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Editorial

Anemia and Raised Cholesterol Level Increases Alzheimer's Risk

Mohsin Masud Jan
Editor

There are currently an estimated 24 million people in the world with dementia. Two thirds of these live in developing countries. Dementia is a progressive degenerative brain syndrome which affects memory, thinking, behavior and emotions. Alzheimer's disease is the most common cause of dementia.

Declining memory, especially the short-term memory, is the most common early symptom of dementia. Other symptoms include difficulty in performing familiar tasks; disorientation to time and place; poor or decreased judgment; and changes in personality. Dementia is not a normal part of ageing. Age is an important risk factor but not the only one. Dementia affects 5% over the age of 65 and 20 % over the age of 80.

This alarming figure is expected to rise dramatically to 81 million by the year 2040, as the life expectancy increases. In Pakistan alone, one million people are estimated to be suffering from dementia and with the increase in life expectancy; these figures will shoot up as well.

Older adults suffering from anemia — lower than normal red blood cell levels — may be at increased risk for dementia, a new study suggests.

Anemia affects as many as 23 percent of seniors, the researchers say. "We found a 60 percent increased risk of dementia with anemia. After controlling for other factors such as other medical illness, demographics, etcetera, the risk remained elevated 40 to 50 percent," said lead study author Dr. Kristine Yaffe, a professor of psychiatry, neurology and epidemiology at the University of California, San Francisco. "Given how common both anemia and dementia are in older adults, more attention to the connection between the two is important. The study of more than 2,500 men and women in their 70s doesn't actually prove that anemia causes dementia, however.

"Because we studied this prospectively, we do think, as best we can tell, that anemia is casually related to dementia, but with observational studies one can never say for sure. But we did our best to exclude other explanations," Yaffe said. The job of red blood cells is to carry oxygen throughout the body. When you are anemic, less oxygen is delivered to brain cells, Yaffe explained. "We think the association is about low oxygen being carried to the brain," she said. Anemia could also indicate poor overall health, the study authors noted. Causes of anemia include iron deficiency and blood loss. Cancer, kidney failure and certain chronic diseases can also lead to anemia.

The study — published online July 31 in Neurology — should remind doctors that many conditions can lead to dementia, and treating them might ward off mental decline, one expert said. "One concern about the increased visibility and prevalence of Alzheimer's disease is that some physicians will be tempted to jump straight to that diagnosis without first having followed the 'rule out reversible causes' rule," said Dr. Sam Gandy, director of the Mount Sinai Center for Cognitive Health in New York City. Alzheimer's disease is the most common form of dementia. "We must always seek to exclude treatable, reversible causes of dementia such as depression, nutritional deficiencies, endocrine disorders and metabolic disorders before rushing into a diagnosis of Alzheimer's," he said.

During the study, all of the participants were tested for anemia and took memory and thinking tests over 11 years. Almost 400 participants were anemic at the study's start. Over the course of the study, about 18 percent of participants — 455 — developed dementia, the researchers found. Of participants with anemia, 23 percent developed dementia, compared with 17 percent of those who weren't anemic. People who were anemic at the study's start had a 41 percent higher risk of developing dementia than those without anemia after the researchers took into account factors such as age, race, sex and education. Additional research is needed to confirm this association before recommendations are made regarding dementia prevention, the study authors suggested.

A study from the University of California, Davis, found that low levels of "bad" (LDL) cholesterol and high levels of "good" (HDL) cholesterol are linked to lower levels of so-called amyloid plaque in the brain. A build-up of this plaque is an indication of Alzheimer's disease, the researchers said in a university news release.

The researchers suggested that maintaining healthy cholesterol levels is just as important for brain health as controlling blood pressure. "Our study shows that both higher levels of HDL and lower levels of LDL cholesterol in the bloodstream are associated with lower levels of amyloid plaque deposits in the brain," the study's lead author, Bruce Reed, associate director of the UC Davis Alzheimer's Disease Center, said in the news release.

"Unhealthy patterns of cholesterol could be directly causing the higher levels of amyloid known to contribute to Alzheimer's, in the same way that such patterns promote heart disease," Reed said. The study, which was published in the Dec. 30 online edition of the journal JAMA Neurology, involved 74 men and women recruited from California stroke clinics, support groups, senior-citizen facilities and the UC Davis Alzheimer's Disease Center. All of the participants were aged 70 or older. Of this group, three people had mild dementia, 33 had no problems with brain function and 38 had mild impairment of their brain function.

The investigators used brain scans to measure the participants' amyloid levels. The study revealed that higher fasting levels of LDL cholesterol and lower levels of HDL cholesterol both were associated with more accumulation of amyloid plaque in the brain. Exactly how cholesterol affects amyloid deposits in the brain remains unclear, however, the researchers said.

In the United States, cholesterol is measured in milligrams of cholesterol per deciliter of blood, or mg/dL. HDL cholesterol should be 60 mg/dL or higher, the researchers said in the news release. LDL cholesterol should be 70 mg/dL or lower for those at very high risk for heart disease. Reed and his colleagues said it's important to maintain healthy cholesterol levels in those who are showing signs of memory problems or dementia, regardless of their heart health.

"This study provides a reason to certainly continue cholesterol treatment in people who are developing memory loss regardless of concerns regarding their cardiovascular health," said Reed, who also is a professor in the UC Davis department of neurology. "It also suggests a method of lowering amyloid levels in people who are middle-aged, when such build-up is just starting," Reed said in the news release.

Original Article

Reliability of Cast Index for Dental Caries Detection

Dental Caries

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ABSTRACT

Objective: To access the inter-examiner reliability of CAST (Caries Assessment Spectrum and Treatment) index for detecting dental caries status among patients visiting a public sector dental hospital of Karachi, Pakistan.

Study Design: Cross sectional study.

Place and Duration of Study: This study was conducted in the dental diagnostic outpatient department of a public sector dental hospital, Karachi, Pakistan, over a period of one month from September 2013 to October 2013

Materials and Methods: Selected/consented participants were examined for dental caries status by the two trained and calibrated examiners using CAST index. A structured and validated proforma was used to record the findings. The inter-examiner reliability was undertaken to find out the reproducibility of this novel method of caries examination. Data entry and analysis was done using SPSS software at 5% level of significance. Descriptive statistics were performed that involved the frequencies of age and gender. Inter-examiner reliability of CAST was assessed using percentage agreement and Cohen's Kappa value.

Results: A total of 100 subjects were recruited for the present study. There were 63% females and 37% males with a mean age of 31±17 years. The percentage agreements obtained for the two examiners were between 70-100% for 9 different codes of the CAST index. The Cohen's Kappa value identified was 0.99.

Conclusion: A strong inter-examiner reliability has been observed for scoring the CAST index which exemplifies the entire patho-physiological phases of dental caries. Results of this study substantiate the potential of CAST index for reproducibly scoring the enamel, dentine and pulp lesions.

Key Words: Dental Caries, Primary Prevention, Reproducibility of Results.

INTRODUCTION

In order to control the caries development by the execution of various caries-preventive strategies, diagnosis of the preliminary stages of dental caries is imperative and entails reliable and validated tools that can recognize the various stages of enamel carious lesions; both the cavitated and non-cavitated stages[1].

Dental caries has been evidently established as a multifactorial and highly preventable[2] oral disease that marks clinically as a path from preliminary visual change in enamel to frank cavitation. White spot enamel lesion is the foremost visible sign of dental caries that can be reversed and arrested through recommended preventive measures from being changed into a cavitated lesion[3, 4].

DMFT (decayed missing and filled teeth) index has been established almost eighty years ago and still it is used as an effective tool to measure the dental caries status[5]. However, after an exceptional change that took place in the history of preventive dentistry which shifted the paradigm from curative to preventive dentistry[6], critical questions raised against DMFT index. This was because of the incapability of this index to measure the early enamel and dentinal lesions and therefore may not be applied in low dental caries communities[7].

In this context inventiveness began in order to develop an index that records the diverse spectrum and all the patho-physiological stages of dental caries[8]. ICDAS (International Caries Detection and Assessment System) was introduced ten years back and demonstrated the potential to record the carious status from most primitive visual change to frank cavitation. But, ICDAS also presented with certain limitations such as complex recording standards, non-compatibility with DMF/S, difficult outcome measure elucidations, non-differentiated criteria for measuring dental caries in primary and secondary dentition and incapability to document the complications of dental caries involving pulp and surrounding tissues[9,10]. In developing countries, cavitated teeth are not being treated for diverse reasons[11], but when in 2010, PUFA/pufa (Pulpal involvement, Ulceration, Fistula, Abscess) index was reported it claim to measure the later infectious stages of dental caries ahead of the pulpal involvement and depicted the burden of untreated carious lesions. However, this index can only be complementarily applicable with other caries detection indices[10, 12].

In this state of affairs, CAST (Caries Assessment Spectrum and Treatment) index was evolved in 2011. This index demonstrated the strengths of ICDAS, PUFA and DMF/S. CAST index has a simple,

convenient and reliable 9 digit coding system which demonstrates the complete spectrum of dental caries[10]. The face and content validity of CAST has already been reported and a monograph has published[13], but, this novel index can only be recommended for use in epidemiological world, when its reliability and validity will be tested across the globe. Therefore, the present study was planned to access the inter-examiner reliability of CAST index, for detecting dental caries among patients visiting a public sector dental hospital of Karachi, Pakistan.

MATERIALS AND METHODS

This Cross sectional study was conducted in the dental diagnostic outpatient department of a public sector dental hospital, Karachi, Pakistan, over a period of one month from September 2013 to October 2013. Informed verbal consent was obtained from all the participants. Subjects with any systemic or oral disease, dental prosthesis, poor manual dexterity, absence of any indexed teeth and non consenting cases were excluded from the study. The two trained and calibrated examiners (AM, MM) performed the dental examination using a mouth mirror and a probe on cleaned and dry tooth surfaces. The novel caries assessment index; CAST was employed to record the dental caries status of all the selected participants. A structured and validated proforma including the demographic details and dental chart (for primary and secondary dentition) was used to record the findings.

Inter-examiner reliability in evaluating the sound teeth, sealants, restorations and carious lesions affecting enamel, dentine and pulp in both primary and permanent dentitions, was clinically determined. This was undertaken to find out the reproducibility of this novel method of caries examination.

Data was entered and analyzed using Statistical Package for Social Science (SPSS) version 16. The 'P' value was assigned at 5% and the power of the test was kept at 80%. Descriptive statistics were performed that involved the frequencies of age and gender. Inter-examiner reliability of CAST index was assessed using percentage agreement and Cohen's Kappa value. Kappa values above 0.75 signified excellent agreement, while values between 0.40 and 0.75 signified good agreement[14].

RESULTS

A total of 100 subjects were recruited for the present study. There were 63% females and 37% males with a mean age of 31±17 years and a range of 65 years. The percentage agreements obtained for the two examiners were between 70-100% for different codes (0-9) of the CAST index (table 1). The Cohen's Kappa value identified was 0.99.

Table No.1: CAST Codes and Inter-Examiner Percentage Agreements

CAST Codes	Code Descriptions	Percentage Agreements
0	Sound	100%
1	Sealed	80%
2	Restored	80%
3	Distinct visual change in enamel	90%
4	Internal caries-related discoloration in dentine	90%
5	Distinct cavitation into dentine	70%
6	Involvement pulp chamber	70%
7	Abscess / Fistula	70%
8	Lost	100%
9	Does not match with any of the other categories	100%
A	Absent	100%

Table No.2: The Codes and Description of CAST.

Codes	Charac-teristic	Description
0	**Tooth**	Sound. No visible evidence of a carious lesion is present
1	**Sealed**	Sealed. Pits and Fissures have been at least partially covered with a sealant material
2	**Restored**	Restored. A cavity has been restored with an (in)direct restorative material, currently without a dentine carious lesion and no fistula/abscess present
3	**Enamel**	Distinct visual change in enamel A clear carious related discoloration (white or brown in color) is visible, including localized enamel breakdown without clinical visual signs of dentinal involvement
4	**Dentine**	Internal caries-related discoloration in dentine The lesion appears as shadows of discolored dentin visible through enamel which may or may not exhibit a visible localized breakdown
5	**Dentine**	Distinct cavitation into dentine. No (expected) pulpal involvement is present
6	**Pulp**	Involvement of pulp chamber Distinct cavitation reaching the pulp chamber or only root fragments are present
7	**Pulp**	Abscess /Fistula. A pus containing swelling or a pus releasing sinus tract related to a tooth with pulpal involvement is present
8	**Lost**	The tooth has been removed because of dental caries
9	**Other**	Does not match with any of the other categories
A	**Absent**	The tooth has not been erupted

DISCUSSION

So far very limited data is available that can recommend the use of this newly developed pragmatic index, CAST in dental epidemiology, therefore this study was undertaken to evaluate the reliability of CAST index for identifying and recording the whole progressive spectrum of dental caries. This is one of the first epidemiology studies on CAST, which has revealed the inter-examiner reliability of this index.

The two examiners (AM, MM) were trained, calibrated and supervised by an experienced epidemiologist trained from Department of Global Oral Health, College of Dental Sciences, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. Examiners undergone theoretical training for using CAST index, summary of the codes and criteria are shown in Table 2. The training involved recording of the index on individual subjects by the two examiners, followed by discussion sessions. This training process continued on different subjects until the two examiners consistently scored the same value of each tooth surface, achieving at least a 90% agreement for the whole mouth.

Even being a latest analytical tool employed to assess dental caries, CAST index has given a strong inter-examiner reliability in this study. The overall Cohen's kappa value found in this study was 0.99, which suggest an excellent agreement between the two observers. On the basis of these results CAST index can be proposed to have the potential for reproducibly scoring enamel, dentine and pulp lesions. In contrast, the reported kappa values are 0.51 and 0.86 for ICDAS and DMFT indices, respectively[15, 16], whereas it was found to be 88% for another developing index for dental caries detection, the Nyvad's new caries diagnostic criteria[1].

Also this was not an unexpected finding while recording CAST scores, that 100% agreement was observed on codes 0, 8, 9 and A (sound and missing teeth). However, 90% agreement on code 3 & 4 (enamel and dentine lesion) was highly substantial and recognition should be given to the training and calibrating team of department of community and preventive dentistry, DIKIOHS, DUHS. Results demonstrated that 80 and 70% similarity was observed for restorative status (code 1 & 2) and later consequences of dental caries (code 6, 7 & 8) respectively.

CAST index has laid down the foundation to identify the pathogenesis of dental caries including the basic reversible and avertable stages of this pandemic disease. This is imperative to figure out in order to improve the oral health status especially in developing countries like Pakistan where 70% of the total population living in rural areas[17], cannot afford an extra burden of treating dental diseases, specifically caries which has been recognized as forth expensive disease to get treated[18].

The likelihood that some proportion of examiners agreement can occur by chance is a recognized limitation[19, 20], and this study is not an exception.

CONCLUSION

A strong inter-examiner reliability has been observed for scoring the simple but structured and pragmatic CAST index which exemplifies the entire patho-physiological phases of dental caries. Results of this study substantiate the potential of CAST index for reproducibly scoring the enamel, dentine and pulp lesions. However, there is a need for more research on this unexplored endeavor.

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Original Article

Frequency of Hepatitis C in General Surgical Patients at Teaching Hospital Khairpur Sindh

Hepatitis C

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ABSTRACT

Background: Viral hepatitis is a global issue. Hepatitis C virus is worldwide public health problem. This is related to the continued occurrence of new infections and the presence of a large reservoir of chronically infected population.

Objective: To observe the frequency of Hepatitis C virus (HCV) infection and find out the risk factors in general surgical patients.

Study Design: Prospective Observational type.

Place and Duration of Study: This study was carried out in the Surgical Department of Ghulam Muhammad Mahar Medical College Teaching Hospital KhairPur Sindh during one year period from May 2012 to April 2013.

Materials and Method: All patients admitted in surgical department either for emergency or elective surgery was included in the study. All patients were screened for HbSAg and Anti-HCV by using immumochromatography (ICT) method. The data of sero-positive patients for hepatitis C were taken for further study. The data was collected through pre- designed Performa and analyzed through SPSS version 15.

Results: Total 1030 patients were admitted in surgical department for emergency or elective surgery. During screening Anti-HCV +ve was found in 165(16.0%) patients. Out of these, 95(9.2%) were male and 70 (6.7%) were female. Mean age of these patients was 40.7 years. Among positive patients, most belongs to rural area with poor socioeconomic status. Multiple injections by quacks, shaving by barbers, history of blood transfusion, previous surgery were found to be risk factors in male, while in female history of Gynae and obstetrics procedure, partner +ve for HCV, blood transfusion were found main risk factor. No any risk factor was found in 20 (12.1%) male and 35 (21.2%) females.

Conclusion: In the absence of any vaccine for Hepatitis C virus, emphasis should be made on health education and about the risk factors for virus transmission. Health care providers must be committed in the formulation of policies and strict adherence to the safe practices.

Key Words: Hepatitis C, risk factor, surgical procedure, prevention.

INTRODUCTION

Viral hepatitis is a major health problem affecting approximately two billion populations worldwide. Current data shows that about 160 million people worldwide are infected with hepatitis C virus.[1] with the prevalence rate of 4-6% in Pakistan.[2]

Hepatitis C virus (HCV) infection is increasing even more rapidly and has occurred in endemic situation in most parts of the world, with a prevalence rate of about 3% worldwide.[3]

Hepatitis C virus infection progresses slowly and carries a high risk of chronic liver disease (70-80%) and latter Hepatocellular carcinoma.[4]

In Pakistan the prevalence of hepatitis C according to provinces is different and was found to be high in Punjab and Sindh (5-6%).[5]

Hepatitis is transmitted by contaminated blood transfusion, un-sterilized syringes, surgical instruments, dental surgery, sexual contact, drug abuse and shaving by barbers. Health care providers especially surgeons and operation theater staff has significantly high risk of infectivity along with further transmission of the disease if pre-operatively screening and standard precautions are not followed strictly. 60-70 percents of patients with chronic liver disease (CLD) are positive for anti-HCV [6] and can be associated with coagulopathy causing bleeding problems during surgery. Routine screening before any surgical intervention reduces the potential risk for its transmission, which is a part of standard care.[7]

The objective of this study was to identify patients with anti-HCV positive presenting to surgical department for emergency or elective procedures.

MATERIALS AND METHODS

This observational study was carried out in surgical department of Ghulam Muhammad Mahar Medical College Teaching Hospital Khairpur Sindh, during one year period from May 2012 to April 2013. Total 1030 patients were admitted in department for emergency or elective surgical procedures. Routine screening test were performed in all patients and in 165 patients become HCV positive, anti- HCV positive patients were included in study after taking informed consent. Further detailed history with regards to various risk factors such as in males past history of any surgery, blood transfusion, shaving by barbers, drug abuse,

partner positive for HCV and past history of jaundice, same as in positive female patients detailed history of jaundice, mode of delivery, place of delivery, any gynaecological procedure, blood transfusion, partner positive for HCV status were obtained in all study population. In all positive cases specific investigations like LFT, PT, APTT and ultrasound especially upper abdomen were performed.

All information was recorded through a pre-designed Performa. Data was analyzed by using SPSS version 15.

RESULTS

Teen hundred and thirty (1030) patients were admitted in surgical ward during a one year of study period for emergency or elective surgical procedures. All patients were screened for anti-HCV status. Out of 1030 screened patients 165 (16.0%) become anti-HCV positive.

Thee age range of patients between 11-70 years and more. In 165 positive patients 95(9.2%) were male and 70(6.7%) were females. Majority of positive patient were belongs to rural areas, uneducated and have had poor socioeconomic status and none of them had knowledge about disease and its importance (table: 1).

Table No. 1: Demographic characteristics of study population N=165

parameters	number	percentage
-Total patients for surgery	1030	-
-Anti-HCV +ve patients	165	16.0%
-Male	95	9.2%
-Female	70	6.7%
-Emergency cases	35	21.2%
-Elective cases	130	78.7%
-Belongs to Rural areas	135	81.8%
-Belongs to Urban areas	30	18.1%

Table No. 2: Age distribution of anti-HCV reactive patients N=165

Age in years	HCV+ve	Percentage
11-20 years	08	4.8%
21-30 years	12	7.2%
31-40 years	50	30%
41-50 years	68	41.2%
51-60 years	18	10.9%
61-70+ years	09	5.4%

More positive cases were seen in age between 30-50 years. Age distribution of the patients is shown in table: 2.

Among 95 anti HCV positive males, 42(44.2%) had history of shaving by barbers, in 35(36.8%) history of multiple injections, while among 70 anti-HCV positive females, 30(42.8%) had history of blood transfusion, history of injections positive in 25(35.7%). In 20 males and 35 females no any related risk factors found for hepatitis C transmission shown in table: 3.

Table No. 3: Risk factors identified in Hepatitis C positive Males & Females

Risk (males) 95	No: %	Risk (females) 70	No: |%
-Shave by barbers	42 (44.2%) jjjjj	-Previous surgery = D&C =LSCS	25 (35.7%) 10 (14.2%)
-Parenteral injections	35 (36.8%)	-h/o blood transfusion	30 (42.8%)
-Past h/o surgery	18 (18.9%)	-Multiple injections	25 (35.7%)
-h/o blood transfusion	15 (15.7%)	-h/o jaundice	20 (28.5%)
-Partner +ve for HCV	08 (8.4%)	-Partner +ve for HCV	15 (21.4%)
-No risk factor	20 (21.0%)	-No risk factor	35 (50%)

DISCUSSION

In Pakistan the frequency of Hepatitis C is significantly higher than in the neighboring countries.[8]

According to Pakistan Medical Research Council (PMRC) Survey 2008, Province Sindh had 5.0-6.0% frequency in its Obstetrics.[9]

In our study frequency of anti-HCV is 16.0% and the mean age of hepatitis C seropositivity 45.5 years; this may be due to fact that frequency of HCV increases with age.[10]

The results of our study are comparable with two international studies conducted in Japan, one shows seropositivity of HCV was 16.9%, while other shows HCV frequency was 7.1%.[11, 12] But our study results are slightly higher to studies done in different cities of Pakistan, HCV seropositivity in Karachi 11.3%[13], Rawalpindi 7.5%[14], Nawabshah 11.6% [15] and in Jacobabad HCV positivity 14% .[16]

Weis and his co-workers reported the prevalence rate of HCV 35% in their patients operated at John Hopkins.[17] another study conducted at Egypt out of 5909 patients evaluated, showed anti HCV frequency seen in 29.8% patients.[18]

The risk factors recognized in this study are same seen in the study by Zubia et al. they have noted history of multiple injection therapy in 95.4% I anti-HCV positive patients.[13] Poor health and low educational standard in Pakistan also contribute for disease transmission,[2] as seen in our study, most of our study populations were illiterates and belong to poor socioeconomic class.

Regarding risk factors in female patients in our study, previous history of gynecological (D&C) and Obstetrical (LSCS) was a major risk factor for transmission of anti-HCV seen in 35(50%) and the same was reported by Jaffary [19] and Batool as 42.2%.[20].

CONCLUSION

In the absence of any vaccine for Hepatitis C virus, emphasis should be made on health education and about

the risk factors for virus transmission. Health care providers must be committed in the formulation of policies and strict adherence to the safe practices.

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Original Article

Older Persons Health

Older Persons, Familial Care and Psychological Stresses: An Anthropo-Gerontological Approach on Health

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ABSTRACT

Objective: The aim of study was to explore the interrelationship of older persons' health with various psychological stresses in Rawalpindi city.

Study Design: Cross Sectional

Place & Duration of Study: The study was commissioned to the research team on behalf of Help Age Pakistan (an INGO based in Islamabad). The data collection was done in various union councils of Rawalpindi city. The study duration was three months and lasted from September 2013 to December 2013.

Materials and Methods: Structured questionnaire was developed to collect information on Older Persons' health, economic and psychological status. In this regard, an extensive questionnaire was designed and pre-tested vigorously. Questionnaires were administered with the help of a research team that comprised the graduates of department of Anthropology of PMAS-Arid Agriculture University along with professionals of Regional Development Network (RDN) as well as field staff of Pakistan National Center on Ageing (PNCA).

Results: 414 (41.4%) respondents said that they felt lonely because they feel age gaps due to which they thought nobody at home could understand what they feel. As regards the frequency of visits by the kids or family members, the responses were Never (36.7%), Monthly (29.6%), Weekly (18.9%). To kill their time 16.2% OPs spent their time in mosque, shops, or parks, 14.1% spent time while staying at home.

Conclusion: The large majority of the OPs felt lonely because of the ignorance on behalf of the kids, families and indifferent attitude of society. There is a strong relationship between the mental stresses, economic instability of families and gradual loosening up of familial bond. The psychological stresses later on are increasing health problems and complications for OPs.

Key Words: Anthropology, Gerontology, Ageing, Older Persons (OPs), Health Issues, Mental Health, Psychological Stress, Loneliness, Social Isolation, Social Exclusion

INTRODUCTION

Psychological anthropology is one of the most contemporary of academic studies; the scholarly study of the relationship between the individual and culture arguably began in the late nineteenth century, when W. H. R. Rivers and his colleagues undertook an expedition to Melanesia to test the perceptions of the local people. The heyday of the discipline was reached in the 1930s and 1940s with the investigations of Margaret Mead, Ruth Benedict, and others[3-14].

Considered historically, a renewed interest in psychological anthropology makes good sense, since the discipline addresses fundamental questions about the nature of humanity that have become especially pressing in the present era of multiculturalism and globalization, as taken-for-granted, everyday realities have been challenged within a fluid and dynamic world. Today, perhaps more than ever, people want to know to what degree their perceptions, emotions, beliefs, values, and even their experiences of themselves may be shaped and changed by shifts in culture and context. What about us is consistent? What is malleable? What does it mean to be an individual and also a member of a community?

In order to provide older people with better healthcare, Help Age International and United Nations Population Fund (UNFPA) illuminates that 'input can be allocated from two sources: government and the community. The focus of the discussion was not on prolonging human life, but ensuring that older people live actively for the entire length of their life. The participants discussed three categories of older people's health as follows: Group 1 - Good health; Group 2 - Fair health; and, Group 3 - Poor health. Each group requires different health strategies. Group 1 will need a preventive healthcare while Group 2 will require both preventive and curative treatments. Intense medical attention should be provided to older people who fall into Group 3."

United Nations Principles for Older Persons was adopted by General Assembly resolution 46/91 of 16

December 1991. The Articles 10 to 14 of UN Principles exclusively focus on the physical and psychological health issues of Older Persons. The article 11 solely puts its emphasis on health issues by uttering that "Older persons should have access to health care to help them to maintain or regain the optimum level of physical, mental and emotional well-being and to prevent or delay the onset of illness".

Policies on ageing have been formulated at an international level (e.g. by the UN), at regional levels (e.g. by the European Commission) and at national levels (e.g. in government strategy, programmes and legislation). Implementation depends on the area of policy being targeted – for policies affecting public service provision (for example, health and social care), devolution of budgetary and administrative responsibility to local authorities and communities is a common feature in many countries. Thus, policies are usually set centrally but implemented locally. This dichotomy brings about tensions that have been articulated elsewhere in the literature on decentralization and devolution[14].

There are a number of differences between the challenges posed by ageing in developed versus less developed countries. Developed nations are mostly concerned about the sustainability of their social protection systems, whereas less developed countries have to deal simultaneously with the challenges of population ageing and those of development. Older people in developed countries are concentrated mostly in urban areas, whereas, in poorer nations, up to half of the population, including many older people, reside in rural areas. Older people in developing countries often reside in multigenerational homes, whereas this is less the case in developed countries[15].

Poorer older people are also at greater risk of social exclusion and exclusion from public services. This can also have an ethnic and cultural dimension. For example, in the UK, 17% of pensioners overall live in poverty, yet this proportion is 42% among the Pakistani and Bangladeshi communities[16].

With respect to the contributions that the anthropology of ageing has made to understanding how cultural change impacts on the lives of older people, Holmes and Holmes (1995) have proposed a number of generalizations that have implications for how cross-cultural gerontologists think about the impact of cultural, societal, economic, religious and political factors on old age and ageing. These are as follows: (1) Modernization affects the way in which we conceptualize old age; (2) Longevity is directly related to the degree of modernization; (3) Modern societies have a relatively high proportion of older people in their population; (4) Older people are accorded more respect in societies where they constitute a low proportion of the total population; (5) Societies in the process of modernizing tend to favor the young (while the old are at an advantage in more stable societies); (6) Respect for older people tends also to be greater in societies in which the extended family has not lost its importance (especially when the extended family functions as the household unit); (7) In pre-industrial societies the family is typically responsible for the economic security of older people, whereas in industrial societies the responsibility falls partially or totally on the state; (8) The proportion of older people who retain leadership roles is lower in modern than in pre-industrial societies; (9) Religious leadership is more likely to be a role one can continue with once one becomes older in a pre-industrial society; and (10) Retirement is a modern invention found only in modern and highly productive societies. These considerations guide most cross-cultural and/or anthropo-gerontological enquiries[17].

An additional consideration with respect to globalization and the age of migration is that these phenomena are expected to intensify the existing gaps in wealth an d resources between the rich and the poor nations, between the First and the Third Worlds, and between what sociologists tend to refer to as 'the centre and the periphery' (i.e. the West and the rest)[18,19].

Victor et al. (2002), for example, distinguish between these concepts. Whereas being alone refers to spending time by oneself, living alone can simply refer to a particular household arrangement, and social isolation to the ways in which individuals are integrated into their broader social environment, through, for example, the number and frequency of contacts they have with others[20].

Some of the key factors which have been found to affect loneliness among older people include personal circumstance and characteristics such as age, marital status, ethnicity, gender and health status; characteristics such as the size of mediating structures of kin and non-kin networks which may facilitate contact with others; and the norms and values influencing expectations about roles and relationships in later life[21]. The risk factors of loneliness and social isolation in later life have been identified as socio-demographic factors, individual health status, life events (bereavement, retirement) and material circumstances such as low income and poverty.

MATERIALS AND METHODS

Structured questionnaire was developed to collect information on Older Persons' health, economic and psychological status. In this regard, an extensive questionnaire was designed and pre-tested vigorously. Questionnaires were administered with the help of a research team that comprised the graduates of department of Anthropology of PMAS-Arid Agriculture University along with professionals of Regional Development Network (RDN) as well as field staff of Pakistan National Center on Ageing (PNCA).

RESULTS

Despite the fact, that most of the respondents were living with their children in their families 414 (41.4%) respondents said that they felt lonely because they feel age gaps due to which they thought nobody at home could understand what they feel. On the other side, 586 (58.6%) said that they don't feel lonely because they regularly visited their friends, and relatives to kill their time and thus kept themselves mentally engaged instead of merely sitting idle and feeling lonely.

Table No.: OPs Feeling Lonely

Response	Frequency	Percent
Yes	414	41.4
No	586	58.6
Total	1000	100.0

The purpose of this question was to know the frequency of visits paid by their sons or daughters in case the OPs were not living with the immediate families then what was the. The largest percentile was 367 (36.7%) cases in which the question was not applicable. The reasons were tri-fold. Firstly, the OPs were already living with their off springs, secondly, they did not have any kids and thirdly their kids stopped visiting them. 29.6 percent uttered that their off springs visited them monthly, 18.9% said that they meet their kids on weekly basis. 10.7 percent of the total respondents selected replied that their kids visited them on six-month basis just because their kids lived in other cities due to which it was hard for them to come to meet the older parents. Only 4.1 percent said that their kids lived abroad therefore they come once in a year to visit their parents.

Above table recorded the responses of OPs that how did they cope their loneliness in their routine life. In 16.2% of the male OPs of the sample used to visit mosque, men's room or going out from home to cope their loneliness. Staying home with spouse were recorded to be 14.1%, socialization with family, children or both were reported to be 9.8%. Only 1.3% interacted with friends of colleagues. The remaining 58.6% cases were not applicable in this situation because these were mostly females who were supposed to stay at home or they had no options to kill their loneliness or boredom.

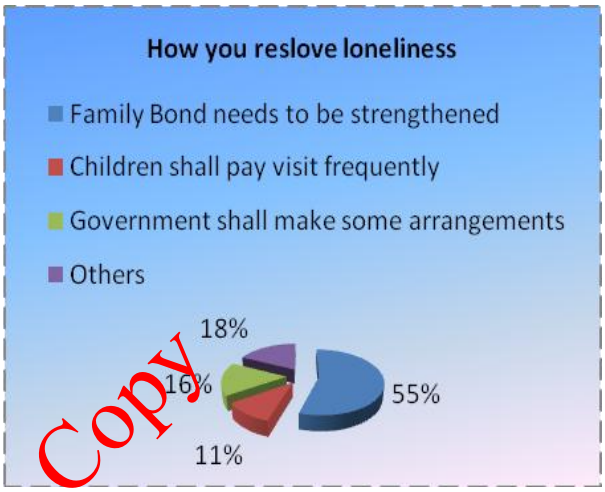
Table No.2: Tenure of Visits paid by Children

Response	Frequency	Percent
Weekly	189	18.9
Monthly	296	29.6
Six Monthly	107	10.7
Yearly	41	4.1
Never / NA	367	36.7
Total	1000	100.0

OPs' Measures to Cope Loneliness

Table: Coping with Loneliness

Response	Frequency	Percent
Mosque/ Club/ GoingOut	162	16.2
Staying with Spouse at home	141	14.1
Socialization with Family/ Children	98	9.8
Interacting with Friends/ Colleague	13	1.3
NA	586	58.6
Total	1000	100.0



Graph: Remedies to Resolve Loneliness

This graph provides further insights into the previous question to understand the perception of the OPs' about how did they resolve the issue of loneliness if they felt so. 227 respondents said that they thought if the family ties are made strengthened then this issue could easily get solved. 68 respondents narrated that the government should come forth and make some alternate arrangement for the OPs so that this matter could be solved on sustainable basis. The government interventions could depend on initiating some social clubbing for the OPs so that they could spend time among their age fellows. 45 respondents of the total 414 respondents stated that the children and rest of the family members should feel their responsibility to visit them frequently.

DISCUSSION

The current study primarily focused on older persons' health and its relationship with familial care and psychological stresses prevailing among them. The study presented very vital statistics regarding the primal inquiries. It was generally found that OPs feel loneliness due to many reasons. First of all the economic burdens of families kept the off springs busy in their professional chores due to which they could not spare quality time to spend with the parents. It was felt

that there has to be a community-run integrated program that provides the OPs a platform to socialize and spend their time productively.

The importance of mental health is quite established in academics as well as in the responses of the OPs during the course of the study further reinforcing the strengths of the arguments as posed by UN Principles for Older Persons. Research sophistication has also highlighted the importance of social protection and its relation with the health indicators.

The champions of World System Theory and modernization paradigms seem true in their sayings regarding the 'Center-periphery dichotomy' which elucidates that third world countries with their so-called development agenda is largely putting the OPs at the risks of their families and society that obviously has no real place for them other than merely categorizing them as 'economic burden or liability'[18-19,22-23].

The cases in which older persons did not live with their families were even more stigmatized in terms of poor health and high frequencies of psychological complications. It was so because these OPs were totally lacking people to care for OPs. In such cases, these OPs were found to be spending their time in shops or public parks thus escalating their social isolation. This social isolation was established to be devastating factors for the physical and mental well being of the OPs.

In 586 cases OPs had no options to socializing or spending their time productively. The socializing measures adopted by the OPs were in most the cases visiting mosques, shops or parks. Secondly the second highest frequency was staying at home in case OPs' life partners were alive. Thirdly, socializing somehow with family and fourthly interacting with friends or colleagues. OPs gave various suggestions to resolve their loneliness like strengthening the family bond, increasing the frequencies of visits paid by the kids. OPs also suggested that government and community are supposed to commence some community based initiatives where they could avoid their mental stresses and sense of loneliness. It was because the OPs felt that the children, families and society have abandoned them which according to them were a clear sign of deliberate ignorance of religious preaching as well.

CONCLUSION

Pakistan is member of today's third world club with numerous developmental issues and challenges in the domain of economic self-reliance as well as political instability. The traditional social institution of family that has been a hall-mark of South Asian culture has unfortunately proven to be insufficient for the effective redressal of psychological issues faced by the OPs. The economic burdens have doubled their problems of social isolation and social exclusion. There is a need to prioritize the human rights agenda as an essential component of development policy and practices in Pakistan in which the OPs have loads to offer in the light of their life long experience.

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Original Article

Weaponry Pattern & Incidence of Homicidal Deaths - 5 Year Study

Homicidal Deaths

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ABSTRACT

Objective: To analyze the 5years data of autopsies with reference to weaponry pattern may offer some help in controlling law and order situation in the country.

Study Design: Retrospective Study

Place and Duration of Study: The study was conducted at THQ hospital Taxila. 5 years data of autopsies conducted during the years from 2009-2013 was taken and analyzed.

Materials and Methods: Autopsy registers from 2009 to 2013 were taken from THQ Hospital Taxila and analysis of the available data was done regarding weaponry pattern, age, sex, area of body targeted and nature of injuries.

Results: During 5years 2009-13 total 279 autopsies were conducted. 234 (83.87%) dead bodies were belonged to male and 45 (16.13%) to females. Most of the dead bodies were adult age group, 138 (49.46%) dead bodies were between age 20-40 years, out of which 112 (81.16%) of males and 26 (18.84%)of females. Firearm remained the most common weapon used claiming 177 (63.44%) lives. In 22 (7.88%) deaths blunt weapons were used and only 7 (2.5%) deaths were caused by sharp edged weapon. Head remained the most targeted area as in 88(31.54%) cases. In 76 (27.24%) persons chest was the target. 33 (11.83%) persons was hit on abdomen, while 28(10.04%) dead bodies were found with injuries on neck. In 40 cases (14.34%) no cause of death was detected.

Conclusion: The analysis may be used to control law and order situation in the society.

Key Words: Weapons, crimes, firearms, Homicidal

INTRODUCTION

Rate of homicidal autopsy is the index of crime rate in the society. Crimes are on rise not only in the whole world but people of our country are particularly very much affected by rapid raise in crimes.

A weapon, arm, or armament is any device used in order to inflict damage or harm to living beings, structures, or systems[1]. Broadly the weapons are of 3 types blunt, sharp and firearm weapons[2]. Most common weapons in the world are the blunt weapons. But in the presence of most modern and sophisticated firearm weapons, blunt weapons are not frequently used to cause homicidal injuries.

Our study shows that most common weapon used in homicidal deaths is the firearms.

These are broadly divided into 2 types, smooth bored and riffled firearm weapons. In riffled firearms bullets, while in smooth bored weapons shot cartridges are used. Any small arm designed to be fired while held in one hand is called hand gun (as pistols and revolvers) and are frequently implicated in homicide, suicide and occasionally in accidental cases [3].

The use of firearm as a weapon of homicide is not only prevalent in Pakistan but in other countries of the world also, as these are very effective mode of causing deaths with remote chances of retaliation, as the culprit is at safe distance from the victim. Gunshot wounds are more destructive than other injuries[4] and highly destructive when fired at close range[5].

Homicide means killing of one human being as a result of conduct of other. It is broadly divided into two types, lawful as killing in self defense, or homicide by law enforcement agencies to control the riots, and un-lawful as murder (homicide with intension) and manslaughter (homicide without intension). [6] The crime of homicide is unacceptable for all types of societies [7].

Unfortunately Pakistan is the country where the crimes are growing very rapidly. This rise in crimes is directly connected with increase in homicidal deaths. An autopsy is always required in homicidal cases[8]. In addition to rising crimes the ever growing terrorism is also playing havoc with the psychology of the nation. Sharp rise in homicidal deaths leading to heavy load of medico-legal autopsies as law and medicine have been interrelated and interdependent since antiquity [9].

The causes of more use of firearms are the easy availability of illegal weapons, fearless possession and flaws in our judiciary system. The firearms may be imported or smuggled from other countries or made in the tribal area of Pakistan as the country made guns are also common in India, Sri Lanka and other Asian areas[10]. All types of firearm weapons are freely available in our country[11].

Analyzing the data about homicidal deaths in a clan with reference to weaponry pattern, age, sex, nature of deaths, and targeted area involved, plays a pivotal role in controlling the crimes and maintaining the law and order situation in a community.

MATERIALS AND METHODS

The autopsy reports from 2009-13 were taken from THQ Hospital Taxila and analysis was done on the basis of weaponry pattern, age, sex, body area involved, address, opinion, material collected for dispatch to Chemical Examiner/Histopathologist, cause of death and injury markings on the postmortem register used as variables. Total 279 autopsies were conducted during 5 years tenure.

RESULTS

Total 279 autopsies were carried out at THQ Hospital Taxila during the period from 2009 to 2013 (during calendar year of 2009, 42 autopsies, in 2010, 44 autopsies, in 2011, 61 autopsies, during 2012, 64 autopsies and in 2013, 68 autopsies). Out of total 279 autopsies 234 (83.87%) belonged to males while 45 (16.13%) belonged to females. (Table 1, Figure 1).

Table No.1: Year wise Male and Female Homicidal Deaths

Year	No.	M	F
2009	42	34	8
2010	44	37	7
2011	61	53	8
2012	64	56	8
2013	68	54	14
GT	279	234	45

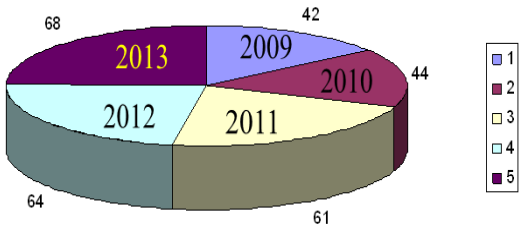

Figure No.1: No. of Autopsies

Regarding weaponry pattern 177 (63.44%) deaths were caused with firearm weapons. While 22 (7.88%) deaths were claimed by blunt and only 7 (2.51%) deaths were caused by sharp edged weapons. Complete breakup of the weaponry pattern is given year wise in shown in the table-2.

As for as the age group is concerned most cases belonged to adult age (20-40 years). During total 5 years duration 138 (49.46%) persons were belonged to age group 20-40 years among them 112 (81.16%) were males and 26 (18.84%) were females. Age wise detail is mentioned in table-3.

Head injuries remained on top as present in 88(31.54%) cases. In 76 (27.24%) persons chest was the target. 33 (11.83%) persons was hit on abdomen, while 28(10.04%) dead bodies were found with injuries on neck. Cause of death in 40 (14.34%) cases remained undiagnosed as negative autopsy.

Table No.2: Year wise Homicidal deaths due to weapons and other reasons

Year	No.	FA	%	Blunt	%	Sharp	%	Hanging	%	Poison	%	Drowning	%	Burns	%	Nil	%
2009	42	30	71.42	1	2.38	1	2.38	4	9.52	1	2.38	-	-	2	4.76	3	7.14
2010	44	30	68.18	7	15.91	-	-	3	6.82	1	2.27	-	-	-	-	3	6.82
2011	61	37	60.65	3	4.92	2	3.28	4	6.56	3	4.92	-	-	-	-	12	19.67
2012	64	33	51.56	9	14.06	4	6.25	-	-	-	-	3	4.69	-	-	15	23.44
2013	68	47	69.12	2	2.94	-	-	8	11.76	2	2.94	1	1.47	1	1.47	7	10.29
GT	279	177	63.44	22	7.88	7	2.51	19	6.81	7	2.51	4	1.43	3	1.07	40	14.34

Table No.3: Year wise age and sex pattern of Homicidal Deaths

Year	0-12 years	M	F	12-20 years	M	F	20-40 years	M	F	Ab.40 years	M	F	GT
2009	2	1	1	10	8	2	19	15	4	11	10	1	42
2010	1	-	1	10	9	1	25	21	4	8	7	1	44
2011	1	1	-	10	9	1	29	24	5	21	19	2	61
2012	3	3	-	12	11	1	33	29	4	16	13	3	64
2013	4	3	1	11	8	3	32	23	9	21	20	1	68
GT	11	8	3	53	45	8	138	112	26	77	69	8	279

DISCUSSION

Crime is an evil against society for which the man is punished by the laws made by the parliament. It is generally believed that good and evil lie embedded together in human nature and it has been seen often in actual life that many good souls commit evil deeds simply because evil in them gets the upper hand over the good in them.

Relation of human being and crimes is as old as the human being itself. Crimes can never be eliminated from a society altogether. Crime control is the desired target. In general there is a global increase in the crimes and so in homicides also[12]. As the fear of law enforcement agencies and law has been faded away from our society so people are involved in the criminal activities without any hesitation.

The most common weapon used in homicidal cases remained the firearms (63.44 %). In USA also the most frequent method of killing is the firearms[13]. In Turkey during the years of 1997-2001, in 54.83% cases of homicidal deaths, firearms remained the weapon used[14]. The firearm is the leading weapon used in homicidal deaths in our study which is consistent with other studies in Pakistan[15-16]. Despite stringent legislation in the UK and elsewhere in the world, the use of firearms in the criminal activities continues to increase [17]**.** But Rate of homicide has been effectively controlled in Brazil by effective legislation and public education[18].

The easily available country made guns are quite unsafe as while firing they may burst also and kill the person who is firing them. The quality is very poor but since they are quite cheap and easily available are quite frequently used[19]. In Pakistan even the authorized dealers of the firearms don't maintain the proper record of the weapons present and sold out. But In USA federally licensed gun dealers are required by law to maintain record of serial numbers of all firearms in their inventories and to report the serial numbers of all weapons sold. Consequently the serial number of a firearm is important to tracing the ownership of a firearm used in the commission of a crime[20].

Regarding causes of high homicide rate in our country in addition to traditional Zan, Zer and zameen, other causes are old family feuds, revenge and traditional honor killings[21].

Homicides may also be triggered by violence shown on TV[22].

As for the age is concerned it is quite evident from the study that usually adult generation is involved in the crimes and mostly this generation is the victim also. Most common age in homicidal cases remained between 20-40years (49.46 %). Emotional element of the young persons plays a key role in increasing violence in a community.

Regarding most common targeted area head remained at no. 1, showing the cruel mentality of the criminals who want to eliminate the chances of survival of victims. The 2nd most common targeted area is the chest. This is consistent with the study conducted at Khyber Medical College Peshawar[23].

Regarding gender involvement male remained the clearly dominant as compared with female as only 45 females were killed as compared with 234 males during 5 years. Almost similar results in a research conducted in Lahore[24]. The females are physically weak, less aggressive and not frequently exposed to outside environment as compared with males.

In 40 cases no cause of death was declared by the Causality Medical Officers showing the high rate of negative autopsy. As there is shortage of qualified well trained staff of Forensic Medicine in the country the medico-legal autopsies are often being performed by doctors inexperienced in forensic procedures[25].

CONCLUSION

Prevention is better than cure is also very much true for crimes also. To control the crimes in a society regular analysis regarding the weaponry pattern, total autopsies carried out in that area , age of victims, targeted area and age, motive, sex and other information of the offenders play a key role to control the law and order situation in the country. This study also may be helpful in this regard.

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Original Article

Vag Birth after CS

Vaginal Birth after Cesarean Section - A Continuing Challenge

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ABSTRACT

Objective: The purpose of this study was to assess the antenatal and intrapartum factors influencing the success of vaginal delivery in women with one cesarean section. Identification of modifiable risk factors which could help in developing local guidelines to improve the management and success rate of patients undergoing vaginal delivery after one previous cesarean section.

Study Design: Prospective cohort study

Place and Duration of Study: This study was carried out at the Department of Obstetrics and Gynecology, Aga Khan University, Hospital, Karachi from 01.01.2008 to 30.06.2008.

Materials and Methods: A sample size of 21 women, undergoing induction of labor (IOL) and 54 women with spontaneous labor were needed. All women with singleton, cephalic, term pregnancies with history of previous one caesarean section were included. Data collected through the Performa and statistical analysis performed using the SPSS computer statistics programme. To compare proportions, the χ^2 test and Fisher's exact test were used and student-t test were used to compare means.

Results: Both groups were comparable and there was no statistical difference between them, except for the Bishop score which in the induction of labor (IOL) group was 4 ± 1.54 and in the spontaneous labor group was 5.7 ± 2.18, which is statistically significant (p value = 0.001). The results suggest that there is no affect of previous vaginal delivery, epidural analgesia, fetal distress and baby's gender on the outcome of trial of labor (TOL). The rate of successful vaginal birth after cesarean section (VBAC) is not significantly different in the group of IOL and spontaneous labor.

Conclusion: The current clinical evidence suggests that VBAC is advantageous to the mother and has no adverse effects on the fetus but it is no risk free. It is actually the responsibility of the obstetrician to ensure best care and appropriate management plan.

Key Words: Cesarean section (CS), uterine rupture, trial of labor (TOL), vaginal birth after cesarean section (VBAC), induction of labor (IOL), augmentation of labor.

INTRODUCTION

Once a cesarean, always a cesarean[1], was the rule in United States of America for most of the last century. In 1980s, vaginal birth after cesarean section (VBAC) grew in popularity and the pendulum began to swing away from routine repeat elective cesarean delivery but recently, the wisdom of this transition has been questioned.

A trial of labor (TOL) after previous cesarean delivery has been accepted as a way to lower down the overall cesarean delivery rate and published evidence suggests that the benefits of VBAC outweigh the risks [2, 3, 4].

Although there is no doubt that trial of labor (TOL) is a relatively safe procedure, it is not risk free and should not be undertaken in a casual fashion. It is the decision to perform the primary cesarean section (CS) that forever alters a women reproductive performance.

The American College of Obstetrician and Gynecology has formally supported the management plan of TOL after a lower segment cesarean section and it was reflected by the significant rise in women delivering vaginally after one CS in 1993 [2].

The reluctance to permit the TOL after one lower segment CS is probably due to a variety of reasons including; fear of uterine rupture, threat of maternal and fetal damage, possible subsequent litigations, many obstetrician think that CS is simple and convenient so why accept a risk [3].

Pakistan being a developing country with poor recourses cannot afford the burden of high rate of CS. In its tertiary hospital the success rate of 64.2% has been reported and these results can be improved with proper patient selection and monitoring [5, 6, 7, 8]. Most recent studies and reviews quote VBAC success rate of 60 - 80% [9, 10].

The success rate may vary and influenced by multiple antenatal and intrapartum factors. Induction of labor (IOL) has been suggested as one of the risk factor which is associated with significantly reduced rate of successful VBAC and maternal morbidity [11, 12]. Previous vaginal delivery [13, 15], maternal age [16], maternal height [16], and fetal birth weight are significant predictors of the failure to deliver vaginally while epidural analgesia appears to have no effect on failed TOL[17]. These findings have led to an approach

illustrate the need for the re-evaluation of VBAC recommendations.

One has to accept the each delivery method has advantages and disadvantages. It is ultimately the responsibility of the obstetrician to ensure that delivery plan is appropriate for each individual.

To assess the antenatal and intrapartum risk factors influencing success of vaginal delivery in women with one cesarean section. Identification of potentially modifiable risk factors which could help in developing local guidelines to improve the management and success rate of patients undergoing vaginal delivery after one previous CS.

MATERIALS AND METHODS

A prospective cohort study was carried out in the Department of Obstetrics and Gynecology, Aga Khan University, Hospital, Karachi. Women undergoing TOL after one cesarean section were included after the approval of protocol and recruitment was stopped once the sample size achieved that is 21 women undergoing induction of labor and 54 women with spontaneous onset of labor.

Data collected through the Performa and statistical analysis performed using the SPSS computer statistics programme. To compare proportions, the χ^2 test and Fisher's exact test were used and student-t test were used to compare means. In women undergoing spontaneous TOL after one previous cesarean section, 20% higher successful vaginal delivery rate has been reported in literature as compared to ones who underwent induction of labor i.e. 77.1% v 57.9% .

At least 40 % difference in success rate of vaginal delivery would be clinically significant and that was our bases of calculating the sample size for this study.

A sample size of 21 women, underwent IOL and 54 women with spontaneous labor was needed to achieve 80% power (1-β) to detect difference of 40% in success rate of vaginal delivery in women undergoing TOL after one previous cesarean section, with 5% level of significance (α).

Singleton, cephalic, term pregnancies with history of previous one CS were included.

If type of previous CS was not known, or it was a classical cesarean section. Patients with medical disorders and obstetric complications which can influence the chances of vaginal delivery were excluded.

RESULTS

Demographic and physical characteristics of both groups were comparable and there was no statistical difference between them, except for the Bishop score which in the IOL group was 4 ± 1.54 and in the spontaneous labor group was 5.7 ± 2.18, which is statistically significant (p value = 0.001) **(Table 1)**. The mean maternal age of the IOL group was 28.38 years ± 4.37 and in the spontaneous labor group was 28.9 years ± 4.83 (p = 0.66). The mean maternal height in the IOL group and the spontaneous labor group was 155.3 cm ± 3.82 and 158.5 cm ± 4.48 respectively (p = 0.06). Mean gestational age in the IOL group and in the spontaneous labor group was 39 weeks ± 1.22 vs 38.6 ± 1.12 (p = 0.19).

Factors affecting outcome of TOL include history of previous vaginal delivery, epidural analgesia, fetal distress and baby's gender. It shows that 12 patients out of 21 in the group of IOL had the history of previous vaginal delivery, out of those 12 patients, only 10 (83.3%) delivered vaginally and 2 (16.7%) had repeat CS. Out of those 21 patients, 9 never had vaginal delivery in the past, among them 6 (66.7%) delivered vaginally and 3 (33.3%) delivered by CS (**Table 2)**. It shows that the history of vaginal delivery increases the percentage of successful vaginal delivery, but our results did not show statistically significant difference (p = 0.35). The second variable was the use of epidural analgesia. In the group of IOL, out of 21 patients, 5 took epidural analgesia and all of them delivered vaginally (100%) and 16 patients who did not take epidural analgesia, 11 (68.8%) delivered vaginally and 5 (31.2%) delivered by CS. However in the group of spontaneous labor (54 patients), 2 patients took epidural analgesia, out of which, 1 (50%) delivered vaginally and 1 (50%) underwent CS. 52 patients who did not take epidural analgesia, 37 (71.2%) delivered vaginally and 15 (28.8%) delivered by CS, but the results were not statistically significant (p = 0.21). Fetal distress and baby's gender do not appear to have any significant effect on the outcome of TOL.

Rate of successful vaginal delivery after TOL in the group of IOL and spontaneous labor was 76.2% vs. 70.4% respectively (p = 0.614) **(Table 3)**. There was no statistically significant difference in the outcome of two groups with respect to their success rate. The total duration of labor, baby's birth weight, Apgar score at one minute and at five minutes was similar.

Table No.I: Demographic and Physical Characteristics

	Induced labor n =21	Spontaneous labor n =54	p value
Total number(n)	21	54	
Maternal Age (years) (mean ±SD)	28.38 ± 4.37	28.91 ± 4.83	0.66
Maternal Height (cm) (mean ±SD)	155.3 ± 3.82	158.5 ± 4.48	0.06
Gestational age (weeks) (mean ±SD)	39 ± 1.22	38.6 ± 1.12	0.19
Bishop score (mean ±SD)	4 ± 1.54	5.7 ± 2.18	0.001*

n = number of patients * p value < 0.05 is significant
SD = standard deviation

Table No.2: Analysis of Factors Affecting Outcome of Trial of Labor

Factors	Induced labor (n = 21)		Spontaneous labor (n = 54)		P value
History of previous vaginal delivery	**Yes n (%)**	**No n (%)**	**Yes n (%)**	**No n (%)**	
Spontaneous vaginal delivery	10 (83.3)	6 (66.7)	20 (83.3)	18 (60)	0.35
Cesarean section	2 (16.7)	3 (33.3)	4 (16.7)	12 (40)	0.07
Epidural analgesia					
Spontaneous vaginal delivery	5 (100)	11 (68.8)	1 (50.0)	37 (71.2)	0.21
Cesarean section	0 (0)	5 (31.2)	1 (50.0)	15 (28.8)	0.52
Fetal distress					
Spontaneous vaginal delivery	1 (50.0)	15 (78.9)	1 (25.0)	37 (74.0)	0.42
Cesarean section	1 (50.0)	4 (21.1)	3 (75.0)	13(26.0)	0.07
Baby's gender	**Male n (%)**	**Female n (%)**	**Male n (%)**	**Female n (%)**	
Spontaneous vaginal delivery	12 (85.7)	4 (57.1)	15 (68.2)	23 (71.9)	0.18
Cesarean section	2 (14.3)	3 (42.9)	7(31.8)	9 (28.1)	0.50

n = number of patients p value < 0.05 is significant

Table No.3: Outcome of Trial of Labor

	Induced labor n (%)	Spontaneous labor n (%)	p value
N	21	54	
Spontaneous vaginal delivery	16 (76.2)	38 (70.4)	0.614
Cesarean section	5 (23.8)	16 (29.6)	
Total duration of labor (minutes)	323.2	267.8	0.11
Baby's weight (kg)	3.26	3.16	0.42
APGAR score at one minute	7.8	7.9	0.75
APGAR score at five minute	8.8	8.9	0.13

DISCUSSION

The increasing incidence of cesarean birth has focused attention on the subject of VBAC and as a result, the literature on the subject has extensively been reviewed. Many recent reports document the relative safety of a TOL as an alternative to CS, but when a trial fails the patient is at increased risk of infection, higher rates of uterine rupture, endometritis, wound infection, operative injury, hysterectomy, and maternal or fetal death.

IOL as a variable of success has had a disparate impact, with reported vaginal delivery rates ranging from 45% to 79%[11]. In 1992 Troyer and Parisi established a scoring system for VBAC success, which proved IOL to be a significant variable associated with a lower rate of vaginal delivery [10].

Many studies supports that IOL is associated with higher rate of cesarean section as compared to spontaneous labor (77.1% vs 57.9%) and uterine scar separation as compared to the elective cesarean section group (7% vs 1.5%). While this study, did not show such association [14].

The use of epidural analgesia in the presence of previous scar remains controversial. Some authors have expressed fear that it may mask the pain of uterine rupture while others have advocated its relative safety provided continuous fetal monitoring is used [77]. This study didn't show association of epidural analgesia with increased risk of CS and the risk of uterine dehiscence [17].

If a woman has not had a previous vaginal delivery, the incidence of repeat emergency CS after induction is high and the need to induce labor should be reconsidered [77]. This study didn't show the difference in success rate of two groups with or without history of previous vaginal delivery.

Most of the studies have identified different factors which affect the successful VBAC; these factors are induction of labor, previous vaginal delivery, indication of previous cesarean section, bishop score, use of epidural analgesia, fetal birth weight, maternal age, maternal height and gestational age. Some authors have concluded that in women, contemplating TOL after previous cesarean section, there is less chance of successful vaginal delivery if; at the index pregnancy, oxytocin is used, contractions last longer than 12 hours, or cervical dilatation progressed slowly [58, 66], but this study has failed to show their association with the outcome. We accept that the small numbers in the studied subgroups limits its power to draw significant conclusions. Therefore studying a larger group would help draw more significant results.

A TOL after previous CS has been accepted as a way to lower down the overall CS rate and published evidence suggests that the benefits of VBAC outweigh the risks.

The stimulus for the interest in VBAC was the progressive rise in CS rate. The current clinical evidence suggests that VBAC is advantageous to the mother and has no adverse effects on the fetus. Although there is no doubt that TOL is a relatively safe procedure, it is not risk free and should not be undertaken in a casual fashion.

CONCLUSION

This study is concluded by saying that there is no affect of previous vaginal delivery, epidural analgesia, fetal distress and baby's gender on the outcome of TOL. The rate of successful VBAC is not significantly different in the group of IOL and spontaneous labor. The IOL does not result in increased risk of failure to deliver vaginally, as compare to the women presenting in spontaneous labor.

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Original Article

Atypical Nephrotic Syndrome

Histopathologic and Clinicopathologic Correlations in Children with Atypical Nephrotic Syndrome

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ABSTRACT

Objective: To find histopathologic and clinicopathologic correlations in children with atypically presented nephrotic syndrome.

Study Design: Retrospective observational study

Place and Duration of Study: This study was carried out at the Department of Paediatric Nephrology, Children's Hospital & Institute of Child Health, Multan, Pakistan **f**rom December, 2005 to January, 2014.

Materials and Methods: Medical record and the biopsy reports of 80 children (age 1-15 years) with nephrotic syndrome, who had atypical features at presentation and had a renal biopsy, were analyzed. Atypical features included hypertension, gross hematuria, hypocomplementemia, impaired renal function, and age more than 12 years, or manifestation of other systemic diseases in children.

Results: Overall results showed hypertension as the commonest (90%) atypical feature followed by impaired renal function (65%), atypical age (53.7%), gross hematuria (41.3%), and hypocomplementemia (31.3%). Histopathologic reports revealed non-MCD lesions in 76 (95%) cases. The commonest lesion was FSGS (25%) followed by MesPGN (23.8%), MCGN (17.5%), and LN (12.5%). Out of the total 80 patients, 62 were idiopathic atypical nephrotic syndrome cases and 18 were secondary (due to some underlying systemic cause) nephrotic syndrome cases. Secondary causes, in decreasing frequency, included lupus nephritis/nephrosis (LN) (n=10; 55.5 %), hepatitis B virus associated nephrosis (HBVAN) (n=4; 22.2%), Henoch Schonlein Purpra nephritis/nephrosis (HSPN) (n=2; 11.1%), hepatitis C virus associated nephrosis (HCVAN) (n=1; 05.5%), renal amyloidosis (RA) (n=1; 05.5%).

Conclusion: Renal biopsy done at the onset of atypically presented nephrotic syndrome provides useful guidance to the final diagnosis. Non-MCD lesions predominate. Some secondary nephrotic syndrome patients also present as atypical nephrotic syndrome; further clinical and laboratory evaluation reveals the secondary cause.

Key Words: Atypical nephrotic syndrome, secondary nephrotic syndrome, children, renal biopsy.

INTRODUCTION

Nephrotic syndrome in children is the most common renal disease with median age at presentation of 4 years. It is characterized by heavy urinary protein losses. Typical cases of nephrotic syndrome are mostly (> 90%) steroid responsive with minimal change disease being the commonest histopathology (~ 80%).[1] Therefore, these children are started on steroids without recourse to renal biopsy. However, renal biopsy may be indicated in children who present clinically with nephrotic syndrome and who also have some atypical features which may indicate other unusual underlying histopathologial lesions or systemic diseases that affect the kidneys.[2-6] These atypical cases may require specific management protocols and other supportive care. The atypical features may include age less than 12 months or greater than 12 years, persistent hypertension, impaired renal function, gross hematuria, hypocomlementemia (low C3), or presence of extra renal clinical manifestations.[1,5] There is limited data about histopathological variants in nephrotic children and adolescents who present with atypical features and those with underlying systemic diseases. Available results also show changing trends of histopathological lesions.[7-13]

The Children's Hospital and the Institute of Child Health, Multan, Pakistan is a tertiary care referral hospital draining pediatric patients from a wide population area. Nephrotic syndrome is one of the commonest renal diseases being referred to this hospital for detailed evaluation. The present study was designed to elucidate the spectrum of underlying glomerular lesions in the atypically presenting nephrotics with primary renal disease or with any underlying secondary cause and also to evaluate the clinicopathologic correlations in these patients.

MATERIALS AND METHODS

In this observational retrospective analysis, medical record of 80 nephrotic children, who had one or more atypical features at presentation, was reviewed. These children were biopsied between December, 2005 to January, 2014. The inclusion criteria were nephrotic syndrome with one or more atypical features at disease onset which include age $\geq$ than 12 years, gross hematuria, persistent hypertension, deranged renal function tests, decreased C3 level, or extrarenal

systemic disease manifestations. Congenital (age < 3 months) or infantile onset (age < 1 year) nephrotic syndrome cases were excluded because these may be hereditary, syndromic or due to congenital infections. Also, the patients with typical acute post-streptococcal glomerulonephritis and those with any absolute contraindication to renal biopsy were excluded. For the purpose of this study nephrotic syndrome was defined as massive proteinuria of > 40mg/m^2/hour or spot urinary protein-creatinine ratio >2(mg:mg), presence of edema, and serum albumin <2.5g/dl. Gross hematuria was defined as urine grossly red or cola colored with RBCs field full or numerous on microscopy. Hypertension was labeled when systolic and/or diastolic blood pressure was persistently $\geq$ 95th centile for age, gender and height on 3 separate readings. Hypocomplementemia was taken as C3 level less than age specific lower limit (< 77mg/dl for age 1-10 years and <83mg/dl for age more than 10 years). Impaired renal function was defined as serum creatinine more than the upper limit of normal for age. Age $\geq$ 12 years was considered an atypical feature in this study.

In the prepared patients, ultrasound guided percutaneous renal biopsy was performed with Dr. J Fine Core Disposable Semiautomatic Biopsy Needle (size 16 G x 150 mm) under local anaesthesia. Two to three cores of renal tissue were taken. Biopsy specimen, preserved in formalin, were sent to the histopathologist at Dr. Zia-ud-Din University Hospital, Karachi for histopathological review by light microscopy (LM) and immunofluorescence (IF) study.

Patients' name, age, date of admission, registration number, presenting complaints, details of history and physical examination, related laboratory tests and biopsy indications and results were obtained by a careful review of the record and the biopsy reports. The atypical features and the outcome variable, that is histopathological lesions, were noted.

Data was analyzed using statistical software SPSS-19. Descriptive statistics were applied to analyze the data. The quantitative variables were calculated by mean and standard deviation and qualitative variables by percentages and frequencies. Various crosstabulations were used to evaluate the clinicopathologic correlations.

RESULTS

In the present study a total of 80 patients, who were biopsied due to atypical nephrotic syndrome, were included. Mean age was 10.94 $\pm$ 2.82 years with an age range of 4 to 15 years. Age at presentation was highest in the age group 12 to 15 years (n=43; 53.7%) with a mode of 13 years. There were 23 (28.7%) patients in the age group 8 to 11 years and 14 (17.5%) patients in the age group 4 to 7 years. No atypical nephrotic syndrome patient was seen between 1 to 4 years age. Sex- wise break-up showed 50 (62.5%) males and 30 (37.5%) females with a male to female ratio of 1.7.(Table I).

Table No.I: Demographic characteristics of patients (N=80)

Age Group (Years)	Male	Female	Total
1-4	00	00	00
>4-7	10 (12.5%)	4(5%)	14(17.5%)
>7-11	14 (17.5%)	9(11.25%)	23(28.75%)
>11-15	26(32.5%)	17(21.25%)	43(53.75%)
Total	50(62.5%)	30(37.5%)	80(100%)

Table No.2: Correlation between histopathological lesions and atypical features.

Histopathological Lesion	Gross Hematuria	Low C3	Hypertension	Impaired Renal Function
FSGS (N=20)	01 (05%)	01 (05%)	19 (95%)	15 (75%)
MesPGN (N=19)	08 (42.1%)	02 (10.5%)	16 (84.2%)	08 (42.1%)
MCGN (N=14)	09 (64.3%)	09 (64.3%)	13 (92.9%)	12 (85.7%)
LN (N=10)	07 (70%)	10 (100%)	10 (100%)	08 (80%)
MGN (N=05)	00	00	04 (80%)	04 (40%)
MCD (N=04)	00	00	03 (75%)	00
CGN (N=04)	04 (100%)	03 (75%)	04 (100%)	04 (100%)
HSPN (N=02)	02 (100%)	00	02 (100%)	02 (100%)
IgAN (N=01)	01 (100%)	00	00	00
RA (N=01)	01 (100%)	00	01 (100%)	01 (100%)

Key: FSGS= Focal Segmental Glomerulosclerosis, MesPGN= Mesangioproliferative GN, MCGN= Mesangiocapillary GN, LN= Lupus Nephritis, MGN= Membranous GN, MCD= Minimal Change Disease,CGN= Crescentic GN, HSPN= Henoch Schonlein Purpra Nephritis, IgAN= IgA nephropathy, RA= Renal Amyloidosis

Renal biopsy reports showed focal segmental glomerulosclerosis (FSGS) as the most common lesion (N=20; 25%) followed by mesangioproliferative glomerulonephritis (MesPGN)(N=19; 23.8%), mesangiocapillary glomerulonephritis (MCGN)(N=14; 17.5%), lupus nephritis (LN)(N=10; 12.5% [08 had

diffuse proliferative LN and 02 had membranous LN]), membranous glomerulonephritis (MGN)(N=5; 6.3%), crescentic glomerulonephritis (CGN)(N=4; 05%) and minimal change disease (MCD) (N=4; 05%). Two patients of Henoch Schonlein Purpura nephritis (HSPN) with associated nephrotic state showed diffuse mesangial proliferation with crescentic GN.

One patient showed IgA nephropathy (IgAN) and another had renal amyloidosis (RA) detected on biopsy. Distribution of atypical features showed that seventy two (90%) patients had persistent hypertension, fifty two(65%) patients had impaired renal function at presentation, 33(41.3%) had gross hematuria, and hypocomplementemia (low C3) was present in 25(31.3%) patients. Clinicopathologic correlation between different atypical features and histopathologic lesions is given in table 2.

Table No.3: Causes of secondary nephrotic syndrome presenting as atypical nephrotic syndrome (N=18).

Causes	No. of patients	Positive serology	Histopathology
LN	10	Low C3, Low C4, anti dsDNA	DPGN(N=08), MGN(N=02)
HBVAN	04	HBsAg, HBV DNA(PCR)	MN(N=03), MesPGN(IgMN)
HSPN	02		MesPGN+CGN
HCVAN	01	anti HCV, HCV RNA (PCR)	MCGN
RA	01	RAF	RA

Key: LN= Lupus Nephrosis/Nephritis, HBVAN= Hepatitis B Virus Associated Nephrosis, HSPN= Henoch Schonlein Purpra Nephrosis/ Nephritis, HCVAN= Hepatitis C Virus Associated Nephrosis, RA= Renal Amyloidosis, anti dsDNA= anti double-stranded DNA antibody, RAF= Rheumatoid Arthritis Factor, DPGN= Diffuse Proliferative Glomerulonephritis(WHO class IV), MGN= Membranous Glomerulonephritis(WHO class V), MN= Membranous Nephropathy, MesPGN(IgMN)= Mesangioproliferative Glomerulonephritis with IgM nephropathy, CGN= Crescentic Glomerulonephritis, MCGN= Mesangiocapillary Glomerulonephritis

Eighteen (37.5%) patients had clinical or laboratory manifestation of other systemic diseases upon further evaluation. Ten patients (12.5% of total patients) had positive antinuclear antibody (ANA), low C3, low C4, and raised anti-double stranded DNA (dsDNA) antibodies; these were all cases of Lupus nephritis/nephrosis (LN) and renal biopsy showed diffuse proliferative LN in 8 patients and membranous LN in 2 patients. Four patients (05% of total patients) were Australia antigen (HBsAg) positive and HBV DNA by PCR (polymerase chain reaction) was also detected in blood; these proved to be hepatitis B nephritis/nephrosis and renal biopsy had supportive features (membranous nephropathy in 3, and mild mesangial proliferation with IgM nephropathy in one patient). One patient had positive anti-hepatitis C (anti HCV) antibody and HCV RNA was detected by PCR showing active viral replication; renal biopsy revealed MCGN secondary to HCV infection. Liver function tests were normal in these hepatitis B an C positive cases. (Table 3).

DISCUSSION

Atypical presentation amongst nephrotic syndrome cases in children and adolescents is not an uncommon occurrence.[11,12] The atypical features may include atypical age (<12 months and ≥ 12 years), hypertension, deranged renal function, gross hematuria, low complement[3], or some extra renal clinical manifestations of a systemic illness which may present with secondary nephrotic syndrome.[1,5] These patients are mostly steroid resistant and are associated with a high risk of developing chronic kidney disease. Hence, renal biopsy is required for diagnosis and specific treatment.[2-4] The incidence of various histopathological subtypes in atypically presented nephrotic syndrome varies from the typical idiopathic nephrotic syndrome and reports from around the world show changing trends.[7-14] Garg AK et al[14] in a study in 2009 in India on clinicopathological spectrum of renal biopsy in children showed that the commonest renal pathology in atypical nephrotic syndrome was MesPGN (38%) followed by MCD(18.2%) and FSGS(14.4%). They biopsied 51 out of 85 children with nephrotic syndrome at onset because of atypical presentaion. A study by Ejaz I et al[16] at King Edward Medical college, Mayo Hospital, Lahore, Pakistan in 2001 showed FSGS 42%, MCD 22%, MCGN(MPGN) 14% and MesPGN 12%. The indications for biopsy in these patients were atypical presentation, initial or late steroid resistance, or steroid dependant patients relapsing on <1mg/kg/day prednisolone. On presentation, 40% had hematuria, 20% were hypertensive, 12% had renal insufficiency, and in 4% C3 was low. A study at Sindh Institute of Urology and Transplantation, Karachi, Pakistan showed an increasing prevalence of FSGS over the years in Pakistani population with higher prevalence of atypical features.[7] A study done at Chittagong, Bangladesh by Mehmud NU et el[17] showed that in atypically presented nephrotic syndrome in children, there was male predominance with a M:F of 1.7. The most common atypical feature was atypical age (55.9%) followed by hematuria (13.6%), hypertension (10.2%), and low C3 level (1.7%). They took age < 2 years and > 8 years as atypical. We decided to include atypical age spectrum to < 1 year and ≥12 years because many patients between 1-2 years and between 8-12 years may present with no other atypical feature and may also be steroid responsive. Hence, undue renal biopsies were avoided. However, the biopsy was performed in these borderline

age group patients later on if they did not respond to steroid therapy. In another study done at Bangabandhu Sheikh Mujib Medical University, Dhaka by Begum A et al[12], in 40 children with atypical nephrotic syndrome, hypertension, gross hematuria, impaired renal function, and hypocomplementemia were observed in 50%, 45%, 19%, and 15% cases respectively. Histopathology revealed that 90% cases had lesions other than MCD. The results of our study also indicate that nephrotic children and adolescents presenting with atypical features are very likely to have histopathological lesions other than MCD, as only 4 patients out of the total 80 had MCD. It also showed that more the number of atypical features in any individual patient, more the chances of non-MCD glomerular lesion or some secondary cause of nephrotic syndrome. MesPGN was the commonest lesion (47.5%) in their study but it was the second commonest lesion in our study. The majority (56.8%) of their atypically presented nephrotic syndrome were resistant to steroid therapy. Gooden M et al[11] in 2010, in Jamaica, West Indies also showed that MesPGN was the commonest (31.2%) histology in atypical nephrotic syndrome. In our study, majority of patients had two or more atypical features at the first presentation. Overall, hypertension was the most frequent atypical feature followed by impaired renal function and atypical age. Persistent high blood pressure was present in the vast majority of atypical nephrotic patients in all the histopathological subtypes. Except for patients with MCD, most of the patients with other glomerular lesions had impaired renal function at presentation. Patients in the age group of 12-15 years had the highest number of atypical features. Also, the number of patients in this age group .was significantly higher than younger age groups (P value< 0.05). Sex predilection was female in cases of LN (8/10) and male in all other categories. This might be explained by the higher number of male patients in our study. Overall, gross hematuria was seen most frequently in patients with MCGN (27.3%), followed by MesPGN (24.2%), and LN (21.2%). It was also seen in all patients with CGN, HSP, IgAN and RA. As expected, hypocomplementemia was present in all patients with LN, 9/14 (64.3%) in patients with MCGN, and 3/4 (75%) patients with CGN. Hypocomplementemia in two patients with MesPGN and one patient with FSGS was unexplained.

Our study also included 18 patients with secondary nephrotic syndrome because their initial presentation was as atypical nephrotic syndrome but further clinical and laboratory evaluation done due to atypical features revealed the final diagnosis of secondary nephrotic syndrome. Ten patients were diagnosed to have lupus nephrosis with low C3 and C4, and positive anti dsDNA antibodies. Out of these 10 patients, 8 had diffuse proliferative LN (WHO class IV), and 2 showed membranous LN (WHO class V) on renal biopsy. Hafeez F et al[18] in a case series of LN in 26 children showed that diffuse proliferative LN was the commonest lesion (n=14), followed by membranous nephropathy (n=6). In their study, the commonest clinical manifestation was edema (80.76%) followed by hypertension (46.15%), hematuria (38.46%), and azotemia (19.33%). Proteinuria was present in 100% cases with nephrotic range proteinuria seen more commonly in WHO class III and IV. The results of an Italian Collaborative Study of lupus nephritis in children and adolescents showed that many patients have only renal disease at onset and lack sufficient criteria to diagnose SLE clearly.[19] Our LN patients also presented initially as nephrotic syndrome with some atypical features; but after further laboratory and clinical evaluation, they proved to be cases of SLE. In our study, Hepatitis B and C nephroses were detected because we routinely screen all the nephrotic patients for HBsAg and anti-HCV antibody status as a prerequisite before starting induction with steroids because there is risk of HBV or HCV reactivation with steroids. Positive cases on screening tests are confirmed with either ELISA (Enzyme Linked Immunosorbent Assay) or ECI (enhanced chemi-illuminescence). With normal liver function tests and positive immunoassay tests, the patients are further requested for PCR test. If PCR detects active viral replication, these patients are subjected to renal biopsy. Biopsies consistent with HBV and HCV associated nephritides are the candidates for specific anti-viral or interferon therapy. Many studies from around the world have shown that hepatitis B virus (HBV) may induce extrahepatic lesions in different organs. HBV associated glomeulonephritis is one of the more important extrahepatic diseases and nephrotic syndrome is its most common clinical manifestation.[20-22] According to these studies,the most common pathology is membranous nephropathy ; other lesions may be minimal change nephropathy, MesPGN, MPGN, and IgAN.[23,24] IgM nephropathy is rare but it was seen in one of our 4 patients; the rest 3 had MGN. One patient in our study proved to have hepatitis C virus (HCV) associated MCGN which manifested as nephrotic syndrome. Other studies favour such presentation.[25] Two patients with HSPN and one each with IgAN and RA had nephrotic proportion proteinuria at presentation. These are the rare cases with such presentation and have poor prognosis.[26-29] Our study combined primary atypical nephrotic syndrome cases with some secondary nephrotic syndrome patients who also presented as atypical nephrotic syndrome. It was after further evaluation that the secondary cause could be elucidated.

CONCLUSION

Vast majority of atypically presented nephrotic syndrome in children and adolescents had

histopathological lesions other than minimal change disease which is the commonest lesion in typical cases of nephrotic syndrome. Some atypically presented cases finally proved out to be secondary to systemic underlying cause. Renal biopsy at the onset of atypical nephrotic syndrome is very helpful to the final diagnosis.

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Original Article

Methicillin-Resistant Staphy.Aureus

Study on Alternative Therapeutic Agents on Methicillin-Resistant Staphylococcus Aureus from Clinical and Environmental Isolates

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ABSTRACT

Introduction: The in vitro antimicrobial activity of Sea buckthorn (SBT) (Hippophaerhamnoides), Green tea (Camellia sinensis) and Dandasa (Juglansregia) on selected methicillin resistant Staphylococcus aureus (MRSA) isolates from clinical samples was tested. The in vitro antimicrobial activity of six antiseptics/disinfectants against MRSA isolated from environmental samples was also evaluated.

Study Design: Experimental Observational.

Place and Duration of study: This study was conducted in Immunology and Infectious Diseases Research Laboratory (IIDRL) Lab, University of Karachi from January 2011 to July 2011.

Materials and Methods: Minimum Inhibitory Concentration (MICs) of plant extracts was determined by micro-broth dilution method and, susceptibility of MRSA isolates from environmental samples against antiseptics/ disinfectants was estimated by the agar disk diffusion and agar well diffusion methods.

Results: None of the plant extracts inhibited the isolates originating from blood samples. SBT offered comparatively more inhibitory zones and among the antiseptics/disinfectants, savlon was the most effective.

Conclusions: In view of the rising antibiotic resistance, exploring possible natural plant extracts for their antimicrobial action seems like an attractive substitute. The results showed some degree of susceptibility and can be suggested for use in vivoafter standard clinical trials.

Key Words: Antiseptics/Disinfectants, Methicillin Resistant, Plant Extracts.

INTRODUCTION

Pharmaceutical companies have a task of manufacturing multitudes of new antimicrobials with broad spectrum activity but the bacteria in turn become rapidly resistant. Therapeutic actions of plants and herbs have been investigated since ancient times due to their availability as locally grown, inexpensive, and applicable in a large spectrum of medical conditions. Medicinal plants are the only source of treatment for some communities[1], and especially have a role in primary health care. The practice of employing herbal medicine is widespread in Pakistan, India, Sri Lanka and the Far East. In United States, the use of herbal products has also increased from 33.8% to 42.1% between the years 1990 and 1997[2]. World Health Organization (WHO) estimates that 80% of world population uses herbal medicine for some form of primary healthcare[3]. Around the world, 35,000 to 70,000 plant species are used as traditional medicine, out of these, 20,000 species are commonly used in the developing countries. Approximately 6,000 species of plants grow in Pakistan and about 700 of them are known to have therapeutic properties, but less than 5% have been evaluated.[1] SBT has been used in traditional Chinese therapeutics since the Tang Dynasty, dating back more than 1,000 years. The leaves, flowers, fruit and roots of SBT are used in Pakistan for the last 2,000 years, for their anti-spasmodic and anti-helminthic properties[2]. The root extract of Glycyrrhiza is widely used as a cough medicine in Pakistan. Hyssop extract derived from Hyssopusofficinalis is used in the treatment of stomach ailments.[1] In our study, anti-microbial action was tested for Greentea (Camellia sinensis)[4] a widely consumed beverage; Dandasa (Juglansregia)[5], the stem of walnut tree, used as a common tooth cleaning agent; and, SBT (Hippophaerhamnoides)[6], the leaves and berries of this plant are widely eaten in the northern areas of Pakistan.

Contact spread puts a massive burden for infection control in the hospital and the environment. In, some studies staphylococcus organisms were retrieved for a period of up to two months after contaminating hospital environment.[7,8] It was therefore, instructive to assess commonly employed antiseptics and disinfectants in healthcare facilities for their antimicrobial potentials.

MATERIALS AND METHODS

The three plants used in this study were dried bark of the walnut tree: Dandasa(Juglansregia), Green tea (Camelliasinensis), berries of SBT (Hippopphaer-hamnoides).

Four strains of MRSA isolated from urine, pus, high vaginal swab and blood clinical samples were selected.

50 samples for culture from hospital environment were obtained from Civil Hospital Karachi, from door knobs, privacy curtains and toilets. Pre-moistened sterile swabs were applied to a 25 cm^2 area followed by direct plating on blood agar plates (Oxoid). Out of these, 11 (22.0%) isolates were characterized as MRSA.The isolates were tested as MRSA by Cefoxitin disk diffusion test and molecular characterization for mecA gene was done by Polymerase Chain Reaction (PCR) method of Geha et al[9]. ATCC 43300 was used as positive control for mecA gene.

Preparation of Aqueous Plant Extracts: A 5% solution of each of the dried plant material was prepared by heating in sterile distilled water at temperature of 95°C in water bath for two minutes followed by cooling for 2 minutes. The extracts obtained were centrifuged at 10,000 rpm for half an hour. Supernatants were filtered through sterile membrane filter 0.22 µm filter unit (Millex-GS, Millipore), stored at -20°C.

Determination of MICs of Plant Material by Microbroth Dilution Method: Concentrations tested ranged from "neat" (undiluted) in well #1 (concentration: 5000 µg/ml) to 1:512 in well #10 (concentration: 9.77 µg/ml). In sterile flat-bottomed 96 well plates (Becton-Dickinson, Oxford, England), two fold serial dilutions of each extract were prepared in Mueller Hinton Broth (Oxoid). The inoculum size was $5x10^5$ CFU/ml, final volume of broth achieved in each well was 100 µl. Well inoculated with the control strains (ATCC 43300) (#12) were taken as positive control. Negative control wells (#11) consisted of plant extracts only. Highest dilution of the plant extracts showing no turbidity were recorded as MIC.

Effect of Antiseptics and Disinfectants on selected S. aureus Isolates: Dettol: Antiseptic. (Chloroxylenol solution: Para-chloro-metaxylenol 1.44% w/v, terpineol 1.8% w/v) (Reckitt Benckiser, Lysol: Antiseptic. (Cresol 500ml, linseed oil 180 gm, potassium hydroxide 42 gm, solution) (LCPW/Howards), Pyodine: Antiseptic. (Povidone-iodine 10%, aqueous solution) (Brooks Pharmaceutical Lab,), Hibiscrub: Disinfectant (Chlorhexidinegluconate 4%) (ICI), SteriliumVirugard: Antiseptic/disinfectant. (Ethanol) (BODE), and Savlon: Disinfectant. (0.3% w/v Chlorhexidinegluconate, 3% w/v Cetrimide, aqueous solution).

a) **Agar-Disk Diffusion Method:** Whatman's 12.6'' filter paper disks (6 mm diameter) were punched out and placed in Petri dishes at a distance of 2 to 4 mm, and sterilized in hot air oven at 160°C for 1 hour. 30 µl of the antiseptic/disinfectant were transferred onto one of these disks, and dried in incubator at 37°C for 1 hour. The disks filled with antiseptic/disinfectant were labeled and stored at 4°C. MRSA isolated from hospital environment (n=11) were prepared for the inoculum turbidity to match 0.5 McFarland standard. A lawn of the isolate was made on a Mueller Hinton media, disks of each antiseptic/ disinfectant were placed at a distance of 15 mm. The plates were incubated at 37°C for 24 hours.

b) Agar-Well Diffusion Method: A lawn of the bacterialsuspensions was made on (MHA) plates six wells of 3 mm diameter spaced at equal distances were punched out. 30 µl from each antiseptic/disinfectant were transferred to the corresponding well. The plates were incubated at 37°C for 24 hours. The inhibitory zone around each well was measured.

RESULTS

The isolates positive for mecA gene 310 bp are shown in Fig 1.The MICs by microbroth dilution method using aqueous extracts Dandasa (Juglansregia), SBT (Hippophaerhamnoides) and Green tea (Camellia sinensis) in serial dilutions ranging from a concentration of 5000 µg/ml (undiluted) to 1:512 (concentration: 9.77 µg/ml) using the flat bottomed 96-well microtube tray were determined and shown in (Table 1a, 1b, 1c).

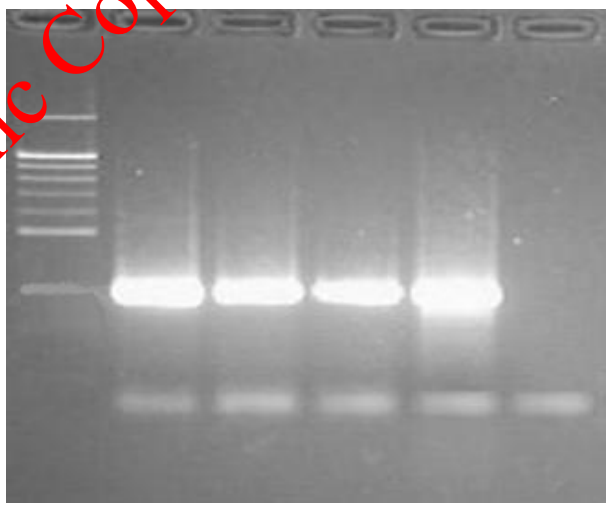

Figure No.1: Agarose Gel showing 310 bp products of *mecA* gene by PCR

Lane 1 --- DNA ladder
Lane 2 --- mecA gene positive control
Lane 3-5 --- mecA gene positive isolates
Lane 6 --- mecA negative control

The highest dilutions of extracts showing no visual turbidity in the microtubes were recorded as the MIC.None of the plant extracts, in concentration of 5000 µg/ml inhibited MRSAstrainsoriginating from blood samples (Table 1a, 1b, 1c). SBT offered comparatively more inhibitory zones as compared to Green tea and Dandasa on isolates from high vaginal swab (MIC ≤ 156.25µg/ml) and significant effects in a dilution of 1:256 (MIC ≤ 39.06µg/ml) on urine and pus

strains. Green tea extract had a (MIC ≤ 1250 mg/ml) on strain high vaginal swab and (MIC ≤ 625µg/ml) on both strains urine and pus. The Dandasa extract was the less effective (MIC ≤ 2500µg/ml) on strains urine and pus, but more on strain high vaginal swab (MIC ≤ 312.5 µg/ml).

The inhibitory action of antiseptics/disinfectants by well-diffusion in a Petri dish is illustrated in (Fig. 2). Savlon was the most effective antiseptic/disinfectant. Lysol, Hibiscrub, Dettol and Iodine displayed "intermediate" zones of inhibition. Sterilium was the least effective.

Table 1a: MIC Estimation Sea buckthorn against MRSA

Sr.	Dilution	MIC (µg/ml)	A*	B*	C*	D*
1	Neat	5000	-	-	-	+
2	1:2	2500	-	-	-	+
3	1:4	1250	-	-	-	+
4	1:8	625	-	-	-	+
5	1:16	312.5	-	-	-	+
6	1:32	156.25	-	-	-	+
7	1:64	78.13	-	-	+	+
8	1:128	39.06	-	-	+	+
9	1:256	19.53	+	+	+	+
10	1:512	9.77	+	+	+	+
11	Negative control	-	-	-	-	-
12	Positive control	+	+	+	+	+

*Isolates used;
A- Code No.m-7723 (Urine)
B- Code No. m-7709 (Pus)
C- Code No. m-7936 (High Vaginal Swab)
D- Code No. m-8376 (Blood)

Table 1b: MIC Estimation of Green Tea against MRSA isolates.

Sr.	Dilution	MIC µg/ml	A*	B*	C*	D*
1	Neat	5000	-	-	-	+
2	1:2	2500	-	-	-	+
3	1:4	1250	-	-	-	+
4	1:8	625	-	-	+	+
5	1:16	312.5	+	+	+	+
6	1:32	156.25	+	+	+	+
7	1:64	78.13	+	+	+	+
8	1:128	39.06	+	+	+	+
9	1:256	19.53	+	+	+	+
10	1:512	9.77	+	+	+	+
11	Negative control		-	-	-	-
12	Positive control		+	+	+	+

*Isolates used;
A- Code No.m-7723 (Urine)
B- Code No. m-7709 (Pus)
C- Code No. m-7936 (High Vaginal Swab)
D- Code No. m-8376 (Blood)

Table 1c. MIC Estimationof Dandasa against MRSA isolates.

Sr.	Dilution	MIC µg/ml	A*	B*	C*	D*
1	Neat	5000	-	-	-	+
2	1:2	2500	-	-	-	+
3	1:4	1250	+	-	-	+
4	1:8	625	+	-	-	+
5	1:16	312.5	+	+	-	+
6	1:32	156.25	+	+	+	+
7	1:64	78.13	+	+	+	+
8	1:128	39.06	+	+	+	+
9	1:256	19.53	+	+	+	+
10	1:512	9.77	+	+	+	+
11	Negative control		-	-	-	-
12	Postive control		+	+	+	+

*Isolates used;
A- Code No.m-7723 (Urine)
B- Code No. m-7709 (Pus)
C- Code No. m-7936 (High Vaginal Swab)
D- Code No. m-8376 (Blood)

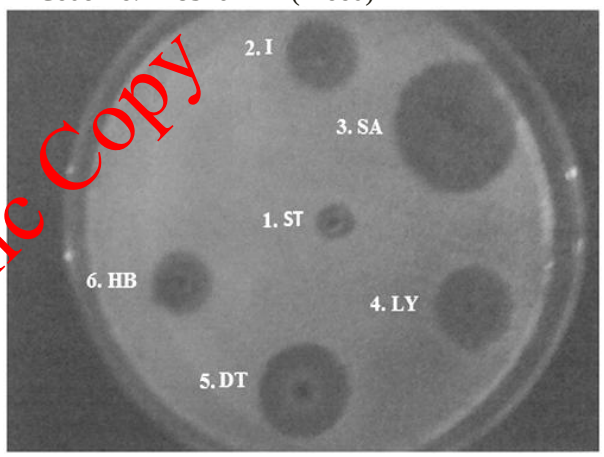

Figure No.2: Zones of Inhibition by Disk Diffusion method of antiseptics/disinfectants against MRSA.
[1. Sterillium (ST), 2. Iodine (I), 3. Savlon (SA), 4. Lysol (LY), 5. Dettol (DT), 6. Hibiscrub (HB)].

DISCUSSION

Pakistan has an abundant plant flora, including those with medicinal properties that are being used for centuries for therapeutic purposes.[10] Our study evaluated the efficacy of crude extracts of three locally grown plants on MRSA isolates retrieved from clinical samples. These included Green tea(Camellia sinensis), Dandasa (Juglansregia), and SBT (Hippophaer-hamnoides). A chemical analysis of active fractions from SBT leaf extracts has led to the finding of a phytochemical drug Hiporamin that possesses a wide spectrum of anti-microbial and anti-viral activity. Hiporamin is a purified form of polyphenol fraction, containing hydrolysable tannins. Green Tea (Camellia Sinensis) has been reported to consist of a variety of components, including polyphenols like catechins and

flavonols.Some of the important actions include its ability to activate leucocytes, and act as an antioxidant, antimutagenic[11], it also reduces plasma cholesterol levels[12]. Walnut (Juglansregia) has anti-inflammatory, antidiarrheic, antihelmintic, antiseptic and astringent properties.[13,14] In our study, none of these extracts had any inhibitory action on the isolate recovered from blood. It may be that when a pathogen enters the blood it is a lethal strain combining multidrug resistance and other virulent properties. SBT had relatively more antibacterial because it is a good source of antioxidants and contains lipophilic and polyunsaturated fatty acids.[15] In a medicinal research, the consumption of SBT berries in 229 healthy individuals markedly raised the fasting plasma concentration of flavonols which has been reported to possess antifungal, antiviral and antibacterial activities[16]. Antioxidant potential of fractions is due to dienes, along with hydroxyl groups, which penetrate through the bacterial wall, disrupting and inhibiting the growth of bacteria[15]. The Total Phenolic Content (TPC) of crude SBT stem extracts has been calculated by a study to be 84 ± 29 mg gallic acid equivalent/g dry extract.[17,18] Studies have shown that SBT inhibits the growth of Bacillus cereus, Pseudomonas aeruginosa, Staphylococcus aureus and Enterococcus faecalis It decreasesTumor Necrosis Factor (TNF-α),and increased Interferon (IFN-γ) secretion from macrophages[19]. In a study MRSAwas isolated from the quarters of 73% infected patients, and 69% of colonized patients. It was concluded that every-day articles used by infected or colonized patients may well be converted into sources of dissemination.[20] In light of the above mentioned facts, the evaluation of six selected antiseptics/ disinfectants on 11 (22%) of MRSA strains retrieved from hospitalenvironment was valuable. Savlon was most and Sterillium was the leasteffective. Savlonhas both bacteriostatic and bactericidal activities, its main mechanism of action being membrane disruption. Its antimicrobial action is associated with the attractions between chlorhexidine (cation) and negatively charged bacterial cells membranes. Cetrimide is a cationic quarternary ammonium compound, which acts a surfactant. Sterilium was the least effective a fact that should be noted by hospitals[21]. The action of biocides varies by concentration, time and temperature[22].

CONCLUSION

In view of the fact, that there is a growing demand for finding new effective drugs due to the rising resistance to existing antibiotics, derivatives from some plants look like an attractive substitute. These plant derivatives do not have any side effects, are easily available and can be used for treatment as eye/ear drops, or topical treatments. They have an important role in the prevention of biofilm formation on medical devices and catheters.

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Original Article

Trachiobronchial Foreign Bodies

Types, Management and Complications of Trachiobronchial Foreign Bodies

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ABSTRACT

Objective: To determine the types, management and complications of tracheobronchial foreign bodies.

Study Design: cross sectional study

Place and Duration of Study: This study was conducted at ENT Department of Nishtar Hospital Multan from January 2010 to December 2011.

Patients and Methods: 150 patients underwent rigid bronchoscopy under general anesthesia after routine investigations and x-rays chest where feasible.

Results: A total 150 patients underwent bronchoscopy for diagnostic as well as therapeutic purposes. Most common foreign bodies were peanuts (40.66%), beetle nuts (18.66%) and whistles (18.66%). In 137 (91.33%) patients, foreign bodies were removed on bronchoscopy at first attempt. 10 (6.67%) cases were diagnostic and only 2 (1.33%) cases were subjected to open surgical removal. One (0.67%) of the patients died in ICU after removal of foreign body.

Conclusion: Early diagnosis and timely management of foreign bodies with bronchoscopy saves patients life and avoids complications. Younger children should not be offered peanuts, whistles or toys that can be inhaled.

Key Words: Foreign body airway, Tracheobronchial tree, Bronchoscopy

INTRODUCTION

Foreign body (FB) aspiration causes thousands of deaths each year as they sometime do not reach in time for intervention all over the world[1].It is 4th leading accidental cause of death under 3 years of age and 3rd most common cause of death under one year of age[2]. FB aspiration is one of the most life threatening conditions which need urgent intervention. In this context, bronchoscopy is a life saving procedure for FB removal in emergency set-up as well as a therapeutic procedure and a diagnostic tool for tracheobronchial tree[3]. Most of the time FB aspiration is encountered in children.The patients may present with respiratory distress, chocking, protracted wheeze, dysphagia, stridor or recurrent chest infections or unilateral recurrent pneumonia. Types of FBs usually differ with geographical locations[4]. Watermelon seeds in Turkey, fish bones in Greece and Asia are the most frequent causes of FB inhalation[5]. In Pakistan, by contrast, peanuts, coins, small toys, betel-nuts and whistles are the most common FBs[6].

For the establishment of diagnosis, definite history and proper examination play a major role. Management of inhaled FBs depends on the sight of impaction. Laryngeal or subglottic FBs need urgent intervention in the form of tracheostomy or urgent bronchoscopy, where asFB in the bronchus cause comparatively less air way problem[7]. Most of the procedures are carried out with the rigid ventilating bronchoscope and grasping forceps under GA. Flexible bronchoscope has also been used for the removal of FBs in the tracheobronchial tree[8]. Sometimes FB inhalation may be asymptomatic[9] leading to pneumonia and even lung collapse, not responding to conservative treatment[10].

Nishtar Hospital Multan comprising 1400 beds including 48 beds of ENT department is one of the leading hospitals and drains a large area of Southern Punjab, Baluchistan and K.P.K. Most of the cases of FBs are referred from remotes areas. So we conducted a study to determine the type of FBs, mode of presentation, management and complications in terms of age and sex distribution so that we may design such a system to offer immediate management without any unnecessary delay.

MATERIALS AND METHODS

A cross sectional prospective study of 150 patients was conducted at ENT Department of Nishtar Hospital Multan (NHM) from January 2011 to December 2012 with the permission from the Ethics and DisciplineCommittee of NHM. Most of the patients were referred from remote areas as emergency cases and some of the patients were admitted through OPD or referred from Pediatric Department of Nishtar Hospital Multan and Children Complex Multan for urgent and sometimes for planned bronchoscopy.Mandatory investigations such as CBC, PT, APTT and viral markers were run and chest x-rays were obtained where feasible.

All the patients underwent rigid ventilating bronchoscopy. Risks and complications were explained

to the relatives and informed consent was taken. Some patients having chest pathology and resistant to conservative treatment underwent planned diagnostic bronchoscopy. All the patients presenting in emergency with the history of FB inhalation in the upper air way were subjected to urgent bronchoscopy and those in whom FB had settled to either of the main bronchus were put on routine elective list for bronchoscopy.All the patients were kept under observation for next 24 hours and x-ray chest were taken in each patient on next day of bronchoscopy except those in whom foreign body was in subgllotis or in the larynx. The patients were discharged to home or referred back to pediatric units after the observation of 24 hours. The patients who suffered from any complications were put for further observation and management. Data was analyzed using SPSS version 16 and tables were created to elaborate the results.

RESULTS

All the patients with definite history of foreign body aspiration or suspicion of foreign body lodged in their airway underwent bronchoscopy under general anesthesia. Male to female ratio was 1.56:1. Most of the patients (65.33%) were under 3 years of age. Duration between impaction and removal of FBs was from 24 hours to one year. 137 (91.33%) patients presented with definite history of FB inhalation while in rest of the patients(13 cases, 8.67%) they came into knowledge on x-ray or bronchoscopy. Most common type of FB encountered was peanut (40.66%), following were those of beetle-nuts (18.66%) and whistles (18.66%).

Table No.1: Types of foreign bodies.

Sr. No.	Types of foreign Bodies	No. of Cases	Percentage
Organic			
1	Peanut	61	40.66%
2	Beetle nuts	28	18.66%
3	Maize grains	9	6%
4	Peanut shell	6	4%
5	Beans	5	3.33%
Inorganic			
6	Whistles	28	18.66%
7	Beads	4	2.6%
8	Toy pistol bullets	3	2%
9	Metallic tracheostomy tube prong	3	2%
10	Steel nails	2	1.33%
11	Nose pin	1	0.6%

Different types of FBs are shown in table-1. In 137 (91.33%) patients, FBs were removed easily, successfully and uneventfully on bronchoscopy at first attempt, either from the bronchus or from the space between the vocal cords. 10 (6.67%) cases were diagnostic, 2 (1.33%) cases were subjected to preoperative tracheostomy and 3 (2%) patients underwent postoperative tracheostomy due to respiratory distress. One (0.67%) of the patients died in intensive care unit (ICU) after removal of foreign body. Site of FB impaction was right main bronchus in 108 (72%) cases, left main bronchus in 32 (21.33%) cases, glottis in 7 (4.6%) cases, and trachea in 3 (2%) patients.Difficult removal was associated with circular or oval shaped FBs such as toy pistol bullets and beads (table-2). Special grasping forceps were used for the removal of these FBs. Table-3 shows the incidence of foreign bodies in different age groups.

Table No.2: Difficult removal of foreign bodies

Sr. No.	Type of foreign body	No. of cases	Percentage
1	Peanut	8	44.4%
2	Beads	4	22.22%
3	Toy pistol bullets	3	16.66%
4	Nose pin	1	5.5%
5	Metallic Tracheos-tomy tube prong	2	11.11%

Table No.3: Foreign body aspiration in different age groups

Age in Years	No. of cases	Percentage
0-1	13	8.66%
1-3	98	65.33%
3-5	16	10.66%
5-12	18	12%
Above 8 years	4	2.66%

DISCUSSION

As we mentioned earlier that FB aspiration is fourth leading accidental cause of death in children under 3 years of age and third most common cause of death in children under one year of age[2]. It therefore refers to the acquisition of prompt diagnosis and instant management of the patients with FB aspiration. Sometimes it may lead to fatal consequences due delay in the removal of FB or when they are missed or left unnoticed[11].In this regard, our study reveals that NHM is offering its best services to the patients who present with the history of FB inhalation. It also indicates that in-time bronchoscopy is the best measure to deal with FB aspiration as over 90% FBs were removed at the time of the procedure and the patients were sent home after 24 hours.

In our study male to female ratio was slightly less than that reported by Kiyanet al[12]and Ezer et al[13]in Turkey. In Iran, Saki et al[14] reported male to female ratio 1.73:1. It means, regarding FB aspiration, male to female ratio is almost same in many areas of the world. In our study, children were the common sufferers (65.33%). In another study ontracheobronchial FBs carried out at Ayub Teaching Hospital, Abbottabad by Asifet al[15] from Pakistan, 77.8% patients were under five years of

age.In a study done by Yadavet al[16] in India, majority of the patients (46%) were under three years.Recently, Foltranet al[17] conducted a meta-analysis of English written articles referring to foreign body inhalation over a 30 years period (1978-2008) and reported that 20% of the patients were of 0-3 years.

In our study, the most common type of foreign body was peanuts (40.66%) while in the study by Ezeret al[13]in Iran seeds (63.87%) were the most common FB with peanuts making 9.8%.In another study by Asifet al[15], peanut (55.6%) was the most common FB. It reveals that in Pakistan, peanut is the most common FB, especially in children below three years of age. So, peanuts and other such edibles must be avoided until the children are able to adequately chew them.

In our study, we removed FBswith rigid bronchoscopy under general anesthesia as it is considered the gold standard management of airway FBs. More than 90% FBswere easily removed at first attempt. The advantage of rigid bronchoscope for the airway FB removal is that, at the same time, it works as an endotracheal tube[18]. Aydoganet al[19] studied 1887 patients with FB aspiration and used rigid brochoscopyto remove the FBs. However, other bronchoscopy techniques such as flexible bronchoscopy, suspension laryngoscopy, and fluoroscopy can also be used.

Most of the foreign bodies were removed from right main bronchus which is in line with trachea as seen in other studies also.In the study by Asifet al[15], 74.1% FBs were found in right main bronchus. Saki et al[14] reported 55.1% FBs lodged in the right main bronchus. Similarly, Gilyoma and Chalya[20] reported 75% FB impaction in the right bronchus in their study 98 patients with FBs in aerodigestive tract.

In our study, only4% patients experienced complications and 0.7% patient died postoperatively. This occurrence ofcomplications is low as compared to other studies. Tang et al[21] conducted a retrospective study in China and reported severe complications in 21.38% patients with the death of the three. Another retrospective study conducted in Turkey by Soysaletal[22] reported the requirement of thoracotomy in three patients and morbidity in 7.9% patients after bronchoscopy. Similarly, in a study on FB inhalayion by Passali[23] et al in Italy reported complications in 12.7% children. However, a study of 45 patients carried out in Poland by Korlackiet al[24]reported no complications at all. Here, we can comment that ENT department of Nishtar Hospital Multan is working wonderful in the management of foreign body inhalation with least incidence of complications.

CONCLUSION

Early diagnoses and bronchoscopy reduces the risk of complications as well as mortality in patients with foreign body aspiration.Whistles should not be packed as gifts in candies and necessary awareness should be offeredto the manufacturers.Edibles like peanuts and small toys should be kept out of the reach of children, especially from those who are less than 3 years of age.

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Original Article

Fungal Sinusitis

Role of MDCT in Diagnosis of Fungal Sinusitis

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ABSTRACT

Objective: To evaluate diagnostic accuracy of MDCT in diagnosis of fungal sinusitis.
Study Design: Cross sectional study.
Place and Duration of study: This study was conducted at the Department of Radiology PNS SHIFA Hospital Karachi from 18th April 2012 to 17th October 2012.
Materials and Methods: 126 patients of all ages and gender with clinical suspicion of fungal sinusitis were included in the study. Non-contrast enhanced axial and coronal CT performed on 16slice MDCT. 76%patients were male, 24% female, 98.4% were immunocompetent and 1.6% were immunocompromised. CT finding of mucosal thickening with hyper-attenuating areas in effected sinuses was considered CT diagnostic criteria for fungal sinusitis. Biopsy and histopathology performed in every case and histopathological diagnosis was considered as 'Gold standard' for comparison of CT findings. Findings of every patient were recorded on a specially designed Performa. SPSS version 10 used to calculate diagnostic accuracy of MDCT in fungal sinusitis.
Results: 32 (25.4%) patients showed mucosal thickening with internal hyper-attenuating areas in the sinuses representing fungal rhinosinusitis. Results compared with biopsy reports. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of CT scan in detection of fungal sinusitis were 100%, 93%, 78%, 100% and 94%. 5 (4%) patients showed intraorbital extension and 3 (2.4%) patients showed both intraorbital and intracranial extension of disease.
Conclusion: MDCT is very useful and accurate in diagnosis of fungal sinusitis. It should be considered as first investigation of choice to confirm or to rule out fungal sinusitis in clinically suspected patients. MRI should supplement MDCT in those cases of fungal sinusitis in which intraorbital or intracranial extension of disease is suspected.
Key Words: MDCT, Fungal sinusitis, hyper-attenuating areas in sinuses.

INTRODUCTION

Fungal sinusitis is a relatively common, but often misdiagnosed disease process involving the para-nasal sinuses. It is a serious condition as certain forms of fungal sinusitis are associated with a high rate of mortality [1]. Over the last two decades the incidence of fungal sinusitis has increased dramatically [2]. Successful treatment requires a prompt diagnosis and frequently relies upon radiologic imaging, specifically computed tomography and magnetic resonance imaging [3]. Now a days MRI is considered the imaging modality of choice for evaluation of suspected fungal sinusitis and has high accuracy in its detection and characterization [4]. Availability and its cost is a limiting factor for MRI. Multi-slice computed tomography (MDCT) is more easily available. So we conducted a study to see the sensitivity and specificity of MDCT in diagnosis of fungal sinusitis.

MATERIALS AND METHODS

This Cross sectional study was conducted at the Department of Diagnostic Radiology, PNS SHIFA Naval Hospital, Karachi from 6 months, 18th April 2012 to 17th October 2012.
Sample Size: 126 patients
Sampling Technique: Non-probability purposive sampling
Sample Selection Inclusion Criteria: Patients of all age groups and gender, with suspicion of fungal rhino-sinusitis presenting with all or any two of the following were included in study:

- Nasal obstruction with nasal discharge and Postnasal drip
- Chronic rhinosinusitis resistant to routine treatment
- Sinusitis with suspected intracranial extension
- Sinusitis with suspected intraorbital extension
- Sclerosis of sinus walls seen on plain x-ray in sjnusitis patients

Note: Already diagnosed cases of fungal sinusitis were not included in study.
Data Collection Procedure: All patients were explained Purpose & procedure of study including the risks & benefits. After taking informed consent from patients study proforma were filled. Approval from ethical committee of the institute, PNS SHIFA hospital, was also taken. Computed Tomography performed on **Toshiba Aquilion 16 Multi-detector CT (MDCT)** scanner. Non contrast enhanced CT was performed every patient in axial and coronal planes with scanning protocol of section thickness 3mm, collimation 3mm, reconstruction interval 3mm, mAs 140 and KV 120.

Scanning in every patient was done from hard palate to the top of the frontal sinuses. The image interpretation of the lesions in every case was done by a consultant radiologist having minimum 3 years of post FCPS experience. CT findings of every patient, regardless of scan result suggestive of either presence or absence of fungal rhino-sinusitis, were recorded on the proforma and histopathological finding of each patient whether positive or negative for fungal sinusitis were collected and documented on proforma.

Data Analysis Procedure: Data was analyzed on SPSS version 10. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of MDCT in detecting fungal rhino-sinusitis was calculated by considering histopathological findings as "gold standard".

Stratification was done with regards to age, gender and duration of symptoms to see the effects of these factors in CT diagnosis.

RESULTS

126 patients with suspected fungal rhinosinusitis, included in the study, were between 21 to 60 years of age. Out of 126 patients, 96 (76%) were male and 30 (24%) were female. 124 (98.4%) patients were immunocompetent and 2 (1.6%) were immune-compromised.

Out of 126 patients, 32 (25.4%) patients showed mucosal thickening and soft tissue areas with internal hyper-attenuating areas with calcifications in the sinuses representing fungal rhinosinusitis. Other 32 (25.4%) patients showed only mucosal thickening without hyper-attenuating areas consistent with simple chronic sinusitis. 7 (5.6%) patients showed mucous retention cyst. 10 (7.9%) patients showed neoplastic lesions involving para-nasal sinuses.

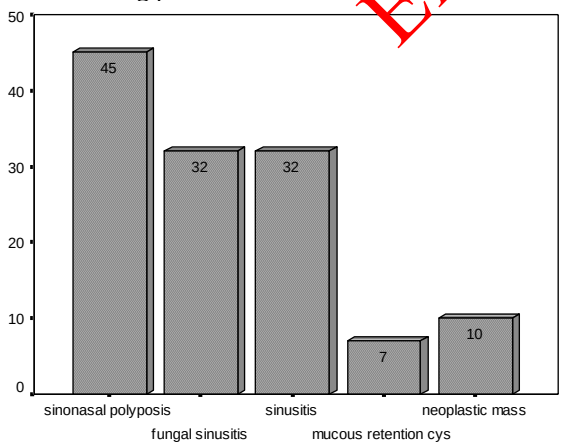

Figure-1: Graph showing CT Scan Diagnosis of Paranasal Sinuses Lesions (n = 126)

True positive and negative outcome of CT scan and histopathology in detection of fungal infections of paranasal sinuses is presented in the table-1 appended below:

Table No.1: True positive and negative outcome of CT scan and histopathology in detection fungal infections in our study.

Computed Tomography Findings	Histopathological		Total
	Positive	Negative	
Positive	25 (TP)	7 (FP)	32(25.4%)
Negative	0 (FN)	94 (TN)	94(74.6%)
Total	25(19.8%)	101(80.2%)	126

The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of CT scan in detection of fungal infections of paranasal sinuses were 100%, 93%, 78%, 100% and 94% respectively as shown in figure below.

5 (4%) patients showed intraorbital extension and 3 (2.4%) patients showed both intraorbital and intracranial extension of disease which was later confirmed on MRI during further management.

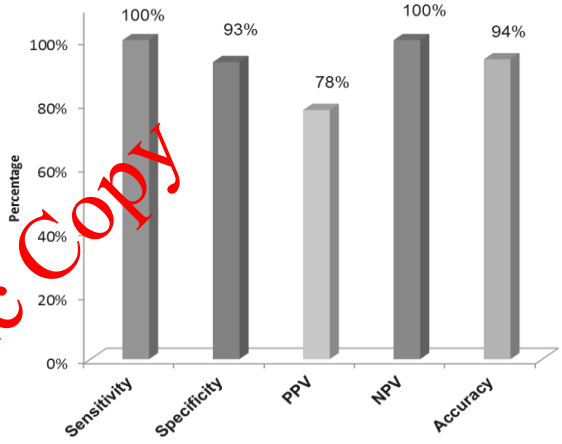

Figure No. 2: Diagnostic accuracy of CT scan in detection of fungal infections of para-nasal sinuses (n=126)

DISCUSSION

CT scan, with its inherent high contrast resolution, allows for excellent demonstration of bony architecture, air in the sinuses and soft tissue masses in paranasal sinuses and nasal cavity. CT scan should thus be superior to plain radiography in demonstrating fine areas of increased attenuation in soft tissue masses [5] .CT is the imaging study of choice in both adult and pediatric patients [6] . On plain X-Ray presence of bony sclerosis along with mucosal thickening is considered important in suspecting diagnosis of fungal sinusitis[7] whereas on CT presence of hyper-attenuating areas in sinuses is considered diagnostic of fungal sinusitis [8] .With fungal sinusitis, the maxillary and ethmoid sinuses are most commonly involved. Allergic fungal sinusitis can involve complete opacification of multiple paranasal sinuses, unilateral or bilateral; sinus expansion and erosion of a wall of the involved sinus; and high-attenuating areas scattered amid mucosal thickening on nonenhanced scans.

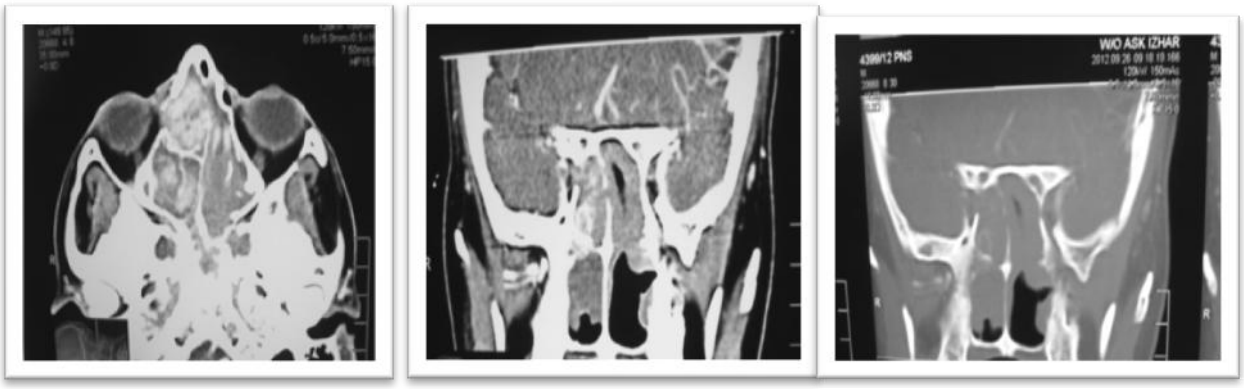

Fig No.3: Fungal sinusitis showing hyperdense areas in sinuses and bone erosion

These areas are due to inspissated secretions or heavy metals, such as iron, manganese, and calcium [9,10]. In our study out of 32 patients of fungal sinusitis, bony sclerosis was noted only in 8 patients (25%) on plain X-Ray whereas on CT internal hyper-attenuating areas with calcifications representing fungal rhinosinusitis was present in 25 out of 32 patients (78%). Vartanian and Meyers in 2012 noted hyperattenuating areas on CT in fungal sinusitis in 81%.[11] Intrasinus calcification on CT with aspergillosis is a characteristic feature of fungal sinusitis and is present in 69–77% of cases [12]. Hyperattenuating areas are due to calcium and magnesium salts deposited in the necrotic areas of the mycelia and fungus-infected mucin [13]. Calcification may occur with other pathologic processes, such as bacterial sinusitis, mucoceles, and neoplasms, but it is uncommon in nonfungal inflammatory sinonasal disease [14]. Intrasinus calcification on CT with aspergillosis is a characteristic feature of fungal sinusitis and is present in 69–77% of cases [13]. The shape and location of calcification in nonfungal cases are different from those of fungal sinusitis. Calcification in fungal cases is primarily centrally located in the maxillary antrum, whereas the calcification in nonfungal cases is usually peripheral, near the wall of the maxillary sinus. Fine punctuate calcification has been identified only in fungal sinusitis, although smooth, marginated, round, or eggshell calcification has been found exclusively with non-fungal disease [15]. So, presence of hyper-attenuating areas or calcification in sinuses on CT is an important diagnostic feature of fungal sinusitis. Pattern and location of calcification in the sinus should also be considered while making the diagnosis of fungal sinusitis and ruling out other causes of calcification in sinuses.

Other noteworthy CT features of fungal sinusitis are reactive changes in bones of sinus wall and infiltration of adjacent soft tissue with bone destruction in the case of invasive fungal sinusitis [16] CT is very sensitive for early detection of bone erosion. CT is the primary imaging modality and is probably more accurate than MRI in diagnostic specificity and determining the extent of bone erosion [17]. In this study, erosions of lamina papyracea was noted in 28 patients (87%) out of 32 patients of fungal sinusitis. Del Gaudio in a study in 2003 found bone destruction / erosion in 71 % of his patients of invasive fungal sinusitis [8] Difference is due to stage and severity of disease process and pattern of sinus involvement. Bone destruction is common in advanced disease and when there is involvement of ethmoid sinuses [18]. In 1998, Silverman and his colleagues described soft tissue changes in the sinus with thickened reactive bone inflammation or with associated nasal inflammation as an early predictor of fungal disease [16]. Ramadan H and his colleagues in a study carried out on management of fungal sinusitis in 2011 found CT as an extremely useful diagnostic modality in detection of intracranial and intraorbital extension of disease process, an important factor in treatment planning .[19]

In many institutions, a limited CT scan costs about the same as a full radiographic series but provides more useful information [20,21,22]. Multiplanar reconstruction of images that is in axial, coronal and sagittal planes and viewing scans at both soft tissue and bone window levels was found very useful to depict and localize hyper-attenuating areas in sinuses and to detect bone erosion. It is recommended by others in their studies as well [18]. A noncontrast CT scan is usually sufficient, except for complicated acute sinusitis (e.g., periorbital cellulitis or abscess). We did not find any difference in CT appearance of fungal sinusitis with reference to age and sex of the patient. However disease was more aggressive in two immunocompromised patients and bone erosion was more common when ethmoid sinuses were involved which may be attributed to their small size and thin walls.

One limitation in our study was that we did not give IV contrast in these patients due to whom we felt difficulty in the differentiation of mucosal thickening from pus-filled areas of sinuses and in interpreting intraorbital and intracranial extension of disease.

CONCLUSION

CT, now commonly available radiological modality, is most practical primary imaging modality for suspected fungal disease of the para nasal sinuses. It has very high diagnostic sensitivity, specificity, positive predictive

value, negative predictive value and accuracy in detection of fungal sinusitis in the range of 100%, 93%, 78%, 100% and 94% respectively. It is probably more accurate than MRI in terms of defining degree and extent of bone erosion, whereas MRI is more sensitive to detect early inflammatory changes in intraorbital or intracranial soft tissues. While doing the CT in addition to routine axial scanning direct coronal scans should be obtained and IV contrast should be given in every patient. MRI should be used to supplement CT to further evaluate the extent and pattern of involvement of soft tissue structures once intracranial or intraorbital disease extension is suspected on CT.

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Original Article

Increasing Tendency of Rape with Females in Pakistan

Rape with females

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ABSTRACT

Objectives: To study the increasing tendency of rape with females in Pakistan.

Design of study: Observational study

Place of study: This study was conducted at the Emergency Departments of Gangaram Hospital Lahore, Mayo Hospital Lahore, Services Hospital Lahore, Shahina Jamil Hospital Abbottabad from 1st January 2012 to 31st May 2013

Materials and Methods: The cases of rape were selected from Services hospital Lahore, Mayo hospital Lahore, Shahina Jamil Teaching hospital Abbottabad and Gangaram Hospital Lahore. The data of rape with female was collected on proforma and analyzed for results.

Results: The incidence of rape was maximum at the age range 21 – 30 years (39 %) as compared to age range 60 and above (1 – 2 %). It was seen that incidence of rape was maximum in labor class of women as compared to house wives and business man wives 5 – 9 % which was minimum. In this study the incidence of rape with women was 55 % (55 cases) in lower class, 30 % in middle class (30 cases) but the victim of rape in high gentry was 15 % (15 cases). The Rape victims were 64 % (64 cases) in unmarried women and 36 % (36 cases) in married women. The incidence of rape was 41 % in urban area (41 cases) and 59 % (59 cases) in rural area. In this study 37 % (37 cases) were semen positive and 63 % (63 cases) were of semen negative. The injuries of private parts and rest of the body were present in 83 % victims of rape (83 cases) and 17 % (17 cases) were those victims in which the injuries were absent. At the last 91 % (91cases) were brought by the police for medico legal examination / certification and 9 % (9 cases) were come on their self request.

Conclusion: The tendency of rape with females is a global problem/sex assault due to, 1) internet use for sex stimulation, 2) Indian sexy movies, 3) the female mixing with males, 4) Co education, 5) Joint possession of offices, 6) Sexy Movies on cable, 7) Non religious gatherings & 8) Unawareness of Islamic teaching

Key Words: Rape, Sex behavior, Female, Islamic Teachings, Seminars, restricted internet, cable, Indian movies, sex related news/journals & literature.

INTRODUCTION

Rape, forceful sexual intercourse without her/his will, consent and marriage.

There are following types of rape,

a) Male to Female
b) Female to Male
c) Female to Female
d) Male to Animal

The causes of rape are followings

1) Internet use for sex stimulation
2) Indian sexy movies
3) The female mixing with males
4) Co education
5) Joint possession of offices
6) Sexy Movies on cable
7) Non religious gatherings
8) Unawareness of Islamic teaching

Statistics on rape and sexual assault are commonly available in advanced countries and are becoming more common throughout the world. Inconsistent definitions of rape, different rates of reporting, recording, prosecution and conviction for rape create controversial statistical disparities, and lead to accusations that many rape statistics are unreliable or misleading. According to USA Today reporter Kevin Johnson "no other major category of crime – not murder, assault or robbery – has generated a more serious challenge of the credibility of national crime statistics" than rape.[1]

The incidence of rape was much more in eureopeon countries as compare to Asian & especially Islamic countries[2], going to be increased day by day due to above causes and sexual frustration[3]. The incidence of rape with female is on the top which is evident from statistical reports of rape recorded by

a) Law and Force agencies
b) Doctors at emergencies department
c) On personal reports to the examination department[4].

Source:	Current or Former Intimate Partner	Another Relative	Friend or Acquaintance	Stranger
US Bureau of Justice Statistics	26%	7%	38%	26%
Australian Government Statistics[5]	56%	10%	27%	8%
UK Home Office (for comparison)[6]	45.4%	13.9%	29.6%	11%

MATERIALS AND METHODS

In this study 100 cases of female different rapes were selected at the Emergency Departments of Gangaram Hospital Lahore, Mayo Hospital Lahore, Services Hospital Lahore, Shahina Jamil Hospital Abbottabad from 1st January 2012 to 31st May 2013.
The data of rape with female was collected on proforma and analyzed for results.

RESULTS

The incidence of rape was maximum at the age range 21 – 30 years (39 %) as compared to age range 60 and above (1 – 2 %) as shown in Table No.1. It was seen that incidence of rape was maximum in labor class of women as compared to house wives and business man wives 5 – 9 % which was minimum as shown in Table No.2. In this study the incidence of rape with women was 55 % (55 cases) in lower class, 30 % in middle class (30 cases) but the victim of rape in high gentry was 15 % (15 cases) as shown in Table No.3. The Rape victims were 64 % (64 cases) in unmarried women and 36 % (36 cases) in married women as shown in Table No.4. The incidence of rape was 41 % in urban area (41 cases) and 59 % (59 cases) in rural area as shown in Table No. 5. In this study 37 % (37 cases) were semen positive and 63 % (63 cases) were of semen negative as shown in Table No.6. The injuries of private parts and rest of the body were present in 83 % victims of rape (83 cases) and 17 % (17 cases) were those victims in which the injuries were absent as shown in Table No. 7. At the last 91 % (91cases) were brought by the police for medico legal examination / certification and 9 % (9 cases) were come on their self request as shown in Table No. 8.

Table No.1: Incidence of rape with women with relation to age

S. #	Age (Year)	Cases	Percentage
01	10 – 20	10	10 %
02	21 – 30	39	39 %
03	31 – 40	31	31 %
04	41 – 50	17	17 %
05	51 – 60	02	02 %
06	61 – 70	01	01 %
	Total	**100**	**100 %**

Table No.2: Incidence of Rape with women with relation to occupation

S. #	Occupation	Cases	Percentage
01	Students	15	15 %
02	Laborer	31	31 %
03	Factory worker	15	15 %
04	Home wives	09	09 %
05	Business wives	05	05 %
06	Framer wives	25	25 %
	Total	**100**	**100 %**

Table No. 3: Incidence of Rape with women with relation to Socio – economic status

S. #	Socio – economic Status	Cases	Percentage
01	Lower class	55	55 %
02	Middle class	30	30 %
03	High gentry	15	15 %
	Total	**100**	**100 %**

Table No.4: Incidence of Rape with women with relation to Marital Status

S. #	Marital Status	Cases	Percentage
01	Married	37	37 %
02	Unmarried	63	63 %
	Total	**100**	**100 %**

Table No. 5: Incidence of Rape with women with relation to residential area

S. #	Residential area	Cases	Percentage
01	Urban	41	41 %
02	Rural	59	59 %
	Total	**100**	**100 %**

Table No. 6: Incidence rape with women with relation to semen positive / negative cases

S. No	Semen positive / negative	Cases	Percentage
01	Semen positive	37	37 %
02	Semen negative	63	63 %
	Total	**100**	**100 %**

Table No. 7: Incidence of rape with women with relation to injuries of private parts / rest of the body

S. No	Injuries private part & rest of body	Cases	Percentage
01	Injuries present	83	83 %
02	Injuries absent	17	17 %
	Total	**100**	**100 %**

Table No. 8: Incidence of rape with women with relation to case brought by police or on self request

S. No	Cases brought by	Cases	Percentage
01	Brought by Police	91	91 %
02	Self request	09	09 %
	Total	**100**	**100 %**

DISCUSSION

The Rape is global problem, it is increasing day by day even in Muslim countries like Pakistan, Bangladesh, Afghanistan and Arabic countries where these offences are prohibited (Haraam) in Islam [13]. The causes of Rape are following [14]

1) Internet use for sex stimulation
2) Indian sexy movies
3) Mix gathering of Male and Female
4) Co education

5) Joint possession of offices
6) Sexy Movies on cable
7) Non religious gatherings
8) Unawareness of Islamic teaching

CONCLUSION

The increasing tendency of rape with females in Pakistan can be reversed or minimized due to

a. Seminars on side effects/complications of mix gathering
b. Islamic Teachings about Sex behavior
c. Restricted use of internet, cable, Indian movies, sex related news/journals & literature by adolescents/ adults
d. Education about sexual behavior
e. Early marriage

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Original Article

Bio-Safety, Biohazards of Ht. Staff

Evaluation of Knowledge Attitude and Practice of Health Care Staff on Bio-Safety and Biohazards, District Pakpattan - Punjab

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ABSTRACT

Objectives: To evaluate the knowledge, attitude and practice of health care staff on bio-safety and biohazards in District Pakpattan.

Study Design: Cross Sectional epidemiological Study.

Place and Duration of Study: This study was conducted in District Pakpattan Punjab, Pakistan from 1st August 2013 to 30th August 2013.

Materials and Methods: The study was carried out to evaluate the knowledge attitude and practice on bio-safety and biohazards of health care providers, who are directly involved in the patient handling e.g. doctors, lady doctor, laboratory and blood bank technicians, Nurses, Dispensers, Lady Health Visitors, Vaccinators ,OT Assistants, dental technicians, dental surgeons, while others were excluded. The target population was 552, and 33% (N=184) population was included in the study as non probability sample to reduce the bias in this reference epidemiological study. A standard questioner was pretested to identify weaknesses and strengths. Respondents interviewed individually and data was analyzed by using SPSS.15.0 for Widows Evaluation Version. Keeping Ethical Consideration in view, formal consent and permission was obtained from concerned Authorities and respondents.

Results: The study results on the variables were as; 27(14.6%) had specific training on bio-safety and biohazards,157(85.3%) had no structured training. 96(52%) respondents had habit of eating at work place, laboratory, dressing or examination rooms , 83(45%) don't have this habits or practice while 6 (3.2%) do this practice sometimes. 98(53%) had habits of storing edibles in the refrigerators meant for vaccines or laboratory purpose, 84(45.6%) don't have this habits and 2(1.0%) do this practice sometimes. Among females(N=91), 35(38.4%)using cosmetics at work place,42(46%) don't have this habits or practice,11(12%) do this practice sometimes. 0ut of 161 the 62(40%) had habits of smoking or sniffing at work place, 99(60%) don't have this habits or practice . 89(48.3%) had habits of cutting nail with teeth and putting pen in the mouth at work, rest 93(50%) don't have this habits or practice.

Conclusion: The study results are consistent and supported by many studies already conducted. Results showing poor knowledge, attitude and poor practices. It demonstrates the serious need of trainings on bio-safety and continuous monitoring on the practices to minimize the health risk, which is a hidden public health problem.

Key words: Bio-safety, bio-hazards, knowledge, attitude and practices, health care providers

INTRODUCTION

Sharps and the biohazardious materials are the major risk among health care and laboratory workers who are threatened by human pathogens. The biological hazards are defined as "A biological agent or condition (as an infectious organism or insecure laboratory conditions) that constitutes a hazard to man or his environment; also a hazard posed by such an agent or condition".[1]

Blood and certain fluids of all patients are considered potentially infectious for HIV,HBV and blood born pathogens[2]. Laboratory workers are exposed to large pool of specimens from patients suffering from infectious such as HBV & HIV[3-4].However they seems to have poor perception of risk of infection and are not compliant with the basic principles of universal precautions.[5-6]

Around 250,000 tonnes of medical waste is annually produced from all sorts of health care facilities in the country which has bad affect on the environment and surrounding and 15 tons of waste is produced daily in Punjab.

Different types of exposure, contact with highly dangerous agents, lack of limit values able to compare all exposures, presence of workers with defective immune systems and therefore more susceptible to the risk.

Vaccination represents an effective tool to minimize risk of occupational and nosocomial transmission for many relevant communicable diseases.

Occupational exposures to biological agents can occur in several sectors, such as health, agriculture, forestry, animal husbandry, food, veterinary, biotechnology,

waste processing and disposal, laboratories, and dentistry, [7-8]

The likelihood of acquiring an infection after occupational exposure is < 0.3% for HIV, 0.5% for HCV, and 18% to 30% for HBV[9].

Transferring the knowledge of preventive measures into practice by health care personals remains inadequate[10]. In Italy most of the data has been collected in hospital settings and, more specifically, by surveys of nurses[11-12].

Percutaneous exposure incidents (PEIs) (needle stick, sharp injuries, as well as splashes leading to exposure of the skin or mucosa to blood) are a major concern in hospitals even in developed countries such as the United States [13-14]. PEIs may increase hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) transmission risk in the healthcare setting has been thoroughly reviewed in the literature and post exposure prophylaxis, when available, is therefore recommended [15]. The under reporting of PEIs by doctors may be related to their unwillingness to reveal the incidence or lack of motivation due to the belief that they can handle the issue themselves [16]. Other studies have shown that a vaccination program in healthcare workers against HBV is cost-effective, decreases the anxiety of an employee after needle stick and sharp injuries, and prevents the transmission of HBV after exposure in the majority of cases [17-18].

Exposure to chemical and physical hazards, lack of safety training, and low levels of safety climate and safety practices remained significant risk factors for Work Related Injuries[19].

MATERIALS AND METHODS

This was cross sectional epidemiological study. Sample size was (N=184) Health care providers under effect of this study were 552, pertaining to the categories mentioned in inclusion criteria. 33% health care providers were selected randomly to reduce the bias in this reference epidemiological study.

Health staff who were directly involved in the patient handling e.g. doctors, lady doctors, laboratory and blood bank technicians, Lab Attendants, Nurses, Dispensers, Lady Health Visitors, Vaccinators ,Operation Theatre Assistants, dental technicians, dental surgeons, surgeons and gynaecologists were included while other health care personals were excluded. Keeping Ethical Consideration in view, formal consent and permission was taken from concerned Authorities and respondents.

Data Collection, Procedure and Data Tools

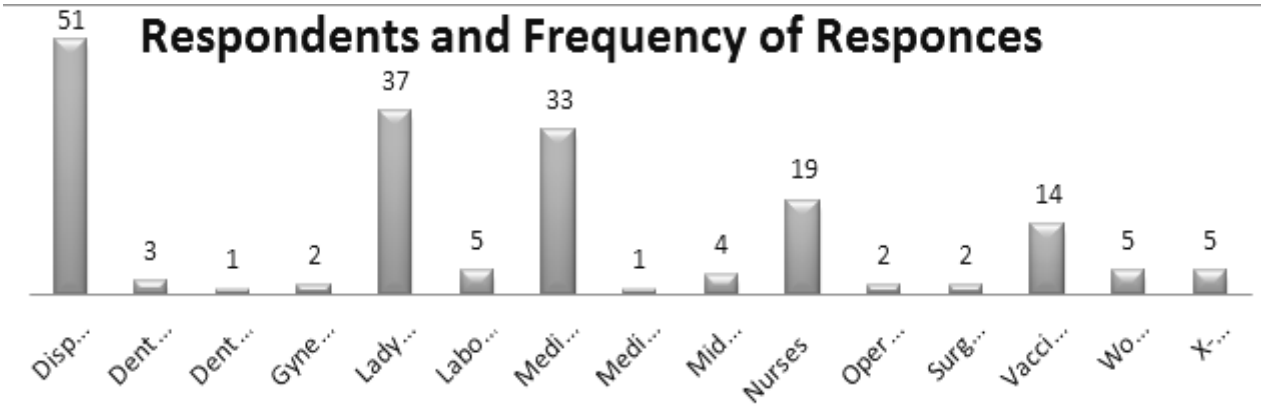
A Standard questioner was developed and pretested, to identify the weaknesses and strengths.

The following variables were included ; training on biohazards, eating in Lab, operation theatre or at other work places, storage of food in vaccine & medicine fridge, application of cosmetics in lab, operation theatre or at examination place, smoking or sniffing in Laboratory or dressing rooms, cutting of finger nails with teeth or putting of pen in mouth, wearing hand gloves during surgical examination or Laboratory work, putting on of white coat during the work, immunization against the hepatitis B, washing of hands after removal of hand gloves, participated in tuberculosis skin testing, taking shower after laboratory work, needle pricks during last one year period and cuts or injury during work.

For data collection school health and nutrition supervisors were trained and sent to the health facilities Data was compiled in the excel format.

RESULTS

In this study we found that only 27(14.6%) health care providers had specific training on bio-safety and biohazards. 96(52%) health personals had habits of eating at work place, laboratory, dressing or examination rooms, 83(45%) don't have this habits or practice and 6 (3.2%) do this practice sometimes. 98(53%) respondents had habits of storing edibles in the refrigerators meant for the vaccines or for laboratories, 86(45.6%) don't have this habits or practice.



Graph No.1: Showing Frequencies of Responses

Table No.1: Study Variables, Responses and Frequencies

		Yes	No	Some time
1.	Do they have any training on Bio - hazards?	27	157	-
2.	Eating in the laboratory/OT/Dressing Room/ Examination Room/Work place.	96	83	6
3.	Storage of food and water in the refrigerator meant for body Fluids, drugs, chemicals, vaccines or other specimens.	98	84	2
4.	Application of cosmetics (for female staff) in Lab. Examination Room, OT.(N=91)	35	42	11
5.	Smoking or sniffing in the Laboratory, OT or Dressing rooms.(N=161)	62	95	1
6.	Cutting of finger nails with teeth or putting the pen in the mouth.	89	92	1
7.	Wearing of hand gloves during surgical procedures/ Examination or Laboratory work.	103	80	1
8.	Putting on of white/lab coats while working.	91	34	57
9.	Immunization against Hepatitis B.	100	84	-
10.	Washing of hands after removal of hand gloves.	78	106	-
11.	Participation in periodic tuberculosis skin testing.	47	137	-
12.	Taking of shower immediately after participating in laboratory work, Wearing of gloves.	50	120	14
13.	Do you have needle prick during your job in last 1 year?	119	65	-
14.	Do you have any injury or cut on your hands during work?	110	74	-

Among females 91(N=91),35(38.4%) had habits of using cosmetics at work place, 42(46%) female don't have this habits or practice and 11(12%) do this practice sometimes. 0ut of 161 the total 62(38.5%) had habits of smoking or sniffing at their work place, rest 96(59%) don't have this habits or practice. 89(48.3%) had habits of cutting nail with teeth and putting pen in the mouth at work, 93(50%) don't have this habits. 47(25.5%) participating in the periodic tests for Tuberculosis, 137(74.5%)don't participate.

Out of 184(N=184), 119(64.6%) had needle pricks during job in last one year, 65(35.3%) were not exposed to the needle stick injuries and similarly 110(60%) had other injuries during work, 74(40%) don't have injuries. A total 100(54.5%) were immunization against hepatitis B, 84(45.5%) were unimmunized.

DISCUSSION

Studies conducted in Pakistan and in other countries of the world on the same topic are consistent with results of this study and results are strongly supported.

In this study we found 27(14.6%) health care providers had specific training on bio-safety and biohazards, 157(85.3%) don't have any structured training. The results are supported as "Exposure to chemical and physical hazards, lack of safety training, and low levels of safety climate and safety practices remained significant risk factors for Work Related Injuries. In 96(52%) health personals had habits of eating at work place, laboratory, dressing or examination rooms, 83(45%) don't have this habits or practice and 6 (3.2%) do this practice sometimes. 98(53%) respondents had habits of storing edibles in the refrigerators meant for the vaccines or laboratories, 84(45.6%) don't have this habit, 2(1.0%) do this practice sometimes. Among females(N=91), 35(38.4%) had habits of using cosmetics at work place, 42(46%) don't use, rest 11(12%) do this practice sometimes. 0ut of 161 the 62(38.5%) respondents had habits of smoking or sniffing at their work place, 96(59%) don't have this habits or practice. 89(48.3%) cutting their nails with teeth and putting pen in mouth at work, 93(50%) don't have this habits. The study results are consistent with many other studies in which safe environment and separate place for health care professional are recommended for eating and for other personal needs.

Out of 184 total 103(56%) had habits of wearing surgical gloves during surgical procedures or examination, 81(43.5%) don't have use. 91(49.5%) health care providers had habits of wearing white coat/lab coats during surgical procedures or examination, rest 34(18.5%) don't wear rest 57(31%) wear occasionally. Non use of appropriate equipments or barriers has been shown in another study which support the result of our study. [15].

A study in Karachi Pakistan, Results showed that 46% of the respondents (34.2% from Punjab, 61.9% from Sindh, 25.2% from Balochistan and 85% from KPK) said they reused syringes either occasionally or regularly. 30.7% of the respondents said they discard used syringes directly into municipal dustbins. The majority (66.7%) claimed there are no separate bins for sharps, so they throw these in municipal dustbins. Standard operating procedures were not available in 67.2% labs, and accident records were not maintained

in 83.4%. No formal bio-safety training had been provided to 84.2% of the respondents [20].

In our study among total respondents (N=184), 100(54.5%) health care providers had immunization against hepatitis B , rest 84(45.5%) are unvaccinated. Vaccination program in healthcare workers against HBV is cost-effective, decreases the anxiety of an employee after needle stick and sharp injuries, and prevents the transmission of HBV after exposure in the majority of cases [17-18].

A total 78(42.3%) respondents had habits of washing hands after removal of surgical gloves, 106(57.6%) don't wash. 50(27%) health care providers had habits of taking shower immediately after participating in laboratory work and wearing of gloves, 120(65.2%) don't have this habits or practice and 14(7.6%)do this practice sometimes. Non use of shower after work or washing hands can cause many diseases, especially latex allergy and other disease.

In this study 47(25.5%) health personals were participating in the periodic tests for Tuberculosis, 137(74.5%) don't participate in the tuberculosis test. Many studies proved that precautionary measures and tests in this regards can minimise the risk of the disease development.

Total respondents were 184(N=184), out of which 119(64.6%) had needle pricks during job in last one year, 65(35.3%) were not exposed. Similarly 110(60%) had other injuries during work, 74(40%) don't have injuries in this period. Needle stick and sharp injuries may be combined with failure to use appropriate barrier garments (e.g. hand gloves of proper size) [13-14]

CONCLUSION

The study results are consistent and supported by many studies showing poor knowledge, attitude and practices. This demonstrates the serious need of trainings on bio-safety and continuous monitoring on the practices to minimize the health risk, which is a hidden public health problem. Health care workers belong to a high risk occupational group so keeping in view, it is essential to take all available and effective organizational technical and medical measures to protect the health care personals.

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Original Article

Effect of Atenolol in BP

Efficacy & Biochemical Evaluation of Pharmaceutical Optimized Atenolol 50mg (F-9) with Essential Hypertension

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ABSTRACT

Objective: The objective of this double-blind, Placebo control study evaluating efficacy and biochemical effects of optimized Atenolol 50mg (F-9) as monotherapy in adult patient with essential hypertension.

Study Design: Double-blind, Placebo control study.

Place and Duration of Study: This study was conducted at the Department of Biochemistry, University of Karachi from February2011 to September 2011.

Materials and Methods: This was multicenter randomized, double-blind, Placebo control study. Patients were randomized to receive once Atenolol (F-9) daily for 8 weeks and at the end of study efficacy and biochemical evaluation was done

Results: The patients treated with optimized Atenolol 50mg (F-9) alone, blood pressure reduction was lower, although significant; reaching values of 140.9 ± 11.3 / m88.9 ± 5.5 mmHg ($p < 0.05$ versus Placebo) by the end of eight weeks of treatment. . No significant variation of blood glucose was observed and different parameters of lipid profile were also observed during the eight weeks of treatment with antihypertensive regimen used. Thus, the drug regimens used may be considered neutral as regards glucose and plasma lipid metabolism profile because drug used at low doses.

Conclusion: We can suggest that the high antihypertensive efficacy, good tolerability and no biochemical effects of the optimized Atenolol50mg (F-9) it is an excellent option for the treatment of hypertension in a wide range of hypertensive patients, with a high potential to reduce cardiovascular risks.

Key Words: Hypertension, Atenolol , Biochemical effects

INTRODUCTION

Hypertension is one of the strongest modifiable risk factors for cardiovascular and kidney disease and has been identified as the leading risk factor for mortality[1].In European countries the prevalence of hypertension in adults is estimated to be approximately 44%.[2] Current guidelines for the management of hypertension recommend a target blood pressure of 140/90 mmHg, with a stricter target for patients who have a high risk of cardiovascular events (< 130/80 mmHg).[3,4]

Atenolol is a β1-receptor selective antagonist and is mainly used in treating hypertension, angina, heart failure and myocardial infarction; chemically, it is 4-(2-hydroxyl-3-isopropyl aminopropoxy) phenylace-tamide.[5,6] The phys-icochemical properties of atenolol, i.e., slight water solubility, low molecular weight (266.336), and its suitable elimination half-life (t1/2= 6–7h).[6]

Comparative safety and efficacy trials indicate that angiotensin receptor blockers like olmesartan medoxomil have superior tolerability and antihypertensive efficacy[7]. Similar investigation using olmesartan, medoxomil and amlodipine besylate showed great effectiveness and tolerance in patient with hypertension[8]. Combination therapies reduced B.P to a greater extent than with amlodipine besylate alone as indicated with benazepril hydrochloride with valsartan and with perindopril[9, 10.]

Therefore, the objective of this comparative study evaluating the efficacy and biochemical effects of optimized Atenolol 50mg (F-9**)** with placebo in the treatment of patients with essential hypertension.

MATERIALS AND METHODS

This was multicenter, randomized, placebo-controlled study. Patient was randomized to receive optimized Atenolol 50mg (F-9) once daily and Placebo once daily for 8 weeks. The study was conducted in Department of Biochemistry, University of Karachi from February 2011 to September 2011, Patients were selected from four different hospitals of orange Town and 80 patients were selected for the study. Therefore 80patients were effectively analyzed for efficacy and tolerability the analysis of antihypertensive efficacy and biochemical effects of a therapeutic regimen in the long term becomes important. The primary efficacy variable was change from baseline in MSDP at the end of study. Secondary variable was change in mean sitting systolic blood pressure from baseline. Safety biochemical parameters (complete blood count, renal function, liver function, electrolytes, protein profile, and enzymes) and electrocardiogram at rest were also determined in all

patients at the baseline (week O) and at the 8th week of antihypertensive treatment. At the same time points, glucose metabolism parameter values and plasma lipids (total cholesterol, HDL-cholesterol, LDL-cholesterol, and triglycerides) were also recorded. Biochemical parameters were determined using an automated method.

RESULTS

The patients treated with optimized Atenolol 50mg (F-9) alone, blood pressure reduction was lower, although significant; reaching values of 140.9 ± 11.3 / m88.9 ± 5.5 mmHg ($p < 0.05$ versus Placebo) by the end of eight weeks of treatment. Variations in blood pressure measurement in the standing position during treatment were similar to those recorded in the sitting position, and no episode of orthostatic hypotension was reported in either of the therapeutic regimen. No significant variation in leg volume measurement was observed among the both groups studied during the eight weeks of treatment. No significant variations of blood glucose were observed and different parameters of lipid profile were also observed during the eight weeks of treatment with antihypertensive regimen used. Thus, the drug regimens used may be considered neutral as regards glucose and plasma lipid metabolism profile because drug used at low doses.

Table No.1: Baseline characteristics

	Atenolol (F-9) (n=60)	Placebo (n=20)
Age (years)	50.2 ± 9.3	51.5 ± 9.8
Male / Female (%)	43.4 / 56.6	35.0 / 65.0
Body weight (Kg)	68.9 ± 13.5	71.2 ± 12.2
BMI (kg/m2)	27.5 ± 3.8	27.8 ± 3.4
SBP sitting (mmHg)	149.5 ± 11.5	148.8 ± 10.9
DBP sitting (mmHg)	95.7 ± 7.4	94.9 ± 7.8

Table No.2 Ambulatory blood pressure monitoring. Mean values of blood pressure

	Atenolol (F-9) (n=60)	**Placebo (n=20)**	**P-value**
Systolic BP – 24 hrs (mmHg)			
Baseline	149.8 ± 11.2	149.2 ± 11.5	NS
Week 8	140.9 ± 11.3	148.9 ± 11.2	0.0074
Diastolic BP – 24 hrs (mmHg)			
Baseline	97.6 ± 7.4	95.4 ± 8.8	NS
Week 8	88.9 ± 5.5	94.9 ± 7.9	0.0003

NS: Non significant, p: probability

Table No.3: Baseline Biochemical characteristics

	Atenolol (F-9) (n=60)	**Placebo (n=20)**
Fasting Blood Glucose(mg/dl)		
Baseline	97.4 ± 11.5	99.1 ± 8.8
Week 8	95.5 ± 11.9	98.9 ± 9.2
Total Cholesterol (mg/dl)		
Baseline	197.2 ± 43.2	195.2 ± 33.3
Week 8	199.7 ± 43.5	193.9 ± 34.1
	LDL - Cholesterol (mg\dl)	
Baseline	114.4 ± 34.1	117.9 ± 25.9
Week 8	114.9 ± 34.5	116.8 + 24.7
HDL - Cholesterol (mg\dl)		
Baseline	52.9 ± 13.1	48.9 ± 11.7
Week 8	51.8 ± 12.8	48.7 ± 11.5
	Triglycerides (mg\dl)	
Baseline	137.2 ± 88.5	145.5 ± 88.1
Week 8	136.1 ± 89.3	144.2 ± 88.9

DISCUSSION

The baseline characteristics of the population included in the study are shown in Table no1. We can observe that the groups were not different in relation to age, body mass index and weight, heart rate, and systolic and diastolic pressure values .No significant variations of blood glucose and different parameters of lipid profile were observed during the eight-week of treatment with any of the three antihypertensive regimens used. Thus, the drug regimens used may be considered neutral as regards glucose, plasma lipid metabolism. The results of this study showed that the optimized product Atenolol 50mg (F-9) as a high antihypertensive efficacy that is sustained in the long term with a quite reduced percentage of loss of blood pressure control in table No.2 We observed that more than 71.8% of the patients treated with optimized product of Atenolol 50mg (F-9) remained with diastolic blood pressure levels equal to or lower than 90 mmHg, thus achieving the goals for the treatment of hypertension. The difficulty to achieve the goal of controlling systolic blood pressure explains why the international guidelines for studies on antihypertensive drugs still use criteria based on diastolic blood pressure to describe the antihypertensive efficacy of a drug, in spite of the fact that guidelines indicate the real need to control systolic blood pressure as well. It is important to point out that blood pressure reduction provided by the treatment with optimized product of Atenolol 50mg (F-9) did not cause any secondary Increase in sympathetic activity, since no significant variations of heart rate occurred. In addition to a high efficacy in reducing blood pressure, keeping it at controlled levels, an antihypertensive drug should also have a good biochemical profile, since the presence of adverse effects may decrease the degree of compliance of the patient to the therapeutic regimen, thus ultimately

leading to treatment dropout. Our results showed that the optimized product of Atenolol 50mg (F-9) at low doses has a very good biochemical profile with a low incidence of adverse events. The good biochemical profile of the optimized Atenolol 50mg (F-9) may be explained by the use of lower doses of each of the hypotensive drugs, since the existence of a strong relation between the dose of the hypotensive drug and the frequency of adverse events is known. However, some drugs used in the treatment of hypertension, such as diuretics and beta-blockers, are known to be able to promote harmful alterations in lipid metabolism, especially in glucose metabolism. In our study we observed that the use of the optimized Atenolol 50mg (F-9) did not change parameters of either glucose metabolism or plasma lipids, thus having a neutral biochemical profile even when used for 8 weeks. Table.No.3 Based on these results we can suggest that the optimized product Atenolol 50mg (F-9) is safe and adequate for the treatment of hypertension in patients with metabolic syndrome, diabetes mellitus and dyslipidemia; because alterations in these parameters are very frequently observed in hypertensive patients. Incidentally, hypertension is frequently associated to the metabolic syndrome; also, the frequency of this association increases with age. However, some drugs used in the treatment of hypertension, such as diuretics and beta blockers, are known to be able to promote harmful alterations in lipid metabolism, especially in glucose metabolism. Based on these results we can suggest that this therapeutic modality is safe and adequate for the treatment of hypertension in patients with metabolic syndrome, diabetes mellitus and dyslipidemia.

CONCLUSION

In brief, the results of this multicenter study demonstrated that the optimized Atenolol 50mg (F-9) has a high antihypertensive efficacy, allowing approximately 72.1% of the patients treated to achieve and maintain for eight weeks. We can suggest that the high antihypertensive efficacy, good tolerability and no biochemical effects of the optimized Atenolol 50mg (F-9) it is an excellent option for the treatment of hypertension.

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Original Article

Viral Hepatitis

Prevalence of Viral Hepatitis in Patients attending Medical Camp

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ABSTRACT

Objective: Objective of this study was to check prevalence of Viral Hepatitis in Patients attending Medical Camp
Study Design: Cross sectional study
Place and Duration of Study: This study was conducted in free Medical Camp of Shaheed Mohtarma Benazir Bhutto Medical University Larkana from 01.07.2011 to 31.12.2011.
Materials and Methods: An advertisement was given one week prior via media for awareness of people. The camp was organized by the faculty of Medical unit III on 1st July 2011. This camp, apart from necessary medicines, equipped with diagnostic facilities to diagnose hepatitis B & C viruses. Patients willing to participate in this study were enrolled; patients with known hepatitis B & C were excluded. ELISA technique was used to diagnose. This study was approved by Ethical committee of Shaheed Mohtrama Benazir Bhutto Medical University. SPSS version 19 was used for data analysis.
Results: Total of 400 peoples were seen at the camp, 96 of them were already known cases of hepatitis B and C and were excluded from analysis. Of 304 patients 246 were males and 154 were females. From 304 patients 32 (10.5%) patients had hepatitis C and 16 (5.3%) had hepatitis B and rest were seronegative. The frequency of HCV and HBV was common in patients with age between 20 to 40 years.
Conclusions: This was a small effort to increase awareness in local population regarding the course of viral hepatitis. We also collected data regarding present prevalence of chronic viral hepatitis in rural areas of interior Sindh. Much more is to be done to control this misery of our community.
Key Words: Viral Hepatitis, Patients, Medical Camp

INTRODUCTION

Hepatitis B virus (HBV) and hepatitis C virus (HCV) are among the principal causes of severe liver disease, including hepatocellular carcinoma and cirrhosis-related end-stage liver disease.
The World Health Organization (WHO) estimates that there are 350 million people with chronic HBV infection and 170 million people with chronic HCV infection worldwide.[1,2]Hepatitis B is estimated to result in 563 000 deaths and hepatitis C in 366 000 deaths annually.[3] Given its large population (165 million) and intermediate to high rates of infection,[1,2]
Pakistan is among the worst afflicted nations. Pakistan has one of the world's highest fertility rates, exceeding four children per woman.[4] It is approximately 800 000 sq km area slightly less than twice the size of the state of California in the USA and Pakistan is larger than either Turkey or Chile.[4-5] Pakistan is divided into five provinces, Punjab, Sindh, Northwest Frontier Province (NWFP), Balochistan, and gilgit baltistan as well as federally administered areas including the capital (Islamabad), Federally Administered Tribal Areas (FATAs), and the western third of Jammu and Kashmir.[6-7] Considering Pakistan's size and large, growing population, there is a surprising dearth of information about hepatitis prevalence, although more is known about its risk factors. We prospectively conducted this study to know the prevalence of hepatitis.

MATERIALS AND METHODS

This cross sectional study was conducted in free medical camp of Shaheed Mohtarma Benazir Bhutto Medical University Larkana. Chandka Medical College was gifted by Praiseworthy Ex-Prime Minister of Pakistan Shaheed Zulfiqar Ali Bhutto. His dream was not only to make this institute the premier institute of Pakistan but to ultimately expand it to the level of a University, which was fulfilled in 2008.
An advertisement was given one week prior via media for awareness of people. The camp was organized by the faculty of Medical unit III on 1st July 2011. This camp, apart from necessary medicines, equipped with diagnostic facilities to diagnosis hepatitis B & C viruses.
Patients willing to participate in this study were enrolled; patients with known hepatitis B & C were excluded. Two ml blood was collected for detection of HBV and HCV. ELISA technique was used to diagnosis.
Ethics: This cross sectional study was approved from ethical committee of Shaheed Mohtarma Benazir Bhutto medical university Larkana,
Statistics: SPSS version 19 was used for data analysis. Frequency and percentages were reported for

categorical variables and mean and SD was reported for continuous variables.

RESULTS

Total of 400 peoples were seen at the camp, 96 of them were already known cases of hepatitis B and C and were excluded from analysis. Of 304 patients 87 (28.6%) were <20 years of age, 76 (25%) were 20-40 years of age, 117 (38.5%) were 40-60 years of age and 24 (8%) were >60 years of age (Figure 1).Overall 246 (61%) were male and 154 (39%) were female (Figure 2).

Out of 304, 32 (10.5%) patients had hepatitis C and 16 (5.3%) had hepatitis B and rest were seronegative (Figure 3).The frequency of HCV and HBV was common in patients with age between 20 to 40 years of age. Of 32 HCV cases patients, 20 (62.5%) were male and 12 (37.5%) were female, and of 16HBV cases 11 (68.7%) were male and 5 (31.2%) were female.

Table No.1: Stratification of Hepatitis based on age:

Hepatitis	< 20 years n=84	20-40 years n=76	40-60 years n=117	>60 years n=24
Yes	11 (13.09)	16 (21.05)	18 (15.38)	3 (12.5)
No	73 (86.90)	60 (78.94)	99 (84.61)	21 (77.5)

Table No.2: Baseline characteristics on participant

Characteristics	Hepatitis positive (n=48)	Hepatitis negative (n=256)	P-value
Mean Age	36±12	38±10	0.12
Male	31 (64.5)	215 (83.9)	0.004
Female	17 (35.4)	41 (16.0)	

Table No.3: Comparison of baseline characteristics of patients with HBV and HCV

Characteristics	HBV positive (n=16)	HCV positive (n=32)	P-value
Mean Age	34±13	36±13	0.24
Male	11 (68.7)	20 (62.5)	0.46
Female	5 (31.2)	12 (37.5)	

DISCUSSION

We observed highly variable seroprevalence estimates for both HBV and HCV. Unlike highly contagious diseases like measles that have a more predictable seroprevalence, blood-borne illnesses like hepatitis are transmitted sporadically or in micro-epidemics. These micro-epidemicsmay account for the wide variations in prevalence seen within a nation, a province, or even acommunity. Identification of the causes of these micro-epidemics provides an opportunity to limit the transmission of these diseases.[8-9] However, methodological differences in sampling strategies may also contribute to differences in seroprevalence within similar regions or populations. For example, one study of the general population did a staged cluster random sampling of the entire city's study population,[10] while another study of putative 'random samples' in a different city recruited persons with the aid of newspaper advertisements[11] that may have distorted the risk profile of respondents compared to the former study.`

The published literature regarding risk factors for HBV and HCV transmission in Pakistan is informative. WHO estimates that in Southeast Asia, an average person receives four injections per year, most of which are unnecessary and up to 75% are unsafe or reused.[12] Unnecessary injections are given commonly in Pakistan out of the prevalent view in the population that injected medicines are more effective than oral medications.[13-14] Intramuscular injections are frequently used for fever, fatigue, and general ailments, while intravenous drips are used for the treatment of weakness, fever, and 'severe' diseases.[15-16] Some people use IV drips to cool down during the summer (HQ, personal observation). These injections are given by physicians at clinics, by informal, untrained providers, by health workers who do home visits, and by pharmacists both trained and informal.[17-18] The healthcare providers mayeven encourage the injection-seeking behavior because patients are more willing to pay an additional physician's fee for injections but will not pay this added fee for oral medications.[18] Syringes are reused and sterility of injections is often not maintained due to financial limitations and lack of risk awareness among the healthcare providers and the population ingeneral.[17]These injections appear to be the single most significant factor in the spread ofHBV and HCV in the general population of Pakistan.

There are about 1.5 million units of blood products transfused each year in Pakistan.[19] Data on the safety of this transfusion process are scanty – perhaps due to the lack of a system of reporting infectious or non-infectious adverse events.[20] The transfusion network is poor lyorganized and likely contributes significantly in the transmission of serious infectious diseases. In fact, the leading hepatologist and public health scientist of Pakistan and editor of the country's premier medical journal for 30 years died in 2004 of cerebral malaria that she acquired through a blood transfusion given during bilateral knee replacement surgery. Her case dramatized the need for regulation and control of the transfusion practices in Pakistan. Under the umbrella of National Blood Policy, comprehensive measures are needed in both public andprivate sectors of all four provinces. These measures should include a situational analysis and a realistic assessment of the blood requirement in the area, followed by recruitment and maintenance of voluntary, non-remunerated blood donors and standardization and regulation of appropriate blood screening procedures. IDUs are numerous in Pakistani society and though they have a disproportionately high burden of health problems, they

have been inadequately studied. Limited data suggest the likely hood that the prevalence of hepatitis is very high in this community. Urgent efforts need to be made to better study this population and to apply globally effective programs like needle exchange and condom distribution together with appropriate counseling and therapy for their drug addiction. Unless serious infections are controlled in IDUs, they will continue to be the source of HBV, HCV, and now HIV to the general population in Pakistan.

CONCLUSION

This was a small effort to increase awareness in local population regarding the course of viral hepatitis. We also collected data regarding present prevalence of chronic viral hepatitis in rural areas of interior Sindh. Much more is to be done to control this misery of our community, but the main hurdle in achieving this goal is lack of financial and institutional supports.

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Original Article

Breastfeeding

Prevalence of Ghutti and Breastfeeding: An Ethnographic Study of Lactating Women of Khewayaali, Wazirabad

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ABSTRACT

Objective: The objective of present study was to investigate level of interdependence between prevalence of Ghutti and education of newborn's mothers.

Study Design: Cross-sectional

Place and Duration of the Study: This study was carried out at Village Khewayaali, Tehsil Wazirabad, District Gujranwala from Aug-2013 to Oct-2013.

Materials and Methods: Data was collected while administrating a fully structured questionnaire. Tool was implemented with the help of women enumerator after improving the areas highlighted during the pre testing. A sample of 324 lactating women was randomly selected out of total population of lactating mothers. SPSS was used for data analysis.

Results: As 95 % of lactating women respondent of this research confirmed that they had given their child Ghutti prior to the breastfeed. But on the other side, 80% of the total respondents also confirmed that they had fed their child in first 04 hours after birth and did not waste the highly nutritive Colostrum. Whereas, comparison of mothers' education with the use of Ghutti delineated that the practice is equally common among illiterate and educated mothers both. Illiterate mothers were 21% of the total respondents and use of Ghutti was equally present in rest 79% educated mothers as well thus the practice was found among 100% respondents.

Conclusion: Current study explored that education has no influence over this deeply rooted a cultural practices and norms. As mothers despite being educated and much aware with the benefits of breastfeed performed this tradition under the persuasions of adult relatives especially mother in law.

Key Words: Ghutti, lactating mothers, breastfeeding, newborn, prelacteal feed.

INTRODUCTION

Pakistan is among the list of developing countries, where situation of health and education is not is not satisfactory. If we express anthropologically, cultural values and their practitioners founds very rigid and majority of the population feels proud to follow the practices of forefathers. Concepts in health domains such as breastfeeding, Ghutti, supported liquids have their own cultural importance within Pakistan and also people belongs to Pakistani culture practice this while living in other countries.

In Pakistani society, on average 72 newborns were expired out of 1000 live births each year. But from those 72 deaths, 53 are those who died earlier before attaining the age of 1 month because of different diseases like pneumonia, diarrhea, respiratory infections and malnutrition. Commonly found/recorded starting place of these diseases is being absence of exclusive breastfeeding, use of formula milk, supported liquids and unhygienic bottles. These births can be secured if they are protected through natural defense of mother's milk without use of any other food item like Ghutti, honey, rose subtract or water for the first six months[1].

Variations among breastfeeding practices are normally based on educational status, socioeconomic rank, cultural concerns, and other factors. These factors are associated with the general decline in breastfeeding comprising on socio-cultural factors, values & traditions practice in health care services, marketing and promotion of newborn feeding items[2,3].

For a reference to cope the knowledge medical students on breastfeeding practices in Pakistan a study was conducted, in which 14% of students were of the view that the colostrums should be discarded and in 12% cases they said that it is harmful for the baby's health, so one can say that these are the strong traditional believes still exist even in educated families through their grand parents[4]. And in Pakistani society families are more motivated to use the Ghutti as first intake for baby after birth. This also presents some cultural myths passed from generation to generation where Ghutti is taken as source of family's traits transfusion to the newborns. And, parents request their family elders to

perform this tradition in order to get their traits into their children through Ghutti.

In countries of the Indian subcontinent, breast feeding is usually started 2 to 3 days after delivery. During the interim, babies in South India are usually given water, diluted cow's milk, honey, or dates followed by Ghutti[5].

The prevalence of pre-lacteal feeds was more commonly found (79%) in an existing study conducted in Hyderabad Pakistan, by Memon et al., in 2006[6]. The practices of pre-lacteal feed are not only common in Pakistan but are frequently observed in many other Asian countries. In rural India as WHO reported, nearly 93% of the surveyed infants were given pre-lacteal feeds in first two days of their life. Situation is not too different in Bangladesh where Infants are reported to be fed honey or mustard oil for three days in blend with or followed by breastfeeding for a month[7-10].

Exiting studies explains the situation quite clearly in the Asian sub-continent that majority of the population used to practice pre-lacteal feeds. Normally they welcome newborn by giving him/her a traditional recipe that is commonly known as Ghutti, and they had strong beliefs that through this Ghutti the cultural and social traits of one's transferred to the young one. This study tries to find that relationship between the education of respondents and prevalence of Ghutti among lactating mothers and cultural importance of Ghutti.

MATERIALS AND METHODS

The present research was conducted in village Khewayaali in Tehsil Wazirabad of Gujranwala district. Out of 1700 lactating mothers Khewayaali, 234 were randomly selected at 90% confidence interval by using an online sample calculating formula. A structured questionnaire was implemented for data collection from the randomly selected women. The said questionnaire was comprised of questions regarding women's demographics, knowledge, attitude and practice of Ghutti and breastfeeding. The questionnaire was improved after piloting under similar rural settings of Gujranwala. Women enumerators took interviews after briefing the subjects about purpose of study. Data was punched into EPiData and SPSS was utilized to draw tables, graphs and charts.

RESULTS

Table 1 shows the age distribution of respondents. Majority of the respondents were in the category of 27-30 years (42.90%) that shows the participation of age-wise mature females in the data collection phase. 29.23% of the respondents belonged to the age category of 31 and above.

Table No. 1: Age of the respondents

Age	Frequency	Percent
15-18	5	1.55
19-22	19	5.87
23-26	64	19.75
27-30	139	42.90
31 and above	97	29.93
Total	324	100.00

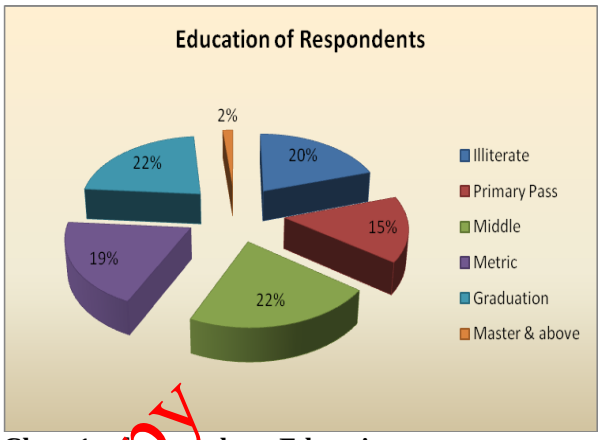

Chart 1: of respondents Education

Education seemed to play a vital role in every domain of life. The above results above show that 20.06% respondents lacked formal education, 15.12% received 1-5 years of schooling, 21.61% were in the category of 6-8 years of schooling. In the category of 9-10 years the percentile remained 19.44%. The largest fraction that was 22.22% constituted the category of 11-14 years of education.

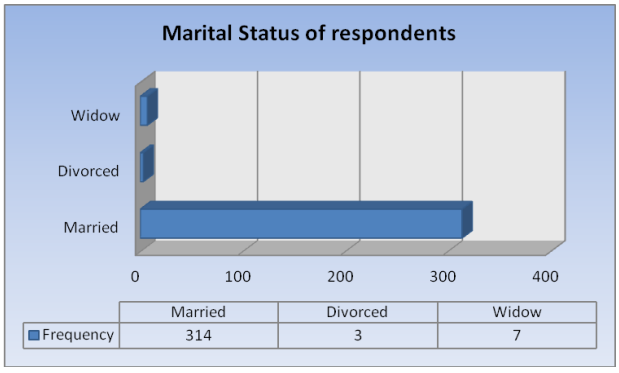

Chart 2: of respondents Marital Status

Chart 2 shows the current marital status of the respondents. Among 324 respondents 96.92% were married at the time of study following 2.16% widows and 0.92% was divorced.

Table 3 shows that 94.14% of women breastfed their child whereas 5.86% could not do that however they did not share any particular reason of the same with the researcher.

Table No.3: Breastfed to youngest child

Response	Frequency	Percent
Yes	305	94.14
No	19	5.86
Total	324	100.0

Table No.4: Initiation of breastfeeding of Infant after Delivery

Hours	Frequency	Percent
Within 1 hour	135	44.26
Within 2 hours	69	22.62
Within 3 hours	41	13.44
Within 4 hours	5	1.64
5 hours and above	55	18.03
Total	305	100.00

Above given table number 4 specifies the time duration in which mother fed their child after the birth and out of total, 82 percent fed the child within first 04 hours after birth while majority (44%) lying in the category of within 01 hour. Results demonstrate a very positive trend as colostrums encompassing all essential nutrients stays for up to 05 hours maximum after delivery of baby. And only 18% mother took more than 5 hours to feed the child.

Table No.5: Did you use Ghutti for your newborn

Response	Frequency	Percent
Yes	307	94.75
No	17	5.25
Total	1324	100.00

At the same time, table 5 highlights significant aspect of cultural practices concerning newborns immediate intake after delivery e.g., use of any other ingredients like water, honey, rose extract and most commonly Ghutti. Above table confirms the strong cultural tradition of presence of Ghutti to the newborns right after birth as 94.75% women reported that they had given Ghutti to their child.

Table No.6: Family Member Advice for Ghutti

Family Member	Frequency	Percent
Husband	68	20.98
Mother-in-law	134	41.37
Father-in-law	66	20.37
Mother	41	12.65
Others	15	4.63
Total	324	100.00

Table 6 depicts the degree of social, cultural and family pressure even over the diet of a newborn. As in all cases some close relative has suggested the use of Ghutti right after birth and mother in law comes forward as the most influential figure in this regard. Overall, none of the family adult is ready to leave this cultural practice and playing a substantial role in keeping this tradition alive regardless of the facts about its no benefit for the newborn's health.

Table No.7: Care Provider advised Breastfeeding

Care Provider	Frequency	Percent
Doctor	262	80.86
LHV	19	5.86
LHW	14	4.32
Others	29	8.96
Total	324	100.00

The role of health care providers is always very significant to create awareness about innumerable salubrious effects of child immediate and long term health and life. Surprisingly, all of the respondents' confirmed that their health service providers sensitized them about the breastfeeding and among them 80% mentioned the name of doctor.

Table No.8: Comparison; Education of Respondents and use of Ghutti

Education	Use of Ghutti	Percentage
Illiterate	65	21
Primary	48	15
Middle	68	22
Higher Secondary Education	58	19
Intermediate and Bachelors	69	22
Masters and Above	4	1
Total	**312**	**100**

Above table presents the findings which revealed that education of respondents had no impact on use of Ghutti, and it's equally common among both respondents educated and illiterate. This confirms that this practice of using Ghutti is purely influenced by culture and traditions and has no relationship with the literacy or educational status of the mother. And educated women too gave Ghutti to their children regardless of their educational level.

DISCUSSION

Around the world lactating women adapt feeding practices to their own circumstances and the socio-cultural setting they live in. Women adapt to their infant's needs, and infants adapt to their mothers' availability. In every culture, it is important to note that there are circumstances where a mother avoids breastfeed, and also, mothers who choose not to breastfeed for multiple reasons[11]. Start and continuity of breastfeeding is influenced by a complex relationship of tradition, culture, social support and socio-economic status[12].

The findings of the earlier studies clearly reveal that due to various cultural beliefs and taboos, initiation of breastfeeding right after delivery gets delayed for many days. Aged female member of the family plays imperative function in initiation of breastfeeding and giving of prelacteal feed (*Ghutti*). Cases were in record

when giving colostrum to the infant was avoided, from other studies from South Asian Countries. A study from Turkey have also depicted that only 9.9% of the mothers had initiated breastfeeding within 4-hour after birth and 68.8% started colostrum in relation to characteristics related to delivery breastfeeding after 2 day[13-17].

The training of health workers in breast feeding and lactation management enhances professional recommendations on breast feeding. Important components of breast feeding promotion include prenatal support, hospital management and subsequent pediatric and maternal visits[18-20].

CONCLUSION

Findings of present study demonstrate and verify the presence of multiple factors which effect breastfeeding practices and are strongly influenced by the culture, norms and local traditions.

This study shows that mothers confirmed that their health service providers have orientated them about the strength of breast milk but still they gave their children *Ghutti*. However, the number of women who fed the child in first hours of after birth is also very encouraging but still the roots of *Ghutti* use are quite deep. Doctor's advice and mother's education both have not played the desired role in eradicating this useless practice so far.

To address this issue, health services providers should not only approach the mothers but as well as their family members including mother in laws and husband. In our strongly patriarchal society women has no say in decision making particularly in rural settings, thus, for effective results, decision makers should be taken into confidence first. Health service providers must have separate sessions with husband and mother of law to sensitize them about the health benefits of breast feed compare to Ghutti. Based on a particular beliefs system, final eradication of this futile exercise will take concerted and incessant efforts by the media, health department, and educated mothers too.

Results of study confirm the findings of previously conducted researches that show this practice relates more to culture than to health. Major factor of persistent use of *Ghutti* as prelacteal diet is persistent pressure by the family elders and highly patriarchal society where women cannot exercise their will despite being educated.

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Original Article

Acute Myocardial Infarction

Risk Factors for Acute Myocardial Infarction

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ABSTRACT

Objective: Objective of the study is to identify risk factors for Acute Myocardial Infarction (AMI).
Study Design: Prospective cross sectional study
Place and Duration of Study: This study was carried out at AK CMH/SKBZ Muzaffarabad from August 2012 to September 2013.
Materials and methods: This study of first ever AMI patients was carried out in a tertiary care teaching hospital. Standard methods were followed to elicit risk factors. Chi-square and Fishers exact tests on SPSS 20 were done for analysis of risk factors.
Result: A total of 210 patients (male (M) = 118and female (F) = 92) with age range from 30 to more than70 years were included. The mean age of patients was 56.30±13.79 years. The risk of developing AMI was statistical significantly in both males and female (<0.001). The significant risk factors for all AMI were: Hypertension (p=0.039), diabetes (p=0.001), Hypercholesterolemia (p=0.05), smoking (p=0.001) and family history of AMI (p=<0.001).Age (p=<0.001 and age category (p=0.045) were also identified as statistical significance risk factor for AMI. Mortality was 24 (11.4%).
Conclusion: Thus we conclude that CAD is more common in adult and has significant association with modifiable major risk factors in our population. Targeted interventions that reduce/modify these modifiable CAD risk factors could substantially reduce the mortality and morbidity of AMI. Health educations on life style modification, programs to diagnose, control of diabetes, hypercholesterolemia and hypertension have to be initiated at community level in order to reduce the occurrence.
Key Words: Coronary artery disease, Adults, Risk factors.

INTRODUCTION

Cardiovascular disease (CVD) is a major global health problem[1]and accounting for very high mortality.[2]Modifiable risk factors such as smoking, diabetes mellitus, hypertension and dyslipidemia are associated with coronary artery disease (CAD).[3] The CAD can occur in non-obese.[4]Obese individuals.[5] with high visceral fat even with low BMI.[6-7]. The present study was undertaken to elicit important risk factors for acute myocardial infarction (AMI).

MATERIALS AND METHODS

This prospective study was undertaken in tertiary referral and teaching hospital SKBZ/CMH Muzaffarabad and was approved by the institutional ethical committee. The verbal informed consent was obtained from all patients. Cases confirmed by electrocardiogram and diagnostic enzyme changes, were included. Patients with previous history of MI, stroke, heart disease, type 1diabetes, and other co-morbid illnesses were excluded. Hypertensive patients were defined as having persistent elevation of blood pressure (≥140/90 mmHg) or who were on anti-hypertensive drugs. Dyslipidemia was defined as hypercholesterolemia, hypertriglyceridemia and high low density lipoprotein (LDL) or patients whoever on drugs to lower cholesterol.[8] Diabetes in our dataset were only type 2 diabetes mellitus (DM)) and was defined as by preadmission history of diabetes mellitus or venous plasma glucose concentration of 7.0mmol/l ,after an overnight fast on at least two separate measurement and or 11.1 mmol/l two hour post prandially using the American Diabetes Association criteria.[9]Smoking was defined as who smoked at least one cigarette/tobacco per day for preceding three months or more.[10-11]Demographic,clinical and laboratories characteristics were recorded in the proforma and entered. Data analysis was employed for all independent and dependent variables. Chi-square and Fishers exact test for categorical versus categorical and other data analysis were carried out to elicit relationship with risk factors by SPSS 20.

RESULTS

A total of 210 patients (male (M) = 163 and female (F) = 48) and mean age 56.2±13.79 with their ages varying from 30 to >70 years were enrolled. In our dataset adults male and female both had significant association with AMI. Demographics distribution of risk factors among MI is shown in Table. The commonest risk factor for AMI was smoking 150(71.4%) followed by hypercholesterolemia 118(58.2%) and both are independent risk-factors for Acute coronary syndrome.

None had any medical checkup earlier. Isolated hypertensions, family history of AMI and diabetes mellitus were statistical significant risks for AMI. The statistical associations between different variables of AMI are shown in Table.

Table No.1: Characteristics of Acute Myocardial Infarction according to Demographics and Risk Factors

	Total	Anterior Myocardial infraction	Inferior & Posterior Myocardial Infraction	*P-value
N (%)	**210**	**118 (56.2)**	92(43.8)	
Age (year) mean age +-SD	**56.30± 13.79**			<0..001**
<30	5 (2.3)	2 (40.0)	3 (60.0)	.045**
30-39	17 (8.0)	10 (58.8)	7 (41.2)	
40-49	34(16.1)	20 (58.8)	14 (41.2)	
50-59	58 (27.6)	32 (55.1)	26 (44.8)	
60-69	64 (30.5)	35 (54.7)	29 (45.3)	
>70	32 (15.2)	19 (59.4)	13 (40.6)	
Risk factors				
Male	162 (77.1)	90 (55.6)	72 (44.4)	<0.001
Female	48 (45.9)	28 (58.3)	20 (41.7)	<0.001
Hypertension	63 (30.0)			.039*
Hypercholesterolemia	118 (56.2)			0.05**
Smoking	150 (71.4)			<0.05**
Diabetes	33 (15.7)			<0.001***
Family History	155 (73.8)			<0.001
Mortality	24 (11.4)	19 (69.2)	5 (20.8)	.05*

*Pearson Chi-square (two tailed); **Independent t test;*** one sample test

DISCUSSION

This study aimed to analyze the risk factors for AMI in adults. This study revealed that smoking, diabetes, hypertension and dyslipidemia were found to be an independent risk factor for AMI, as observed in previous studies .[12-13] All forms of tobacco produce free radicals that deplete antioxidants and cause oxidative damage to DNA, proteins and lipids and risk for AMI.[14]Diabetes type 2 was not only independent but also along with one or other risk factors were found to have an strong association with AMI. In diabetic patients 80% of deaths are attributable to CAD as result of dyslipidemia .Isolated hypertension and hypertension with one or other risk factors were significantly associated with AMI .Hypertension is in turn correlated with salt intake 8.5 grams/day, alcohol intake and obesity.[15] Salt restriction reduces blood pressure at 6-12 months and weight reduction of 9 kg, can lower systolic blood pressure (SBP) by 6 mm Hg.[16-17]Dyslipedemia is widely accepted as risk factor for AMI. Dyslipidemia was independently associated as a significant risk factor (p=0.05) in our study. However dyslipidemia was also associated with one or other risk factors for AMI .[18-19]

CONCLUSION

Our results suggest that appropriate measures are needed for screening and awareness of putative risk factors of AMI in targeted population. In order to achieve such objective all clinicians should search routinely for risk factors among every case and counsel the identified victim. At the county level, reducing the burden of CAD will require continuous public education and focus on controlling common risk factors by early recognition of symptoms.

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Original Article

Helicobacter Pylori

Helicobacter Pylori Infection may be a New Risk Factor in Developing Acute Myocardial Infarction

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ABSTRACT

Objective: The purpose of present study was to find out the relationship between helicobacter pylori infection and acute myocardial infarction

Study Design: Experimental / Case control study

Place and Duration of Study: This study was carried out the Biochemistry Department, Dow University of Health Sciences, Karachi from 11.02.2013 to 15.12.2013.

Materials and Methods: Serum samples of age and gender matched 80 each of Cardiac and non-cardiac patients with H. Pylori were investigated for the levels of IgG and IgA by kit methods.

RESULTS: Patients who were H.pyloric AMI compared to non-h.pyloric nomal had relationship with increased IgG in Acute myocardial infarction patient with H.pyloric infection as compare to control.

Conclusion: The results of present study suggest that H. pylori is a new risk factor for the development of atherosclerosis and enhance the risk factor. Therefore proper treatment and diagnosis can be helpful for cardiac patients.

Key words: H. pylori, Atherosclerosis, Myocardial infarction, IgG, IgA.

INTRODUCTION

Coronary artery disease is known to be the most leading cause of death in industrialized societies[1]. A cardiovascular risk factor is due to the inflammatory response to irritation, lipid peroxidation and infection[2]. H. pylori cause chronic gastritis, a persistent low grade inflammatory response increase fibrinogen, a coagulation factor which is a predictor of ischemic heart disease[3]. Cardiac risk factors can cause impairment of endothelial vasodilator function of coronary resistance arteries[4-6].

Most of the patient infected by H.pylori never experience symptoms and complications[7]. 10 – 20% patients with symptoms are risk of developing peptic ulcer while 1-2% is at risk of acquiring gastric carcinoma[8]. H. pylori is present in mucus on the inner lining of epithelium and inside cells[9]. For the first time Mendel et al suggested the relationship between coronary heart disease with H.pylori[10].

MATERIALS AND METHODS

In this study 88 persons with no history of cardiac disease and 87 myocardial infarction patients having age between 35 to 70years old were compared in two separate groups. The case group admitted in CCU ward was selected by convenient non probability sampling method.Patients were all diagnosed MI with confirmed clinical symptoms, ECG changes high cardiac enzymes, while the control had no history of any cardiovascular disease, ECG changes or any positive physical or clinical examination. Gastrointestinal drugs users excluded in both groups.

Five ml blood sample was drawn from every MI patient and controls which were involved in the study by venupuncture using a 05 ml sterilized disposable syringe. After clotting, serum was separated by centrifugation and stored at -20 ^{0}C until analyzed. Levels of parameters were measured by ELIZA methods using monobind kit..Data were analyzed using Chi-square (X2) and T- test in SPSS version 16 software.

RESULTS

Table No.1: Comparison of relative frequency of Positive IgG and IgA in both groups.

	Negative N (%)	Positive N(%)	Total N(%)	p
IgG				
Case	38(43%)	50 (56.81%)	87 (100%)	0.003
Control	60 (68%)	38 (31.8%)	88 (100%)	
IgA				
Case	50 (58.8%)	38 (43%)	87 (100%)	0.45
Control	45 (51.1%)	43 (48.8%)	88 (100%)	

There were all males cases and control, the mean ages in the control and case groups 55.3 $\pm$ 11.8 and 57.8 $\pm$

13.7 years respectively (p = 0.1). there were also no significant differences were found between case and control groups in diabetes, hypertension and obesity.

50 patients (56.81%) from case group were IgG positive against H. pylori and 38 (31.8%) persons in control group were IgG positive against H.pylori. The statistically difference was significant (p = 0.002), while there were no significant difference between IgA levels of two groups (p = 0.44) (Table 1). 38 (43%) cases and 43 (48%) controls had positive IgA against H.pylori.

Table No. 2: Relative frequency of positive IgG and IgA in case group.

	IgG	Negative N (%)	Positive N (%)	Total N(%)
IgA				
Positive		10 (26.3%)	28 (73.6%)	38 (100%)
Negative		28 (66.6%)	14 (33.3%)	42 (100%)
Total		38	42	

$X^2 = 6.125$ df = 1 p = 0.01 OR = 3.5Cl: 95% 1.3 – 9.5

DISCUSSION

There is a significant difference in our study, in which there is IgG levels of H.pylori was shown between cases and control (0.002).

According to some researchers, H.Pylori infection is seen in lower socioeconomic society peoples[10] and their frequency is higher in older age people[11,12]. In our study there is a significant difference between control group and cases with IgA and IgG. The antibodies against H.pylori compared with the cardiovascular risk factors were shown significantly diversity.

HDL levels are significantly lowers in H. pylori seropositive cases according to En-zhi-jin[13]. Chronic infections which may be viral and bacterial may play a role in aggravation of atherosclerosis[14]. Like infections, hypertension, diabetes and smoking are also major risk factors which cause cardiovascular events[15].

Release of inflammatory cytokines during chronic infections which causes endothelial dysfunction and blockage of small vessels that leads to decrease blood flow[16,17,18,19]. H. pylori infection is considered as a new risk factors in developing atherosclerosis due to increased risk in chronic inflammation. This disease may increase risk in the patients with low birth weight[20].

CONCLUSION

From this study, it may be concluded that H. pylori infection can a considered as a new risk factors in developing chronic inflammation in developing atherosclerosis. Therefore proper treatment and diagnosis can decrease the hazards of atherosclerosis.

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Original Article

Electromagnetic Radiations on Thyroid

Effects of Electromagnetic Radiations on Thyroid Follicles of Mice

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ABSTRACT

Objective: To study the effects of electromagnetic radiations on follicles of Thyroid gland of mice.
Study Design: Laboratory based randomized controlled trials.
Place and Duration of Study: The study was carried out in department of Anatomy, Army Medical College Rawalpindi in collaboration with National Institute of Health, Islamabad from November 2009 to November 2010.
Materials and methods: Twenty adult Balb/C male mice were divided randomly into two study groups, comprising of 10 animals in each group.Group A was kept under experimental conditions without mobile phone exposure, group B exposed to radiations for 1 hour /day, for two months from mobile phone set. Thyroid glands were removed and sectioned after exposure period. Sections were stained with hematoxylin and eosin for microscopic examination.
Results: Results showed statistically significant difference in number and mean size of Thyroid follicles in gland of experimental groups.
Conclusion: Thus it is concluded that exposure to EMFs causes decrease in size and increase in number of follicles of thyroid gland of mice, indicating hyperactivity of gland.
Key Words: Mobile Phone, Thyroid Follicles, Balb/c and Mice.

INTRODUCTION

Electromagnetic field (EMF) and its potential harmful effects on the human body are heavily researched in the medical field. Electromagnetic field is an area that is generated by the source of the radio frequency and distributed in space[1]. All the electronic equipment we use in our daily life, without thinking how much we use or how often we use, create EMF[2]. Electromagnetic sources can be classified as Natural Electromagnetic Sources like Sun, stars, atmospheric discharges like thunder and Unnatural or Human Made Sources like Cables that carry electrical currents, television (TV) and computers, electrical home gadgets, radio and TV base stations, cell phones and their base stations[3].

Frequency is number of vibrations of electromagnetic waves in a particular time, at certain points. One cycle of an electromagnetic wave in one second is 1 Hertz (Hz), and one megahertz (MHz) is equal to one million cycles in 1 second. Analog phones work at frequencies between 800 and 900 MHz whereas digital phones work at 1850 to 1990 MHz[4].

Harmful Effects of EMF Sources: Due to the frequent use of cell phones, they have a unique place in EMF studies. The effects of cell phones on the human body can be categorized as thermal and non-thermal effects[5]. Mobile phone is considered one of the important sources for the EMF generation, Even though they have internal safety mechanism they still present a risk factor[6].

Decreasing of the area of vision[7] heavy stress and feeling of tiredness, loosing of concentration and attention, voices in the ears and warming of ears, reversible hearing problems[8], headache, electrical burn[9] and such can be seen as the short term effects.

The long term effects that commonly encountered are; irreversible hearing problems, damaging of the embryonic development[10] increasing risk of miscarriage, decrease in the number of sperms[11], damaging of the brain tissue[12] heart related problems, weakening of the memory[13], lymphoma[14] and damaging of the genetic structure[15]. Purpose of this study was to see the harmful effects of these radiations on the size of thyroid gland follicles because secretion of thyroid hormone is directly related with the size of thyroid gland follicles.

MATERIALS AND METHODS

The study was carried out in department of Anatomy, in collaboration with National Institute of Health, Islamabad from November 2009 till November 2010. Twenty adult Balb/C male mice were taken. Animals were given standard diet and kept at standard temperature 21 ± 2 C and animal room was maintained on 12 hour light/dark cycle. They were divided randomly into two study groups, comprising of 10 animals in each. Experimental animals were housed in the standard plastic cage with the exposure device (mobile phone) kept in centre of the animal cage, in a separate small cage. Group A (Control Group) kept

under same experimental conditions without a mobile phone. Group B exposed to mobile phone radiations for 1hour/day for two months. At the end of experiment, animals sacrificed by over dose of ether, midline incision given in neck, overlying muscles, lymph nodes and salivary glands were removed thyroid gland taken out along with trachea and esophagus. Tissue preserved in 10% formalin, for forty-eight hours then taken and processed for paraffin embedding, 5µm thin sections of tissue prepared and mounted on glass slides. Hematoxylin eosin stain used. Sections of thyroid were examined microscopically for:

- Size of follicles under high power field.
- Number of follicles under low power field.

For the calculation of size of follicles an ocular micrometer was used in calibration with a standard stage micrometer. Two measurements were taken for each follicle. One measurement was taken at the maximum transverse diameter of follicle and another at perpendicular to the first one (16) so the average diameter of the thyroid follicle was measured by taking the mean of the two diameters i.e Max transverse diameter + max perpendicular diameter = 2

Three observations were made in each lobe of gland in this way six observations in each section and 60 observations in each group.

Number of follicles was counted in each lobe of thyroid gland at 10X moving from pole to pole and from medial side (that is trachea) to the lateral side.

Data were entered in a database using SPSS version 15. Descriptive statistics were used to describe the data i.e mean and standard error (SE) for follicular size (ANOVA) followed by Post_hoc tukey test. The difference was regarded statistically significant if the "p" value was equal to or less than 0.05. "p" value was found by means of "t" distribution table.

RESULTS

Group A (control): On microscopic examination thyroid gland revealed normal morphology (fig 1) The thyroid gland of control animals was characterized by the predominance of macro follicles rich in a colloid material. There diameter was 117 ± 5.03/m (table 1)

Table No. 1: Comparison of Follicular diameter in thyroid Tissue between Control and Experimental Groups.

Groups	Mean±SE	P-Value
Control Group A	117.56 ± 5.03	<0.00**
Experimental Group B	92.50 ± 2.25	

Number of follicles in control group was 163 ± 5.53 **(**table 2)

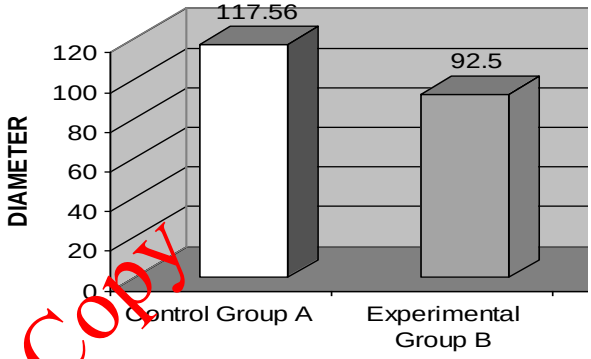
Group B (experimental): Lobes in the exposed group showed numerous micro follicles with less colloid content. (figure 2)

Mean diameter of follicles was 92.50 ± 2.2 (Tab 1, bar chart 1)

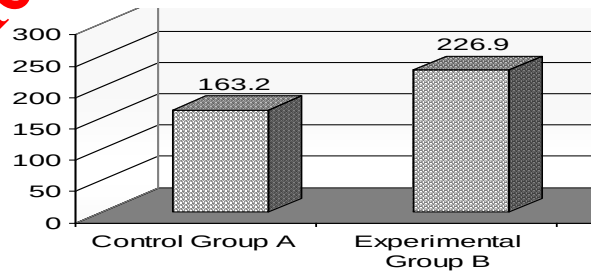
Total number of follicles was increased, number was 226.9 ± 8.949. (Tab 2, bar chart 2)

Table No. 2: Comparison of number of follicles in thyroid Tissue between Control and Experimental Groups.

Groups	Mean±SE	P-Value
Control Group A	163.2± 5.53	<0.00**
Experimental Group B	226.9 ± 8.949	



Bar Chart No.1. Comparison of Follicular diameter in thyroid Tissue between Control and Experimental Groups



Bar Chart No.2: Comparison of number of Follicies in thyroid Tissue between Control and Experimental Groups

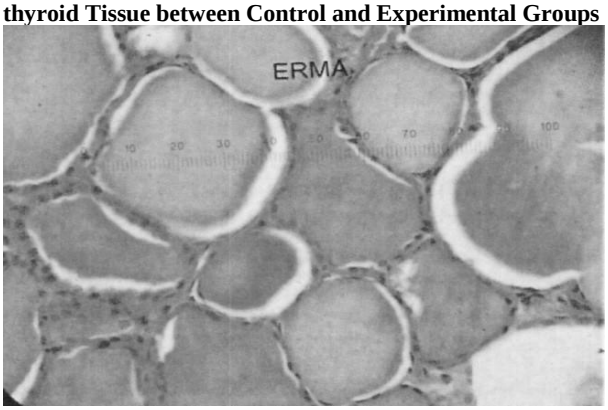


Figure No.1. Photomicrograph of a cross section from thyroid gland of animal of control group showing follicular diameter H&E stain.

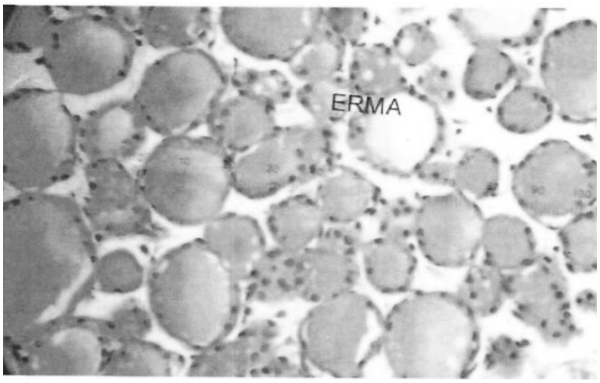


Figure No.2: Photomicrograph of a cross section from thyroid gland of animal of experimental group showing follicular diameter H&E stain.

DISCUSSION

The widespread use of mobile phones has been going sky-high over the past decade and now its use is an essential part of business, commerce and society. The fact that so many people own mobile phones attests to their perceived importance to the general public. The use of mobile phones and related technologies will continue to increase for the foreseeable future[17]. Mobile phones are low power radio devices that transmit and receive radio frequency radiation at frequencies in the microwave range of 900-1800 MHz[18]. Despite repeated horror stories on mobile phones in the media; nearly more than 500 million people worldwide use mobile phones[19]. The extensive use of mobile phones has been accompanied by public debate on the possible adverse effects on human health. The concerns relate to the emissions of radio frequency (RF) radiation from the mobile phones and the base stations that receive and transmit the signals.

In the evaluation of biological effects of radiofrequency fields, many studies were focused on the endocrine system, because of its crucial role in human health status. Due to proximity of thyroid gland to the cell phone during its normal use, the thyroid gland could be involved in interaction with electromagnetic field emissions.

It is certain from literature that; EMF has potential harmful effects on tissues in human and experimental animals. Moreover; it had concluded that there are roles of molecular pathways such as oxidative stress on electromagnetic field-induced diseases. Electromagnetic field reduces the speed of destroying free radical compounds thus allowing them to affect longer periods of time. Therefore, the fact that electromagnetic field increases the amount of free radicals makes us believe that they can also cause cell damage as well as tumors[20]. Results of the present study have shown that histomorphology of thyroid gland in male Balb/C mice after exposure to EMFs generated by mobile phone for two months demonstrated increased activity of thyroid gland; this is indicated by decreased size and increase in number of thyroid follicles.

CONCLUSION

Turnover of hormone within the lumen of follicle depend on diameter of the follicles. Thus, it could be suspected that the synthesis and secretion of thyroid hormone was more intense and faster in smaller follicles suggesting an increase activity of the thyroid gland. There is rapid multiplication of smaller and more active follicles to meet the secretary needs of the gland.

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Original Article

Obstetric Fistula

Knowledge of Medical Students About Obstetric Fistula in Pakistan - Still A Tragedy

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ABSTRACT

Objective: To assess the knowledge of medical students about obstetric fistula in Pakistan—still a tragedy.
Study design: Cross sectional study.
Place and Duration of Study: This study was conducted at Hamdard University Hospital, Karachi from 01.01.2014 to 15.03.2014.
Materials and Methods: A cross sectional study of knowledge of medical students of Final Year MBBS was conducted using a pretested self-administered questionnaire. Total 100 questionnaires were filled out of which, 87 were filled by medical students and 13 by house officers. The data was evaluated and analysed on SPSS.
Results: The results shows that the overall knowledge of our students and junior doctors regarding obstetric fistula was below average. They are not well aware of the substantial burden of obstetric fistula in our community, its root causes and preventive measures to be taken. This shows the need to giving more weightage to this topic in curriculum and re-structuring their training program.
Conclusion: The presence of trained professional is crucial for the early detection and timely management of such complications. To achieve this within limited resources these students and young doctors are an important cadre of health professionals, therefore the curriculum should lay emphasis on community based clinically oriented teaching.
Key Words: Obstetric Fistula, Vesicovaginal Fistula, Rectovaginal Fistula, Maternal Mortality.

INTRODUCTION

The World Health Organization (WHO) defines an obstetric fistula (OF) as an "abnormal opening between a woman's vagina and bladder and/or rectum through which her urine and/or faeces continually leak".[1] Classifications of fistula vary, but they generally include fistulae from obstetric causes including vesicovaginal fistula (VVF) and rectovaginal fistula (RVF).

OF is a devastating complication of complicated labor, it disables millions of women and girls in developing countries. Several million cases of OF are currently thought to exist in sub-Saharan Africa and south Asia.[2]

Worldwide each year more than half a million healthy young women die from complications of pregnancy and childbirth. The WHO estimates that, globally, over 300 million women currently suffer from short or long-term complications arising from pregnancy or childbirth, with around 20 million new cases arising every year [3]. Worldwide, obstructed labour occurs in an estimated 5% of life births and accounts for 8% of maternal deaths [4]. The United Nations Population Fund (UNFPA) recently launched a global campaign to end fistula, labelling this condition a preventable and treatable tragedy.[1]

The development of OF is directly linked to one of the major causes of maternal mortality and that is obstructed labour. Where mother's pelvis is too small to enable the baby to be delivered without help. Adolescent girls are particularly susceptible to obstructed labour, because their pelvises are not fully developed. The labour can last many days and often results in the death of both the mother and the baby. If the mother will survive, she will probably develop a fistula and her baby will most likely be dead. With access to skilled maternal care, such labour can be predicted, identified and treated.[5]

This problem has been eliminated from developed countries but it is still a major public health problem in third world countries. In Pakistan each year over five million women become pregnant, and of these 700,000 (15%) are likely to experience some obstetrical and medical complications. An estimated 30,000 women die each year from pregnancy-related causes.The obstructed labor is one of the major cause of maternal mortality and the development of obstetric fistula.[6]

The WHO has suggested that over two million women, mostly from sub-Saharan African and Asian countries, have fistula.[7] Given an estimated population of 645 million women of reproductive age in sub-Saharan Africa and South Asia in 2010, suggest that 3 per 1000 women of reproductive age have a fistula, which is considerably higher for low and middle income countries. Overall, it is estimated that over one million women may have a fistula in these regions, and that there are over 6000 new cases per year in these regions. Given the devastating consequences, this represents a very substantial burden.[8, 9]

Because of the complex interactions among medical, social, economic, and environmental factors it is less clear which strategies effectively prevent fistulas. The most effective short-term strategies for obstetric fistula prevention will involve enhanced surveillance of

labour, improved access to emergency obstetric services and competent medical care for women both during and after obstructed labour and the development of specialist fistula centres to treat injured women where fistula prevalence is high. The long-term strategies to eradicate obstetric fistula must include universal access to emergency obstetric care, improved access to family planning services, increased education for girls and women, community economic development, and enhanced gender equity.[7]

This is well known fact that OF, have the highest prevalence where maternal mortality is high.[10] Currently there is a worldwide effort to reduce maternal mortality in line with the Millennium Development Goals (MDGs) to reduce maternal mortality by 75% by 2115 [11]. This was restated and re-emphasized on World Health Day 2005, which was dedicated to maternal and new born health.

In order to achieve this target apart from social, financial, medical and political strategies, we can utilize our medical students young doctors and general physicians who are already practicing in communities, they can play vital role by creating awareness regarding risk factors resulting serious maternal mortality and maternal morbidities like obstetric fistula. They can identify high risk patients and arrange their transfer to tertiary care. They can also sensitize the family towards prenatal, intrapartum and postpartum care of mother as well as baby [9].

The purpose of this study was to assess the knowledge of young graduating medical students and junior doctors, about the burden of this tragic disease in our community, where it is still a major health problem.

MATERIALS AND METHODS

The study was conducted at Hamdard University Hospital. A cross sectional survey of knowledge of medical students of Final Year MBBS was conducted using a pretested self-administered questionnaire. Total 100 questionnaires were filled out of which, 87 were filled by medical students and 13 by house officers. The data was evaluated and analysed on SPSS.

RESULTS

Total 100 questionnaires were filled, out of which 87 were filled by medical students and 13 by house officers.

As table 1 shows that only 28% reported correctly about the definition of Obstetric fistula and 70% gave wrong answer while 2% didn't respond. The correct answer was, that it is a medical condition in which a communication develops between rectum and vagina. The other choices given to answer this question were wrong.

Regarding the prevalence of obstetric fistula 60% knew correctly about its prevalence in sub-Saharan Africa and Asia. 38% were wrong and 2% didn't respond.

The symptoms of obstetric fistula varies widely, in our questionnaire the most common symptom was asked and the answer was faecal and urinary incontinence. Only 45% answered correctly, 54% answered wrong and 1% didn't answer.

Regarding risk factors of obstetric fistula, almost all the risk factors are mainly related to low socio economic status, which was correct answer in our questionnaire. It was an eye opening that only 17% reported correctly, 2% didn't respond and 81% reported wrong answer.

In Pakistan, the most important direct cause is unmonitored labor which is mostly conducted by conventional dais at home. 34% reported correct reason though 63% answered wrong and 3% not responded.

Table No. 1: Statement showing correct, incorrect or no response on the issue

	Correct	Incorrect	No response
What is obstetric fistula?	28%	70%	2%
Is it prevalent in Pakistan?	60%	38%	2%
Commonest symptoms of OF?	45%	54%	1%
Commonest risk factors of OF in Pakistan?	17%	81%	2%
Most important cause of OF in Pakistan?	34%	63%	3%
Commonest belief of our community about OF?	31%	65%	4%
Usual attitude of families toward effected patients in Pakistan?	39%	56%	5%
What are the treatment options available in Pakistan?	65%	32%	3%
Are there any special fistula repair centres in Pakistan?	42%	31%	27%
How can we prevent it?	50%	46%	4%
What is the role of students and young doctors in its prevention and eradication?	68%	32%	0%
Is there any need to give extra weightage to this topic in undergraduate curriculum?	100%	0%	0%

OF is still present in under developed countries because of low socioeconomic status, malnutrition, negligence and difficulty in accessing tertiary care. Those who marked any of these causes were marked correct, 61% answered correct and 36% replied wrong while 3% had no answer.

The commonest belief in community regarding obstetrical fistula is curse or punishment from nature which was correctly answered by 31% though 65% answered incorrect and 4% didn't reply. Usual attitude of community is to abandon such miserable women, it was correctly responded by 39%, incorrectly by 56% and 5% didn't respond.

In our study, 59% knew that it is treatable while 17% didn't know and surprisingly 24% had no idea so not responded. Among treatment choices 50% answered for surgical treatment and 15% for catheterization, 32% answered wrong choices and 3% not responded. For special treatment centers in Pakistan only 42 % answered correct, 31% thought that there are no such centers and 27% didn't respond this question.

To overcome this health issue, the correct step to take is creating awareness, only known by 50% and 46% didn't know while 4% had no answer.

In order to reduce this morbidity, their contribution was asked, in which 33% chose by creating awareness, 16% by developing medical strategies, 26% for early referrals and 16% chose special training of doctors. However 9% responded that they can't play any role. They were also asked about their role in community to prevent it and 68% replied correctly which included counselling for antenatal care and avoiding home deliveries. However 32% gave wrong answers like no harm by Dai delivery.

But most importantly, everyone was in favor of giving extra importance and weightage to this topic in their curriculum, which is the need of time. For this, 100% responders favored it.

DISCUSSION

The study was to assess the knowledge of our junior doctors and final year MBBS students about the prevalence, risk factors, causes, community belief and availability of treatment of OF in Pakistan. It was also to assess their attitude towards its prevention and identification of their role in eradication of this problem.

The results, clearly shows that the overall knowledge of our students and junior doctors regarding OF was below average. Which needs to be noticed and careful strategies to be developed, to obtain our target of prevention of this stigma.

Our survey shows that our young doctors and students were not aware of the definition, as 70% replied incorrect, which is primarily required to understand the pathology. This is an eye opening situation for the trainers at under graduate level. This problem can be rectified by giving more weightage to this topic in curriculum and re-structuring their training program.

OF is still prevalent in developing countries including South Africa and countries of Middle East Asia. According to an estimate, introduced by Waaldijk in1993, an incidence rate is 1 to 2 per 1,000 deliveries. This incidence rate suggested a worldwide incidence of 50,000 to 100,000 new cases annually; and a worldwide prevalence of 2 million cases of obstetric fistulae [12]. In Pakistan where each year over five million women become pregnant, and of these 700,000 (15%) are likely to experience some obstetrical and medical complications. An estimated 30,000 women die each year from pregnancy-related causes. The obstructed labor is one of the major cause of maternal mortality and the development of obstetric fistula.[6] our survey revealed that only 60% of our doctors and students were aware of its prevalence in Pakistan.

The commonest symptoms were only known by 45%, which is again related to lack of understanding of the topic which in return related to weakness in training program. It is suggested that Training program should incorporate the principles of risk management as developed in the spheres of psychology, aviation and high reliability organization, they should be at the core of undergraduates, post graduates and lifelong.[13]

Social factors responsible for OF are mainly related to low socio economic status, 81% of them reported wrong. This was because of the fact that community based education is never included in their curriculum. It is also vital to improve overall literacy rate to improve social condition, which is not an easy target in low income country like Pakistan but still povert is not the only determinant. There are various examples of countries with modest levels of GNP have achieved low maternal mortality by establishing community based maternal health care system, examples are Brazil, China, Malaysia and Bangladesh.[14] This explains that even in Pakistan appropriate strategies would indeed lower down the incidence.

Causes of OF include the place of birth, presence of a skilled birth attendant, the duration of labor, the use of a partograph, the lack of prenatal care, early marriage, young age at delivery, older age, lack of family planning, and a number of other poorly defined additional factors.[15,16] Fifty two percent of the women in Pakistan alone give birth without skilled help, either by a relative or someone else and two percent deliver alone.[17] In Pakistan OF is most often the result of obstructed labor.[18]

In our survey this fact was correctly reported by only 34% where as 63% answered wrong and 3% not responded. WHO guidelines suggest that in countries where the prevalence of OF is high, all curricula for trainee midwives, nurses and doctors should include not only theoretical training and prevention but also

treatment. Midwives and obstetricians should be trained in the clinical prevention of OF.

Living with fistula has a profound effect on women's quality of life, as their families and communities tend to view them as defective. They have to cope with pain, discomfort, shame, depression, isolation, and stigma from the community, as well as from their own spouse. In our survey less than 40% were aware about community belief and their attitude towards these poor women. In India and Pakistan, 70% to 90% of women with fistula had been abandoned or divorced, therefore, that some women can no longer cope with the pain and suffering, and resort to suicide.[19, 20] The other reported consequences are social ostracisation [21, 22] and marginalization, high rates of divorce or separation, absence of sexual intercourse [23, 24], loss of fertility and amenorrhea [25] and depression.[26]

In some developing countries, a few specialized fistula hospitals exist, particularly in parts of Ethiopia, Nigeria, Pakistan, Sudan and Tanzania. Over 90% of women can be cured with one operation. However many women and their families, may not even know that a treatment exists and these services are often too far away or too expensive. But most of the doctors lack training in fistula repair, and most hospitals and clinics are unable to treat fistula successfully. It is evident that simple use of an indwelling urinary catheter can help to prevent fistula formation in between 15% to 20% of cases. [27, 28]

Knowledge of our students regarding availability and options of treatment is found out below average. Only 59% knew that it is treatable. Among treatment choices 50% answered for surgical treatment and only 15% for catheterization. For special treatment centers in Pakistan only 42 % answered correct, 31% thought that there are no such centers and 27% didn't respond this question.

To reduce this morbidity, their contribution was assessed and sadly 9% thought that they have no role, if such survey was conducted on larger scale this percentage could even go higher. Regarding their role in community, 68% replied correctly but 32% gave wrong answers including no harm by Dai delivery.

These trained professionals should be utilized in the community and in rural areas provided they are trained on these lines. If trained health professionals are available at BHU they can give basic first aid and arrange transfer to tertiary care center. All over Pakistan there are 57 Medical colleges both private and public sector producing around 8000 fresh graduates each year. They can help in counseling at the community level regarding health education, utilization of medical facilities and awareness about the female health. They can also perform data collection in these areas. PMDC can make it mandatory to have one month job in rural areas to get M.B.B.S. certificate.

CONCLUSION

Clearly, the presence of trained professional is crucial for the early detection and timely management of such complications. To achieve this within limited resources these students and young doctors are an important cadre of health professionals, therefore the curriculum should lay emphasis on community based clinically oriented teaching as also was the same opinion by 100% of the students. WHO has also suggested that undergraduate, curriculum must include a basic understanding of OF.

Limitation of our study was its small sample size and it is the need of time to conduct such surveys on larger scale, to assess the knowledge and perception of youth about health care situation of their country and progress toward MDG goals.

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Original Article

Effect of Cefixime in Typhoid

Efficacy of Cefixime in the Treatment of Uncomplicated Typhoid

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ABSTRACT

Objective: To determine the efficacy of cefixime in the treatment of uncomplicated typhoid fever in children.
Study Design: It was a descriptive case series.
Place and Duration of Study: this study was carried out at the Department of Pediatrics, Teaching Hospital D.G Khan Medical College from April 2013 to September 2013.
Materials and Methods: A total of 110 cases fulfilling the inclusion/exclusion criteria were enrolled in the study.
Results: In this study 8.78±3.87 years was the commonest age, 68(61.82%) male cases and 42(38.18%) female cases, efficacy of cefixime in the treatment of typhoid fever in children was calculated and in 96(87.27%) cases, efficacy was recorded while only 14(12.73%) cases could not treated effectively. The results of the study reveal that cefixime is safe and effective drug for the treatment of typhoid fever in children.
Conclusion: The results of the study reveal that cefixime is safe and effective drug for the treatment of typhoid fever in children.
Key Words: Typhoid Fever, Cefixime, Children

INTRODUCTION

In 1948 John Woodward successfully used chloramphenicol to treat patients with typhoid fever (TF). After this accomplishment, the first choice for the therapy of TF was chloramphenicol until the 1970s, when the first outbreaks of infection by antibiotic resistant bacteria appeared. The loss of sensitivity by Salmonella typhi to the antibiotics used for the treatment of typhoid fever was noted in the years following the beginning of antimicrobial therapy. Resistant strains frequently are resistant to chloramphenicol, trimethoprim-sulfamethoxasole and ampicillin. Resistance to these drugs is called multi-drug resistance (MDR). In places with high incidence of MDR strains of Salmonella typhi, quinolones like ciprofloxacin are the chosen agents for the treatment of TF[1].

In 2006, the World Health Organization (WHO) estimated incidence of 16 to 33 million typhoid fever cases globally every year, with 500,000 to 600,000 deaths and case fatality rate of between 1.5 and 3.8%.[2] With more than 80% of global cases, South Asia is the most commonly reported region for the acquisition of typhoid fever since 1996 to 2005. There are several hospital based studies carried out in Pakistan that described high incidence rate of typhoid fever in children. According to an estimate, 250,000 deaths occur each year in Pakistan among which typhoid fever is one of the leading cause[3].

Pakistan is one of the 6 countries with 80% resistance to these drugs. The emrgence of developing MDR to ampicillin, chloromphenicol and trimethoprim-sulfamethaxazole leads to use of other druge like ciprofloxacin, ceftriaxone, and azithromycin. Flouroquinolones or third generation cephalosporins are the drugs of choice for the treatment of typhoid fever [4,5,7]. In recent years, however, the emergence of resistance to quinolones has placed tremendous pressure on public health system in developing countries as treatment options are limited [6,7].

Widespread emergence of multidrug-resistant S. typhi has necessitated the search for therapeutic options for TF. Fluoroquinolones have proven effective, but to date they are not recommended for use in children, and quinolone resistant strains of S. typhi have been reported[8].

Azalides are another class of antibiotics which have shown promise in the treatment of typhoid fever. Studies comparing the efficacy of Azithromycin with cefixime in adults and in children with typhoid fever have reported it to be safe and efficacious[9].

Only cefixime allow oral administration for use in ambulatory patients. Cefixime is a third generation cephalosporin, for oral use in children, administered once or twice daily with good antimicrobial activity against S. typhi. Due to emergence of multi-drug resistance (MDR) S. typhi alternative drugs for the treatment of TF are required. We conducted this study to assess the efficacy of Cefixime in the treatment of TF.

The emergence of multidrug resistance in Pakistan as well as in other countries leads to use of other antimicrobial agents. So, this study is designed to assess the efficacy of cefixime in their treatment of typhoid fever in children and will help in the better selection of

drugs in the treatment of enteric fever in children. The low cost of this drug and its single dose per day is going to be very economical for the patients.

MATERIALS AND METHODS

A total of 110 children, who were diagnosed as typhoid fever on the basis of their clinical presentation of febrile illness supported by positive typhoid IgM, between 3 to 15 years of age of either gender were included in the study while patients of typhoid fever who developed complications of the disease were excluded from the study. Informed consent was taken from the parents of the children and they were explained in detail regarding treatment procedure. All patients were given cefixime in single dosage of 20mg/kg/day. Patients were admitted and examined daily by the researcher and efficacy to treatment was noted. Efficacy of treatment was established (complete resolution of fever (98.6F) within 96 hours of treatment and patients remain a febrile for next 48 hours). The data was collected on a pre-designed proforma. Effect modifier (duration of fever before treatment) were addressed through stratification.

The data was entered in the SPSS version 12.0 and analyzed accordingly. Age was presented as mean and standard deviation. Gender and efficacy of treatment was presented as frequency and percentages. Data was stratified for duration of fever (<2, >5 days) before treatment.

RESULTS

Age distribution of the patients was done, 29(26.36%) were recorded between 3-5 years, 65(59.09%) were between 6-10 years and 16(14.55%) were between 11-15 years of age and 8.78+3.87 was recorded as mean and s.d.(Table 1). Gender distribution of the patients shows 68(61.82%) male cases and 42(38.18%) female cases (Table 2). Efficacy of cefixime in the treatment of typhoid fever in children was calculated and in 96(87.27%) cases, efficacy was recorded while only 14(12.73%) cases could not be treated effectively (Table 3).

Table No.1: Age Distribution (n=110)

Age(years)	n	%
3-5	29	26.36
6-10	65	59.09
11-15	16	14.55

Table No.2: Gender Distribution of the Patients (n=110)

Gender	n	%
Male	68	61.82
Female	42	38.18

Stratification of efficacy of cefixime in treatment of typhoid fever in children with regards to duration of fever reveals that 77(70%) cases were suffering from fever >5 days before treatment and out of them 69(89.61%) were treated effectively while <2 days of duration of fever before treatment was recorded in 33(30%) cases and out of them 27(81.82%) cases were treated effectively (Table 4).

Table No.3: Efficacy of Cefixime in the Treatment of Typhoid Fever In Children (n=110)

Efficacy	n	%
Yes	96	87.27
No	14	12.73

Table No.4: Stratification of Efficacy of Cefixime in the Treatment of Typhoid Fever In Children with Regards to Duration of Fever (n=110)

Duration of fever before treatment	No. of cases	%	Efficacy	
			No. of cases	%
>5 days	77	70	69/77	89.61
<2 days	33	30	27/33	81.82

DISCUSSION

The emergence of multi drug resistance in Pakistan as well as in other countries leads to use of other antimicrobial agents. This study was designed to assess the efficacy of cefixime and will help in the better selection of drugs in the treatment of enteric fever in children. The low cost of this drug and its single dose per day is going to be very economical for the patients.

For many decades, antibiotics such as chloramphenicol, ampicillin, and cotrimoxazole were used for treating enteric fever. The emergence of multiple-drug-resistant (MDR) Salmonella strains, which are resistant to chloramphenicol, ampicillin, and cotrimoxazole, have changed treatment options. MDR strains of S. Typhi have been reported from all parts of the world[10].

In one study, cefixime accomplishes the desired characteristics of an antibiotic and may be the treatment of choice of MDR and non-MDR typhoid fever, particularly in children from endemic areas with high prevalence of MDR typhoid fever. In that study, cefixime showed clinical efficacy around 100%, with low-rate of relapses. All strains isolated were sensitive to cefixime[11].

To date, the Fluoroquinolones are the agents of choice for the treatment of TF. However, the role of these agents in the pediatric patient is controversial, as they can cause damage to the articular cartilage[12]. In another study, cefexime accomplishes the desired characteristics of antibiotics and may be the treatment of TF, particularly in children and all age groups. In that study Cefixime showed clinical efficacy around 92.5% [13].

Ciprofloxacin and ofloxacin resistance was first reported in Bangladesh in 8% of enteric fever cases in the year 2000 [14]. In the year 2005 a resistance pattern of 71% was observed. In year 2009 the scenario was that of 90% resistance to second generation fluroquinolones cases[14,15,16,17]. Ciprofloxacin is no

more a drug for empirical therapy for the treatment of enteric fever in almost all countries of the world unless a complete ciprofloxacin susceptibility is proved [18,19]. However WHO recommends ciprofloxacin and ofloxacin for MDR cases and azithromycin, third generation cephalosporin and high dose older generation fluroquinolones in nalidixic acid resistant cases [17,20,21]. Resistance to azithromycin and Cefixime is rarely reported and this is why they can be used as empirical therapy in enteric fever [22,23].

The limitation of the study was that we did not compare cefixime with any other antibiotics and any side effects of the drug but considering the other studies mentioned above, we may consider cefixime as a safe drug and further trials may be conducted for comparison with other antibiotics as well. However, the low cost of this drug and its single dose per day is going to be very economical for the patients in our setup.

CONCLUSION

The results of the study reveal that cefixime is safe and effective drug for the treatment of typhoid fever in children.

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Original Article

Treatment Outcome of Childhood Hodgkin Lymphoma after Chemotherapy Alone

Hodgkin Lymphoma

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ABSTRACT

Objective: To find the outcome of Hodgkin lymphoma treatment in children without radiotherapy using chemotherapy as a single treatment modality.

Study Design: Descriptive retrospective study.

Place and Duration of the Study: This study was conducted at the Pediatric Oncology Department, Children's Hospital & Institute of Child Health, Multan from January, 2006 to January, 2014.

Materials and Methods: All newly diagnosed children with Hodgkin lymphoma up to the age of 15 years were included in the study. Diagnosis was made on history, clinical examination and lymph node biopsy for histopathology & immunohistochemical staining. X-Ray chest, CT scan of the abdomen, bone scan and bone marrow biopsy were done for staging the disease. Chemotherapy was given to all children according to UKCCSG (United Kingdom Childhood Cancer Study Group) protocol for treatment of Hodgkin lymphoma. Response to treatment was noted after completion of chemotherapy.

Results: Among 60 children with Hodgkin lymphoma, 55(92%) were male with M: F = 11.5:1.Age range at presentation was 3.5-15 years with mean of 8.5 years. Cervical lymphadenopathy was noted in 52(87%) & mediastinal lymphadenopathy in 8(13%) patients. Stage I, II, III & IV were found in 13(22%), 4(7%), 34(56%) & 9(15%) respectively. Mixed cellularity (MC) was the most common histopathological type, found in 43(72%) patients, followed by nodular sclerosis(NS) in 13(22%) and lymphocyte predominant (LP) in 3(5%).Lymphocyte depleted(LD) type was found in only one patient. On immunohistochemical staining CD30 was positive in all patients. So far, 53 (88%) children have completed their treatment and showed complete response to chemotherapy alone, 4(7%) got relapse & 3(5%) expired during treatment.

Conclusion: Most of the children with Hodgkin lymphoma show complete response to the chemotherapy alone and can be treated without radiotherapy. However more patients and long-term follow up is needed for making definite conclusions.

Key Words: Hodgkin Lymphoma, Lymph Node Biopsy, Immunohistochemical Staining, Chemotherapy.

INTRODUCTION

Treatment for children with Hodgkin lymphoma may involve radiotherapy, chemotherapy or combined modality therapy. High-dose large volume radiotherapy administered to young and prepubescent children is known to result in impairment of soft tissue and bone growth. The growth disturbance is related largely to the age of the child at the time of radiotherapy and the radiation dose administered.[1] The most marked impairment is observed when radiation dose >35 Gy are given to children <13 years old.[2] The risk of Hypothyroidism appears to be related to radiation dose.[3] Among children who receive neck irradiation of < 26 Gy, the incidence of hypothyroidism is only 17%compared with 78% incidence among children who receive dose > 26 Gy.[4] Standard-dose radiotherapy has also been implicated in the development of late thyroid, cardiac, and pulmonary toxicity.[5,6] A major late effect among survivors of pediatric Hodgkin's disease is an increased risk for second malignant tumors, particularly breast cancer or other solid tumors, which commonly occur in previously irradiated fields.[7,8,9,10] Therapeutic trials in adults with Hodgkin's disease have compared outcome between patients treated with chemotherapy alone and those treated with combined-modality Therapy. In some studies, patients treated with combined modality therapy have an event-free survival (EFS) benefit but no increased survival benefit. In other studies, EFS and overall survival (OS) are similar.[11] One pediatric trial that compared chemotherapy with or without radiation for patients with advanced stage Hodgkin's disease indicated no benefit with the addition of radiation.[12] The British experience of radiation alone as a single treatment for stage 1 showed a 92 % overall survival, but 30 % of the children relapsed and required salvage chemotherapy.[13] This rate seems too high considering the results of the similar patients treated by a short chemotherapy course and low dose radiation.[14, 15]

The rationale for most protocols based on chemotherapy alone was always based on the experience of the Olweny et al.[16] in Uganda where radiotherapy machines were not available. On the basis

of these encouraging results, the earliest chemotherapy-alone studies used 6-12 courses of MOPP (nitrogen mustard,oncovin,prednisolone,procarbazine) or MOPP like regimens.[17,18,19] In pediatric and adult experience ,six cycles of MOPP induce male sterility in > 90% of the patients[20] as well as an increased risk of secondary leukemia [21] that were considered unjustifiable. In 1984, Chemotherapy was changed from MOPP to ABVD (Adriamycin , Bleomycin , Vincristine & Dacarbazine) which was reported to be less toxic owing to the lower dosages of alkylating agents [22],but high relapse rate was observed with this regimen[23] Treatment was switched to combination of MOPP and ABVD in all Hodgkin lymphoma cases irrespective of stage or size of the involved lymph nodes ,considering the fact that cure can be achieved using non cross-resistant drugs from onset and because male gonadal dysfunction is reported to be reversible after three MOPP courses[24]

Our study analyzes the results of chemotherapy-alone modality for treatment of Hodgkin lymphoma at the Children's Hospital and the Institute of Child Health, Multan according to UKCCSG protocol for Hodgkin Lymphoma (HD 2000-2002).

MATERIALS AND METHODS

It is a retrospective descriptive study conducted at the Children's Hospital and the Institute of Child Health, Multan from January, 2006 to January, 2014. Sixty newly diagnosed children with Hodgkin Lymphoma up to the age of 15 years were included in the study. Patients with relapsed Hodgkin lymphoma and those who were already given chemotherapy at some other center were excluded from the study. Data was collected from the record of all patients registered for the treatment of Hodgkin lymphoma and age,sex ,clinical presentation & previous drug history specially for anti tuberculosis drugs were noted. Local examination of the involved lymph nodes for site, size & consistency was noted. Abdominal examination for hepatosplenomegaly and chest examination for any signs & symptoms related to mediastinal mass were noted. Lymph node biopsy of the primary site was sent for histopathology & immunohistochemical staining to the histopathologist at Shaukat Khanam Memorial Cancer Hospital & Research Center Lahore.CD 30 staining was done in all patients but CD 15 & CD 20 could not be done due to limited financial resources. X-Ray chest was done in all patients for the detection of any mediastinal mass. CT scan of the neck, chest, abdomen & pelvis, bone scan and bone marrow trephine biopsy were done for staging the disease.

Chemotherapy was given to all children according to UKCCSG protocol for Hodgkin Lymphoma (HD 2000-2002). We used the hybrid regimen with alternating courses of ChlVPP and ABVD to lessen the pulmonary and cardiac toxicity associated with ABVD. ChlVPP regimen consists of Chlorambucil , Vinblastine , Procarbazine & Prednisolone and ABVD consists of Adriamycin , Bleomycin , Vincristine & Dacarbazine .Four to eight courses were given depending upon the stage of the Hodgkin lymphoma. At the end of the treatment, response to chemotherapy was assessed by regression/persistence of the lymph nodes clinically and on CT scan.

Data was analyzed using statistical software SPSS 19.Descriptive statistics were applied to analyze the data. The quantitative variables were calculated by mean and standard deviation and qualitative variables by percentages and frequencies.

RESULTS

Among 60 children with Hodgkin Lymphoma, 55(92%) were male with M: F = 11.5:1.Age range at presentation was 3.5-15 years with mean age of 8.5 years. Most of the patients were referred from different areas of Southern Punjab and remaining belonged to some areas of Baluchistan. Previous history of receiving anti tuberculosis drugs for a duration of 3 - 9 months was noted in 12(20 %) patients. Cervical lymphadenopathy was noted in 52(87%), being the most common site of Hodgkin lymphoma presentation ,axillary in 3(5%) and generalized in 5(8%) patients with a variable duration of 3 months to 3 years**.** Mediastinal lymphadenopathy was noted in 8(13%) children (table 1). Stage I, II, III & IV were found in 13(22%), 4(7%), 34(56%) & 9(15%) respectively (table 2). Among the four known histological types of classical Hodgkin lymphoma; Mixed cellularity (MC) was the most common histopathological type, found in 43(72%) patients, followed by nodular sclerosis(NS) in 13(22%) lymphocyte predominant (LP) in 3(5%) & Lymphocyte depleted(LD) type in only one patient.(Table. 3) .On immunohistochemical staining CD30 was positive in all patients. So far, 53 (88%) children have completed their treatment and showed complete response to chemotherapy, 4(7%) got relapse & were given EPIC regimen (Etoposide, Prednisolone,Ifosfamide,cisplatin). During chemotherapy, 3(5%) patients expired due to herpes encephalitis, tuberculous meningitis and pulmonary aspergillosis. (Table 4).

Table No.I: Clinical characteristics of the patients (n=60)

Clinical Characteristics	Patients
Age	3.5 – 15 Yrs
Mean Age	8.5 Years
Males	55 (92%)
Females	05(08%)
Male: Female	11.5 :0 1
Took ATT	12(20%)
Cervical Lymphadenopathy	52 (87%)
Pallor	42 (70%)
Fever	40 (67%)
Weight Loss	12 (20%)
Mediastinal Mass	08 (13%)

Table No.2: Staging Distribution of Hodgkin Lymphoma (n=60)

Stages	Patients
Stage I	13(22%)
Stage II	04(07%)
Stage III	34(56%)
Stage IV	09(15%)

Table No.3: Histopathological Types of Hodgkin Lymphoma (n=60)

Histopathological Type	Patients
Mixed Celularity	43 (72%)
Nodular Sclerosis	13 (22%)
Lymphocyte Predominant	03(05%)
Lymphocyte Depleted Type	01 (01%)

Table No.4: Outcome

Total Patients	60
Compete Response to treatment	53(88%)
Relapse	04(07%)
Expired	03(05%)

DISCUSSION

Since the introduction of MOPP chemotherapy in addition to extended field radiotherapy, combined therapy has become a standard mode of treatment for Hodgkin lymphoma in most centers [25, 26] The first report on children treated without radiotherapy was from Ziegler et al [27]In 1978, Olweny et al. reported survival rates of 75% and 60% for low and high stage patients respectively.[28] In 1988, Ekert et al, gave disease free survival rates (DFS) of 92% for all stages using chemotherapy only.[29] In 1989, a randomized study showed equal results using chemotherapy with or without radiotherapy [30]

In our study, all patients were enrolled onto a single protocol regardless of the stage and histopathological type of the Hodgkin lymphoma. Chemotherapy alone modality was used with ChlVVP -ABVD regimen for a duration of 4-8 months depending upon the stage of the disease. Majority of the patients i.e. 88% showed complete response to treatment with regression of lymph nodes at the primary site clinically and on CT scan. These results of our study are in concordance with a study conducted in Costa Rica where Lobo-Sanahuja et al. gave results of 86 children treated with chemotherapy alone with DFS rates of 90% and 60% for stage I- IIIA and IIIB- IV, respectively. [31]The reported decrease in DFS in patients with more advanced stage is not seen in our patients. But in our series only a few stage IV patients i.e 09(15%) are included, also the case in many other reports. From a retrospective analysis on several reports, Bader et al. concluded that only stage IVB patients benefit from combined therapy. [32] The data from our patients are in line with mentioned reports.

Although the follow-up for our study is not yet long enough to conclude that survival will be equivalent in our patients to the patients receiving radiotherapy, other studies that have longer follow-up have indicated no survival benefit for post-chemotherapy radiation therapy. [33] Loffler et al. conducted a meta-analysis that included eight trials for patients with Hodgkin's disease in which the randomized study question was chemotherapy with or without additional radiation therapy. Overall, patients who received radiation had an 11% higher rate of continuous complete remission at 10 years (15% higher for patients with stage I to III disease). The advantage was less pronounced for patients with mixed-cellularity Hodgkin's disease, and same response might be expected in our patients as mixed-cellularity was the most common type in our patients i.e. 72%. However, overall survival was better in the chemotherapy-alone arm because of an increased rate of death after relapse and from non–relapse-related causes in patients who received radiation before relapse. In the only other randomized study of radiotherapy versus no further treatment in children with Hodgkin's disease achieving a complete response to initial chemotherapy, Weiner et al [34] treated patients with advanced-stage disease who achieved complete responses to eight cycles of MOPP-ABVD with total nodal radiation or no further therapy. There was no difference in EFS or overall survival at 5 years for patients in the two randomized treatment groups.

Although survival is an excellent measure of outcome, EFS is equally important end point when treating patients with Hodgkin's disease. Although many patients who relapse can be cured, salvage therapy is more toxic and is associated with a high rate of late effects. In a study of survivors of pediatric Hodgkin's disease from Stanford, [35] relapse was the most significant risk factor for the development of a second malignancy. In our study, relapse was observed in 4(7%) patients and these patients were given salvage therapy with EPIC regimen. The follow-up for our study is not yet long enough to conclude about the toxicity and late effects of this salvage therapy. Considering long-term effects, it is known that ABVD courses combined with radiotherapy cause parenchymal lung damage. Gonadal toxicity is lower using ABVD instead of MOPP. [36, 37] The occurrence of secondary malignancies for MOPP or ABVD in combination with radiotherapy is probably similar.[38] The use of hybrid chemotherapy programs that decrease total exposure to alkylating agents, anthracyclines, and bleomycin has decreased, but not eliminated, the incidence of chemotherapy-associated late effects. These observations are in concordance with our study, as we did not found these effects associated with chemotherapy in our patients. Similarly, no

endocrinological dysfunction was noted in our patients during chemotherapy after regular evaluation by endocrinologist of our hospital. This observation may be due to use of hybrid regimen with alternating ChlVVP - ABVD courses, secondly the follow-up for our patients is not yet long enough to conclude about the late effects.

In our study, 3(5%) patients expired during the treatment due to causes other than the disease itself or the chemotherapy. One patient expired due to complicated tuberculos meningitis, other due to pulmonary aspergillosis and third one due to herpes encephalitis. These causes of death are due to increased risk of infections in these children as they are immunocompromised due to disease itself and chemotherapy as well.

CONCLUSION

Chemotherapy alone with ChlVVP – ABVD regimen gives a high cure rate in all children with Hodgkin lymphoma without use of radiotherapy. This treatment modality is effective and safe, however more patients and long-term follow up is needed for making definite conclusions.

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Original Article

Efficacy of Low Dose Isotretinoin (20 Mg) for the Treatment of Mild to Moderate Acne Vulgaris

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ABSTRACT

Objective: To determine the efficacy and safety of low dose (20 mg) isotretinoin for the treatment of mild to moderate acne for a duration of six to nine months.

Study Design: This was an observational, non-comparative, uncontrolled study.

Place and Duration of Study: This study was carried out at the Department of Dermatology, Shalamar Hospital Lahore from 01-1-2010 to 31-12-2013.

Materials and Methods: Six hundred adult patients of either sex with mild to moderate acne and, ages between 15 to 25 years were enrolled. They were treated with a fixed low dose of isotretinoin daily irrespective of weight, for six to nine months. Patients were evaluated clinically at baseline, then monthly during the treatment and follow-up.

Results: Of the 600 patients enrolled, 580 completed the study. 94% of patients were completely cured in six months with a cumulative dose of 62.37 mg/kg.Treatment was continuedfor 6 % of patients, who still had active acne lesions.The cure rate reached 98.96 % at the end of ninth months. Patients were followed for another six months and a relapse rate of 4.48% was observed. Mild cheilitis and xerosis were common. Laboratory abnormalities were mild and transient.

Conclusion: Six to nine months treatment with a daily dose of 20 mg/day isotretinoin was found to be effective in patients with mild to moderate acne. The drug was well-tolerated and showed almost negligible clinical and laboratory side effects.

Key Words: Acne, Low dose Isotretinoin, efficacy, side effects

INTRODUCTION

Acne Vulgaris is one of the most common skin disorder that involves pilosebaceous glands. It mainly affects adolescents, between 12 to 25 years of age, though may occur at any age[1]. Acne has a complex pathogenesis: increased seborrhoea, ductal comification and colonization of pilosebaceous ducts by propioni bacterium acne with consequential inflammation. An elevation in gene markers such as Insulin like growth factor-1 (IGF-1), interleukin-1 beta(IL-1β) and tumor necrosis factor-alfa (TNF-α) is also a commonly observed [2].

Isotretinoin, an FDA approved drug for treatment of severe nodulo-cystic acne,has revolutionized the treatment of acne as it affects all the factors involved in the pathogenesis of acne[3]. Since its worldwide introduction, it has been accepted as the most effective mode of treatment for acne [4]. Its recommended dosage is relatively high, 0.5 mg/kg to 1.0 mg /kg per day for four to eight months until a cumulative dose of 120 mg/kg to 150 mg/kg is reached[5]. This regimen is widely used and produces good results, though a large number of dose dependent side effects are reported[6]. Due to these side effects, and high cost of the medicine, patients have difficulty in completing the treatment [7].

Common practice in some areas of the world is to administer low dose regimen, for the less severe cases of acne but this practice has not yet been well-established[8]. Recent studies have reinforced the view that low-dose isotretinoin is useful for mild to moderate acne, with less side effects (cutaneous, systemic and laboratory based) as compared to standard dosage [9]. As to date there is no data on use of fixed daily dose in mild to moderate acne,in population of Lahore, therefore, we planned to conduct this study.

The aim of this open label, observational study was:

1. To assess the efficacy of fixed daily low dose (20 mg/day) isotretinoin in the treatment of mild to moderate acne.
2. To determine the various side effects with oral isotretinoin in fixed low dose (20 mg/day).

To evaluate the incidence of relapse after treatment with low dose oral isotretinoin.

MATERIALS AND METHODS

Description of Participants: This was an observational, non-comparative, open label and, uncontrolled study. Six hundred patients from Lahore district and surrounding areas having mild to moderate acne were selected randomly from the outpatient of the department of dermatology at Shalamar Hospital Lahore. The study period was from 1st January 2010 to 31st December 2013.

Following criteriaswas used in selecting the study group:

Inclusion Criteria:

1. Patientsof age group 15 to 25 years irrespective of

sex or race.
2. Patients diagnosed as having mild to moderate acne (GAGS score of 10 to 38), no nodule or cystic lesion.

Exclusion Criteria:

1. Diabetes mellitus, hypercholesterolemia and hypertriglyceridemia.
2. Patients having acute or chronic liver disease.
3. Patients on oral contraceptive use or taking other drugs known to exacerbate acne.
4. Patients with severe nodulo-cystic acne.

All patients were advised to take isotretinoin 20 mg daily after a fatty meal for a period of six months and those not cured (GAGS score > 0) will continue for another three months. All other treatments except moisturizers were restricted for these patients.

Patients were examined clinically, were graded and recorded using the GAGS score at first visit and then every subsequent monthly visit. Information regarding age, sex, weight, duration of acne, and history of previous treatment was recorded (see Table-1). Non-inflammatory lesions (comedones) and inflammatory lesions (papules and pustules) were counted on first visit and then monthly for six to nine months, depending on how long the treatment was continued. Side effects caused by the treatment were also recorded at each visit.

We considered a six monthfollow-up to be adequate for detection of relapses. During this period, clinical evaluations and acne severity grading were regularly performed at monthly intervals. At the end of the study, the degree of satisfaction on a four-point scale was also documented by the participants where, 4-very satisfied; 3-satisfied; 2-slightly satisfied and 1-unsatisfied.

Serum lipid profile, Liver Function Tests (LFTs) and complete blood picture was done at the baseline before starting the treatment, after 1 month and thenevery three months during the treatment and during the six months follow-up period. Females with signs ofvirilization and hirsutism underwent ultrasonography to exclude Polycystic Ovarian Disease and adrenal hyperplasia.

Global Acne Grading System (GAGS)[10]: The GAGS global score was calculated by rating six different locations (forehead, right cheek, left cheek, nose, chin and chest/upper back) and then multiplying each rating by a factor that is specific to that area. Rating is based on the surface area and distribution /density of pilosebaceous units as follows:

Score of 0 = no lesion, Score of 1 = one or more comedo, Score of 2 = +one or more papule, Score of 3 = +one or more pustule, Score of 4 = +one or more nodule

Multiplication factor used for each location is as follows,

Forehead =2, right cheek =2, left cheek =2, nose =1, chin =1, chest and upper back =3.

The global score is the sum of all six-location scores, and the global acne grade according to the global score is defined as follows:

Nonefor global score = 0, Mild for global score = 1-18, Moderate for global score = 19-30, Severe for global score = 31-38, Very Severe for global score >38.

Statistical Analysis: Statistical analysis was done in R statistical computing software. T-tests and chi-squared were used where appropriate.

RESULTS

Of the 600 patients, enrolled in this study, 442 females and 138 males completed the study. Twenty patients dropped out of study for unknown reasons.Their ages ranged between 15 to 25 years (mean=17.69± 1.86 years), weight ranged from 45 kg to 75 kg (mean=57.8 ± 3.27 kg) and disease duration ranged between six months to three years (mean=6.4±10.7 months) (Table 1).

Table No.1: Study Details

Clinical Characteristics	
Gender	Male=144, Female=436
Age (Years)	17.69± 1.86
Weight (Kg)	57.8± 3.27
Previous history (Months)	6.42± 10.7
GAGS Score	
GAGS at Study Start	25.3± 6.27
GAGS at Month 1	15.74± 6.46
GAGS at Month 2	8.7± 5.81
GAGS at Month 3	3.67± 4.37
GAGS at Month 4	2.33± 3.59
GAGS at Month 5	1.36± 2.8
GAGS at Month 6	0.72± 2.05
Relapse	
Relapse (Percentage)	4.48

For the 580 patients whocompleted the study, the Isotretinoin dose was 20mg/day that according to weight ranged between 0.28 mg/kg to 0.49 mg/kg per day (mean=0.34 ± 0.017mg/kg/day). Patients received treatment for six to nine months. Total Isotretinoin dose range was 62.37mg/kg in six months to 93.55 mg/kg in nine months. Most patients started showing improvement at the end of first month and by the end of sixth months 94% (n=545) of the patients were free of any active acne lesions (GAGS score= 0) and the treatment was stopped (fig 1). Remaining 6% (n=35)

patients continued treatment for another three months, 3.96 %(n=23) patients were declared cured after nine months (GAGS score= 0). The total cure rate after nine months of treatment was 97.96%. Recurrence was observed in 4.48% (n=26) patients and was predominant in females.

About patient satisfaction, 94.6% of patients were very satisfied (4 points), 3.9% of patients were satisfied (3 points), 0.5% of patients were slightly satisfied (2 points) and 1 % of patients were not satisfied (1 point).The mean satisfaction rate was 3.92 points (±0.02).

Laboratory Abnormalities: Triglycerides and total cholesterol levels before and after completion of treatment were also compared. A slight increase in triglycerides and cholesterol (up to 15% higher than the upper limit of normal values) was detected in 4.28% (n=28) of patients. Slight elevation of alanine aminotransferase (ALT) was detected in 0.34% (n=2) of patients. Both the lipid profile and LFTs reverted to normal level within one month after stopping the treatment.

Side effects: The most common side effects reported were mild cheilitis in 91% of patients, mild xerosis in 42.93% of patients and Epistaxis in 2.5% of patients. No patient developed depression or any other psychological side effect.

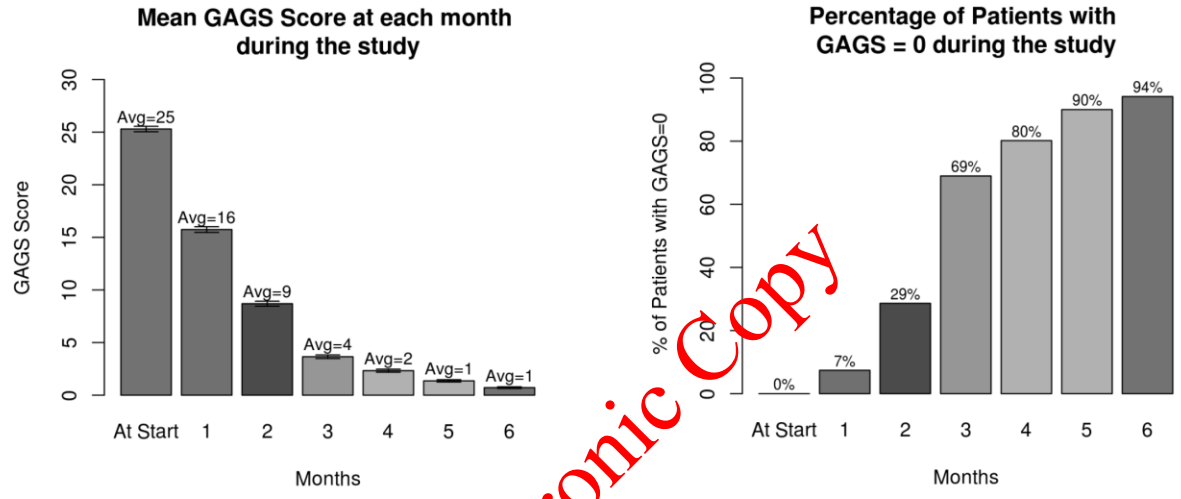

Figure 1: Improvement in patients observed by GAGS score assessment. **(A)** Barplot of the average GAGS score of patients (N=580) who completed the study over the period of six months. The error bars show the standard error for GAGS score. **(B)** Percentage of patients with GAGS Score=0 increases as the study progresses and indicates the improvement in patients' acne with this treatment.

DISCUSSION

The 20 mg fixed low-dose isotretinoin produced good results (GAGS=0) in 94% of patients after six months (Table 1). The cure rate increase to 97.96% after nine months of treatment. Our results were found to be similar to those reported in the literature in patients with moderate acne using the classical dosage of 0.5 mg/kg to 1.0 mg/kg per day[11]. A few studies like ourshave been carried out using low doseisotretinoin irrespective of patients' weight and have shown complete response in majority of patients. Gan et al [11] carried out low dosage treatment for seven to eight months and showed complete response in 93.9% of the patients. Similarly, Kubaisiet al[12] achieved excellent results in 93.5% of patients who also received a fixed dose of 20 mg/day of isotretinoin for a duration of four months. Our results are also supported by the findings of Beneret al[13], Sardana et al [14] and of Lee et al[15]who demonstrated the effectiveness of low-dose isotretinoin in the treatment of acne conglobate and moderate acne, respectively. A larger study (n=638) by Amichaiet al.[16], reported successful treatment of 94.8% of patients with moderate acne by a low-dose 20 mg/day for a total period of six months. Other reports have also supported the efficacy of the low-dose treatment[17].

The present study showed that lower dose of isotretinoinis well tolerated with milder side effects and is cost effective. Our patients showed muco-cutaneous changes like cheilitis, mild xerosis and/or epistaxis and the results are similar to that reported in previous studies with smaller dose[18]. Although no depression was reported in our patients throughout the study, one cannot postulate that low-dose isotretinoin would necessarily reduce the potential for this rarely reported idiosyncratic reaction [19]. In our study, triglycerides and total cholesterol level increased in 4.28% (n=28)of patients, liver enzymes increased in 0.34% (n=2) of patients. These increased levels were still lower when compared to other studies[20]. Laboratory abnormalities

reported in the literature include triglycerides (25% to 44%), total cholesterol (30% to 31%), and liver enzymes (10% to 20%) in patients treated with a standard dose of 0.5 mg/kg to 1.0 mg/kg per day for five to six months[21]. Abnormal laboratory findings in our study were of low grade and these effects were generally transient and reversible and did not alter the treatment course. Furthermore, no study patient discontinued isotretinoin therapy as a result of developing side effects or laboratory abnormalities.

We investigated the recurrence rate and long-term efficacy of our study, by carrying out a monthly follow-up evaluation for six months after the stopping the treatment. Majority of our patients were disease-free during the follow up period. The recurrence rate in our study was 4.48% (n=26), similar to the results shown by Amachi et al. [16]. The recurrence rate was higher in patients with six months of treatment than those with nine months of treatment which shows that the cumulative dose does affects the recurrence rate [21]. Factors shown to influence a relapse have included female gender, younger age (< 16 years of age), truncal acne, severity and, a prolonged history of acne [22].

We verified that the low-dose treatment had effects similar to the conventional treatment with same GAGS scores. The mean patient satisfaction score was 3.92±0.02. This result suggests that the low-dose regimen is superior to other regimens (conventional or intermittent) in terms of patient satisfaction and has similar effects, as compared with the conventional regimen for maintaining remission.

Limitations: The limitations of this study include study design, and the fact that it investigated outcomes of the treatment within a single institution. Our low incidence of reported side effects was based upon complaints documented. In addition, this study did not include patients with nodulo-cystic acne.

CONCLUSION

Our findings encourage 20 mg/day isotretinon as first-line therapy for mild-to-moderate acne. These results suggest that, when we consider tolerability, efficacy and patient satisfaction, the low-dose treatment regimen is the most suitable for patients with mild to moderate acne, with very little side effects.

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Case Report

Glycogen Storage Disorder

Glycogen Storage

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ABSTRACT

Glycogen Storage Disease (**GSD**, also called **Glycogenosis** and **Dextrinosis**) is the result of defects in the processing of glycogen synthesis or breakdown within muscles, liver, and other cell types. Patients usually present with low blood sugar, enlarged liver, slow growth, muscle cramps, seizures and anemia. Von Gierke disease is the most common type of glycogen storage disorder. Von Gierke[1] described the first patient with GSD type I in 1929 under the name hepatonephromegalia glycogenica. In 1952, Cori and Cori [2] demonstrated that glucose-6-phosphatase (G6Pase) deficiency was a cause of GSD type I. Other types are Pompe, Forbes, Cori, Hers and Anderson types.GSD type 5 McArdle disease affects skeletal muscles [3].

Key Words: Glycogen storage disease, Liver, Hypoglycaemia

INTRODUCTION

Glycogen storage disorders are inherited enzyme defects that cause glycogen to be improperly stored in the body. In the United States, they are estimated to occur in 1 per 20,000-25,000 births. Overall, according to a study in British Columbia[4], approximately 2.3 children per 100 000 births (1 in 43,000) have some form of glycogen storage disease. A Dutch study estimated it to be 1 in 40,000[5].

Symptomatic therapy is very important, in type 1 and 3 preventing hypoglycemia is the target. In type 2 GSD DNA recombinant alglucosidase alfa has been found effective. Gene therapy is an effective mode of treatment but not yet available.

Prognosis depends upon the type of GSD. Complications that might occur are renal failure, malignant alteration of hepatic adenomas, progressive cardiorespiratory insufficiency and rhabdomyolysis.

CASE PRESENTATION

Four years old male child was referred to Paediatrics Unit 2, Civil Hospital due to fever, growth retardation and muscle weakness. He was born to a 25 years old healthy woman after a smooth and uneventful pregnancy at 39 weeks gestational age. He had low grade fever, intermittent in character and partly relieved by medicines. He was not gaining weight since 1 year of age and didn't walk or run like children of his age and got tired easily. He was admitted a year back in a local hospital and received blood transfusion twice for being anemic. Hemoglobin was stated to be 3 in old CBC reports. He was fully vaccinated.

On examination he weighed 4.8kg, height, hypoactive, with abdominal distension. Respiratory rate was 38/min, heart rate 128/min, axillary temperature 37.5c, liver was palpable 3cm below costal margin and spleen was 4cm palpable below the costal margin. Subcutaneous fat was lost with loose axillary and gluteal folds.

The Labs showed Hb 6.7 g/dl, MCV 75.9, TLC 6100/cmm with normal differential count, Platelets 76000/cmm. Urine DR and chest Xray were found to be normal. RBS was 88mg/dl. Metabolic profile was all normal except low calcium levels of 7.8mg/dl. Ultrasound abdomen showed mild parenchymal changes in liver. Hb Electrophoresis showed 97.1% HbA1 and other normal patterns of Hemoglobin excluding thallessemia. All culture results were negative.Liver biopsy revelaed multiple tiny fragments of liver tissue showing effacement of normal architecture by large cells with abundant cytoplasm containing glycogen as demonstrated on special stains, on immunohistochemistry the cells showed positivity with cytokeratin CAM 5.2 and negative for CD 68.

He was transfused with blood to maintain hemoglobin around 10, antipyretics were given for fever and regular monitoring of RBS was done with advice about feeding.

DISCUSSION

There is incomplete degradation of glycogen due to deficiency of various enzymes which breakdown glycogen at various levels of its metabolism. Severe hypoglycemia stimulates epinephrine secretion, which activates lipoprotein lipase and the release of free fatty acids. These fatty acids are transported to the liver, where they are used for triglyceride synthesis and are exported as very-low-density lipoprotein (VLDL), which is elevated in these patients. The lipid abnormalities include hypercholesterolemia (decreased high-density lipoprotein [HDL] cholesterol and increased low-density lipoprotein [LDL] cholesterol), Recent evidence suggests that sera from patients with glycogen-storage disease Ia are able to more efficiently promote scavenger receptor class B type I–mediated cellular cholesterol efflux and that an increased antioxidant effect of these sera is directly related to the increased urate concentration.[6]. However, a recent report suggests that affected individuals may sustain an

increase in carotid artery intimal thickness and arterial dysfunction.[7]

The cause of severe anemia in the absence of renal function compromise in children with glycogen-storage disease it has remained unclear. Some have recently proposed that hepcidin production by hepatic adenomas plays central in patients with glycogen-storage disease. Hepcidin is a peptide hormone that is also a key regulator of the egress of cellular iron; in excess, it may interfere with intestinal iron transport as well as iron release from macrophages.

- Long-term consequences of glycogen storage include the following:
  - Hepatic adenomas
  - Hepatocellular carcinoma
  - Progressive renal insufficiency
  - Hyperuricemic nephrocalcinosis
  - Hyperlipidemic xanthomas
  - Short stature
  - Hypoglycemic brain damage

Blood glucose levels, glucose tolerance test, glucagon tolerance test, LFTs, anion gap, Glycogen content and CPK levels along with electromyography and muscle biopsy are diagnostic aids. Liver biopsy is the confirmatory test.

Management is mainly by maintaining satisfactory blood glucose levels and preventing lactic acidosis. Evidence suggests better control of hypoglycemia in persons with GSD type I and III and an extended duration of euglycemia and better metabolic control for patients[8]. Allopurinol, Cholesterol lowering agents and ACE inhibitors have some role. Currently, efforts are underway in animal models to develop gene therapy in patients with both forms of glycogen-storage disease type I. Type 1 GSD requires nocturnal intragastric feedings of glucose and frequent snacks. Additionally, for patients with GSD type I, the future may bring in adeno associated virus vector – mediated gene experimental therapy, which may result in curative therapy, as is possible in patients with GSD type II[9].

Weekly administration of granulocyte colony–stimulating factor (GCSF), in addition to prophylactic PO iron and prompt treatment of intercurrent infections, is critical in patients with glycogen-storage disease type Ib. in 2006, Roe and Mochel reported a clinical benefit with anaplerotic diet therapy in an adult-onset GSD type II patient with skeletal muscle weakness[10]. Liver transplantation is an option in severe cases.

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In this link write the goals of the study but avoid unqualified statements and conclusions not completely supported by data.

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When appropriate, may be included.

ACKNOWLEDGMENTS

List of all contributors who do not meet the criteria for Authorship, such as a person who provided purely technical help, writing assistance or department chair who provided only general support. Financial & Material support should be acknowledged.

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