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Editorial

Exercise may Fight Depression in Heart Failure – Different Studies

Dr. Mohsin Masud Jan
Editor

Exercise helps people with heart failure feel a bit better, physically and emotionally, a new study shows. It may also lower a person's risk of dying or winding up in the hospital.

Up to 40% of people with heart failure grapple with depression. The combination often leads to poor health outcomes. One study found seriously depressed people with heart failure were more than twice as likely to die or be hospitalized over the course of a year compared to other people with heart failure who weren't depressed. "Whenever patients are more depressed, their motivation goes down. Their ability to keep up with their doctors' recommendations goes down. Their ability to get out and do basic physical activities like walking goes down," as does their health, says David A. Friedman, MD, chief of Heart Failure Services at North Shore-LIJ Plainview Hospital in New York. "It's a vicious cycle."

"This [study] ... shows a non-drug way to try to improve patients' mood and motivation. That's the best thing you can do," says Friedman, who was not involved in the research. For the study, which is published in the Journal of the American Medical Association, researchers assigned more than 2,322 stable heart failure patients to a program of regular aerobic exercise or usual care. Usual care consisted of information on disease management and general advice to exercise.

The exercise group started with a standard exercise prescription for patients in cardiac rehab: three 30-minute sessions on either a treadmill or stationary bike each week. After three months, they moved to unsupervised workouts at home. At home, their goal was to get 120 minutes of activity a week. Just as happens in the real world, most exercisers fell short of their weekly goals.

Despite the fact that they weren't as active as they were supposed to be, they still had slightly better scores on a 63-point depression test than the group assigned to usual care. There was a little less than a one-point difference between the two groups. But the differences persisted even after a year, leading researchers to think the result wasn't a fluke. And the exercisers were about 15% less likely to die or be hospitalized for heart failure compared with the group getting usual care.

Researchers think the differences between the two groups were small because most people in the study weren't depressed to begin with. Only 28% had test scores high enough to indicate clinical depression. But the more depressed a person was, the more they had to gain from regular exercise. After a year, test scores of depressed patients were about 1.5 points better in the exercise group compared to those assigned to usual care. "We know that exercise is beneficial in terms of improving cardiovascular fitness. Now we know depression is also reduced in these patients," says researcher James A. Blumenthal, PhD, a professor of psychology and neuroscience at Duke University in Durham, N.C. "For people who were more depressed, they experienced a greater reduction in their depressive symptoms with exercise," he says. The study shows exercise "is in the same ballpark" as other established treatments, particularly antidepressant medications, Blumenthal tells WebMD.

Original Article

Risk Factors and Fetomaternal Out Come of Placenta Previa at Teaching Hospital Khairpur

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ABSTRACT

Objectives: To explore the relative risk factors for placenta previa and to measure the maternal and perinatal complications with placenta previa at teaching hospital, so that a preventive strategy can be made to optimize fetomaternal outcome.

Study Design: Prospective descriptive study.

Place and Duration of Study: This study was conducted at the Department of Obstetrics and Gynecology, Ghulam Mohammad Maher Medical College Hospital, Khairpur, Sindh, Pakistan from 1st January to 31st December 2011.

Materials and Methods: All Patients who presented with antepartum hemorrhage and diagnosed on ultrasound as placenta previa were included in this study. A total of 161dignosed cases of placenta previa were included in the study. The data was collected on predesigned proforma and analyzed on SPSS version 15.

Results: Total obstetric admission was 2796 during study period and frequency of placenta previa was 161 (5.7%), Mean maternal age was 31.09±5.38. Mean were 3.4 for parity and 4.8 for gravidity. The ratio between unbooked and booked cases was 3:1. Maternal and perinatal morbidity was very high with increased rate of caesarean section 110(83.9%), 20 patients received in shock at the time of admission, 145 (90%) needed blood transfusion. Post partum hemorrhage was seen in 25(19%), Maternal death 5(3.8%) was seen in study population. Regarding perinatal outcome preterm delivery was seen in 73(55.7%), low APGAR score <7 at birth 41(31%), low birth weight 60(45.8%) and perinatal mortality rate was 35(26.7%).

Conclusion: It was concluded that Placenta previa is a serious condition with manifestation of significant maternal & perinatal morbidity and mortality. These complications can be reduced by provision of adequate antenatal care to every women and ultrasound examination for early diagnosis of placenta previa before symptoms arrival, reduce rate of caesarean section and provision of family planning services to reduce family size.

Key Words: Placenta previa, maternal morbidity, Perinatal mortality, Risk factors.

INTRODUCTION

Placenta previa is an infrequent type of impaired placental localization in the lower segment of uterus over or near the internal cervical os[1]. Placenta previa complicates 0.3% to 0.5% of the pregnancies[2].

Its incidence is higher among Asian women as compared to white women.[3] Notably 1.2% of the total 37.702 pregnancies analyzed in an Asian population had placenta previa.[4] While an incidence of 3.5% in Pakistani population and 65% pregnancies associated with a previous cesarean section in Pakistan. Significant maternal and perinatal morbidity and mortality can be attributed to this condition.[5]

Etiology of placenta previa is unknown but it is thought to be caused by repeated trauma to the endometrial tissue which leads to endometrial scarring resulting in requirement of greater area and abnormal position for placentation.[6]

Other risk factors including cesarean section[7], high parity,[8] history of previous spontaneous or induced abortions,[9] Previous uterine operation, Previous placenta previa,[10] Multiple gestation,[11] male sex of the fetus.[12] All of these risk factors have been found in the western population. Risk factors in Pakistani women according to studies done to date in Pakistan include increasing maternal age,[13] increasing parity, previous Caesarean section,[9] Smoking,[14] low socio-economic status , residence in urban areas, working during pregnancy were the risk factors associated in an Asian population. Although the risk factors associated with placenta previa in both the Eastern and the Western population are comparable but there are certain risk factors,[15] which are unique to Asian population.

Maternal complication of placenta previa are APH, mal presentation, shock, the risk of massive hemorrhage is 12 times more likely with placenta previa.[20] It also includes higher rate of cesarean section, peripartum hysterectomies,[21] coagulation failure or even death.

Fetal complications are preterm birth, low birth weight, IUGR and intrauterine death. The rate of birth defects is 2.5 times more often in pregnancies affected by placenta previa; the cause is unclear.[16] Birth asphyxia is also high[17]. The rate of admission of neonates to NICU and duration of stay in hospital were increased in pregnancies complicated with placenta previa.[18]

Lack of antenatal care is associated with increased fetal and maternal mortality, and is a matter of great concern as antenatal is not given the due consideration as it demands in underdeveloped countries of the world such as Pakistan.

Women with placenta previa mostly need to deliver the baby by cesarean section; this prevents the death of the mother and the baby. Most complications can be avoided by hospitalizing a mother who is having symptoms, and delivering her by planned C-Section.[19]
The Objective of our study is to evaluate the Potential role of risk factors for placenta previa and to measuse the maternal and perinatal morbidity and mortality associated with placenta previa and to develop proposal to reduce maternal and fetal complications in these cases.

MATERIALS AND METHODS

It was a prospective study carried out at department of Obstetrics and Gynecology, Ghulam Mohammad Maher Medical College Hospital Khairpur, over a one year period. All patients who presented with antepartum hemorrhage and diagnosed on ultrasound as placenta previa were included in the study, after obtaining informed consent. Exclusion criteria were antepartum hemorrhage with normally situated placenta, placenta abruption, and placenta previa with multiple gestations.
The study group included the 161 cases diagnosed as placenta previa contributing the 7.5% of total obstetric admission. Data was collected including age, parity, booking status, severity of hemorrhage and the risk factors for placenta previa were noted on predesigned pro-forma. Maternal outcome measures with number of blood transfusion mode of delivery, postpartum hemorrhage and maternal deaths. Our primary variables for the neonatal outcomes were gestational age in weeks, birth weight, live birth, stillbirth, Apgar score at one minute, admission in Neonatal Intensive Care Unit, neonatal death and take home baby (discharge from hospital).
Data was analyzed on SPSS version 15.0 by frequencies, means with standard deviations and ratios. P-value < 05 was considered significant.

RESULTS

During the study period total obstetric admissions were 2796 and number of placenta previa cases was 161 (5.7%), only 23% patients were booked and 77.4 were unbooked. Mean maternal age was 31.0.9±5.38, minimum 18 and maximum 42 years. Mean were 3.4 for parity and 4.8 for gravidity.
Out of 161 placenta previa cases 131 delivered in ward and 30 cases that presented with mild bleeding were managed expectantly and discharged when bleeding settled down. Out of 131, 21 patients delivered by vaginal route and 110 (83.9%) by caesarean section.
It was further observed that maximum patients presented at 33-36 weeks of gestation 120(74.5%)
Regarding risk factor (Table:1) multiparity was found in 103 (63.9%) of cases, history of previous caesarean section in 40 (24.8%), placenta previa in previous pregnancies 30 (18.6%), history of Dilatation and Currettage was found in 35 (21.7%) cases, No risk factor was found in 40 (24.8%) of placenta previa cases.

Table No.1: Risk factors of placenta previa

Risk Factors	No of Patients	%age
Multiparity	103	63.9%
Previous c/s	40	24.8%
Past history of pp	30	18.6%
History of d&c	35	21.7%
No risk factor	40	24.8%

c/s=caesarean section, pp= placenta previa, d&c= dilatation and curettage.
Studying maternal complications (Table:2), 145(90%) patients needed blood transfusion and 6% needed massive transfusion 8-10 units, Rate of caesarean was very high 110(83.9%), Postpartum hemorrhage were seen in 25 (18%) patients, 4 (3%) patients ended on Peripartum hysterectomy, maternal mortality 5 (3.8%) was seen in study population.

Table No.2: Maternal morbidity and mortality

Maternal Complications	No of Patients	%age
Blood transfusion	145	90%
Caesarean section	110	83.9%
Postpartum hemorrhage	25	19%
Peripartum hysterectomy	4	3%
Shock	20	15.2%
Maternal Death	5	3.8%

Perinatal outcome data revealed that out of 131 babies born, 73(55.7%) were preterm, 26(19.8%) were fresh stillborn, neonatal death were seen in 18 (13.7%), Neonatal Nursery admission were seen in 45 (34.3%) babies and 87 (66.4%) were discharged from hospital alive (Table:3).

Table No.3: Fetal out come in cases of placenta previa

Variables	No of cCases	%age
Live birth	105	80%
Prematurity	95	72.5%
Still birth	26	19.8%
Neonatal deaths	18	13.1%
Low birth weight	60	45.8%
NNICU	45	34.3%
Take baby home	87	66.4%

NNICU= Neonatal intensive care unit.

DISCUSSION

Bleeding in late pregnancy is important cause of fatal and maternal morbidity and mortality. According to WHO estimates 25% of all maternal deaths are due to hemorrhage. Study from other countries indicates that life threatening hemorrhage occurs 1 in 1000 deliveries. The reported frequency of placenta previa varies from 0.6-1.65%[22] that is 1 in 200 births. The incidence of

placenta previa in our study is quiet high that is 5.7%, while it is quoted to be 2-5%, 3.01% and 2.53% in other studies from other parts of the world. The reason of high incidence of placenta previa in our study may be because of large number of referred cases to a tertiary care hospital, but still this may be an underestimate of actual figure as many patients with hemorrhage fail to reach to hospital. In present study highest number of patients, 90 (55.9%) were of 31- 40 years. This is supported by a study were placenta previa was 54.6% in a wide range of 26- 35 years.[22] The booking status in the current study is only 22.3%, similar to a study done in Saudi Arabia. Out of the rest 77.6%, most had not received antenatal care from anywhere. This clearly shows the importance and necessity of antenatal care in prevention and early detection of placenta previa to reduce morbidity and mortality.

In a study conducted at university of Oslo, age was studied as a significant risk factor with mothers over the age of 40 years being significantly more likely to have severe hemorrhage. But in our study, mean age of the patients is 33.6 years, similar to the study done in another tertiary care hospital of sindh. The reason may be practice of early marriages in our society as compare to other part of the world. the incidence of placenta previa is more in multipara(95%) as compared to nulipara (4.9%). So being a problem of multiparity, reduction in family size and the issues of contraception are highly applicable. Study from Brazzaville University Hospital on 126 cases of placenta previa also reported that 73.6% women had more than two previous deliveries.[22] High rate of blood transfusion in this study and other studies as well.[23]which increases the risk of transfusion reaction and contacting infectious disease such as hepatitis B.

There is high incidence of cesarean section among patients with placenta previa[24] 85.2% in some studies this is close to our study where 110 (83.9%) underwent cesarean section. The incidence of postpartum hemorrhage is 18%, which is almost the same as mentioned by crane et al. Commonest cause of PPH was uterine atony, placenta acreta, followed by coagulation failure. Maternal mortality in this study is 3.8%, contributing to 20.3% of the total maternal deaths in the ward, while mortality quoted by another study due to hemorrhage is (20%).[25]

Considering the perinatal outcome, 95(72.5%) women had preterm deliveries, which is almost the same as found in various other studies. In most of the cases delivery was iatrogenic in maternal interest.

Perinatal mortality was 29%, while other studies from Sindh have quoted 41.6% and 20% perinatal mortality in cases of antepartum hemorrhage, 19.8% were fresh stillborns indicating that severe hemorrhage and hypovolemic shock on arrival exposed the fetuses to hypoxia and ultimately death and this again proves the importance of early and rigourous management of placenta previa.

CONCLUSION

Based upon observations made during this study, it is concluded that placenta previa is as a serious condition with significant maternal & perinatal morbidity and mortality. Factors increasing lost of babies are lack of antenatal care prematurity and low birth weight.

Recommendation:

These placenta previa related complications can be reduced by provision of antenatal care to every woman at their doorstep. Family planning should also be emphasized as a strategy towards reductions of parity and there by the incidence of placenta previa. Considering very high perinatal morbidity and mortality, neonatal care units should further be improved.

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Original Article

Neopterin Screening Significantly Improves Safety of Blood Donations

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ABSTRACT

Introduction: The transfusion of blood borne infections is one of the most important transfusion associated hazards in many parts of the world specially in developing countries. Potentially hazardous agents include certain viruses, bacteria and parasites such as HIV, HCV, HBV, Syphilis, Malaria and other pathogens. These may remain undetected either because they are known and not screened or they may also be unknown by usual screening methods. Moreover it is also possible that blood is donated during the diagnostic window period. Neopterin is a sensitive indicator of activated cell mediated (T helper cells type1) immune response. Its significant role in blood screening was acknowledged after many years of trials therefore we hypothesized that additional non-specific screening using highly sensitive immune marker like neopterin could significantly improve the safety of blood donations

Study Design: A cross-sectional prospective study

Place and Duration of Study: This study was carried out in the department of Physiology, BMSI in collaboration with JPMC blood bank from May 2011 to Oct. 2011.

Patients and methods: A total of 174 blood donors were included in the study who were screened for HIV, HBV, HCV, Malaria and Syphilis by routine screening (ELISA, RPR and slide method). Serum neopterin level was measured using ELISA.

Results: 174 subjects participating in this study, 21 showed increased serum neopterin levels beyond the acceptable cut-off level of 10nmol/l. Out of them 7 were positive for HBV, 6 for HCV and one of the blood donors was found to have HIV and HCV co-infection. Thus increased neopterin levels were found to be highly significant with a p value of 0.001 in donors having viral infections. Further testing of the remaining 7 samples with increased neopterin level that were seronegative by routine screening, led to the detection of acute CMV infection in three of these donors. These subjects were asymptomatic at the time of donating blood. Three subjects tested positive for syphilis by RPR but their neopterin level was found to be within normal range.

Conclusion: Screening of blood donations for serum neopterin levels significantly increases the safety of blood donations regarding various viral pathogens in a non-specific way.

Key Words: Neopterin, Blood donations.

INTRODUCTION

Blood transfusion is an essential component of health care which saves millions of lives each year.[1] Currently known dangerous infectious agents associated with transfusion include HIV, Hepatitis B and C , Malaria, Syphillis, Acute CMV, EBV, Parvo virus, West Nile virus and agents responsible for Filiriasis Leishmaniasis, Toxoplasmosis and Chagas disease.[2,3] The W.H.O. recommends that blood donations worldwide should at least be screened for Hepatitis B Surface Antigen ,Antibody to Hepatitis C ,Antibody to HIV, usually subtypes 1 & 2 and Serologic test for Syphilis.[4]In 2006 the W.H.O report on blood safety revealed that in the area of blood testing, 56 out of 124 countries did not screen all of their donated blood for HIV, hepatitis B & C and syphilis. Reasons given for this include scarcity or unaffordability of test kits, lack of infrastructure and shortage of trained staff. [5] In Pakistan there is high prevalence of Transfusion transmitted infections, with the paid donors showing 25% HCV and 10% HBV infection. In the family donors HCV infection was found to be 2.5% and HBV was 5%, where as the voluntary donors showed 2% prevalence for Hepatitis B and 0.5% for HCV infection.[6]

Neopterin is a sensitive indicator of activated cell mediated (T helper cells type 1) immune response.[7] Human monocytes/macrophages produce and release large amounts of neopterin following activation by T-lymphocyte-derived gamma-interferon.[8,9] It is determined by RIA, ELISA and HPLC in body fluids. It concentrations measure 5.3 ± 2.7 nmol/l in the serum of healthy adults.[10] Activation of the immune system and subsequent rise in neopterin concentration is a key feature of various pathologies like: viral infections, autoimmune diseases , malignant tumours, allograft transplantation and cardiovascular disease. Neopterin screening of blood donations allows to detect and exclude viral infections during the acute phase and allows to further shorten the diagnostic window in addition to specific serologic screening methods.[11] For

blood donation screening serum neopterin level is acceptable below 10nmol/l .[12]There are a number of studies have proved the capability of Neopterin screening to improve safety of blood donations regarding the transmission of viral infections such as HIV, Hep B, Hep C, EBV, Parvo Virus B19 and acute CMV infection.[13]So additional non-specific screening using immune response marker like Neopterin could reduce this risk.[14] This study was under taken to study neopterin relationship with transfusion transmitted infections and assess the potential role of Neopterin screening as a safety marker in blood donations.

PATIENTS AND METHODS

This cross-sectional prospective study was carried out in the department of physiology BMSI, in collaboration with JPMC blood bank. The study comprised of a single group which included 174 blood donors. All healthy blood donors of both gender age between 18-60 years were included in the study. Patients with history of Cancers, history of heart disease, history of active tuberculosis, history of known infectious diseases e.g. HIV, Hepatitis B and C and history of STD / High risk sexual behavior were excluded from this study. These were screened for HIV, HBV, HCV by ELISA, Malaria by slide method and Syphilis by RPR. Serum neopterin level was measured using ELISA.

RESULTS

This study was conducted on blood donors at the JPMC blood bank. A total of one hundred and seventy four blood donors were selected, who were all male and the age group in our study was in the distribution of 18-50 yrs. All the donors were screened for routine basic screening tests (HIV 1 and 2, HBs Ag, HCV , MP and RPR for syphilis). After screening out of 21 donors with elevated neopterin , 14 were positive for infections screened routinely which includes HBs Ag (7) HCV (6) and HCV + HIV co-infection (1). The remaining 7 donors with elevated neopterin were screened for CMV IgM and Dengue IgM antibodies. Three of these asymptomatic donors showed presence of CMV IgM antibodies.

Table No.1: Age distribution of blood donors with Neopterin level

Age group (in years)	Number	Percent	Neopterin level (nmol/L)	
			Mean ± S.D.	Elevated neopterin level
<20	5	2.9	9.24 ± 5.01	1 (20.0%)
20-24	58	33.3	7.36 ± 3.58	8 (13.8%)
25-29	60	34.5	7.15 ± 4.06	8 (13.3%)
30-34	37	21.3	7.03 ± 4.09	3 (8.1%)
35-39	10	5.7	6.51 ± 1.42	-
≥ 40	4	2.3	8.57 ± 6.35	1 (25.0%)
Total	174	100.0	7.25 ± 3.87	21 (12.1%)

Average neopterin level (Mean ± S.D) and Elevated neopterin level according to age were not significant difference p>0.05

Table No.2: Neopterin levels in donors with positive and negative screening tests

Screening test	No. (%)	No. of positive with elevated neopterin level (>10 nmol/L)	Neopterin level (nmol/L)	
			Mean ± S.D	P-value
Negative	154 (88.51)	4 (2.6%)	6.23 ± 2.19	0.001*
Positive	20 (11.49)	17 (85.0%)	15.10 ± 4.93	

Table No.3: Neopterin levels in transfusion transmitted infections

Transmitted disease	No. (%)	No. of positive with elevated neopterin level (>10 nmol/L)	Neopterin levels nmol/l	P value
Hepatitis "B"	7 (4.02)	7 (100%)	16.39 ± 3.21	0.001*
Hepatitis "C"	6 (3.45)	6 (100%)	15.59 ± 1.63	
HIV + Hepatitis "C"	1 (0.57)	1 (100%)	25.01 ± 0.00	
CMV	3 (1.72)	3 (100%)	17.03 ± 1.83	
Syphilis	3 (1.72)	0	1.86 0.78	

Table No.4: Distribution of neopterin levels in various transfusion transmitted disease

Neopterin range (nmol/L)	No. of subject	Transfusion transmitted disease				
		Hep "B"	Hep "C"	Hep "C" & HIV	CMV	VDRL
3.1 – 6.0	70	0	0	0	0	1
6.1 – 10.0	83	0	0	0	0	2
10.1 – 14.0	4	2	1	0	0	0
14.1 – 18.0	11	3	4	0	2	0
18.1 – 22.0	5	2	1	0	1	0
22.1 – 26.0	1	0	0	1	0	0
Total	174	7	6	1	3	3

DISCUSSION

The specific testing cannot control newly emerging and/or unrecognized infections. Additional non-specific screening using immune response marker like Neopterin could reduce this risk. In 1994 nationwide screening for elevated Neopterin was introduced in whole Austria when its significant role in blood screening was acknowledged after years of trials. One of the major goals of this non-specific screening

strategy was to build a kind of umbrella against virus infections which are not routinely screened for.[15] Recent data further supports the concept that neopterin screening should be able to detect a wide range of acute viral infections, and thus also newly emerging viral infections should be detectable by elevated neopterin concentrations e.g highly elevated neopterin levels were observed in patients suffering from acute dengue virus infections. [16]

Considering this background we designed this study to estimate serum Neopterin levels in blood donors of local population and to study its relationship with transfusion transmitted infections. We also intended to assess the potential role of Neopterin screening as a safety marker in blood donations in our local population as it will be a pilot study for the south Asian population with regards to blood donation safety and role of neopterin.

In our study out of 174 donors 21(12.06%) showed elevated neopterin level which is in accordance with the study done by Banu et al[17], who showed 19.09% (58)donors with elevated neopterin level. In another study conducted by Honlinger et al[18] only 1.6% (12) blood donors showed increased neopterin level.

In our study the age distribution of blood donors was between 18-50 yrs. Most of the blood donors were in the age group of 25-29 years i.e 34.5% (60) donors and 20-24years i.e 33.3% (58) donors. This was followed by 21.3% (30) donors in the age group of 30-34 years , 5.7% (10) donors in the age group of 35-39 years, 2.9% (5) donors below the age of 20 years and 2.3% (4) donors over the age of 40 years.

The results of our study showed that the average Neopterin level (Mean ± S.D) and elevated Neopterin level according to age were not significant statistically.(difference P>0.05) This is not in agreement with the study of Spencer et al[19] who found a positive correlation between neopterin level , age and gender This could be due to the fact that all of our study subjects (blood donors) were male in the age distribution of 18-50 yrs in contrast to the age distribution of 20-80 yrs in their study who belonged to either gender. Furthermore in that study, they suggested that the relative contribution of age and gender to modulating neopterin levels in normal physiological events may reflect the biology of underlying aging, late-age onset diseases, and perhaps gender differences in morbidity and mortality.

In our study out of 174 subjects, 154 were negative for the screening of transfusion transmitted infections. The Neopterin content in the sera of these blood donors was 6.23±2.19 nmol/l where as in the blood donors who tested positive for TTIs either by routine screening or our advanced panel of screening markers, the neopterin level was elevated to 15.10±4.93 nmol/l. When compared statistically the difference between these values was found to be highly significant with p value of 0.001.

Among blood donors CMV IgM was positive in 3 donors (1.724%). When compared to study conducted by Honlinger et al[18] it was almost half which showed 3.7% positivity (12) donors. The neopterin level in the sera of these CMV positive donors was 17.03 ± 1.83 nmol/l which is in agreement with the study of Schennach et al [20] who found similarly elevated neopterin levels in CMV positive asymptomatic blood donors. who reported a 20 fold increased incidence of Acute CMV infection in blood donors with elevated neopterin level, where increased neopterin level was found even before CMV IgM seroconversion. Another study conducted by Schennach et al[21] Who also found that in donors with increased neopterin levels the occurrence of an acute Epstein-Barr virus or Parvo virus infection was 4 to 6 times more likely than in donors with neopterin level within the normal range.

In conducted study out of 174 donors 7 (4.02%) were positive for Hbs Ag . The neopterin content in the the sera of viral Hepatitis B positive donors was 16.39 ± 3.21nmol/l. The data was obtained for an evident increase in neopterin levels associated with viral B hepatitis, this was well supported by another study done by Samsonov et al[22] (1992) who found elevated neopterin level of 19.9±5.7 nmol/l in the serum of Hepatitis B positive patients. Kalkan et al[23]in their study also found elevated neopterin levels of 15.6±5.1 nmol/l in chronic HBV positive patients which is in well agreement with our study. The study done by Banu et al [17] also found similar results of neopterin elevation in Viral Hepatitis B positive blood donors.

In our result one HIV positive donor showed elevated neopterin level of 25.01nmol/l. The Study conducted by Fuchs et al also showed increased neopterin level in 100% HIV positive donors. They found that in HIV infection, neopterin levels increase with progressive disease and inversely correlated with CD4+/CD8+ T cell subset ratios and are of predictive significance [24]. Recently in the study of Nubling et al [25] concluded that the diagnostic sensitivity of neopterin screening during the HIV window phase is similar to p24 antigen test therefore neopterin screening of blood donors may identify window phase of HIV infection.

Hepatitis C virus infection also correlated with elevated neopterin levels. The 6 (3.4%) HCV samples had neopterin values in the range of 15.59 ± 1.63nmol/l.Similar results were obtained by Schennach et al[26] and Banu et al[17] in their studies.

Three of the donors in the study were positive for syphilis .The neopterin concentration in their serum was 5.86±0.78 nmol/l which was below the cutoff level of 10nmol/l. Similar findings were observed by N'Gom et al [27] who did not find any neopterin elevation with syphilis. This is probably due to the fact that in contrast to the viral infections which trigger the cytotoxic immune response involving TH1 cells, the systemic bacterial infections invoke the humoral immunity thus involving TH2 instead of TH1, and therefore no change in neopterin levels was observed.[12]

CONCLUSION

Screening of blood donations for serum neopterin levels significantly increases the safety of blood donations regarding various viral pathogens in a non specific way.

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Original Article

Clinical Profile of Patients in Relation to Different Presentations of Acute Appendictis

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ABSTRACT

Objective: To study the different presentations of acute appendicitis and to find out its morbidity and mortality.
Study Design: Descriptive prospective study.
Place and Duration of Study: This study was conducted at Ghulam Mohammad Mahar Medical College and Hospital Sukkur during the period of two (02) years, from April2010 to March 2012.
Patients and Methods: This prospective study included 120 patients. Major criteria for diagnosis were symptoms and signs suggestive of acute appendicitis. Patients were operated within 12-24 hrs of admission. In majority of patients Lanz-incision were made. The appendix was submitted for histopathological examination in every case .Mostly patients were discharged on second post-operative day except the complicated cases which were discharged between 3-5 days.
Results: Out of 120 patients 80 were male and 40 were female with male to female ratio of 2:1, the highest incidence of disease is found in second and third decade of life. Common presenting symptom was anorexia seen in 85 patients. 62 patients were presented with periumblical pain which then shifted and localized at right iliac fossa. Common examination finding was rebound tenderness observed in 91 patients. 18 appendices were found perforated and 08 were gangrenous. The negative appendicitis was found in 16 patients. Commonest post-operative complication was wound infection seen in 22 patients.
Conclusion: Early presentation and surgical intervention can reduce the rate of morbidity, mortality and post-operative complications in patients of acute appendicitis.
Key Words: Acute appendicitis, anorexia, periumblical pain.

INTRODUCTION

Appendicitis is common with life time occurrence of seven (07) percent [1]. Riginald Fitz was the one who named appendicitis to be a disease which was previously diagnosed as an initial process of perityphlitis.[2] Highest incidence is in 10-19 years old.[3] .Appendicitis is one of the most common causes of emergency abdominal surgery. It usually occurs when the appendix become blocked by faecolith, hypertrophied lymphoid tissue or rarely a tumor[4]. Despite technologic advances the diagnosis of appendicitis is still based primarily on patient history and physical examination[5]. The classic history of anorexia and periumblical pain followed by nausea, right lower quadrant pain and vomiting occur in only 50% of patients. Nausea is present in 61-92% of patients; anorexia is present in 74-78% of patients. Diarrhea or constipation is noted in 18% of patients. The pain migration is most discriminating feature of patient's history with sensitivity and specificity of approximately 80% [6]. The symptoms of appendicitis can vary. It can be hard to diagnose appendicitis in young children, elderly and women of child bearing age [7].In some cases other tests may be needed including abdominal ultrasound and ct-scan abdomen[8]. Diagnostic laparoscopy may be useful in selected cases (e.g. infants, elderly and female patients) to confirm the diagnosis of acute appendicitis. Complications of acute appendicitis may include wound infection, dehiscence, bowel obstruction, abdominal/pelvic abscess and rarely death[9]. The mortality rate in non-perforated appendicitis is less than 1%, but it may be as high as 5% or more in young and elderly patients in whom the diagnosis may often be delayed thus making perforation more likely [10]. The goal of therapy of acute appendicitis is early diagnosis and prompt operative intervention [11]. Many surgeons using an aggressive approach, accepting the certain number of negative appendicectomies traditionally 15% , although the use of imaging studies appear to have reduce the negative appendicectomy rate to less than 10% [12]. Perforation in acute appendicitis is responsible for increased morbidity (6-17%), mortality, prolonged hospital stay and financial burden in the patients [13].

PATIENTS AND METHODS

This prospective study was carried out on 120 patients during the period of two years from April 2010 to March 2012 in Ghulam Mohammad Mahar Medical College Hospital Sukkur. Patients with suspected diagnosis of acute appendicitis were hospitalized and relevant Proforma was filled. After detailed history thorough general physical and systemic examination

was performed and positive findings recorded. After admission routine laboratory investigations were sent along with the regular monitoring of vital signs of patients. Ultrasound abdomen was done in all patients. Metronidazole was given to all patients but in cases of perforated appendix third generation cephalosporin were added. Patients were kept nill orally, I/V fluids were given and appendicectomy done within 24 hrs of admission. In majority of patients we used Lanz incision but in those cases whose diagnosis was not clear we used lower midline incision. The special attention was given to technical and anatomical details of findings and dissecting the appendix with least trauma to adjacent structures. In few patients a cleavage plane could not be found and with careful sharp dissection appendix was separated from surrounding structures and removed. In few patients of perforated appendices drains were used. Appendix was submitted for histopathological examination in every case. Majority of the patients were discharged on 2nd post-operative day except complicated cases which were discharged on 3-5 post operative days. Patients were followed as out patients for removal of stitches and then up to the period of three months regularly.

RESULTS

Total patients were 120, out of them 80 were male and 40 were female with male to female ratio of 2:1. The highest incidence of disease is found in second and third decade of life, which decreases gradually as age advances above thirty years.

Table No. 1: Age incidence of appendicitis

Age Group	Male	Female
11-20 YRS	43	23
21-30 YRS	29	12
31-40 YRS	05	02
41-50 YRS	02	02
51-60 YRS	01	01
	Total:80	Total:40

All patients came with pain abdomen. In 62 (51.6%) patients pain started at umbilical region and then shifted and localized at right iliac fossa. The common presenting symptom was anorexia seen in 85 (70.8%) patients followed by nausea observed in 80 (66.6%) patients.

Table No. 2: Clinical presentation of various symptoms.

Symptoms	No: of patients	Percentage
Periumblical pain	62	51.6
Epigastric pain	25	20.8
Pain in RIF	30	25
Pain in hypochondrium	05	4.1
Nausea	80	66.6
Vomiting	68	56.6
Fever	60	50
Anorexia	85	70.8
Absolute constipation	15	18

While examining the different patients it was found that rebound tenderness was present in 91 (75.8%) patients followed by tachycardia which was present in 80 (66.6%) patients.

Table No. 3: Physical findings in the patients.

Signs	No: of patients	Percentage
Temperature	60	50
Tachycardia	80	66.6
Rebound tenderness	91	75.8
Guarding	75	62.5
Rigidity	23	19.1
Psoas sign	34	28.3
Obturator sign	17	14.1
Rovsing sign	48	40
Rectal tenderness	20	16.6

In 18(21.6%) patients appendix was found perforated and in 08(9.6%) patients it was gangrenous. The negative appendicitis was found in 16 (19.5%) patients, of which 04 (4.8%) patients were having Meckle's diverticulitis, 03 (3.6%) have Amoebic typhlitis, in 01 (0.83%) patient ectopic pregnancy was found and 02 (2.4%) were having salpingo-oophoritis, in 03(3.6%) patients we found mesenteric adenitis and in 03 (3.6%) patients appendix found macroscopically normal.

Out of 120 patients the 85 (70.8%) patients presented with the duration of symptoms of 12-24 hrs, in rest of 35 (29.1%) patients the duration of symptoms was 36-72 hours.

In 38 patients complications developed post-operatively, among them 22 (18.3%) patients developed wound infection.

Table No.4: Post-operative complications.

Complication	No: of patients	Percentage
Wound infection	22	18.3
Wound dehiscence	03	3.6
Wound haematoma	03	3.6
Faecal fistula	01	0.83
Intestinal obstruction	02	2.4
Pelvic abscess	03	3.6
Paralytic ileus	04	4.8

DISCUSSION

Acute appendicitis is one of the most common causes of acute abdominal pain. Present day treatment of choice for acute appendicitis is appendicectomy, however complications are inherent to operative treatment [14].Appendicitis occur most frequently in second and third decade of life. The incidence is highest in 10-19 yrs age; it is also higher in men (male to female ratio of 1.4:1). Clinical presentation of acute

appendicitis may mimic other abdominal and chest inflammatory conditions and the classical symptoms of migrating lower abdominal pain, fever, anorexia and vomiting may be evident in only 50-60% of patients [15].

In our study the highest incidence of disease is found in second and third decade of life, out of total 120 patients 80 were male and 40 were female with male to female ratio of 2:1.In one study the incidence was highest in male, age 20-29 yrs where as in female the highest incidence was observed in 10-19 yrs age group [16]. Another study gives the gender ratio of 1.2:1; the mean age was 25.7 yrs and majority of the cases occurring in third decade of life. Abdominal pain, fever, anorexia and vomiting were common symptoms. Commonly elicited signs include RIF tenderness, rebound tenderness, and localized guarding and right rectal wall tenderness [17]. In one study from Hong Kong the mean age of the patients having appendicitis is reported to be 33 yrs. In a retrospective review of 140 patients of appendicectomy, 52 female developed acute appendicitis with male to female ratio of 1.7:1 [13].

A Meta- analysis of the symptoms and signs associated with a presentation of acute appendicitis was unable to identify any one diagnostic finding but showed that migration of pain was associated with diagnosis of acute appendicitis. Tenderness on rectal examination may be present. Percussion tenderness, guarding and rebound tenderness are most reliable clinical findings indicating the diagnosis of acute appendicitis [18]. In our study the most common symptom was anorexia seen in 85(70.8%) patients, followed by nausea in 80(66.6%) patients, the migrating pain was present in 62 (51.6%) patients. The most frequent sign was rebound tenderness observed in 91(75.8%) patients followed by tachycardia in 80 (66.6%) patients. On study showed that presence of pyrexia with tachycardia is common, abdominal examination revealed localized tenderness and muscular rigidity [19]. Acute appendicitis continues to be a diagnostic challenge because of its variable presentation. The negative appendicectomy rate reported in surgical literature varies from 8-33% [20].

In our study the negative appendicectomy rate is 16%.

Appendicitis is most common cause of surgical abdomen in all ages, late diagnosis and surgical intervention is regarded as an important cause of morbidity in acute appendicitis [21].

In our study the appendix found perforated in 18 (21.6%) patients and it was gangrenous in 08(9.6%) patients, and majority of these patients presented with duration of symptoms of 36-72 hours. Careful attention to patient's history, a thorough physical examination and early clinical review help to minimize the possibility of delayed diagnosis of appendicitis. Appendicitis with a delay in treatment usually leads to high perforation rate and unfavorable outcome [22].One study concludes that delayed presentation to hospital is significant factor which leads to perforation in acute appendicitis [23].A retrospective study suggested that the risk of appendiceal rupture is minimal in patients with less than 24-36 hours of untreated symptoms [24]. Another retrospective study suggested that appendicectomy within 12-24 hours of presentation is not associated with an increase in hospital length of stay, operative time, advanced stages of appendicitis or complications [25]. The average rate of perforation at presentation is between 16-30%. Wound infection rate vary from less than 5% in simple to 20% in cases with perforation and gangrene [26].

In our study post operative complications occurred in 38 patients, among them wound infection was observed in 22(18.3%) patients. One study showed that the rate of post operative wound infection vary from 5-20% [27]. Another study showed that after appendicectomy the wound infection was seen in 80% patients, and the overall complication rate was 13.5% [17].

CONCLUSION

Early presentation and surgical intervention can reduce the rate of morbidity, mortality and post-operative complications in patients of acute appendicitis.

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Original Article

Frequency of Congenital Anomalies in New Born & Associated Maternal Risk Factors in the Rural Setup of Nawabshah

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ABSTRACT

Objective: To determine the frequency of congenital anomalies alongwith the assessment of maternal risk factors.
Study Design: Cross sectional observational study.
Place and Duration of Study: This study was conducted at the Department of Obstetrics & Gynaecology at PUMHS Hospital Nawabshah from 01.01.2010 to 31.12.2011.
Materials and Methods: This cross sectional observational study was conducted in the Department of Obs & Gynae, PUMHS Hospital Nawabshah. All the newborn delivered with CA during the specified time comprised the study group. The study population was evaluated according to maternal demographic features like age, gestational age, BMI, birth order and consanguinity. Significant maternal illness, BOH, diabetes mellitus, drug ingestion, smoking and exposure to radiation were recorded. All the newborns were examined by Paediatricians and anomalies were recorded. Mean ± SD were used for age & parity and frequency, pattern of CA alongwith associated maternal risk factor described in number and percentage.
Result: During the study period, 11608 babies were born in which 178 showed evidence of CA giving a frequency of 15.33 / 1000 births. The mean maternal age was 32.24 years while the mean parity was 3.6. Consanguinity was the most significant factor (48.31 %) followed by BOH (14.60 %). Diabetes mellitus was found in 10.67 % while past history of CA was found in 7.30 %. Multiple risk factors were responsible in 9.55 % of cases. Regarding the systemic involvement, CNS anomalies contribute 35.39 %, GIT 18.53 %, muscular skeleton 14.04 % and urogenital 13.43 %. 57.30 % babies were stillborn while 43 % died in early neonatal period and 33 % were referred to Paediatrics ward for further management.
Conclusion: Congenital anomaly is an important cause of perinatal mortality. Its elimination need health education programmes, folic acid supplementation, early recognition by 3D ultrasound and termination in those cases which are not compatible with life.
Key Words: Congenital anomalies, Risk Factors, Folic acid supplementation, Role of ultrasound.

INTRODUCTION

Congenital anomalies (CA) are structural defects of prenatal origin that results from defective embryogenesis or deviation from normal development[1, 2]. It is the 3rd leading cause of perinatal mortality after birth asphyxia & prematurity in developing countries[3]. In Pakistan it accounts for 6-9% of perinatal deaths[4]. Its management involves complex medical issues, behavioral concerns & parental distress with psychological trauma.

65-75% of congenital malformations are multifactorial in origin. The recognizable risk factors are chromosomal aberration, hereditary predisposition, viral infections[5], maternal obesity[6], diabetes mellitus[7], consanguinity[8,9], IVF[10] and drugs[11, 12]. Diabetes mellitus is associated with a 3-4 fold increase risk of CA[7] while consanguinity could be responsible up till 60%[8, 9].

The advancement of ultrasonography is very much appreciated for the diagnosis of CA which offers a 70-80% detection rate in hands of expert sonologist[13]. The beneficial role of folic acid must not be forgotten in the prevention of CA and needs a continuous folic acid supplementation throughout reproductive life[14].

The frequency of congenital anomaly is variable and depend upon the availability of sophisticated investigations like karyotyping and autopsy.

We conducted this study to determine the frequency of CA alongwith the assessment of associated risk factors in the deliveries occurring in the rural setup of Nawabshah.

MATERIAL AND METHODS

This cross sectional study was conducted in the Department of Obs & Gynae at Nawabshah from 1st Jan 2010 to 31st Dec. 2011. All the newborns delivered with CA during the specified time comprised the study group. The study population was evaluated according to a preformed Performa. Maternal demographic features like age, gestational age, BMI, birth order, consanguinity were documented. Significant maternal illness, BOH, diabetes mellitus, drug ingestion, smoking and exposure to radiation were recorded. All the newborns with CA were thoroughly examined by Paediarician at birth and anomalies were recorded. Antenatal anomaly scan were sought for the detection of cardio vascular and GIT anomalies.

Mean ± SD of maternal age and parity were calculated. Frequency, pattern of CA and associated maternal risk

factors describe in numbers and percentage were determined. SPSS version 16 was used for statistical analysis.

RESULTS

During the study period, 11608 babies were born in which 178 showed evidence of CA giving a frequency of 15.33/1000 births. > 85% of mothers were non-booked (< 3 antenatal visits). Maternal age ranged from 15–42 years, the mean age was 32.24 years. Considering the age group, the women who were 26–35 years and > 35 years had highest number 30.84 % and 42.05 % of malformed babies. The parity ranged from 1–8 and the mean parity was 3.6.

Table No.1: Maternal Demographic Features

Age (Years)	n	%age
15 – 25	34	19.10%
26 – 35	58	32.58%
36 – 42	86	48.31%
PARA		
0 – 1	58	32.58%
2 – 4	54	30.33%
4 – 8	66	37.07%
BMI		
18 – 25	31	17.41%
25 – 30	68	38.20%
> 30	79	44.38%

The most significant maternal risk factor associated with CA was Consanguinity (48.31 %), followed by B.O.H (Recurrent abortion, Previous H/o IUDs) (14.60 %) and Diabetes Mellitus (10.67 %). Past History of congenital anomalies contribute 7.30 % and multiple factors operated in 9.55 % of cases.

During the study period, 178 babies were delivered with CA, males were dominated (n = 113, 68.48 %), while females were 36.51 % (n = 65).

Table No. 2: Associated Maternal Risk Factors For Ca

Risk Factor	n	%
Consanguineous Marriage	86	48.31%
B.O.H	26	14.60%
Diabetes Mellitus	19	10.67%
Past H/o of CA	13	7.30%
H/o of Fever/Infection	07	3.9%
Family H/O Diabetes Mellitus	06	3.37%
H/O of drug intake	04	2.24%
Combination factors	17	9.55%
Total	**178**	**100 %**

Table-3 showed the system wise distribution of anomalies. Anomalies affecting central nervous system were found in 63 (35.39 %) in which anencephaly contributes 11.79 % and 8.42 % had hydrocephalus. GIT anomalies were 18.53 %, Urogenital 13.43 %, musculoskeletal system 14.04 % and involvement of CVS was found in 10.67 % of cases. Small contribution was found from skin (3.93 %) and Eyes (2.24 %). Multisystemic involvement (Syndrome) was found in 1.12 % of cases.

Table No. 3: System wise distribution of ca (n=178)

System Involved	Types of Defect	N	%
CNS		63	35.39%
	Anencephaly	21	
	Hydrocephalus	15	
	Hydrocephalus with Meningocele	4	
	Meningocele	12	
	Encephalocele	5	
	Teratoma-Sacral, Fronto Orbital	2,1	
	Holoprosencephaly	1	
	Microcephaly	2	
Urogenital		24	13.48%
	Polycystic Kidney	6	
	Renal Agenesis	4	
	Hydroureter	2	
	Hypospadias	4	
	Ambigious Genitilia	3	
	Undescended Testis	5	
GIT		33	18.53%
	Combine Cleft lip & cleft palate	9	
	Cleft lip	6	
	Cleft palate	5	
	Imperforated Anus	5	
	Duodenal atresia	3	
	Omphalocele	2	
	Extrophy of Bladder	2	
	Diaphragmatic Hernia	1	
Musculo Skeletal		25	14.04%
	Talipes	12	
	Polydactily	10	
	Craniosyntosis	3	
Skin		7	3.93%
	Large hairy neavus	2	
	Haemingioma	5	
Eye		4	2.24%
	Congenital Ptosis	2	
	Anophthalmia	1	
	Single Eye	1	
Syndrome		2	1.12%
	Prune Belly Synd	1	
	Down Syndrome	1	

Majority of newborns in study population were stillborn (n = 102, 57.30 %), while 24.15 % (n = 43) died in early neonatal period, while 33 (18.54 %) were referred to Paediatric ward.

None of the mother had received folic acid supplementation in the preconceptional period and very

few had taken folic acid irregularly in the first trimester of pregnancy. 04 (2.24 %) number of patients were using antiepileptic medicines.

The methods used to diagnose congenital anomaly were USG and clinical examination. Chromosomal analysis and genetic studies were not performed due to poor socioeconomic background of patients and lack of facility in the hospital.

DISCUSSION

Congenital anomalies are important causes of perinatal mortality and now diagnose more frequently due to advancement in ultrasonography. It is the third commonest cause of perinatal death in the developing world and accounts for 6 – 9 % of perinatal mortality in Pakistan[3,4].

The scenario could be change by offering selective termination in early pregnancy complicated by life threatening congenital anomalies and by the provision of adequate care to babies with CA compatible with life.

The frequency of CA in the study population was 15.33/1000 births which is comparable with other local studies[5,15]. The reported incidence could be rises once the more sophisticated investigations and autopsy involved in the protocol.

Most of CA were found with maternal ages 26 – 35 years (48.31 %) while 32.58 % were in > 35 year. Increasing age of mother is a recognizable risk factor of CA in many studies[5,16,17].

Increasing birth order increases the risk of CA[16] but we could not found such association in our study.

Maternal obesity is a recognized risk factor[6] was also found in 82.58 % of cases in the present study. Regarding maternal risk factors, consanguinity was most significant (48.31 %) comparable with other local studies[8,15]. Consanguinity was also found as a major risk factor in India[3,16] an avoidable factor eliminated by health awareness programmes.

10.67 % women were diabetic which causes a 3 – 4 folds increase risk of malformations as compared to general population[7]. This proportion of congenital anomalies could be avoided by planned pregnancies and a better periconceptional diabetic control.

Neural tube defect (35.39%), mainly Anencephaly & hydrocephalus were the commonest congenital malformations comparable with a local study[15]. NTD was also seen in 1 in 1000 US population and 4 to 15/1000 births in India[18]. NTD are more common among Hispanic, Ireland, China and UK population. Use of anti-epileptic drugs, maternal diabetes mellitus, obesity and previous NTD affected pregnancies are the risk factors. Maternal folic acid supplementation during periconceptional period and life style modification play a major role in the reduction of major congenital malformations. The others systems involved are GIT (18.53%), Musculo Skeletal (14.04%) and Urogenital(13.48%). The rate of detection of cardiac anomalies were only 10.67% most probably it is because of lack of sophisticated USG in the institute.

Considering the frequency of congenital anomalies and its share in the perinatal mortality we need to create health care programmes addressing towards genetic counseling, avoidance of consanguineous marriages, periconceptional folic acid supplementation along with screening and offering early termination in pregnancy with lethal CA.

CONCLUSION

Congenital anomaly is an important cause of perinatal mortality. Its elimination need health education programmes, folic acid supplementation, early recognition by 3D ultrasound and termination in those cases which are not compatible with life.

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Original Article

Role of Thyroxine in Minocycline Induced Hypothyroidism in Guinea Pigs

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ABSTRACT

Background: Minocycline has been used for decades for the treatment of infections caused by a wide range of Gram negative and Gram positive organism. Minocycline has reported to cause hypothyroidism and goiterogenic affects which results in inhibition of thyroid hormones formation.

Objective: The thyroid gland is mostly affected by many drugs; these drugs include lithium, amiodarone, nitroprusside, perchlorate, sulfonylurea, minocycline, phenylbutazone, and betadine. The long term use of these drugs is usually associated with hypothyroidism. So the present study was undertaken to observe the role of thyroxin in Minocycline induced thyroidal hormonal disturbance in Guinea pigs.

Study Design: Prospective experimental study

Place and Duration of Study: This study was conducted in the Department of Anatomy, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre (JPMC), Karachi from 10.10.2010 to 10.11.2010.

Materials and Methods: 30 adult male Guinea pigs were taken from the animal house weighing between 450-650 Grams. The animals were divided into three groups A, B and C on the basis of treatment given. Group A received control diet, Group B received minocycline (0.02mg/g/day) and Group C received minocycline (0.02mg/g/day) with 0.5ug/g/day thyroxin tablet for 8 weeks at the end of which they were sacrificed, blood sample were taken for serum TSH, T3 and T4.

Results: There was highly significant decrease in body weight, increase in both absolute and relative weight of thyroid gland, marked increase in serum TSH, but the serum level of both T3 and T4 were found decreased in guinea Pigs receiving minocycline. Increase in body weight and decrease in both absolute and relative weight of thyroid gland, the level of TSH decreased, while serum levels of T3 and T4 increased in group C animals receiving minocycline with thyroxin.

Conclusion: This study was proved that use of thyroxin along with minocycline minimizes the harmful effects of minocycline on thyroid gland to a great extent and thyroxin was effective in preventing the hypothyroidism in experimental Guinea pigs.

Key words: Minocycline, thyroidal hormones, thyroxin, Guinea pigs.

INTRODUCTION

The long term use of different drugs is usually associated with hypothyroidism (Vasudevn et al., 2011)[1].The tetracyclines are drugs which remain drugs of first choice for infection with chlamydia, rickettsia (Q fever, typhus), vibrio cholera (cholera) and in acne (Bennettand Brown 2009)[2]. Minocycline is a semisynthetic broad spectrum antibacterial agent that was introduced in 1967 by the Erstwhile Le drele Laboratories (EisenD & Hakim MD, 1998)[3].The percentage of an oral dose that is absorbed with an empty stomach is high for Minocycline i.e.100% (Brunten et al., 2009)[4]. The lipophilic properties of minocycline, with complete oral absorption and good sebum penetration, make it the most widely prescribed systemic antibiotic used to treat acne vulgaris, often given for months or years (Ramakrishna. et al., 2009)[5]. Minocycline with proven safety, which has been commonly used to treat pneumonia and acne as well as infections of the skin, genital and urinary systems ,Central nervous system, gonorrhea, meningitis, shigellosis, conjunctivitis, psittacosis, Q fever, relapsing fever, and syphilis (Elewa H. F et al., 2006)[6].Minocycline has several immunomodulatory and neuroprotective properties independent of its antimicrobial functions (Skripuletz et al., 2010)[7]. The drug persists in the body long after its administration is stopped possibly due to retention in fatty tissues (Brunten et al., 2009)[4]. Minocycline is associated with hypothyroidism, predominantly with concurrent chronic lymphocytic thyroiditis (Tacon et al., 2008)[8]. Minocycline has goiterogenic effects with inhibitory effects on thyroid function resulting in inhibition of thyroid hormone formation. Iodination of thyroglobulin is inhibited by minocycline, which also strongly inhibits coupling of triiodothyronine (T3) and thyroxin (Taurog et al., 1996)[9].

Thyroxin has an antioxidant activity in microsomal and mitochondrial fraction from liver and can prevent to formation of free radicals in neutrophils (Golkina et al., 2001)[10]. Synthetic thyroxin is today the most commonly used drug for treating congenital hypothyroidism or post-operative thyroid cancer (Chao et al., 2009)[11]. Administration of L- thyroxin is a common medical treatment for nodular goiter (Fiore et

al., 2010)[12]. The general effect of thyroid hormone is to activate nuclear transcription of large numbers of genes. Therefore, in virtually all cells of the body, great number of protein enzymes, structural proteins, transport proteins and other substances are synthesized. The net result is generalized increase in functional activity throughout the body. The thyroid hormones increase the metabolic activities of almost all the tissues of the body.In adult, thyroid hormone helps to maintain brain function food metabolism and body temperature, among other effects (Saicic et al., 2006)[13].

MATERIALS AND METHODS

This study was conducted in the Department of Anatomy, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre (JPMC), Karachi, for 8 week. This is a prospective experimental study.

Thirty (30) healthy and active adult male Guinea Pigs, weighing between 450-650 gm. were selected for the present study. The animals were divided into three groups A, B and C according to the treatment given to them.

In this study, minocycline was used, in the dose of0.02mg/g/day and Tablet thyroxin was use in the dose of 0.5ug/g/day

Group A: This group comprised of 10 animals and they will serve as control. The animals were maintained on standard laboratory diet and water ad libitum.

Group B: This group comprised of 10 animals. The animals were given 0.02mg/g/day minocycline (Steifel Laboratories Pakistan (Pvt) Ltd, Steifel Laboratories Inc.Coral Gables, FL33134, and USA) orally.

Group C: This group comprised of 10 animals. The animals were given 0.5ug/g/day thyroxin tablet (GlaxoSmithKline Pakistan Ltd, RN 000374, Ml 000017 & 000233) orally and minocycline (Steifel Laboratories Pakistan (Pvt) Ltd, Steifel Laboratories Inc.Coral Gables, FL33134. USA) orally.

Throughout the study period the animals were observed for their general health, activity and behaviour. Weight of the animals was done at the commencement of study and just before sacrifice.

After completion of study period (at the end of 8 weeks, the incision was made in neck region from chin to xiphisternum, infrahyoid muscles were retracted to expose the thyroid, and thoracic viscera were exposed by careful removal of skin, fascia and muscles to take blood sample by intra cardiac puncture and were kept in labeled tubes containing 10µl sodium EDTA, kept on ice until centrifuged. After centrifugation the plasma was aliquot and kept frozen at -70ºC until assay. The thyroid function test (TSH, T3 and T4) was assessed by Total ELISA Kit from diagnostic systems laboratories. Thyroid glands was removed from the site and washed with normal saline.

The statistical significance of differences of various quantitative changes between treated and control rats were evaluated by the paired sample‘t’ test[12]. The numerical data was subjected to SPSS software for statistical analysis. The difference was regarded as statistically significant if the P-value was equal to, or less than 0.05.

RESULTS

Relative weight of thyroid gland: The mean values of relative weight of thyroid gland in control group A was 10.3 ± 0.23 gm. A highly significant increase ($p<0.001$) was observed in group B when compared with the mean values of relative weight of thyroid gland in group A. There was moderately significant ($P<0.01$) decrease in relative weight of thyroid gland of group C when compared with group B, however a significant ($p<0.05$) difference was noted when compared with mean value in group A with C (Table-1 & figure: 1).

Table No.1: Mean relative weight of thyroid gland in different groups of guinea pigs

Groups	Treatment	Thyroid gland relative weight (mg/100gm body weight)
A	Normal diet (ND)	10.3 ± 0.23
B	Minocycline	25.9 ± 1.47
C	Minocycline + Thyroxin	17.4 ± 0.65

*Mean ± SEM

Statistical analysis of the mean relative weight of thyroid gland between different groups

Groups	P-value
A Vs B	P<0.001****
B Vs C	P<0.01***
A Vs C	P<0.05**

Key: Insignificant* Significant moderately significant*** highly significant****

Table No.2: Mean plasma levels of TSH, T3 and T4 in different groups of guinea pigs

Groups	Serum TSHµl/ml	Serum T3 ng/dl	Serum T4µg/dl
A	0.2 ± 0.01	4.9 ± 0.31	34.5 ± 2.34
B	6.5 ± 0.26	2.3 ± 0.15	15.5 ± 1.23
C	0.7 ± 0.05	4.1 ± 0.28	29.3 ± 1.57

Statistical analysis of the mean plasma TSH, T3 and T4 levels in different groups of guinea pigs

Groups	Serum TSH	Serum T3	SerumT4
A Vs B	P<0.001****	P<0.001****	P<0.001****
B Vs C	P<0.01***	P<0.01***	P<0.01***
A Vs C	P<0.05**	P<0.05**	P<0.05**

Key: Insignificant* Significant moderately significant*** highly significant****

Hormonal essay: The mean values of plasma TSH in group A was 0.2 ± 0.01 µl/ml. The increase in hormone level in group B was highly significant ($P<0.001$) when compared with group A and there was a moderately significant ($p<0.01$) decrease in group C when compared with the group B. The mean value of TSH is

increased significantly ($p<0.05$) when compared with group C with group A (Table-2 and figure: 2).

Plasma tri-iodothyronine (T3) levels were estimated in all animals. The decrease in hormone levels in group B was highly significant ($p<0.001$) when compared with group A and there was moderately significant ($p<0.01$) increase in group C when compared with group B. The mean value of T3 in group C was decreased significantly ($P<0.05$) when compared with group A. (Table-2 and figure: 3).

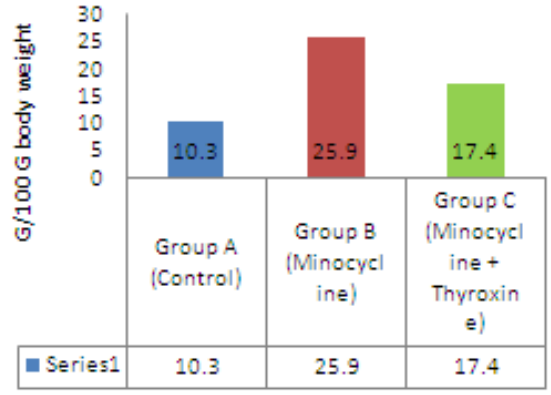

Figure No.1: Mean Relative Weight of Thyroid gland

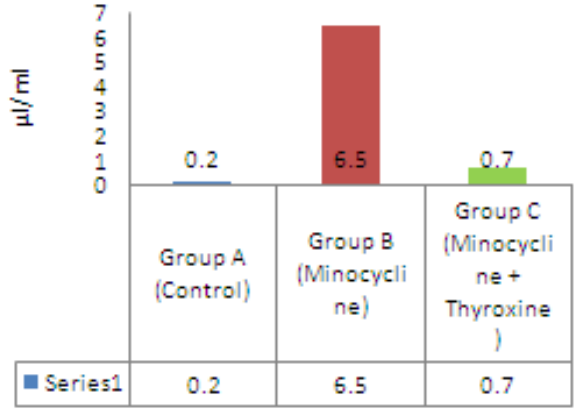

Figure No.2: Mean Plasma Level of TSH

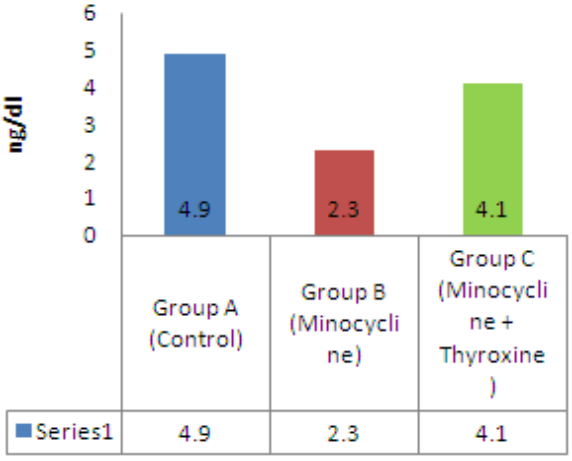

Figure No.3: Mean Plasma Level of T3.

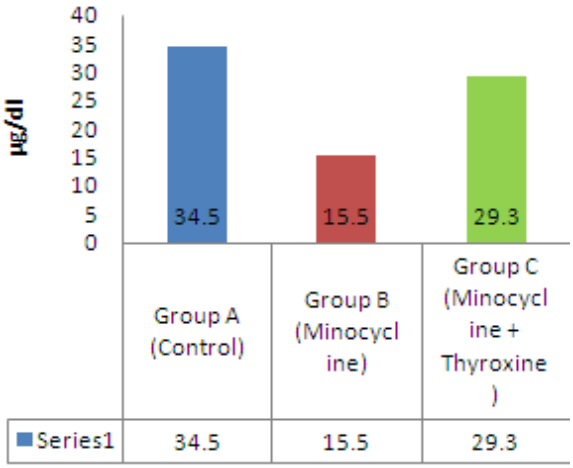

Figure No.4: Mean Plasma Level of T4.

Plasma T4 (Thyroxin) levels were estimated in all animals. The decrease in hormone levels in group B was highly significant ($p<0.001$) when compared with group A and there was a moderately significant decreased in B when compared with group C. The mean value of plasma T4 level was significantly ($p<0.05$) decreased in group C when compared with group A (Table-2 and figure: 4).

DISCUSSION

The present study was carried out by observing and recording the effects of minocycline on the relative weight of thyroid gland and estimation of hormonal levels (TSH, T3 and T4). Numerous studies on minocycline have shown that it possesses potent antithyroid effects probably by inhibiting the iodination of thyroglobulin and also by inhibiting the coupling of diiodotyrosine residues to form triiodothyronine and thyroxine (Bowles et al., 1998)[14]. Understanding the mechanism of action of antithyroid effects is important in elucidating not only the cause of hypothyroidism in human being exposed to solve this problem but also its prevention.

Relative weight of thyroid glands was highly significant increase in group B animals. The increase in weight could be due to hypertrophy of follicular cells and deposition of melanin pigment inside the follicular cells and within the colloid. Inuwa and William (1995)[15]suggested that, it might be due to the increased follicular epithelial height (from basement membrane to surface) in hypothyroid rats, he observed that the epithelial height in hypothyroid rats given thyroxine was not significantly increased when compared with euthyroid rats.

In minocycline and thyroxin treated group C animals, the relative weight of the thyroid gland was decreased when compared to minocycline treated group B animals; it might be due to decreased cellular hypertrophy and less inflammatory changes. This is in agreement with Joffe et al (2007)[16] who proved that in

the presence of thyroxine the height of cells of follicles comes to near in height of follicular cell of control group and colloid was again restored in the lumen of follicles.

There was highly significant increase in serum TSH (thyroid stimulating hormone) hormonal level in minocycline treated group B animals. In ultra-structural study of black thyroids, Taurog et al (1996)[9] reported that patient taking minocycline presented with clinical and laboratory evidence of thyroid hypo function (decreased serum T4 and increased serum TSH). Capen (1997)[17] observed that the lowers circulating T3 levels, which results in a compensatory increased secretion of thyroid stimulating hormone (TSH), follicular cells hypertrophy and hyperplasia.

There was significant increase in levels of both T3 and T4 hormones and significant decrease of TSH hormone in group C animals. Suppression of serum TSH concentration by administering exogenous thyroid hormone may interfere with the growth of established nodules as well as with the formation of new thyroid nodules (Fiore E et al, 2010)[12]. Chao et al (2009)[11] stated that the treatment with thyroxin (T4) is probably safer than treatment with a combination of T4 and T3. Therefore, T4 alone contuse to be the most appropriate therapy for patients with hypothyroidism. Carroza et al (1999)[18] has proved that the most of T3 is derived from thyroxine.

CONCLUSION

The present study shows development of hypothyroidism as a result of administration of minocycline. The study further emphasizes a definite preventive role of thyroxine on minocycline induced hypothyroidism in case of long term use of minocycline.

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Original Article

Comparison of Body Weight and the Weight of Stomach after Simultaneous Administration of Ibuprofen and L-Arginine Albino Rats

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ABSTRACT

Objective: To observe the effects of ibuprofen and L-Arginine when given simultaneously on the body weight and absolute weight of stomach of albino rats and statistical analysis of the results.

Study Design: A prospective experimental study.

Place and Duration of study: This study was conducted at Department of Anatomy, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre Karachi during 2008.

Materials and Methods: This study was conducted in the Department of Anatomy, Basic Medical Sciences Institute Jinnah Postgraduate Medical Center Karachi where 45 albino rats of either sex between 90-120 days were selected and were divided into three groups, 'A', 'B' and 'C', containing 15 animals each, which were further sub-divided into three sub-groups containing 5 animals each according to time of sacrifice, i.e. 4, 6, and 8 weeks respectively. Group 'A' served as control. Group 'B' received ibuprofen at the dose of 70 mg per kilogram body weight per day with feed and L-Arginine 300 mg per kilogram body weight per day with feed. Animals were weighed on sartorius balance before and after their stipulated time period. Animals were fixed on a dissecting board, the abdomen was opened with a long midline incision and the stomach was removed and opened along the greater curvature with an incision extending from cardiac to the pyloric end. After removing the contents of the stomach the absolute weight of the stomach was recorded on a Sartorius balance.

Results: Observations on body weight (G) in Group-'A' There was a significant increase ($P<0.05$) in the weight of all subgroups. In Group-'B' their was moderate decrease in weight subgroup 'B'1 and significant decrease in subgroups 'B'2 B''3 when compared to control. No difference was observed in Group C when compared with control. Observations of absolute weight of stomach (G) the weight was increased significantly ($P<0.05$) when compared with control. No difference in weight was noted between Group 'C' and control group.

Conclusion: The effects of ibuprofen on the body weight and absolute weight of the stomach could be minimized when given simultaneously with L-Arginine**.**

Key Words: L-Arginine, ibuprofen, albino rats.

INTRODUCTION

Ibuprofen is a nonsteroidal analgesic, antipyretic and anti-inflammatory agent that is a propionic acid derivative used for relief of pain, reduction of fever and in the treatment of osteoarthritis and rheumatoid arthritis. It acts by inhibiting the enzyme cyclooxygenase (COX) which catalyzes the conversion of the arachidonic acid to prostaglandins (Yip-Schneider et al., 2001; Takeeda et al., 2004)[1-2]. The non-steroidal anti-inflammatory drugs (NSAIDs) are the major cause of peptic ulcers in patients who do not have Helicobacter pylori infection. The magnitude of gastro-duodenal toxicity caused by these agents is quite large; risk factors for these drugs are increasing age, higher doses and prolonged use. In the USA, about 16,500 people per year die as a result of NSAID-associated gastrointestinal complications (Mizushima, 2008)[3]. Drug-induced injury of the gastrointestinal tract is increasingly common but generally under-recognized. Acute gastritis and peptic ulceration are also caused by the heavy use of the non-steroidal anti-inflammatory drugs, particularly aspirins (Bagshaw et al., 1987; Kumar et al, 2003)[4-5].The principal therapeutic effects of NSAIDs derive from their ability to inhibit prostaglandins production (Underwood, 2004)[6].

It has been proved that non steroidal anti-inflammatory drugs like indomethacin and ibuprofen cause the topical mucosal injury and it is the critical factor in the, development of intestinal injury (Seager et al, 2000)[7]. Gastrointestinal adverse drugs reactions from ibuprofen usage include mucosal ulcers and bleeding (Abraham et al., 2005)[8]. According to Gilman et al (2006)[9] the most common symptoms associated with Ibuprofen are anorexia, nausea, dyspepsia, abdominal pain, and diarrhea. These symptoms may be related to the induction of gastric or intestinal ulcers, which is estimated to occur in 15% to 30% of regular users. Ulcerations may range from small superficial erosions to full thickness perforations of muscularis mucosa. There may be single or multiple ulcerations accompanied by gradual blood loss leading to anemia or by life threatening hemorrhage(Maricic et al 1999)[10].

L-arginine is an essential amino acid in children, which participates in many important biochemical reactions associated to the normal physiology of the organism (Jimenez et al., 2004)[11]. It is an essential amino acid for the infants and the children and it is semi essential in the adults. Although the arginine is made by the liver as a step in the synthesis of the urea, children cannot produce arginine rapidly enough to support growth requirements (Nakaki, 1994). Nitric oxide synthesized from L-arginine plays an important role in the gastric mucosal integrity by interacting with endogenous prostaglandins (Takeuchi et al., 1993)[13]. Endogenous prostaglandins play a protective role on endotoxin-induced gastric mucosal micro circulatory disturbance and mucosal damage (Pique et al., 1998)[14]. Arginine supplementation did not affect plasma glucose levels in non diabetic rats. Thus, dietary L-arginine supplementation stimulates endothelial Nitric oxide synthesis by increasing BH provision, which is beneficial for vascular function and glucose, homeostasis in diabetic subjects (Kohli et al., 2004)[15]. Adding L-arginine to diet of the mice intoxicated with mercury, restoration to normal homeostatic conditions were achieved (Santarelli et al., 2007)[16]. L-arginine augments myotube formation and increased nitric oxide production in a process limited by cellular L-arginine uptake (Long et al., 2006)[17]. Keeping in mind the effects of ibuprofen and L-Arginine on the gastrointestinal tract, we decided to study simultaneous use of above drugs and find their effects on the body weight and the absolute weight of stomach.

MATERIALS AND METHODS

This study was conducted in the Department of Anatomy, Basic Medical Sciences Institute Jinnah Postgraduate Medical Center Karachi where 45 healthy and active adult albino rats of either sex between 90-120 days were selected for present study. The animals were divided into three groups, 'A', 'B' and 'C', containing 15 animals each and were further sub-divided into three sub-groups containing 5 animals each according to time of sacrifice, i.e. 4, 6, and 8 weeks respectively. Group 'A' served as control. Group 'B' received ibuprofen available in the market as "BRUFEN" by Bayer Laboratories, Karachi Pakistan) at the dose of 70 mg per kilogram body weight per day orally with feed (Dokmeci et al., 2007) and L-Arginine available in the market as "ARGININE", General Nutrition Corporation, Pittsburg, USA. The dose of the L-Arginine was 300 mg per kilogram body weight per day with feed (Takeuchi et al., 1993). At the end of respective time period the animals were weighed on Sartorius balance and then anaesthetized with ether in a glass container and sacrificed. Animals were fixed on a dissecting board, the abdomen was opened with a long midline incision and the stomach was removed and opened along the greater curvature with an incision extending from cardiac to the pyloric end. After removing the contents of the stomach the absolute weight of the stomach was recorded on a Sartorius balance. Statistical significance of difference of various quantitative changes between the groups was evaluated by student "t" test. The difference was regarded statistically significant if the 'P' value was equal to or less than 0.05. All calculations were done by utilizing computer software SPSS version 16.

RESULTS

Observations on Body Weight (G)

Group-A: The body weight of animals in all subgroups was increased during their respective period of time. The mean initial weights in 'A'1, 258.00±11.38; 'A'2, 261.20±7.24 and 'A' 3, 255.80±4.60 were observed. The mean final weight of subgroups 'A'1, 'A' 2 and 'A' 3 were 270±11.66, 273.80±8.33 and 274.00±4.50 respectively. There was a significant increase ($P<0.05$) in the weight of all subgroups (table-1 and graph-1).

Group-B: The mean initial body weight in 'B'1, 'B'2 and 'B'3 were observed as 250.40±4.20; 253.60±2.13, and 252.40±3.35 respectively while the mean of final weight observed in same subgroups were 229.20±3.54, 236.60±2.13, and 237.20±3.45 respectively, this decrease was moderately significant in subgroup 'B'1 ($P<0.001$) while it was significantly decreased ($P<0.05$) in subgroups 'B'2 and 'B'3. There was a decrease in the final body weight in subgroup 'B'1 was moderately significant when compared with 'A'1, while in subgroups 'B'2 and 'B'3 this decrease was significant ($P<0.05$) when compared with subgroups 'A'2 and 'A'3 (table-1 and graph-1).

Group-C: The initial body weight of animals in subgroups 'C'1, 'C'2 and 'C'3 recorded was 235.60±5.37, 256.60±5.09 and 259.00±7.11 respectively. While the final weight recorded in subgroups 'C'1, 'C'2 and 'C'3 were 245.80±6.65, 264.20±6.02 and 272.60±6.41. There was increase in mean final body weight in all subgroups when compared with their initial body weight and this increase was moderately significant in group 'C'1 and 'C'3 ($P<0.001$) while it was significant in group 'C'2 ($P<0.05$). There was increase in mean of final weight in all subgroups 'C'1, 'C'2 and 'C'3, this increase was significant ($P<0.05$), when compared with subgroups 'B'1, 'B'2 and 'B'3. There was a decrease in final body weight in all subgroups 'C'1, 'C'2 and 'C'3 and this decrease was insignificant ($P>0.05$) when compared to subgroups 'A'1, 'A'2 and 'A'3 (table-1 and graph-1).

Observations of Absolute Weight 0f Stomach (G)

Group-A: The mean weight of stomach in subgroups 'A'1, 'A'2 and 'A'3 was 1.85±2.33; 1.90±9.24 and 1.85±2.18 respectively (table 2 and graph 2)

Table No. 1: Mean* value of Body Weight (G) in Different Groups of Albino Rat

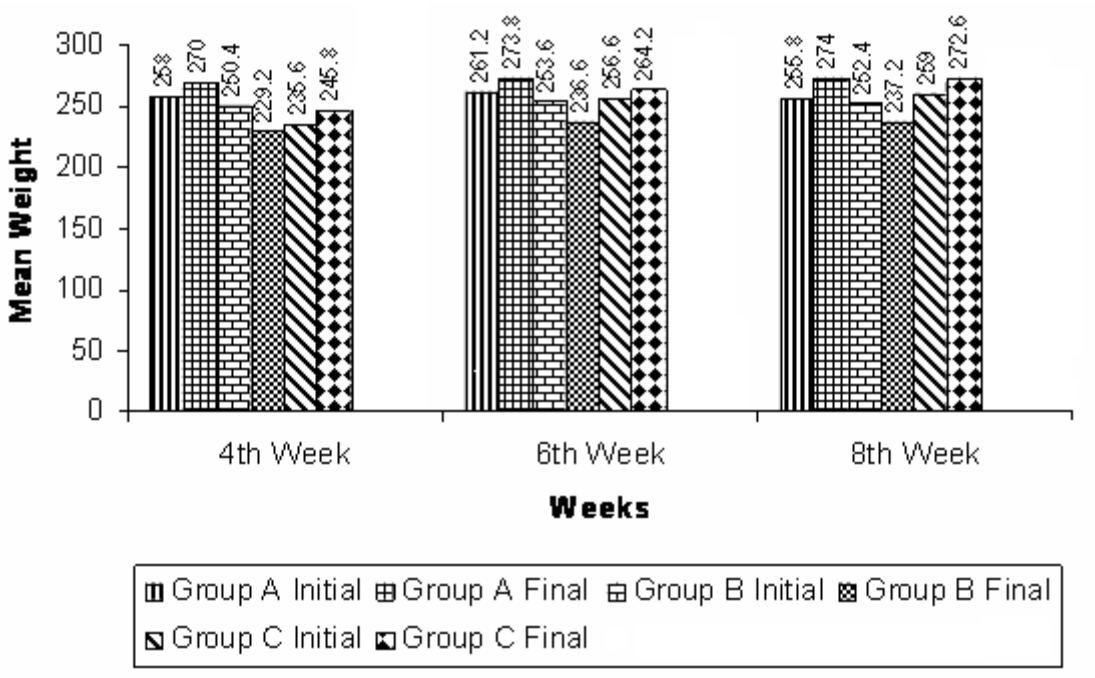
Groups	Sub-groups	Treatment Given	Initial Weights	Body Weights (G)		
				Final Weights at Sacrificial Time		
				4th Week	6th Week	8th Week
A (n=15)	A1	Control	258.00±11.38	270.00±11.66	--	--
	A2		261.20±7.24	--	273.80±8.33	--
	A3		255.80±4.60	--	--	274.00±4.50
B (n=15)	B1	Ibuprofen	250.40±4.20	229.20±3.54	--	--
	B2		253.60±2.13	--	236.60±2.13	--
	B3		252.40±3.35	--	--	237.20±3.45
C (n=15)	C1	Ibuprofen + L-Arginine	235.60±5.37	245.80±6.65	--	--
	C2		256.60±5.09	--	264.20±6.02	--
	C3		259.00±7.11	--	--	272.60±6.41

*Mean±SEM

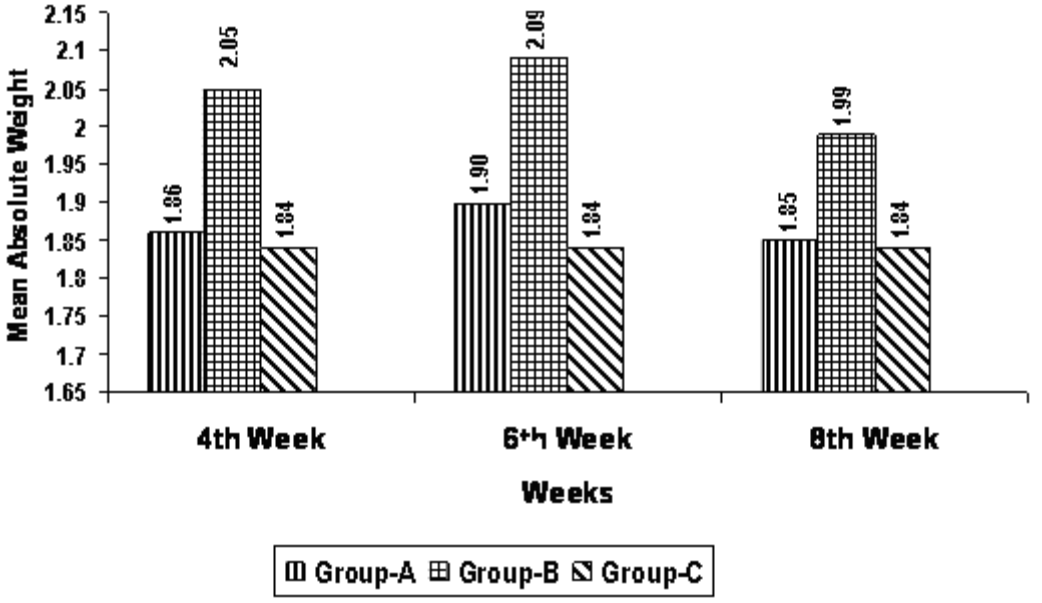
Table No. 2: Mean* value of Absolute Weight (G) of stomach in Different Groups of Albino Rats

Groups	Sub-groups	Treatment Given	Absolute weight (G) of stomach at the time of sacrifice		
			4th Week	6th Week	8th Week
A	A1	Control	1.858±2.33	--	--
	A2		--	1.90±9.24	--
	A3		--	--	1.85±2.18
B	B1	Ibuprofen	2.05±5.22	--	--
	B2		--	2.09±3.80	--
	B3		--	--	1.99±1.88
C	C1	Ibuprofen + L-Arginine	1.84±1.45	--	--
	C2		--	1.84±1.46	--
	C3		--	--	1.84±1.87

*Mean±SEM



Graph No. 1: Body Weight (G) in Different Groups of Albino Rats



Graph No. 2: Absolute Weight (G) of Stomach in Different Groups of Albino Rats

Group-B: The mean weight of the stomach in subgroups 'B'1, 'B'2 and 'B'3 was 2.05±5.22; 2.09±3.80 and 1.99±1.88 respectively. The weight was increased and significant (P<0.05) when compared with subgroups 'A'1, 'A'2 and 'A'3 respectively (table 2 and graph 2).

Group-C: The mean weight of the stomach in subgroups 'C'1, 'C'2 and 'C'3 observed was 1.84±1.45, 1.84±1.46, and 1.84±1.87 respectively. The mean weight of the stomach was decreased and significant (P<0.05) in subgroups 'C'1 and 'C'3 when compared with subgroups B1 and B3, while this decrease was moderately significant (P<0.05) in subgroup C2 when compared with B2. There was a decrease and insignificant (P>0.05) in absolute stomach weight in all subgroups 'C'1, 'C'2 and 'C'3 when compared with control subgroups 'A'1, 'A'2 and 'A'3 (table 2 and graph 2).

DISCUSSION

Ibuprofen is a commonly used non-steroidal anti-inflammatory drug that produces gastric mucosal injury and that inhibition of nitric oxide synthase, reduces gastric mucosal injury (Abraham et al., 2005). Nitric oxide synthesized from L-arginine plays an important role in the gastric mucosal integrity by interacting with endogenous prostaglandins (Takeuchi et al., 1993).

The animals treated with Ibuprofen in group-'B' appeared ill looking with loss in their body weight because of the injurious effects of Ibuprofen due to loss of appetite (because of erosions/ulcers on the gastric mucosa) and it is agreement with same Dudkiewicz (1981) who observed in an experimental study on Ibuprofen-induced gastrointestinal changes in rats, and demonstrated that Ibuprofen caused disturbances in intestinal motor functions which might lead to the development of malabsorption syndrome. The findings of the present study are in disagreement in response to appetite but in agreement in response to body weight with the study of Esther et al (1997) who observed the effects of non-steroidal drugs on glutathione S transferase of the male Wistar rat digestive tract. They noted that the animals' food consumption was increased and body weight was decreased.

The animals of group 'C' appeared normal active and healthy, it appeared that their activity is more or less same as compared to group 'A'. These animals put on weight, which could be explained due to increase in the appetite caused by L-arginine and reduction to minimum of damage to stomach; it is in agreement to Mahmoud et al (2002).

The absolute weight of the stomach in group-'B' animals showed an initial increase in subgroups-'B'1 and 'B'2, as compared to corresponding controls. The increase in weight may also be due to inflammatory infiltration in lamina propria and submucosa and dilatation of glands, these finding are same as of Kumar et al (2004), that in active ulcers with on-going necrosis beneath the superficial necrotic debris a zone of inflammatory infiltrate was present. The increase in weight might be due to edema and accumulation of the mucus content in surface epithelial cells and mucus neck cells as compared to control. In subgroup-'B'3 the absolute tissue weight was less than from groups-'B'1 and 'B'2, but slightly increased as compared to corresponding control.

In group-'C' animals the absolute weight of the stomach was significantly decreased when compared to

their corresponding group-'B' animals, while the weight was insignificantly decreased when compared with group-'A'.

In the light of above consideration, the net results of the study suggest that the gastric ulcer occur more frequently in people who use Ibuprofen as reported by Jimenez et al (2004) and Kumar et al (2004). The body weights of all animals were changed, the animals of group 'A' gained body weight between four and eight weeks. The animals of group 'B' loss weight than group 'A', this decrease in weight was due to loss of appetite as observed by Takeeda et al (2004) who studied role of endogenous prostaglandin and cyclooxygenase isoenzyme in mucosal defence of inflamed rat stomach. They observed that body weight gradually decreased depending on the duration of treatment. In relation to body weight the absolute weight of the stomach of ibuprofen treated rats showed a significant increase in weight which may be attributed to mucosal edema.

CONCLUSION

The effects of ibuprofen on the body weight and absolute weight of the stomach could be minimized when given simultaneously with L-Arginine

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Original Article

Effect of Fructosemia and Hyperuricemia on Antioxidant Enzyme Level

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ABSTRACT

Objective: To measure effects of fructose and uric acid on superoxide dismutase and find out the relationship among them in animal model.

Study Design: comparative study

Place and Duration of Study: The study was conducted at Basic Medical Sciences Institute JPGMC from November 2009 to June 2010.

Materials and Methods: Total forty male albino rats with an average weight of 180±2g were selected. The rats were grouped. The animals were fed on standards diet and given tap water ad libitum until treatment. The protrocols for experiment was according to institute of laboratory animal resources on life sciences, US National research council,1996 and institutional animal ethical committee (IAEC) of basic medical sciences institute, Karachi. Albino rats were divided into four groups. Group A(10) – control given only standard diet, group B(10) fed on 60%fructose with standard diet , group C(10) fed on fructose, standard diet and intraperitonially oxonic acid 250mg/kg and group D (10) only on injection intraperitonially oxonic acid 250mg/kg. At the end of study 10 ml of blood was drawn from heart of rats. Then blood was estimated for superoxide dismutase and urate done by kit methods randox-manual /Rx monza UA230/UA 233.

Results: In Group C superoxide dismutase was found to be 32%(244mg/dl±2.23) which was more than control. In the same group the uric acid concentration was highly significantly correlated with control.

Conclusion: The urate concentration does increase when we take fructose upto 60%in our diet .It also increase superoxide dismutase concentration. More than this value may have inverse effect on the uric acid level and its role as an antioxidant may become inversed.

Key Words: Urate, Superoxide Dismutase, Fructose, Al Bino Rats, Induced Hyperuricemia.

INTRODUCTION

Free radical can be defined as any molecular species capable of independent existence that contains an unpaired electron in an atomic orbital [1].They are capable of triggering chain reactions which can damage the different cell constituents.

The most important free radicals in many disease states are oxygen derivatives, particularly superoxide and the hydroxyl radical. Superoxide is formed from several molecules by oxidation including adrenaline, flavine nucleotides, thiol compounds, and glucose .Superoxide is also produce during important biological reactions including electron transport chain in mitochondria.[2]

In order to check free radicals formation to avoid oxidative stress , body has different anti- oxidant defence systems. An antioxidant can be defined as: "any substance that, when present in low concentrations compared to that of an oxidisable substrate, significantly delays or inhibits the oxidation of that substrate. The physiological role of antioxidants, as this definition suggests, is to prevent damage to cellular components arising as a consequence of chemical reactions involving free radicals.[3] Superoxide dismutase is believed to serve as first line of defence against toxicity of superoxide radicals .Also takes part in cell signaling regarding to reactive oxygen species levels.[4]Superoxide is one of the main reactive oxygen species in the cell and as such, SOD serves a key antioxidant role. The physiological importance of SODs is illustrated by the severe pathologies evident in mice genetically engineered to lack these enzymes. Mice lacking SOD2 die several days after birth, amid massive oxidative stress[5] Mice lacking SOD1 develop a wide range of pathologies, including hepatocellular carcinoma[6] an acceleration of age-related muscle mass loss,[7] an earlier incidence of cataracts and a reduced lifespan. Mice lacking SOD3 do not show any obvious defects and exhibit a normal lifespan, though they are more sensitive to hyperoxic injury.[8]

Uric acid now is not considered as merely a metabolic waste. It has been proposed that increase in life span observed in human evolution to some extent might be due to protective action of uric acid [9]**.** Increase uric acid levels have been found in oxidative stress and ischemia which might be compensatory mechanism of protection against free radicals[10].Urate radicals do not react with oxygen to form another peroxy radical which is seen with the ascorbic acid, thus increasing the efficacy of uric acid as an antioxidant[11].Uric acid cause inactivation of Nitric oxide and peroxynitrite radicals.[12,13]Another important function of urate is found in its ability to form chelating agents with transition metals ions like iron and copper thus scavenging them. We carried out a study to assess the relationship of uric acid with superoxide dismutase in an induced hyperuricemic rats.

MATERIALS AND METHODS

Locally bred forty(40) male Albino rats with an average weight of 180±20g were purchased. The rats were grouped and housed in environmentally controlled room(ambient temperature 24±2°C and relative humidity of 55±5%) in the animal house and acclimatized for 07 days**.** The animals were fed standard diet and given tap water ad libitum until treatment. The protocols for experimentation was approved and performed in strict accordance with the Guide for the care and use of laboratory animals (Institute of Laboratory Animal Resources on Life Sciences, US National Research Council, 1996) and the Institutional Animal Ethical Committee (IAEC) of Baqai Medical University, Karachi. Pakistan. The cage size was 8"X18"X10" to keep a group of 05 animals in the cage to prevent from cannibalism.

Sodium Tungstate 10%, 2/3N sulphuric acid,10% sodium bicarbonate,LiCO3, 40%Formaline,Acetic acid, Fructose, Oxonic acid. Spectrosol grade reagents and acids from B.D.H, Poole, UK, were employed. All purified enzymes, coenzymes, substrates, standards and buffers will be purchased from Sigma Chemicals Company, USA. All other chemicals were of analytical grade and will be procured from SRL and Qualigens, USA.

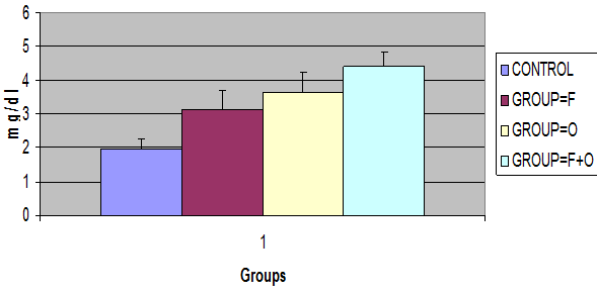
All animals housed in standard conditions were initially fed standard diet and allowed adaptation of one (01) week.Albino rats were divided in four(04) groups; A,B,C & D.

Group A:Ten (10) male albino rats as Control were kept as control and were fed standard diet and water ad libitum for 10 weeks. Group B: Ten (10) male albino rats [F]were fed 60% fructose mixed in standard diet and water ad libitum for 10 weeks. Group C:Ten (10) male albino rats [FO]were fed 60% fructose mixed in standard diet and water ad libitum for 10 weeks. They were also injected intraperitonealy oxonic acid 250mg/kg every third day for 10 weeks.Group D:Ten (10) male albino rats [O]were injected intraperitonealy oxonic acid 250mg/kg every third day for 10 weeks. They were fed standard diet and water ad libitum for 10 weeks.Body weights were measured at the commencement and at the end of study. The amount of diet was measured before giving and then subtracted from the amount of food left over daily. At the end of study, rats were dissected in a nearby room separate from experiment area. Approximately 10 mls of blood was drawn from heart using disposable syringe. 8 mls of blood was transferred in heparanized tube, mixed and centrifuged to separate plasma and divided in two epindorf cups for estimation of uric acid and SOD done by kit methods by randox-manual /Rx monza UA230/UA 233.

RESULTS

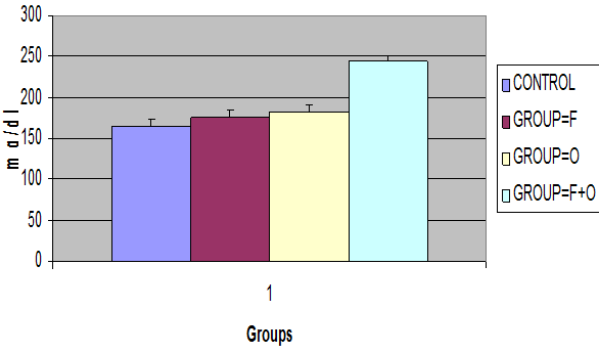
Graph 1: Shows the comparison of mean plasma uric acid levels of Control with rest of the groups. Mean plasma level of uric acid of Control is found to be 1.97 mg/dl(±0.09) .Group "F"(fructose) showed mean plasma uric acid of 3.15 mg/dl(±0.17) .This reflects that uric acid was raised to 37% in rats which were exposed to diet comprising 60% Fructose than control. On comparing both groups i.e., Control with Group "F"(highly significant statistical correlation(P <0.001) was observed.

The mean plasma uric acid levels of Group "O" (oxonic acid) was 3.63 mg/dl(±0.22)which is 45% higher than Control. The probability calculated was highly significant (P<0.001) when both groups were evaluated.



Bar Graph No.1: Comparison of Serum Uric Acid levels of all study groups.

Serum Uric Acid				
Groups	Control	Group F	Group O	Group F+O
M.V	1.97	3.15	3.63	4.43
S.D	0.3	0.55	0.63	0.43



Bar Graph No.2: Comparison of Serum SOD levels of all study groups.

Serum Uric Acid				
Groups	Control	Group F	Group O	Group F+O
M.V	165.15	176.65	181.25	244
S.D	8.38	8.23	9.96	6.69

While comparing Group "F+O"(Fructose +Oxonic acid) with Control, highly significant correlation was observed(P<0.001).It was due to high mean plasma serum uric acid level of Group "F+O" which was 4.41mg/dl(±0.14) .The combination of fructose with uricase inhibitor ,Oxonic acid raises uric acid to 55% from control and this level is highest of all these groups.

Graph 2: shows the comparison of mean plasma SOD levels of Control with rest of the groups. Mean plasma level of SOD of Control was found to be 165.15mg/dl (±2.65) .Group "F" (Fructose) showed mean plasma SOD level of 176.65mg/dl (±2.60) reflecting SOD levels were raised to 6.5% in rats which were exposed to diet comprising 60% Fructose.On comparing both groups i.e., Control with Group "F" significant statistical correlation (P<0.01) was observed.The mean plasma SOD levels of Group "O" (oxonic acid) has been measured to 181.2mg/dl(±3.52)which is again 8% more than Control. Therefore, significant (P<0.01) correlation was observed on comparison of both groups. While comparing Group "F+O" (Fructose +Oxonic acid) with Control, highly significant correlation was observed (P<0.001).It was due to high mean plasma SOD levels of Group "F+O" which was 244mg/dl(±2.23) which is highest of all these groups. In this group SOD was 32% more than control which might be due to antioxidant action of uric acid.

DISCUSSION

Uric acid has long been described as metabolic waste of purine metabolism with strong relation to number of pathologies involving many organs of body. On the other hand scientific research has also revealed its role as an antioxidant making its pathological status ambiguous. In present study it was tried to elaborate antioxidant status by incorporating different antioxidants and evaluating their relationship with uric acid as described in many studies.

One of the important features of this study was the method by which hyperuricemia have been induced in animal model. The group B was given fructose, group D was treated with "oxonic acid" and group C was offered both fructose and oxonic acid (G=Fructose+ Oxonic acid). The principle hyper-uricemic factor in this study was fructose as it is extensively used in beverages and food .Its a rather controversial factor as number of studies both animals and human, are in the favour that fructose can induce hyperuricemia[14] but many studies have opposed this hypothesis[15] and even mixed response has been shown[16] .Present investigation has tried to verify this theory. Very few studies have used this combined model of fructose plus oxonic acid.In order to make conditions similar to human, uricase inhibitor oxonic acid was incorporated to abolish the effect of this enzyme in rats. Also these different regimens were used to establish the extent of hyperuricemia caused by fructose.

Superoxide dismutase levels were found to be raised in all three groups in comparison to control.The highest level was observed in group C of 244 mg/dl as shown in graph 1.They were 32% more than the control. This was in agreement with H. Ulrich Hink, Nalini Santanam et al. The possible explaination can be drawn from number of studies showing that superoxide dismutase during catalyzing dismutation of $O_2^{\cdot-}$ to H_2O_2 can form copper bound hydroxyl radical from hydrogen peroxide H_2O_2. [17].Hydroxyl radical when gets bounded to SOD, then it can attack adjacent histidine residue which is attached to copper resulting in inactivation of both SOD1 and SOD 3 [18].This might be prevented when small anions or reductants including Uric acid are coincubated [19] . as shown in graph 1 the comparison of mean plasma SOD levels of Control with rest of the groups. Mean plasma level of SOD of Control was found to be 165.15mg/dl (±2.65) .Group B (Fructose) showed mean plasma SOD level of 176.65mg/dl (±2.60) reflecting SOD levels were raised to 6.5% in rats which were exposed to diet comprising 60% Fructose. On comparing both groups i.e Control with Group B significant statistical correlation (P<0.01) was observed.

The mean plasma SOD levels of Group D (oxonic acid) has been measured to 181.2mg/dl(±3.52)which is again 8% more than Control. Therefore , significant (P<0.01) correlation was observed on comparison of both groups .

While comparing Group C (Fructose +Oxonic acid) with Control, highly significant correlation was observed(P<0.001).It was due to high mean plasma SOD levels of Group "F+O" which was 244mg/dl(±2.23) which is highest of all these groups.In this group SOD was 32% more than control which might be due to antioxidant action of uric acid.

It has been suggested that in group C there was significant increase in the concentration of uric acid . this was in accordance with some studies done on human that high dietary intake of fructose contributes significantly to hyperuricemia.[20] In a large study in the United States, consumption of four or more sugar-sweetened soft drinks per day gave an odds ratio of 1.82 for hyperuricemia.[21] Increased production of uric acid is the result of interference, by a product of fructose metabolism, in purine metabolism. This interference has a dual action, both increasing the conversion of ATP to inosine and increasing the synthesis of purine.[22] Fructose also inhibits the excretion of uric acid, apparently by competing with uric acid for access to the transport protein SLC2A9.[23] The effect of fructose in reducing excretion of uric acid is increased in people with a hereditary (genetic) predisposition toward hyperuricemia and/or gout.[22]

Starvation causes the body to metabolize its own (purine-rich) tissues for energy. Thus, like a high purine diet, starvation increases the amount of purine converted to uric acid. A very low calorie diet without carbohydrate can induce extreme hyperuricemia; including some carbohydrate (and reducing the protein) reduces the level of hyperuricemia.[24] Starvation also impairs the ability of the kidney to excrete uric acid, due to competition for transport between uric acid and ketones.[25] Many studies are controversial to our results all were done on human some supported that high doses of fructose (200 g/day for 2wks) raise the blood

pressure and cause the features of metabolic syndrome. Some suggested that lowering of the uric acid level prevents the increase in mean arterial blood pressure. Excessive intake of fructose may have a role in the current epidemics of obesity and diabetes.[26] some authors also suggested that increased dietary fructose was not associated with increase uric acid level. [27]

CONCLUSION

The urate concentration does increase when we take fructose upto 60%in our diet e.g., beverages soft drinks. It also increases superoxide dismutase concentration. It has been concluded that more than this value of fructose may have inverse effect on the uric acid level and its role as an antioxidant may become inversed. Therefore, it is suggested from our study that further work need to be done on the effect of fructose on uric acid levels on human

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Original Article

Serological, Biochemical and Radiological Comparison of Triple Hepatitis (Hepatitis B, C & D Virus) and Dual Hepatitis (Hepatitis B & D Virus) at a Hepatology Clinic

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ABSTRACT

Objectives: To compare the serological, biochemical and radiological parameters of triple hepatitis (Hepatitis B, C & D) and dual hepatitis (Hepatitis B & D) infection.

Study Design: Cross Sectional Study.

Place and Duration of Study: This 3½ study conducted at Hepatology clinic and wards of Medicine Department, Chandka Medical College (C.M.C), Larkana from January 2008 to June 2011.

Materials and Methods: Blood sample of 1713 HBsAg positive patients were drawn, for detection of anti-HDV Antibodies, anti – HCV antibodies on ELISA, HBV DNA, HCV RNA and HDV RNA on PCR and liver function tests (LFT). Ultrasound of all patients was performed. Serological, biochemical and radiological parameters were compare in triple hepatitis and dual hepatitis patients by chi-square test. P value of less than 0.05 was taken as statistically significant.

Results: Of 1713 patients, anti-HCVAb was detected in 420 (24.5%) and anti-HDVAb in 1116 (65.1%). 268 (15.6%) had triple hepatitis and 848 (49.5%) had double hepatitis. HDV RNA was detected in 100% patients of TH positive as compared to 74.1% of DH ($p < 0.001$). TH patients tend to have normal liver span [OR: 11.28 (95% CI: 8.19 – 15.13). TH and DH patients, had features of advanced liver diseases, but no other statistically significant serological, biochemical or radiological difference was noted between both.

Conclusion: TH infection was documented in 15.6% and DH in 49.5% HBsAg positive patients. Infected patients had advanced liver disease. There was no statistically significant major difference noted in serological, biochemical or radiological parameters of TH and DH.

Key Words: Triple hepatitis, Dual hepatitis, HBsAg, HBV DNA, anti-HCV Ab, HCV RNA, anti-HDV Ab, HDV RNA.

INTRODUCTION

Hepatitis B virus (HBV) is a hepatotropic virus, belonging to hepadnaviridea family. It has infected approximately one third of world population and at least 350 million individuals worldwide are harboring this virus in active state. 80 – 85% individuals infected with it, clear it spontaneously, but the remaining go into chronic phase of infection. After a mean period of 15 – 25 years, 25 – 40% of these go on to develop cirrhosis and Hepatocellular carcinoma at the rate of 2 – 5% per year.[1,2,3] Pakistan comes in the category of intermediate prevalence zone for HBV infection where the prevalence of carrier of HBV is 2.11% to 10%.[4,5,6]

There are two important dilemma associated with HBV infection. First, there is no curative therapy available for it and secondly, HBV infected patients are the only individuals at risk of acquiring hepatitis Delta virus (HDV) infection. HDV is a defective virus which can only infect and replicate in the patients who are infected with HBV. This combined infection of HBV and HDV is called dual hepatitis (DH). When both viruses infect an individual simultaneously, the course of disease is not much different from isolated HBV infection. But, if super infection occurs, the rate of liver damage increases exponentially. This eventually leads to severe disease with higher rates of progression to cirrhosis and Hepatocellular Carcinoma.[7,8]

Three major problems are encountered with DH infection. First, rapid and aggressive progression of disease (hepatitis), second, no response to oral nucleoside / nucleotide drugs used for suppression of HBV proliferation, and third, marginal response (20%) to higher doses of interferon alpha. These problems make the management of dual hepatitis (HBV and HDV co infection or super infection) a challenging task.[9,10,11,12,13]

This situation is even complicated if HCV infect an individual already harboring DH. This is called triple hepatitis (TH). The exact course and natural history of triple hepatitis is un-determined and treatment guidelines unclear regarding drugs, dosing and duration.[14,15,16,17] The magnitude of both entities i.e. DH and TH is reported to be very high in our country, ranging from 20 – 90% for DH and 3.4 – 11.8% for TH.[18,19,20,21,22] So, we designed this study to observe the serological, biochemical and radiological differences

between dual and triple hepatitis infection. This study may help in understanding the characteristics of dual and triple hepatitis.

MATERIALS AND METHODS

This was a hospital based cross-sectional and observational study for a period of three and half years from January 2008 till June 2011. The patients were enrolled from weekly Hepatology clinic and wards of Medicine Department, Chandka Medical College (C.M.C), Larkana. The study population / participants were the same that we studied for determination of frequencies of dual and triple hepatitis.[23]

Sampling Technique: Purposive sampling.

Inclusion Criteria: All new known HBsAg positive patients of either sex visiting Hepatology clinic of C.M.C Larkana for further evaluation and management were enrolled.

Exclusion Criteria:

- Patients younger than 15 years and older than 75 years.
- Patients previously diagnosed as seropositive for HCV antibodies (anti-HCV Ab) and / or HDV antibodies (anti-HDV Ab).
- Patients receiving oral or injectable therapy for viral hepatitis or previously non responders to such therapy.

Data Collection: Collection of data was started after approval of ethical review committee of Shaheed Mohtarma Benazir Bhutto Medical University, Larkana. Patients meeting our selection criteria were enrolled, study protocol was explained in detail and informed written consent was taken from each to draw blood sample and undergo ultrasonological evaluation. Blood samples were taken and sent to central laboratory C.M.C Larkana for detection of anti – HCV antibodies (anti-HCV Ab), Hepatitis D Virus antibodies (anti-HDV Ab) on ELISA, Hepatitis B Virus (HBV) DNA, Hepatitis C Virus (HCV) RNA and HDV (HDV) RNA by Polymerase Chain Reaction (PCR), and Liver Function Test as serum bilirubin, serum Alanine aminotransferase (ALT) and serum asparate aminotransferase (AST). LFTs were performed by Slectra – E Merck (Germany) auto-analyzing machine.

Ultrasound (US) examination of abdomen was done for liver parenchymal changes, liver size, portal vein (PV) size, spleen size and the presence of ascites. Ultrasound examination of abdomen was done by a senior radiologist with more than 10 years experience, at the Radiology Department C.M.C Teaching Hospital. Toshiba SSA-70 U/S machine was used to carry out U/S examination. A separate Performa was filled for each patient enrolled for the study to record the data of these investigations and demography. All investigations were performed at the laboratory of CMC teaching hospital.

Data Analysis: The collected data was transferred to and analyzed using SPSS version 19. Means of numeric response variables as age, serum bilirubin, serum ALT, serum AST, portal vein diameter and splenic size were calculated and compared in triple hepatitis and dual hepatitis. Categorical response variables as age (16-35years, 36-55years, 56-75years), gender (male, female), liver size (normal, decreased, increased), liver echo texture (normal, altered), portal vein diameter (normal, dilated) and ascites (present, absent) were compared in triple hepatitis and dual hepatitis patients by Chi-square test. Odd ratios (OR) and 95% Confidence Interval (CI) were calculated. Probability value (p-value) of less than 0.05 (<0.05) was considered to be statistically significant.

RESULTS

Table No 1: Demographic Profile of 1713 HBsAg Positive Patients

Characteristic	Number, n (%)
Age	
Mean ± SD	43.45 ± 14.83
Range	56 (72 - 16)
Age Categories	
16 – 35 Years	565 (33.0%)
36 – 55 Years	705 (41.2%)
56 – 75 Years	443 (25.8%)
Gender	
Male	1225 (71.5%)
Female	488 (28.5%)
Liver Function Test	
Serum Bilirubin (mg/dl)	1.82 ± 0.58 mg/dl
Serum ALT (IU/L)	67.96 ± 40.93 IU/L
Serum AST (IU/L)	172.16 ± 62.12 IU/L
Radiological Features	
Liver Size	
Normal (8 - 12 cms)	516 (30.1%)
Decreased (< 8cms)	814 (47.5%)
Increased (> 12 cms)	383 (22.4%)
Liver Echo Texture	
Normal	652 (38.1%)
Altered	1061 (61.9%)
Splenic Size (cms)	12.73 ± 1.81 cm
Portal Vein Diameter (cms)	1.63 ± 0.48 cm
Normal	1084 (63.3%)
Dilated	629 (36.7%)
Ascites	
Present	576 (33.6%)
Absent	1137 (66.4%)
Serological Test	
HBsAg Positive	1713 (100%)
Anti – HDV Ab Positive	1116 (65.1%)
Anti – HCV Ab Positive	420 (24.5%)
HBV DNA PCR Positive	308 (18%)
HCV RNA PCR Positive	148 (8.6%)
HDV RNA PCR Positive	896 (52.3%)
Dual / Triple Hepatitis	
Triple Hepatitis	268 (15.6%)

(HBV+HCV+HDV)	
Dual Hepatitis (HBV + HDV)	848 (49.5%)

A total of 1713 known HBsAg positive patients were enrolled in our study during the specified period with mean age of 43.45 ± 14.83 years. 1225 (71.5%) were male and 488 (28.5%) female. HBV DNA was positive in 308 (18%) patients. Anti – HCV Ab was documented in 420 (24.5%) and HCV RNA in 148 (8.6%). Anti – HDV Ab was documented in 1116 (65.1%) and HDV RNA in 896 (52.3%). Mean serum bilirubin, ALT and AST was 1.82 ± 0.58 mg/dl, 67.96 ± 40.93 IU/L and 172.16 ± 62.12 IU/L respectively. Liver span was decreased in 814 (47.5%), liver echo texture altered in 1061 (61.9%), portal vein dilated in 629 (36.7%), and ascites was present in 576 (33.6%) patients. 268 (15.6%) patients were HBsAg, anti-HCV Ab and anti-HDV Ab positive and were labeled as triple hepatitis. A total of 848 (49.5%) patients were HBsAg and anti-HDV Ab positive and were labeled as dual hepatitis. Table 1.

Table No 2: Comparison of Triple Hepatitis and Dual Hepatitis Patients

Characteristic	Triple Hepatitis (268)	Dual Hepatitis (848)	P values*	or (95%CI)
Age				
Mean ± SD	43.38 ± 14.33	43.85 ± 15.03	0.394	NA
Range	56 (72 - 16)	54 (71 - 17)		
Age Categories				
16 – 35 Years	86 (32.1%)	270 (31.8%)	0.939	1.01 (0.75 – 1.35)
36 – 55 Years	118 (44.0%)	342 (40.3%)	0.283	1.16 (0.88 – 1.53)
56 – 75 Years	64 (23.9%)	236 (27.8%)	0.204	0.81 (0.59 – 1.11)
Gender				
Male	220 (82.1%)	712 (84.0%)	0.471	0.87 (0.60 – 1.25)
Female	48 (17.9%)	136 (16.0%)		
Serological Test				
HBV DNA PCR Positive	60 (22.4%)	176 (20.8%)	0.568	1.10 (0.79 – 1.53)
HCV RNA PCR Positive	32 (11.9%)	00(0%)	0.234	NA
HDV RNA PCR Positive	268 (100.0%)	628 (74.1%)	0.001**	0.70 (0.67 - 0.73)

*Chi – square test (2-sided significance) **Statistically significant p values (<0.05)
+Significant and high odd ratios NA. Not Applicable

Table No.3: Comparison of liver function test of triple Hepatitis and dual Hepatitis Patients

Characteristics	Triple Hepatitis (268)	Dual Hepatitis (848)	P values*
Serum Bilirubin (mg/dl)	2.04 ± 0.44	2.02 ± 0.54	0.364
Serum ALT (IU/L)	83.84 ± 40.70	75.05 ± 47.35	0.137
Serum AST (IU/L)	212.05 ± 84.97	185.54 ± 55.6(	0.069

***Chi – square test (2-sided significance)**

Mean age of triple hepatitis positive patients was 43.38 ± 14.33 years as compared to 43.85 ± 15.03 years in dual hepatitis patients. HBV DNA was detected in 60 (22.4%) triple hepatitis ($p < 0.568$) as compared to 176 (20.8%) in dual hepatitis patients with odd risk of 1.10 (95% CI; 0.79 – 1.53). HCV RNA was detected in 32 (11.9%) triple hepatitis patients ($p < 0.234$). HDV RNA was detected in 268 (100%) triple hepatitis patients ($p < 0.001$) as compared to 628 (74.1%) patients in triple hepatitis negative patients with odd risk of 0.74 (95% CI; 0.71 – 0.78) as given in table 2.

Table No 4: Comparison of Radiological features of triple hepatitis and dual hepatitis patients

Characteristic	Triple Hepatitis (268)	Dual Hepatitis (848)	P values*	or (95%CI)
Liver Size				
Normal (8 - 12 cms)	164 (61.2%)	104 (12.3%)	0.001**	11.28 (8.19 – 15.53)+
Decreased (< 8cms)	104 (38.8%)	540 (63.7%)	0.001**	0.36 (0.27 – 0.48)
Increased (> 12 cms)	000 (0.00%)	204 (24.1%)	0.001**	1.41 (1.35 – 1.47)
Liver Echotexture				
Altered	148 (55.2%)	704 (83.0%)	0.001**	3.96 (2.93 – 5.35)+
Splenic Size (cms)	13.31 ± 1.55	13.46 ± 1.60	0.736	NA
Portal Vein (cms)	1.27 ± 0.20	1.25 ± 0.21	0.071	NA
Dilated	130 (48.5%)	415 (48.9%)	0.902	0.98 (0.74 – 1.29)
Ascites Present	110 (41.0%)	410 (48.3%)	0.067	0.74 (0.56 – 0.98)

*Chi – square test (2-sided significance) **Statistically significant p values (<0.05)
+Significant and high odd ratios NA. Not Applicable

There was not statistically significant difference in biochemical profile (serum bilirubin, serum ALT, serum AST) of triple hepatitis and dual hepatitis patients, as illustrated in table 3.

In patients having triple hepatitis, the liver span was normal in 164 (61.2%) as compared to 104 (12.3%) patients in dual hepatitis ($p < 0.001$) with odds of 11.28 (95% CI: 8.19 – 15.53). Liver echo texture was altered in 704 (83.0%) dual hepatitis patients as compared to 148 (55.2%) triple hepatitis with odds of 3.96 (95% CI: 2.93 – 5.35) as shown in table 4.

DISCUSSION

In our study, we observed that both triple and dual hepatitis patients had biochemical, serological and radiological evidence of advanced chronic liver disease. Triple hepatitis was documented in 15.6% HbsAg positive patients and dual hepatitis in 49.5%. The only serological difference between Triple Hepatitis and Dual Hepatitis was more frequent detection of HDV RNA. So, we assume that, HCV may have permissive effect on HDV, as it was detected in 100% patients of TH and 74% of DH ($p < 0.001$). There was no significant biochemical (LFT) difference noted between both Triple Hepatitis and Dual Hepatitis. Radiological comparisons were also statistically insignificant, except two important findings. TH patients tend to have normal liver size ($p < 0.001$) with odds of 11.28 (95% CI: 8.19 – 15.53) and DH patients were more likely to have altered echo texture of liver ($p < 0.001$) with odds of 3.96 (95% CI: 2.93 – 5.35).

Morsica G et al., (2009), studied the dual hepatitis and triple hepatitis infection in HIV positive individuals. He was of the view that HCV and HBV had suppressive effect on each other, while the presence of both viruses had permissive effect on HDV proliferation. So, HDV may be the predominant virus in triple hepatitis. Similar, observations were made by Jardi R et al.(2001). Liaw YF et al., (1998), while studying the virological and clinical course of triple hepatitis, found completely different results. He reported that triple hepatitis is associated with severe acute disease, but relatively benign, slowly progressive chronic infection. Clinical, biochemical and serological course of triple hepatitis infection was dominated by HCV infection.[24,25,26]

Mathurin P et al., in 2000 at France studied replication status and histological features of patients with triple and dual hepatic infection. Multiple infection was associated with a decrease of HCV replication. Cirrhosis was more frequently observed in patients with multiple infection. In patients with triple infection, serum HCV RNA and markers of HBV replication were absent in 80%, suggesting that HDV acts as a dominant virus. In patients with dual infection, HBV and HCV exerted an alternative, dominant replication.[27]

Whether HCV or HDV is the pre-dominant virus in triple hepatitis or what should be the ideal therapy for triple hepatitis, is still unknown and controversial issue. Our study and international literature bring focus to these issues.

CONCLUSION

- Triple and dual hepatitis is associated with advanced liver disease.
- Triple hepatitis and dual hepatitis seen in 15.6% and 49.5% respectively.
- HDV RNA was detected more frequently in triple hepatitis.
- Liver echo texture was altered more frequently in dual hepatitis.
- Triple hepatitis patients tend to have normal liver span.

Recommendations:

- ❖ Studies (multicentre) should be performed to answer the issues raised by our study, so that the collected data can be used to by international authorities, societies and associations to formulate recommendations for triple and dual hepatitis management.
- ❖ Community awareness regarding prevention of viral hepatitis should be intensified, so that we get rid of these silent killers (dual and triple hepatitis).
- ❖ Government should make immunization mandatory and compulsory, so that we can save our future from developing dual and triple hepatitis, because prevention is much better than cure.

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Original Article

Study to Compare the Results of Transvesical VS Transurethral Prostatectomy in respect to Incidence of Post Operative Urinary Incontinence

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ABSTRACT

Objective: To compare the results of transurethral resection of prostate with transvesical prostatectomy in respect to the incidence, and severity of postoperative urinary incontinence.

Study Design: Comparative cross sectional study.

Place and Duration of Study: This study was carried out in GMMMC Hospital Sukkur, Pakistan, where all transvesical prostatectomies were performed. It was two years study from feburvoury 2008 to March 2010.

Materials and Methods:280 patients were selected, they were diveded in two groups and 140 Patients underwent TURP were kept in group A, and 140 patients transvesical prostatectomy group was titled as B. Patients having associated stricture urethra, urinary bladder stones or bladder diverticulum and later on proved a scarcinoma of prostate were excluded form the study.

Results: From group-A (TURP Group) 20 (14.28%) Patients developed incontinence postoperatively and all had stress type of incontinence. While in group B Transvesical prostatectomy 37 (26.4%) patients developed urinary incontinence. 30(21.4) patients had stress incontinence and 7(5%) patients developed continuous urinary leakage. Rate of recovery after conservative measures remained rapid with group A as compared to group B.

Conclusion: Frequency and severity of postoperative urinary incontinence is more with transvesical approach. But the facility of TURP is not freely available. Therefore improvement in the technique of open prostatectomy is mandatory. For which recommendations have been given.

Key Words: TURP, Transvesical, Transurethral Prostatectomy, intracorporeal lithotripsy

INTRODUCTION

TURP is the classic treatment for urinary symptoms due to the prostate (prostatism) or BPH. Prostatic tissue is removed and so the physical bulk of the prostate is reduced. Obstruction is reduced and urinary symptoms considerably improved. The operation is performed through the penis and usually there are no cuts or surgical incisions. The procedure is tolerated reasonably well, although associated with retrograde ejaculation. It is the gold standard treatment for BPH with many years of history to support its use.

Indications: According to the Agency for Health Care Policy and Research guidelines for the diagnosis and treatment of BPH and the recommendations of the Second International Consultation on Benign Prostatic Hypertrophy, the absolute indications for primary surgical management of BPH are as follows:[2]

- Refractory urinary retention
- Recurrent urinary tract infections due to prostatic hypertrophy
- Recurrent gross hematuria
- Renal insufficiency secondary to bladder outlet obstruction
- Bladder calculi
- Permanently damaged or weakened bladders
- Large bladder diverticula that do not empty well secondary to an enlarged prostate

Contraindications: The only absolute indication for an open prostatectomy over a TURP is the need for an additional open procedure on the bladder that must be performed at the same time as the prostatectomy. Such indications include open surgical resection of a large bladder diverticulum or removal of a bladder stone that cannot be easily fragmented by intracorporeal lithotripsy.

A relative indication for the selection of an open prostate surgery over a TURP is generally based on prostatic volume and the ability of the surgeon to complete the TURP in less than 90 minutes of actual operating time (although < 60 min is considered optimal).

In general, open prostatectomy can be justified in a patient with a prostate of 45 g or larger, but this is totally dependent on the skill and experience of the endoscopic urological surgeon. Most experienced urologists use a prostatic volume of 60-100 g as the upper limit amenable to endoscopic removal, but some

highly skilled resectionists are capable of safely treating a 200-g prostate with TURP in less than 90 minutes.

MATERIALS AND METHODS

This study was carried out in Ghulam Muhammad Mahar Medical College hospital (GMMMC) sukkur, Pakistan, to compare the results of TURP with transvesical prostatectomy in respect to post procedure incontinence from feburvoury 2008 to March 2010. Two groups were made and 100 cases of BPH were selected for each group by non-probability convenient sampling technique. Patients who underwent TURP were put in group A and transvesicle prostatectomy group was titled as group B. Decision for the approach was based on institution. Transurethral approach was adopted at Ghulam Muhammad Mahar Medical College Hospital, sukkhur. Patients having associated urethral stricture, urinary bladder stone or diverticulumwere excluded from the study. Urinary incontinence was compared between both groups after the procedures by following the patients weekly up to 24 weeks. Symptoms of incontinence were controlled by pelvic floor exercise, drugs (Anticholinergic) i.e. Oxybutynin 5-mg 2-4 times/day, Imipramine hydrochlorid 25-mg 2-4 times/day, Nusculotropic Flavoxate hydrochloride200-mg 3-4 times/day. Prostate size/weight was calculated by the formula: $\pi/6 \times$ anteroposterior $\times$ transverse diameter $\times$ sagittal diameter. A well-informed consent was obtained from all study subjects. A predesigned proforma was used to record information regarding demographics, presenting complaints, history, examination, investigations, treatment outcomes, complications and follow-up. SPSS version 16 was used to analyze data. Chi-square test was used to differentiate the proportions, while continuous data were analyzed by applying t-test. P-value up to 0.05 was considered significant.

RESULTS

Among group A 83 patients were admitted with acute retention of urine and 07 patients were operated due to more irritating symptoms. Among group B 85 patients were operated for urinary retention and 5 patients with more irritating symptoms. Mean prostate size was 70-g and 76-g for group A and group B respectively (P=0.12). Mean age of group A subjects was 63±8.9 years while it was 69±9.6 years in group B (P=0.14). Majority of the patients in both groups were in their 6th decade of life (Table 1). Urinary incontinence was observed in 30 patients after TURP (Group A) and in 35 subjects after TVP (Group B) which was insignificant (P=0.298). No continuous leaking of urine in the absence of intra-abdominal pressure was observed in any subject of group A (Table 2). During follow up symptomatic improvement was observed in all 30 subjects of group A latest up to 10th week, whereas 1 subject of group B remained nonresponsive to conventional therapy (Table 3).

Table No.1: Age distribution of study subjects

Age range	Group A(n=140)	Group B(n=140)
50-60 years	70 (50%)	68 (48.5%)
61-70 years	52 (37.1%)	50 (35.7%)
71-80 years	10 (7.14%)	14 (10%)
> 80 years	08(5.7%)	08 (5.7%)

Table No.2: Comparison of urinary incontinence between study groups

	Group A (n=140)	Group B(n=140)
No incontinence	120 (85.7%)	103 (73.5%)
Stress incontinence (associated with coughing and sneezing)	20 (14.2%)	30 (21.4%)
Continuous leaking (without increased intra-abdominal pressure)	0	7 (5%)

Table No.3: Follow up observations for symptomatic improvement

Follow-up Period	Group A (n=20)	Group B (n=37)
2-3 weeks	9 (45.00%)	11(29.73%)
4-6 weeks	7 (35.00%)	15(40.54%)
7-8 weeks	2 (10.00%)	4 (10.81%)
9-10 weeks	2 (10.00%)	3 (8.11%)
11-12 weeks	0	3 (8.11%)
Non-respondent	0	1 (2.70%)

DISCUSSION

In recent decades, various interventional procedures for the treatment of symptomatic benign prosthetic hyperplasia (BPH) have been developed. Most of them have been considered potential alternative to open prostatic surgery such as transurethral resection of prostate (TURP), or transurethral incision of prostate (TUIP)5. Despite good results observed in the initial clinical studies, most concepts and procedures were never generally accepted6. However, they contributed considerably to knowledge regarding treatment of symptomatic and obstructive BPH7. Only a few procedures have stood the test of time and became part of the urological armamentarium8. Currently interventional methods are classified by their effect on prostate tissue in procedures with immediate tissue ablation (open prostatectomy, TURP, vaporization techniques, laser resection technique), procedures with delayed tissue ablation (transurethral high energy microwave thermo therapy, transurethral needle ablation, interstitial laser coagulation) and other

procedures (TUIP, stents) with relief in obstruction without tissue ablation9. Out of these the cost and results of open prostatectomy and transurethral resection of prostate are compatible10. Whichever procedure is adopted, two main concerns that make operating surgeons most worried are bleeding during and in immediate postoperative phase and incontinence at the time of removal of catheter. In our study two most popular procedures for BPH were compared for post operative urinary incontinence. The patients were divided in group A and group B. Group-A underwent transurethral resection of prostate. In this group 20 (14.2%) patients developed post-operative urinary incontinence. In group-B patient underwent transvesical prostatectomy. In this group 37 (26.4%) patients developed postoperative urinary incontinence. We have sub-classified incontinence in two categories, stress incontinence and continuous leaking of urine. In group A all 20 (14%) patients had stress incontinence i.e. with coughing and sneezing. While in group B 30 (21.4%) had stress incontinence and 07 (5%) had continuous dribbling of urine. This proportion is consistent with other studies11. Measures used for controlling the symptoms were pelvic floor muscle exercise and medicine including anticholinergic drugs (Oxybutynin, imipramine hydrochloride)12. Antihistamine (Chlorpheraireaminemaleate)13, and Musculotropic relaxants (Flavoxate hydrochloride)14.

Improvement observed in group A was rapid as 16 (80%) patients become symptoms free within 6 weeks duration and remaining 4 (20%) in 10 weeks. While in group B, it took upto 12 weeks to improve. Similar observations have also been made in a study by Margel D et al15. One patient in group B remained incontinent with continuous leaking of urine and required condom catheter. The analysis of clinical studies shows a great variety of different results. The main reason is that the design of past and present studies ignored the pathophysiological aspect of BPH, especially the obstructive component and the fact that the outcome of most procedure depends on the operator/user16.In a study at Japan TURP is found superior to transurethral vaporization of prostate (TUVP) and transurethral radiofrequency thermotherapy (TURF), interstitial laser coagulation of prostate (ILCP) and transurethral microwave thermotherapy (TUMT) with regard to efficacy and overall usefullness17. One study showed that the functional length of the sphincter unit is the portion with positive closure pressure, and this is where urethral pressure is greater than bladder pressure18. In men the functional length is longer and the maximum closure pressure builds up in the prostatic segment, reaches a peak in the membranous urethra and drops as it reaches the level of bulbous urethra19. The entire functional length in men is about 6-7cm20. After prostatectomy, there is usually no positive pressure in the entire prostatic fossa, minimal closure pressure at the apex of the prostate and normal or greater than normal pressure within the voluntary sphincter segment of the membranous urethera21. It means that it is the functional length of the sphincter segment above the genitourinary diaphragm that determines the degree of incontinence22. High pressure is almost always recorded within the voluntary sphincter despite the common belief “Itrogenically induced incontinence” is due to damage to the voluntary sphincter. Its true incidence is very low and makes patients become permanently incontinent23. Postoperative urinary incontinence is multifactorial and its main cause is decreased functional length of prosthetic urethera. Sometimes hypertrophic overactive urinary bladder may lead to incontinence with frequency and urgency. Infrequently trauma to external sphincter mechanism lead to permanent incontinence. In this study only one patient became permanently incontinent. In that patient prostate was fibrosed in that patient and during enucleation probably trauma to external sphincter mechanism may have occurred. Rest of the patients in both groups who developed incontinence, recovered within few weeks time.

CONCLUSION

Frequency of postoperative urinary incontinence is higher and more severity in transvesical approach than in TURP. As the facility of TURP is not freely available improvement in expertise with transvesical approach is mandatory**.**

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Original Article

Comparative Study of add-on Therapies, Salmeterol and Montelukast to Inhaled Corticosteroids in Mild to Moderate Asthmatic Patients

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ABSTRACT

Objective: The aim of this study was to compare the effect of both add-on therapies; Salmeterol plus Inhaled Corticosteroid and Montelukast and Inhaled Corticosteroid on asthma control in poorly controlled asthma.

Study Design: Randomized clinical trial.

Place and Duration of Study: Department of Pharmacology and Therapeutics, Basic Medical Sciences Institute, Jinnah Post-graduate Medical Centre, Karachi from December 2007 to June 2008.

Materials and Methods: 75 patients aged between 15-65 years, suffering from mild to moderate asthma were randomly divided in three groups. Group A was given Salmeterol 50µg and Fluticasone propionate 250µg twice daily, Group B was given tablet Montelukast 10mg at night in addition to Beclomethasone Dipropionate 500µg twice daily and Group C was given Beclomethasone Dipropionate 500µg twice daily. Improvements in Peak Expiratory Flow Rate (PEFR) and FEV_1 were assessed by Peak Expiratory Flow Meter and Spirometry, fortnightly at the beginning and end of treatment respectively. Student paired t test was applied to analyze data.

Results: An improvement of 46.58 %(P-value <0.001), 38.59% (P-value <0.005) and 21.2% (P-*value* not significant) in PEFR was noted in Group A, B and C respectively. In Group A and B FEV_1 increased from1.17L/min (±0.12) to 1.41L/min (±0.13), and 1.42L/min (±0.13) to 1.62L/min (±0.13) respectively, while in Group C it was from 1.24L/min (±0.12) to 1.26L/min (±0.13).

Conclusion: Salmeterol is slightly more effective than Montelukast as add-on treatment in increasing PEFR in patients suffering from mild to moderate persistent asthma.

Key Words: Salmeterol, Montelukast, Inhaled Cortcosteroids(IC), Peak Expiratory Flow Rate (PEFR).

INTRODUCTION

Asthma is a growing public health problem in many countries around the world. Asthma current affects approximately 300 million individuals worldwide and remains a global respiratory health concern[1]. Asthma is an inflammatory disease of the airways associated with intermittent episodes of bronchospasm[2]. Unfortunately, regardless of disease severity, patients have a tendency to underestimate their level of asthma control, and many patients with asthma live with significant symptoms and restrictions. Asthma is a chronic potentially life-threatening condition that is increasing in both prevalence and severity. In mild-to-moderate asthma, there is persistent bronchial inflammation involving primarily lymphocytic and eosinophilic infiltration associated with remodeling of the airway wall[3]. Airway obstruction can lead to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning[4].

For optimal management, patients with persistent asthma require daily controller therapy. According to the NIH guidelines, inhaled corticosteroids (ICSs) are the most effective anti-inflammatory medications available. Inhaled corticosteroids have been shown to reduce symptoms, reduce risk of hospitalizations for asthma, reduce deaths from asthma, improve lung function, and improve or prevent several of the pathologic alterations associated with airway remodeling[5].

Many patients do not have adequate symptom control while receiving low-dose inhaled corticosteroid treatment and additional second-line therapy is necessary. Combining a long-acting β_2-agonist with low-dose inhaled corticosteroid has been shown to provide equivalent or superior asthma control than using higher doses of inhaled corticosteroid alone, as is reflected in current asthma management guidelines[6].

The introduction of inhaled long-acting inhaled β_2-adrenoceptor agonists (LABAs; Salmeterol and Formoterol) represented an important advance in asthma therapy. Treatment with LABAs provides better

control of symptoms and lung function than short-acting β_2- agonists[7,8].

Several studies show that the combined use of long-acting β_2-agonists with low-to-moderate doses of inhaled corticosteroid therapy appears to provide greater clinical benefit than further increasing the dose of inhaled corticosteroid[9].

In fact, when combined with moderate doses of inhaled glucocorticosteroids, these drugs have been shown to improve symptoms and lung function more effectively than doubling the dose of inhaled corticosteroids[10] .

Leukotriene receptor antagonists (LTRA) are a novel class of therapy available in the management of asthma. They have both anti-inflammatory and bronchodilator activity, although not as great as that of inhaled corticosteroids or long-acting β_2-agonists, respectively[11].

Montelukast is a potent, specific LTRA. Administered once daily in tablet form, Montelukast reduces the signs and symptoms of persistent asthma in children as young as 2 years of age[6]. While the improvements in FEV_1 are modest (6 to 10%), asthma symptoms and quality of life appear to be improved to a greater degree with Montelukast administration than is FEV_1[12,13]. There has been speculation about whether symptom improvement with the systemic delivery of Montelukast could be due to systemic effects on both the small and large airways[14] .

As long-acting β_2-agonist and leukotriene antagonists act on the different parts of inflammatory cascade, aim of this study was to compare the effect of both add-on therapies; Salmeterol plus ICS and Montelukast and ICS on asthma symptoms and Peak expiratory flow rate (PEFR).

MATERIALS AND METHODS

Study Design: This was a randomized, open-label, parallel group study carried out at the department of Pharmacology and Therapeutics, BMSI, in collaboration with Department of Chest Medicine, JPMC, Karachi. The ethical committee of this institution approved the study protocol.

Patients: A total of 75 mild to moderate asthmatic, male and female patients were recruited in the study. These patients aged between 15-70 years were receiving ICS therapy for asthma. Patients were excluded from study if: they were taking systemic steroids or have taken systemic steroids in past 6 months; have had respiratory infections and taken antibiotics in past 4 weeks. Patients suffering from diabetes, heart disease, hypertension, hepatic and renal diseases were also excluded from study.

Study Procedure: The study extended over 12 weeks period which was preceded by 2 weeks run-in period. Subjects were assessed in run-in period to determine eligibility for randomization based on pre-specified criteria i.e patients of either sex suffering from mild to moderate persistent asthma not controlled by ICS. During treatment period patients were randomized to either Group A, given Salmeterol 25µg/Fluticasone 125µg inhaler (Salmicort), two puffs twice daily; Group B, given Tab. Montelukast 10mg (Ventec) at night along with Beclomethasone Dipropionate inhaler 250µg (Beckson Forte) two puffs B.D. or Group C, given Beclomethasone Dipropionate inhaler, 250µg, two puffs B.D. for 12 weeks with follow up visits fortnightly.

Peak expiratory flow rate (PEFR) was measured by Micropeak. Peak flow meter. Reg. Design no. 2100423, Made in UK, on every clinical visit and recorded. The safety and tolerability of Salmeterol and Montelukast was assessed by monitoring adverse events (including exacerbation of asthma) blood pressure and heart rate at clinic visits throughout the study.

Statistical Analysis: All the values are taken as mean ±SEM. The primary efficacy measurement was the change in the PEFR fortnightly throughout the study period from baseline to end point. Student pair test was used to analyze the data.

RESULTS

Patients: Of 100 patients enrolled in study 75 were randomized to treatment, 25 in each treatment group. Five patients withdrew during treatment period. One patient withdrew from Salmeterol group two patients each from Montelukast and ICS groups because of non-compliance. Demographic data and baseline PEFR are given in Table-1. Patients in all three groups were matched for age, sex and type of asthma they were suffering from. Male to female ratio was same as observed in international studies i.e. 25:75 in all groups.

Peak Expiratory Flow Rate: Both add-on therapies, Salmeterol and Montelukast significantly improve PEFR, after each fortnight treatment while patients of ICS group showed non significant improvement in PEFR, as shown in Table-2.

By week 12 in Group A patients (Salmeterol plus ICS), improvement in PEFR was from 189.4 L/min (±16.12) to 354.58 L/min (±7.61) which is 46.58% as compared to baseline value, while in Group B (Montelukast plus ICS), improvement of 38.59% in PEFR from 201.3 L/min (±14.72) to 327.82 L/min (±12.41) was observed as compared to baseline value. Whereas in Group C (ICS), PEFR improved to only 21.2% from 182.60 L/min (±17.05) to 231.73 L/min (±13.84) in comparison to baseline observation as shown in Figure 1.

Spirometry: Improvement in Spirometric values from baseline to end of study was significant in Group A, Group B and non-significant in Group C patients. In Group A and in Group B, FEV_1 increased

from1.17L/min (±0.12) to 1.41L/min (±0.13), and 1.42L/min (±0.13) to 1.62L/min (±0.13) respectively, while in Group C it was from1.24L/min (±0.12) to 1.26L/min (±0.13). FEV_1/FVC improved from 67.75 (±2.84) to 83.14(±1.58), and 73.84 (±2.61) to 87.81(±1.7) in Group A and B respectively while in Group C it was from 68.27(±2.88) to 69.95 (±2.88) as shown in Table 3.

Table No.1: Demographic and Baseline Characteristics of Patients

Characteristics	GROUP A (Salmeterol plus Inhaled Corticosteroid)	GROUP B (Montelukast plus Inhaled Corticosteroid)	GROUP C (Inhaled Corticosteroid)
Total Patients	25	25	25
Remained in study	24 (96%)	23 (92%)	23 (92%)
Left out	01 (4%)	02 (8%)	02 (8%)
Age			
Mean	34	36	35
Range	15-65	15-65	15-65
Gender			
Male	6 (25%)	6 (26%)	6 (26%)
Female	18 (75%)	17 (66.6%)	17 (66.6%)
Type of Asthma			
Mild	13 (54.1%)	12 (52.1%)	12 (52.1%)
Moderate	11 (45.8%)	11 (47.8%)	11 (47.8%)
Family History			
Positive	19 (79.1%)	19 (82.6%)	18 (78.2%)
Negative	5 (20.8%)	4 (17.3%)	5 (21.7%)
Spirometry			
FVC L/min	1.7 (±0.145)	1.88 (±0.158)	1.70 (±0.14)
FEV1 L/min	1.2 (±0.128)	1.41 (±0.134)	1.20 (±0.12)
FEV1/FVC	68.55 (±2.84)	73.61 (±2.61)	68.37 (±2.8)
PEFR L/min	189.4 (±16.4)	201.3 (±14.72)	189.8 (±17.0)

Values are expressed in Mean (±SEM) (Percentage)
SEM: Standard Error of Mean
FVC: Forced Vital Capacity
FEV_1: Forced Expiratory Volume in First Second
PEFR: Peak Expiratory Flow Rate L/min: Liters per minute

Table No.2: Improvement In Peak Expiratory Flow Rate Among All Groups From Day 0-90

Groups	Day 0	Day 90	Percentage change	P-value
Group A	189.4 L/min (±16.12)	354.58 L/min (±7.61)	46.58%	<0.001***
Group B	201.3 L/min (±14.72)	327.82 L/min (±12.41)	38.59%	<0.005**
Group C	182.60 L/min (±17.05)	231.73 L/min (±13.84)	21.2%	N.S
Group A versus Group B				N.S
Group A versus Group C				<0.001***

Values are expressed in Mean (±SEM)
SEM: Standard Error of Mean
P-value: Probability value
***: Highly Significant
**: Moderately Significant
N.S: Not Significant

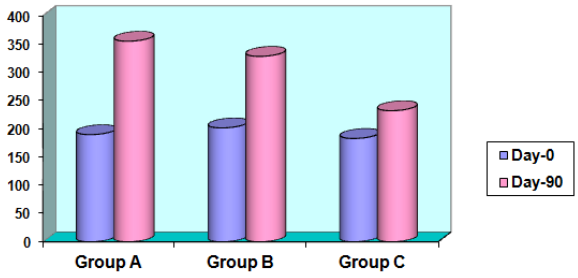

Figure No.1: Comparison of Peak Expiratory Flow Rate among all groups from day 0-90

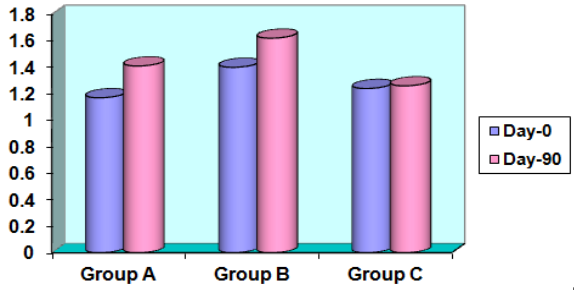

Figure No.2: Comparison of FEV1 among all groups from day 0-90

Safety: Both add-on treatments are well tolerated by patients. Side effects reported by patients were mild and did not require cessation of therapy.

Table No.3: Comparison of Spirometry in All Three Groups from Day 0-90

GROUPS	Spirometry	Day-0		Day-90		P-value
GROUP A	FEV_1 L/min	1.17	(±0.128)	1.41	(±0.133)	<0.001***
	FEV_1/FVC	67.75	(±2.84)	83.14	(±1.58)	<0.005**
GROUP B	FEV_1 L/min	1.40	(±0.13)	1.62	(±0.133)	<0.005**
	FEV_1/FVC	73.84	(±2.61)	87.21	(±1.7)	<0.01*
GROUP C	FEV_1 L/min	1.24	(±0.12)	1.26	(±0.13)	N.S.
	FEV_1/FVC	68.27	(±2.88)	69.95	(±2.82)	N.S.

Values are expressed in Mean (±SEM) P-value: Probability value SEM: Standard Error of Mean
***: Highly Significant FEV_1: Forced expiratory volume in First Second **: Moderately Significant
FVC: Forced Vital Capacity *: Significant N.S: Not Significant L/min: Liters per minute

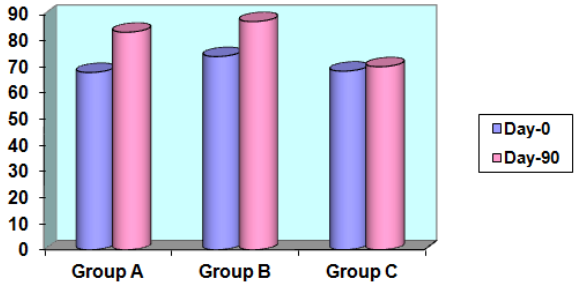

Figure No.3: Comparison of FEV1/FVC among all groups from day 0-90

DISCUSSION

Substantial variations in asthma outcomes persist despite the development and dissemination of national and international guidelines for the diagnosis and management of asthma[15].

Our study is the comparative study regarding the treatment options for patients with symptomatic asthma, despite taking low dose inhaled corticosteroids. Our aim was to evaluate the effectiveness of these treatments in clinically realistic situation with clinically relevant outcomes. Overall, the benefit provided by each add-on treatment on PEFR and spirometric values was significant in both treatment groups (group A and group B) recorded fortnightly and at the start and end of study respectively.

Adding a leukotriene modifier to ICS versus using SAL with an ICS has been evaluated in several randomized clinical trials. These trials have demonstrated greater efficacy of using SAL with an ICS compared with either Zafirlukast or Montelukast as add-on therapy to ICSs in patients with persistent asthma.

The present trial demonstrates that adding Salmeterol or Montelukast provided more benefit than ICS alone as evident by improvement in PEFR. Moreover, Salmeterol/ICS combination has shown more increase in PEFR as compared to Montelukast/ICS, 165.18L/min and 126.5L/min respectively. These results are consistent with the result of Cochrane review[16] which suggested superiority for the long-acting β_2-agonist and ICS combination over the combination of a leukotriene receptor antagonist and an ICS, with significantly greater improvements in lung function, symptom control and quality of life[16].

Busse and coworkers observed that improvement in morning PEF more than doubled in patients using SAL (29.6L/min) when compared with patients receiving zafirlukast (13.0 L/min; P<0.001) [17]. In a clinical trial by Nelson and associates, it was evident that patients treated with the combined FP and SAL had greater overall asthma control with significantly greater improvements in morning and evening PEF (P<0.001), FEV_1 (P<0.001), rescue-free days (P<0.032), and shortness of breath symptom scores (P<0.017) compared with patients receiving FP plus montelukast[18].

A clinical trial done by Bjermer and co-workers supports our study, as patients receiving salmeterol and fluticasone had a significantly larger increase in morning peak expiratory flow (litres per minute) compared with patients receiving montelukast and fluticasone (least squares mean (SE) change from baseline of 34.59 (1.70) versus 17.73 (1.69), P < 0.001). Both treatments significantly improved peak expiratory flow over baseline values (P < 0.001)[19].

Comparing combination of Salmeterol and ICS with ICS alone, this study is in line with trial conducted by Bergmann et al, which showed that combined Salmeterol Fluticasone (SFC) therapy resulted in significantly greater improvements in PEFR and symptom control than doubling the dose of FP. At week 12, morning PEFR had increased by 52 L/min from baseline in patients on SFC and by 36 L/min in subjects receiving FP. The adjusted difference between groups was 16.6 L/min (95% confidence interval, 1.1 to 32.0 L/min)[20] .

Pavord et al in 2007 conducted a similar study comparing the same treatment groups as we did in this study and found Salmeterol plus ICS led to better symptom control and improvement in lung function than the Montelukast plus ICS combination with

significantly more rescue medication-free nights and greater increases relative to baseline in morning and evening PEF [21] same results seen in our study.

CONCLUSION

In this study, we have shown that the Salmeterol and Montelukast are both effective in improving PEFR (Salmeterol is a better than Montelukast) when given in addition to inhaled corticosteroids. Longer-term studies are required to evaluate the effects of Salmeterol and Montelukast on asthma control and exacerbation rates when administered as second-line therapy in addition to inhaled corticosteroids.

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Original Article

The Protective Role of Taurine in Oxytetracycline - Induced Hepatotoxicity in Albino Rats

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ABSTRACT

Objective: To study the protective effects of taurine in oxytetracycline induced hepatic steatosis in albino rats.
Study Design: Prospective Experimental Study.
Place and Duration of Study: This study was conducted in the Department of Anatomy, Khyber Medical College, Peshawar from July 2011-December 2011.
Materials and Methods: Four groups of male albino rats, each comprising 8 animals, were treated for 21 days as follows: Group A served as control, group B treated with oxytetracycline 120 mg/kg body weight intraperitoneally for three consecutive days, group C treated with oxytetracycline 120mg/kg body weight intraperitoneally for three consecutive days plus taurine 1% solution as their sole source of drinking water for 21 days, and group D treated with taurine 1% solution alone as their sole source of drinking water for 21 days.
The animals were weighed at the start and end of treatment and were sacrificed on 22nd day of start of treatment under deep ether anaesthesia. Blood samples were collected for enzyme study by intracardiac puncture. The livers were removed, washed in normal saline and weighed. They were fixed in 10% formalin and embedded in paraffin. 4 µ thick sections were cut and processed for H & E staining, and were examined microscopically. Statistical analysis of the data was done and results were tabulated.
Results: Groups A (data not shown) and D showed normal results with no significant differences across the groups. The relative liver weights in group B increased significantly (P value <0.05) in comparison with group C and D. The relative liver weights decreased significantly (P value <0.05) in group C and D as compared to group B. There was moderately significant decrease (P value <0.01) in the values of serum hepatic enzymes (SGPT, SGOT, and ALP) in the animals of group C as compared to group B. Histologically the livers of group B animals showed generalized microvesicular steatosis. In group C the fatty change was much less pronounced as compared to group B.
Conclusion: The data show that the hepatic steatosis induced by oxytetracycline can be reversed / attenuated by taurine supplementation for 21 days, in albino rats.
Key Words: Oxytetracycline, Hepatic Steatosis, Taurine.

INTRODUCTION

Oxytetracycline is a broad spectrum antibiotic from the tetracycline group active against many gram-positive and gram-negative bacteria including anaerobes, reckettsiae, chlamydiae, mycoplasmae and protozoa. It is very effective against vibrio cholera, and in combination with other drugs, against Helicobactor Pylori[1].

Tetracyclines in excessive doses are hepatotoxic and are known to induce microvesicular steatosis in liver, the underlying mechanism being deficient ß-oxidation of fatty acids[2,3,4]. In different studies it has been used to create experimental hepatic steatosis in rats[4,5,6]. Hepatic steatosis can progress into steatohepatitis, cirrhosis and hepatocellular carcinoma[7].

Taurine (2-aminoethanesulfonic acid), is a non essential, sulphur containing amino acid found in many tissues and synthesized in the liver as an end product of L-cystein metabolism[8]. The protective role of taurine against tissue injury has been reported by many authors, and the physiological actions attributed to taurine include antioxidation, cell membrane stabilization, neuromodulation, osmoregulation and bile acid conjugation[9, 10, 11].

In rats taurine attenuates the oxidative stress and injury in the urinary bladder and kidney induced by nicotinamide[12]. It reduces the severity of cyclophosphamide - induced hemorrhagic cystitis[13], and ameliorates the hypoxia induced lactic acidosis in brain, liver and heart [14].

In the liver taurine attenuates the injury induced by agents such as cyclosporine A[15], carbon tetrachloride[16], acetaminophen[11], and thioacetamide[17]. Its restorative role in experimentally induced non - alcoholic steatohepatitis has been observed[18]. It has been suggested that taurine reverses hepatic steatosis by enhancing the secretion of hepatic triglycerides and enhances the removal lipid peroxides by increasing the flow of bile[19].

The purpose of this study was to find the histological and biochemical evidence of the hepatotoxicity caused

by overdose of oxytetracycline in rats; and to find if taurine, a sulphur containing amino acid, can offer any protection against such toxicity.

MATERIALS AND METHODS

This study was conducted in the Department of Anatomy, Khyber Medical College, Peshawar. Oxytetracycline (STAR Pak) and taurine (GNC, USA) were purchased from the local market.

Thirty two healthy adult male albino rats 90-120 days of age and 200-300 gram in weight were selected for this study. They were fed on the standard chow and were divided into four groups with eight animals in each group. They were treated for 21 days as follows:

Group A served as control and were injected normal saline 1 cc intraperitoneally for three consecutive days. They were allowed to have free access to drinking water and were kept for 21 days.

Group B animals received injection oxytetracycline 120mg per Kilogram body weight, intraperitoneally for three consecutive days, with free access to drinking water for 21 days. This dose regime of oxytetracycline has been shown to induce fatty change in rat liver [5, 6].

Group C animals received injection oxytetracycline 120mg per Kilogram body weight intraperitoneally for three consecutive days and 1% taurine solution as their sole source of drinking water for 21 days[15,18].

Group D received normal saline 1 cc intraperitoneally for 3 consecutive days, and 1% taurine solution as their sole source of drinking water[15, 18] for 21 days.

On the 22nd day of the start of the treatment, all the animals were sacrificed under deep ether anaesthesia. Blood samples for liver enzymes were collected by heart puncture. Enzyme studies (Serum gltutamic pyruvate transaminase -SGPT, Serum glutamic oxaloacetic transaminase -SGOT, Alkaline phosphatise -ALP) were done to measure the amount of liver injury and for correlation with morphological findings. Livers were removed, washed with normal saline and weighed. They were fixed in 10% formalin and embedded in paraffin. 4µ thick sections were stained with hematoxylin and eosin, and examined microscopically for cell morphology and lobular architecture. Histological diagnosis was made and the results were tabulated.

RESULTS

The findings in all parameters in group A (control, data not shown) and group D (taurine only) were comparable without any significant difference across the groups. The relative liver weight in group B (Oxytetracycline group) increased significantly (P value <0.05) in comparison with group C (Oxytetracycline plus taurine treated) as shown in table 1. The relative liver weights in group C was comparable to group D with an insignificant increase (p value >0.05), but the relative liver weights of animals of group C decreased significantly (P value <0.05) in comparison with group B. These findings are shown in table 2.

Table No.1: Comparison of *Mean relative liver weight (G/100G) between groups B, C and D

Relative liver weight	Group B	Group C	Group D
	4.99±0.30	3.66±0.05	3.58±0.06

*Mean +SEM

Table No.2: Statistical analysis of differences in mean relative liver weight between different groups

Groups	P-Value
B vs C	P<0.05**
B vs D	P<0.05**
C vs D	P>0.05*

Key (P-value): Insignificant* Significant** Moderately Significant***

The mean values (IU/L) of serum glutamic pyruvate transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT) and serum alkaline phosphatise (ALP) levels of albino rats in group B were raised moderately significantly (P value <0.01) as compared to both group C and D, but were decreased moderately significantly (P value <0.01) in group C in comparison with group B (table 3).

Table No.3: Comparison of Mean (Mean±SEM) serum levels of liver enzymes in different groups

Liver Enzymes	Normal value	Group B	Group C	Group D	P Value	
SGPT (ALT)	0-45 IU	107±2.28	67.99±1.89	42.02±0.95	P1	<0.01***
					P2	<0.05**
SGOT (AST)	5-45 IU	124.20±5.83	65.20±3.15	45.31±4.14	P1	<0.01***
					P2	<0.01***
Alk Phosphatase	80-306 IU	376.6±20.02	196.4±22.47	146.6±17.73	P1	<0.01***
					P2	<0.01***

Key (P Value): Insignificant* Significant** Moderately Significant*** P1=Group B versus Group C P2=Group C versus Group D

The livers of animals in groups A and D exhibited normal histological features in the H&E stained sections (Figure-1). In group B there was some distortion of lobular architecture and dilatation of central vein (Figure-2). Swelling of hepatocytes and narrowing of sinusoids were seen. Hepatocytes showed

microvesicular steatosis with plenty of fatty vacuoles. Increase in the number of mononuclear cells in the region of portal triad was observed. Few ballooned hepatocytes were seen in the acinar zone III.

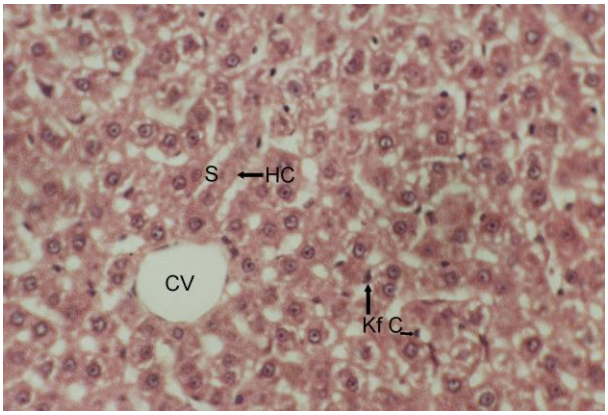

Figure No.1: Photomicrograph of H&E stained section of rat liver (control) (CV- central vein, HC – hepatic cords, S – sinusoids, Kf C- Kupffer cells x400).

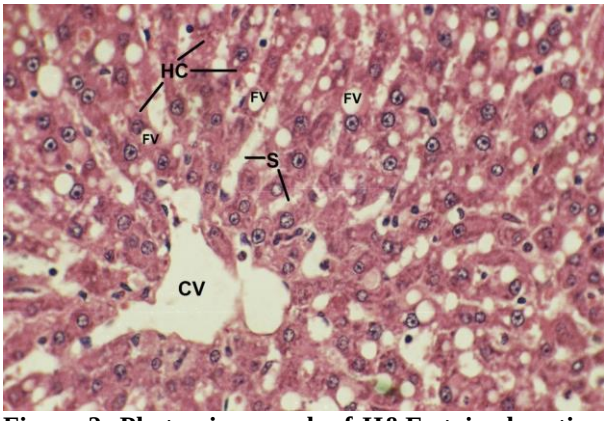

Figure 2: Photomicrograph of H&E stained section of rat liver treated with oxytetracycline (CV- central vein, HC – hepatic cords, FV – fat vacuoles, S – sinusoids, x400).

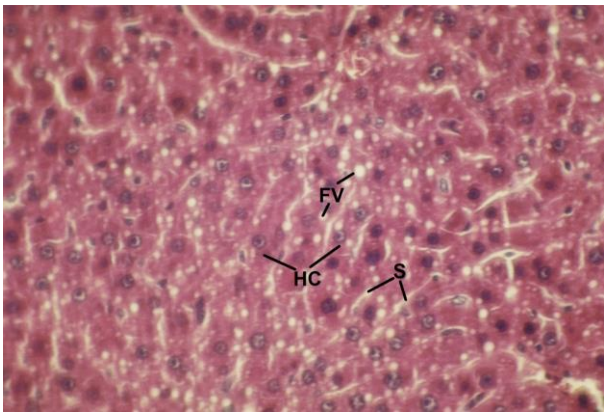

Figure No.3: Photomicrograph of H&E stained section of rat liver treated with oxytetracycline and taurine (HC – hepatic cords, FV – fat vacuoles, S – sinusoids, x400)

In group C (figure 3), the H&E stained sections showed markedly reduced fatty change in comparison to group B. There was marked decrease in the size of fatty vacuoles. The lobular architecture showed little distortion and the arrangement of cells in cords was obvious. The central vein showed less dilatation, and the walls were not distorted.

DISCUSSION

Drug-induced liver diseases are clinicopathologic patterns of liver injury related to drugs; about 900 medications have been identified as potentially hepatotoxic, ranging in severity from mild toxicity to fatal injury[20].

Fatty liver (hepatic steatosis) is a condition in which fat accumulates in liver cells[5]. This condition can progress into steatohepatitis, cirrhosis and hepatocellular carcinoma[7,21].

The protective role of taurine against various hepatotoxic agents has been observed in a number of studies. In a study, Kerai et al (1999)[19], demonstrated for the first time that hepatic steatosis and lipid peroxidation, occurring as a result of chronic alcohol consumption can be reversed by administration of taurine to rats. Waters et al (2001)[11] demonstrated that taurine supplementation attenuates lipid peroxidation and hence the liver injury by acetaminophen, represented by significant decrease in serum hepatic enzymes and reduced hepatocyte apoptosis and necrosis[11].

Keeping in view the different studies wherein the protective effects of taurine against drug-induced hepatotoxicity has been documented, it was considered worthwhile to try to find out if taurine can offer any protection against the oxytetracycline-induced fatty liver in albino tats.

The increase in relative liver weight in oxytetracycline treated (group B) animals was due to hypertrophy of hepatocytes and accumulation of fat as described in the morphological findings. These findings coincide with the study of Huang et al (2011)[22] who noted significant increase in the relative liver weight in rats with fatty liver induced by high fat diet.

The significant decrease in relative weight of liver in group-C animals as compared to the group-B can well be due to the antioxidant effect of taurine administration. In this group there was a reduction in the deposition of fat (fatty change) in liver and a decrease in the swelling of hepatocytes. Chen et al (2006)[18] observed that taurine treatment resulted in a significant decrease in liver weight, liver index and plasma lipid and glucose levels, and oxidative stress in experimentally induced non-alcoholic steatohepatitis in rats.

The serum levels of liver enzymes (SGPT, SGOT, ALP) were found to be significantly (P value < 0.01) raised in both groups B and C as compared to group D.

The damage to hepatocytes increases the permeability of the cell membrane with the resultant leakage of the cytosolic enzymes into the sinusoids and thence into circulation. The increase in serum hepatic enzymes is in agreement with the findings of Helal et al (2011)[5,6]. The authors observed that the administration of oxytetracycline caused highly significant increase in the activity of SGPT and SGOT. The elevated values of serum hepatic enzymes also correlated with the histological findings in the present study.

The significant decrease (P value <0.01) of these enzymes in the group-C animals speak of the membrane protection offered by taurine administration and are in conformity with the findings of Waters et al (2001)[11], Dorgru-Abbasoglu et al (2001)[17], and Jagadeesan and Pillai (2007)[24]. They noted significant decrease in the serum hepatic enzymes, after taurine treatment, in the liver toxicity induced by acetaminophen, thioacetamide, and mercury, respectively.

The morphological examination of H&E stained sections of liver in group-B animals demonstrated microvesicular fatty change and swelling of hepatocytes. Some ballooned hepatocytes were also seen. The findings coincide with a number of studies[4, 5, 6], where oxytetracycline has been used to induce experimental steatosis in rats.

The morphological examination of H&E stained sections of liver in group-C demonstrated that hepatic lobular architecture was comparable to control. The fatty change was of a much lesser degree than in group B and the fat vacuoles were very much reduced in size. These findings can be attributed to the antioxidant, membranoprotective and detoxifying properties of taurine. These findings match with the findings of Chen et al[18], who observed significant improvement in both histological and biochemical parameters in the experimentally induced nonalcoholic steatohepatitis in rats fed on high fat diet. Kerai et al[19] suggested that the taurine-induced reversal of hepatic steatosis in the ethanol treated rats is due to increased triglycerides secretion from the liver. They also suggested that an increased bile flow enhances the removal of peroxides.

CONCLUSION

This study suggests that the attenuation of fatty change by taurine administration is a finding of great importance. As it has been shown that non alcoholic fatty liver disease can progress into steatohepatitis and cirrhosis, dietary supplementation of taurine to patients receiving drugs such as oxytetracyclie can save them from fatty liver disease. Further studies are needed to confirm the findings on this topic.

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CORRIGENDUM

The name of the College / Hospital mentioned with the names of Abid Ali, Assoc. Prof of Anatomy and Iftikharud Din, Assoc. Prof. of Pharmacology appeared at Sr. Nos. 1 & 3 respectively in the article "Protective Role of Taurine on Tamoxifen-induced liver damage in Rats: A Morphological Study", published in the Medical Forum Monthly, in the month of August 2012 at pages 6-9 may be read as Kabir Medical College, Peshawar instead of Khyber Medical College, Peahawar.

Chief Editor.

Original Article

Emergency Obstetrical Hysterectomy (One Yr Review) at Nishtar Hospital Multan

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ABSTRACT

Objective: The objective was to study the cases of obstetrical hysterectomy in one year period in the teaching hospital and to determine incidence, indications and maternal outcome of the patients and suggesting ways to improve outcome.

Study Design: Observational retrospective study.

Place and Duration of Study: This study was conducted at Nishtar Hospital Multan from Feb 2011 to Feb 2012.

Materials and Methods: One year observational retrospective study of 71 consecutive cases of obstetrical hysterectomies performed during study period (i.e. from Feb 2011 to Feb 2012) in Nishtar Hospital Multan were analyzed.

Results: Total number of deliveries conducted during study period were 10406 and 71 obstetrical hysterectomies were undertaken. Frequency of obstetrical hysterectomies being 0.68% and booked cases 39.43%. The most common cause of procedures were morbid adherence of the placenta, uterine atony and uterine rupture. Total hysterectomies were 57.74% and subtotal were 42.25%. Number of maternal deaths were 12.6%. Patients who died were in critical condition with massive blood loss, late arrival , dai handling and non availability of blood beacase of uncooperative attendants and malpractices of doing caesarean sections at peripheries without any indication.These were main factors for maternal mortality.

Conclusion: Emergency obstetrical hysterctomy remains essential life saving procedure especially for high risk cases. Proper antenatal care, early admission in labour ward, proper resuscitation and in time refferal, increase favour of normal deliveries and reduced caesarean section rates will go long way to reduce the incidence of this procedure.

Key Words: Emergency obstetric hysterectomy, postpartum haemorrhage, Caesareans section.

INTRODUCTION

Postpartum hemorrhage according to WHO causes 25% maternal deaths[1]**.** The most common cause of maternal mortality is hemorrhage[2,3]. Obstetrical hysterectomy is a life saving procedure in obstetrical hemorrhage and it is considered "near miss" event[4]. Obstetrical hysterectomy was first attempted 200 years ago as surgical attempt to manage the hemorrhage and infections[5]. In the last few decades, uncontroled hemorrhage has become a major indicative factor. Causes such as uterine atony, placenta previa, and ruptured uterus vary from area to area and influenced by standards of practice and quality of antanatal care[6,7]**.** Obstetrical hysterectomy is more common in developing countries like ours because of high incidence of unbooked and improperly supervised deliveries outside the hospital. One of the main indications of obstetrical hysterectomies is high incidence of caesarean sections. Sometimes patients present delayed in hospitals which makes obstetrical hysterectomies to be associated with high maternofetal morbidity and mortality[8,9]. The purpose of the present study was to determine frequency, indications and maternal outcome of obstetrical hysterectomies and suggestion of some ways to improve the outcome.

MATERIALS AND METHODS

This study was conducted in the Nishtar Hospital Multan over a period of one year i.e. form February 2011 to February 2012. Patients were identified from all three units. Record was taken from labour ward registers and operation registers. Results analysed were according to age , parity, social status, previous history of caesarean section, mode of delivery, indications for obstetrical hysterctomy and maternal morbidity and mortality. All data were evaluated and analysed by using SPSS 10.

RESULTS

During one year period 10406 deliveries including 4997 caesarean sections and 5409 vaginal deliveries were conducted. Frequency of obstetrical hysterectomy was 0.68%. After caesarean section frequency of obstetrical hysterectomy was 1.42% and after vaginal deliveries frequency of hysterectomies was found to be 1.31%. Majority of the patients (43.66%) fall in 30-35 years age group. 36.61% of th patients were multiparous with parity >5 (Table 1). Out of 71 patients 37 patients were delivered by caesarean section and 34 (47.88%) patients were delivered vaginaly. Highest rate was found in unbooked cases (43 patients) and it was 60.56%. Booking status matters alot in incidence of obstetrical hysterectomies (Table 2). Morbid adherence of placenta

was most common cause of obstetrical hysterectomies (25.35%) and incidence of morbid adherence was increased because of increase in the rate of caesarean sections.

Table No.1: Demographic features of the patients undergoing obstetrical hysterectomy (n=71)

Age(yrs)	Number	Percentage
15-25	5	7.04%
26-30	18	25.35%
30-35	31	43.66%
>35	17	23.94%
Parity		
0	6	8.45%
1-2	16	22.53%
3-4	23	32.39%
>5	26	36.61%
Booking status		
Booked	28	39.43%
Unbooked	43	60.56%

Table No.2: Number of previous caesarean deliveries, mode of delivery and type of obstetrical hysterectomy (n=71)

Number of previous caesarean deliveries	Number	Percentage
1	18	25.35%
2	16	22.53%
3	22	30.98%
4	15	21.12%
Mode of delivery		
Vaginal delivery	34	47.88%
Caesarean delivery	37	52.11%
Type of hysterectomy		
Total	41	57.74%
Subtotal	30	42.25%

Table No.3: Causes of haemorrhage in women undergoing emergency obstetrical hysterectomy. (n=71)

Causes	Number	Percentage
Morbid adherence of placenta	18	25.35%
Placenta previa	17	23.94%
Uterine atony	13	18.30%
Rupture uterus	12	16.90%
Abruption	4	5.63%
Other causes	7	9.85%

Out of 71 cases of obstetrical hysterectomies (17) 23.94% were due to placenta previa, 13 cases (18.3%) were due to uterine atony, 8 cases were after vaginal deliveries. Five cases of uterine atony were after caesarean sections. Two interesting cases were seen during study: One patient was operated due to previous 1 caesarean section. She was also a patient of chronic myeloid leukemia. She bled a lot on the operation table. Her obstetrical hysterectomy was done due to uterine atony but she didn't survive. She died after one day due to underlying qualitative platelet defect. Second patient was with fibroid uterus who also bled heavily on operation table but survived after obstetrical hysterectomy. Complications were rare in the study because most of the hysterectomies were done by the consultants. Complications seen during the study were anemia, sepsis, 21 cases were reported due to disturbed clotting profile. Maternal mortality Rate was 11.26%. 8 patients died due to severe hemorrhage. So the well known causes of obstetrical hysterectomies were morbid adherence and placenta previa.

DISCUSSION

The frequency of obstetrical hysterectomy in the present study was 0.68%. It is very high comparative to study done in Bahawalpur. Reported rate of emergency obstetrical hysterectomies in developed countries is very low(0.4/1000-0.2/1000) deliveries[10].

Difference in the incidence may be explained by unbooked cases for antenatal care and mostly reffered patients with detrimental health conditions. Majority of the patients(43.6%) were 30-35 years old and were multiparous. It is similar to the study of Berclay and Ahmad[11-12].

The most frequent indication for emergency obstetrical hysterectomy(EOH) in the present study was morbid adherence of placenta i.e. 25.35% and 23.94% hysterctomies were due to placenta previa. Almost similar results were generated by other studies done in different hospitals of Pakistan1[13-16].

Abnormal placentation has emerged as an important etiological factor since the last two decades and reported worldwide as well as in the third world countries. Well known risk factors are morbid adherence of placenta, placenta previa and previous caesarean births[10].

Obsterical hysterctomy is a life saving procedure for morbid adherence of placenta. Subtotal hysterectomies were done during studies. Although it is superior due to low degree of hemorrhage and speedy procedure but it has certain problems such as cyclical discharge, spotting and cervical carcinoma due to cervical stump remanent. It is not effective in placenta accreta and increta because of excessive bleeding from uterine artery but in our study it was probably surgeons's decision regarding situation whether to go for total or subtotal hysterectomy.

Our study also confirm the previous observation that obstetrical hysterectomy is associated with perinatal mortality and morbidity and post operative complications were anemia and sepsis[8,9].

Maternal deaths in this study were mostly in unbooked and refer cases because of their delayed arrival and lack of antenatal care and in most of the patients death occurred due to hypovolemic shock. Maternal mortality

in our study was 12.6 which is very high comparatively to developed countries[9].

CONCLUSION

EOH helps in reducing maternal mortality rate. High risk patients should receive proper antenatal care after booking. Vginal deliveries should be conducted by trained persons and caesarean sections should be done by qualified persons. By this we can reduce the caesarean section rate. Increase in maternal mortality is due to malpractice by mobile surgeons and unqualified persons in the obstetrics. They are doing unnecessary caesarean sections in peripheries and this practice should be snubbed.

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Original Article

Students' Perception on Acquisition of Basic Clinical Skills

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ABSTRACT

Objective: To analyze the perception of medical students towards the basic clinical skills workshops conducted during their final year in a Pakistani medical college.

Study Design: Cross sectional survey

Place and Duration of Study: This study was conducted at the Department of Medical Education, Wah Medical College, Wah Cantt, Rawalpindi during February 2012.

Materials and Methods: Fifty final year students were divided into five batches for the workshop. Each batch rotated through five stations with allocated basic clinical skills. The students practiced the skills on dummies and manikins after demonstrations and instructions by the facilitators. A predesigned likert scale questionnaire with thirteen close ended questions with five options each was filled by students anonymously at the end of the workshop. Frequencies of answers were calculated.

Results: Majority of students gave positive response about the conduct of the workshop and quality of facilitation. They agreed on having an improvement in their level of clinical competence post workshop. Majority suggested that the workshop should be conducted at the beginning of the final year. Although 70% thought that the skills included were relevant, however, almost a quarter remained undecided on the matter.

Conclusion: The students appreciated the importance, conduct and arrangements of the workshop, and quality of facilitation. Kinesthetic learning based workshops on basic clinical skills should be a regular practice and must be conducted at the beginning of final year class of undergraduate medical education.

Key Words: Students. Clinical competence. Education. Undergraduate.

INTRODUCTION

Background theoretical knowledge and basic clinical skills go hand in hand and form two equally important foundation pillars of medical education and an undergraduate trainee should acquire both[1]. In "traditionally oriented" medical schools, the students are usually expected to learn clinical skills by observing the clinicians, by interviewing and examining patients, and finally presenting findings for discussion [2]. Before graduating, the students are exposed to basic clinical skills unequally. To prepare medical students for their experience and postgraduate training, basic clinical skills should be addressed specifically in the curriculum[3].

Surgical skills laboratories have become an increasingly important component of technical skills training for students and learners entering surgical fields[4]. They have emerged in response to observations that completion of an accelerated skills course results in comparable levels of student performance postcourse across a variety of preclinical backgrounds and clerkship experiences [5].Graduating class students can provide valuable feedback on what they have learned in the existing system[6].

The current project was designed to analyze the perception of medical students towards the clinical skills workshops conducted during their final year in a Pakistani medical college.

MATERIALS AND METHODS

This cross sectional survey was carried out with prior permission from the college authorities in which fifty final year students were included after informed consent. Students were divided into five batches for the activity. Five stations were established in different rooms in the skills lab and were allocated skills to be practiced by the students. All batches were rotated through each station where they were demonstrated and facilitated by clinicians experienced in relevant fields with an objective to let the students learn and practice basic clinical skills Each batch attended the workshop for a duration of two days (12 hours). The students were given a chance of hands on practice of following skills on dummies and manikins after demonstrations and instructions by the facilitators:

- Station 1 was allocated to basic surgical skills including aseptic measures, gowning and gloving, suturing and knotting, intramuscular injections, fine needle aspiration cytology (FNAC) and true cut biopsy.
- Skills learnt at station 2 were male and female catheterization.
- Station 3 was for various types of bandages including plaster cast.
- Station 4 was allocated for airway management including emergency airway management, endotracheal intubation and tracheostomy

- Students learnt and practiced obstetric skills like normal vaginal delivery, breech delivery, instrumental delivery (outlet forceps and vacuum extraction) and episiotomy at station 5.

A predesigned likert scale questionnaire having thirteen close ended questions with five options (on a scale of five, i.e., from strongly agree to strongly disagree) each was given to students at the end of the workshop. The students were asked to anonymously fill in their responses honestly and without any teacher or peer pressure because their answers would have an impact on future policy regarding improvement of basic clinical skills in graduating doctors.

The questions of the questionnaire were grouped into four categories. Category I (question 1-7) dealt with arrangement and conduct of the workshop. Category II (question 8-10) was related to competence of facilitators and quality of facilitation. Category III (question 11 &12) was about outcome of the workshop. Category IV (question 13 & 14) had queries, the responses to which might help in defining future strategy and policy.

The results were entered into SPSS version 19 and frequencies of answers calculated.

RESULTS

All students attended the workshop and rotated through all the stations. They learnt and then practiced the clinical skills enthusiastically and generally appreciated the kinesthetic mode of learning with the help of dummies and manikins. When asked to fill the questionnaire, all fifty students replied promptly. In general they gave positive response regarding the conduct and outcome of the workshop and the quality of facilitation. The specific pattern of their perception about the basic clinical skills workshop as showed through the feedback proformas they filled is shown in Table-I.

Table No.1: Student's responses (in percentage) to the questionnaire on basic clinical skills workshop

S. No.	Question Category	Question	Percentage of responses				
			SA	A	UD	DA	SDA
1	I	Were you informed about the schedule in time?	40%	46%	10%	2%	2%
2		Were you given enough time on each station?	38%	42%	4%	12%	0
3		Was rotation among different stations smooth?	44%	40%	4%	8%	4%
4		Were you given enough chance of hands on practical experience?	26%	50%	12%	0	2%
5		Did you find contents of workshop useful?	58%	42%	0	0	0
6		Did you like the arrangements of workshop?	38%	58%	2%	0	2%
7		Would you like to have similar workshops in future?	58%	42%	0	0	0
8	II	Were facilitators able to hold your interest?	48%	46%	4%	2%	0
9		Were relevant examples discussed?	26%	66%	4%	2%	2%
10		Would you like to attend workshops in future facilitated by these facilitators?	48%	46%	2%	4%	0
11	III	Were the objectives of workshop achieved?	40%	52%	4%	4%	0
12		Did the workshop improve your clinical skills	84%	16%	0	0	0
13	IV	Should these workshops be conducted in the beginning of academic session of Final year?	48%	44%	8%	0	0
14		Were all the skills included in the workshop important to be learnt at undergraduate level	20%	50%	24%	2%	4%

SA = Strongly agree A = Agree UD = Undecided
DA = Disagree SDA = Strongly disagree

DISCUSSION

The necessity of learning skills through "integrated skills training" at an undergraduate level has been supported by several studies. This training is a more effective method of learning basic clinical skills, compared to traditional skill training and reinforcement in 12 month clinical internships [7]. Skills instruction for senior students entering surgical internship results in a higher perception of preparedness and improved skills performance [8].

The skills included in the workshop under discussion encompass several surgical disciplines. The skills included (general surgery, obstetrics, airway management, orthopedics and urology) form a part of suggested curriculum of practical clinical skills in undergraduate medical education [9]. The fact that the surgical resident must have thorough cognitive understanding of the process as well as technical mastery of non surgical airway management [10] further justifies inclusion of these skills in the workshop. Acquisition of core obstetric skills during student life would help the graduating doctors and interns in future.

The same is in practice in United Arab Emirates University [11]. Training on catheterization was included in this workshop which during student life is not a routine practice. Such procedure carried out by untrained hands especially in male patients can lead to severe complications and injury and thus merits inclusion in curriculum [12]. We endorse this suggestion.

Use of manikins and dummies for the workshop enabled to students to use their tactile senses amply thus enhancing learning process. This mode of hands on kinesthetic learning is generally enjoyed and preferred by the students [13].

The results of the category-I questions show that the students were generally satisfied with the conduct and arrangement of the workshop. However, the indecision and disagreement showed by students in question 1 (10 and 4% respectively) might indicate a lack of interest by few students. Better motivation, planning and counseling in future might solve this problem. The indecision and disagreement by few students regarding enough time on each station, smooth rotation among stations and enough chance of hands on practice might reflect on the length of the workshop which could be increased from two days (12 hours) in order to improve the quality of clinical skills learnt by the graduating class as young medical graduates undertaking their housejob are naturally expected to demonstrate reasonable competence in basic practical skills. Lack of the same may be a source of anxiety to the doctor and a potential hazard to the patient [14]. A 100% agreement shown by the students on want of attending the similar workshops in future (question 7) reflect upon their desire to avoid the same dilemma.

The category-II dealt with quality of facilitation, wherein majority of students either strongly agreed or just agreed that the facilitators were able to hold their attention, discussed relevant examples and would be suitable for facilitating future workshops. This endorses the effectiveness of teaching in the learning process. Moreover as each batch comprised of ten students only, this small size might have enhanced the student facilitator interaction thus rendering the workshop effective through small group teaching (SGT) which creates the perfect environment for learning and discussion, without the need for didactic teaching and leads to improvements in the quality of teaching and learning [15]. SGT is considered an effective methodology in relevance to clinical teaching [16].

The category-III questions related to the outcome of the workshop. Majority of the students were of the opinion that the objectives of the workshop were achieved while only 4% each remained undecided and disagreed. In response to the next question where students were asked whether this training improved their clinical skills, an absolute agreement was achieved. These results further endorse the effectiveness of the workshop. This is in accordance with a previous study where the integrated curriculum which included clinical and technical skills did improve confidence and would enhance baseline abilities for clinical internship [17]. As in a traditional setting, medical students' first experience in the operating theatre often takes place during their electives and is therefore separated from the university's medical curriculum [18], learning of these skills during student life is important and might prove to be beneficial for the graduating doctors as well as the students they would treat during their house job.

As category-IV questions dealt with students' perception regarding contents and timing of the workshop their response might have an effect on future planning. In opinion of majority of students the workshop should be conducted at the beginning of the final year MBBS class. This consensus might be based on the fact that the students would have a whole academic year ahead of them before graduation and would get chance of practicing and consolidating these skills during this time.

As far as contents of the workshop were concerned, a mixed pattern of response was observed. Although half of the students agreed that all skills practiced should be learnt at undergraduate level, but a noticeable 24% remained undecided and 4% disagreed as well. This might reflect upon the inexperience of students. There are gaps between what is required and what exists at present. Inputs of all stakeholders are needed to identify these gaps. Being important stakeholders feedback from medical students regarding the deficiencies they faced plays an important role in developing and revising training programmes [19]. Although an integrative medical curriculum with a student-centered strategy of education interests most medical students[20], several other factors like teacher's perception, cost and time needed for training, needs of the community and patient's expectations must be kept in mind while revising policies.

CONCLUSION

The students appreciated the importance, conduct and arrangements of the workshop, and quality of facilitation. In light of their response, it is suggested that kinesthetic learning based workshops on basic clinical skills should be a regular practice and must be conducted at the beginning of final year class.

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Original Article

A study on Correlation of Portal Vein Diameter and Splenic size with Gastro-Oesophageal Varices in Cirrhotic Patients

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ABSTRACT

Objective: This study was conducted to find out the correlation of portal vein diameter and splenic size with gastro-oesophageal varices in diagnosed cases of cirrhosis of liver.

Study Design: A cross-sectional study.

Place and Duration of Study: This study was conducted at the Liver Clinic, Ghulam Mohammad Mahar Medical College Hospital, Sukkur from January 2011 to December 2011.

Materials and Methods: One hundred sixty four patients with cirrhosis of liver were selected for the study. Ultrasonography was performed in all cases to note the portal vein diameter and splenic size. Oesophagoa-gastr-duodenoscopy was done to detect presence of varices with grades.

Results: In the study it was found that fourty patients had no varices (grade O) and the rest one hundred twenty four patients developed varices. Average portal vein diameter of patients without gastro-oesophageal varices was 11.545 ± 1.514 mm and of patients with varices 13.998 ± 1.123 mm. The difference was statistically significant ($p < 0.05$). Average spleen size of patients without gastro-oesophageal was 13.129 ± 1.102 cm and with varices 14.997 ± 1.992 cm. This variation was also statistically significant ($p < 0.05$). There was a positive correlation between grading of oesophageal varices and portal vein diameter ($r = 0.707$; $p < 0.001$) and between splenic size with oesophageal grades ($r = 0.467$; $p < 0.001$).

Conclusion: The study portrays that with increase in portal vein diameter and splenic size, the chance of formation of gastro-oesophageal varices also increases and a positive correlation exists. Thus, measurement of portal vein diameter and splenic size by ultrasonography is a non-invasive predictive indicator of the development of gastro-oesophageal varices in cirrhosis of liver.

Key Words: Cirrhosis of liver, portal vein diameter, gastro-oesophageal varices.

INTRODUCTION

Portal hypertension is the most common complication and also one of the important causes of death in chronic liver disease. Increased resistance to portal blood flow due to alteration of the hepatic architecture leads to dilatation of portal vein, splenomegaly; and formation of oesophageal and gastric varices, variceal haemorrhage, ascites, hypersplensim, encephalopathy, etc.

In cirrhosis, increased intrahepatic vascular resistance is thought to be located mainly in the hepatic sinusoids[1]. Recent studies have demonstrated that in addition to the increased resistance caused by the morphologic changes of chronic liver diseases, a dynamic component of increased resistance (resulting from the active contraction of vascular smooth muscle cells, myofibroblasts and hepatic stellate cells) is also present[2].

Portal hypertension leads to dilatation of portal vein, splenomegaly, and formation of portal systemic collaterals at different sites. The portal system and the systemic venous circulation are connected at several locations[3]. Gastro-oesophageal collaterals develop from connections between short gastric and coronary veins and the oesophageal, azygos, and intercostals veins; the result is the formation of oesophageal and gastric varices. Collaterals develop in areas where anatomic connections exist between the portal venous and systemic circulation. These are vascular channels that are functionally closed in normal conditions but become dilated in portal hypertension as a consequence of increased intravascular pressure and blood flow. Theses gastro-oesophageal varices are responsible for the main complications of portal hypertension and massive upper Gl bleeding **Error! Bookmark not defined.**.

It is a well-known fact that portal vein diameter is usually increased in cirrhosis of liver with portal hypertension and spleen is also enlarged in size. A few previously reported studies showed that there was a definite correlation between portal vein diameter and presence of gastro-esophageal varices. Sarwar et al reported that patients with portal vein diameter more than 11 mm are more likely to have oesophageal varices[4]. Another study by Dib et al showed that oescophageal varices developed when the portal vein diameter exceeded 13 mm[5]. On the other hand, Li et al found that haemodynamics of the portal vein were unrelated to the degree of endosopic abnormalities in cirrhosis of liver[6].

Oesophago-gastro-duodenoscopy is required to detect the gastro-oesophageal varices. But the procedure is invasive, painful to the patient, and is not available in all centres. Whereas portal vein diameter and splenic size can be measured by an easily available, painless and non invasive method likes ultasonography (USG). The study was done to find out the correlation between the portal vein diameter and splenic size with the development of gastro-oesophageal varices.

MATERIALS AND METHODS

Total one hundred & sixty four patients attending the Liver Clinic of Ghulam Mohammad Mahar Medical College Hospital, Sukkur, were selected for study, from January 2011 to December 2011.

Either previously diagnosed or newly diagnosed cases with cirrhosis of liver were taken into account. The following cases with portal hypertension were excluded from the study:

1. Cirrhosis of liver with previous history of gastrointestinal bleeding.
2. Cirrhosis of liver with portal vein thrombosis.
3. Other cases with portal hypertension, i.e. non cirrhotic portal fibrosis, Budd-Chairi syndrome, extra-hepatic portal venous obstruction.

Salient features in the history included occupation, alcohol intake, appetite, jaundice, swelling of abdomen, disorientation, unconsciousness, etc. Patients with history of haematemesis and malena were not taken into account. A through general survey was done to assess pallor, cyanosis, jaundice, oedema engorged neck veins, palpable neck glands, pulse, and blood pressure. The gastrointestinal system was clinically examined with focus on the size of the spleen, liver span, ascetic fluid, fluid thrill, and presence of any venous prominences over the abdomen. The investigations like routine blood including platelet count, liver function tests (LFTs), prothrombin time including INR were recorded from reports of previously diagnosed cirrhotic patients or performed for the newly diagnosed cases. Ultrasonography was performed in all cases and diameter of portal vein in mm and spleen size in cm was recorded. Upper gastrointestinal endoscopy was done to locate the varices.

Spleen size measurement: Spleen size was measured ultrasono-graphically by placing the patient in supine position, using 2-5 MHz curvilinear transducer in the coronal plane of section posteriorly in one of the lower left intercostals spaces. The patients were examined in various degrees of inspiration to maximize the window to the spleen. The plane of section was then swept posteriorly and anteriorly to view the entire volume of spleen. The average adult spleen measurers 12 cm in length. The spleen parenchyma is extremely homogeneous and it has a uniform mid-to-low echogenicity. When the spleen enlarges, it can be more echogenic. Splenomegally commonly accompanies portal hypertension and is a noteworthy finding[7,8]. A maximum cephalo-caudal measurement exceeding 13 cm indicates enlargement with a high degree of reliability[9].

Portal vein diameter measurement: The portal venous supply for the left lobe can be visualized using an oblique, cranially angled sub-xiphoid view (recurrent subcostal oblique projection). The main and right portal veins are best seen in a sagittal or oblique sagittal plane[10]. In normal individuals, the portal vein diameter does not exceed 13 mm in quite respiration, measured where the portal vein crosses anterior to the inferior vena cava[11,12,13,14]. This assessment is usually conducted with ultrasound views along the long axis of the portal vein. Respiration and patient position greatly affect the size of the portal vein and its tributaries; therefore, diagnostic measurements must be standardized by examining the patient in the supine position and in a state of quite respiration. We followed the above method to measure portal vein diameter.

Upper gastrointestinal endoscopy: Endoscopy was performed in all selected cases to look for gastro-oesophageal varices and other associated signs of portal hypertension like red weal marks, cherry red spots. Grading of oesophageal varices was done according to Paqet[15].

Grade I- small varices without luminal prolapsed;
Grade II – moderate-sized varices showing luminal prolapse with minimal obscuring of the gastro-oesophageal junction;
Grade III – large varices showing luminal prolapsed substantially obscuring the gastro-eosophageal junction;
Grade IV- very large varices completely obscuring the gastro-oesophageal junction.

Statistical analysis: Results were analyzed by statistical methods like average, standard deviation, student's "t" test and Pearson's correlation co-efficient.

RESULTS

A total of 164 patients with cirrhosis of liver were selected for the study. Among them, 112 were males (68%), the remaining were females (32%). Median age of the study group was 40 years; range 19-64 years.

In the study it has been found that 40 patients out of 164 had not developed gastro-oesophageal varices. Among the rest of the 124 patients, 38 had low-grade varices (grade 1 and II) and 86 patients had high-grade varices (grade III and IV).

Average serum albumin level of these 164 patients was 2.76 ± 0.585 gm/dl and globulin 3.898 $\pm$ 0.792 gm/dl. And average serum albumin level in variceal and non-variceal group was 2.52 ± 0.421 gm/dl and 3.484 $\pm$ 0.402 gm/dl respectively. Average platelet counts were

1,11,000 ± 2840 and 215,000 ± 5500/cu mm of blood in the same groups respectively.

Average portal vein diameter (PVD) of patients without gastro-oesophageal varices was 11.545 ± 1.514 mm and of patients with varices 13.998 ± 1.123 mm. this difference is statistically significant (t = 2.27517E-11; $p < 0.05$).

Average spleen size of patients without varices was 13.129 ± 1.102 cm and with varices 14.997 ± 1.922 cm. And this variation is also statistically significant (t = 9.12963E-05; $p < 0.001$).

Hence it had been found that gastro-oesophageal varices developed when PV diameter was > 11.5 mm and spleen size was > 13.1 cm.

It had also been found that there was a positive correlation between grading of oesophageal varices and portal vein diameter ($r = 0.707$) and it is statistically significant ($p < 0.001$). That means when portal vein diameter increases, oesophageal varix also increases in size.

There was also a positive correlation between splenic size and oesophageal grades ($r = 0.467$; $p < 0.001$). So, oesophageal varix also depends on spleen size. (Table I)

Table No.I: Showing different values in the variceal and non-variceal group.

Parameters	Variceal group (n=62)	Non-variceal group (n=20)	P value
Average portal vein diameter (mm)	13.998 ± 1.123	11.545 ± 1.514	p < 0.05
Average spleen size (cm)	14.997 ± 1.922	13.129 ± 1.102	p < 0.001
Average platelet count (per/ cu mm)	1,11,000 ± 2,840	2,15,000 ± 5,500	p > 0.10
Average albumin level (gm/dl)	2.52 ± 0.421 gm/dl	3.484 ± 0.402	p > 0.10

DISCUSSION

A total of 164 patients were selected in our study: males were 112 and females were 52. Median age of the study population was 40 years, range being 19 to 64 years. In another Indian study by Sharma and Agggarwal, proportion of male patients (87 males out of 101 patients) was slightly higher than our study, but median age was more or less similar (median age 45 years) to ours[16].

Average serum albumin and platelet count was 2.52 gm/ dl and 1,11,000/cu mm of blood respectively in the variceal group. Though the differences of these values with those of the non-variceal group were not statistically significant, it had been found that these values corroborated to other studies. In the study of Thomopoulos et al the patients with the varies had the platelet count less than 1,18,000/ cu mm[17]. Serum albumin level was less than 2.95 gm/ dl in the variceal group as shown by the Sarwar et al **Error! Bookmark not defined.**.

Upper Gl Endoscopy of the study population revealed that a total of 124 patients had developed gastro-oesophageal varices and 40 patients were yet to develop these. Ultrasonography showed that average portal vein diameter (PVD) of the patients with gastro-oesophageal varices (GEV) was 13.998 ± 1.123 mm and without gastroesophageal varices (GEV-0) was 11.545 ± 1.514 mm. This difference was statistically significant ($p < 0.05$).

Radiologically, average spleen size of the patients with GEV was 14.997 ± 1.922 cm and spleen size in the GEV-0 group was 13.129 ± 1.102 cm, and the difference was highly significant ($p < 0.001$).

So, it can be concluded that gastro-oesophageal varices developed in cirrhotic patients with portal vein diameter more than 11.545 mm and larger than 13.1 cm spleen size.

These observations were more or less similar to other studies. In the study by Prihatini et al, portal vein diameter 11.5 mm and spleen size of 10.3 cm were predictive factors for oesophageal varices in liver cirrhosis[18]. Here, spleen size was smaller than our study, but portal vein diameter was corroborative to ours. Portal vein diameter for development of gastro-oesophageal varices was also nearer to the Sarwar et al study (portal vein 11 mm) **Error! Bookmark not defined.**. Thomopoulos et al showed that the majority of patients with gastro-oesophageal varices had spleen size more than 13.5 cm which was nearly similar to ours **Error! Bookmark not defined.**.

In our study, it was also found that in patients with gastro-oesophageal varices, grading of varices directly correlated with portal vein diameter and spleen size ($r=0.707$ and 0.467 respectively). That implied, when portal vein diameter and spleen size increased, gastro-oesophageal varices also transformed to higher grades. Average portal vein diameter and spleen size in higher grade varices were 14.43 ± 0.86 mm and 15.36 ± 2.14 cm. In a study by Schepis et al portal vein diameter 13 mm was associated with higher grade varices[19]. Sharma and Aggarwal had noted that a clinically palpable spleen was associated with high grade varices; however, they did not measure the splenic size radiologically.

Hence, it can be concluded that gastro-oesophageal varices in cirrhotic patients (without previous history of gastrointestinal bleeding), directly correlates with portal vein diameter and splenic size.

CONCLUSION

We can conclude that in cirrhosis of liver with portal hypertension, without previous history of upper gastrointestinal bleeding.

- Portal vein diameter increases with development of varices.
- Spleen size increases with formation of gastroesophageal varices.
- There is a positive correlation between portal vein diameter (r=0.707) and spleen size (r=0.467) with gastro-oesophageal varices which was the aim of our study.

Hence, measurement of portal vein diameter and splenic size by ultrasonography is a non-invasive predictive indicator of the development of gastro-oesophageal varices in cirrhosis of liver.

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Original Article

To Correlate the Serum Levels of Adiponectin with Systolic and Diastolic Blood Pressure in Hypertensive's and Healthy Individuals

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ABSTRACT

Background: To correlate the serum levels of adiponectin with systolic and diastolic blood pressure in hypertensive's and healthy individuals.

Study Design: Cross-sectional, case control study.

Place and Duration of study: This study was conducted at the Department of Physiology BMSI JPMC in colaboration with Abassi Shaheed hospital karachi from Dec 2008 to June 2009.

Materials and Methods: This study included total 100 subjects, 50 subjects with known case of hypertension and 50 normal healthy age and gender matched controls

Results: Adiponectin serum concentration was found lower in coronary artery disease patients when compared with control subjects. (7.10) verses (11.98).

Conclusion: This suggests that higher levels of serum adiponectin is protective against the development of hypertension.

Key Words: Coronary heart disease, Adiponectin, Case Control study.

INTRODUCTION

Hypertension is a major risk factor for cardiovascular disease, it is the leading cause of morbidity and mortality worldwide. In developed countries, hypertension ranks as the top contributing factor for mortality and third in causing disability-adjusted life years.[1] Hypertension is a polygenic and complex disease with rising prevalence. More than 25% of the adult population is affected by hypertension, and two thirds of those individuals reside in developing countries.[2] With the present trends, the prevalence of hypertension is predicted to increase to 30%, or ≈1.5 billion people, on the globe in the next 20 years.[3]

Hypertension causes injury to the endothelium leading to endothelial dysfunction which may develop atherosclerotic changes[4]. In hypertension the concentration of angiotensin II, the principal product of renin angiotensin system are often elevated, angiotensin is the potent vasoconstrictor. In addition to cause hypertension it contributes to atherogenesis by stimulating the growth of smooth muscle[5].

Adiponectin is the most abundant known secreted factor produced by adipocytes, was originally identified by four independent groups in mid 1990´s, in both mice and human[6]. The adipose tissue has traditionally been regarded as a silent organ that passively stores excess energy. However the recent evidence suggests that adipose tissue especially visceral fat is to be considered as an endocrine organ, directly involved in the pathophysiology of metabolic syndrome and cardiovascular diseases.[7] As the biologically active molecule, adiponectin appears to protect the vasculature at each stage of atherogenesis. First stage of atherosclerosis involves endothelial dysfunction in response to the traditional cardiovascular risk factor, such as hypertension[13].

MATERIALS AND METHODS

A total of 100 subjects were recruited in the study, and divided into 2 groups:-

A group consisting of 50 normal healthy control subjects with no history of hypertension. The other group included 50 subjects which were known cases of hypertension. Normal and diseased subjects were from both sexes of age ranging from 40 years to 80 years.

A written consent was taken from all the participants of the study six ml of the venous blood was drawn from the subjects under all aseptic procedures. The blood sample was transferred to the gel tube. After 30 min to 60 min the blood was centrifuged for 10 minutes at the speed of 3000 rounds per minutes (rpm). Serum was separated to dry clean aliquot tube and stored at -20 degree centigrade. Before analyzing, the samples were thawed and allowed to attain the room temperature. Serum adiponectin was measured by enzyme linked immunosorbant assay, using the kit provided by Biosource France.

RESULTS

Table 1 shows the comparison of mean ages among 2 groups i.e. normal healthy control group and the group having diagnosed cases of hypertension. Mean ages of 2 groups were comparable on average, as the samples were collected from the matched cases. Table 1 also

shows the comparison of height among the 2 groups i.e. between cases and control subjects; non significant changes were recorded in the height among the 2 groups. On comparison of weight among the 2 groups i.e. between cases and the control subjects, weight in group B was significantly increased as compared to control subjects (73.5±0.5)and (66.0±0.10) respectively ($p < 0.001$) . Independent t-test was applied.

Table 2 shows comparison of systolic and diastolic blood pressure among hypertensive subject and control group. The systolic blood pressure shows statistically significant increase in hypertensive patients (170.1± 19.1) than the systolic blood pressure in control group (146.7±20.9). Similarly diastolic blood pressure shows statistically increased significance ($p < 0.001$) in hypertensive patients (95.7±12.6) than in control subjects (82.8±13.2).

Table 3 shows comparison between serum adiponectin concentrations in hypertension subject with that of control. The adiponectin concentration shows significant ($p < 0.001$) decrease in hypertensive patients (7.10±1.40) than in controls (11.98±0.59).

Table No.1: Comparisons of age, height and weight in control &hypertensive groups

Variables	Group A	Group-B
Age(yrs)	Control	hypertensive
	Mean±SEM	Mean ± SEM
Height (meter)	55.18 ± 1.12	54.17 ± 2.24
	1.60 ± 0.02	1.56 ± 0.02
Weight (kg)	66.0 ± 0.10	73.5 ± 0.19**

**P < 0.001highly significant when compared to controls

Table No.2: Comparison of systolic and diastolic blood pressure in hypertensive patients (group B) with normal healthy (Groups).

Variables	Group A	Group B
SBP (mmHg)	Control	Hypertensive
	Mean ± SEM	Mean ±SEM
	146.7 ± 20.9	170.1 ± 19.1**
DBP(mmHg)	82.8 ± 13.2	95.7 ± 12.6**

**P < 0.001 highly significant when compared to controls.

Table No.3: Comparison of serum adiponectin concentration in normal control group a with hypertensive subjects Group B

Variables	Group A	Group B
Serum Adiponectin (µgm/ml)	Control	Hypertensive's
	Mean±SEM	Mean±SEM
	11.98±0.579	7.10±1.40**

**P < 0.001 highly significant when compared to controls

Table 4 shows correlation coefficient (r) among serum adiponectin with systolic and diastolic blood pressure, among the two groups. Highly significant negative correlation was found between control group and hypertensive patients (r = 0.55 and r = -0.76). Similarly significant negative correlation was found between diastolic blood pressures among controls and hypertensive (r = 0.65 and r = - 0.86).

Table No.4: Correlation of serum adiponectin concentration with systolic and diastolic blood pressure in Group A & B

Variables	Group A	Group B
	Serum adiponectin	Serum adiponectin
SBP mmHg	r = -0.54	r = -0.76**
DBP mmHg	r = -0.65	r = -0.86**

**Correlation is significant at the 0.01 level.

DISCUSSION

Hypertensive subjects are always at high risk of developing coronary heart disease, endothelial dysfunction caused by hypertension leads to the inflammatory process which may cause the initiation of atherosclerotic phenomenon[8]. As expected from our results the relationship between hypertension and adiponectin was inversely related. Our study showed that decrease in serum adiponectin levels in hypertensive subjects as compared to control group. Our observations suggested that subjects having low serum adiponectin levels are more prone to develop hypertension and this observation is in agreement with the studies of Adamezeck et al. (2005) and Kasumi et al. (2002) who did their study in japanese hypertensive men. Our results showed strong negative correlation of systolic and diastolic blood pressure with serum adiponectin which are in agreement with the study done by Funuhashi et al. (2003) and Mallamaki et al. (2002). According to Ouchi et al. (2003) serum adiponectin levels were independently correlated with vasodilator response to reactive hyperemia, so it can be an independent parameter for endothelial dysfunction which is an important feature of hypertension and atherosclerosis[9]. Our study agreed with the above statement and suggests that hypoadiponectemia may affect the pathogenesis of hypertension at very early stage.

Lower concentration of serum adiponectin has been associated with both hypertension and dyslipidemia.[12] Patients with essential hypertension appears to have significantly lower levels of plasma adiponectin when compared with normotensive patients[13]. In another case-control study, after adjusting for confounding factors such as obesity, insulin resistance, and diabetes, significantly lower concentrations of circulating adiponectin were present in patients with hypertension compared with those without. (Iwashima et al., 2004). Adiponectin may also be involved in the progression of hypertension. On a high-salt diet, Ohashi et al showed that adiponectin-deficient animals display significantly

higher systolic blood pressure compared with wild-type control animals independent of insulin resistance.

CONCLUSION

This suggests that higher levels of serum adiponectin is protective against the development of hypertension.

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Original Article

Analysis of Medicolegal Autopsies in Quetta, Balochistan

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ABSTRACT

Introduction: Medicolegal autopsies can be valuable source of data on ascertainment of specific causes of reported deaths, particularly homicides in a particular geographic area. The present study provides information regarding the medicolegal deaths which autopsied in Quetta Balochistan.

Objectives: The aim of this study is to analysis the pattern of injuries, age group, gender, causative agent, cause and manner of medicolegal death found on autopsies of Quetta and its suburbs that follows the traditional pattern of life and considers as a backward society.

Study Design: Retrospective study of Medico Legal autopsies referred by police for complete medicolegal autopsy at Police Surgeon medicolegal department of Sandeman Civil Hospital, Quetta Balochistan.

Place and Duration of Study: This study was conducted at Medicolegal Department of Sandeman Civil Hospital Quetta from 1st January 2006 to 31st December 2008.

Materials and Methods: The present study is based on record of 122 medicolegal deaths autopsied during the study period in the mortuary of Sandeman Civil Hospital Quetta affiliated with Bolan Medical College Quetta from 1st January 2006 to 31st December 2008.

Results: Out of 122 medicolegal autopsies Males accounted for 90.16% and Females were 9.84%. Male: female ratio 9.16:1. The majority cases 45 (36.88%) were in the age group of 20-29 years followed by 34 (27.86%) cases in age group of 30-39 years.

Most common cause of deaths in majority of cases was firearm 59 (48.36%), bomb blast explosions 12 (9.83%), sharp force injuries 9 (07.38%), blunt injuries 5 (04.10%), burn 4(03.28%). Homicidal deaths constituted 90 (73.77%), accidental deaths (9.84%), suicidal 3 (2.46%), undetermined 2 (01.64%) and natural deaths 15 (12.29%). The head and trunk is most affected area in cases of physical trauma

Conclusion: study concludes that homicidal deaths by firearms were observed in majority of medicolegal deaths.

Key Words: Deaths, medicolegal autopsy, Quetta.

INTRODUCTION

Quetta is the capital of the Balochistan, a province of Pakistan, with modern and traditional ways of living. According to census report of 2005, Quetta had the population of 815,914 and is the 8th populous city of Pakistan.[1] Balochistan constitutes about 44% of the country's land area, with a population of about 8 million people. The community is very conservative and follows the traditions.[2] However with spread of education and awareness among local peoples, social scene and life style is changing.

Civil Hospital Quetta is named after Sir Robert Sandeman the first British Agent of the Governor General and Chief Commissioner in British Balochistan.[3] British Balochistan remained a part of the British Empire till 1947, when the partition of British India gave birth to two states, Pakistan and India, and Balochistan merged in Pakistan.[4]

Medicolegal autopsies provide evidence for legal action, and show and make available data on ascertainment of specific causes of unnatural death (homicides, accidents, suicides, etc.) in a particular geographic area. The unnatural death is one of the indicators of social and mental health status of the society.

Homicide refers the death of one human being as the result of conduct of another. Homicide rates differ from country to country and community to community all over the world. Globally the homicide toll is 1.6 million deaths per year.[5]

Many workers have studied the different topics of medicolegal interest in different parts of the world, but here in Balochistan, not a single study was carried out on this subject. So, this study is carried out to find demographic information and find out cause and pattern of unnatural deaths in Quetta. We present baseline data obtained from our study results and analysis.

MATERIALS AND METHODS

Study design: The study is retrospective study

Place of study: This study was conducted on all medicolegal deaths referred by Police for complete medicolegal autopsy at Sandeman Civil Hospital Quetta, a teaching hospital of Bolan Medical College Quetta during January, 2006 to December, 2008. The autopsies were performed in mortuary of medicolegal department.

Duration of study: From 1st January, 2006 to 31st December, 2008.

Sample size: material for this study consists of 122 complete medicolegal autopsies performed in Sandeman Civil Hospital Quetta during a period of 3 calendar years (from 1st January 2006 to 31st December 2008).

Sample Selection: The cases selected on the basis of Police inquest, history and circumstances of case, relative's statement, medicolegal autopsy findings and hospital record case files. The medicolegal autopsies consists of general physical examination, cloth examination, external and internal examination of deceased persons were thoroughly and carefully carried out in mortuary.

Data Collection: Data were collected on especially designed proforma related brief information pertaining to age, gender, address, incident as per police record, circumstances leading to death, type of offending weapon causing death, the wounds found on the body and location of wounds was compiled.

The death cases disposed off/handed over without medicolegal autopsy were not included. The postmortem examination of decomposed body and exhumations were not included.

Data analysis: The data thus collected and analyzed on M.S Excel.

Ethical consideration: Permission was obtained from Police Surgeon, Sandeman Civil Hospital, Quetta for collection of the relevant data from record for entire study.

RESULTS

A total of 122 medicolegal deaths were reported to the Sandeman Civil hospital Quetta and subjected to medicolegal autopsy over 3 years (2006-2008) period.

Table No.1: Demographic Data of Autopsies (n-122).

Variables	Number of cases	Percentage
Age group (in years)		
1-9	06	04.92%
10-19	09	7.38%
20-29	45	36.88%
30-39	34	27.87%
40-49	16	13.11%
50-59	09	7.37%
60-69	02	1.64%
> 70	01	0.82%
Gender		
Male	110	90.16%
Female	12	9.84%
Locality		
Urban	75	61.47%
Rural	47	38.53%

In this study the age range was from less than 9 years to more than 70 years. The majority cases 45 (36.88%) were in the age group of 20-29 years followed by 34 (27.86%) cases in age group of 30-39 years. While a small number of autopsies were aged below 9 years 06 (04.92%) and above 70 years 1(0.82%).

Males outnumbered the females with a ratio 9.16:1

The number of autopsies of victims reported from urban areas was high as compared to the urban areas (Table-I). The age and gender distribution is presented in Table-I

Table-2 shows maximum cases of deaths were due to firearms injury 59 (48.38%) followed by bomb blast explosions (9.83%), sharp edged weapon (07.37%), Blunt weapon (04.09%), Natural (Sui) gas poisoning (03.27%), Burns (03.27%).

Table No.2: Cause Leading to Death Ascertained on Autopsies (N-122)

Cause leading to death	Number of cases	Percentage
Firearm injury	59	48.36%
Sharp force injury	09	07.38%
Blunt weapon injury	05	04.10%
Bomb blast injuries	12	09.83%
Burns	04	03.28%
Electrocution	02	01.64%
Coalmine accident injury	01	00.82%)
Custodial deaths	03	02.46%)
Mechanical asphyxia	03	02.46%
Drowning	02	01.64%
Poisoning	03	02.46%
Natural gas poisoning	04	(03.28%
Natural disease	15	12.29%
	122	100%

Table 3 shows homicide was cause of 90 (73.77%) deaths, accidents were cause of 12 (9.84%) deaths and suicides were the cause of 3(02.46%) deaths.

Table No.3: Manners of Deaths

Manner	Number of cases	Percentage
Homicide	90	(73.77%)
Accidents	12	(09.84%)
Suicide	03	(02.46%)
Natural deaths	15	(12.29%)
Undetermined	2	(01.64%)
Total	122	100

Table 4 shows 59 persons died due to firearm inflictions. The maximum number of firearm fatalities 27 (45.76%) were seen in the age group of 20-29 years followed by 12 (22.33%) deaths in 30-39 years age group. All victims were male and manner of death was homicide.

Table No.4 Age Distribution Of Firearm Fatalities (N-59)

Age (in years)	Number of cases	Percentage
1-9	01	01.69%
10-19	05	8.47%
20-29	27	45.76%
30-39	12	22.33%
40-49	08	13.55%
50-59	04	06.77%
60-69	02	03.38%
70 & above	Nil	Nil
Total	59	All males

Table 5 shows the number of fatal injuries sustained and their distribution in body. Most of the injuries of head, neck and face 86 (34.81%) followed by those of chest 63 (25.50%) and abdomen.

Table No.5: Regional Distribution of the Firearm Injuries

Regions involved	Number of cases	Percentage
Head, face & neck	86	34.81%
Chest	63	25.50%
Abdomen	52	21.05%
Upper limb	34	113.76%
Lower limb	12	04.86%
Total	247	100

DISCUSSION

Death is inevitable to every live creature. Allah says in His Holy Book, Quran "Every soul has to taste death".[6] The loss of a human being especially in uncertain circumstances inflicts enormous psychosocial trauma and grief to individuals and close relatives. The death of a patient due to terminal illness is believed as desire or wish of God but death resulting due to violence, deliberate act or negligence of others; makes a loud demand for justice and prevention.

The necessity for searching answers to various questions in doubtful cases of death was evident to mankind since beginning. The legal system and forensic medicine both have attempted to resolve such problems amicably. The purpose of a post-mortem examination was to find a definite cause of death. Every country has its own legal system regarding post mortem examinations and issuance of death certificates. Medicolegal autopsy is performed in pursuance of law to establish the cause and manner of death and to establish or rule out foul play. These autopsies comprise the cases of deaths due to criminal assault, poisoning and accidents.[7]

The cause of death could be defined as disease or injury which results in death of the individual. The manner of death explains how the cause of death came about. These include natural deaths**,** accidental deaths, homicidal deaths, suicidal deaths and undetermined deaths. Natural deaths are consequences of many pathological conditions and endogenous as well as exogenous factors are responsible for those. But unnatural deaths are due to exogenous factors alone. An unnatural death involving a cognizable offence attracts police investigation, postmortem examination, prosecution, finally trial by the court of law and Justice.[8,9]

Deaths are often not autopsied, or ignored by the people for various reasons.[10] Autopsy is not in police or public interest or when the cause of death is evident**.** Occasionally, the deceased's family refuses the autopsy and aborts prosecution because of social, cultural and religious traditions and beliefs.[11] Objections to autopsy have been reported from studies in Asia and Africa and reasons for refusing autopsy usually include, religious objections, dislike of the procedure, fear of mutilation of body, cultural reasons, deceased is too young or female.[12] For civilian, in Sandeman hospital Quetta, medicolegal officer conducts postmortem autopsy examinations and a senior medical officer, the Police Surgeon, is the supervisor of all medicolegal work and In-charge of the department.

The United Nation's global study on homicide statistics; "on trends and patterns in homicide" estimates that the total number of annual homicides in the year 2010 was 468000. Findings connect firearm availability and higher homicide levels; 42 percent of global homicides are actually committed with firearms.[13]

During study period 122 medicolegal autopsies were carried out in this hospital. Males outnumbered the females 110 (90.16%) to 12(9.84%). Male to female ratio in the studied period was 9.16:1. This finding is consistent with other studies.[11,14,16,23,29]

This may be due to males' predominant contribution in daily working life, exposing them to all sorts of violence and facing many stress factors. While great majority of women in Balochistan are housewives and remain dependent on men.

The commonest age group of the subjects was 20-29 (36.88%) followed by the age group 30-39 years ((27.86%). These findings are consistent with the findings of studies conducted in Pakistan[18-21]and other countries.[11,30,31]

This age group represents economically active age and depicts an economic loss to family and nation. Person of this age travel more and work widely in search of livelihood and are more likely to be involved in accidents and fatal disputes.

Our study shows that firearm was the most common causative agent in medicolegal deaths 59 (48.38%) followed by bomb blast explosions (9.83%). sharp weapons (7.37%), blunt weapon (4.09%) and burn death (03.27%).

Results are also comparable with forensic data from Rawalpindi[15,] Peshawar[16], Dera Ismail Khan[35],

Lahore[18], Faisalabad[28], Hyderabad[26] and Bahawalpur.[19] The studies revealed that primary method of committing homicide was by firearm weapon. The high number of criminal homicides has now become a major problem of our country and researchers pointed out the involvement of firearms in such deaths. The reason is that Afghanistan war created illegal firearms trafficking in Pakistan. Obviously number of deaths due to firearm weapons has also increased due to easy availability of all sophisticated and modern weapon firearms without a legal control.[34]

However, a study from Karachi[24] conducted in year 2002 showed that road traffic accident and firearms both were likewise responsible for majority of unnatural deaths. This may be due to the fact that Karachi is a mega city with high population and large number of vehicles on roads. Quetta has road traffic of low density as compared to Karachi.

Humayun M et al in a recent study from Dera Ismail Khan[25] observed that the firearm was most common method followed by bomb blast injuries in homicide. This is in line of our present report. Bomb blast injuries in Pakistan especially in Province of Khyber Pakhtunkhawa and Balochistan are becoming increasingly common over the last three decades mainly due to being front state in Afghanistan war.

In present study 4 people were suffocated to death from natural (Sui) gas poisoning. The reason is Quetta region remains severe cold in extreme of winter and temperature drops to below freezing point and people use natural (Sui) gas for room heating purpose particularly in night. One death was reported due to coal mining accident injury which occurred inside a coal mine in Quetta range.

Our study shows that firearm fatalities were 59 (48.38%), the most vulnerable age group seen of 20-29 years followed by 30-39 years. People of these age groups expected to be more productive and active from socioeconomic point of view. The study is in line with other studies.[28,32,33]

Our study revealed that the target area in firearm injury cases were found maximum in head area 86 (34.81%) followed by chest 63 (25.50%) and abdomen 52 (21.05%). Targeting upper part of body areas signify that aim of the attackers was shooting to kill the victim. Upper body torso contains vital organs brain, lungs and heart. Lethal injury to body's vital leads to rapid death. In agreement with these results, a study on firearm fatalities in Dammam, Saudi Arabia[36], observed the most common sites of firearm injury were the head (36.7%) and the chest (28.7%).

Homicide was the most dominant manner of death followed by accidents. Out of 122 cases, 90 (73.77%) were homicidal while only 12 (9.84%) were accidental in nature. Suicide counts 3 (2.46%) cases and natural 15 (12.29%) cases and undetermined 2 (1.63%). Similar studies were also conducted at Peshawar[14], Dera Ismail Khan[35], Faisalabad,[28,32] where homicidal deaths predominates. Our study differs from studies conducted at Hyderabad[23], Nigeria [17] and Dacca [27] which show accidental deaths predominated rest of unnatural deaths. Comprising percentage of homicidal deaths of our study, less number of homicides occurred in Lahore[18] and Nawabshah[22] as observed by researchers. This may be attributed to better policing, industrialization, employment, higher literacy, availability of health care facilities.

In 15 (12.29%) cases pronounced as natural death, the reasons were history of natural disease and absence of antemortem external injuries on bodied.

CONCLUSION

Firearm weapon was the most common weapon of offence used for homicide. The young adult male in age group 20-39 years are at the risk.

Efforts should be made for

- Strict implementation of firearm control legislation
- To design prevention measures through education and awareness
- To establish more trauma care facilities

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Original Article

Role of Magnetic Resonance Cholangiography (MRC) in Patients with suspected Choledocholithiasis

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ABSTRACT

Objective: To evaluate the diagnostic accuracy of magnetic resonance cholangiography (MRC) in patients with suspected choledocholithiasis.

Study Design: Cross sectional / comparative diagnostic procedural study

Place and Duration of Study: This study was conducted at the Department of Radiology & Gastroenterology Nishtar Medical College & Hospital, Multan from March 2011 to March 2012

Materials and Methods: 50 patients (25 men and 25 women) having mean age of 50 years with suspected choledocholithiasis on sonography were included in the study.MR cholangiogram with two dimensional turbo spin echo sequences were acquired.ER cholangiogram was performed as a reference imaging technique.

Results: 48 out of 50 patients had bile duct stone on reference imaging technique. Two patients were truly negative for choledocholithiasis.MR cholangiogram was positive in 45 patients.MR cholangiogram missed CBD calculi in three patients that were positive on ER cholangiogram having size of calculi <6mm.33.3% patients had single calculus, while 66.7% have multiple CBD calculi. Stone size was 6mm in 25(55.5%) patients,6-10mm in 15(33.3%) patients and >10mm in 5(11.2%) patients

Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV),and accuracy of MR cholangiogram were 93.7%,100%,100%,40% and 94% respectively

Conclusion: MR Cholangiogram provides results comparable with the ER cholangiogram in patients with suspected bile duct obstruction due to choledocholithiasis. In patients in whom an interventional endoscopic procedure is unlikely, MR Cholangiogram can replace ER Cholangiogram as a diagnostic tool, as it is non invasive and well tolerated by patients

Key Words: Magnetic Resonance Cholangiography, Endoscopic retrograde cholangiography,Choledocholithiasis.

INTRODUCTION

Accurate methods detecting bile duct abnormalities in patients with obstructive jaundice are important to both surgeons and endoscopists. Biliary obstruction may be the result of choledocholithiasis, tumors, trauma or infection. The most common cause is choledocholithiasis[1,2]. The prevalence of common bile duct (CBD) stones in patients who undergo cholecystectomy has been reported to be in the range of 10-20%, and the frequency of undetected CBD stones is approximately0%-4.2%.[3]. Accurate identification of CBD stones is important to avoid the surgical morbidity associated with residual stones.[4]

Endoscopic reterograde cholagiography (ERC), percutaneous transhepatic cholagiography(PTC), and intraoperative cholagiography(IOC) are considered to be the best diagnostic methods for common bile duct (CBD) stones; however, these procedures are invasive. Transcutaneous ultrasonography is generally used for the initial evaluation of patients presenting with symptoms consistent with choledocholithiasis but its diagnostic yield is low.[5] The diagnostic accuracy of endoscopic ultrasonography for biliary tract stone disease is greater than 95% and compares favorably with ERC. However; the accuracy of both techniques is highly operator dependent.[6, 7]

Magnetic Resonance Cholagiography (MRC) is a non invasive method of imaging the biliary tract. No contrast medium, sedation, or analgesics are needed. Several reports have shown the ability of MRC to display the biliary tree by combing the advantages of projectional and cross sectional views. The major challenge for MRC is whether it will reach the diagnostic accuracy of ERC and endoscopic ultrasonography for CBD stones and assume a diagnostic role.[8]

Many authors have compared the accuracy of MR cholangiography (MRC) with that of endoscopic reterograde cholangiography (ERC). In one study, the sensitivity, specificity, and accuracy of magnetic resonance cholangiography (MRC) in identifying CBD stones with reference to direct cholangiography (ERC or IOC) were 96%,97% and 97% respectively.[9]

In Pakistan, where health care facilities are limited and limited data is available nationally regarding the diagnostic accuracy of MR cholangiography in detecting choledocholithiasis in patients with symptomatic gall stones. A study of this kind is deemed necessary to generate local database that will be helpful

to determine the diagnostic value of MR cholangiography that is a non-invasive technique in comparison with endoscopic reterograde cholangiography. If the diagnostic accuracy of this method is found to be high then it can be utilized in such cases.

MATERIALS AND METHODS

Study was conducted from March 2011 to March 2012 to determine the diagnostic value of magnetic resonance cholangiography (MRC) in patients with suspected choledocholithiasis comparing with the reference imaging that is endoscopic reterograde cholangiography (ERC).

Fifty consecutive in-patients with suspected CBD stones were prospectively included in the study over a period of 12 months. There were 25 men and 25 women with mean age of 50 years. The patients were referred for magnetic resonance cholangiography (MRC) with suspicion of choledocholithiasis on ultrasonography.

Magnetic resonance cholangiography (MRC) examination was performed on 1.5 T unit (Philips) with a body coil.MR cholangiogram were acquired using non breath holding fat suppressed respiratory triggered turbo spin echo (TSE) sequences. Two dimensional TSE imaging was performed in the axial and coronal planes. The source images obtained were reformatted into targeted small volume maximum intensity images.

The presence of stone within biliary system, its location and size were determined by consultant radiologist with five year experience. Associated findings i.e. biliary, pancreatic duct dilatation and any associated mass were noted.

Endoscopic reterograde cholangiogram (ERC) was performed with TJF 100 or TJF 130 duodenoscopes in 50 patients. The presence of stone within biliary system, its location and size were determined along with associated findings.

Data collection was twofold, i.e. part- I includes demographics of patients like age, sex and presenting symptoms and part-II looked at the magnetic resonance cholangiography (MRC) and endoscopic reterograde cholangiography (ERC) findings. Statistically analysis was performed using SPSS. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy indices of magnetic resonance cholangiography (MRC) were calculated taking endoscopic retrograde cholangiography (ERC) findings as gold standard.

Regarding ethical considerations, this study uses ionizing radiation during fluoroscopy in endoscopic reterograde cholangiography (ERC), which could cause harmful effects on population, so we included only those patients, having clinical, sonographic and magnetic resonance cholangiography suspicion of choledocholithiasis.

RESULTS

From total 50 patients, 25(50%) were male and 25(50%) were female. The mean age was 50 years.

MR Cholangiogram giving complete delineation of the CBD were obtained in all cases and were technically adequate for interpretation. Cholangiogram of diagnostic quality were obtained in all the patients who underwent endoscopic reterograde cholangiography

Results of MR Cholangiogram: MR Cholangiogram detected calculi in 45(90%) patients out of total fifty patients with clinical suspicion of choledocholithiasis. A single stone was found in 15 patients (33.3%), and 30 patients had two or more calculi. Stone size was 6mm in 25(55.5%) patients, 6-10mm in 15(33.3%) patients and >10mm in 5(11.2%) patients. 40 (88.8%) patients has calculi in CBD, In 4(8.8%) patients calculi were found in CHD and in one (2.2%) patient in cystic duct.

Results of ER Cholangiogram: Forty eight out of total fifty patients were positive for CBD stone on ER cholangiogram that is gold standard. Three additional patients were positive for CBD stone on ER cholangiogram that were falsely negative on MR Cholangiogram. Other radiological findings like size, location and number of calculi were comparable with MR Cholangiogram

MR Cholangiogram showing CBD Stone

Table No.1: Sensitivity, Specificity, PPV, NPV& Accuracy of MR Cholangiogram

MR Cholangiogram	ER-Cholangiogram	
	Stone +ve	Stone -ve
Stone +ve	45	00
Stone –ve	03	02

Sensitivity =93.7% Specificity =100%, PPV =100%, NPV=40%, Diagnostic Accuracy =94%

Correlation of Results from MR Cholangiogram with gold standard (ER Cholangiogram): Of the Forty eight patients with CBD stone disease, only forty five were detected on MR Cholangiogram. Three patients that were negative on MR Cholangiogram, found positive on ER cholangiography with stone size of <6mm.Calculated Sensitivity, Specificity, PPV, NPV and diagnostic accuracy were 93.7%,100%,100%,40% and 94% respectively (Table-I).

DISCUSSION

Transcutaneous sonography and CT scan are currently advocated for the initial evaluation of patients with symptoms consistent with choledocholithiasis with a few exceptions, the reported sensitivity for CBD stone diagnosis does not exceed 50% whereas specificity is higher than 90%(10,11,12).Direct cholangiography is generally still considered to be the ideal method for CBD stone diagnosis, although ERC may miss small stones :endoscopic sphincterotomy involving instrumental exploration is usually required to rule them out, especially in a dilated CBD (13,14).

Preliminary early reports indicate that MRC could be used to delineate the anatomy of the biliary tract and depict dilated bile duct and biliary obstruction(15,16).MRC images is based on the use of heavily T2 weighted sequences to highlight static or slowly flowing fluid which provide high signal intensity whereas the background appears hypointense(17).Diagnostic accuracy for choledocholithiasis and stenosis ranges from 71 to 100% (18) .To expand the clinical use of this less invasive diagnostic imaging modality technical refinements such as the use of fast spin echo variants allowing rapid acquisition within a few seconds.

Few reports have specifically addressed the use of MRC for diagnosis of gall stone disease(19).To our knowledge, only five reports has focused on choledocholithiasis(20) and only two were prospective: one include 126 patients with clinically suspected bile duct obstruction, of which thirty two were shown to have CBD stones; in the six cases not diagnosed by MRC,the stones were small (2-7mm):The other prospective study of 47 patients with suspected CBD stones confirmed 19 cases: MRC picked up 18 (95%),and one 6mm stone was missed. However the median stone size in this series was well above that of the present series, often exceeding 10mm (21, 22).

In our study of patients with high suspicion of CBD stone, 48(96%) actually had biliary stone disease, and 45 of these were diagnosed by MR Cholangiogram. Three patients having calculi were missed on MR Cholangiogram. The present study showed 93.7% sensitivity, 100% specificity and 94% diagnostic accuracy that is much higher than most of the studies mentioned in literature, however comparable with one study that is showing sensitivity, specificity and diagnostic accuracy of 96%,97% and 97% respectively[9].

Optimal patient management needs timely coupling of diagnosis and therapy; MRC is a purely diagnostic .Nevertheless, it may give valuable information on patients in whom ERC is not available.

CONCLUSION

In conclusion, MR Cholangiogram provides comparable results to ER cholangiogram in patients with suspected bile duct obstruction due to choledocholithiasis. In patients in whom an interventional endoscopic procedure is unlikely, MR Cholangiogram can replace ER Cholangiogram as a diagnostic tool, as it is non-invasive and well tolerated by patients.

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Original Article

Major Electrolytes Imbalance in Chronic Heart Failure Patients

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ABSTRACT

Objective: To assess the major electrolytes (Magnesium, Calcium, Sodium, Potassium, Chloride) in chronic heart failure patients.

Study Design: Case Control Study.

Place and Duration of Study: This study was conducted at Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, National Institute of Cardiovascular Diseases from April to December 2003.

Materials and Methods: A sample size of 90 was drawn through non- probability purposive sampling, 45 were diagnosed cases of chronic heart failure, 45 healthy people. Age, sex were matched. Serum electrolytes (Mg^{++}, Ca^{++}, Na^{+}, K^{+}, Cl^{-}) were determined. Renal function parameters urea, creatinine was determined. Age group was b/w 35-65 years. Data was analyzed on the SPSS 16.

Results: Mean values of serum electrolytes (Magnesium, Calcium, Potassium, Chloride) were significantly low (1.72+- 0.48, 7.46+-1.23, 3.78+_ 0.54, 99.80+-8.89) respectively in chronic heart failure patients when compared with control people.

Conclusion: The study concluded patients with chronic heart failure manifest a variety of electrolyte abnormalities hypomagnesaemia, hypocalcaemia, hypokalemia, hypochloremia, as a result of diuretics, digoxin therapy.

Key Words: Electrolytes, Abnormalities, Chronic heart failure, Imblance

INTRODUCTION

Heart failure is a chronic, progressive illness. Electrolyte instability is common in patients with congestive heart failure (CHF) during extensive time management. Digitalis was the first pharmacologic agent with positive ionotropic actions gained common use in the cure of chronic heart failure ,augment diminish cardiac contractility by inhibiting the activity of sodium potassium adenosine triphosphatase the resulting increase in the concentration of intracellular sodium enhances the entry of calcium into cells by increasing calcium-sodium exchange.[3] Diuretic agents (especially the non-potassium sparing groups) are potent kaliuretic agents,[4] promote cation excretion almost exclusively in association with chloride.[5] As with potassium there may be a magnesium dependent serum calcium deficiency.[6] Increased rate of electrolyte abnormality, cardiac arrhythmias among patients showing to digoxin–diuretic interactions has been documented in many studies. The joint therapy of digoxin, diuretic triple increases the risk of digoxin intoxication 7. The major electrolytes abnormalities are hyponatremia, hypokalemia, hypomagnesaemia. These derangements are of immense clinical importance; their development not only represents an immediate threat to the CHF patient (e.g., dysrhythmias secondary to hypokalemia), indicative of necessary pathophysiologic events, an unfavorable clinical course, an adverse therapeutic response 8.The study was designed to determine the serum electrolytes level in chronic heart failure patients as electrolyte abnormalities are common among them due to drugs .Determination have made the rapid, accurate measurement as a useful clinical tool in a prevention of variety of disease states.

MATERIALS AND METHODS

The study was carried out in the Department of Biochemistry, BMSI, JPMC, NICVD, Karachi from April to December 2003.A total of 90 people, 45 cases of chronic heart failure from NICVD, Karachi, 45 healthy normal age, gender matched people were selected as control group. Patients diagnosed, treated with diuretic, digoxin for heart failure were included. Patients with risk factors of heart diseases hypertension, diabetes mellitus, cigarette smoking, positive family history of cardiac diseases were included in study. Blood samples were collected under aseptic measures. To minimize the variability of the analytical method, all samples were processed at one time. Serum magnesium, calcium were determined by colorimetric kit method (Kit Cat No. 0137, No.0151-3) supplied by STANBIO Laboratory by (microlab-200) analyzer. Serum Sodium, Potassium, Chloride were determined by ion-selective electrode (Easy-lyte analyzer) method.

Statistical Analysis: Data analysis was done on SPSS 16. The results were given as numbers, percentage for qualitative data (gender) mean standard deviation for quantitative data (age, electrolytes). Student t-test was

used for quantitative data for comparison between cases and controls. P-value < 0.05, < 0.001 were considered significant.

RESULTS

The results were expressed as mean value (SD). Demographic distribution 0f study subjects were given in figure-1a, and 1b.

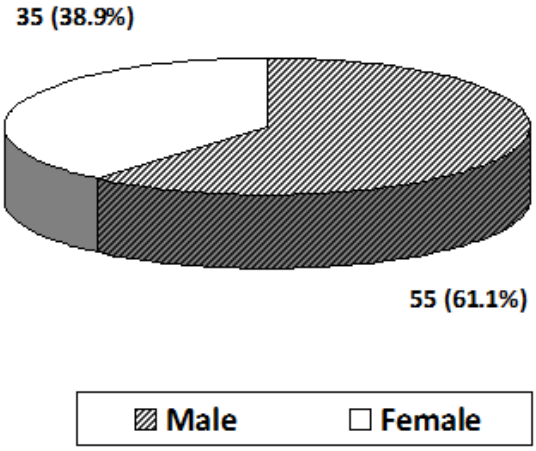

Figure No.1: Male/ Female Distribution of Chronic Heart Failure patients and Control subjects

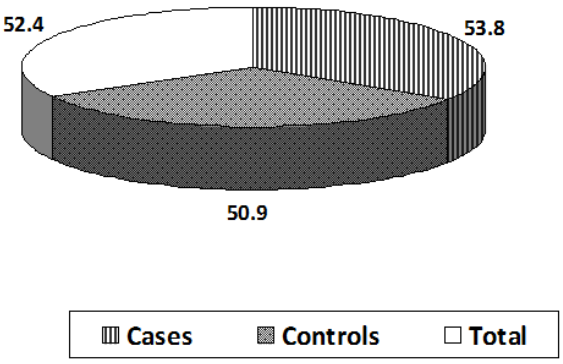

Figure No.2: Age Distribution of Chronic Heart Failure patients and Control subjects.

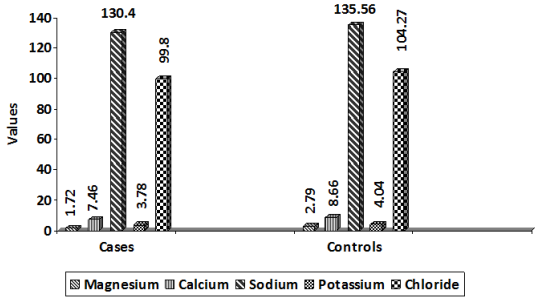

Figure No.3: Biochemical Parameter of Cases of Chronic Heart Failure & Controls groups

A total of 90 subjects, 45 were patients of chronic heart failure, 45 were control subjects. Out of 90 cases 55 (61.1%) were male, 35 (38.9%) were female. Age of 45 cases was 53.8+-9.63 and age of 45 control subjects was 50.9+-5.67. Age range was 52.4±7.98. Mean values of serum electrolytes, Magnesium, Calcium, Potassium, chloride were observed as significantly low (1.72+-0.48, 7.46+-1.23, 3.78+-0.54, 99.80+-8.89) respectively.

DISCUSSION

The study compared an important serum electrolytes magnesium, calcium, sodium, potassium, chloride in chronic heart failure patients receiving diuretics, digoxin. Chronic heart failure is metabolically demanding condition. Resting energy consumption is increased, shift from anabolic to catabolic processe[9.] Most physicians are comfortable with diagnostic, therapeutic strategies for the recognition, treatment of patients with hypokalemia. Age range was 35 to 65 years, the mean was 52.4± 7.98. Males comprised 61.1%, females38.9%.Lavie et al[10] confirmed prognostic ability with exercise cardiopulmonary variables for predicting prognosis in patients with chronic symptomatic systolic heart failure, while Tang et al[11.] Define the fluid retention after thiazolidine initiation in patients with established heart failure. In contrast to this study Pulligano[12] showed mean age of patients with heart failure was higher than 70 years, due to magnesium intake of the elderly tends to be low, their susceptibility to magnesium deficiency was diminished intestinal absorption, increased urinary output of magnesium.

Magnesium is an essential element as a cofactor in various enzymes important in metabolic homeostasis. After calcium, it is the second most abundant divalent cation present in serum13,14.Patients receiving digoxin are predisposed to the magnesium deficiency ,toxic effects of digoxin. The magnesium deficiency impairs the sodium-potassium pump, allows potassium to escape from the cell, to be lost in urine[15,16.]Magnesium reduces coronary artery tone, increases coronary blood flow by 22% in normal human subjects. At the cellular level magnesium was found to protect against ischemia, hypoxic injury by preventing intra-mitochondrial calcium accumulation, improving mitochondrial ATP synthesis essential for the functioning of enzymes in the aerobic cellular metabolism 17.Magnesium deficiency in 55% of Purvis and Morahed[18] study was observed because of diuretic agents. Pronounced diuresis by diuretics, increased renal excretion of magnesium was the cause of magnesium deficiency. Patients who received loop diuretics (furosemide) the magnesium deficiency was prominent. Ceremuzynski et al[19] assessed the role of electrolyte imbalance in cardiac arrhythmias related to increased magnesium excretion

was a feature of heart failure associated with complex ventricular arrhythmias. Clinically important electrolyte disturbances such as hypokalemia, hypocalcaemia had been described in patients with hypomagnesaemia of various causes 20. These heart failure patients are prone to magnesium deficiency as a result of diuretic, digoxin administration, neuro-hormonal activation.[21] the diuretics, digoxin causing major electrolyte disturbances were also observed by Nicholls[22] loop, thiazide diuretics induces deficits of sodium, potassium, magnesium in patients with heart failure. Eichhorn et al[23] showed diuretic, digoxin, rennin angiotensin aldosterone activation, inadequate nutrition in patients predispose congestive heart failure to hypomagnesaemia. Cohen et al[24] showed magnesium depletion, hypomagnesaemia are common among furosemide treated patients with chronic congestive heart failure. Milionis et al[25] stated patients with severe decompensate CHF exhibit acid-base, electrolyte disturbances due to the activation of neurohormonal mechanisms, drugs regularly used in patients. Leier et al observed hyponatremia, hypokalemia, hypo-magnesium were the most common electrolyte abnormalities in heart failure patients

CONCLUSION

The study concluded patients of chronic heart failure manifest a variety of electrolyte abnormalities. Diuretic (furosemide),digoxin are magnesium losing drugs with other electrolytes Calcium , Potassium ,Chloride .Recent advances in the analytic methods for serum electrolytes determination have made the rapid, accurate measurement as a useful clinical tool in a prevention of variety of electrolyte abnormalities and also apply treatment immediately to prevent disease states.

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Original Article

Knowledge and Practices of Complementary and Alternate Medicine among Cancer Patients

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ABSTRACT

Background: To assess the knowledge, practices of Complementary and Alternative Medicine in Cancer patients.
Study Design: A Cross sectional Hospital based study.
Place and Duration of Study: This study was conducted in Jinnah Postgraduate Medical Centre, Karachi from May to November 2010.
Materials and Methods: The study was conducted by using non- probability purposive sampling with structured questionnaire on 375 cancer patients of JPMC oncology OPD's. Informed consent was taken. Data was entered, analyzed on Statistical Package for the Social Science version 19.
Results: Out of 375 patients, commonest age group was 40-49 (48.5%) of the patients had used complementary, alternative medication for the cure of their cancers. The major reasons assessed for using alternative medicine was the high cost of conventional medication (82.4%). 43.4% had gone to Peer/ Faqeer/ Moulvi, 32.4% had taken medication from Hakim, 24.2 % homeopathic medication. 22.9% were illiterate as compared to 9.1% matric passed with average monthly income of Rs.5000-10,000. 48.5% of the patients claimed using complimentary, alternate medication at some stage during their illness. 80% of the patients using complementary, alternative medications had been diagnosed with Gastrointestinal Tract cancers as compared with other cancers. The patients that were previously using Complementary, alternative medicine (48.5%) preferred using allopathic medication (90.9%) in future.
Conclusion: Every patient has the right to choose, decide newer, advanced forms of medical Treatment, scientific methods, a relatively high number of patients had used Complementary, alternative medicine for the treatment of their ill ness. An awareness/ procedural program is of utmost important for cancer patients. Government must facilitate cancer patients as cancer is on the rise in Pakistan.
Key Words: Complementary, Alternative Medicine, Cancer, Allopathy.

INTRODUCTION

A health improvement with cost savings for the CIM therapy versus usual care[1]. Complementary and alternative medicine is an umbrella term covering a diverse array of healing modalities[2] According to the definition provided by the National Center for Complementary, Alternative Medicine, Complementary, Alternative Medicine (CAM) is a broad domain of healing resources encompasses all health systems, modalities, practices, their accompanying theories, and beliefs, those intrinsic to the politically dominant health system of a particular society or culture in a given historical period. .Pakistan is a developing country. Majority (66%) lives in rural areas.[3] Low literacy, cultural beliefs , practices leads to self care, home remedies, consultation with traditional healers in rural community.[4] According to one estimate, >80% of the developing world's population still dependence on the complementary, alternative systems of medicine[5] The prevalence of CAM use is estimated at 25% among residents of the United Kingdom,[5] 50% among German, French,[6] and Australian[7] populations, 42% to 69% among residents of the United States.[8] A summary of 26 surveys across 13 countries concluded that the prevalence of CAM use by cancer patients overall was 31.4% (range, 7% to 64%).[9] Most cancer patients combine CAM with conventional therapy[10] The increasing interest in CAM among cancer patients is due to limitations of conventional cancer treatment, side effects by allopathic medical therapies (e.g., chemotherapy and radiation therapy), low-invasive nature of treatment, increased advertising, media coverage of CAM, or the desire for holistic or natural treatments. As cancer incidence increases, survival time lengthens, the population seeking information about and access CAM is likely to increase.In Pakistan use of spiritual practices, prayer, worships for the purpose of cure or an improvement in an illness are common. Faiths healers have been reported to be major source of care for people with mental problems especially women with low literacy.

MATERIALS AND METHODS

A cross sectional Hospital based study was conducted May to November 2010.Sample size of 375 patients was drawn using non- probability purposive sampling. Data was collected through structured questionnaire

.The study was conducted on cancer patients presenting to Jinnah Post Medical Center oncology Out Patients Department's. Informed consent was taken from the respondents. Data was entered, analyzed on Statistical Package for the Social Science (SPSS) version 19.

RESULTS

Out of 375 patients 62.7% were female, 37.3% male respondents. Commonest age group was 40-49 years. Use of Peer/ Faqeer/ Moulvi was the most prevalent choice (43.4%). The remaining 32.4% had taken medication from Hakim, 24.2% had taken homeopathic medication. The use of alternative modalities decreased with the increasing level of education and household income. Majority of them were illiterate with average monthly income of Rs.5000-10,000. 48.5% of the patients claimed using complimentary, alternate medication at some stage during their illness.

Table No.1: Comparison of literacy level among patients using complementary and alternative medication

Literacy Level * Prior CAM Use					
			CAM Use		Total
			No	Yes	
Literacy Level	Illiterate	Count	98	86	184
		% of Total	26.1%	22.9%	49.1%
	Primary	Count	34	39	73
		% of Total	9.1%	10.4%	19.5%
	Matric	Count	38	34	72
		% of Total	10.1%	9.1%	19.2%
	Interme-diate	Count	9	13	22
		% of Total	2.4%	3.5%	5.9%
	Above Interme-diate	Count	14	10	24
		% of Total	3.7%	2.7%	6.4%
Total		Count	193	182	375
		% of Total	51.5%	48.5%	100.0%

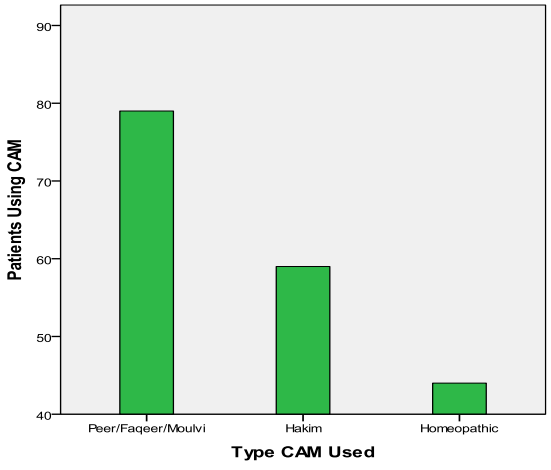

Figure No.1.1: Type of complementary & alternative medicine used by patients prior coming to hospital.

The major reasons cited for using alternative medicine were the high costs of conventional medication (82.4%) followed by persuasion from family or other patients. 67.2% believed in the effectiveness of alternative medicine and 32.8% doubted the efficacy of alternative treatment.

With increased literacy level the usage of CAM decreased. 52% frequency difference b/w illiterate & matric passed. The major source of information for alternative medicine was friends, family. The patients previously used CAM (48.5%) preferred using allopathic medication (90.9%) in future. Most patients shifted to allopathic mode of treatment after using CAM due to no improvement in their conditions or after they had awareness about allopathic medication & procedures.

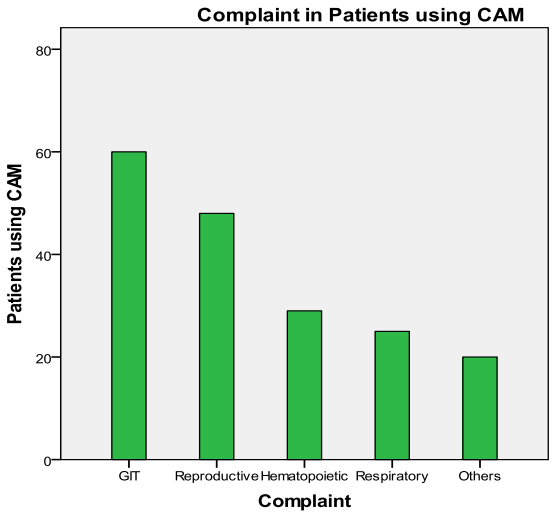

Figure No.1.2: Comparisons of different Cancers among CAM users

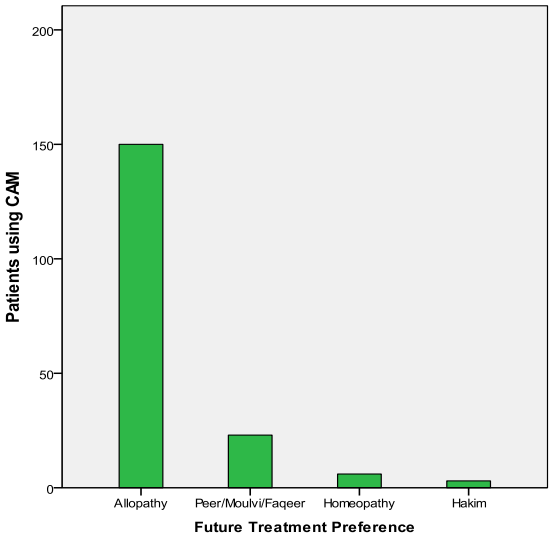

Figure No.1.3: Future treatment preferences in Cancer patients.

DISCUSSION

Almost half (48.5%) of the patients that were included in this study had used complementary, alternative medication for the cure of their cancers. In a study from Rawalpindi, more than two third of the study participants had used alternative modalities at some point of their illness. The commonest was Quranic verses/Dam darood, spiritual healing which corresponded to the cultural, religious beliefs of their population [10] Most patients who used Complementary, alternative medicine were found to have GIT cancers followed by reproductive system cancers, blood cancers, respiratory cancers and others.

Patients wanted to maximize their chances for survival by opting different treatment options other than Allopathy. Patients with advanced disease turned to CAM for hope after conventional treatment failed. Most patients used CAM to feel more hopeful. Although reasons for hope are not well measured nor the term well-defined, [11] hope may be the single greatest reason for using CAM therapies. One third of the outpatients expected CAM to cure their disease, which confirms other studies**.** [12, 13, 14]

Alternative therapies had experienced a revival over the past decade, fueled in part by the public's desire to participate in their own health care, a perception that the medical profession had failed to find a cure for cancer, despite almost three decades of war on cancer.[15] Expanded research initiatives are needed to determine the safety, efficacy of drug and herb or vitamin interactions. Whether we call these approaches medicines, alternatives, unconventional or complementary approaches, or natural herbal remedies, interest in them is here to stay. [16]

CONCLUSION

The study proved the use of complementary, alternative medicine (CAM) is part of social scope of oncology patients. A relatively high number of patients had used CAM for the treatment of their illness. While the CAM modalities used are diverse, peer/ Faqeer are most popular. The increasing and concomitant use of CAM with conventional allopathic medicine underlines the need for implementation of a surveillance system to report, monitor possible threatening drug-herb interactions and urge the oncologists to openly address their patient's knowledge, attitude and practices of CAM.

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Original Article

Urinary Tract Infection is the Most Common Complication in Diabetic Patients

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ABSTRACT

Objective: The urinary tract infection are more frequent complications in patients with diabetes mellitus.

Study Design: Experimental Study.

Place and Duration of Study: This study was conducted at GMMMC Hospital, Sukkur, Pakistan from April 2008 to July 2009.

Materials and Methods: The patients which were selected in study all were more than 20years of age, of either gender were known diabetes for more than 3 years duration. The infection was labeled when >5/hpf leukocyte in urine and growth of organism on urine for C/S. The blood sugar and hemoglobin A1C (HbA1C) was also advised to evaluate the status of their diabetes i.e. control or poorly control.

Results: in this study total 200 diabetic patients were evaluated for urinary tract infection, of which 142(71%) had UTI. Out of 142 patients 130(91%) had diabetes type 2 and 12(8.4%) were diabetes type 1. The male to female ratio was 1:2. The age of patients with type 2 and type 1 diabetes mellitus was 50.52±9.74 and 18.77±2.65 whereas the mean random blood sugar level in patients with type 2 and 1 diabetes was 240 and 290. The duration of diabetes type 2 and 1 was 3.80±2.31 and 2.54±1.42. The isolated microorganism were Staphylococcus aureus, Escherichia coli, Proteus, Pseudomonas aeruginosa, Klebsiella, Enterobacteriaceae and C.albicans.

Conclusion: The urinary tract infection is more common complication in patients with diabetes mellitus.

Key Words: Pseudomonas aeruginosa, Klebsiella, Enterobacteriaceae, C.albicans, neurogenic, pyelonephritis

INTRODUCTION

Diabetes Mellitus is a chronic disease that can cause another serious health complications such as heart disease, kidney failure, stroke, and even blindness. Diabetes mellitus is also a condition where the pancreas not able to produces insulin in its proper amount. In this condition in which glucose, often mentions as blood sugar, is too high and could not be controlled. Glucose is made in the liver and muscle but mostly comes from the food we eat. In order to use this sugar, the pancreas produces a hormone called insulin. Urinary Tract Infection, (UTI) is a common ailment and can affect people of all ages, sex, and from all cultures. However, there are certain groups of people that are more prone to UTI than others. Women, for example, for reasons yet to be firmly established, carry a greater risk of UTI. Diabetic patients too fall under this category. Going further, pregnant women with diabetes are probably amongst the most vulnerable to UTI. Diabetic women are at a higher risk of developing to urinary tract infection (UTI) after menopause as compared to non-diabetic women. In fact, a study by University of Washington, Seattle revealed that the risk of UTI in diabetic women was 80% higher than others. UTI in diabetic patients is not only more severe but also is more recurrent as compared to non-diabetic patients. The sugar content of urine in a diabetic patient provides a breeding ground for bacteria once they enter the bladder. The most serious but rare types of UTI like pyelonephritis, widespread infections, abscesses, inflammation of the bladder wall, occur mostly in diabetic individuals. The risk of UTI increases with any negative change in the immune system of the body. Diabetes, like many other disorders, affects the immune system, increasing the risk of a urinary tract infection. Another characteristic of UTI in diabetic patients is that of the risk of presence of asymptomatic (having no symptoms of illness or disease) bacteriuria - presence of bacteria in urine - is much greater than in others. Treating this condition, according to study conducted in 2003, is of little value as it

does not prevent complications. Diabetes may cause conditions of overactive bladder or neurogenic bladder. Whereas, an overactive bladder is common, neurogenic bladder is rare but more a severe condition. Diabetic men and women commonly face problems like feeling of urinary urgency, incontinence, frequency and getting up at night often to urinate. A severe condition often manifests in the shape of painful urination and retention of urine in the bladder.

UTI in diabetic patients can be a traumatic experience leading to complications if not treated in time. Urinary tract infection cure for diabetic patients requires a longer period, lasting from anything between seven to fourteen days, of antibiotic treatment even for uncomplicated infections. In many cases it may have to be accompanied by bladder infection treatment. This study concerned with evaluation of urinary tract infection in patients with diabetes mellitus.

MATERIALS AND METHODS

This descriptive case series study was carried out in the department of Urolody at GMMMC Hospital Sukkur, Pakistan, from april 2008 to July 2009. Patients were more than 20 years of age, of either gender were known diabetes for than 3years duration presented with fever with chills & rigor, burning during urination, altered colour of urine with foul smelling discharge, urgency to void, blood in the urine, discomfort in lower abdomen (supra pubic pain and flank pain) with nausea and vomiting, through outdoor & indoor patients in our study. The detail history of all such patients was taken; complete clinical examination and routine investigations were performed. The blood sugar and hemoglobin A1C (HbA1C) was also advised to evaluate the status of their diabetes i.e. control or poorly control.Urine microscopy were done in these patients to evaluate UTI the method for quantitating the number of leucocytes in the urine was glass slide microscopy. The infection labeled when >5/hpf leukocytes in urine, growth of organism on urine culture and sensitivity (C/S) by collecting urine sample in sterilize bottle, labeled it and sent to laboratory for analysis. The data was collected through a pre-formed performa / questionnaire.The frequency and percentage of for age & UTI and associated pathogens was calculated. The chi square test was applied on categorical variables and the p-values ≤ 0.05 was considered as significant.

RESULTS

During study period total 200 diabetic patients were evaluated for urinary tract infection, Out of 200, 142(71%) had detected urinary tract infection. Of 142 patients 130(91%) had diabetes type 2 and 12(8.4%) were diabetes type 1. The gender distribution in relation to urinary tract infection is shown in Table-I.

Table No.1:Gender distribution of patients with UTI

gender		UTI	Total	pValue
	positive	negative		
male	30(28.5%)	27(72.9%)	57(40.1%)	
female	75(71.4%)	10(27%)	85(59.8%)	0.03
total	105(73.9)	37(26%)	142(100%)	

Table No.2: Pathogens identified on culture & sensitivity

pathogens	n=92%
E.coli	58(65%)
proteus	12(13%)
staphylococcus aureus	11(12%)
psuedomonas aeruginosa	4(5%)
klabisella	03(3%)
entrobactericaea	02(2%)
c.albicans	02(2%)

The mean ± SD for age of patients with type 2 and type 1 diabetes mellitus was 50.52 ± 9.74 and 18.77 ± 2.65. The mean random blood sugar level in patients with type 2 and 1 diabetes was 240 and 290. The mean ± SD for duration of diabetes type 2 and 1 was 43.80 ± 2.31 and 2.54 ± 1.42. The isolated microorganism as far as diabetes is concerned are shown in Table II. Regarding the demographical distribution majority of the patients were from rural communities.

DISCUSSION

Urinary tract infections (UTIs) are a common burden in patients with diabetes mellitus. Cystitis, ascending infections leading to pyelonephritis, emphysematous complications and renal and perinephric abscesses are well recognised in this group of patients especially if glycaemic control is poor. Despite the clinical significance of UTI in diabetes, it is inadequately understood and management regimens are mostly not evidence based. Anticipation of potential complications and earlier interventions are vital to reduce serious adverse outcomes. Herein we discuss the aetiology, pathogenesis and management of UTI and its local and more remote complications.

In present study the reported prevalence patients of urinary tract infection in diabetes was 71% of which 91% in diabetes type 2 and 8.4% in diabetes type 1 and it can be compared with the study of Lerman-Garber et al7 which shows that overall prevalence was 46.5% (slightly lower than our study) and proved the association of urinary tract infection and diabetes. The

finding of present study can be comparable with the study of Patel, et al,8 which was a 14 years prospective study, about the complications of urinary tract infection, done on 8793 hospitalized cases. He has reported acute complications, and chronic urinary tract infection in 31.4% of patients with diabetes mellitus. In our study the female population was predominant to acquire urinary tract infection and is consistent with the study by Brauner et al9. In our study 71% patients had poor glcaemic control and Brauner et al hypothesized that good glycaemic control helps in reducing the prevalence of urinary tract infection. Bacteriological studies usually reveal the involvement of gram negative enteric organisms that commonly causes urinary tract infections such as E. coli, Klebsiella species, and the Proteus species10. Similarly, the predominant numbers of pathogens isolated in our study were gram negative bacilli. Among the patients infected with gram negative bacilli in our study, Escherichia coli was isolated from 58(63%) of the subjects, Klebsiella spp. From 03(03%), Pseudomonas spp. from 04(05%), Staph aureus 11(12%) and the Proteus spp in 12(13%) and can be contrast with the study by Brauner et al9 reported prevalence of E.coli 55% of urine culture in diabetic patients. Hoepelman suggested mechanisms of an increased susceptibility to UTI are (a) decreased antibacterial activity due to the 'sweet urine', (b) defects in neutrophil function (c) increased adherence to uroephithelial cells and UTI in diabetics should be treated complicated UTI with agents reaching high tissue levels for 10–14 days11. The diabetes severity and duration are the main determinants of higher UTI and asymptomatic bacteriuria risk-a pattern that resembles the relation between diabetes characteristics and other complications, such as retinopathy or neuropathy Therefore, one would expect that improved diabetes control might yield a reduction in incidence of urinary tract infection.

CONCLUSION

The urinary tract infection is more prevalent in patients with persistent raised blood glucose level or poorly glycaemic control while E.coli is the main cause for UTI in patients with diabetes mellitus.

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Original Article

To Determine the Frequency of Silent Myocardial Ischemia in Type-II Diabetic Patients with Proteinuria

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ABSTRACT

Objective: To determine the frequency of silent myocardial ischemia in type-II diabetic patients with proteinuria.
Study Design: Cross sectional study.
Place and Duration of Study: This study was performed at Department of Medicine in collaboration with department of Cardiology CMC, Hospital larkana from 15-Nov-2011 to 14-May-2012.
Materials and Methods: There was a **n**on probability purposive sampling. All patients who were type-II diabetics and having proteinuria were included in this study. The age of these patients were > 35 years. They were selected for determination of silent myocardial Ischemia. The electrocardiography of all those patients having FBG>126 mg/dl and proteinuria > 150mg/dl was performed. The ETT of all patients was done in cardiology department. Those patients who have normal ETT were labeled negative for silent myocardial ischemia, while ETT positive patients were labeled as having silent myocardial ischemia.
Results: The total no: of 323 patients were included in this study with mean age of 49.9+10.3 years, 270 (83.6%) were male and 53 (16.4%) were female. The ETT was positive in 69 (21.36%) patients.
Conclusion: The frequency of SMI in our study was 21.36%.
Key Words: Silent myocardial ischemia, Diabetes mellitus, proteinuria.

INTRODUCTION

Diabetes mellitus is a disorder that affects the body's ability to make or use insulin. Diabetes results in raised levels of glucose in the blood stream. This can cause severe short-term and long term consequences[1].

Type 2 Diabetes Mellitus accounts for 90% to 95% of all diabetes mellitus cases, caused by combination of complex metabolic disorders that result from coexisting defects of multiple organ sites such as insulin resistance in muscle and adipose tissue, a progressive decline in pancreatic insulin secretion, unrestrained hepatic glucose production, and other hormonal deficiencies. Most affected individuals are obese and, therefore, have variable degrees of insulin resistance. Other risk factor includes increasing age, sedentary lifestyle and is associated with a strong genetic predisposition[2].

Generally, the injurious effects of diabetes mellitus are separated into macrovascular complications (coronary artery disease, peripheral arterial disease, and stroke) and microvascular complications (diabetic nephropathy, neuropathy, and retinopathy)[3].

Diabetic nephropathy is defined as persistently raised urinary albumin excretion rate (UAER) already above arbitrary established normal range, so-called microalbuminuria (UAER >30 mg/24 hours or 20 µg/min, and less than or equal to 300 mg/24 hours or 200 µg/min). Persistently elevated UAER values >300 mg/24 hours or >200 µg/min, should be named macroalbuminuria[4]. Proteinuria is defined as excessive protein excretion in the urine, generally greater than 150 mg/24 h[5]. Angina pectoris has long been considered the cardinal symptom of myocardial ischemia. However it is now known that angina pectoris may be a poor indicator for myocardial ischemia, particularly in patients with diabetes. Coronary artery disease (CAD) in diabetic patients poses diagnostic and therapeutic challenges for clinicians, especially when patients are asymptomatic during episodes of myocardial ischemia. Silent myocardial ischemia (SMI) refers to the presence of objective findings suggestive of myocardial ischemia that is not associated with angina or angina equivalent symptoms. Such objective evidence includes exercise testing or ambulatory monitoring demonstrating electrocardiographic changes, nuclear Imaging studies demonstrating myocardial perfusion defects, or regional wall motion abnormalities illustrated by echocardiography[6]. It is found that the excess of cardiovascular events and mortality occurs in diabetic patients with persistent microalbuminuria, but is particularly evident in macroalbuminuric diabetic patients and results not only from end-stage renal failure (ESRF) but rather from cardiovascular disease (CVD), the latter mainly in type 2 diabetic patients. Microalbuminuria is currently regarded as a marker of generalized endothelial damage; it reflects transvascular albumin leakage, now recognized as an early event in atherogenesis[4]. The prevalence of silent myocardial ischemia (SMI) in asymptomatic microalbuminuric and normalbuminuric type 2 diabetic patients is 30% and 6.6% respectively[7].

The aim of my study is to use proteinuria in type 2 diabetics as useful marker for identifying people with silent myocardial ischemia. Prompt and timely intervention in people found to have silent myocardial ischemia in this way would help in reducing significant morbidity and mortality from cardiovascular events in our country.

MATERIALS AND METHODS

Study design: Cross sectional study.
Setting: This study was performed at department of medicine, in collaboration with department of cardiology CMC hospital Larkana.
Duration of study: This was a six months study from 15-Nov-2011 to 14-May-2012.
Sampling technique: Non probability purposive sampling.
Sample selection:
Inclusion criteria: All patient of age 35 years and above of either sex with type 2 diabetes having proteinuria with duration of type 2 diabetes being more than 5 years.
Exclusion criteria: Following patients were excluded:

1. Patients with known type 1 diabetes.
2. Patients with known ischemic heart disease or any other heart disease.
3. Patients with known renal or urinary tract disease.
4. Patients with fever, pregnancy, regular prolonged standing, regular severe exercise.
5. Patient with hypertension.
6. Patient with hyperlipidemia.

Data collection procedure: The study was conducted after informed written consent, patients were enrolled from Diabetic clinic of Department of Medicine, C.M.C Teaching Hospital, Larkana. Detailed history was taken from all patients aged above 35 years of either sex. Fasting blood samples were taken and sent to CMC hospital laboratory for determination of fasting blood sugar. Patients diagnosed with type 2 diabetes under went 24 hour urinary protein quantification. Those having 24 hour urinary protein greater than 150 mg/dl and fulfilling the selection criteria were selected for determination of silent myocardial ischemia (SMI).
Electrocardiography (ECG) of all patients having FBG ≥ 126 mg/dl and proteinuria > 150 mg/dl was performed. Protocols of Exercise tolerance test (ETT) were explained to selected subjects and sent to Department of Cardiology for determination of silent myocardial ischemi.ETT of all selected patients was done after thorough explanation of procedure in department of cardiology and interpreted by consultant cardiologist with experience of at least 5 years. Those patients who have normal ETT were labeled negative for SMI, while those patients whose ETT is positive for ischemia were labeled as having silent myocardial ischemia.

Data analysis procedure: Data was entered and analyzed on SPSS version17.0. The frequency and percentages were calculated for qualitative variables like gender, proteinuria and silent myocardial ischemia status. Mean±SD was computed for quantitative variables like age and duration of diabetes. Stratification was done with regard to age, gender and duration of diabetes to see the effects on these outcomes variables through chi-square test. P-value≤0.05 was taken as significant.

RESULTS

A total of 323 patients were enrolled in this study. Of 323 patients,112 (34.7%) were 35-45 years of age with mean age of 49.9±10.3 years (Graph 1) and 270 (83.6%) were male with male to female ratio 5.1:1 (Graph 2).
Of 323 patients, 117 (36.2%) had duration of diabetes between 5-10 years with mean duration of 7.6±2.9 years (Graph 3). The frequency of SMI was 69 (21.36%) (Graph 4).
Stratified analysis based on age, sex, duration of diabetes is summarized in table 1-3.
Stratified analysis showed that frequency of SMI increases as age increases. Silent Myocardial ischemia is more common in patients within age group 66-75 years that is33.3% and is statistically significant (P-<0.001).
Stratified analysis based on sex showed that SMI in male patients is 23.3%compared to female 11.3%, it is statistically significant (P-0.03).
Stratification based on duration of diabetes shows SMI in group of >15 years duration is30.6% and is statistically significant (P-0.01).

Table No.1: Stratification of age in Participants having Silent Myocardail Ischemia.

Ischemic changes in ECG	Age group				Total
	35-45 years	46-55 years	56-65 years	66-75 years	
Yes	15 (13.4%)	12 (17.9%)	15 (23.8%)	27 (33.3%)	69
No	97 (86.6%)	55 (82.1%)	48 (76.2%)	54 (66.7%)	254
Total	112	67	63	81	323

P-value: <0.001

Table No.2: Stratification of sex in participants having silent myocardial ischemia.

Ischemic changes in ECG	Sex		Total
	Male	Female	
Yes	63 (23.3%)	6 (11.3%)	69
No	207 (76.7%)	47 (88.6%)	254
Total	270	53	323

P-value: 0.03

Table No.3: Stratification of duration of diabetes in participants having silent MI

Ischemic changes in ECG	Duration of DM			Total
	5-10 years	11-15 years	>15 years	
Yes	18 (15.3%)	20 (19%)	31 (30.6%)	69
No	99 (84.6%)	85 (81%)	70 (69.3%)	254
Total	117	105	101	323

P-value: 0.01

DISCUSSION

Coronary heart disease (CHD) is the leading cause of death in patients with type 2 diabetes is often asymptomatic[8] and may present without warning as acute myocardial infarction, heart failure, arrhythmia or sudden death. In acute myocardial infarction and heart failure, mortality is increased in the presence of type 2 diabetes, thus emphasizing the potential value of identifying high-risk asymptomatic individuals with diabetes[9].

Microalbuminuria is present in approximately 25% of patients with type 2 diabetes and is associated with a doubling of the risk of early death, mainly from CHD[10].Microalbuminuria has been defined by consensus, as a urinary albumin excretion rate between 20 and 200 µg/min, though rates of 10.6 µg/min have been linked to increased macrovascular events in type 2 diabetes[11]. Silent myocardial ischemia (SMI) can be detected by various methods[12]. Using treadmill exercise testing, SMI has been defined as exercise-induced ST-segment depression in the absence of CHD symptoms, and, in men free from known CHD, this finding has been associated with increased mortality[13-14]. There is very little data on the prognostic value of SMI, detected by any method, in asymptomatic patients with type 2 diabetes[15-17].

The aim of this study was to determine frequency of SMI in patient with type II diabetes and proteinuria. We found that frequency of SMI was 21.36% in our study. The study conducted by Hussein AZF and Strak SK reveals the prevalence of silent myocardial ischemia (SMI) in asymptomatic microalbuminuric and normalbuminuric type 2 diabetic patients is 30% and 6.6% respectively[7].

The reported frequency of silent myocardial ischaemia in diabetics is variable[18-20]. This study results are in line with findings of Caraccilo[21],Chipkinet[al22] and Airaksinen et al[23], with no significant difference in which silent myocardial ischaemia in diabetics was 19%. Burgess et al reported incidence of SMI was 16%[6].Impaired symptom perception contributes to the lack of recognition of painful stimuli. For angina, this may occur at different levels. Potential reasons may include a higher pain threshold, an excess of endogenous endorphins, and a generalized defective perception of painful stimuli. Episodes of silent myocardial ischemia may represent less severe or shorter events than those associated with angina pectoris. In diabetic patients, it is suspected that partial or complete autonomic denervation may contribute to the prevalence of silent myocardial ischemia[6].

In this study as age increases the frequency of SMI increases. Similar to Burgess et al reported frequency of SMI which was higher in old age group[22]

In this study SMI was more common in patients with duration of diabetes >15 years. Similarly other studies also reported that as duration of diabetes increased the frequency of SMI is also increased.

The strength of this study is that we have included patients with diabetes and proteinuria. Most of above mentioned studies only represented association of type II diabetes with SMI.

This study has few limitations. First, it was a cross sectional study with no comparative group. Cohort study is appropriate design to conduct this study but cohort studies take a lot of time and resources and it's not possible to complete this within limited time frame. However this study will serve as hypothesis generating study. Second, we did not ask about control of diabetes. It is possible that long standing uncontrollable diabetes is more prone to develop SMI compared to well controlled diabetics. Third, we did not asked about socio-economic status (SES) history so patients with low SES may be more prone to develop SMI. Fourth, since this was a hospital based study it was not representative of population.

CONCLUSION

It is concluded from this study that

- The frequency of SMI in diabetic with proteinuria is 21.36%.
- Frequency of SMI in diabetic patients with proteinuria within age group 66-75 years is 33.3%.
- Frequency of SMI in male diabetics patients with proteinuria is 23.3% compared to female 11.3%.
- Frequency of SMI in diabetic patients with proteinuria with duration of diabetes of >15 years is 30.6%.

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Original Article

A Study of Knowledge, Attitude and Practices Regarding Smoking among Doctors of Nishtar Hospital, Multan

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ABSTRACT

Background: The World Health Organization cites Tobacco use as one of the biggest public health threats the world has ever faced. Tobacco is the number one preventable cause of disability and death. The incidence of Tobacco smoking is increasing across the globe especially amongst the youth. Since Tobacco smoking is associated with serious health problems such as Hypertension, Ischemic Heart Disease and Lung Cancer, there is an urgent need to create awareness among the masses about the health hazards and long term consequences of smoking. In Pakistan, tobacco use is common in general public and the health professionals don't lack behind this habit.
Objectives: To determine the frequency of smoking and to create awareness and health consciousness among doctors about hazards of smoking. To understand the relationship of smoking with other diseases.
Study Design: Observational cross sectional study
Place and Duration of Study: This study was conducted at Nishtar Hospital, Multan over a period of three months 15th Jan. to15th March 2012.
Materials and Methods: A total of 240 male doctors,10 from each ward were selected with their informed consent. A structured questionnaire was designed. Data was collected and analyzed using EXCEL and SPSS.
Results: Out of 240 doctors, 98(40.8%) were smokers and 142(59.2%) were non-smokers. Among smokers,168(69.8%) belonged to age group 20-30 years.70(71.4%) smokers belonged to urban areas and 28 (28.6%) belonged to rural areas.76(77.6%) smokers belonged to literate families and 22(22.4%) belonged to illiterate families.38(38.8%) smokers started smoking before joining medical school and60(61.2%) started smoking after joining medical school. 52 (53.2%) doctors smoked 6-10 cigarettes per day. Among smokers, 44% gave positive history of smoking in friends, 34.1% gave positive smoking history of their fathers, 17.1% gave smoking history of their brothers and 4.8% about their grandfathers. Also among non-smokers, 52.2% gave positive smoking history of their friends. Within families of smokers, there was an increase frequency of hypertension (20.4%), IHD (8.2%) and lung diseases (20.4%). 40.7% doctors (smokers and non-smokers) take smoking as 'Just a habit', 29.6% think it as 'A stress relief', 14.8% as 'Relaxation' and 3.7% for 'Concentration'. 49% smokers smoke outdoors and 19% smoke Indoors and 31.7% at all places. 62% smokers tried to quit smoking but among those, 73% stayed off for less than 3 months and 27% for more than 3 months.
Conclusion: Most of the smoker doctors are young, from urban areas, have literate families and tell positive history of smoking in their friends. Time of start of smoking is after joining medical school. Most doctors smoke outdoors and like smoking as 'Just a habit' but also keeping knowledge for its 'Health problems'. Doctors try to quit smoking but unfortunately majority of them keep themselves stay off for less than 3 months.
Key Words: Smoking, Tobacco, Nicotine, Addiction, Doctors, Health, COPD, Lung Cancer.

INTRODUCTION

The World Health Organization cites Tobacco use as one of the biggest public health threats the world has ever faced. Tobacco is the number one preventable cause of disability and death. The incidence of Tobacco smoking is increasing across the globe especially amongst the youth. Since Tobacco smoking is associated with serious health problems such as Hypertension, Ischemic Heart Disease and Lung Cancer, there is an urgent need to create awareness among the masses about the health hazards and long term consequences of smoking. In Pakistan, tobacco use is common in general public and the health professionals don't lack behind this habit.

Smoking is one of the leading causes of preventable death.. A variety of plant materials are smoked, including marijuana and hashish, but the act is most commonly associated with tobacco as smoked in a cigarette, cigar or pipe.[1]

Nicotine has been consumed in the form of tobacco and other plants for many hundreds of years. High levels of nicotine in cigarette can make it harder to quit smoking[2].

Tobacco is considered to be a mood and behavior altering substance that is psychoactive and amusable. It is believed to be as potentially addictive as alcohol, cocaine and morphine[3].

The tobacco epidemic is one of the biggest public health threats the world has ever faced. It kills nearly six million people a year of whom more than 5 million are users and ex users and more than 600 000 are nonsmokers exposed to second-hand smoke. Approximately one person dies every six seconds due to tobacco and this accounts for one in 10 adult deaths. Up to half of current users will eventually die of a tobacco-related disease. Nearly 80% of the more than one billion smokers worldwide live in low- and middle-income countries, where the burden of tobacco-related illness and death is heaviest. Tobacco users who die prematurely deprive their families of income, raise the cost of health care and hinder economic development. In some countries, children from poor households are frequently employed in tobacco farming to provide family income. These children are especially vulnerable to "**green tobacco sickness**", which is caused by the nicotine that is absorbed through the skin from the handling of wet tobacco leaves[3].

Smoking is generally five times higher among men than women[4] however the gender gap declines with younger age[5,6]. In developed countries smoking rates for men have peaked and have begun to decline, however for women they continue to climb[7].

Individuals who smoke cigarettes are 12 times more likely to die from lung cancer, two to four times more likely to develop coronary heart disease, twice as likely to have a stroke, and 10 times more likely to die from chronic obstructive lung disease[8,9] Women who smoke have a greater degree for ectopic pregnancy and miscarriage[10]. The following are health effects of smoking on young adults according to WHO:

Teens who smoke are three times more likely than nonsmokers to use alcohol, eight times more likely to use marijuana, and 22 times more likely to use cocaine. Smoking is associated with a host of other risky behaviors, such as fighting and engaging in unprotected sex.[11]

On average, someone who smokes a pack or more of cigarettes each day lives 7 years less than someone who never smoked[12].

Teenage smokers are more likely to have seen a doctor or other health professionals for an emotional or psychological complaint[13]

Tobacco use is very common in Pakistan and is still consumed in a variety of ways, like cigarette smoking, chewing tobacco, cigars etc. In addition to these, tobacco is smoked in unique local ways, which include "Beedi" (Tobacco rolled in dry leaves) and "Hookah" (Hubble - Bubble), and "Sheesha" which is an upcoming trend, especially in the higher social classes.[14]

In Pakistan, it is estimated that the prevalence of tobacco smoking is 36% for males and 9% for females. Among young adults especially the university students in Pakistan, the prevalence of smoking is 15% with the majority being male smokers[15]. Approximately 1,200 children start smoking everyday[16]. This represents a huge impact not only in terms of economic costs but it is slowly depriving the country of a healthy workforce and increasing the burden of disease in the already overburdened health sector. The reason young people start to smoke is complex and multi-faceted. It includes a host of interacting biological, genetic, psychological, economic and social variables. Arguably the most modifiable determinants are social and environmental in nature, including exposure to smoking by parents, siblings, friends, and members of the general public[17].

Numerous authors have observed that a young person's decision to smoke is directly influenced by peers' smoking behaviour[18].

Exposure to smoking in private and public places may also influence tobacco use initiation, maintenance, and cessation.[19]

A study investigates smoking habits and attitudes towards smoking in general practitioners, consultants at a university hospital, medical students and students of health policy and management (H.P.M). An anonymous, self-administered postal survey was used. 38% of general practitioners, 27% of the consultants, 18% of the medical students and 31% of H.P.M. students are current smokers.

All the health professionals can contribute to tobacco control[20]. Community usually views physician as exemplars and as such their office and hospital should be a model of non-smoking behaviour[21]. They also serve as providers of support, information and encouragement in helping patients to achieve such a goal[22]. For these reasons and more, it is essential that doctors themselves don't smoke, medical students and students of health policy and management (H.P.M.) However, marked deficits have been found in the amount and type of training medical professionals receive in smoking cessation counseling with little attention paid to determination of effective training methods[23].

MATERIALS AND METHODS

It was an observational cross sectional study conducted at Nishtar Hospital, Multan over a period of three months Jan. to March 2012.A total of 240 male doctors,10 from each ward were selected with there informed consent. A structured questionnaire was

designed. Data was collected and analyzed using EXCEL and SPSS.

RESULTS

Out of 240 participants doctors,98(41.%) were smokers and142(59%) were non-smokers 41% of doctors at Nishtar Hospital Multan smoke. (Table-1). Among smokers,168(69.8%) belonged to age group 20-30 years, 60(25%) had age between31-40 years and only12(5.0)% were 51-60 years old. (Table-2). 70 (71.4%) smokers belonged to urban areas and 28(28.6%)belonged to rural areas. (Table-3). 76(77.6%) smokers belonged to literate families and 22(22.4%) belonged to illiterate families (Table-4). 38(38.8%) smokers started smoking before joining medical school and60(61.2%) started smoking after joining medical school (Table-5). Among the 98 smoker doctors 52(53.2%) smoked 6-10 cigarettes per day (Table-6). Within smokers, there was an increase frequency of hypertension (20.4%), IHD (8.2%) and lung diseases (20.4%) (Table-7). Among smokers, 44% gave positive history of smoking in friends, 34.1% gave positive smoking history of their fathers, 17.1% gave smoking history of their brothers and 4.8% about their grandfathers. Also among non-smokers, 52.2% gave positive smoking history of their friends (Table-8).

Table No.1: Frequency distribution of smokers and non smokers

Variable	No	%age
Smokers	98	41.00
Non-Smokers	142	59.00

41%doctors of Nishtar Hospital,Multan smoke

Table-2: Frequency distribution according to age

Age	Smoker (%)		Non-Smoker (%)
	No.	%age	No. %age
20 – 30	168	69.8	84.5
31 – 40	60	25	09.9
41 – 50	00	00.0	05.6
51- 60	12	5.2	00.0

* Most of the smokers belong to age group of 20-30 years

Table No.3: Frequency distribution of smokers according to residence

Residence	No	%age
Urban	70	71.4
Rural	28	28.6

*The data show, 71% of Smoker doctors belong to Urban areas

Table No.4: Literacy level of parents

Literacy Level	Smokers		Non-Smokers	
	No.	%age	No.	%age
Literate	76	77.6	92	65
Illiterate	22	22.4	50	35

*Majority of Smoker doctors (77%) belong to Literate families

Table-5: Time of starting smoking

Time	No	%age
Before joining Medical School	38	38.8
After joining Medical School	60	61.2

*Fairly good number of doctors started smoking after joining Medical School

40.7% doctors (smokers and non-smokers) take smoking as 'Just a habit', 29.6% think it as 'A stress relief', 14.8% as 'Relaxation' and 3.7% as 'Concentration'(Table-9) 49% smokers smoke Outdoors and 19% smoke Indoors and 13.7% at all places (Table-10). 62% smokers tried to quit smoking but among those (Table-11)., 73% stayed off for less than 3 months and 27% for more than 3 months (Table-12).

Table No.6: Number of cigarettes smoked per day

No. of Cigarettes	No.	%age
0 – 5	8	8.1
6 – 10	52	53.2
11 – 15	12	12.2
16 – 20	16	16.3
>20	10	10.2

*More than 50% doctors smoke 6-10 cigarettes per day

Table No.7: Frequency distribution of diseases among smokers and non-smokers

Disease	Smokers (%)	Non-Smokers(%)
Hypertension	20.4	11.3
IHD	8.2	7
Lung diseases	20.4	4.2

*Incidence of Hypertension and Lung diseases is more common in smokers

Table No.8: Frequency distribution of smoking among friends and family

H/O Smoking	Smokers (%)	Non-Smokers(%)
Friends	44	52.2
Father	34.1	27.5
Brothers	17.1	12.5
Grandfather	4.8	7.5

* A smoker decision to smoke is directly influenced by peers' smoking behavior

Table No.9: Frequency distribution of likes about smoking

Like About Smoking	No.	%age
Just a habit	33	40.7
Concentration	3	3.7
Stress-relief	24	29.6
Relaxation	12	14.8

*40% doctors take smoking as 'Just as a habit'

Table No.10: Frequency distribution according to place of smoking

Place	No.	%age

Indoors	20	19.6
Outdoors	50	49
Work	8	7.8
Driving	6	5.9
All places	14	13.7

*More than 50% doctors prefer to smoke outside

Table No.11: Frequency distribution of smokers who tried to quit smoking

Tried to Quit	No.	%age
YES	60	62
NO	38	39

*62% smoker doctors tried to quit smoking

Table No.12: Frequency distribution of time period smokers stayed off from smoking

Time Period	No	%age
>3 months	16	27
<3 months	44	73

*Unfortunately, 73% of those who tried to quit could not keep themselves off for even 3 months

DISCUSSION

All the health professionals can contribute to tobacco control[20]. Doctors have always had an important responsibility to convince their patients not to smoke. Community usually views physician as exemplars and as such their office and hospital should be a model of non-smoking behavior[21]. They also serve as providers of support, information and encouragement in helping patients to achieve such a goal[22].

We took doctors as the focus of our study as the attitudes and practices towards tobacco use of these health professionals can influence future policies and practice. If the doctors are smoking, then the credibility of anti-smoking messages to the public is lost. Medical doctors are a group that should be more aware than general population about the health hazards associated with smoking.

There is a high prevalence of smoking among doctors and smoking is on rise in Pakistan. According to a study published in American Journal of Preventive Medicine, in the year 2007, 40.7% doctors are smokers[24.] our study also shows 40.8% doctors of Nishtar Hospital are smokers.

A research carried out by Ioic Jessar in 2005 tells 28.7% started smoking before 40 years[25]. Whereas our research tells 69.4% smokers are in 20-30 year age groups.

A survey done among French general practitioners indicates that 84.3% doctors smoke less than 15 cigarettes per day but in our study, 50% doctors smoke less than 15 cigarettes per day.

According to a study on Greek doctors, 41% doctors started smoking after joining medical college[26]. But our study shows 61.2% started smoking after entry in medical college.

According to our study, 50% doctors smoke outdoors but a study highlights only 30% doctors smoke outside[26].

Our research tells 62% tried to quit smoking but some study showed only 37% usually try[21]. This attitude may become a reason in the next few months to quit smoking. A survey indicates 68.35% doctors consider smoking a major threat to health problem[27], and our study shows similar results i.e. 67%. This is very interesting fact that majority of subjects in our study agreed on one point that 'Smoking is harmful for one's health'. This attitude shows very healthy trend that smokers could not deny this fact that smoking is injurious to health'.

According to a study in Saudi, friends influence to smoke about 70% but in our study 52%. Most doctors have 1st degree relatives who are smokers according to a study carried out in Malaysia and our study reveals relatives are second to friends. This shows peer pressure also is an important reason to start smoking, it has been observed most doctors are influenced by their friends instead of their parents. Another study in Saudi tells that 51% smoke for stress relief[28]. but according to our study, 30% smoke for stress relief. Majority of doctors in Nishtar Hospital consider smoking as 'Just a Habit'

CONCLUSION

Most of the smoker doctors are young, from urban areas, have literate families and tell positive history of smoking in their friends. Time of start of smoking is after joining medical school. Most doctors smoke outdoors and like smoking as 'Just a habit' but also keeping knowledge for its 'Health problems'. Doctors try to quit smoking but unfortunately majority of them keep themselves stay off for less than 3 months.

Recommendations:

Tobacco caused 100 million deaths in the 20th century. If current trends continue, it will cause up to one billion deaths in the 21st century.

Unchecked, tobacco-related deaths will increase to more than eight million per year by 2030. More than 80% of those deaths will be in low- and middle-income countries.

From the start of the course, students should be educated about the physiological, pathological, social and moral hazards of cigarette smoking.

Anti-smoking campaigns should be accelerated using print and electronic media.

Smoking in college, hospital and hostel premises should be strictly prohibited.

Tobacco taxes are the most effective way to reduce tobacco use, especially among young people and poor people. Advertising restrictions should be observed.

According to WHO, the six MPOWER measures to control Tobacco use are:

1. Monitor tobacco use and prevention policies
2. Protect people from tobacco use
3. Offer help to quit tobacco use
4. Warn about the dangers of tobacco
5. Enforce bans on tobacco advertising, promotion and sponsorship
6. Raise taxes on tobacco

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Original Article

Medical Students Lifestyle and Health Related Behavior: A Survey from Nishtar Medical College Multan

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ABSTRACT

Background: The health status of people significantly depends upon their health related behavior and lifestyle. Medical students as a distinct and adolescents segment of our population need to address their health and lifestyle problems. This is a unique group of people with special wishes. Our survey aims to identify the lifestyle and behavioral patterns in this group and later come up with issues that demand special attention.

Objective: To determine the Medical Students Lifestyle and Health related Behavior in Nishtar Medical College Multan

Study Design: Cross sectional Descriptive study

Place and Duration of Study: This study was conducted at the Nishtar Medical College Multan from 01.01.2011 to 31.01.2011.

Materials and Methods: There was a non probability convenient sampling A survey was performed in one boy's hostel and one girls' hostels selected randomly. An interview base semi-structured questionnaire proforma was used to collect the data from willing medical students of 4th year MBBS. One hundred and five students (male: 49 & female: 56) residing in Hostels in Nishtar Medical college Multan, were included in the study.

Results: Females were more depressed than males and had more sleep problems and taking the unhygienic junk foods. Quite a few of them (7.1%) were involved in substance misuse and addictions. Nine percent male and 1 % female students were currently smoking cigarettes. Peer pressure was the most common reason (56.1%) to start smoking. As regard the physical exertion was concerned, 53.10 % male and 37.5 % female did exercise half an hour per day five days a week and were of opinion that physical exercise was essential for health.

Conclusion: Majority of the student's lifestyle and health related behavior was not healthy. Insufficient sleep, depression and smoking were the leading unhealthy behaviors among the respondents. Families can play an important role to help the students live a healthier life. Further research studies should be carried out to emphasize issues of concern and achievable solutions in the medical students. A health education campaign should address properly in the students to change their lifestyle and health related behavior.

Key Words: Health related behavior, Lifestyle, Eating habits, Physical activities, Addiction.

INTRODUCTION

Medical student population and health of Medical students is a very special issue and is the focus of interest worldwide for the parents. The demands on young adolescents are new and unmatched; their parents could not have predicted a lot of the pressures they face. How we help youth meet up these demands and provide them with the kind of education, skills and attitude they will need in a changing environment, will depend on how well we are aware of their world. [1]

The population aged 18–24 in Pakistan was estimated to be approximately 27 million in 2000, and it is expected to continue to increase, reaching 44.6 million in 2020. This is an increase of 39 percent in just 20 years. This age group accounts for almost one quarter of the population in Pakistan and the peak number of youth will be reached in the year 2035. [2]

The fundamental data on education among adolescents shows that they are not receiving the adequate schooling and capability building to prepare for the future· [2] Several health related behaviors (e.g. Smoking, alcohol) as well as health ornamental behaviors (e.g. Physical exercise) are adopted in adolescence and they often persist into adulthood. [3]

The most frequently reported behaviors in this population include such as watching TV, playing video games, beating others, smoking and drinking alcohol, as lack of sleep, swearing, throwing things, and vandalism. [4, 5, 6]

Moreover, considerable gender differences can be found with relation to health-related behavior, both in adults and in adolescents. Usually, males exhibit healthier-risk and less health-protective attitude than females. [7, 8] However; in recent years some studies have depicted a remarkable increase in smoking among females. [9, 10]

With increasing evidence that chronic insufficient sleep results in negative daytime consequences e.g. Daytime sleepiness, depressed mood[11, 12] interventions designed to overturn adolescent delayed sleep timing may help ease these problems. [13]

Adolescence often turns away from parents and health care providers towards peers for support, guidance and management of their life. However, a brief look at the accessible information is therefore important to identify and highlight the health, lifestyle and behavioral issues of the adolescents and possible ways to promote a healthier lifestyle in this population. The purpose of the study was to make clear the lifestyle and behavior of the medical students and to identify the major health risk behaviors in this age group.

MATERIALS AND METHODS

A semi structured questionnaire was used to carry out the survey about lifestyle and health related behavior. One hundred and five students were interviewed who were residing in the hotels in Nishtar Medical College Multan. All the respondents were approached whoever came in first contact from a hostel randomly selected from all boys' hostels and one of all girls' hostels. Data collection was continued for four weeks during the month of January 2011. Interviews were conducted by one male and one female doctor, who were also involved in designing the questionnaire.

Variables Measured: The common health and lifestyle behavior variables measured are as follows:

- Hygienic practice
  Washing hands
  Brushing teeth
- Eating habits
  Breakfast Intake
  Fruit intake
  Junk food intake
- Physical exercise.
- Smoking prevalence: smoking is there or not in the respondents.
- Often' feel depressed / anorexic: the term "often" included at least twice every week.
- Bedtime: / Sleep:
  Before midnight, after midnight

Data Analysis: The data were entered in SPSS (Statistical Package for Social Sciences) version 16 and analyzed accordingly. Descriptive statistics included frequencies and percentage for continuous and categorical variables. The results were presented in the form of figure and tables.

RESULTS

A total 114 students including males and females were approached in this survey, nine students (8.5%) declined to participate; therefore the response rate for the study was 91.5%. The total numbers of medical students who took participation in the interview and used for analysis were one hundred and five. About forty seven percent of the respondents were males and 53% were female. The median age of the respondents was 21 years.

As far as satisfaction regarding living conditions in hostel life was concerned, 65.7% students were not satisfied with living conditions whereas 7.6% were satisfied and 26.7% were uncertain.

Hygienic Practices: As regards hygienic practice, 79.6 % males and 80.4% female students washed their hands regularly before taking meal. Only 14.3 % male and 19.6 % female students brushed their teeth twice or thrice a day.

Eating Habits: Regarding the eating habits, the majority stated that they did not take breakfast and were in the habit of eating from the college canteen. The reasonable percentage of respondents stated to be indulged eating unhealthy, junk foods and carbonated drinks. They considered their eating habits as being 'just rights' and a scarce percentage of respondents used fruits, milk and yogurt. (Table 1)

Table No.1: Percentage of different habits of eating n = 105

Activity	Gender	Number (%age)
Taking breakfast daily	Male Female	7 (14.3) 12 (21.4)
Taking meals regular	Male Female	27 (55.1) 29 (51.8)
Taking Junk food daily	Male Female	13 (26.5) 17 (30.4)
Taking 3 or more Carbonated drinks per day	Male Female	26 (53.1) 22 (39.3)
Taking fruits daily	Male Female	8 (16.3) 8 (14.3)
Taking milk/yogurt daily	Male Female	5 (10.2) 17 (30.4)

Females were more depressed than males and had more sleep problems. Substance abuse and other addictions were also documented in a very little number of respondents (Table 2)

Table No.2: Sleep Pattern & use of Anxiolytic Drugs n - 105

Activity	Gender	Number (%age)
Time of going to bed up to 12.00 midnight	Male Female	16 (32.6) 30 (53.5)
Time of wakening (before Fajar prayer)	Male Female	15 (30.6) 27 (48.2)
Taking Anxiolytic drugs	Male Female	3 (6.1) 4 (7.1)

Smoking among the Students: Almost nine percent of male students and 1 % of female students were smoking cigarettes currently. A significant majority were aware of the hazards associated with smoking. Smoking among the respondents is detailed in Table 3.

Table No.3: Percentage of smoking among respondents n - 105

Question	Response	Number	% age
Smoke Cigarettes Currently		Male (12) Female (1)	8.7 1
Smoke (cigarettes / day):	1–5	4	3.8
	6–19	7	6.6
	> 20	2	2
Why started smoking?	Peer pressure	10	9.5
	Father smokes	2	1.9
	Get rid of stress	1	1

Physical Exercise: As regards physical exercise, 53.10% of male and 37.50 % of female were stated to do physical exercise for half an hour five days of the week, while the large majority as detailed in the figure were fond of a sedentary lifestyle. (Figure 1)

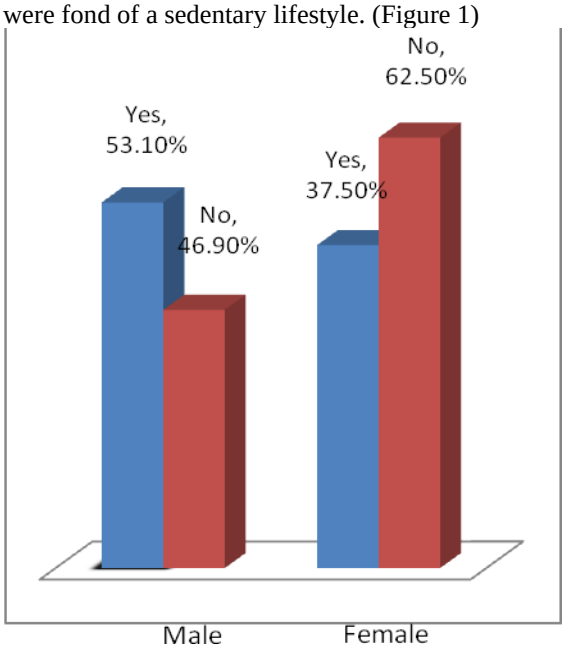

Figure 1: Physical Exercise (30 minutes per day)

DISCUSION

The most commonly reported health and lifestyle risk behaviors among our respondents were unhealthy and unhygienic eating, inadequate sleep, lack of physical exertion,

and smoking was the leading unhealthy and risky behaviors among the medical students. The least prevalent health risk behaviors were use of anxiolytics.

WHO's report that at least 20% of adolescents will experience some form of mental illness mood disturbances, eating disorders. [14] Dental care including brushing of teeth and preventive dental checkups is considered part of a healthy lifestyle. [14] The status of dental care among the medical students needs improvement.

A study carried out among Lebanese university students; it was found that they had better eating habits as 53% of female were taking breakfast as compared to only 12% in our study. Similarly 61% of Lebanese students used to take their meal regularly whereas only 29 % in our study. The findings were not inconsistent with our study. [15] A study at Alexandria University hostels, it was found that 86% ate unhealthy diet, 34% were physically inactive, 17.5% of male students were current smokers & 32% had poor sleep behaviors. These findings did not correlate well with our study[16]. Our results showed that (79%) of the respondents were getting less sleep daily, which is a cause for concern and further inquiry. [17]

The addictive behavior most common amongst medical students was cigarette smoking. Almost half of the 150 million adolescents who continue to smoke will finally end up to their graves by tobacco related diseases. [18]

Smoking among adolescents may also be an indicator of many other lifestyle and health issues.[19, 20] Francis; et al.[21] had reported that adolescents who smoke were at higher risk of psychopathology versus to adolescents who were non-smokers.[22]

There was proof that medical student's decisions to smoke were strongly influenced by the family and friends. Our study also supports the fact that peer pressure was the most common reason to start smoking. Having a friend who smoked might be an influence to initiate smoking. [23] Ten percent of the medical students in our study started to smoke since their associates and friends were smokers. Introducing programs in educational institutions regarding the hazards of smoking be carried out. Moreover bans on advertising companies and an increase in the price of tobacco products must be practiced.

A study carried out among students at university of Brazil, [24] which showed a similar pattern as the present study that male students were regular in physical exercise as compared to female students. Hence there is a strong need to encourage students to devote some time to extracurricular activities.

It was inspiring to note that more than half of the respondents (57.7%) exercised on a regular basis. However we should strive to create further understanding regarding the significance of exercise and physical activity, since very few of them were of the opinion that exercise is essential for health.

This study provided a valuable local point of view with regards to the medical student's lifestyle and behavior. Interventions have been found to be successful for lifestyle change in the student population. [25] significant data are available in favor of lifestyle interventions leading to a better health outcome. [26]

Strengths and Limitations: A very limited research has been done regarding the assessment of medical student's lifestyle and health related behavior; our study is the first of its kind to the best of our knowledge.

The present study at the same time had a few limitations. We used non probability convenience sampling to draw our sample; this method is inferior to probability sampling in representation of the population, and this limits the validity of the study

CONCLUSION

Unhealthy and unhygienic eating, inadequate sleep, lack of physical exertion, smoking and use of anxiolytic drugs were the leading unhealthy and risky behaviors

among the medical students. The students as an adolescents need to be treated as a distinct segment of our population and we suggest that the families of these students can prove to be a great source to help them, live a healthy life. The study has attempted to highlight various areas of concern with respect to medical student's lifestyle and health related behavior. Health promotion and change in lifestyle programs are required for good health of the medical students

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Original Article

Incidence of Low Diastolic Blood Pressure as a Sign of Elderly and a Cardiovascular Risk Factor in the Early Age Post Menopause Women

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ABSTRACT

Objective: To determine the post menopausal changes of diastolic blood pressure in the early age menopause women.

Study Design: A comparative and cross-sectional study.

Place and Duration of Study: This study was conducted at the Department of Physiology BMSI., JPMC, Karachi in collaboration with the Abbassi Shaheed Hospital and National Institute for Cardiovascular Diseases, Karachi from Oct 2009 to June 2010.

Materials and Methods: This study included a total of 100 women, 50 with early age post menopause and 50 with normal age post menopause. For the statistical analysis , the degree of probability was computed by comparing the calculated value of "t" with tabulated value in the table of "t" distribution against the degree of freedom.

Results: Diastolic blood pressure was found to be significantly increased with a P-value of <0.001 in the early age post menopause women.

Conclusion: This suggests that an early age post menopause is more likely to develop a sign of elderly and a cardiovascular risk factor such as decreased diastolic blood pressure.

Key Words: Early age post menopause, Normal age post menopause, Diastolic blood pressure (DBP), A sign of elderly, Cardiovascular (CV) risk factor, Cross sectional study.

INTRODUCTION

In 1998, Tuomilehto et al., indicated that low DBP alone was a significant predictor of CV and non-CV mortality among persons aged >50 years (most >70 years). However, the evaluation of the underlying pathophysiological mechanisms was limited, particularly regarding hemodynamic parameters. Low DBP could also be a marker of cardiac function. Indeed, in the population of North Karelia, especially in patients >70 years of age, the DBP–mortality relation was considered as a direct main result of cardiac failure, and there was an age dependence regarding the effect of low DBP on mortality.[1]

In the recent years, in subjects >50 years of age with advanced renal failure, Blacher et al[7] showed that increased aortic stiffness and low DBP were independent predictors of CV risk. Low DBP could also be a marker of cardiac dysfunction.[2]

A low diastolic blood pressure has been associated with increased cardiovascular mortality.[3]

According to Bots et al, the following proposed mechanisms underlie this phenomenon: a low diastolic pressure that compromises coronary blood flow, a low diastolic pressure that is due to deteriorating health, and a low diastolic pressure that is a consequence of stiffening of the large arteries. [4]

Natural menopause is recognized to have occurred after 12 consecutive months of amenorrhea for which there is other pathological or physiological cause. Early age menopause is a broader term to include those women who have experienced menopause under the age of 45 years.[5] Low or absent estrogen and high levels of FSH and LH, is the picture of menopause.[6]

In Pakistan, the mean age at menopause has been found to be 49 years (+/-3.6 years) in rural areas and 47 years in urban areas.[7] Whereas mean age at menopause in rural chandigarh (India) is 48.22+/_2.47 years and in urban is 49.30+/-2.80 years. [8] Menopause before 45 years of age, is considered to be early age menopause .[9]

After age 60 years, stiffening of the large arteries leads to decreased diastolic pressure and increased pulse pressure, and this changes the relationship between low diastolic pressure and cardiovascular disease.[10]

Menopause may interact with or accelerate event of normal ageing. Early menopause may be a risk factor for early mortality from diseases related to decreased estrogen levels and may promote increased incidence of osteoporosis, heart diseases, diabetes, breast cancer, osteoarthritis and autoimmune diseases .[11,12,13]

MATERIALS AND METHODS

This was a cross sectional and comparative study conducted in the department of B.M.S.I., J.P.M.C. in collaboration with Abbassi Shaheed Hospital and National Institute of Cardiovascular Diseases, Karachi.

A total sample of 100 post menopausal women, was selected for the study. 50 women with a history of

cessation of menstruation since 2 years, ages between 40 – 45 years, were selected as early age post menopause. Whereas, 50 women as normal age post menopause consisting of women with a history of cessation of menstruation since 2 years ,ages between 50 – 58 years.

Systolic blood pressure and diastolic blood pressure were recorded by mercury type of sphygmomanometer. The blood samples of those subjects who fulfilled the criteria were collected after an overnight fasting of 10-12 hrs. About 4 ml of blood was drawn from venepuncture after all aseptic measures while the subjects were sitting in upright position. 2 ml blood was taken for serum cholesterol and hormonal analysis, each. After centrifugation, serum were stored at -20 degree centigrade.

Serum total cholesterol was estimated by the enzymatic colorimetric method. Serum follicle stimulating and serum leutinizing hormones were measured by enzyme linked immunoassay.

Statistical Analysis: The degree of probability was computed by comparing the calculated value of "t" with tabulated value in the table of "t" distribution against the degree of freedom. The difference with mean values of the two groups was regarded as statistically significant, if the P-value was less than 0.05 and it was taken as highly significant if P-value was less than 0.001. Correlation coefficient was detected using Pearson coefficient of correlation SPSS-10. For data feeding the computer package Microsoft Excel was used. Only P-value (<0.05) are considered significant.

Inclusion Criteria: Non obese, non hypertensive and non hysterectomized women who were experiencing menopause, were included in our study. All the subjects were having normal electrocardiographs, fasting blood sugar under normal limits and heamoglobin ≥ 11 g/dl. Overall , they were apparently healthy subjects.

Exclusion Criteria: With history of smoking, any malignancy or psychiatric disorder, were not included in this study. Subjects on hormone replacement therapy and known cardiac patients, were also excluded from this study.

RESULTS

Table 1 shows the comparison of age, height and weight between normal age menopause and early age menopause women.

Age was significantly higher in early age menopause (42.08±0.36 years) than the normal age menopause (53.52±0.44 years) women, whereas height and weight show no statistical difference.

Table 2 shows that the mean diastolic blood pressure was significantly higher with a P value of <0.001 in early age menopause (74.08±1.53 mmHg) than in normal age menopause (89.32±1.35 mmHg) women.

Table 3 shows that the mean systolic blood pressure remained insignificant on both sides . Mean serum cholesterol was significantly higher in EA group (178.82±8.95 mg/dl) than in MA group (149.82±8.85 mg/dl) with a P-value of <0.05. The mean FSH was significant in early age menopause (77.22±5.16 µlU/ml) as well as to the mean value in normal age menopause (61.93±4.15 µlU/ml).There was no statistical difference as far as the mean LH values concerned as they remained non significant on both sides.

Table No.1: Comparison of age, height and weight in normal age menopause and early age menopause. (Values are expressed as Mean ± SEM)

Variables	Normal Age Menopause	Early Age Menopause
Age(years)	53.52±0.44	42.08±0.36*
Height(Meters)	1.55±0.007	1.56±0.008
Weight(kg)	63.52±1.36	64.30±1.51

*showing a significant difference at P-value<0.05

Table No.2: Comparison of diastolic blood pressures in normal age menopause and early age menopause. (Values are expressed as Mean ± SEM)

Variable	Normal Age Menopause	Early Age Menopause
Diastolic Blood Pressure mmHg	89.32±1.35	74.08±1.53**

**showing highly significant difference at P-value <0.001

Table No.3: Comparison of systolic blood pressures, total serum cholesterol, follicle stimulating hormone (fsh) and leutinizing hormone(lh) between normal age menopause and early age menopause (Values are expressed as Mean ± SEM)

Variables	Normal Age Menopause	Early Age Menopause
Systolic Blood Pressure (BP) mmHg	124.62±2.35	124.38±1.98
Total Serum Cholesterol	149.82±8.85*	178.82±8.95*
FSH(µlU/ml)	61.93±4.15*	77.22±5.16*
LH(µlU/ml)	54.74±3.31	55.36±4.50

**showing highly significant difference at P-value <0.001

*showing significant difference at P-value<0.05

DISCUSSION

Christensen et al., assessed various data show that not all the subjects with the same elevation in SBP have the same CHD risk ; those with lower DBP and therefore wider PP, have greater CHD risk, possibly due to great pulsatile stress (Christensen, 1991).[14]

High systolic blood pressure (SBP) increases vascular beds, a determinant of left ventricular (LV) geometry, whereas low DBP may reduce coronary perfusion

pressure. [15]

According to Glynn et al.(2000), after having adjusted for systolic blood pressures and confounding variables (like pulse pressure), the apparent increased risk of cardiovascular disease, is associated with low diastolic blood pressure.[16]

In the study of Protogerou et al. (2007) , the first prospective investigation in an elderly population was performed, in which pressure wave reflections, arterial stiffness, cardiac function, and TPR were measured to investigate the potential pathophysiological association of low DBP and mortality. They showed that, in this very aged population, a J-curved association between DBP and mortality (all-cause or CV) was present. [3]

Under these circumstances, the current study was performed to analyze and compare the difference of blood pressure as well as other variables, in two different age groups of menopause women.

First group i-e normal age menopause group had females with a history of at least two years of amenorrhea or post menopause and ages between 50-58 years taken as control group, and the second group consisted of females of early age menopause with a history of at least two years of amenorrhea or post menopause and ages between 40-45 years of age.

Our study shows the incidence of low diastolic blood pressure as a sign of elderly and cardiovascular morbidity in the early age menopause group, is in accordance with second tertile of the study done by Protogerou et al. (2007) as well as with the study of Glynn et al.(2000).[3,16]

The results of our study suggest that the cardiovascular risk factors were increased with the women who underwent early or premature ovarian failure i-e the early age menopause group as compared to the women with the normal age menopause group. These findings were in agreement of the studies done by Fioretti et al .(2000) and Atsma et al .(2006).[17,18]

According to Kok et al.(2006), blood vessel stiffness increases over time whereas diastolic blood pressure tend to decrease. The women with decreasing diastolic blood pressure level probably had some degree of hardening of arteries". This is like an explanation for the fact that "beneficial" changes in diastolic blood pressure did not result in a statistically significant increase in menopausal age. This observation is also in agreement with our study.[19]

In our study, follicular stimulating hormone and leutinizing hormones levels were significantly higher in both menopausal groups showing an apparent menopausal status in them whereas these levels were decreased in the reproductive or control group, and these observations are in accordance with the findings of the study done by Barnett et al.(2004).[20]

Our group of early age menopause also had as a significant increase in the serum cholesterol in accordance with the findings of the study done by Knauff et al.(2008).[21]

CONCLUSION

Regarding this comparative and cross-sectional study, we conclude that the decreased values for diastolic blood pressure in the early age post menopause group, show the sign of elderly as a cardiovascular risk factor for the early age post menopause women than the naturally occurring normal age post menopause women.

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