (n=100, p=0.010) engineering students agreed to the same.

When asked whether they considered smoking an addictive habit, 79% medical students

(n=205, p=0.004) agreed, but the remaining 21% (n=55) either disagreed or were unsure. On the other hand, when engineering students were asked the same question, 69% (n= 127,

p=0.004) agreed, 20% (n=27, p=0.06) disagreed and 14% (n=26, p=0.055) were not sure of its effects.

Figure 1: Perceptions on Smoking Effecting Disease Occurrence



When enquired whether smokers died at an earlier age than non-smokers, 62% medical students (n=160, p=0.001) agreed, 20% of them (n=53, p=0.006) disagreed and 18% of them (n=47, p=0.065) were not sure.

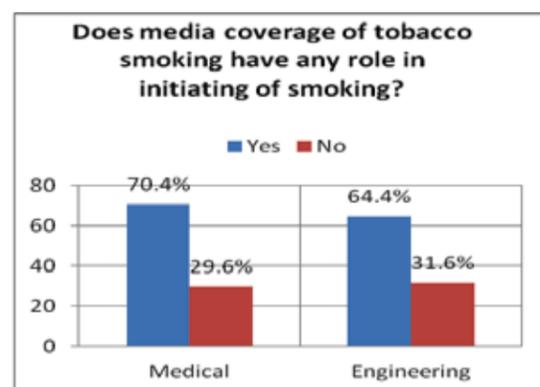
Whereas in the engineering group, 43% of the students (n=82, p=0.001) agreed with the statement, 32% disagreed (n=60, p=0.006) and 25% were not sure (n=48, p=0.065).

Similarly, when asked whether there was an association between lung cancer and mortality, 82% medical students (n=213, p=0.001) and 61% engineering students (n=115 p=0.001) thought smoking was a risk factor. However, 18% of medical students disagreed or were not

sure (n=47 p=0.002) as compared to 40% of engineering students (n=75, p=0.002) in it being a risk factor.

It was even more interesting to note that while 62% of medical students (n=160, p=0.001) agreed that smokers died at a younger age than non-smokers, 20.4 % of them disagreed (n=53). Engineering students were completely divided, as 43.2% of them (n=82, p=0.001) agreed on its effects in reducing life expectancy, 31.6% (n=60, p=0.006) disagreed with this whereas 25.3% (n=48, p=0.065) were not sure.

Figure 2: Media Coverage and Smoker Initiation



Misconceptions bounded about the reversibility of changes, and even more starkly in the group studying medicine. In the medicine group, 25% (n=65) believed that changes caused by smoking were reversible, and a little more in the engineering group (35%, n=66) thought the same (p=0.025). On the other hand, 22% medical students (n=57) and 26% engineering students (n=49) were not sure about the reversibility of the changes.

DISCUSSION

Smoking is such a common habit these days that every nook and corner in the city has a small stall selling paan and cigarettes. Young people who cannot afford to buy an entire cigarette pack ask the shop-keeper to give cigarettes in loose, and so miss a chance to see the warning that "smoking is injurious to health". Even ads that run on television rush through the warnings about the side effects of smoking. Now the key measure to reducing diseases due to smoking is deterring young people from taking up the habit all together.

Internationally, a lot of emphasis has been put on teaching young under-training physicians on preventive measures as they will be future ambassadors of health care. Robyn Richmond in his article, *teaching medical students about tobacco* wrote that future doctors should be educated adequately in medical school so that they become knowledgeable in tobacco control and prevention measures and develop skills in smoking cessation.⁷

In our study we have compared the attitudes and knowledge of medical students with engineering

students to see the differences in perception regarding the habit. The basis of this study was that medical students would have a more mature and knowledgeable approach as teaching about tobacco and its hazards has become part of first and second year curricula in many medical colleges. In Pakistan, to the best of our knowledge, no study has been conducted that compare the attitude and influences on students enrolled in medical colleges with that of engineering colleges.

One-fourth of the survey sample admitted to have tried to smoke at least once in their lifetime, and at least 20% medical students and 35% of engineering students surveyed were currently smoking. Abroad various studies have been conducted to determine the smoking rates among medical a student, which ranged from 0 to 56.9% for men and 0 to 44.7% for women, and surprisingly was more prevalent among Turkish men than among those in other European schools.⁷

Peer pressure clearly played a major role in many students picking up the cigarette in the two groups, but students studying medicine were less likely to be influenced by it. The difference rate was not at a desirable level: a significant 15% of medical students thought that those who smoked looked cool, 16% thought that people who smoked had more friends, and 15% agreed that girls were more attracted to boys who smoked. The percentage of students with similar thoughts in the engineering group was clearly much higher.

Boys are more likely to be influenced by images of their peers smoking has been shown earlier in a study conducted in Islamabad, where 51.2% of the sample thought boys who smoked had more friends, compared to 36.9% who thought girls had more friends, whereas 13.0% thought boys and 11.9% opined girls who smoked looked more attractive.⁴

In USA this phenomenon has been studied in-depth and "social smoking" has been attributed as the reason for initiation where young people hang together and are influenced to smoke in gatherings. A study published in Pediatrics journal, titled "Social Smoking Among US College Students", which sampled 10,904 students enrolled at 119 nationally

representative US colleges revealed that social smoking is common among college students⁸. Smith et al noted similar findings but saw social smokers more likely to be occasional in their habit along with less nicotine dependence⁸.

Rather than medical education playing a deterrent role, study in Turkey found that tobacco consumption by medical students increased progressively with knowledge on harmful consequences not barring students from this habit. It concluded that students smoke more frequently with passage of time and their smoking history prolongs with one third smokers adopting this habit while studying medicine⁹. In the study we conducted, we found that medical students' knowledge about smoking was inadequate when it came to morbidity, mortality and life expectancy (Fig. 1). That the tobacco companies have successfully marketed lighter versions of cigarettes as less threatening to health is reflected in the response to the question whether some cigarettes were less dangerous than the others: 40% medical students (n=105, p=0.010) agreed that some were less dangerous while 53% (n=100, p=0.010) engineering students agreed to the same.

It was even more interesting to note that while 62% of medical students (n=160, p=0.001) agreed that smokers died at a younger age than non-smokers, 20.4 % of them disagreed (n=53). Engineering students were completely divided, as 43.2% of them (n=82, p=0.001) agreed on its effects in reducing life expectancy, 31.6% (n=60, p=0.006) disagreed with this whereas 25.3% (n=48, p=0.065) were not sure.

Misconceptions abounded about the reversibility of changes, and even more starkly in the group studying medicine. In the medicine group, 25% (n=65) believed that changes caused by smoking were reversible, and a little more in the engineering group (35%, n=66) thought the same (p=0.025). On the other hand, 22% medical students (n=57) and 26% engineering students (n=49) were inconclusive about the reversibility of the changes.

Our findings were no different to the study conducted in November 2007 in Berlin, Germany, to determine the competence of fifth year medical students to counsel smokers. In

this study, students underestimated smoking related mortality and its negative effects on longevity with only one third students feeling qualified enough to counsel tobacco dependant patients¹⁰

Influence of media on smoking habits was obvious as 70.5% medical students (n=183) and 69% engineering students (n=130) admitted that media coverage did have a role in initiation of smoking. However, 28% of engineering students (n=53, p=0.001) were impressed by sportsmen and actors smoking versus 9% (n=22) medical students (Fig. 2). The fact remains that tobacco is easily available, and the more young people are exposed to cigarette advertising and promotional activities, the more likely they are to smoke.²

In the 2012 US Surgeon-General report, it was observed that marketing by tobacco industries instigates youths to smoke with 80% smokers influenced by heavily advertised brands². Further a humongous amount is spent on marketing these products promoting low cost tobacco that ends up having a substantial impact on youth.² World Health Organization in 2006 reported that nicotine is made available in doses to maximize addiction and a phony image of tobacco as a clean product is promoted although standards for tobacco products are not regulated appropriately. Hence it is high time that a comprehensive regulation on all tobacco products, ingredients, emissions, manufacture, communications and marketing, as endorsed by the WHO Framework Convention is implemented¹¹

According to afore mentioned discussion nearly three decades ago, the US National Cancer Institute had recommended inclusion of tobacco-treatment education in the curricula of all US medical schools by 1995 to improve the participation of health-care providers in smoking cessation efforts. Another follow up study found that tobacco control training in medical and nursing schools is low.¹²

CONCLUSION

Even though this study is based on a valid questionnaire tested internationally and the large sample size with a good response rate, there were certain limitations. First, all subjects were

Incidentally Diagnosed Lobular Carcinoma-in-Situ in a Case of Multiple Fibroadenomas

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ABSTRACT

A case of lobular carcinoma *in situ* (LCIS) arising within a fibroadenoma. Diagnosis of LCIS was made based on histopathological examination of the excised lumps. The case report highlights the role of histopathology in the diagnosis of this entity coexisting in a fibroadenoma, as ultrasound missed the presence of pre-malignant cells. Fibroadenomas have genetic correlation, as was defined in our case. This case stresses the need for histological evaluation of all breast masses in women.

KEY WORDS: LCIS, fibroadenoma, Histopathology, Non Invasive Breast Cancer.

taken from private education institutes of Karachi. Second, they all had the same level of affordability. Third, only those subjects who were between the age groups 19 to 25 years could be included.

In this study conducted in two colleges of Pakistan, our findings were no different than previous studies conducted abroad. Even though the hazards of smoking have been included in the curriculum, it has not made significant impact in the outlook of students. While students studying medicine were better aware of the risks associated with smoking and tobacco consumption, their overall knowledge of the health risks was unsatisfactory. A significant number of medical students were unable to list and hence effectively counsel about long and short term health benefits. Peer pressure and media played a large role in students picking up the habit.

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INTRODUCTION

Fibroadenoma is the most common benign breast tumor in adolescent girls and young women with a peak incidence occurring in the second and third decades of life. Carcinoma arising within a fibroadenoma is rare and is usually discovered incidentally.¹ Mammography is the standard of reference for the detection of breast carcinoma, yet 10%–30% of breast cancers may be missed at mammography. Possible causes for missed breast cancers include dense parenchyma obscuring a lesion, poor positioning or technique, perception error, incorrect interpretation of a suspect finding, subtle features of malignancy, and slow growth of a lesion.²

In lobular carcinoma in situ (LCIS) cells that look like cancer cells are growing in the lobules of the milk-producing glands of the breast, but they do not grow through the wall of the lobules. LCIS (also called *lobular neoplasia*) is sometimes grouped with ductal carcinoma in situ (DCIS) as a non-invasive breast cancer, but it differs from DCIS in that it doesn't seem to become invasive cancer if it isn't treated. Women with lobular carcinoma in situ (LCIS) have a 7 to 11 fold increased risk of developing cancer in either breast.³ Fibroadenoma considered as a risk factor for development of breast cancer, its reporting has been overshadowed by that of breast cancer. Early diagnosis and treatment can relieve anxiety associated with non-malignant conditions of the breast.

It is deduced that majority of cases diagnosed as fibroadenoma, that were in their second and third decades (16-30 years), may be due to hormonal dependency, participation in lactation, and involution at menopause, which could be a possible contribution to lump formation.⁴

CASE

A 28 years old woman came to surgical OPD at Civil Hospital Karachi, with the complaint of swellings in both breasts since one year, that had increased in size with time. She had no mastalgia, nipple discharge and skin changes or any systemic symptoms. There was absence of family history of benign breast lumps, her

mother and one elder sister were already operated for fibroadenomas few years back, and were uneventful till date. Clinical examination revealed three lumps which were non-tender, mobile, hard, firm and slippery on palpation in both the breast, one in the left breast upper outer quadrant measuring around 3x2cms. Two in the right breast, one in inner lower quadrant measuring 2.5x3cms approximately other lied below the areola towards the upper outer quadrant measuring 2x2cms approximately. No auxiliary and supraclavicular lymph nodes were palpated in both the axilla. Mammography and ultrasonography confirmed their presence of all the three lumps palpated clinically, with no enlarged lymph nodes in both axillas.

The patient opted for excision of the lumps and refused for fine needle aspiration cytology. The patient was admitted for excision biopsy of both breasts. All three lumps were excised and sent for histopathology, in three separate jars, with their site of origin labeled. The excised lumps were firm, solid and slippery to hold, the lump in the left upper outer quadrant was 2.5x2.5cms, the lump in the right lower quadrant measured 2.5x2.0cms, and the lump below the right areola was 2x2cms with a tan gray lesion inside the lump. The post-operative period was uneventful and the patient was discharged after 24 hours with clean wounds next day and with a planned follow-up and biopsy report after two weeks. Histological examination of all the three masses revealed fibroadenomas, but the one which lied below the areola in the right breast revealed a focus of lobular carcinoma-in-situ that was completely confined within the fibroadenoma. After discussing treatment options with the patient, a policy of continued surveillance was decided upon. The patient remains asymptomatic 2 years & 4 months after the procedure.

DISCUSSION

The risk of missing breast cancer in women under 25 years of age who have Fibroadenomas diagnosed by physical examination, sonography, and FNA is 1 in 229 to 1 in 700.⁵ In our case the LCIS was missed in the ultrasound. Carcinomas arising within a fibroadenoma have the same behavior as those developing independently, so their treatment should be the same. The debate

about which therapeutic procedure should be followed in a case of a carcinoma in situ within a fibroadenoma reflects the controversy concerning optimal treatment of LCIS and DCIS. Although DCIS and LCIS are noninvasive breast cancers, their biological behavior differs considerably. Breast conservation therapy is clearly a reasonable treatment option in most women with DCIS within a fibroadenoma, whereas most women with LCIS within a fibroadenoma will prefer to be treated by close surveillance after local excision and biopsy. Although LCIS can be treated by prophylactic mastectomy, the procedure is generally considered an excessively aggressive approach for most women.^{6,7,8}

In our case the diagnosis was made based on the histopathology report, and offering

conservative treatment could have resulted in invasive carcinoma of breast. It appears choosing the excision biopsy was a better option instead. There are two reports on the simultaneous occurrence of CIS (carcinoma-in-situ) arising within multiple fibroadenomas. In both reports a patient is described with two fibroadenomas containing LCIS.^{9,10}

Learning from the case highlight that instead of depending on radiological reports for diagnosis, the FNAC should be mandatory, especially if opting for conservative treatment of Fibroadenoma. Close monitoring of the lump should be done and once excised should be sent for histopathology. There is a familial connection between occurrence of fibroadenomas, just like breast cancers.

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CASE REPORT

Massive Endometroid Ovarian Carcinoma and Synchronous Uterine Malignancy

Shazia Sultana¹, Rubina Hussain² and Wasiya Irfan³

ABSTRACT

The diagnosis of ovarian carcinoma is a challenging task especially when women usually present vague symptoms like abdominal distension and pain. The aim of this paper is to report a case of synchronous ovarian malignancy in a young patient. A 36 year old unmarried female presented with a huge right ovarian cystic mass occupying the whole abdomen, breathlessness, jaundice and urinary retention. She underwent laparotomy for surgical removal of the mass and during the surgical procedure a frozen section was performed that showed malignancy. Total abdominal hysterectomy and bilateral salpingo oophorectomy was thereafter performed on her. Final histopathological report of the mass revealed well differentiated endometroid ovarian cancer and endometroid endometrial cancer. Synchronous endometroid tumors are generally present in young patients; these tumors tend to be of low grade malignancy. Prognosis of endometroid carcinoma is relatively better than other histological types.

KEY WORDS: Endometroid Tumour, Total Abdominal Hysterectomy, Bilateral Salphingo-Oophorectomy, Laparotomy.

INTRODUCTION

Ovarian cysts and tumors grow silently and are often undetected for years. They usually do not cause pain but if large they present with discomfort. Ultrasonographic scanning permits early detection and appropriate treatment. Occasionally, ovarian cysts reach enormous dimensions without raising any symptoms.¹ The simultaneous occurrence of two genital tumors is relatively of unknown etiology. Synchronous endometroid carcinoma of the uterine corpus and ovary is an uncommon but well known phenomenon. Such cases may represent as either separate independent primary or as metastatic tumors requiring careful consideration of a number of gross and histological features. These features illustrate the criteria helpful in distinguishing independent primaries from metastatic carcinomas which have a different therapeutic implication.²

CASE

A 36 year old unmarried female presented to the gynecology and obstetrics department at Ziauddin Hospital Karachi with massive abdominal distension and pain. The patient had been noticing abdominal distension since last two years; she perceived this distension as weight gain and took homeopathic medication for weight reduction. Associated symptoms included breathlessness, loss of appetite and anuria due to pressure effects of the ovarian mass. There was no history of colicky pain, vomiting or any other gastrointestinal symptoms. There was no previous history of any other illnesses or family history of any malignancy. When inquired about her menstrual history her age of menarche was 13 years, menstrual cycles were regular with normal flow for first 5 years after menarche. Thereafter at the age of about 18 years patient developed prolonged menstrual cycles and she menstruated after 8-12 weeks each time. The flow was excessive and patient bled for 8-9 days at each menses.

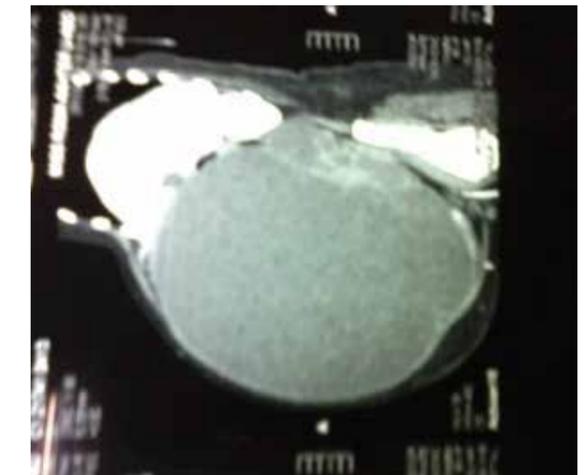
On admission to the hospital the patient weighed 78kgs. General physical examination revealed pallor, jaundice and pedal edema while rest of the examination was unremarkable. Abdominal examination showed generalized abdominal

distention (Fig. 1) with huge mass arising from pubic symphysis to xiphisternum. Percussion over abdomen was dull and there was no shifting dullness present. Bowel sounds were heard normally. A vaginal examination was not performed.

Figure 1: Generalized Distension Of The Abdomen Is Evident.



Figure 2: Abdominopelvic CT Scan Of The Patient



The patient's laboratory investigations revealed Hb 6gm/dl, urea 120mg/dl, creatinine 4mg/dl, indirect bilirubin 4mg/dl and total bilirubin 5mg/dl. Tumor marker alpha feto protein was 3.88ng/ml and CA-125 was 65.44 IU/ml. Patient's transabdominal ultrasound revealed a large solid cystic mass arising from the right adnexa measuring 32.0 by 27.0 by 33.0 cm. It showed internal septations and solid component with low level echoes. The uterus appeared normal and was completely separated from the mass.

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Abdominopelvic CT scan confirmed large right ovarian cystic mass (Fig. 2) with internal septa and solid component. CT scan showed mass causing compression and displacement of small and large bowel loops. The mass was abutting gall bladder and undersurface of liver and was compressing the aorta, inferior vena cava and iliac vessels. There was mild right sided hydronephrosis and hydroureter present. Chest X ray showed right lung collapsed due to large mass.

A multidisciplinary team of physicians and surgeons managed the patient preoperatively. She was transfused 2 units of packed cells to correct her anemia and she was maintained on dialysis till her urea and creatinine were under normal ranges. After receiving surgical fitness patient was listed for an elective laparotomy. Preoperatively the patient and her family were counseled about the possibility of malignancy of the ovarian mass and were told that the nature of surgery will depend on the on-table report of the frozen section of the mass. If report would suggest malignancy, the surgery would be converted from cystectomy to transabdominal hysterectomy with bilateral salphingo-oophorectomy.

The patient underwent laparotomy with a midline incision extending above the umbilicus. After opening layers, a large tense, smooth surfaced cystic mass was noted (Fig. 3). There was no free fluid in the abdomen. The mass observed was large and could not be removed intact. Approximately 9 liters of purulent dark brown yellowish foul smelling fluid was drained and after that the cyst measuring 30 x 24 x 25cm was removed and sent for frozen section. Frozen section reported malignant tumor. The family of the patient was informed followed by proceeding of hysterectomy and bilateral salphingo-oophorectomy with omentectomy.

Figure 3: The Mass Post Abdominal Layer Opening



The postoperative period was uneventful and patient was discharged on 10th postoperative day. The patient's weight was reduced from 78kgs to 62kg postoperatively. The histopathological report later confirmed synchronous endometrioid ovarian and uterine tumor. After consultation with the multidisciplinary team the patient was suggested to be further managed by chemotherapy and radiation both.

DISCUSSION

The presence of two genital tumours at the same time is relatively uncommon and makes 0.63%³ of all genital malignancies. Initial challenge for gynaecologic oncologist is to classify diseases of women with associated genital malignancies, especially of the endometrial carcinoma of the uterus and ovary. If endometrial carcinoma is present only in one half of the myometrium this is stage IA, while the stage IIIA tumor spreads to the serosa or adnexa. Carcinoma localized at the ovary without the rupture of the capsule is of stage IA, while ovary carcinoma that spreads to the fallopian tube or uterus is of stage IIA.

The association of endometrial ovarian carcinoma with uterus carcinoma is the most. While both etiology and pathogenesis are unknown, this may be attributed to the development of the surface epithelium of the ovary which has the same embryologic derivation from the mullerian duct. There is an assumption that those might, as particular objects, develop into independent neoplasm at the same time under the influence of some hormones.^{4, 5} It is needed to classify disease

correctly as further treatment and prognosis depend on it. Some authors prefer histology criteria to make a difference between metastatic disease and independent occurrence. Sometimes, this distinction is difficult or even impossible.⁶ The major criterion for endometrial carcinoma and ovarian metastasis is a multiple nodular ovarian tumor. Minor criteria are ovaries smaller than 5cm, bilateral affection, deep myometrial invasion, vascular invasion and fallopian tube affection. Major criterion, two or more minor criteria, as well as the absence of ovarian endometriosis is enough to make the diagnosis of metastatic disease.⁷

The tumor in our case penetrates more than half of the myometrium and invades cervical stroma but does not extend beyond the uterus nor does it involve both fallopian tubes; therefore, it can be classified as stage II. Tumor that penetrates deeply into the myometrium might indicate ovarian metastases, because it is well known there is no invasion or the invasion is superficial in cases of independent tumors. On the other hand there is a huge right ovarian cyst that comes out to be well differentiated from endometrioid carcinoma of the ovary; the tumour involves the ovarian surface along with element of endometriosis in cases of metastases from ovaries to uterus. There are no signs of lymphovascular invasion or penetration into fallopian tube, which speaks in favor of independent growth. Left ovary was enlarged 10 x 6 x 5 cm, showed endometrioid carcinoma, well differentiated type (histological grade I), nuclear grade II, omentum with massive areas of necrosis but no viable tumor and lymph node involvement which classify it as IB stage.

Our patient was 36 years of age, and it is well known that independent tumors occur in younger women more frequently, in contrast to independent tumors of endometrial or ovarian carcinoma which most frequently occur in the seventh decade of life, median age 41–52 years, obese, premenopausal and nulliparous women.⁸ Synchronous tumors have also been linked to hyperestrogenic conditions (chronic anovulation, polycystic ovarian syndrome (PCOS), obesity, estrogen producing ovarian tumors, or unopposed estrogen replacement therapy). Our case is different in a way as the patient presented with an enormous cyst, she was young and her BMI was 22kg/m² but there was

history of prolonged cycle. Hyperestrogenemia may cause endometrial hyperplasia and in some cases endometrial carcinoma. Correlation between corpulence and ovarian carcinoma is not so clear. Certain studies suggest that corpulence in the adolescence increases the risk of ovarian carcinoma. Our patient has endometrioid tumor of the ovary and uterus. It is known that women present with simultaneous tumor of ovary and uterus are barren women in one third to one half of all cases. There are several reasons for that. Hormonal influence is very important. Some studies claim that the uterine body fallopian tubes and ovarian epithelium are one morphologic entity, which explains an independent development of the tumor in different compartments of mullerian tubes. The estrogen impact is crucial. Families with hereditary nonpolyposis colorectal carcinoma (HNPCC), and Lynch's syndrome have more probability for endometrial carcinoma.

Immunohistochemical analysis of some receptors might be a good indicator of the process development and treatment success.¹⁰ Because of the lack of sufficient evidence clarifying whether it was the case of synchronic (based on clinical and PH findings) or metastatic endometrial carcinoma of endometrium and ovary, patient was classified as higher stage due to rupture of huge cyst during surgery and cervical involvement of endometrioid carcinoma, so she underwent complete radiation and chemotherapy. The five-year survival in synchronous tumors is excellent, 79%, in contrast to single primary ovarian cancer.⁹

To conclude ovarian cysts can present in any way management of ovarian cysts depends on the patient's age, the size, structure of the cyst and fertility issues and menopausal status. Risk factors and clinical outcome indicators in women with synchronous tumors are different from those based on histology division. It is necessary to identify synchronous primaries and metastatic tumors correctly as staging, prognosis and further management depend on it. In fact, standard criteria for differentiating between primary and metastatic tumors are likely to be misleading in this situation and additional testing is required. In the future, a better evaluation of the etiology of these diseases is needed; also, molecular diagnosis of

Morgagni Hernia - Presenting as Vague Abdominal Pain Since 8 Years

Tahir Muhammad Yaseen¹, Syed Asif Ali Zaidi² and Shafiq-ur-Rehman³

ABSTRACT

Morgagni hernia is the rarest type of Congenital Diaphragmatic Hernia(CHD). It accounts for 2% of all CHD cases and is detected incidentally through a chest xray. The hernia occurs mostly on right side of diaphragm with incidence of 90%, 8% occur bilaterally and 2% limited to left side. It is predominant in females presenting symptom of abdominal pain. The presence of colonic sounds on chest examination is a significant finding in diagnosis. CT scans usually reveal a retrosternal or parasternal mass or fat density which represents omentum and air containing viscus. A case of a middle aged lady presenting with vague abdominal pain for the last eight years is reported. Suspicion was raised over a chest xray which highlighted the right dome of diaphragm being pushed up and the presence of gaseous shadow under the right dome. Subsequent computed tomography showed morgagni hernia. The patient underwent open transabdominal of the stomach and omentum, where the hernia sac not resected and a primary closure of the defect was performed. The post operative course was uneventful. Morgagni though rare, often remains undiagnosed and can lead to life threatening complications. Surgical intervention regardless of patient's asymptomatic state should be offered to avoid complications.

KEY WORDS: *Congenital Diaphragmatic Hernia, Morgagni, Surgery.*

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tumors in endometrium and ovary would give us a real confirmation.

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INTRODUCTION

The domain of Congenital Diaphragmatic Hernia(CHD) involves birth defects involving abnormal development of the diaphragm . With a probability of 1:2,000/ 1:3,000, it accounts for 8% of all major congenital anomalies.¹ CHD is one of the three morgagni types which is rare. It is often referred to as retrosternal / parasternal hernia. CHD was first described by the Italian anatomist and pathologist Giovanni Morgagni in 1769² and accounts for 2% of all CHD cases located anterior to the xiphoid process of the sternum.³ Majority of the adults diagnosed with morgagni hernia remain asymptomatic with a few developing symptoms of dyspnea, cough or sternal pain depending on severity.⁴

CASE

A 68 year old known hypertensive female presented with history of intermittent upper abdominal pain, dyspepsia, bloating, non bilious vomiting, along with intermittent constipation since 8 months. She had history of ventral hernia repair with mesh 8 year ago .On physical examination her blood pressure was 100/70 mmhg, pulse 86/min, and temperature of 37 degree celsius. Abdominal examination revealed a midline infra-umbilical scar; abdomen was soft and non-tender and a digital rectal examination was unremarkable. Breath sounds were diminished at right basal region while rest of the examination was unremarkable.

Laboratory investigations revealed hemoglobin of 13g/L, white cell count 7 μ L, platelet 216 μ L; electrolytes normal range, amylase 34U/L, lipase 27U/L, blood glucose 94mg/dl. Chest x-ray revealed right dome of diaphragm pushed up and gaseous shadow under the right dome. Abdominal ultrasonography showed multiple gall with a left renal cortical cyst measuring 8.3 x 1.7 cm.

The patient underwent computed tomography scan of the abdomen due to the elevated right dome of diaphragm reported on chest x-ray. The CT scan revealed the herniation of stomach and transverse colon towards right hemithorax causing pressure over mediastinum. The right dome of diaphragm was termed questionable

with a normal liver. The examination of the gall bladder revealed multiple stones. CT diagnosis of eventration for diaphragm/ morgagni hernia were sought but as liver was not pushed up, therefore the final diagnosis of morgagni hernia was made.

Initially the patient was admitted under the team of internal medicine, however with the progression of the case the surgery team was also taken on board. After findings presented by the CT scan a repair of the hernia was planned. The patient was optimized preoperatively. An informed consent was acquired and blood products arranged.

An open transabdominal repair was performed through an upper midline incision. The contents of the hernia sac included transverse colon, fundus of stomach and omentum. The contents reduced after the adhesions were taken down. The hernia sac not resected; and the defect was using a 1- gauge synthetic non-absorbable interrupted/ mattress suture. There was no prosthetic material (mesh) or drain employed. A cholecystectomy was also performed.

Figure 1: Pre-Operative Chest X-Ray



Patient's postoperative course was unremarkable. A nasogastric tube was removed on first day after the operation and an oral feed was permitted from the second post operative day. The patient was subsequently discharged.

DISCUSSION

Congenital diaphragmatic hernia includes bochdalek hernia, morgagni hernia, and hiatus

hernia.¹ bochdalek hernia represent 98% of CHD cases while morgagni hernia represent only 2%.⁵ The morgagni hernia is rarely diagnosed in childhood being more prevalent in adults. The overall morgagni hernia is the rarest type of diaphragmatic hernia⁶ and is detected incidently through chest x-ray⁷

Figure 2: Pre-Operative Abdomen CT Scan

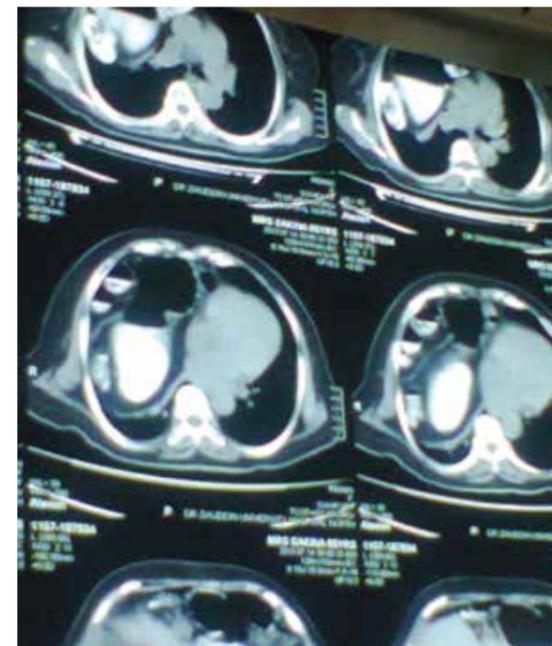


Figure 3: Pre-Operative Picture



Figure 4: Hernia opening can be seen on right side

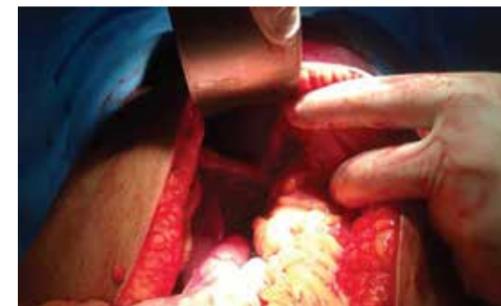


Figure 5: Post-Operative Chest X-Ray



The pleuroperitoneal membrane's lack of fusion/ muscularization anteriorly leads to defect in costosternal trigones known as foramen of morgagni. It is located posterolateral to sternum at the level of seventh rib on either side of xiphoid process. Morgagni hernia is via right hiatus, whereas larrey hernia is via left hiatus.⁸ The hernia can occur on both sides but mostly develops on right side of the diaphragm with incidence of 90%, 8% occur bilaterally and 2% limited to left side.⁶ The rarity of occurrence on left side is due enhancement of diaphragm by heart and pericardium.⁹ The occurrence morgagni hernia is more common amongst females. The frequency of diagnosing morgagni hernia increases with age, especially after 50 years.⁹

The most frequently occurring symptoms reported for it are abdominal pain and constipation.¹⁰ Cardiopulmonary symptoms such as dyspnea and palpitations are less common than gastrointestinal symptoms.⁶ A decrease in respiratory sounds or presence of colonic sounds on chest examination is a significant finding in diagnosis of the hernia.⁹ Factors that

predispose onset of symptoms of morgagni hernia include conditions producing prolonged / sudden increase in intra-abdominal pressure such as pregnancy, trauma and exercise.⁶ Computed tomography is also a tool for diagnosing morgagni hernia. CT scans usually reveal a retrosternal or parasternal mass or fat density which represents omentum or omentum and air containing viscus.⁶ Magnetic resonance imaging (MRI) yields similar information. In cases of visceral herniation, barium study can confirm the diagnosis.⁶

The diagnosis of morgagni hernia is made through radiological assessment. Depending on the contents of the hernia sac; a chest roentogram will show either right, left or bilateral pericardiophrenic density where omentum is the content. Where the content is present in the transverse colon, small intestine or the stomach, air fluid can be observed.⁶ The viscus trapped in the hernia sac can undergo intestinal obstruction, incarceration or strangulation. Therefore the treatment of morgagni hernia

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whether symptomatic or asymptomatic is surgical.⁶ Choice of surgical approach for morgagni hernia remains controversial¹¹. Some argue in favor of transthoracic,^{12,13} transabdominal,¹⁴⁻¹⁶ or video assisted endoscopic technique.¹⁷⁻²² The transabdominal approach is reported in most of the cases as the preferred approach.⁶ The contents of sac are reduced into the peritoneal cavity and margins of sac identified and sac is generally resected.⁶ Mesh is used in cases of large defects or muscular weakness while small defect can be closed by direct suturing.²³ Operative mortality and morbidity are low especially for elective repairs.²⁴

In conclusion morgagni hernia being rare is often not diagnosed. The lack of proper diagnosis can lead to dreadful consequences such as strangulation of the hernia contents. It is determined that computed tomography of thorax and upper abdomen are the best methods for diagnosis with a surgical approach being the best option for repair.

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REVIEW ARTICLE

Molecular Epidemiology of Hepatitis B Virus in Pakistan: Link with Southern Asia

Saeeda Baig¹**ABSTRACT**

Viruses and their genotypes reflect the relationship of their hosts. How these strains evolve, is one question and how they cross the borders is another. Since the HBV genotypes have been described by Okamoto and colleagues in 1988, Hepatitis B virus is expressed by a classification of different HBV strains into genetic genotypes and sub-genotypes. A degree of 8% divergence between the groups has since then become the definition for HBV genotype. Now HBV is known by its geographic genotype and sub-genotype distribution. They also exhibit combination of both separately or in the form of a hybrid and hybrid of HBV genotypes is a common event in countries where movement of people is frequent across the borders, thus, providing a mixture of variation within individuals and in the population in general. It is seen that if travelling is by road then the different genotypes are prevalent around the borders, but if travelling is by air then they exist in general population as a less prevalent genotype. This review highlights the genotypic link between Pakistan and its South Asian neighbors.

KEY WORDS: *Hepatitis B Virus, Genetics, Genotypes.*

INTRODUCTION

Several scientific fields such as archaeology, anthropology and linguistics were used previously for the study of human migration. In the recent years, genetics has opened up new avenues and routes of human movement through study of mitochondria, viruses, Y chromosome and DNA sequence analysis.¹¹ Consequently, evaluation of nucleotide sequences showing their genotypes and sub-genotypes determine how much of their evolution can be reconstructed. HBV, especially changes form every time it crosses borders. These are ornamental changes which are part of the HBV armor associated with immunity and genome size, related to HBV genotypes.

Worldwide a strong correlation has been reported between HBV genotype and ethnicity since the genotypes have been described by Okamoto and colleagues in 1988.² HBV strains found worldwide differ having more than 8% genetic variability and eight HBV genotypes namely A, B, C, D, E, F, G, and H have been established on this basis.^{3,4} Advances in phylogenetics has further resulted in recognition of subgenotypes of HBV genotypes based on more than 4% intra-genotypic divergence. Until now, the presence of 5 subgenotypes have been recognized for each of the HBV genotypes A, B, C and D, while 4 subgenotypes have been well reported for genotype F.⁵⁻⁷

In South East Asia the most prevalent genotype of hepatitis B virus is D. This review highlights the genotypic link between Pakistan and its South Asian neighbors. (Figure 1)

DISCUSSION

In Asia, initially, research on genotyping of HBV was conducted extensively in Japan and China, therefore, B and C the genotypes of these countries were considered as the most prevalent genotypes of Asia. Later on, it was found that all the seven HBV genotypes can be found in Asia⁶, with predominance of D in South East Asia. Majority of South Asian countries where HBV genetics studies have been done genotype D has been found as predominant, whereas, the less prevalent genotype depends on the

predominant genotype of the neighboring country. Thus HBV isolates sequences have shown that genotype D is predominant in India⁸, Afghanistan⁹, Iran.^{10,11} Likewise, a similar pattern of genotype prevails in Pakistan with genotype D being the most prevalent.¹² Genotype D particularly happens to be the most widely distributed genotype and has been found scattered universally on the globe. However, the highest prevalence is in the belt stretching from Southern Europe and North Africa to India. Similarly Western and Southern Africa are of concern. Within the populations affected it has been noted that the intravenous drug users are the ones that fall prey to this genotype.¹³⁻¹⁵

HBV Genotypes of Pakistan

In Pakistan, multiple studies based on various population groups have been conducted to find out the prevalence of HBV infection.¹⁶⁻¹⁸ All such studies present a varying rate of infection based on the study design, population selected, diagnostic assays and demographical and epidemiological variation. These study groups report HBV prevalence rate as 2–10% among healthy blood donors; 5–9% among health care personnel, 3.6–18.66% among the general population, 3.16% among the pregnant women, 10–20% in patients with provisional diagnosis of hepatitis and 3.16–10.4% among professional blood donors.¹⁸

HBV Genotypic Link with Neighbors**India:**

Pakistan shares 2900 km of border with India. Population of Pakistan is ethnically and linguistically connected to India because of the several waves of migration from India to Pakistan. After partition in 1947 the immigrants settled in various parts of the country. Studies from India have generally reported predominance of genotype D coexisting with A and AD in lesser percentages. Hence a similar pattern is being seen in Pakistan. The appearance of genotype A has been linked to the migration from Europe over the time.¹⁹ Since such migration was more prevalent in the Western and Northern states of Colonial India than in the Eastern region, this may well explain the rarity of genotype A in Eastern India as well as in Pakistani population. Further this has been

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confirmed by genetic studies from India involving mitochondrial DNA and Y chromosome.²⁰ Genotype C is also present in the populations of both countries. Genotype B has been reported from Pakistan but not from India although both B and C are the dominant genotypes reported in studies from South-East Asia and the Far East.^{21, 22}

Bangladesh:

Bangladesh had been part of Pakistan from 1947 to 1971 and was known as East Pakistan. In Bangladesh, the predominant genotype is D (50%)²³ as that of rest of the subcontinent.²⁴ But Bangladesh also has C 37.5%, mixed C+D 7.5% and A and B each 2.5%.²⁵ Genotype A is present in a small percentage of population in the same way as in Pakistan and India. Since Bangladesh was also part of Indian subcontinent therefore, it exhibits the same pattern. The high prevalence of genotype C in the Bangladeshi population can be explained by their borders facing towards Far East and South-east Asia.²⁶ The Bangladeshis have had migratory links with the Mongolian ethnic group, hence a mixture of genotypes C and D is present. This is the only explanation available for the prevalence of genotype C is prevalent here, while elsewhere in the rest of Southeast Asia it is prevalence of D is more dominant. The reason for the presence of Genotype B in Bangladesh, as well as in Pakistan²⁷, is difficult to explain given that it has been designated as genotype characteristic of the Far East.²⁸

Middle East:

HBV gene sequences analysis of these countries are consistent with Pakistan and show that HBV genotype D subtype *ayw2* is the most dominant.^{29,30} Thousands of Pakistanis are residing in the Middle East for employment reasons. The majority of the countries which harbor Pakistani immigrants are UAE, Saudi Arabia, Qatar and Iran.

Iran:

Studies from Iran, another border sharing neighbor, show predominance of genotype D. Iran shares 912 km of border with Pakistan. Pilgrims in groups from Pakistan visit various holy places in Iran. Studies from Iran confirm

that only genotype D exists in different regions of Iran.³¹⁻³³ Iran had also been a victim of influx of immigrants from neighboring countries which allows a potential introduction of other genotypes showing a mixed genotypic pattern in the general population. But phylogenetics in a recent study showed all isolates were clustering in a distinct branch of genotype D.³⁴ This probably can be explained on the basis that genotypic exposure was only limited to genotype D, whether they were refugees from Afghanistan or pilgrims from Pakistan.

Saudi Arabia:

Saudi Arabia has a very special place in Muslim world. Hundreds and thousands of Muslims visit holy places as pilgrims from all around the globe. Being a resource rich country thousands of migrants reside in Saudi Arabia for employment including Bangladeshis, Indians, and Pakistanis etc. From Pakistan every year millions visit the holy places as religious pilgrims. Majority of the pilgrims travel to the holy cities of Mecca and Medina, while the rest are scattered all over Saudi Arabia, especially in regions close to universities and medical colleges. If we look at Hepatitis B genotype in Saudis, it is a reflection of crowd that gathers. The Saudi study³⁵ on HBV shows that the majority of patients (64%) acquired HBV through unknown risk factors. Hepatitis B genotyping in patients revealed that major genotype is D (81.4%), whereas, other genotypes and their mixture are present in small percentages; A - 1.4%, C-1.4% and E- 5.7%. Also 10% had mixed genotype ADG, DE, DF and ADFG. This study needs to be further verified through bigger sample size.

Figure 1: graphic representation of genotypes distribution in Pakistan and neighboring countries.



Afghanistan:

Afghanistan shares 2640 km of border with Pakistan. The geographical terrain is difficult to maneuver around, much of this being quite mountainous, making crossing the border only practical through the numerous passes in the mountains. Yet border crossings are very common, which largely remain unchecked or uncontrolled. The prevalence of chronic HBV infection in Afghanistan was reported as 6.7% in 2003. The prevalence of HBsAg among Afghan refugees residing in camps in Balochistan, Pakistan was reported to be 8.3% in 2003 (WHO- UNICEF 2005). The predominant HBV genotype in Afghanistan was found to be genotype D having 95% bootstrap value on phylogenetics analysis.³⁶ Afghanistan is one place where people have been internally and externally displaced conferring higher chances of infected population of HBV and other viruses. Prevalence of Genotype D of HBV shows that mixing of strains is within the population.

China:

The genotype distribution of HBV in China is most interesting. China lies in the north of Pakistan and India. China shares 510 km with Pakistan, and trade ventures between Pakistan and China are through the Khunjerab pass 16002 feet in the Karakoram Mountains connecting Pakistan's Gilgit-Baltistan Hunza - with the southwest border of the Xinjiang region of China. The most common genotype of northern China is C, southern is B³⁷, whereas, in western China genotype D is found. Since China is an enormous country national travel is a normal phenomena and HBV recombinant viruses have been identified which are C/D recombinant hybrids.³⁸ Keeping in mind the geographical location of the China-Pakistan border, the area surrounding is related to the northern part of China, hence genotype C is prevalent in the adjoining part of Pakistan.³⁹

CONCLUSION

Researchers in general agree that the prevalence of HBV genotypes throughout the world is clearly linked to trade and migration. Hepatitis B genotype D is the most prevalent genotype worldwide but its epidemiological tracking history is still not very clear. Zehender et al⁴⁰ has done Phylogeographical analysis of HBV genotype D by reconstructing the epidemiological history of HBV-D genotype through phylodynamically and phylogeographical studies. Their study shows that Indian sub-continent had the highest posterior probability to be the location of the tree root of genotype D which suggests that the India was the place in which HBV-D originated. As a result of frequent exchanges with neighbors this genotype penetrated into neighboring areas.

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STUDENTS' CORNER

Majority of the Population Disregards Obesity as a Health Risk: Obesity among different Socioeconomic Strata in Karachi - A Hospital Case study

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ABSTRACT

Background: Obesity is a chronic disease which requires aggressive management. Obesity, although not a direct cause of most diseases, unfavorably alters the risk factor profile. It may lead to high blood pressures and high cholesterol levels, which can result in cardiovascular diseases or strokes. In addition to these diseases, the quality of life is also severely impaired. Successful treatment of obesity not only alleviates the associated medical problems, but also improves the quality of life dramatically.

Objectives: To observe and compare obesity, its perception and complications among different socioeconomic classes in Karachi.

Methods: A predesigned questionnaire was filled out at two hospitals of Karachi for a sample representing patients from lower and higher socioeconomic strata. BMI of these patients was calculated and assessed with respect to their income, education level and occupation, eating patterns, frequency of exercise. The presence of associated non-communicable diseases like hypertension and diabetes mellitus was also recorded. Data was analyzed using SPSS software.

Results: The patients' population comprised 31 males and 19 females. The mean age was 45.56 (SD ± 12.08). Minimum age was 15 years, while maximum was 75 years. Pathological analysis revealed that majority of SCC cases were moderately differentiated, SCC with clinical stage T2 or T3, N0,M0/N1,M0. Most common oral sites came out to be buccal mucosa of cheeks followed by lateral borders of tongue and lips. All patients underwent primary resection ± neck dissection and reconstruction when necessary.

Conclusion: Obesity was observed in all classes irrespective of the education, income and occupation of the respondents with sedentary lifestyle being the main causal factor. There exists lack of awareness of the harmful consequences of obesity

KEY WORDS: BMI, Obesity, Morbid Obesity.

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INTRODUCTION

The common perception in our part of the world is that obesity is characteristic for the developed countries. Recent results have revealed an alarming rise in the incidence of obesity globally including in the developing world. Considered to be more threatening than smoking¹ a 2001 WHO report reveals obesity has reached epidemic proportions globally, with more than 1 billion adults overweight and at least 300 million of them clinically obese. It has become a major contributor to the global burden of chronic disease and disability. Often coexisting in developing countries with under-nutrition, obesity is considered by experts to be a complex condition, with serious social and psychological dimensions, effecting virtually all ages and socioeconomic groups.²

Decreased physical activity and overconsumption of cheap, energy-dense food have led to globally increasing incidence of obesity with tripled rates in the last 20 years. The prevalence of overweight among them children has increased from 10% to 25% with the prevalence of obesity ranging from 2% to 10%. The Middle East, Pacific Islands, Southeast Asia, and China face the greatest threat.³ Data from the National Health Survey of Pakistan for 1990-1994 revealed prevalence of obesity (BMI > or = 27) in 25-44 year olds in rural areas (9% males, 14% females) and in urban areas (22% males, 37% females) respectively. For 45-64 year olds, prevalence was higher (11% males, 19% females) in rural areas and (23% males, 40% females) in urban areas respectively.⁴

The rapid increase in the prevalence of obesity suggests a trend that is largely due to social, environmental and behavioral changes rather than changes in hereditary factors.^{5,6} Obesity results from an imbalance between caloric input and its expenditure. Nutrition plays a direct role in caloric balance, being the sole factor responsible for calorie intake while calorie expenditure is dependent on specific variables of physical activity, basal metabolic rate and the thermogenic effect of food.^{7,8} Recent evidence, from Western countries, suggests that sedentary activities, such as watching television or using a

computer, are associated with increasing obesity, independent of purposeful physical activity.^{9,10}

The relationship between obesity and socioeconomic factors, though complex, has been demonstrated in different populations. Low income and low education may be associated with obesity and obesity related co-morbidities.¹¹ Some developing countries face the paradox of families in which the children are underweight and the adults are overweight. This combination has been attributed by some people to intrauterine growth retardation that results in low birth weight apparently predisposing to obesity later in life through the acquisition of a "thrifty" phenotype.¹² The "thrifty phenotype" hypothesis proposes that as an adaptation to malnutrition in fetal life, permanent metabolic and endocrine changes occur which would be beneficial if nutrition remained scarce. However, if nutrition becomes abundant, these changes predispose to obesity and impaired glucose tolerance and an increased susceptibility to cardiovascular disease. The "thrifty phenotype" hypothesis proposes that as an adaptation to malnutrition in fetal life, permanent metabolic and endocrine changes occur which would be beneficial if nutrition remained scarce. The etiology of obesity in the low socioeconomic strata is believed to be multi-factorial. Physical activity, nutrition and certain psychosocial factors like self-esteem, depression and body image are some of the elements associated with risk of obesity in the low socioeconomic class. People of lower socioeconomic status are less health conscious and have stronger beliefs in the influence of chance on health. This in turn is associated with unhealthy behavioral choices.¹³

METHODOLOGY

A descriptive cross sectional study was conducted in a public and a private sector hospital over a period of two months from July 1, 2012 to August 31, 2012. Sample size was calculated to be 114 with CI 97%, precision at 5% & prevalence at 8%. Wastage was added and the sample size was inflated to increase validity of the study. A total of 125 adults between the ages of 18-60 years were included employing convenience sampling. Pregnant women, mentally challenged patients & non-

cooperative patients were excluded from the sample.

Weight and height of patients were measured using height scale/measuring tape and calibrated weighing scale at the two hospitals. Height was recorded in meters and weight in kilograms with BMI calculated by using the formula $\text{weight}/\text{height}^2$. Socioeconomic status was measured in terms of overall family income, occupation and education level. Respondents were categorized according to WHO's classification of Body Mass Index (BMI) based on their weight and height.

Table 1:WHO Classification of BMI and Categories

BMI Range	Category
BMI of 25-30kg/m ²	Overweight
B BMI between 30-35kg/m ²	Obese
BMI >35kg/m ²	Morbidly Obese

A predesigned questionnaire was the data collection instrument. The questionnaires were filled out by interview and translated to Urdu for patients who did not understand English. Data was entered and analyzed using SPSS version 17. All quantitative variables were presented as mean and standard deviation and all qualitative variables as percentages and frequencies. Chi-
Table 2:Cross Tabulations

	Overweight	Obese	Morbidly Obese	P value
Gender				
Male	26.4	12.8	8	0.201
Female	21.6	21.6	9.6	
Monthly Income				
PKR 10,000-19999	11.2	2.4	3.2	0.294
PKR 20,000-49,999	4	0	0.8	
PKR 50,000-74,999	4	0.8	1.6	
PKR 75,000-99,999	4	4.8	0.8	
PKR 100,000-149,999	4	3.2	1.6	
PKR 150,000 and above	0.8	0.8	0	
Marital status				
Single	16	10.4	1.6	0.088
Married	32	24	16	
Education Level				
Uneducated	19.8	9.1	5.8	0.758
Primary	0.8	0.8	0	
Matriculate	2.5	1.7	0	
Intermediate	3.3	5	3.3	
Bachelors	13.2	9.9	4.1	
Masters	8.3	9.1	3.3	
Occupation				
House-maker	12.8	14.4	7.2	0.458
Banker	6.4	4	0.8	

square test of significance was applied and p-value <0.05 was considered as significant. The limitations presented for this study pertain to the small sample size of 125 respondents which is small to draw definitive conclusions. The samples were also limited to only two hospitals which restricts generalization or results.

RESULTS

A total 125 questionnaires were filled out at two hospitals. Table 2 shoes distribution of respondents according to their BMI

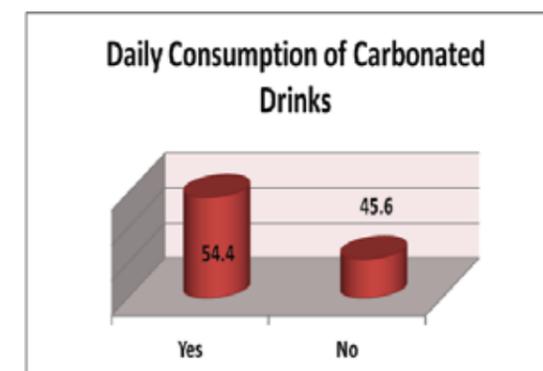
Table 2: BMI Distribution of Respondents

BMI	n	%
Overweight (25-30)	60	48.0
Obese (30-35)	43	34.4
Morbidly Obese(>35)	22	17.6

Cross tabulations were used with BMI as the independent variable. The association of BMI was assessed with different variables like gender, monthly income, marital status, education level, occupation, family history of obesity, associated co-morbidities and the frequency of physical exercise.

Driver	3.2	1.6	2.4	
Family History				
Yes	18.4	9.6	20	0.111
No	29.6	14.4	8	
Frequency of Exercise				
Nil				0.047
Twice a week	41.94	28.23	10.48	
Three times or more	3.23	4.03	3.23	
	2.42	2.42	4.03	
Associated co morbidities				
None				0.127
Hypertension	28	16.8	5.6	
Diabetes mellitus	8.8	8	6.4	
Asthma	10.4	4.8	4	
Joint pains	0	3.2	1.6	
	0.8	1.6	0	

The respondents were asked about identified factors directly related to obesity. The results provided 81.6% of the respondents confirmed of snacking between their meals while 18.4%



refrained from eating between meals. 54.4% of the respondents consumed carbonated drinks every day while 45.6% did not drink carbonated drinks every day.

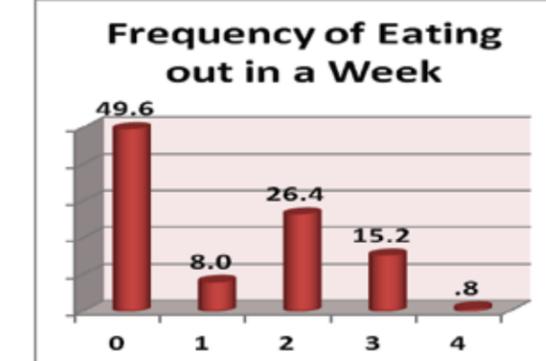
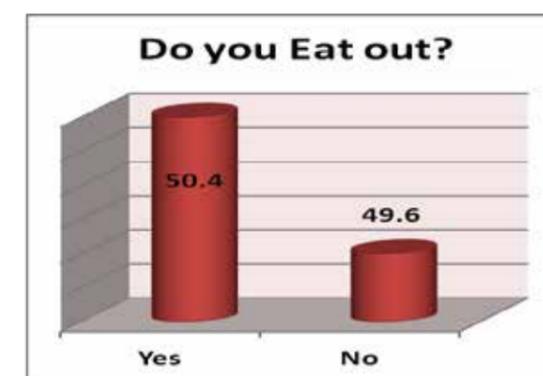


Table 3:Frequency

Frequency of Weekly Exercise		
BMI Range	n	%
No Exercise	100	80
Twice	13	10.4
More	12	9.6
Want to Lose Weight		
BMI Range	n	%
Yes	41	32.6
No	84	67.4



DISCUSSION

There is a significant percentage of obesity in all classes irrespective of the socioeconomic stratification. This finding was not consistent with Nanan's report that obesity was directly associated with socioeconomic status with more

prevalent in urban areas with increasing income as compare to rural areas.⁴

The study showed increase in obesity in the uneducated category while less number of obese in the graduate & postgraduate category. This was consistent with the study of AJ Stunkard in 1993 where obesity and lack of

education were positively associated.¹⁴ An alarming 56% of the study population did not consider obesity a hazard to health. Only 33% of the respondents wanted to lose weight while 67% were not keen to lose weight. This again suggested a lack of awareness regarding the ill effects of obesity, resulting from poor education.

The study showed fifty percent association of co morbidities with excess weight, consistent with the study *"The relation of gender, race and socioeconomic status to obesity and obesity co morbidities in a sample of US adults. International Journal of Obesity (2002)"* depicting a graded increase in diabetes, hypertension and high serum cholesterol with increasing body weight in nearly all gender, racial and socioeconomic groups. The results of this study suggested a substantial disease burden associated with obesity and this burden increases with increasing severity of obesity.¹⁵

The study showed a strong relationship between obesity & positive family history of obesity, as respondents having positive family history were found to be more obese. National Health & Nutrition Examination Survey III reported similar findings that prevalence of obesity (BMI=30) is twice as high in families of obese individuals than in the population at large.¹⁶

Another important finding was the lack of physical activity in the study population. overweight (41.94%), obese (28.23%) and morbidly obese (10.48%) respondents did not exercise even once a week. Exercise twice a week was indulged by overweight (3.23%), obese (4.03%) and morbidly obese (3.23%) respondents exercised. Few exercised three or more times a week overweight (2.42%), obese (2.42%) and morbidly obese (4.03%). This was consistent with findings reported in other studies^{17,18,19} where physical activity was shown to induce health related benefits and was the most beneficial prevention practice for losing and successfully maintaining weight. A study by La Torre et al²⁰ showed that boys and girls of higher socioeconomic status were more likely to participate in extra-curricular physical activities.

CONCLUSION

Females tend to be more obese irrespective of the socioeconomic status with married

respondents more overweight compared to their single counterparts. Although high socioeconomic status has an increased incidence of obesity, it is also observed groups of socioeconomic status. Lower socioeconomic status has been associated with less health consciousness i.e. doing things to keep one healthy, stronger beliefs in the influence of chance on health and lower life expectancies. These attitudinal factors have been implicated in unhealthy behavioral choices.²¹ Obesity was found to have a positive association with co-morbidities. This translates into an increased burden of diseases and an economic drain on the country due to the costs incurred in treating these conditions. In 2004 in the Pacific Islands, the economic consequences of non-communicable diseases, mainly obesity and diabetes mellitus amounted to \$1.95 million-almost 60% of the health care budget of Tonga.² There was generally a low awareness towards importance of physical activity. Increased sedentary behaviors and lower levels of physical activity are evident in lower segments of socioeconomic society around the world¹⁹ Education levels are positively associated with health knowledge and leisure time physical activity and higher education levels have been shown to increase physical activity participation and other healthy behaviors.²²

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