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Editorial

How to Check Brain Drain from Pakistan

Dr. Azhar Masud Bhatti
Editor in Chief

Most of Pakistani students going abroad for higher, or specialized, education every year, very often never return to their homeland. Though Pakistan has a number of institutions for higher education, various students prefer going abroad.

Presently, there are 68 public universities and 56 private universities in Pakistan. Eight public and 18 private institutions have a degree-awarding status. According to a BBC report, Gallup-Pakistan survey indicates that not only qualified professionals and university graduates want to leave the country, but even semi-skilled and unskilled workers want to migrate in search of better prospects. About 62 per cent of the adults interviewed for the survey expressed the desire to go abroad to work, while 38 per cent say that they would prefer to settle permanently outside the country. This shows that many Pakistanis are gradually losing faith in the country's economic future. Higher Education Statistics Agency (HESA) statistics of July, 2007, show that the total number of Pakistani students enrolled in the UK was 9,335 in 2006- 2007, with 6,205 students in postgraduate and 3,130 in undergraduate courses. The number increased to 9,840 in 2007-2008, out of which 6,550 Pakistani students were postgraduate and 3,290 were under-graduate.

There are mainly two types of students who go abroad: First are our absolute brightest and most talented students; they generally go to elite schools and are fortunate enough to not only attain the best education the country or even the world has to offer, but also to excel at it. These students set their sights on the world's best universities such as Cambridge, Harvard, Yale or Oxford. While not everyone makes it, they still wind up going abroad to their "safe choices" of universities, which might not be great but are still outside of Pakistan. It is not just about education, but also about a lifetime experience. They either get scholarships, or their parents are able to arrange for their expenses on their own, while a few struggle to find other ways.

The elite educational institutions charge them heavily for their "services" to enable them to make this journey, often making false transcripts and writing fabricated stories about them as recommendations.

One often sees advertisements of these schools boasting about how many students they got admitted to universities abroad. Many of these students do hope to come back to Pakistan after attaining their education and changing things, but frankly that seldom happens.

The second type is made up of students who are from middle or even lower middle class. These students have not had a chance to obtain a quality education, nor have their financial circumstances allowed it. These students have a dream of going abroad, not primarily to study, but also to work, to sustain themselves and, perhaps, send some money back home. Lured by dreams of a utopia abroad, they become victims of "agents" who, in the interest of making money, send these students to mediocre/low level or even non-existent universities. They mostly end up staying illegally abroad, away from their families and are forced to do menial labour jobs at low wages.

According to Ali Moeen Nawazish, the Youth Ambassador of the Geo/Jang Group, the mass demand for going abroad is primarily fuelled by a lack of opportunities both in number and quality in Pakistan. The favourite destinations of the students are situated mainly in Europe, North America, China and Australia. Every year, nearly 10,000 foreign student visas are granted in Pakistan. There are nearly 10,000 Pakistani students studying in the United Kingdom. All in all, between 2004 and 2008, as many as 42,000 Pakistani students were admitted into the UK. As of 2010, there were 5,222 Pakistani students in the United States, putting Pakistan among the top 25 countries sending students to the US. There are some 1,000 Pakistani students in Cuba, all of whom are studying medicine on scholarships provided by the Cuban government. There are over 2,000 Pakistani students of medicine in the Central Asian state of Kyrgyzstan. China also attracts a large number of students from Pakistan, with 2006 estimates putting their number well over 1,000; in Xinjian alone, there are over 500 Pakistanis in universities. Another most favoured destination for Pakistani students is Australia. There were 1,626 Pakistani students in Australia in 2005; in entirety, some 5,000 Pakistani students chose the country for studies in 2011.

There is another aspect of the issue also, and that is the brain drain. We are losing our best brains to the developed nations fast, and it is unfortunate that no serious steps are being taken to check the trend. Successive governments have made no well-thought-out policies in this regard. The government does not persuade Pakistani students to come back and serve their country. They are not offered proper jobs, according to their qualifications. According to a British Council report in July 2009, the driving force for all Pakistanis to study overseas is increased employability in a competitive marketplace. This whole map shows that in coming years, people aged between 18 and 38, the age when people prefer to study and make their careers, the trend will continue. There is no denying the

fact that the Higher Education Commission (HEC) is a success story when it comes to the provision of higher education in Pakistan, and it has changed the higher education landscape in the country. However, the government also needs to cooperate more with the HEC in terms of funding. Reducing this brain drain is pivotal for the development of the country as a whole. We need more universities to accommodate the increasing number of students. The HEC needs to ensure quality and regulate higher education especially in private sector ‘business oriented’ universities. There also needs to be an effort towards excellence in research, which is an inherent university feature which we clearly lack in Pakistan. We also need to look to industry to create employment for our graduating students and the government to ensure fair wages.

Pakistan’s neighbouring country, India, is a clear success model in this regard as a BBC documentary showed that most Indian students now prefer to stay in India for higher education than going abroad. This has been fuelled by an intense focus on quality, and a heavy government subsidy for local students, along with employment opportunities. Nobody can say that going abroad to attain an education is wrong; our students should go abroad. But our most talented students not coming back to Pakistan is wrong, especially after having been given the best opportunities in the country.

It is sad that those given the best opportunities are not using them to add value to the country and society.

Secondly, there is no point in paying ten times more for the same quality education that is available in Pakistan. Going abroad is not a magical thing where everything will be better than in Pakistan. There is no point for our students to go to mediocre, or low-level, universities abroad when we can provide them better education here in Pakistan.

Original Article

'Vitamin A' a Potential Teratogen

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ABSTRACT

Objective: To determine the teratogenicity of Vitamin A excess on intrauterine development of thymus in albino rats.

Study Design: Experimental study

Place and Duration of Study: This study was conducted at the Department of Anatomy/ Histopathology, Shaikh Zayed Postgraduate Medical Institute, Lahore from September 2008 to September 2009.

Materials and Methods: Study was conducted with 18 pregnant female albino rats, of Sprague-dawley variety. These female rats were randomly separated into equal groups, A, B and C (n=6). Vitamin A was used in the form of Isotretinoin (13-cis retinoic acid). The dose of isotretinoin used in this study was constant i.e, 2.5mg/kg body weight of rats for every experimental group. Taking the trimester of pregnancy as variable of the study dose was given on 9 (mid trimester) and 17 (late trimester) days of pregnancy to the mother rats. The sample size was obtained by collecting 18 foetuses from each group. Thymuses were collected from the rat foetuses of each group after dissection.

Results: The foetuses of experimental group whose mother rats received the dose of Vitamin A in mid trimester showed thymic ectopia in a significant number of foetuses ($P<0.01$), while dose of Vitamin A given in late trimester caused thymic hypoplasia ($P<0.01$) in fetuses of albino rats. **Conclusion**: It is obvious with these findings that single dose of Vitamin A can cause deleterious effects on developing thymus in albino rats.

Recommendations: Caution must be taken while administration of Vitamin A to a pregnant woman.

Key Words: Vitamin A, Albino rat, thymus, development, teratogenesis.

INTRODUCTION

Vitamin A is an essential human nutrient. It is essential for the maintenance of visual and reproductive function and for proliferation and differentiation of epithelial tissues.[1]

Vitamin A is a generic term used for a large number of related compounds. Retinol (an alcohol) and retinal (an aldehyde) are often referred to as preformed Vitamin A, found in animal food sources, such as liver, kidney and milk.[2]Vitamin A is also found in different vegetables (like carrots, spinach, peas) in the form of carotenoids (especially B-carotene). [3] These carotenoids can be converted by the body into retinal.[8] Retinal can be converted by the body to Retinoic acid, the form of the Vitamin A known to affect gene transcription. Retinol, retinal, retinoic acid and related compounds are collectively known as retenoids.

The effects of retinoids, biologically active derivatives of Vitamin A, are transduced by nuclear receptors, the Retinoic Acid Receptors - RARs (α-β-γ) and Retinoic X Receptors - RXRs (α-β-γ).[5,6]

The recommended daily amount of Vitamin A for male is 3000 IU/day and for female is 2300 IU/day.[7] However Teratology Society (1987) recommended daily intake of 8000 IU/day for pregnant women as maximum intake during pregnancy.[8]Excessive intake of Vitamin A produces a toxic syndrome called hypervitaminosis A.

Vitamin A is widely used in clinical practice to treat Xerophthalmia, dermatological problems, such as acne and psoriasis and chronic infections.[9]

The excess or deficiency of Vitamin A causes abnormal morphological development (teratogenesis).[10] Too much or too little retinoids at the wrong stage or at the wrong time can adversely affects the developing embryo.[11]In the case of excess the teratogenic effects of Vitamin A appears to occur at an undetermined level above 8000 IU/day. Vitamin A is especially harmful during early pregnancy when organogenesis occurs. Embryonic exposure to RA causes a wide spectrum of severe malformation in the offspring of human and rodents.

Due to the known teratogenic effect of retenoids, therapeutic doses are contra indicated during pregnancy.[12] Much of the knowledge about the toxicity of Vitamin-A in pregnancy arose from research with the drug isotretinoin.[8] A constellation of birth defects termed retinoic acid Embryopathy (RAE) resulted from oral administration of 13-Cis-retinoic-acid (isotretinoin).[13]

Several mouse studies have demonstrated potential adverse effects of RA when administered during mid and late pregnancy in mice.[11]

MATERIALS AND METHODS

This experimental study was conducted in Department of Anatomy/ Histopathology, Shaikh Zayed Postgraduate Medical Institute, Lahore.

In this experimental study 18 female rats, weighing about 200-250 g and 6 adult male rats, weighing 250-300 g of Sprague-dawley variety of albino rats were used. They were obtained from National Institute of Health, Islamabad. All animals were kept separately in animal house of the Punjab Postgraduate Medical Institute, Lahore. The food and water was provided ad libitum.

Study Design: After conception 18 female rats were randomly separated in to equal groups, A, B and C (n=6). Total gestational period in rats is of 21 days and each trimester was of 7 days. Vitamin A was used in the form of Isotretinoin (13-cis retinoic acid), given in oral form to the rats by nasogastric tube (N/G Tube). The dose of isotretinoin used in this study was constant i.e, 2.5mg/kg body weight of rats for every experimental group. Taking the trimester of pregnancy as variable of the study dose was given on 9 (mid trimester) and 17 (late trimester) days of pregnancy to the mother rats, while Group A was the control group in this group pregnant rats were given 1ml of olive oil as vehicle.

Sample collection: Cesarean sections of rats were carried out on gestational day 21. Their foetuses were removed, weighed and, killed by euthanasia. Three foetuses from each animal were then selected randomly and labeled as sub groups A1,B1 and C1 respectively. These selected foetuses were then immersed in 10% formalin for ten days and examined under a binocular dissecting microscope for external congenital anomalies. Afterward, their thymuses were dissected under binocular dissecting microscope and weighed then external morphological study of thymus was carried out. These thymuses were then fixed in zenker's solution. After fixation thymus was embedded in paraffin. Serial 5µm sections were cut and stained with hematoxylin /eosin and reticulin stains for detailed histological study of thymus.

Statistical Analysis: Qualitative data was analyzed statistically by Chi-square (X2) method, while quantitative data was analyzed by analysis of variance (ANOVA) using Statistical Package for Social Sciences (SPSS) Version 16.

All the quantitative variables were described by Mean, ± SD and all qualitative variables were described by frequency and percentages. P-value of < 0.05 was considered significant.

RESULTS

The gross congenital anomalies of thymus (small and ectopic thymus) were noticed. In group B1 (mother rats received dose in 2nd trimester), 4 out of 18 thymuses were ectopic (22.2%). Further analysis showed that mean weight of thymus and RTWI was not affected in this group.

Table No.1: Effects of Vitamin A on Gross Appearance of rat thymuses of control and experimental groups

Group	Normal	Abnormal	Total	Gross mal-formations observed	
				Ectopia	Thin thymus
A1	18	0	18	0	0
B1	14	4	18	4	0
C1	10	8	18	0	8
Total	42	12	54	4	8

p < 0.001**

A1: Control Group B1: Mid trimester Group
C1: Late trimester Group
** Highly significant difference(P<0.01)

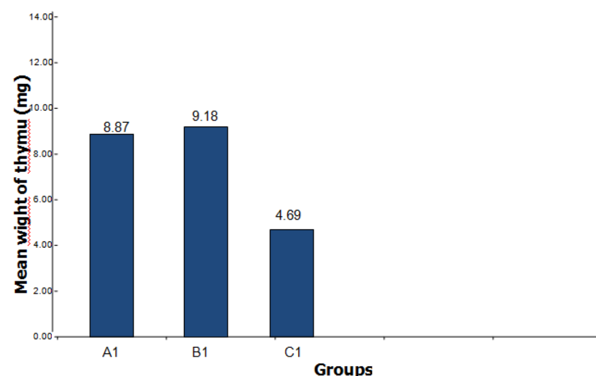

Figure No.1: Mean weight of thymuses of control and experimental groups exposed to Vitamin A during gestation

A reduction in mean thymocyte population was not observed in this experimental group.In group C1 (mother rats received dose in 3rd trimester), 8 out of 18 thymuses were found small and thin (44.4%). The mean weight of foetal thymus in experimental group C1 was significantly reduced when compared with control group A1 (P<0.01).

Table No.2: Weight of thymus (mg) of foetuses of control and experimental groups exposed to Vitamin A during gestation

Groups	Mean Weight	S.D	Minimum Weight	Maximum Weight
A1	8.8667	±1.67650	5.45	12.60
B1	9.1778	±2.89821	4.80	15.20
C1	4.6911	±1.61691	3.18	8.50

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A1: Control Group B1: Mid trimester Group
C1: Late trimester Group
SD: Standard Deviation

Table No.3: Comparison of effects of Vitamin A on Weight of thymus (mg) of control and experimental groups Contrast Tests

Contrast	Value of Contrast	Std. Error	t	df	P – Value
A1 Vs B1	-.3111	0.78917	-.394	27.231	0.696++
A1 Vs C1	4.1756	0.54899	7.606	33.956	0.000**
B1 Vs C1	4.4867	0.78223	5.736	26.648	0.000**

A1: Control Group B1: Mid trimester Group
C1: Late trimester Group
** Highly significant difference(P<0.01)
* significant difference (P<0.05)
++ Non significant difference(P<0.05)
Based on one way ANOVA

Table No.4: Relative tissue weight index of rat foetuses of control and experimental groups treated with Vitamin A during gestation

	Mean RTWI	S.D	Minimum RTWI	Maximum RTWI
A1	0.1670	±0.34880	0.119	0.268
B1	0.1775	±0.57267	0.107	0.320
C1	0.1103	±0.50801	0.074	0.236

A1: Control Group B1: Mid trimester Group
C1: Late trimester Group
SD: Standard Deviation
RTWI: Relative Tissue Weight Index

Table No.5: Comparison of effects of Vitamin A on Relative Tissue Weight Index of control and experimental groups Contrast Tests

Contrast	Value of Contrast	Stdandard Error	t	Df	P – value
A1 Vs B1	-0.0738	0.15805	- 0.467	28.088	0.644++
A1 Vs C1	0.5983	0.14525	4.119	30.114	0.000**
B1 Vs C1	0.6722	0.18044	3.725	33.523	0.001**

A1: Control Group B1: Mid trimester Group
C1: Late trimester Group
** Highly significant difference(P<0.01)
* significant difference (P<0.05)
++ Non significant difference(P<0.05)
Based on one way ANOVA

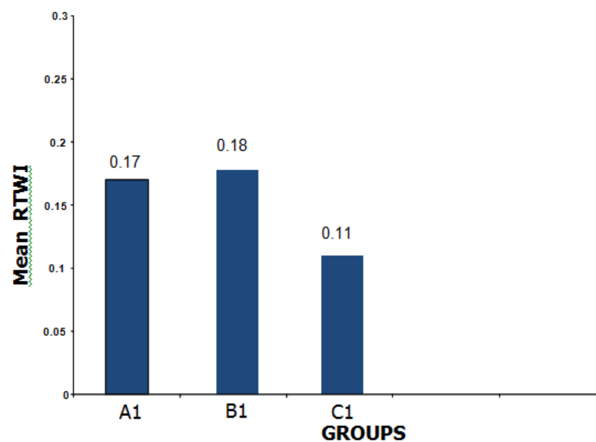

Figure No.2: Relative tissue weight index for thymuses of rat foetuses of control and experimental groups exposed to Vitamin A during gestation

Table No.6: Thymocyte Population in foetal thymuses of control and experimental groups treated with Vitamin A in different trimesters of pregnancy

Groups	Mean/ mm^2	S.D	Minimum/ mm^2	Maximum/ mm^2
A1	32.2778	±6.71088	23.00	44.00
B1	29.0000	±8.11679	20.00	45.00
C1	29.1111	±4.28251	24.00	37.00

A1: Control Group B1: Mid trimester Group
C1: Late trimester Group
SD: Standard Deviation

Table No.7: Comparison of effects of Vitamin A on Thymocyte Population of control and experimental groups Contrast Tests

Cont-rast	Value of Contrast	Standard Error	t	df	P -Value
A1 Vs B1	3.2778	2.48236	1.320	32.840	0.196++
A1 Vs C1	3.1667	1.87640	1.688	28.876	0.102++
B1 Vs C1	-.1111	2.16310	-.051	25.784	0.959++

A1: Control Group B1: Mid trimester Group
C1: Late trimester Group
** Highly significant difference(P<0.01)
* significant difference (P<0.05)
++ Non significant difference(P<0.05)
Based on one way ANOVA

Relative tissue weight index is an important parameter which should also be taken under consideration whenever the weight of tissue is discussed. It was found out that decrease weight of thymus in group C1 was also confirmed by decreased relative tissue weight index of

experimental group C1 as compared to control group A1. A reduction in mean thymocyte population was observed in experimental group C1, but this reduction had no statistical significance.

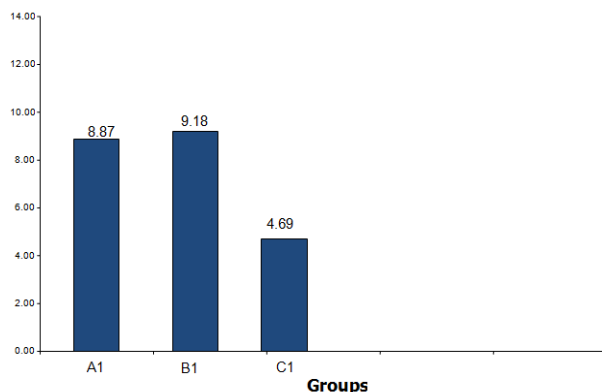

Figure No.3: Mean thymocyte population of experimental and control groups exposed to Vitamin A during gestation

DISCUSSION

Although RA is required for normal embryonic growth and development, it is also a powerful teratogen in excessive dose. Infants born to mothers exposed to retinoids during pregnancy have a 25-fold increased risk for malformations, nearly exclusively of cranial neural crest-derived tissues.[14,15] The neural crest, a transient, multipotential population of cells, originates from the dorsal neural folds, and cells migrate to a variety of sites within the developing embryo. Crest cells move in coherent streams and follow highly defined migratory patterns, a hallmark behaviour of these cells.

The present study was intended to assess the effects of Vitamin A on prenatal development of thymus in albino rats exposed to the drug during various trimesters of pregnancy.

In the current study Vitamin A was used in the form of isotretinoin. It was eminent that even in therapeutic dose, 2.5 mg /kg body weight, given in different trimesters of pregnancy Vitamin A exhibited teratogenic potentials.[16,17]

In this study exposure to rat foetal thymuses to Vitamin A on gestational day 9 (2nd trimester) resulted in ectopic thymus. Retinoids decrease neural crest cell adhesion to the substrate and their ability to migrate; this inhibition is dose dependent. Following in vivo exposure, RA also disrupts migratory pathways such that crest cells end up at the wrong target.[15]

In group C1, dose was given in third trimester on gd:17. In rats during development by the gd:15 thymus migrates into thorax and it increases in weight afterwards. So interference at this stage by Vitamin A on thymic development may lead to hypoplastic thymus, which was evident in group C1. These hypoplastic thymuses had shown significant reduction in weight, insignificant decrease in size of thymic lobules and insignificant decreased thymocyte population. These results coincide with the study of Makori *et al.* who found same hypoplastic thymuses in monkeys exposed to 2.5 mg/kg of 13-cis-RA (isotretinoin). Histological analysis of hypoplastic thymus tissues from exposed fetuses of these monkeys indicated a slight decrease in size of thymic lobes, but no identifiable changes in cellularity.[17]

Researchers have proved that in mice RA causes anatomical and functional thymic anomalies (thymocyte dysmaturation) that are probably related to abnormal expression of HOXA3 and Pax-1 genes.[18]

This study suggests that the administration of RA to pregnant rats results in the rapid transfer across the placenta to the developing embryo and teratogenic effects depends on the dosage and time of gestation.

CONCLUSION

The result of this research work clearly indicates that Vitamin A is capable of having direct influence on developing thymus (thymic ectopia and hypoplasia) even in single dose administration in prenatal period in mid and late trimesters of pregnancy. So caution must be taken while administrating Vitamin A to a pregnant woman.

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Original Article

Frequency of Same Day Discharge and its Feasibility after Transradial Percutaneous Coronary Intervention

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ABSTRACT

Objective: To observe the frequency of same day discharge and its feasibility after transradial percutaneous coronary intervention (PCI).

Study Design: Observational Study.

Place and Duration of Study: This study was conducted at the Coronary Care Unit and Angiography ward of the Punjab Institute of Cardiology, Lahore from January 2007 to June 2007.

Materials and Methods: Non-probability purposive sampling technique was used to enroll 100 subjects. A total of 790 PCIs were performed from January 2007 to June 2007 at the Punjab Institute of Cardiology, Lahore via transradial approach. Out of these 790 patients, one hundred patients (12.66%) had same-day discharge after transradial PCI. These patients were evaluated and information was obtained regarding entry site complications and adverse cardiovascular events at the time of discharge and at one month follow up after the procedure.

Results: Out of 100 patients, who had same day discharge, 2(2%) patients had hematoma at the time of discharge, 1(1%) had asymptomatic loss of radial pulse and 6(6%) patients had weak but palpable radial artery. At one month follow up 4(4%) patients had asymptomatic loss of radial pulse. However, none of these patients had major access site complications which required blood transfusion or admission to the hospital. Only 1(1%) patient had repeat coronary angiogram for chest pain, which revealed patent stent and TIMI III flow in distal vessel. One patient had repeat PCI but it was done to another vessel and previously placed stent was patent. There was no death and none of the patients underwent coronary artery bypass grafting (CABG).

Conclusion: The radial artery is the route of choice for most coronary procedures. The radial approach virtually eliminates access site complications after PCI, and allows rapid mobilization of the patient.Same-day discharge after radial PCI is a safe and feasible strategy.

Key words: Transradial percutaneous coronary intervention, same-day discharge, angioplasty, access site complications, adverse cardiovascular events.

INTRODUCTION

There is increasing data in the literature that same-day discharge is a safe approach for certain low-risk patients undergoing percutaneous coronary intervention (PCI) via radial approach,[1-5] but overnight stay is still considered the standard approach for the majority of patients. In recent years, the practice of intracoronary stenting using modern techniques and new developments in antiplatelet therapies have made percutaneous coronary intervention procedures much safer, with a diminished risk of complications such as acute/subacute stent thrombosis. These observations along with limited health care resources have led many invasive cardiologists to consider the feasibility of PCI to be carried out on an outpatient basis. It has been shown that a few hours observation period is safe after elective PCI,[6] and pilot studies suggest that outpatient PCI performed via the transradial route is feasible in selected patient populations.[1,4] Major advantages of radial PCI are earlier ambulation of the patient and lower rates of access site complications.[7-9]

However as in this study, the previus studies also excluded subjects who received platelet glycoprotein IIb/IIIa inhibitors. As these potent antiplatelet agents are increasingly used in clinical practice, this is clearly a major issue that needs to be clarified as they are often given an intravenous infusions of 12–18 hours duration, which would limit the feasibility of same-day discharge. Although the beneficial effects of these agents in PCI have been well documented in a number of large randomized placebo-controlled trials,[10,11] it remains controversial if all patients undergoing PCI should receive these antiplatelet agents. The benefit of these drugs is greatest in Troponin positive or diabetic subjects.[12,13]

Over the past 30 years, dramatic improvements have been achieved in the safety of percutaneous coronary intervention procedures, despite the increasing complexity of clinical and anatomic conditions treated.

The rate of vascular complications has declined dramatically as techniques have improved and procedural experience has increased. Several previous investigators have explored the safety of same-day discharge after low-risk elective coronary intervention, and almost all have supported the safety of the practice.[6,14-20]

As the burden of IHD is increasing and the number of patients undergoing PCI is increasing, there is a need for better utilization of hospital resources. It has been reported that same-day-discharge PCI is safe in certain low risk patients[1] and is preferred by patients.[2] But data on this at national level is lacking so this study was designed to evaluate the feasibility and safety of same day discharge after transradial PCI.

MATERIALS AND METHODS

This observational study was conducted at the Coronary Care Unit and Angiography ward of the Punjab Institute of Cardiology, Lahore.

Non-probability purposive sampling technique was used to enroll 100 subjects. A total of 790 PCIs were performed from January 2007 to June 2007 at the Punjab Institute of Cardiology, Lahore via transradial approach. Out of these 790 patients, one hundred patients (12.66%) had same-day discharge after transradial PCI.

Inclusion Criteria were age 30-70 years, positive Allen's test, any indication for elective percutaneous coronary intervention.

Exclusion Criteria were age >70, primary PCI, administration of glycoprotein IIb/IIIa inhibitors, prolonged chest pain and ECG changes (Fresh ST segment elevation or depression of 1mm or more and any new T wave inversion) after the procedure, prolonged resuscitation, intracoronary thrombus and access site complications.

Local complications were, hematoma, asymptomatic loss of radial pulse, pseudo aneurysm, arteriovenous fistula, dissection of artery.

Adverse cardiovascular events were myocardial infarction, cardiac death, repeat PCI and coronary artery bypass grafting. Stent thrombosis was defined as partial or total thrombotic occlusion of stent, documented by coronary angiography after stent implantation. Acute Stent Thrombosis was stent occlusion intraprocedural or within 24 hrs of stent implantation.[21] Subacute Stent Thrombosis was stent occlusion after 24 hrs till 30 days following stent implantation.[21]

All patients were given antiplatelet therapy (aspirin 150mg and 600mg clopidogrel) 2–4 hours before angioplasty as loading dose. Following angioplasty, all patients were prescribed antiplatelet therapy (aspirin 150mg once daily and clopidogrel 75mg twice daily).

After successful PCI, the radial sheath was removed and a pressure bandage was applied and patients were fully ambulated after 3-4 hours. If there were no complications (chest pain, entry site complications) after 1 hour of ambulating, they were allowed to leave the hospital. Patients were asked to remove the pressure bandage the next morning and to visit for follow-up after 2-4 weeks.

Informed consent was taken from all patients included in the study. A detailed history and clinical examination was done. All the information was collected on a predesigned proforma regarding sociodemographic profile i.e. name, age, and socioeconomic background, risk factors for ischemic heart disease, history of previous myocardial infarction, procedure to be performed; procedure time, hemostasis time, time for ambulation, time for discharge and local complication profile. Patients were followed up after 4 weeks and they were assessed regarding puncture site complications i.e. hematoma, asymptomatic loss of radial pulse, pseudo aneurysm, arteriovenous fistula, and dissection of artery and information was obtained about adverse cardiac events like myocardial infarction, need for repeat PCI, coronary artery bypass grafting and cardiac death. Patients who were discharged on the same day during the study period were those with stable and unstable angina, single or multivessel disease and undergoing single or multivessel PCI. The patients with access site complications, administration of IIb/IIIa inhibitors, or increased risk for post discharge complications (suboptimal PCI result etc) were not discharged. Some patients were not discharged for social reasons like coming from distant areas.

Statistical Analysis: The collected data was entered and analyzed by using Statistical Package for Social Sciences (SPSS) Version 10 for Windows. Demographic profile, risk factors for ischemic heart disease like diabetes mellitus, smoking, hypertension, family history of ischemic heart disease and elevated lipid profile were presented as frequency tables. Qualitative variables such as occupation, socioeconomic status and variables of the history were presented as frequency tables showing proportions. Variables in examination and local complications were presented as frequency distribution tables. Continuous variables are presented as mean ± SD.

RESULTS

A total of 790 PCIs were performed from January 2007 to June 2007 at the Punjab Institute of Cardiology, Lahore via transradial approach. Out of 790, 100(12.66%) patients had same-day discharge after transradial PCI within 14 hours of procedure.

Descriptive Statistics of the patients who underwent same day discharge after radial PCI are shown below in table 1. Mean age of the patients was 53.04±10.05

years, mean procedure time was 31.30±13.1 minutes and these patients remained admitted in hospital for a mean duration of 11.44±2.01 hours. Pulse, blood pressure, temperature and respiratory rate and heparin dosage given during PCI are shown in table 1.

Table No1: Descriptive Statistics

Variables	Mean± SD
Age in Years	53.04±10.05
Pulse in minutes	80.26±6.7
Systolic BP	126.4±24.6
Diastolic BP	78.68±13.3
Respiratory	16.04±1.4
Temp	98.328±0.46
Heparin dose	7625.00±2172.34
Procedure time (in minutes)	31.30±13.1
Hemostasis time (in minutes)	10.81±2.85
Hospital Stay time(in hours)	11.44±2.01

Table No.2: Baseline characteristics

Characteristics	Frequencies(%) n=100
Age mean years	53.04±10.05
Sex	
Men	74(74%)
Women	26(26%)
Hypercholesterolemia	21(21%)
Smoking current/previous	39(39%)
Diabetes mellitus	29(29%)
Hypertension	36(36%)
Previous MI	13(13%)
Family history of IHD	20(20%)
Chest pain symptom	75(75%)
NYHA angina classification	
I	4(4%)
II	18(18%)
III	68(68%)
IV	10(10%)
Single vessel disease,	82(82%)
Multivessel disease	18(18%)
Obesity	23(23%)

n=number of patients, MI=myocardial infarction, IHD=ischemic heart disease, NYHA=New York Heart Association

Table No.3: Puncture site complications at discharge

Puncture Site Complications	Frequencies (%) n=100
Hematoma	2(2%)
Asymptomatic loss of radial pulse	1(1%)
Radial artery palpable	91(91%)
Radial artery palpable but weak	6(6%)

Baseline characteristics of the study population are shown in table 2. The study comprised of 100 patients out of which 74(74%) were males and 24(24%) were females. Ninety three percent of the patients were taking both aspirin and clopidogrel. Eighty two percent patients had single vessel PCI and 18% had multivessel PCI. Right radial approach was used in 95% of the patients and in 5% of the patients left radial approach was used.

Table No.4: Puncture site examination and adverse cardiovascular events at follow up

Follow-Up Events	Numbers (%) n=100
Puncture site complications	
Asymptomatic loss of radial pulse	4(4%)
Radial artery palpable	96(96%)
Adverse cardiovascular events	
Repeat angiogram	1(1%)
repeat PCI	1(1%)
None	98(98%)

Cannulation was done smoothly in 87% patients and 13% had difficulty during cannulation. In 68% patients cannulation was done in the first attempt, in 22% in the second attempt, in 9% in the third attempt and in one patient it was done in fourth attempt. Verapamil alone was used in 16% of the patients and both verapamil and glyceryl trinitrate was used in 81% patients and in 3% paitens only glyceryl trinitrate was used.

At the time of discharge hematoma was observed in 2% patients but it was minor, there was weak but palpable pulse in 6% of the patients and in 1% there was asymptomatic loss of radial pulse. Table 3.

At one month follow up physical examination showed palpable radial pulse in 96% patients and in 4% patients there was loss of radial pulse. In terms of adverse cardiovascular events only one patient had repeat coronary angiogram for chest pain, which revealed patent stent and TIMI III flow in distal vessel. One patient had repeat PCI but it was done to another vessel and previously placed stent was patent. Table 4.

DISCUSSION

Same-day discharge is an attractive approach for PCI due to more efficient utilization of hospital resources. Transradial PCI has been demonstrated to be a safe and effective method of percutaneous revascularization.[1,4,7] After transradial PCI, patients have significantly less vascular complications compared to the transfemoral approach and can mobilize earlier.[1,7-10] For this reason, the radial approach makes same-day discharge PCI feasible and safe. The use of the radial approach also leads to improved quality of life after the procedure compared to the femoral approach, and is preferred by the majority of patients.[11]

Several studies have reported the effect of PCI on patients' quality of life.[12-17] Expansion of the indications for PCI, including the elderly patients and primary PCI for acute myocardial infarction, and increasing utilization of stents, coupled with improved procedural success rates, has resulted in increasing

patient volumes in many catheterization laboratories. Management of this large number of patients, often with no increasing resources, is a challenge for many centers. Same-day discharge PCI can potentially reduce hospital cost of PCI and improve bed utilization. However, the major concerns for same-day discharge PCI are the risk of entry site complications and adverse cardiovascular events especially related to occlusion of the target vessel after discharge. Our study shows that same-day-discharge PCI is feasible and safe for the patients regarding post-discharge access site complications and adverse cardiovascular events.

In the current study in terms of adverse cardiovascular events only 1 had repeat coronary angiogram but it did not reveal any evidence of in-stent restenosis and stent was patent with TIMI III flow in the distal vessel. One patient had repeat PCI but it was done to another vessel and previously placed stent was patent.

Incidence of stent thrombosis varies between 2-10 % in literature.[7-10] This difference could be due to the fact that our study population was small. Patients were considered suitable for same-day discharge, based on certain criteria already mentioned, which were also negatively related to acute stent thrombosis and low risk for access site complications. Another factor was that the majority of patients undergoing stenting in our hospital were pretreated with clopidogrel several days before the procedure. Thus, in this stable group of patients with low risk of stent thrombosis, same-day discharge did not culminate in any increase in patient risk.

Complications at the angioplasty access site (radial artery) in current study were minor. None of the patients had major access site complications. At the time of discharge hematoma was observed in 2% of the patients but it was minor and no blood transfusion was required, there was weak but palpable pulse in 6% of the patients and in 1% there was asymptomatic loss of radial pulse.

At one month follow up physical examination showed palpable radial pulse in 96% of the patients and in 4% of the patients there was loss of radial pulse.

The absence of major access site complications substantiates the safety of same-day discharge. Significant radial bleeding or hematoma after discharge does not occur with any frequency in patients selected to be eligible for same-day discharge.

In OUTCLAS study[1] same day discharge was applied to 106 patients while in current study same day discharge was applied to 100 patients. The largest study so far in this respect was the study by Ziakas et al,[17] where same-day-discharge PCI was applied to 943 patients. Larger catheters were used in study by Ziakas et al, 7F in half of the procedures, whereas only 6F were used in the OUTCLAS and in current study. Another safety and feasibility study is RADICAL study[18] which was conducted on 150 patients. Baseline characteristics of patients were similar in all three studies and are comparable to current study. The results of all these studies show that same-day PCI can be applied to larger variety of patients.

In current study none of the patients had major access site complications or required admission to the hospital. In the study by Ziakas et al[17] within 24 hours from discharge only 1(0.1%) required a repeat angiogram, which did not show target vessel occlusion while in this study none of the patients underwent repeat angiogram within 24 hours. In study by Ziakas et al[17] during the first month, 11(1.3%) underwent a repeat angiogram, out of which 4 had subacute vessel closure and 3 underwent a new PCI (performed in a lesion that was also present at the first procedure but was left untreated, while in this study only 1 patient underwent repeat angiogram but it did not show any evidence of in-stent restenosis.

In study by Ziakas et al,[17] 27(2.8%) visited their doctor and/or the hospital within 24 hours after discharge because of entry site complications, and 38(4%) patients visited within 1 month. However, none of the patients had major access site complications or required admission to the hospital. In our study at the time of discharge hematoma was observed in 2% patients but it was minor, there was weak but palpable pulse in 6% of the patients and in 1% there was asymptomatic loss of radial pulse.

It is obvious that same-day discharge can not be applied to all patients undergoing PCI. In our study, 12.66% patients undergoing PCI (100 of 790 patients) were discharged on the same day of the procedure. Some patients have clinical (PCI for acute myocardial infarction, and so forth) or social reasons that make same-day discharge not possible and other patients are considered at high risk for post-discharge complications. Same-day discharge is also not feasible for patients receiving glycoprotein IIb/IIIa inhibitors, as these agents require an at least 12-hour infusion. Recent clinical trials have shown the benefit of glycoprotein IIb/IIIa inhibitor administration in patients undergoing PCI.[4,6,19,20] Although the beneficial effects of these agents in PCI have been well documented in a number of large randomized placebo-controlled trials.[12,13] It remains controversial if all patients undergoing PCI should receive these antiplatelet agents. The benefit of these drugs is greatest in Troponin positive or diabetic subjects.[12,13]

One of the issues in same-day-discharge PCI is that it does not allow serial measurement of cardiac enzymes, and so it is possible that patients discharged home may have undetected enzyme elevation. In our study, patients who were most likely to have enzyme elevation were not discharged the same day (patients with

prolonged chest pain or electrocardiographic changes after the procedure, prolonged resuscitation, major side branch occlusion, intracoronary thrombus, poor intracoronary flow).

CONCLUSION

The radial artery is the route of choice for most coronary procedures. The radial approach virtually eliminates access site complications after PCI, and allows rapid mobilization of the patient.Same-day discharge after radial PCI is a safe and feasible strategy.

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Original Article

Knowledge, Attitude and Practices regarding Dengue Fever in People of Lahore

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ABSTRACT

Background: Dengue fever has emerged as an important public health problem in recent years and has become endemic throughout major cities in Pakistan. In Lahore, capital of Punjab it has appeared as an epidemic during last few years. Lahore has been worst hit by Dengue and emerged as an epidemic with terrible implications on health and economy of the populations and collapsing the health systems. Study was conducted during the peak of epidemic in 2011.

Objectives: To establish a baseline of knowledge, attitude and practices for dengue prevention.

Study Design: Cross Sectional Study.

Place and Duration of Study: This study was conducted in Lahore, Capital of Punjab province. Lahore has been divided in to eight administrative zones called ‘towns’. Allama Iqbal and Gulberg towns were selected for the study. Study was conducted during the month of September 2011, at the peak of epidemic

Materials and Methods: The study was focused on densely populated 6 areas and a total of 219 household were randomly selected and interviewed and all information stored in a structured Proforma.

Results: Among 219 households, showed that electronic media was the most common source of information within the community, followed by Friends and family. Areas of deficit knowledge were information about vector and its biting time and seasonal prevalence. The identified deficit areas of practices were keeping water storage tanks uncovered and less use of insecticides. Whereas, negative attitude noted was about elimination of larval breeding sources.

Conclusion: Overall level of knowledge and practices were low however, study showed positive attitude of community toward Dengue prevention.

Key Words: Dengue fever, Knowledge, Attitude, Practices.

INTRODUCTION

Dengue is a mosquito-borne infection that had become a major public health concern. It is a disease found in most tropical and subtropical areas of the world and had become the most common arboviral disease of human. Nearly 40% of the world's population lives in Dengue endemic area[1-3]. Dengue fever and dengue hemorrhagic fever (DHF) are viral diseases and virus is contracted from the bite of a striped Aedes aegypti mosquito that has previously bitten an infected person. Dengue outbreaks have also been attributed to Aedes albopictus, Aedes polynesiensis and several species of the Aedes scutellaris complex.[4-7] The mosquito flourishes during rainy seasons but can breed in water-filled flower pots, plastic bags, and cans year-round. One mosquito bite can cause the disease[5]. The virus is not contagious and cannot be spread directly from person to person. There must be a person-to-mosquito-to-another-person pathway. Because it is caused by one of four serotypes of virus (DEN-1 through DEN-4) it is possible to get dengue fever multiple times.[8-10] However, an attack of dengue produces immunity for a lifetime to that particular serotype to which the patient was exposed.[11-14] However, secondary infection with another serotype or multiple infections with different serotypes leads to sever form of dengue. Because dengue fever is caused by a virus, there is no specific medicine or antibiotic to treat it. For typical dengue fever, the treatment is purely concerned with relief of the symptoms (symptomatic).

Dengue fever now believed to be the most common arthropod-borne disease in the world. Some 1.8 billion (more than 70%) of the population at risk for dengue worldwide live in member states of the WHO South-East Asia Region and Western Pacific Region, which bear nearly 75% of the current global disease burden due to dengue. Dengue inflicts a significant health, economic and social burden on the populations of endemic areas. Available data from South-East Asia is largely derived from hospitalized cases among children but the burden due to uncomplicated dengue fever is also considerable. In a prospective study of schoolchildren in northern Thailand the mean annual burden of dengue over a five-year period was 465.3 DALYs per million, with non-hospitalized patients with dengue illness contributing 44 - 73% of the total[4-7].

Recent outbreaks of suspected dengue have been recorded in Pakistan, Saudi Arabia, Sudan and Yemen, 2005--2006. In Pakistan, the first confirmed outbreak of DHF occurred in 1994. A DEN-3 epidemic with DHF was first reported in 2005. Since then, the expansion of

dengue infections with increasing frequency and severity has been reported from large cities in Pakistan as far north as the North-West Frontier Province in 2008. Dengue is now a reportable disease in Pakistan. A pertinent issue for this region is the need to better understand the epidemiological situation of dengue in areas that are endemic for Crimean-Congo hemorrhagic fever and co-infections of this pathogens[15, 16].

The instant study is an attempt to establish a baseline of knowledge, attitude and practices for dengue prevention and point out deficit areas in knowledge and practices among residents of Lahore.

Operational Definitions:

Knowledge: The knowledge that the respondent have regarding the cause, transmission, clinical manifestation and prevention of Dengue fever.

Attitude: The feeling and beliefs of the respondents with regard to Dengue fever and its prevention.

Practice: The actions intended to do in order to prevent from Dengue fever.

MATERIALS AND METHODS

Study Setting: Study was conducted in Lahore, Capital of Punjab province. Lahore has been divided in to eight administrative zones called 'towns'. Allama Iqbal and Gulberg towns were selected for the study.

Study duration: Study was conducted during the month of September 2011, at the peak of epidemic.

Sample Technique: Purposive and cluster sampling technique was used for the study and a total of 219 house hold were interviewed. Allama Iqbal and Gulberg were chosen purposively among eight towns being more affected in the current epidemic of Dengue fever. Within these towns study was focused on densely populated areas of these towns. Six such areas/clusters were selected for the study. From each area, 35 households were visited for interview, on the assumption that sample of more than 30 is sufficient and representative for a KAP study.

Inclusion Criteria:

- Age: 15 - 60 yrs of age.
- Either Sex:
- Permanents residents.

Data Collection Procedure: A survey questionnaire was prepared and was translated into Urdu and pre-tested. Survey questionnaire comprised of five parts each part has specific questions to obtain information on; i) socio-demographic information, ii) knowledge, iii) attitude, iv) practices, and v) observations. For the purpose of data collection, 3 teams of surveyors, comprising of two members each were selected. One day training was organized for the field teams, in which the survey methodology and questionnaire was discussed in detail. Field simulation exercise followed by a debriefing session was also part of the training.

Data Analysis Procedure: Data was entered in Microsoft Excel. Before data entry desk editing was carried out, followed by data cleaning. Analysis was done using Microsoft Excel. Descriptive statistics (frequency, percentage, mean, standard deviation) were used primarily to summarize and describe the data to make it more understandable. Frequency distribution used in terms of Socio-demographic characteristics, Level of knowledge, Attitude towards dengue fever, Practice regarding dengue fever prevention. Participants answered a total of 14 close ended, multiple choice questions about Dengue fever. Each correct response was given one mark with a total of 14 marks. Participants' level of knowledge on Dengue fever was classified in to High (11-14 scores), Medium (07-10 scores) and Low (00-06 scores).

RESULTS

This study was conducted in Lahore City; 219 respondents were interviewed. The average age of the respondents was 35.4 years (SD 13.2). Most of the participants were female (61%). Majority of the respondents were married (78%). Most of the respondents were literate (60%) while the illiterate were (40%). Majority of the respondents were employed (95%) and majority of respondents had income (47%) between 6,000 to 10,000 More than half of the respondents (58%) were told having up to 2 rooms, (36%) had 3-5 rooms and (7%) had more than 5 rooms.13% families were comprised up to 4 members, (47%) had 5-8 members and (39%) had more than 8 members. More than half of the respondents (68%) told having no Dengue fever to any family member; while (32%) reported having fever to family members. More than half of the respondents (63%) told they look for doctors for treatment of fever; while (1%) for Hakeem and 2% for paramedics. Majority of the respondents knew about Dengue fever includes (86%) knew through electronic media; (13%) knew through printed media; (26%) knew through friends and family, and the (4%) through health personal. Distribution of knowledge on Dengue fever of the respondents showed that 50 % of subjects had "low knowledge", 37% of them had "moderate knowledge" while 13% had "high knowledge". (Table No: 1).

Table No.1: Distribution of knowledge level on Dengue fever

Level	Knowledge	
	Number	% age
High	28	13
Moderate	82	37
Low	109	50
Total	219	100

Table No.2: Knowledge about Dengue Fever

		Yes	No	Don't know	Yes	No	Don't know
		Number			% age		
1.	The principal mosquito vector for Dengue fever is Aedes aegytpi.	31	58	130	14	26	59
2.	Dengue fever is a severe, flu-like illness that affects infants, young children and adults.	108	35	76	49	16	35
3.	Dengue patients have chills, headache, pain upon moving the eyes, and low backache.	156	13	50	71	6	23
4.	Rainy season is the only epidemic season for Dengue infection.	118	41	60	54	19	27
5.	Mosquitoes transmitting Dengue infection bites only during day time.	68	63	88	31	29	40
6.	The mosquito that transmits Dengue infection lays its eggs in dirty sewage water.	53	94	72	24	43	33
7.	Empty stagnant water from old tires, trash cans, and flower pots can be breeding places for mosquitoes.	112	24	83	51	11	38
8.	Dengue viruses are transmitted to humans through bites of infective female Aedes mosquitoes	20	39	160	9	18	73
9.	Only method of controlling Dengue infection is to combat the vector mosquitoes.	120	23	76	55	11	35
10.	There is no specific treatment for Dengue infection.	112	27	80	51	12	37
11.	Insecticide can be beneficial in killing the mosquito larvae.	118	16	85	54	7	39
12.	Insecticide, if put in the standing water, can help to prevent the mosquito breeding.	71	37	111	32	17	51
13.	Stored water containers/tanks for drinking water without being covered should be cleaned every 7 days.	120	43	56	55	20	26
14.	I am afraid of getting Dengue fever, If one of my family members has DF.	149	29	41	68	13	19

Table No.3: Distribution of Attitude level on dengue fever

Level	Attitude	
	Number	% age
Positive	192	88
Neutral	25	11
Negative	2	1
Total	219	100

The mean knowledge score for the respondents was 6 ± SD 3.65 (Table No: 2). There were 88 % of respondents who had "positive attitude", 11% of them had "neutral attitude", while only 1 % had "negative attitude". The mean attitude score for all respondents were 25.23 ± SD 2.28. (Table No: 3). 12 % of respondents had good practices, 46% fair and 42% had poor practices as shown in Table 5. The mean practices score for all respondents was 4 ± SD 2.70. 77% of respondents were covering water jars after using, 71% had covered their water tanks and 55 % were using mosquito coils/nets in their houses. 55% of respondents were also doing indoor insecticide spray on regular basis. It is also revealed that 78% of respondents never examined mosquito larvae in the water containers in their toilets. Among the interviewed households, 64% had neat and tidy housing environment. 72% of houses had nothing that could hold water around the house. 40% of the household had stored water containers in the toilet.

Only 5% had dirty water in flower vases or indoor plants and 7% of the households had water collection on the plates supporting flower vases. 40 % of the households had covered the stored water containers/tanks. Majority of interviewed households 61% had available mosquito coil / mat or electric mosquito killer, and among these only in 39 % of houses was in use. 57 % of visited houses had wire gauze on doors, windows and ventilators or mosquito net available and among these 43 % had these in use.

DISCUSSION

The results of this study showed 50 % of subjects had "low knowledge", 37% of them had "moderate knowledge" while 13% had "high knowledge". A study was done in Karachi to assess knowledge and practices regarding dengue fever.

Table No.4: Attitude towards dengue fever

No.	Statement	Agree	Disagree	Neither agree nor disagree	Agree	Disagree	Neither agree nor disagree
		Number			**% age**		
1.	DF is a disease that cannot be prevented.	53	122	44	24	56	20
2.	Eliminating the breeding places is the responsibility of the public health staff and health volunteer.	155	35	29	71	16	13
3.	Only method of controlling or preventing dengue and DHF is to combat the vector mosquitoes.	151	21	47	69	10	21
4.	Only smogging is enough to prevent mosquito and no need for other ways.	70	77	72	32	35	33
5.	Everybody has a chance to be infected with dengue virus.	166	21	32	76	10	15
6.	Person who once got dengue infection cannot get dengue infection again.	33	95	91	15	43	42
7.	It is possible to recover completely from dengue infection.	150	10	59	68	5	27
8.	Elimination of larval breeding sources is a waste of time and very complicated.	35	74	110	16	34	50
9.	Strong and healthy person will not get dengue infection.	55	108	56	25	49	26
10.	Sleeping in mosquito net can prevent dengue infection.	120	55	44	55	25	20
11.	You are one of the important people in preventing dengue fever.	102	65	52	47	30	24

Table No.5: Distribution of practices levels (Excluding 'all don't have' responses)

Level of practices	Practices	
	Number	**% age**
Good	26	12
Fair	101	46
Poor	92	42
Total	219	100

About 89.9% of individuals interviewed had heard of dengue fever. Sufficient knowledge about dengue was found to be in 38.5% of the sample, with 66% of these were in Aga Khan University Hospital and 34 % were in Civil Hospital Karachi. Literate individuals were relatively more well-informed about dengue fever as compared to the illiterate people ($p<0.001$). Knowledge based upon preventive measures was found to be predominantly focused towards prevention of mosquito bites (78.3%) rather than eradication of mosquito population (17.3%). Use of anti- mosquito spray was the most prevalent (48.1%) preventive measure. Television was considered as the most important and useful source of information on the disease.[17-18]

A study done on knowledge and practices in Pakistan showed that knowledge had significant associations with education ($p= 0.004$) and socioeconomic status ($p=0.02$). The high socioeconomic group showed better preventive practices. The study concluded that Knowledge of dengue is inadequate in the low socioeconomic class.[19]

Moreover, study had shown positive attitude of community toward Dengue prevention. Concerning negative attitude noted was that 'elimination of larval breeding sources was a waste of time and very complicated'. Study results showed that among the respondents 12 % had good practices, 46% fair and 42% had poor practices. 77% of respondents were covering water jars after using, 71% had covered their water tanks and 55 % were using mosquito coils/nets in their houses.

Table No.6: Practice regarding dengue prevention

No.	Statement	Yes	No	Not present	Yes	No	Not present
		Number			**% age**		
1.	Do you cover water jars after using immediately?	169	36	14	77	16	6
2.	Do you have a cover in your water tanks?	155	5	59	71	2	27
3.	Do you ever examine the mosquito larvae in the flowers pots?	9	50	160	4	23	73
4.	Do you change the water of the indoor plants every week?	24	21	174	11	10	79
5.	Do you ever drain off the water in the plates of the flower pot? How often?	25	20	174	11	9	79
6.	Do you examine any discarded thing that can hold water around your house?	48	105	66	22	48	30
7.	If yes, do you ever put them in the garbage or dispose them.	46	2	0	96	4	0
8.	Do you use mosquito net/mosquito coils in your house. When?	135	64	20	62	29	9
9.	Do you participate when your community has been sprayed fog	46	94	79	21	43	36
10.	Do you participate in any campaigns of dengue infection in your community	45	90	83	21	41	38
11.	Do you ever examine the mosquito larvae in water containers in the toilet?	30	171	18	14	78	8
12.	Do you check and clean your roof gutters in the rainy season.	121	83	15	55	38	7
13.	Do you spray insecticide inside the house regularly?	120	99	0	55	45	0

A study done in Thailand regarding vector knowledge and practices showed that almost all respondents (98%) regarded dengue as a serious to very serious problem in their village and 77% of the respondents thought it would be possible to get rid of the mosquitoes that cause dengue. Volunteers of the local public health offices (43%) were mentioned most common as the main person responsible to control mosquito breeding, followed by residents themselves (32%) and the government (13%). [20]

CONCLUSIONS

This study concluded that:

- Overall level of knowledge and practices were low however with a wide gap between knowledge and practices.
- There is a positive attitude of community toward Dengue prevention.

Recommendations:

- Public education is necessary to address the knowledge gap revealed in the study.
- Behavior change strategy must form an essential part of integrated Dengue prevention and control program.

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Original Article

Determination of Pesticide Residues Hexachlorocyclohexane, Cyclodiene, Diphenylaliphate and their Metabolites in the Breast Milk of Women from Karachi- Pakistan

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ABSTRACT

Purpose: The aim of this study was to determine the presence of pesticide residues hexachloro-cyclohexane, cyclodiene, diphenylaliphate and their metabolites in the milk of women from different regions of Karachi, Sindh-Pakistan.

Study Design: An experimental study.

Place and Duration of Study: This study was conducted in the department of Zoology, University of Karachi from April 2009 to April 2011.

Materials and Methods: A total of 30 human breast milk samples were collected from the Gynae wards of Karachi hospitals. A breast pump was used to collect 5 ml milk sample from each women. The sample was taken in the sterilized and labeled vials. The collected samples were then stored at -20 ^{o} C for analysis. All the samples were analyzed for the presence of pesticide residues. Samples of milk were prepared accordingly and the purified samples injected into the Shimadzu GC-ECD apparatus. The peaks of the samples were compared by the retention time of the standard peaks. The chromatogram obtained indicated the quantity of pesticide residues.

Results: The standard chromatogram of organochlorine pesticides and their isomers were prepared and analyzed on GC-ECD. The standard chromatograms were then matched with the chromatogram of milk samples. The isomers like α, β, γ and δ were detected as major residues of HCH. The cyclodiene compounds such as aldrin and α-endosulfan were detected as common compounds. DDT was found in 43% of milk samples. The percentage of cyclodiene residues was higher than HCH and diphenylaliphate.

Conclusion: A significant bioconcentration of organochlorine residues was found in the breast milk. Total DDT concentrations were found higher than total HCH levels. It is thus concluded that this bioconcentration of pesticide residues clearly indicates that the mother contains a heavy amounts of such toxic chemicals.

Key Words: Hexachlorocyclohexane, Cyclodiene, Diphenylaliphate, Metabolites, Women breast milk.

INTRODUCTION

Pesticides or insecticides are among the most extensively used chemicals in the world today and they are also among the most hazardous compounds to the human being as well. As some pesticides can be beneficial in decreasing the populations of harmful or destructive insects while others can be damaging to the environment and can cause serious disturbances[1]. Organochlorine pesticides are organic compounds that are characterized by their lipophilicity persistence and semi-volatility has been used as pesticides including both insecticides such as DDT, lindane, aldrin, dieldrin and methoxychlor as well as herbicides. The chlorinated hydrocarbon unsecticides were introduced in 1940 and are widely used in agriculture sector to control insect pest species[2]. There is evidence of organochlorine pesticide residues in sediments, water, crops, meat and human fluids including human milk[3-8]. Restriction and bans on the preparation of organochlorine pesticides minimized their usage, as they persist in the environment for long period because of their accumulation in the soil[9]. Also in the industrialized sectors these chemicals are banned and restricted for their use on large scale but in the developing countries DDT is still being used[10]. As OC pesticides are hydrophilic and lipophilic compounds, they enter in the environment and human body via food chain and can cause various ailments such as reproductive, neurological and endocrine dysfunctions[11] as well as disturb the enzyme systems[12].

It has also been reported that mothers are exposed to OC's through food chain contamination and environmental pollution. These chemicals enter in the body through oral, dermal and inhalation and are then absorbed and distributed to different organs[13]. The fetus may receive these chemicals through the placenta of mothers[14] and also transferred from mother to newborn babies through breast milk like organochlronines[15-17]. As breast milk is an important carrier that provides all the necessary nutrients, growth factors and immunological components to the infants[18], several risk factors are involved for the accumulation of OC's in human breast milk e.g., parity, maternal age, timing of

sampling and the nature of diet that are consumed by the mother[19-22].

Very little work has been done to measure the body burden of organochlorines in the women of Karachi-Pakistan especially on human breast milk. Therefore, present study has been carried out to assess the residual levels of organochlorine pesticides and their metabolites in the breast milk of women particularly belonging to the different regions of Karachi, Pakistan.

MATERIALS AND METHODS

Chemicals and Standards Pesticides: The standard mixtures of organochlorine compounds were purchased from Supelco Company of USA. All the chemicals and solvents used were of pesticide scan grade. For the extraction of milk samples methanol, sodium oxalate, diethylether and hexane were used.

Table I. Pesticide residues (mg/kg) in the milk samples.

Name of Pesticides	Positive samples	Positive test (%)	Mean	SD	SE	Range min-mix
α-HCH	10	33	0.006	0.012	0.002	0.007—0.016
β-HCH	15	50	0.405	1.013	0.185	0.432—1.157
γ-HCH	13	43	0.019	0.033	0.006	0.027—0.050
δ-HCH	9	30	0.009	0.020	0.003	0.010—0.024
Σ HCH			0.439			
Heptachlor	4	13	0.002	0.006	0.001	0.001—0.006
Hepta-endo-epoxide	3	10	0.001	0.006	0.001	0.0006—0.005
Hepta-exo-epoxide	9	30	0.022	0.043	0.007	0.028—0.059
Aldrin	10	33	0.062	0.229	0.041	0.040—0.205
Endrin	9	30	0.087	0.443	0.081	0.012—0.329
α-Endosulfan	16	53	0.346	0.945	0.172	0.341—1.018
β-Endosulfan	5	16	0.086	0.466	0.085	0.001—0.335
Endosulfan Sulfate	00	-	-	-	-	-
Dieldrin	7	23	0.029	0.123	0.022	0.014—0.102
Σ Cyclodienes			0.635			
4,4-DDT	7	23	0.016	0.077	0.014	0.004—0.183
4,4 DDE	13	43	0.032	0.012	0.002	0.036—0.066
4-4,DDD	9	30	0.222	0.473	0.086	0.266—0.604
Methoxychlor	8	26	0.175	0.202	0.037	0.271—0.416
Σ Diphenylaliphatic			0.444	-	-	-
Hexachlorobenzene	1	3	0.003	0.016	0.003	0.000—0.013
Σ OCs			1.518			

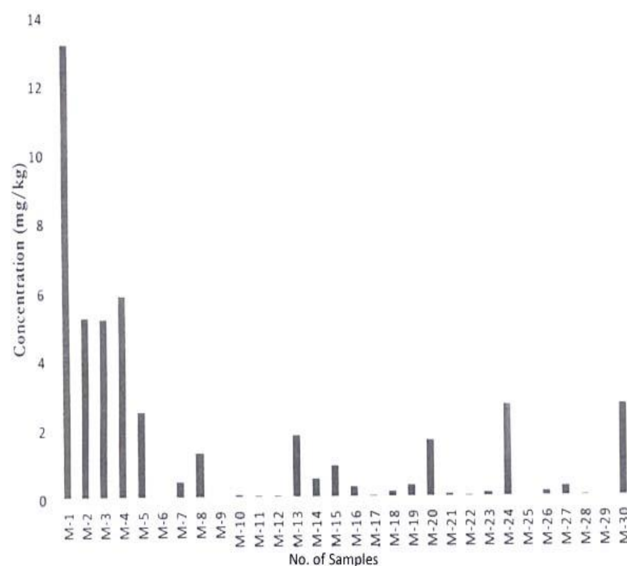

Figure I: Bar graph showing total OC concentration in 30 milk samples

Collection of milk samples: The milk samples were collected from the Gynae wards of Karachi hospitals. A total of 30 breast milk samples were collected for this study. Each milk samples comprises of 5 ml that were taken in the well cleaned and labeled vials. All the samples were kept and stored at -20 °C till analysis.

Preparation of Samples: Out of total 5 ml of milk samples, 4 ml of sample was mixed with equal amount of methanol and shaken for 5 min for proper mixing. Sodium oxalate 0.1 gm was then added and the solution was again shaken by vortex mixer. The mixture was extracted with 10 ml of diethyl ether and n-hexane (1:1 v/v) and was then centrifuged for 15 min at 3000 rpm. The organic phase was separated out after centrifugation. The pellet was again extracted with diethyl ether and n-hexane. This was repeated twice to obtain three organic phases from the mixture. The organic phases were then dried by nitrogen. The dried residues were re-dissolved in 1 ml of hexane for clean up procedure.

Detection and Quantification of Pesticide Residues: Quantitative estimation of pesticide residues in all the extracts was done by Schimadzu GC 17 – A, equipped with Ni 63 Electron Capture Detector (ECD) attached with CBM-102 chromatogram recorder system. Purified nitrogen gas was used as the carrier gas and a known volume 1µl of milk sample was injected in the column through specialized syringe. Different peaks of the samples were identified by comparing the retention times of the standard peaks and the quantification of residues was then obtained from each sample.

RESULTS

The standard chromatogram of 18 organochlorine agricultural pesticides and their isomers were prepared on GC-ECD. The standard chromatograms were then matched with chromatogram of 30 milk samples. Sample 1 has the highest OC concentration 13.2 mg /kg than the rest samples. Samples 6, 9, 25 and 29 had negligible quantities (Fig.1). The results obtained from all samples (n=30) was statistically interpreted (Table 1). The mean concentration of OC ($\sum OC$) was calculated as 1.518 mg /kg. The mean concentration of Hexachlorocyclohexane isomers α, β, γ and δ were calculated as 0.006 mg /kg, 0.405 mg /kg, 0.019 mg/kg and 0.009 mg /kg respectively. The concentration of total HCH isomers was then found to be 0.439 mg /kg.

Among cyclodiene group of compounds, heptachlor was detected in 4 samples out of total 30 samples and the mean value was calculated as 0.002 mg /kg. The isomers of heptachlor i.e., heptachlor endoepoxide and heptachlor exoepoxide were calculated as the mean value of 0.001 mg /kg and 0.022 mg /kg. Aldrin was detected in 10 samples and Dieldrin was found in 7 samples with their mean values of 0.062 mg /kg and 0.029 mg /kg respectively. Endosulfan and their isomers like α-endosulfan and β-endosulfan were detected with their mean values as 0.346 mg /kg and 0.086 mg /kg respectively.

Regarding diphenylaliphate compounds, the mean value of 4,4-DDT was calculated as 0.016 mg/kg and of DDE (major metabolite) was 0.032 mg /kg, where as for DDD it was found to be 0.222 mg/kg. The mean of total DDT (i.e., sum of DDT, DDE and DDD) was found to be 0.270 mg /kg.

DISCUSSION

This study was conducted in the different localities of Karachi to collect the breast milk samples of women from different hospitals for the detection and quantification of pesticide residues and their metabolites due to pesticide exposure.

The present finding of the milk samples showed the heavy concentration of HCH as compared to Diphenylaliphate insecticides. Among all metabolites, β-HCH was reported to be more stable in the environment than its isomers[23]. The present study however indicated that the β-isomer of HCH was in a higher concentration of 0.405 mg/kg than α, β, γ and δ isomers. A study reported that about sixty milk samples were found to be contaminated with HCH isomers[24]. The same finding was also noticed by the present study. Another study reported that the breast milk of Russian women[25] and Chinese women[26] indicated higher β-HCH than α and γ isomers. The present study also agreed with the findings of these reports. Similarly a study reported that the total HCH found in four villages of India[27] showed 0.123 ppm, 0.129 ppm, 0.131 ppm and 0.127 ppm and these values are found significantly in lower level as compared to the present study that showed mean concentration $\sum 0.439$ ppm of HCH.

A study from Victoria, Australia reported that the breast milk samples showed lower levels of aldrin, dieldrin, heptachlorepoxide and HCB[15], while the present investigation indicated higher values of these compounds in the milk samples. The pesticide residues dieldrin and HCB were found to be 60% higher values in the milk samples of Ghana women[28]. However the present study also indicated higher values of these compounds in the milk samples. Many researchers also reported the high concentration of DDT in the breast milk of Victorian's mother[15]. This is almost in line with the present study.

CONCLUSION

A significant bio-concentration of organochlorine residues was noticed in the breast milk of Karachi women by the present work. Total DDT concentrations were found to be higher than total HCH levels. As milk is the most initial natural food source of infants, so there are more chances of the bioaccumulation of the residues and their metabolites in infants and new born provided if their mothers contain or are heavily exposed by such toxic chemicals.

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Original Article

Frequency of Various Causes of Upper Gastrointestinal Bleed (UGIB) at a Tertiary Care Hospital

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ABSTRACT

Objective: To determine the frequency of various causes of upper gastrointestinal bleed (UGIB) at Tertiary Care Hospital.

Study Design: Descriptive cross-sectional study.

Place and Duration of Study: This study was conducted at the Department of Internal Medicine, Nishtar Hospital Multan from August 2009 to January 2010.

Materials and Methods: A total of 88 patients with upper GI bleed were registered. Prior permission was taken from Institutional Ethical Committee to conduct this study. Informed consent was taken from each patient. Upper GI Endoscopy was done to find out the source and cause of bleeding. For identification of each patient, personal data was collected. All the data collected were entered and analyzed using SPSS-11.

Results: Mean age was 41.64±13.56 years with 49 (55.70%) male and 39 (44.30%) female patients. Majority of the patients 38(43.18%) were between 36-50 years of age. In our series the commonest cause of UGIB was oesophageal varices in 56.82% of cases followed by peptic ulcer disease in 38.63% of patients.

Conclusion: Oesophageal varices followed by peptic ulcer disease are the commonest causes of UGIB in our setting.

Key Words: Chronic liver disease, Upper GI bleeding, Esophageal varices.

INTRODUCTION

Upper gastrointestinal bleed (UGIB) refers to the hemorrhage in the upper GI tract. Anatomically it is defined as bleeding occurring proximal to the ligament of Treitz which connects the 4th part of duodenum to the diaphragm near the splenic flexure of the colon.

Upper GI bleed is most important medical emergency and requires urgent admission to the hospital for diagnosis and management. Mortality due to upper GI bleed is 11% in emergency admissions and 33% in inpatients[1].

Usual presentation of UGIB is hematemesis which is vomiting of red blood or coffee ground material. It may present as hematochezia (maroon colored stools) if bleeding is rapid and severe or as melena (black, tarry, foul smelling stools) if bleeding is small and gradual.

The various causes of UGIB are peptic ulcer disease (35-62%), gastroesophageal varices (4-31%), Mallory Weis tears (4-13%), gastroduodenal erosions and erosive esophagitis (2-8%), gastric malignancy (1-4%), angiodsyplasia, dieulafoy's lesions, aortoenteric fistula, hereditary hemorrhagic telangiectasia and uremia. Coagulation disorders may present as upper GI bleed[2].

It is concluded from various studies that 90% of the cirrhotic patients will develop gastroesophageal varices over the span of 10 years but only one third of these will result in upper GI bleed[3]. After stabilization of patient an attempt is to be made to establish the cause of bleeding. The evaluation through history should focus on known causes of upper GI bleed. To establish the site of bleeding history and clinical examination are seldom helpful but some signs and symptoms may give clue to the underlying pathology which has resulted in upper GI bleed. The site of bleeding is determined by upper GI endoscopy whose accuracy and competence has been well documented[4, 5]. Arteriography has its own limitations it can locate the site of bleeding provided, culprit lesion is oozing blood at a rate more than 1 ml per minute. Oespophageal varices due to chronic liver disease are most important cause of upper GI bleed in this part of world which is mostly post viral. One study has reported esophageal varices due to CLD as cause of UGIB in 44% of the cases and peptic ulcer disease in 19.7% of cases [6]. Another study has reported esophageal varices as culprit for UGIB in 65% of the cases and gastric erosion in 15% of cases[7]. The present study was designed to see the frequency of various causes of UGIB at tertiary care hospital.

MATERIALS AND METHODS

This descriptive cross-sectional was conducted in the Department of Internal Medicine, Nishtar Hospital, Multan during the period from August 2009 to January 2010. Permission to conduct this study was obtained from Institutional Ethical Review Board. A total of 88 patients were registered. Informed consent was taken from each patient and upper GI endoscopy was done to

find out the source and cause of bleeding. All information were recorded in a predesigned proforma. Data collected were entered and analyzed through SPSS-11.

RESULTS

A total of 88 patients were included in this study. It included 49 (55.70%) male and 39 (44.30%) female patients with male to female ratio of 1.3:1 (Table-1).

Majority of the patients 38 (43.18%) were between 36-50 years of age. Three (3.41%) patients were having age more than 65 years (Table-2).

There were 54 (61.36%) patients who presented with both hematemesis and melena, 19 (21.59%) patients had melena and 15 (17.50 %) patients had hematemesis alone (Table-3).

Table No.1: Gender Distribution of Patients with UGIB (n=88)

Gender	No. of patients	%age
Male	49	55.70
Female	39	44.30

Table No.2: Age Distribution of Patients with UGIB (n=88)

Age (years)	No. of patients	%age
<20	05	05.68
21-35	22	25.00
36-50	38	43.18
51-56	20	22.73
>65	03	03.41

Mean age ± SD = 41.64±13.56 years.

Table No.3: Presentation of UGIB (n=88)

Complaints	No. of patients	%age
Hemetemesis/melena	54	61.36
Hemetemesis	15	17.05
Melena	19	21.59

Table No.4: Causes of Upper Gastrointestinal Bleed (n=88)

Cause	No. of Patients	%age
Esophageal varices	50	56.82
Peptic Ulcer disease		
Gastroduodenal erosions	14	15.91
Gastric ulcers	11	12.50
Duodenal ulcers	09	10.22
Mellory Weis tear	1	1.14
Gastric carcinoma	1	1.14
Erosive esophagitus	1	1.14
Coagulopathy	1	1.14
Total	88	100

In our study the commonest cause of UGIB was oesophageal varices in 56.82% of cases followed by peptic ulcer disease in 38.63% of patients. Acute gastroduodenal erosions were present in 15.91% patients (Table-4).

Out of the 50 patients of Oesophageal varices due to chronic liver disease, 3 (6%) were less than 20 years of age, 11 (22%) were 21–35 years, 24 (48%) were 36–50 years, 10 (20%) were 51–65 years and 2 patients (4%) were > 65 years of age (Table-5).

Out of the 50 patients having esophageal varices due to chronic liver disease, 29 patients (58%) were male and 21 (42%) were females.

Table No.5: Age Distribution of Patients with UGIB in relation to CLD (n=50)

Age (years)	No. of patients with CLD	%age
<20	03	06.0
21-35	11	22.0
36-50	24	48.0
51-56	10	20.0
>65	02	04.0

DISCUSSION

Upper gastrointestinal bleed is a real medical emergency and is an important cause of morbidity and mortality accounting up to 8% of hospital admissions[8]. The prevalence of UGIB is 170 cases per 100000 per year and its incidence varies from 50 - 150 per year in USA and 100-107 per 100000 per years in United Kingdom[9, 10]. The mortality due to UGIB is 3-14 % and it rises with increasing age. Mortality is also associated with other comorbid conditions. Local data from our country describes that common causes of UGIB are esophageal varices, duodenal and gastric ulcer, gastric erosions, superficial mucosal ulceration and Mallory Weiss tears[7, 11-12]. The most common cause of UGIB in our study is esophageal varices as compared to peptic ulceration in western countries. It may be due to post viral chronic liver disease as hepatitis B and C are common in our setting.

The mean age of patients in our study was 41.64 +- 13.56 years with peak occurrence in 36-50 years of age. Shaikh et al [13] in their study on UGIB from Karachi reported that 65% patients were between 20-50 years. Similar findings have been reported by Sabir et al [14]. Peak incidence of UGIB in western countries is in 5th to 6th decade mentioned by Parente[10] and Golanova[15]. This could be due to higher average life span of western population. In our study there were 55.70% male and 44.30% female patients with UGIB and male to female ration was 1.3: 1. Iqbl in this study reported male to female ratio as 1.5: 1 [12].

Qari[16] in his study has reported that 42 (60%) of cases presented with hemetemesis, 11 cases (15.7%) with melena and 17 (24.8%) cases with both whereas in our study 54 (61.36%) of patients presented with both hemetemesis and melena, 19 (21.59%) patients with

melena and 15 (17.05%) of patients with hemetemesis alone.

In our study frequency of esophageal varices was 56.82% while peptic ulcer disease was 38.63% in patients of UGIB. Several local studies have demonstrated that esophageal varices as leading cause of UGIB in Pakistan followed by peptic ulcer disease. Shaikh et al[13] have labeled variceal bleed in 59.1% of cases, other studies by Chaudhary[7] from Raheem Yar Khan and Khan[17] from Peshawar all have concluded that variceal bleed is a common cause of UGIB. Qari[16] also reported variceal bleed in 57% of cases while Svoboda et al [18] has reported it in 57.4% of cases. It can be explained by much high incidence of hepatitis B&C in our country as compared to western country. In western literature esophageal varices are less common cause as mentioned by Villanueva et al[19] where esophageal varices were noted in 15%. In National American Society for Gastrointestinal Endoscopic Bleeding Survey (ASGE) on UGI tract involving 2225 patients esophageal varices was present in 15.4%[20]. H. Pylori and NSAIDS are important factor included in the causation of peptic ulcer disease. Alcohol also increase the risk of acute UGIB among NSAIDs users. Most of international data as reported by Boonpongmanee[21] and Eirtkin[22] says that peptic ulcer disease is commonest cause of UGIB. Silverstein et al from USA reported that peptic ulcer disease is the commonest cause[20]. The same has been reported by Rockall[1] and Wilcox from UK[23].

In our study more than 70% of patients having esophageal varices were more than 36 years of age, while Shaikh et al[13] has reported esophageal varices in relatively younger age group 20-30 years (22%). The reason may be more prevalence of chronic liver disease at younger age group.

Shaikh et al[13] have also reported peptic ulcer disease as 2nd most common cause of UGIB in 25.8% of cases and Iqbal[12] in 19%. Sub-mucosal lesions which include esophagitus, gastritis, duodenitus and Mellory Weis tears were in 20% of the cases and gastric neoplasm in 4%. In our study gastric carcinoma was the cause of bleeding in 1.14% and the same has been reported in other studies by Shaikh[13] and Qureshi[24].

The patients with variceal bleed had greater morbidity than bleeding from other causes. The fact may be attributed to underlying decompensated disease which appears as independent predictor of mortality in multivarient analyses.

CONCLUSION

Oesophageal varices followed by peptic ulcer disease are the commonest causes of UGIB in our setting.

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Original Article

Prevalence of Hepatitis in Neonates and Children in Karachi

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ABSTRACT

Inflammation of liver is known as "hepatitis" is commonly found in infant as neonatal hepatitis and in children as acute and chronic hepatitis. Neonatal hepatitis is a general term for inflammation of the liver that occurs shortly after birth in newborns (less than 3 months of age) for which a specific cause cannot be identified.

Objectives: To provide an overview of current childhood statistics of hepatitis and jaundice to facilitate analysis of the impact of past research discoveries on outcome and provide essential information for prioritizing future research directions.

Study Design: Experimental Study.

Place and Duration of Study: This study was conducted at the Department of Histopathology, BMSI, JPMC, Karachi from May 2004 to March 2005.

Materials and Methods: Slides / paraffin blocks of liver biopsies from patients under 15 years of age. The cases were of two categories i.e. retrospective and prospective. The distribution of 480 cases of hepatitis was according to Age and Sex. Total 200 (41.7%) cases were encountered in the youngest of 0-5 years age group, 180 (37.5%) cases in 6-10 years and only 100 (20.8%) cases in 11-15 age group.

Results: The distribution of 24 cases of hepatitis was according to Age and Sex. Total 200 (41.7%) cases were encountered in the youngest of 0-5 years age group, 180 (37.5%) cases in 6-10 and only 100 (20.8%) cases in 11-15 age group.

Conclusion: It is observed that the tendency of liver inflammation was decreased with increase in age and sexual differentiation showing male predominance with male to female ratio of 2:1. The inflammation of liver /hepatitis in young children, can be caused by infectious, metabolic, and genetic disorders. Physiological jaundice or neonatal hepatitis is mostly reported in male population than females, in children. In Karachi this is found that neonatal jaundice can be recovered with the growing age and it is found to be a common cause for enlargement of liver and associated liver diseases in infants and children that can lead to higher risks of acute or chronic liver diseases in adulthood.

Key Words: Neonatal hepatitis, chronic Hepatitis, acute hepatitis, inflammation of liver.

INTRODUCTION

Inflammation of the liver/hepatitis is very common in early infancy and childhood.[1,2] In neonatal hepatitis most of the infants are infected by viruses that cause the inflammation of liver before birth or shortly after birth[1]. The neonatal hepatitis is usually associated with jaundice, enlarged liver and spleen[14].If there are no viruses are detected in neonatal hepatitis, and a liver biopsy showed "giant cells", it is known as giant cell hepatitis [3, 4,5]. The symptoms are same in neonatal hepatitis, other type of hepatitis or in biliary atresia, in which the bile ducts are destroyed due to unknown cause. "Hepatitis" can cause liver cells` degeneration or necrosis[6] and the wide range of clinical manifestations are determined by the severity of the hepatocyte`s dysfunctions or by liver functions` tests. Neonatal hepatitis can have a number of causes including infections, metabolic, and genetic disorders. Hepatitis A, B, and C are less commonly occurs in neonates. Hepatitis B, in the neonates appear as chronic hepatitis, with the histological features of active hepatitis[7,8, 9].* Long term follow-up will be required to determine the final evolution of this lesion. The progression from neonatal hepatitis to cirrhosis and hepatocellular carcinoma in a young child was demonstrated by sequential biopsies in a research. In Pakistan, HBV infection rate is increasing day by day. The reason may be the Seventy percent of the all new born have transplacental IgG antibodies against hepatitis A[10,11,12,13] , only that last about 8 months of age. Due to lack of proper health facilities or poor economical status and less public awareness about the transmission of major communicable diseases like hepatitis B, hepatitis C and Human Immunodeficiency syndromes are increasing[2]. Chronic liver disease and jaundice occurring with in the first 24 hours of life may increase the evidence of an underlying pathology[14].

MATERIALS AND METHODS

Slides / paraffin blocks of liver biopsies from patients under 15 years of age. the cases were of two categories i.e. retrospective & prospective.

Retrospective:

1. Slides / paraffin blocks of liver biopsies received during last 10 years in the department of pathology,

Basic Medical Science Institute (BMSI), Jinnah Postgraduate Medical Center, Karachi.

2. Slides / paraffin blocks of liver biopsies received in department of pathology, national institute of child health (NICH) Karachi during last 7 years.

Prospective: Slides / paraffin blocks of liver biopsies received during last 10 years in the department of pathology, basic medical science institute (BMSI), Jinnah postgraduate medical center national institute of child health (NICH) Karachi. A clinical protocol including the particulars about the patients name, age, sex and diagnosis were obtained from the surgical pathology registers, request cards and copies of report.

RESULTS

The distribution of 24 cases of hepatitis was according to Age and Sex. Total 200 (41.7%) cases were encountered in the youngest of 0-5 years age group, 180 (37.5%) cases in 6-10 and only 100 (20.8%) cases in 11-15 age group.

Table No.1: Showing Age and Sex Differentiation in Young Population N-480

Age	Male	%	Female	%	Total	%
0-5	160	50.0	40	25	200	41.5
6-10	120	37.5	60	37.5	180	37.5
11-15	40	12.5	60	37.5	100	20.8
TOTAL	320	100	160	100	480	100

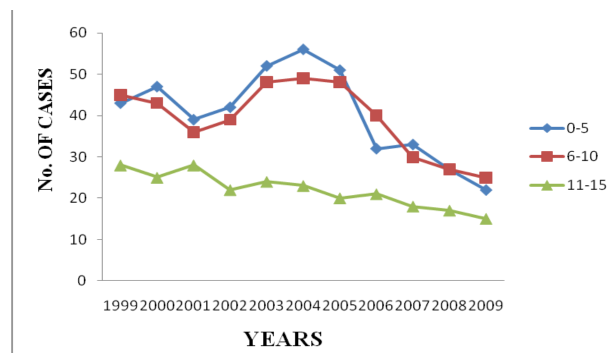

Figure No.1: Showing Year Wise Distribution of 480 Cases Reported for Physiological Jaundice and Hepatitis

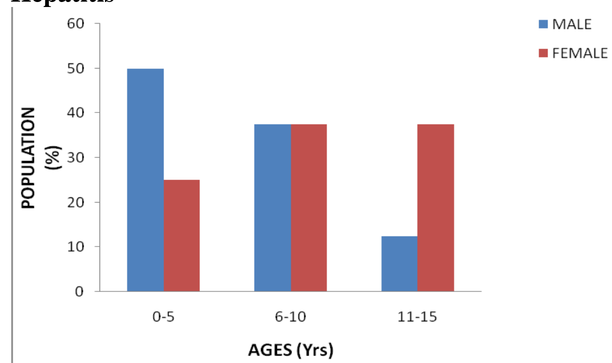

Figure No.2:Showing Age and Sex Differentiation in Young Population

It is observed that the tendency of liver inflammation was decreased with increase in age & sexual differentiation showing male predominance with male to female ratio of 2:1.

DISCUSSION

Hepatitis is associated with the necrosis of hepatocytes is a leading cause of chronic liver diseases[1,6]. In developing countries, hepatitis is common, nearly 100% of the population in some countries has serologic evidence of past hepatitis during childhood[4,7,8,9,10,13]. Hepatitis is considered as the second most important cause of cirrhosis[5], while the major cause of liver cirrhosis can be catarrhal jaundice. Viral hepatitis and especially the hepatitis B is a frequent cause of chronic hepatitis and fulminant hepatitis rarely[6]. Most of the cases of neonatal or chronic hepatitis are associated with [15,16], mild to moderate inflammatory infiltrate or cholestasis[1]. It is also known that neonatal hepatitis and liver fibrosis and can develop cirrohsis[1]. In the western population, prior to targeted vaccination programs, the highest rate of liver infection occurred in children aged 5-14 years[17, 18], in our results we found that there is decline in the symptoms after the age of 12 years. Moreover the classic symptoms of hepatitis are less likely in younger patients. Children less than 5 years of age are highly symptomatic and have jaundice as the major symptom [14] (Fig.2). Our results show a high male to female ratio i.e. 2:1 (Table 1). In Asia neonatal hepatitis and early childhood liver diseases cause liver dysfunction and other complications[19]. The ratio of various types of hepatitis appear to be higher in males than females[2, 20]. Urban communities are more involved than rural areas. Jaundice is occurred more in adults than children below 15 years of age, and the ratio is also increased in males than females[5].

CONCLUSION

The inflammation of liver in infants and young children is an indicator of hepatitis that can be caused by metabolic, infectious, and genetic disorders. It is mainly characterized by physiological jaundice in newborn and mostly reported in male population than females. In Karachi this is found that neonatal hepatitis can be recovered with the growing age and it is found to be a common cause for enlargement of liver and associated liver diseases in infants and children that can lead to higher risks of acute or chronic responses in adulthood.

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Original Article

To see the Gross Qualitative Parameters such as General Appearance of Rats and their testes after Long and Short Term Use of Sildenafil Citrate

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ABSTRACT

Objective: To see the gross qualitative parameters such as general appearance of rats and their testes after long and short term use of Sildenafil Citrate.

Background: As very little attention has been given to explore the effects of a sildenafil citrate on histological aspects of testes, hence this experimental study was designed to check whether the drug which is being used indiscriminately in our country and abroad is safe or it has any harmful effect on the architecture of rat testis.

Study design: Experimental Study

Place and Duration of Study: This study was conducted in departments of Anatomy & Histopathology Shaikh Zayed Hospital Lahore for a period of six weeks from 02.05.2008 to 17.06.2008.

Materials and Methods: Sample size consisted of 45 animals, divided into Group A (Control), Group B and C (Experimental), Each group was consisting of 15 animals. Physical examination of rats and their testis was done every day by the author himself and recorded.

Results: After giving drug, on inspection of rats all the animals were active and healthy and the gross appearance of the testes was normal except in an animal, in which the testes were smaller than the associates of the same group. Eating habits of all the animals were normal, taking food and water freely. After half an hour of giving the drug, they were mounting over each other and looked aggressive. The comparison of all the groups, A vs B, A vs C and B vs C remained statistically non –significant ($P>0.05$).

Conclusion: No significant difference was observed in qualitative parameters (general appearance) of the rats and their testes after giving sildenafil citrate.

Key words: Sildenafil, testis, qualitative parameters.

INTRODUCTION

Impotence and infertility are the great social problems in some communities, regarded as disgrace, a mark of divine displeasure, and ground for divorce or even for compulsory suicide. Males are blamed to be impotent or infertile in some marriage failure cases, therefore in such an atmosphere, abuse of drugs is quite common. In a routine practice, sildenafil citrate is frequently and indiscriminately used to enhance the sexual orgasm by old age people and sportsmen[1]. Infrequent use as an aphrodiasic and performance improving agent may cause harmful effects. Sildenafil citrate is prescribed in cases of erectile dysfunction and pulmonary hypertension but little attention so far has been paid to the indiscriminate and vigorous use of sildenafil handled by medical and paramedical staff, quacks and self –medicants. Although this misdirected therapy is practised for improving the impotence but as a matter of fact, it may result into maturation arrest of spermatozoa, or even toxic for spermatogonia as well[2].

Erectile dysfunction (ED) is a world wide problem which may have significant negative impact on quality of life with particular reference to psychological point of view[3]. Until recently, no effective oral therapy existed, the options present were highly difficult to perform, and majority of people found them un essay solution for a satisfactory response[4]. Ideal oral treatment for erectile dysfunction should have following features: easy administration with a reasonable short time prior to sexual activity, reliable efficacy, good tolerability within therapeutic range, high selectively for the site of action, lack of side effect like CNS problems, that yields prompt onset of action and a plasma half-life that produces an appropriate duration of action while avoiding its accumulation in blood by its daily use[5]. Sildenafil citrate (Viagra) is the first oral agent introduced for treatment of ED, meets this strict criteria. It is rapidly absorbed and acts with in 30 minutes to 1 hour, it has a short plasma half–life of approximately 4 hours; and it is well tolerated in the dosage range studied with no clinically appreciable effects on heart rate or blood pressure.[6-8] In clinical trials, single oral doses, of sildenafil have shown effectiveness in the treatment of ED of organic, psychogenic or mixed etiologies. [7,9-10]

The effects of sildenafil citrate have also been observed on eyes, such as bovine retinas were isolated and perfused for the purpose to understand the physiology of sildenafil on retina with a low and a high concentration, higher concentrations were found to be potential for retinal degeneration[11]. In rats prolong use demonstrated the dilation and congestion of choroidal vasculature[12]. But it has no role to cause any significant changes in foveolar choroidal circulation of age related macular degeneration patinets[13]. Sildenafil on human retinal blood flow, have showed increased retinal venous diameters and retinal blood flow with out causing rise in intra ocular pressure[14]. As this drug is phospho diesterase enzyme (PDE) inhibitor, PDE-5 in addition to PDE-6 enzyme localizations on human retina have been confirmed[15]. But it has also been reported that erectile dysfunction agents including sildenafil citrate had a causative effect on non –arteritic anterior ischemic optic neuropathy [16-22]. In animals, prolong use of sildenafil with mild doses twice daily have reduced myocardial infarction. Myocardial infarction was induced by the ligation of left anterior descending coronary artery [23]. Its protective role against ischemia of heart in mice is also proved [24].

In view of above facts we designed this study to see the gross qualitative parameters such as general appearance of rats and their testes after long and short term use of sildenafil citrate.

MATERIALS AND METHODS

Three groups A,B & C each consisting upon fifteen male adult albino rats of wistar strain weighing 250-300 g were used for this experimental study. The study was conducted in the departments of Anatomy and Histopathology at Shaikh Zayed Federal Post graduate Medical Institute Lahore. The animals were assessed for their sexual maturity on the basis of following criteria.

1. Random fighting and aggressive behavior.
2. Bucking i.c attempt to mount.
3. Free hanging of testes in the scrotal sacs.

This study was carried out over the period of six weeks on 45 animals. Two weeks were given for acclimatization and to check the state of health on the basis of weight gain or loss and four weeks for experiment. All the rats were numbered with a permanent marker and divided randomly into three groups, group A as control, group B & C as experimental, each group comprised of 15 rats. Drug was purchased from Al-Towar Pharmacy, Hor Al Anz, DUBAI, UAE and the expenses were borne by the author himself.

Group A (Control) did not receive drug, while in group B (Experimental) each animal was given sildenafil citrate in a dose of 8 mg /kg orally after dilution with water on alternate days for four weeks i.e total 14 doses. In group C (experimental) each animal was given sildenafil citrate in a dose of 8 mg/ kg orally after dilution with water once a week for four weeks i.e total 4 doses.

Assessment of animals was done by the author every day for a period of four weeks, to exclude any general ailment by their physical activity, eating behavior and general appearance. Gross appearance of testes was also examined for any obvious abnormality.

This study was permitted by Ethical review board of federal post graduate medical institute of Shaikh Zayed Medical Complex Lahore.

RESULTS

The qualitative parameters were.

1. **Gross appearance of albino rats before dissection:** Animals of all the groups were active and healthy looking through out the period of experiment. Eating habits of all animals were normal and they were taking food and water freely. They were active and representing no sign of ailment. Therefore this parameter statistically remained constant as shown in table 1, after half an hour of giving the drug, they were observed to be mounting over each other and looked aggressive.

Table No.1: Comparison of gross qualitative parameters in the rats of control group A (unexposed) and experimental groups B and C (exposed) to sildenafil

Parameters	Groups						Chi-square	P-Value
	A (n=15)		B (n=15)		C (n=15)			
	N (ab)	%	N (ab)	%	N (ab)	%		
Gross appearance of albino rats before dissection	0	0.00	0	0.00	0	0.00	0.000	1.00++
Gross Appearance of testes after dissection	0	0.00	1	6.70	0	0.00	2.05	0.360++

Key: N(ab) : Number of animals with abnormality, **n** : Number of animals in each group
++ Non-significant difference (P>0.05)

Table No. 2: Comparison of gross appearance of testes, in the rats of control group A (unexposed) and experimental groups B and C (exposed) sildenafil

Groups	Group compared	Chi square	P value
A	B	1.034	0.309++
	C	0.000	1.000++
B	C	1.034	0.309++

Key:
A : Control group**B :** Experimental group
C : Experimental group
++Indicate non significant difference (P>0.05)

2. **Gross appearance of testis after dissection:** The gross appearance of testes of group B were also normal in all aspects except in one animal (6.7%) as shown in Table -1, in which the testes were looking relatively smaller and seemed to be atrophied. Seminiferous tubules were not easily plucked out from the testes of that animal and stringing out phenomena was also found decreased. The gross appearance of testes of experimental group C was also normal as seen in Table-1. Both the phenomena stringing and plucking out were normal. The comparision of all groups, A vs B, A vs C and B vs C reveled statistically non – significant difference (P>0.05) Table -2.

DISCUSSION

Since none of the study is available in literature regarding morphological changes in testis of albino rats after giving sildenafil citrate therefore it is almost impossible to relate this study with others. However we were able to find atrophic changes in testis of one of the rats, it is just possible that if the sample size is made larger we may be able to confirm or exclude atrophic changes noted in one of our experimental animal.

There is possibility that this may have happened by chance, as a result of over sight by the author or it may be the result of some sort of infection which may have caused atrophic changes in the testes of albino rat but not manifested on gross general appearance of rats and their testes. But we can not be sure of anything until we do this study taking a large sample size and done at multiple centers to remove the individual bias or occurrence by chance. The smallness in size of testis that we found in one of the rats may be found in other organs of animals after giving this drug and this may have implications in turn over human organs as well. We observed a significant finding that when rats were given sildenafil citrate, after half an hour they were mounting over each other and looked aggressive their by indicating sexual behavioral changes which is in agreement with the findings of study done by Eardley I[6].

CONCLUSION

No satisfactory significant difference was observed in the gross qualitative parameters of rats and their testes after long and short term use of sildenafil citrate.

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Original Article

A Comparative Study of Cross and Parallel Kirschner-Wires Fixation in Gartland Type-III Supracondylar Fracture of Humerus in Children

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ABSTRACT

Aims and Objective: To compare the anatomical and functional results of open reduction and internal fixation of supracondylar fracture of humerus in children with parallel and cross K-wire fixation and to determine the best method of fixation, preventing complications

Study design: A comparative study.

Place and Duration of Study: This study was conducted in Orthopaedics department, District Head Quarter Hospital Dera Ghazi Khan from March 2011 to September 2011.

Materials and Methods: Forty consecutive patients from 4 to 10 years of age (mean age of 6.4 years) with Gartland type-III supracondylar fractures of humerus, received in the emergency department were included in the study.

Results: In this study, patients from 4 to 10 years of age were included. Their mean age was 6.4 years. Their age distribution is shown in Graph-1. Highest numbers of patients were from 6 to 7 years of age. Those were 17 (42.5%). The mean age of the patients in which fracture was fixed by parallel Kirschner wires, was 6.2 years and the mean age of the patients in which fracture was fixed by cross Kirschner wires, was 6.6 years.

Conclusion: On the basis of above mentioned findings and review of the available literature, the conclusion of this study is that cross Kirschner wires configuration is more safer and stronger mode of fixing all Gartland type-III supracondylar fracture of humerus in children.

Key words: Kirschner-Wires Fixation, Gartland Type-III, Supracondylar Fracture of Humerus

INTRODUCTION

It is exclusively a fracture of the immature skeleton[1]. The bone in the supracondylar area is weaker during the last part of first decade because it is undergoing metaphyseal remodeling. As the younger child falls with the outstretched arm, the elbow is hyper extended and the tip of the olecranon is forced into the thinnest portion at the depth of olecranon fossa thus fracturing the Supracondylar area.

Supracondylar fracture is the second most common fracture in children (16.6 %) and the most frequent before the age of seven years[1]. According to Boyd HB, Altenberg AR[2] who studied 713 fractures of the elbow in children, 12 years of age or younger, Supracondylar fracture of Humerus is 65.4% of all the fractures of the elbow in children.

Supracondylar fractures occur as two main types: the common extension type and the rare flexion type. According to Wilkins KE, King RE[3], 97.7% of the fractures were of the extension type, and only 2.2% were of the flexion type.

Supracondylar fractures were described in the writings of Hippocrates[4] during the third and fourth century A.D, but it was not until the 1700s that much was written about supracondylar fractures in the classic medical literature. In a series of pediatric extremity fractures published[5] in 1954, fractures of the supracondylar area had a greater rate of re-reduction, nerve injury, surgical intervention, and poor results than any other type of extremity fracture. In 1959, GartlandJJ[6] described three stages of extension type Supracondylar fracture humerus based on the degree of displacement. Type-I:- Un displaced

Type-II:- Displaced but with intact posterior cortex. Type-III:- Displaced with no cortical contact. These are further divided Into Posteromedial and posterolateral types.

Treatment of supracondylar fractures is controversial and often technically difficult; complications are common. Cubitus varus is the most frequent problem with a mean incidence of 30%[7]. Injury to any of the three major nerves around the elbow occurs in 6-16% of cases[8].

Type I and type II fractures are usually treated conservatively. A variety of methods of treatment for displaced type III fractures has been recommended including closed reduction and immobilisation,[6] traction by various methods[10] and closed[11] or open reduction[12] stabilised by Kirschner wires under image intensifier. Non-operative management by straight lateral traction with the elbow in extension was first reported in 1939[9] and was later reviewed in a study[10].

Open reduction and internal fixation is done in most of the centers in Pakistan, including ours, due to lack of the facility of image intensifier and decrease in the rate of complications as compared to closed reduction.

MATERIALS AND METHODS

This study was conducted in Orthopaedics department, District Head Quarter Hospital Dera Ghazi Khan from

March 2011 to September 2011. Forty consecutive patients from 4 to 10 years of age (mean age of 6.4 years) with Gartland type-III supracondylar fractures of humerus, received in the emergency department were included in the study.

RESULTS

In this study, patients from 4 to 10 years of age were included. Their mean age was 6.4 years. Their age distribution is shown in Graph-1. Highest numbers of patients were from 6 to 7 years of age. Those were 17 (42.5%). The mean age of the patients in which fracture was fixed by parallel Kirschner wires, was 6.2 years and the mean age of the patients in which fracture was fixed by cross Kirschner wires, was 6.6 years.

There were 28 (70%) male patients and 12 (30%) female patients. Out of them, 15 males and 5 females, in which fracture was fixed by parallel Kirschner wires. There were 13 males and 7 females, in which fracture was fixed by cross Kirschner wires.

Left humerus was fractured in 23 (57.5 %) and Right humerus was involved in 17 patients (42.5 %) as shown in Table-3 and Graph-3. Left humerus was fractured in 12 patients and Right humerus was fractured in 8 patients, in which fixation was done by parallel Kirschner wires. Left humerus was fractured in 11 patients and Right humerus was fractured in 9 patients, in which fixation was done by cross Kirschner wires. All the patients included in the study had Gartland type III fracture of humerus. 34 (85%) of them had posteromedial and 6 (15%) of them had posterolateral displacement of distal segment.

In 20 (50%) patients, Supracondylar fracture of humerus was fixed by parallel and in other 20 (50%) patients, fracture was fixed by cross configuration of Kirschner wires.

Table No.1: Metaphyseal-diaphyseal angle

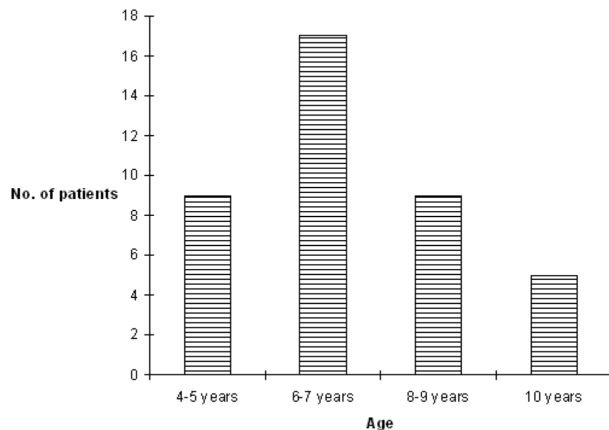
		Parallel wires	Cross wires	P-value
Immediate postoperative Metaphyseal-diaphyseal angle	No. of patients	20	20	0.007878
	Mean	97.25	90	
	SD	11.43345	1.685854	
Metaphyseal-diaphyseal angle at 1st week	No. of patients	16	15	0.001785
	Mean	93.125	90.05	
	SD	3.221949	3.221949	
Metaphyseal-diaphyseal angle at 3rd week	No. of patients	16	20	0.013659
	Mean	93.5	89.95	
	SD	5.853774	1.605091	
Metaphyseal-diaphyseal angle at 6th week	No. of patients	16	19	0.012733
	Mean	93.3125	89.78947	
	SD	5.618051	1.474937	
Metaphyseal-diaphyseal angle at 3rd month	No. of patients	16	19	1.474937
	Mean	93.25	89.78947	
	SD	89.78947	1.474937	
Metaphyseal-diaphyseal angle at 6th month	No. of patients	16	19	0.014496
	Mean	93.1875	93.1875	
	SD	5.36928	1.474937	

Table No.2: Range of motion

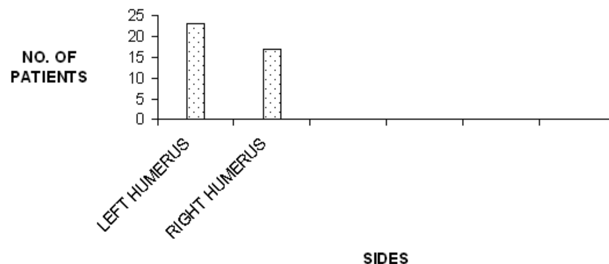
		Parallel wires		Cross wires		P.-value
		Mean	SD	Mean	SD	
3rd post-operative week	Experimental fixation arc	30.625	7.274384	31.05263	6.141604	0.851517
	Supinatiion-pronation arc	109.6875	16.47915	116.0526	13.2894	0.214591
6th post-operative week	Extension-flexion arc	81.25	11.32843	83.68421	9.104655	0.485757
	Supinatiion-pronation arc	126.5625	17.29342	130.2632	13.2784	0.479106
3rd post-operative month	Extension-flexion arc	94.6875	9.393038	96.31579	11.76649	0.658306
	Supinatiion-pronation arc	133.75	16.38088	137.3684	11.82845	0.454235
6th post-operative month	Extension-flexion arc	128.75	17.27233	133.1579	17.57607	0.461581
	Supinatiion-pronation arc	156.5625	28.26769	162.8947	19.38755	0.439279

Table No.3: Complications

	Revised fixation	Pin-track infection	Cubitus varus	Anterior bone block	Tourniquet palsy
Parallel wires	4	2	3	1	0
Percentage	20.0	12.5	18.7	6.2	-
Cross wires	-	2,0	1,0	1.0	1.0
Percentage	-	10.0	5.2	5.2	5.0



Graph No.1: Age Distribution



Graph No.2: Side Involved

DISCUSSION

Supracondylar fracture of humerus is a fracture of the immature skeleton. The bone in the supracondylar area is weaker during the last part of first decade because it is undergoing metaphyseal remodeling. In my study, 40 patients from 4 to 10 years of age were included. Their mean age was 6.4 years. Highest numbers of patients were from 6 to 7 years of age were 17 (42.5%).

Wilkins reviewed 4520 patients with supracondylar fracture of humerus in 31 major series[13]. He observed that most of these fractures occurred between the ages of 5 and 8 years.

In a study, 46 patients of supracondylar fractures of humerus were included. Maximum patients were from 7 to 9 years of age[14].

In another study, 62 patients of supracondylar fractures of humerus were included.Maximum patients were from 4 to 9 years of age[15].

46 patients with supracondylar fractures of humerus were included in a study[16]. The mean age of the patients was 6 years.

The mean age of 71 patients with supracondylar fractures of humerus, included in a study conducted was 6 years[17]. In this study, out of 40 patients, there were 28 males (70%) and 12 female patients (30%).

Boys outnumbered girls by 119 to 111 (52 % and 48% respectively) in a study conducted[18].

In a study, 71 patients with supracondylar fractures of humerus were included[17]. Among them 41 (57.7%) were boys and 30 (42.2%) were girls. In this study, left humerus was fractured in 23 (57.5%) and right humerus was involved in 17 patients (42.5%). These findings were comparable with previous studies as mentioned below.

One hundred and forty-five (63%) of the injuries were in the left elbow and eighty-five (37%) were in the right in a study [18].

In a study conducted on supracondylar fracture of humerus in children, the left side was injured in 22 (62.8%) patients, and the right side in 13 (37.1%) patients[19]. Left humerus was fractured in 35 (74.46%) and right in 12 (25.5%) children, in a study conducted by Richard et al[20]. Posteromedial displacement of the distal segment was observed in more patients as compared to posterolateral,probably secondary to the pull of the triceps, which originates more medially.In this study distal segment of the fracture was displaced posteromedially in 34 (85%) and posterolaterally in 6 (15%) children, which is comparable to the reports of other authors .

Posteromedial displacement of the distal segment was observed in 94 (81.03%) and posterolateral in 22 (18.96%) children in a study[18].

In a study done, Posteromedial displacement of the distal segment was observed in 23 (58.9%) and posterolateral in 16 (41.02%) children[20].

In another, displacement of the distal fragment has been specifically noted, 75% of the time the fragment was displaced posteromedially[9]. Acute compromise of either the neural or circulatory status in the extremity is not uncommon after fractures about the elbow in children. Fortunately, most compromises are transient. In this study transient radial nerve palsy was encountered in 2 (5%) children with posteromedial displacement of the distal segment. Complete nerve functions recovered after 2 months in each case. No other neurovascular

(Brachial artery, Median or Ulnar nerve) injury was observed.

In a retrospective review of displaced extension-type supracondylar fractures of the humerus in 101 children revealed neural injuries in 13 (12.8%) children[22].

In a study it was observed nerve injuries in 3 (8.8%) out of 34 patients of supracondylar fractures, two of which involved the radial nerve and one the median nerve[19]. All resolved spontaneously between four and six months postinjury. One patient had no radial pulse upon presentation. However, the pulse returned promptly with reduction of the fracture.

The incidence of neural injuries in association with supracondylar fracture of humerus has been estimated to range from 5 to 19 per cent in studies done by other authers as well[23].

In a study, transient nerve palsies was observed in 5 (11.1%) out of 46 patients with supracondylar fracture of humerus, 3 of these 5 patients involving the radial nerve and 2 involving the median nerve. Complete nerve functions recovered after 3 months, in each case[24].

Four patients (20%) whose fracture was fixed by parallel Kirschner wires, lost fixation and required revised surgery because in the immediate post-operative radiographs, distal segment of the fracture was seen markedly rotated. Not a single patient required revised fixation, in whom fracture was fixed by cross Kirschner wires. This finding was very significant statistically.

It was also reported loss of fixation in 11(13.75%) of 80 patients in whom only two lateral wires had been used[11]. The loss of fixation was attributed to technical errors, such as failure to engage the proximal and distal cortices and crossing of the wires at the fracture site. The authors concluded that, although the use of two lateral wires eliminates the risk of injury to the ulnar nerve, it is technically very demanding.

In a study the use of parallel wires led to re-displacement of the supracondylar fracture in 4 (57%) out of 7 patients despite an initial anatomical reduction[17].

Cubitus Varus developed in 18.7% of the patients, in which fracture was fixed by parallel wires. Cubitus Varus also developed in 5.2% of the patients, in which fracture was fixed by cross Kirschner wires. This difference was significant statistically. 2 (4.34%) out of 46 patients,whose fracture was fixed by cross wires, developed cubitus varus deformity postoperatively. There was no significant difference in the rate of pin track infection, torniquet palsy and anterior bone block, among both study groups.

CONCLUSION

On the basis of above mentioned findings and review of the available literature, the conclusion of this study is that cross Kirschner wires configuration is more safer and stronger mode of fixing all Gartland type-III supracondylar fracture of humerus in children.

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Original Article

Frequency of Wound Infection in Clean Orthopaedic Surgery Using Single Dose Antibiotic Prophylaxis

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ABSTRACT

Introduction: Wound infection is the disastrous complication after clean orthopaedic surgery. Role of prophylactic single dose parenteral antibiotic is still controversial in prevention of this morbidity.

Objective: Frequency of wound infection in patients underwent open reduction and internal fixation of long bone clean orthopaedic fracture using single dose antibiotic prophylaxis.

Study Design: case series study.

Place and Duration of Study: This study was conducted at the Department of Orthopaedic Unit 1, Civil Hospital, Karachi from 11th August 2010 to 10th February 2011.

Patients and Methods: A total of 231 patients having long bone clean orthopaedic fracture were selected. Patients diagnosed as clean orthopaedic cases and determination of fractures on X-ray with intact skin over fractures were included in the study. Patients with open fracture having co-morbidities already on antibiotics were excluded from the study. Open reduction and internal fixation was carried out using single prophylactic dose of injection cepharadine (2 grams). Wound infection was assess on 5th postoperative day according to Southampton wound grading system.

Results: There were 191 males and 40 females with mean age 36.70 years. Out of 231 patients, 213 had no infection while 18 cases had wound infection on 5th postoperative day.

Conclusion: The use of single dose prophylactic antibiotic prophylaxis is effective in preventing wound infection after management of clean long bones orthopaedic fractures.

Key words: Wound infection, Clean orthopaedic surgery, Antibiotic prophylaxis.

INTRODUCTION

Wound infections are the second most common cause of hospital acquired infection.[1] The National Research Council classified surgical wound infections into four major types, based on peri-operative bacterial contamination: (1) clean, (2) clean contaminated, (3) contaminated and (4) dirty wound infection.[2] Clean cases are those in which skin remains intact without break over fracture site.[3] The reported rate of wound infection after clean orthopaedic surgery is from 5-12%.[4-5]

Surgical wound infection causes postoperative complications and significant postoperative morbidity and mortality, prolongs hospital stay, and adds between 10% and 20% to hospital costs.[6] The history of wound infection took a pathophysiological direction when Lister first introduced antiseptic procedures in surgery.[7] Many methods have been employed for the control of contamination and growth reduction of micro-organisms.[8] The role of perioperative antibiotic prophylaxis in clean orthopaedic surgery is well established.[9] With the advent of aseptic surgery, there is increasing consensus among the orthopaedic surgeons to use single dose antibiotic prophylaxis for clean orthopaedic surgery.[10] In developing country like Pakistan, a 3-5 dose of regimen is still in practice as a precautionary measure.[11] In a study, Ali and Raza[12] showed that rate of wound infection after clean orthopaedic surgery is 8% using single dose prophylaxis versus 6% with 3-dose regimen. Additional antibiotic dosage not only increases the costs and side effects but also decreases the body resistance.[13] Therefore, the rationale of this study was to determine the frequency of wound infection in clean orthopaedic surgery using single dose antibiotic prophylaxis which will help in gaining the confidence of local surgeon to use single dose prophylaxis in our setup.

PATIENTS AND METHODS

This case series study was carried out from 11th Agusut 2010 to 10th February 2011 in the Department of Orthopaedic Unit 1, Civil Hospital, Karachi. A total of 231 patients having long bone clean orthopaedic fracture were selected. Patients diagnosed as clean orthopaedic cases and determination of fractures on X-ray with intact skin over fractures was included in the study. The patients with open fracture having co-morbidities already on antibiotics were excluded from the study. Operative procedures were performed by three assistant professor of the unit with similar clinical experience and expertise. Postoperative, apart from intravenous fluids, parenteral analgesics, and antiemetics, no additional dose of antibiotic was given

to the patient. Open reduction and internal fixation was carried out using single prophylactic dose of injection cepharadine (2 grams). Spinal or general anaesthesia was instituted as per requirement. The patient was assessed for wound infection of the operative site on 5th postoperative day. The wound examination findings were graded according to Southampton wound grading system. The SPSS version 15 was used to analyze the data.

RESULTS

Two hundred and thirty one patients having long bone fractures were included in the study. There were 191 (82.7%) males and 40 (17.3%) females with male to female ratio was 4.8:1. Age of the patients ranged between 18-70 years. Overall mean±SD age of the patients was 36.70±13.35 years (Table 1).

Table No. 1: Frequency distribution of age and sex (n=231)

Parameter	No.	%age
Age (years)		
18 – 30	131	44.2
31 – 40	40	17.3
41 – 50	42	18.2
51 – 60	39	16.9
61 – 70	8	3.5
Sex		
Male	191	82.7
Female	40	17.3

Table No.2: Frequency distribution of long bones involved with respect to final outcome

Long bone involved	No infection (n=213)		Wound infection (n=18)	
	No.	%	No.	%
Femur (n=133)	129	55.8	4	1.7
Tibia/Fibula (n=41)	35	15.2	6	2.6
Humerus (n=22)	18	7.8	4	1.7
Radius/Ulna (n=35)	31	13.4	4	1.7

Table No.3: Duration of time from fracture to surgery with respect to final outcome

Duration (days)	No infection (n=213)		Wound infection (n=18)	
	No.	%	No.	%
≤10 days (n=130)	118	51.1	12	5.2
>10 days (n=101)	95	41.1	6	2.6

Wound infection rates with respect to long bones involved and duration from fracture to surgery are presented in Tables 2 and 3 respectively. Wound infection occurred more in open reduction and internal fixation of fracture of tibia/fibula (2.6%). However, wound infection rates were high (5.2%) in those patients whom surgery was performed ≤10 days after fracture.

DISCUSSION

Long bones fractures are frequently encountered in orthopaedic practice as a consequence of blunt and penetrating trauma. Open reduction and internal fixation is the primary treatment strategy in management of closed long bones fractures.[14] Among various complications, surgical site infection is prove to be disastrous in the presence of metallic implants.[15] The results of current study showed a 7.8% of wound infection rates after open reduction and internal fixation of clean long bones fracture using single dose prophylactic antibiotics. Most of the long bones fractures are encountered in young age group. Dai et al[16] reported that majority of the afflicted patients were between 18 to 30 years of age group with mean being 36.70 years. Ilyas et al[17] also noticed average age of 33 years in their case series, which is nearly comparable to results of this study. The sex ratio distribution in the present study was also in keeping with other literature. Ghauri et al[18] observed 85% of males and 15% of females in their prospective study management of aseptic non-union of diaphyseal fractures of long bones. Whereas in the in the present study, 82.7% of males and 17.3% of females had their long bones fractures.

The role of prophylactic antibiotics in clean orthopaedic surgery has been well established.[9] Percin and associates[19] evaluated a role of single dose parenteral cefazolin prophylaxis in 228 orthopaedic and traumatologic surgical patients. Both major and minor wound infections were reduced in single dose antibiotic treated group. Whereas in the present study, out of 231 clean orthopaedic long bones fracture receiving single parenteral dose of cepharadine, 18 (7.8%) cases demonstrated wound infection on fifth postoperative day according to Southampton wound grading system, which is comparable to the study conducted by Ali and Raza.[12]

CONCLUSION

This study concluded that single antibiotic prophylaxis is effective in preventing wound infection after open reduction and internal fixation of clean long bones orthopaedic fractures. Therefore, this therapeutic strategy is suitable and should be considered in avoiding wound infection after all clean long bones orthopaedic fractures.

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CORRIGENDUM

It is to clarify that the name of Furrakh Mustafa Memon, Asstt. Prof. of Anatomy, DMC, DUHS, Karachi appeared in our Journal Medical Forum Monthly, April, 2012 (page 69) in Article “The Role of Vitamin ‘C’ on the Thickness of the Epidermis after X-Irradiation of the Guinea Pigs A Morphological Study under Light Microscope” may be read as second author instead of first author and Ghulam Mujtaba Kolachi may be read as first author instead of second author.

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Original Article

Disease Pattern and Outcome among Afghan Patients: Our Experience in Tertiary Care Hospital in Quetta

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ABSTRACT

There is paucity of studies focused on Afghan resident patients who come to Pakistan. These patients are either referred or come here due to lack of facilities in their home country. This study was done to show the spectrum of illness brought to Pakistan and if they were different from illnesses in their parent country.

Study Design: Descriptive Cross-Sectional Study.

Place and Duration of Study: This study was conducted at Paediatric Unit-I, Bolan Medical College Hospital, Quetta from June 2006 to May 2011.

Patients and Methods: All admitted patients who were bonafide citizens of Afghanistan were included in this study. The patients were divided into three groups to determine the frequencies of illness in each group. Percentages were calculated for various ages and diseases.

Results: A total of 4416 patients were admitted from June 2006 to May 2011, out of these 110 were Afghan patients and the rest were Pakistanis. 58.18% patients were in group I, 29 % were in group II while 14.5 % were in group III. The 34.5% were suffering from tuberculosis, 13.6% patients were malnourished, 9% had nephrotic syndrome, 10% had various malignancies, 6.6% had infectious diseases, 4.54% had haematological causes, 3.6% had celiac disease, and 4.54 % had liver disorders, while 14% had miscellaneous disorders.

Conclusion: Tuberculosis, malnutrition and infectious diseases are most common in afghan patients.

Key Words: Tuberculosis, Malnutrition, Pattern, Outcome.

INTRODUCTION

While there have been many studies on afghan refugees, there is paucity of studies focussed on Afghan resident patients who come to Pakistan. These patients are either referred or come here due to lack of facilities in their home country.[1] Afghan studies show that Tuberculosis, measles, diphtheria, and typhoid fever are other common infectious diseases.[2] This study was done to show the spectrum of illness brought to Pakistan and if they were different from illnesses in their parent country.[3]

PATIENTS AND METHODS

This descriptive cross sectional study was conducted at Paediatric Unit one BMCH. It lasted from June 2006 to May 2011. All admitted patients who were bonafide citizens of Afghanistan were included in this study. For this purpose data was analysed using files of patients admitted during the study period. All those patients who had sought refuge in Pakistan were excluded from the study. After this the patients were evaluated by a through history, physical examination and relevant investigations which were dictated by the diagnosis. The patients were divided into three groups to determine the frequencies of illness in each group. Group one consisted of patients up to the age of 60 months(5 years), group two included children from 61 months to 120 months(6-10 years) and group three consisted of patients more then 120 months. Percentages were calculated for various ages and diseases.

RESULTS

A total of 4416 patients were admitted from June 2006 to May 2011, out of these 110 were Afghan patients and the rest were Pakistanis (Table 1). Overall the Afghan patients constituted 2.49 % of the total patients admitted over five years. The year-wise distribution is shown in table 1. The male to female ratio was 1.89:1. 58.18% patients were in group I, 29 % were in group II while 14.5 % were in group III. The 34.5% were suffering from tuberculosis, 13.6% patients were malnourished, 9% had nephrotic syndrome, 10% had various malignancies, 6.6% had infectious diseases, 4.54% had haematological causes, 3.6% had celiac disease, and 4.54 % had liver disorders, while 14% had miscellaneous disorders. Among the tuberculous patients 65.9 % patients had tuberculous meningitis, 20.45% had pulmonary tuberculosis, and 9.09 had abdominal tuberculosis while 2.27% each had bone and spine tuberculosis respectively. In the tuberculous meningitis patients 6.89% had stage I, 24.13% had stage II while 68.96 % had stage III tuberculous meningitis. 82.72% percent patients were discharged, 10% patients died and 7.27% left against medical advice.

Table No.1: Year-wise distribution of total Pakistani and Afghan patients

Year	Total	Afghan	Pakistan	%age of Afghan patients per year
2006	306	06	300	1.96%
2007	1172	27	1145	2.30%
2008	758	16	742	2.11%
2009	848	21	827	2.47%
2010	997	25	972	2.50%
2011	335	15	320	4.47%
Total	4416	110	4312	2.49%

Table No.2: Break-up of tuberculosis patients (n=44)

Break-up of Tuberculosis	No.	%age
Tuberculous meningitis	29	65.9
Pulmonary tuberculosis	9	20.5
Tuberculous spine	1	2.3
Tuberculous arthritis	1	2.3
Abdominal tuberculosis	4	9.0

Table No.3: Break-up of tuberculous meningitis patients (n=29)

Grade	No.	%
I	2	6.9
II	7	24.2
III	20	68.9

DISCUSSION

Over five years the tuberculous patients constituted only a fragment of the population. This may be because of difficulties in logistics and war like situation in Afghanistan. Since this study was focussed only on bonafide afghan citizens and did not include those who were in refugee camps or who had settled in various cities of Balochistan, therefore this percentage can be explained. Male patients were twice as much as female patients perhaps owing to cultural and religious factors, whereby boys are more likely to be treated then girls.[4]

Most of the patients were below five years of age, thus showing the increased morbidity and mortality in this age group.[5,6] The number of patients decreased as the age increased thus showing increasing morbidity and inability of medical staff at Afghanistan to treat them.[7]

More then one third of the patients suffered from tuberculosis thus showing the high prevalence of tuberculosis in Afghanistan.[2,8,9] Among the tuberculosis patients more then two thirds suffered from tuberculous meningitis. This shows the delay in diagnosing this condition as most of the meningitis patients came at third stage.[9-11] This may also be because of decreased BCG vaccination among these children.[12-14] The lack of immunization and the malnourished status makes tuberculous meningitis more virulent in these patients.[15]

One fifth of the patients had pulmonary tuberculosis which was the second most common form of tuberculosis.[16,17] The third most common was abdominal tuberculosis.[18] A significant number of patients were malnourished thus contributing to the increased prevalence of tuberculosis.[19-21] The malnutrition was mostly primary and found in group one.

Nephrotic syndrome was also much prevalent in afghan patients, this was mostly steroid sensitive.[22] One tenth patients had malignancies, mostly acute lyphoblastic leukaemia.[23] Infectious diseases and particularly measles were also a significant concern.[24,25] The prevalence of haematological disorders especially aplastic anaemia has substantially increased since the recent war. More studies are needed to validate this. Three fifth of the patients were discharged, and mortality was only one fifth, while one fifth patients left against medical advice.

CONCLUSION

Tuberculosis, malnutrition and infectious diseased are the main diseases that are prevalent in patients referred from Afghanistan.

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Original Article

Transfusion Transmitted Infections (TTIS) Among Blood Donors of Sukkur

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ABSTRACT

Objective: To estimate an approximate disease burden of HIV, HBV, HCV, and Syphilis in healthy blood donors.

Background: Blood transfusion department not only screen transmitted infections but also give clue about the prevalence of these infections in healthy population. The objective of this study was to estimate an approximate disease burden of HIV, HBV, HCV, and Syphilis in healthy blood donors, so as to determine how well we are doing in fight against these killers. As most of these healthy blood donors are first time donors aged 18-60 years, the results can also be utilized to estimate the prevalence in healthy population of this age group.

Study Design: Retrospective Study.

Place and Duration of Study: This study was conducted in blood Bank of Ghulam Muhammad Mahar Medical College Hospital Sukkur from January 2008 to December 2010.

Materials and Methods: All healthy blood donors reporting to the blood bank in the specified study period were screened for HIV, Hepatitis B, C and Syphilis.

Results: A total of 7085 were screened, out of these 364 donors (5.14%) were seropositive for hepatitis C, 268 (3.78%) were seropositive for hepatitis B, 36 (0.5%) were seropositive for Syphilis and only 4 (0.05%) had shown seropositivity for HIV.

Conclusion: Transfusion transmitted infections are a major threat associated with unscreened blood donations. In Pakistan the prevalence of hepatitis B and C is very high in occult form. Selection of healthy blood donors and public awareness programs targeting local community will be an important measure to stop its transmission through blood transfusion.

Key Words: Hepatitis B, Hepatitis C, Syphilis, HIV, Transfusion transmitted infections.

INTRODUCTION

Blood has been used since 1930 for various indications[1]. Transfusion therapy is a well established treatment in various medical and surgical procedures[2]. After the introduction of the blood banks and better storage techniques it becomes more widely used in patients[3].

Transfusion of blood and its components is life saving as well as it has life threatening hazards. With every unit of blood there is a 1% chance of transfusion associated problems including transfusion transmitted diseases[4]. Blood is one of the major sources of transmission of hepatitis B, C, HIV, Syphilis and many other diseases[5, 6]. The hazards of transfusion can be minimized by proper screening and selection of donors before collection of blood[7] .WHO recommends that, at least, all donated blood should be screened for hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV) and Syphilis[8]. The prevalence of transfusion transmitted infections, among blood donors allows for assessment of epidemiology of these infections in the community[9]. The screening of blood for TTIs is mandatory for blood safety as lack of blood screening facilities adds to hazards of blood transfusions[10].

The purpose of this study was to determine the prevalence of TTIs in healthy blood donors coming to GMMMC Teaching hospital, Sukkur, with special entity of HIV, hepatitis B, hepatitis C, and Syphilis. By studying this prevalence, attention will be drawn towards the severity of the situation so that effective action can be taken to prevent further transmission of diseases via blood transfusion.

MATERIALS AND METHODS

Study Population: The subjects screened for HBV, HCV, HIV, and Syphilis were all healthy blood donors.

Study location: Blood bank of Ghulam Muhammad Mahar Medical College Hospital Sukkur.

Inclusion Criteria: Inclusion criteria followed were age 18-60 years, weight more than 50 kg and hemoglobin concentration above 12g/dl.

Exclusion Criteria: All individuals less than 18 years or older than 60 years were not bled. Donors with history of jaundice or documented HIV, HBV, HCV infections also refused for blood donations.

Assay: A total of 7085 healthy donors were screened for hepatitis B, C, HIV, and Syphilis. Enzyme linked immunosorbent assay (ELISA) was used for detection of Hepatitis B, C, and HIV and Veneral Disease Research Laboratory test (VDRL) for Syphilis.

RESULTS

All 7085 people under study were voluntary donors and none of them were paid. Among the donors, 672 (9.48%) had TTIs. Hepatitis C was present in 364 (5.14%) donors, 268 (3.78%) were hepatitis B, 36 (0.5%) were positive for Syphilis and only 4 (0.05%) had shown seropositivity for HIV as shown in table 1

The year wise distribution of donors and their status of seropositivity is shown in table 2

Table No.1 HBsAg, Anti-HCV, VDRL and anti-HIV prevalence in blood donors (n= 7085).

Serological marker	Seropositive	Percentage
HBsAg	268	3.78%
Anti-HCV	364	5.14%
VDRL	36	0.5%
Anti-HIV	04	0.05%

Table No.2: Prevalence of HBsAg, anti-HCV, VDRL, and anti- HIV among blood donors for studied years.

Year	Total number of blood donors	HBsAg	HBsAg	HCV	HCV	VDRL	VDRL	HIV	HIV
		Number	Percentage	No.	%age	No.	%age	No.	%age
2008	2117	97	4.58%	(2008) 117	5.53%	10	0.47%	01	0.047%
2009	2208	79	3.58%	(2009) 124	5.61%	12	0.54%	01	0.047%
2010	2760	92	3.33%	(2010) 123	4.46%	14	0.50%	02	0.072%
Total	7085	268	3.78%	364	5.14%	36	0.5%	04	0.05%

DISCUSSION

Blood transfusion is a life saving intervention and millions of lives are saved each year globally through this procedure[11]. However blood transfusions are associated with the risk of the transmission of infection[12] Globally, more than 81 million units of blood are donated each year3. More than 18 millions units of blood are not screened for transfusion-transmissible infections[12]

In Pakistan more than 1.5 million points of blood are collected each year[3] UNAIDS has estimated that only 50% of the 1.5 million blood bags are screened in Pakistan[13]. The lack of blood screening facilities adds to the risk of transfusion transmitted infections (TTIs) which can be overcome by proper selection of donors[10].

Results of our study shows that seropositivity of hepatitis C in healthy donors is high (5.14%) followed by seroprevalence of hepatitis B (3.78%). The seroprevalence of Syphilis is 0.5% and seropositivity of HIV is 0.05%. HCV was found to be the most common transfusion transmitted infection as compared with HBV, HIV and Syphilis. Our results are similar to study conducted by Asif et al (5.14%) from Islamabad3. For hepatitis B, our results are closer to the study conducted by Ujjan ID et al (3.65%) from Hyderabad[14].

For HIV and Syphilis, our findings are similar to study done by Manzoor I et al (0.05% and 0.5%) respectively from Lahore[15]. A similar study was conducted in other areas of Pakistan like Rawalpindi which showed that HCV was found to be most common (6.21%) whereas HBV was next in prevalence (5.86%) [16]. In another two years study done at blood transfusion center Tehsil Headquarter Hospital Liaquatpur the prevalence of HIV, HBV, and HCV was zero, 5.96% and 0.07% respectively[17], while in Combined Military Hospital Peshawar, HBsAg was positive in 1.75% and anti-HCV was positive in 2.60% of donors[18]. A study done at blood transfusion center Nishtar Hospital Multan and Fatimid Blood transfusion center Multan showed the prevalence of HIV, HBV, and HCV in healthy donors to be zero, 3.37% and 0.27% respectively[19].

In an International study done in India showed prevalence rate of TTIs were 0.35%, 0.35%, 1.66% and 0.8% for HIV, HCV, HBV, and Syphilis respectively[9]. It was noted that in Ethopia that prevalence rates of TTIs in blood donors were 4.5% for HIV, 8.2% for HBV and 5.8% for HCV[20]. In Iranian blood donors these rates were 0.003%, 0.487%, 0.093% and 0.005% for HIV, HBV, HCV and Syphilis respectively[21]. It was estimated that in Malawi HIV prevalence is 10.7%, HBV prevalence is 8.1% and HCV prevalence is 6.8%[22]. Tanzania showed prevalence of HIV, HBV and HCV in blood donors to be 3.8%, 8.8% and 1.5% respectively[23].

CONCLUSION

In conclusion blood is one of the main sources of transmission for hepatitis B, hepatitis C, HIV and Syphilis. The majority of donors are either voluntary, relatives or friends, who are apparently healthy but this study showed that these diseases are prevalent among healthy donors. Pakistan is still in a state of war with these killers.

Recommendations

It is important to follow the WHO guidelines to screen every donor for HBV, HCV, HIV and Syphilis to decrease the transmission of TTIs. Voluntary donors should be promoted and extensive donor selection and screening procedures should be made mandatory at each health care facility. Record keeping should be promoted. The Government of Pakistan should also

encourage blood banks at all levels to follow the National Blood Safety Regulations and to work together for its implementation

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Original Article

A Study of Knowledge, Attitude and Practices Regarding Breast Feeding Among Feeding Mothers

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ABSTRACT

Objectives: To determine the knowledge, attitude and practices regarding child feeding among feeding mothers and to promote breast-feeding practices among lactating mothers.

Study Design: Observational cross-sectional study (KAP Study).

Place and Duration of Study: This study was conducted at OPD and indoors of Obstetrics and pediatrics departments of Nishtar Hospital, Multan during the period from October 2010 to January 2011.

Materials and Methods: A total of 160 feeding mothers were selected by simple random technique.

Results:- In our study out of 160 mothers16 (10%) had matric education and only 08 (5%) had education higher than F.A while 80 (50%) were totally illiterate. Breast-feeding practices were low in lower class and high in middle and upper classes. A total of 61% children were breast-fed while 39% were non breast-fed. Out of 61% breast fed children, 45% were exclusively breast fed while 16% were partially breast-fed. Among the breast-fed children 60% were male while 40% were female. The mothers who started breast feeding with in few hours after birth were 61(38%) and 72 (45%) started breast-feeding on 1st day while 27 (17%) mothers started breast feeding on 2nd day after birth**.** 97%infants were given 'water', 'sugar', 'honey' & 'arq-e-gulag' as ghutti (1st feed) rather than giving breast milk due to different reasons. Duration of breast feeding was less than 1 year in 88 (55%) of the mothers, 56 (35%) breast fed their babies for 1-2 years while 16 (10%) breast fed for more than 2 years.

Conclusion:- Prelacteal feeds were given to majority of babies as first feed by relatives. Male infants are more breasts fed as compared to females. Most of the mothers don't breastfeed their children for the first 2-3 days because of misconception about colostrums**.** The leading cause of early weaning in most of children is next pregnancy. The trend in the breastfeeding is relatively lower in the lower socioeconomic class as compared to the middle and upper classes.

Key words:-Breast-feeding, Lactating mothers, Prelacteal.

INTRODUCTION

Breast-feeding is a normal and natural way of feeding the infants[1]. It provides the primary source of nutrition for infants before they are able to eat and digest other foods. Bbreastfeeding allows mother and baby to emotionally bond in a special way that can not be matched, since breastfeeding meets both the nutritional and nurturing needs[2].

The nutrition survey of Pakistan conducted in 1984-86 indicated that 99.3% mothers started breast-feeding at the time of birth of the baby, but in recent studies it is 90.8%[3].

The breast-feeding is still the first and the preferred method of feeding by the majority of Pakistani women's but the in-appropriate practices such as the provision of pre-lactal feeds, discarding the colostrums and delayed initiation of breast feed are widespread. Many mothers supplement the breast milk with water and other fluids. The supplement of the breast milk with other milk has been reported to increase the childhood mortality tenfold due to poor cleaning of the bottles and dilution With unsafe drinking water[4]. Extended breastfeeding is known to benefit the health of children in developing countries and despite widespread expectations of a decline in breastfeeding in these countries, it has been demonstrated that the incidence and duration of breastfeeding are in fact increasing in many countries[5].

According to WHO research the infant mortality rate in the developing countries is 5-10 times higher in children who have not been breastfed or who have been breastfed for less than 6 months. Despite the marked advantage of breast feeding its popularity has declined significantly in many parts of the world. The W.H.O recommends that infants should be exclusively breast fed for the first 6 months of life. Breast feeding should continue for at least 2 years, with weaning foods added at 6 months of age.

The discontinuation of breast feeding before 2 years of age contribute to the malnutrition and increased susceptibility to infection All these and similar practices lead to lactation failure[6].

In most of the countries with information on breast-feeding trends, recent declines have occurred, although the decreases range from sharp to moderate[7]. Pakistan shows an increase in exclusive breastfeeding under 4 months from 12% (1988) to 25% (1992). Postpartum

care augmented with individualized professional support commenced in the hospital and continued in the community significantly increases the duration of breastfeeding among women who identify themselves as being without support for the first month postpartum[8].

UNICEF and Govt. of Pakistan launched a program called baby friendly hospital initiative in 1992 to improve optimal breast feeding practices in hospitals and other Health facilities[9].

Breastfeeding is associated with decreased risk for many early-life diseases and conditions, including otitis media, respiratory tract infections, atopic dermatitis, gastroenteritis, type 2 diabetes, sudden infant death syndrome, and obesity .Breastfeeding also is associated with health benefits to women, including decreased risk for type 2 diabetes, ovarian cancer, and breast cancer[10].

In 2007, Healthy People 2010 objectives for breastfeeding initiation and duration were updated to include two new objectives on exclusive breastfeeding (i.e. to increase the proportion of mothers who exclusively breastfeed their infants through age 3 months to 60% and through age 6 months to 25%[11].

Research has indicated that less education and lower socioeconomic status are associated with lower rates of breastfeeding among all racial/ethnic groups; however, black women across all socio-demographic variables consistently had lower rates of breastfeeding than white and Mexican-American women[12].

Lower rates of breastfeeding among black women have been attributed to several factors, such as economic pressures to return to work environments that do not support breast eeding, lack of breastfeeding education and supportive social networks, aggressive marketing by formula manufacturers, and cultural environments that do not value breastfeeding or promote positive images of breastfeeding women[13].

However, successful interventions such as the Baby Friendly Hospital Initiative,† in which hospitals adopt 10 practices that support breastfeeding as outlined by UNICEF and the World Health Organization (WHO), have resulted in increases in rates of both overall and exclusive breastfeeding among black women and other subgroups with the lowest breastfeeding rates[14]. According to latest research carried out by WHO %age of breastfed children in different regions was (Eastern Europe, Central Asian countries-17%, Asia Pacific-33%, South Asia (Pakistan, India, Bangladesh) 24-26% & Sri Lanka-75%).

MATERIALS AND METHODS

It was an observational cross-sectional hospital based study (KAP Study), conducted at OPD and indoors of Obstetrics and pediatrics departments of Nishtar Hospital, Multan during the period from October, 2010 to January, 2011. A total of one hundred and sixty feeding mothers were selected by simple random technique. Data were collected from mothers by a pre-tested structured questionnaire. The data was analyzed by applying various statistical tests and formulas such as frequencies, percentages, Means and Chi square test. Level of significance was set at 0.01.

RESULTS

In our study out of 160 mothers 16(10%) had matric education and only 8 (5%) had education higher than F.A while 80 (50%) were totally illiterate (Table-1).

Out of 160 women 76 (47%) were from middle class, 48 (30%) from lower class and only 36 (23%) belonged to upper class. Breast-feeding practices were low in lower class, high in middle and upper classes (Table-2).

The mothers who started breast feeding with in few hours after birth were 61 (38%) and 72 (45%) started breast-feeding on 1st day while 27 (17%) mothers started breast feeding on 2nd day after birth as shown in table-3.

Duration of breast feeding was less than 1-year in 88 (55%) of the mothers, 56 (35%) breast fed their babies for 1-2 years while 16 (10%) breast fed for more than 2-years (Table-4).

A total of 61% children were breast-fed while 39% were non breast-fed. Out of 61% breast fed children, 45% were exclusively breast fed while 16% were partially breast fed. Among the breast-fed children 60% were male while 40% were female. The reasons for early curtailment of breast feeding were the perceptions of mothers 56 (35%) to stop breast feeding during ill health, 72 (45%) were against breast feeding during pregnancy while 32 (20%) mothers thinking was their milk is poor in quality and quantity and is not good for the health of baby.

Table No.1: Literacy status of mothers (n=160)

Education	No. of patients	%age
Nil	80	50.0
Primary	24	15.0
Middle	32	20.0
Matric	16	10.0
F.A and above	08	05.0

Table No.2: Socio economic status (n=160)

Class	No. of patients	Percentage
Upper	36	23.0
Middle	76	47.0
Lower	48	30.0

Table No.3: Status of breast feeding (n=160)

Status	No. of patients	%age
Within in few hours	61	38.0
1st day	72	45.0
2nd day	27	17.0

Table No.4: Duration of breast feeding (n=160)

CDuration	No. of patients	Percentage
< 1 year	88	55.0
1-2 years	56	35
> 2 years	16	10.0

DISCUSSION

The study was conducted at OPD and indoors of Obstetrics and pediatrics departments of Nishtar Hospital, Multan during the period from October 2010 to January 2011. It was hospital based an observational cross-sectional study (KAP Study). One hundred and sixty feeding mothers were selected by simple random method. The aim of our research was to study knowledge, attitude and practices regarding breast feeding among feeding-mothers. The mean age of women was 26 years. 36% were primigravida and 50% of the women were illiterate.

This study showed that 97% infants were given 'water', 'sugar', 'honey' & 'arq-e-gulag' as ghutti (1st feed) rather than giving breast milk due to different reasons. Main reason was the belief that moral of the infant is affected by individual who gives first feed and other reasons were religious applications and as a cleaner of gut. While in one study ghutti was given to 94% of babies[4]. 62% of infants remained devoid of breast feeding for 1st1- 2 days because mostly mothers strictly denied to accept colostrums as beneficial food for their babies.

As far as socio-economic status is concerned, breast feeding practice was low in lower class, same was observed in other studies also[12].

Despite having awareness of breast feeding, the feeding practice is low among working women due to shortage of time. Among breastfed children, next pregnancy is leading cause of early weaning (<1year). In our study exclusively breast fed children were 45% while in a cross sectional study carried out between June and October 2006 in Clang exclusive beast feeding was reported by 23.8%, mixed feeding by 14.5% and infant formula feeding was reported by 52.7% of women

According to WHO researches in 1988 in Pakistan, exclusive breastfeeding was 12% and in 1995 it increased up to 25%. According to our research in this specified region of Multan exclusive breastfeeding has increased up to 45%. Breast fed babies enjoy good health, survive better and show good protection against infectious diseases[15].

In our study only 38% of the mothers gave their first breast feed with in few hours after birth and 45% gave on the first day, almost similar results were observed in another study where it was started by 38% with in few hours and 40% on the first day respectively[14].

Duration of breast feeding was less than 1-year in 55% of the mothers, 35% breast fed their babies for 1-2 years while 10% breast fed for more than 2-years. In a study it was observed that the discontinuation of breast feeding before two years of age contribute to the malnutrition and increased susceptibility to infection[16].

CONCLUSION

Prelacteal feeds were given to majority of babies as first feed by relatives. Male infants are more breastfed as compared to females. Most of the mothers do not breastfeed their children for the first 2-3 days because of misconceptions about colostrums. The leading cause of early weaning in most of children is next pregnancy. The trend in the breastfeeding is relatively lower in the lower socioeconomic class as compared to the middle and upper classes.

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Original Article

Comparison of Intravenous with Oral Iron in Management of Iron Deficiency Anemia in Pregnancy

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ABSTRACT

Objective: To compare the therapeutic effect of intravenous and oral iron therapy in iron deficiency anemia of pregnancy.

Study Design: Quasi experimental comparative study.

Place and Duration of Study: This study was conducted in department of Gynecology and Obstetrics, Fauji Foundation Hospital Rawalpindi from I[st] April 2007 to 31[st]December 2007.

Patients and Methods: One hundred pregnant women of confirmed iron deficiency anemia with hemoglobin levels between 7-8 gm/dl and serum ferritin level < 12ug/l were recruited from antenatal clinic and obstetrical ward and divided in two equal groups and assigned either intravenous or oral iron therapy. Patients not willing for follow up or had anemia due to other causes such as megaloblastic or hemolytic anemia were excluded from study. Pregnancy with renal and liver disease and patients with known allergy to iron were also excluded. Treatment efficacy was assessed after three weeks by estimating the hemoglobin and serum ferritin levels.

Results: An increase in hemoglobin was observed rising from 8.82 ± 1.01 g/dl to 10.9 ± 1.20 g/dl in intravenous group while in oral iron therapy group rise in hemoglobin from 9.32 ± 0.63 to 10.32 ± 0.62 gm/dl was observed (p< 0.00).The serum ferritin levels rise from 8.34 ± 2.73 to 30.3±7.68 ug/l in intravenous iron therapy while it was from 8.34 ± 2.71 to 11.26 ± 2.88ug/l in oral group (p< 0.00).

Conclusion: Intravenous iron therapy is more effective than oral iron therapy in raising the hemoglobin and serum ferritin levels in pregnant patients with iron deficiency anemia.

Key words: Iron sucrose complex, serum ferritin, iron deficiency anemia.

INTRODUCTION

Women in Pakistan suffer a lot of problems during pregnancy and iron deficiency anemia is the commonest single nutritional deficiency anemia[1].More than 50% women in reproductive age group are anemic or iron depleted mainly due to menstrual blood loss, inadequate iron intake or mal-absorption [2].The consequences of iron deficiency are serious and may result in low birth weight baby, increased preterm birth rate, perinatal mortality and irreversible brain damage .To avoid all these consequences intravenous (IV) iron sucrose has been found to be a safe line of treatment which corrects iron deficiency rapidly [3].It is also found that serum ferritin levels are raised more in intravenous therapy as compared to oral iron therapy[4].Intravenous iron therapy also corrects the depleted stores so that iron remains available for erythropoises[5].

Pregnant anemic patients need more iron and this requirement can be difficult to meet by oral iron because of poor compliance, limited absorption, interaction with food and physiological effect of pregnancy on digestion. It has been found that intravenous iron therapy is more effective and has fewer side effects like fever and skin allergy. These side effects can be avoided by dividing the total dose into smaller doses (100-200mg/day) and by the slow administration over 1-4 hours. It is concluded that intravenous iron sucrose complex is safe and effective treatment for iron deficiency anemia of pregnancy which can be successfully used as a day care case without hospitalization[6].

Our study was designed to compare the therapeutic efficacy of oral versus intravenous iron in pregnant patients with iron deficiency anemia by comparing pre and post treatment increase in hemoglobin (Hb) and serum ferritin levels.

PATIENTS AND METHODS

This study was carried out in the department of Gynecology and Obstetrics of Fauji Foundation Hospital Rawalpindi from 1st April 2007 to 31st December 2007.Hundred consecutive patients qualifying inclusion criteria were divided into two equal groups using table of random numbers.

Group A oral iron

Group B intravenous iron

Pregnant women with confirmed iron deficiency anemia between gestational ages of 12-32 weeks with hemoglobin level of 7-10 g/dl were included in the study. Patients not willing for follow up or had anemia due to other causes such as megaloblastic or hemolytic anemia were excluded from study. Pregnancy with renal and liver disease and patients with known allergy to iron were also excluded.

After informed consent patients who met the inclusion criteria were recruited from antenatal clinics and obstetric ward of Fauji Foundation Hospital. History

and ultrasonography were used to identify patients with appropriate gestational age (>12 weeks and <32 weeks).Hemoglobin was estimated to confirm diagnostic criteria (Hb 7-10 gm/dl) and confounding variables were controlled by identifying patients with megaloblastic or hemolytic anemia (peripheral film),renal disease (serum urea and creatinine levels) and liver disease (liver function test).Patients were told about the risk of intravenous iron therapy (skin allergy, fever) and oral therapy (diarrhoea, constipation ,black colored stools).Iron deficiency anemia was confirmed by complete blood picture (Hb 7-10 gm/dl), microcytic hypochromic picture on peripheral film and serum ferritin levels < 12ug/l.

Tests were done at Fauji Foundation Hospital laboratory Rawalpindi. Two groups were allocated to treatment using random number tables. Group A received tablet ferrous sulphate 300 mg (60 mg of elemental iron) orally three times per day (maximum oral dose). Study group B received total calculated amount of iron by following formula:

Hb deficit (g/l) x body weight (kg) x 2.21+1000. Group B received intravenous iron in divided doses in 200 mls of normal saline over one hour on alternate days after an initial test dose. All these cases were followed up after three weeks and their post iron therapy complete blood picture and serum ferritin were repeated from Fauji Foundation Hospital laboratory Rawalpindi. All information was recorded on specially designed proforma for analysis.

Statistical Test: Frequencies, mean and standard deviations for age, weight, hemoglobin and serum ferritin levels were calculated using descriptive statistics of SPSS version 12. One sample t-test was used to compare hemoglobin and ferritin levels before and then after 3 weeks of treatment in both groups. Independent sample t-test was used to compare mean hemoglobin and serum ferritin increase between two study groups. P-values ≤ 0.05 was considered statistically significant.

RESULTS

A total number of 100 patients met the inclusion and exclusion criteria. Fifty cases were given iron sucrose therapy and 50 cases were given oral iron therapy. The age distribution between two groups was not statistically significant i-e (p=0.223).The difference between mean gestational age and weight of two groups was statistically significant (p = 0.007) and (p=0.00) (Table no 1 and 2).The mean pretreatment hemoglobin of patients in Group A was 9.32 ± 0.63 g/dl and the post treatment hemoglobin in this group was 10.32 ± 0.62 gm/dl. The rise in the hemoglobin was statistically significant, p=0.00 by one sample t-test. The mean pre and post treatment hemoglobin of patients of group B was 8.82 ± 1.01 gm/dl and 10.9 ±1.2 gm/dl .The rise in hemoglobin was statistically significant (p=0.00) by one sample t-test. Therefore, both oral and intravenous iron significantly improved the patients post treatment hemoglobin. The mean rise in the hemoglobin in group A was 1.00 ± 0.36 gm/dl while it was 2.09 ± 0.51 gm/dl in group B. The mean rise in hemoglobin after treatment was significantly higher in intravenous route (group B) p = 0.028.The mean pretreatment serum ferritin in Group A was 8.34 ± 2.7ug/l , while the post treatment serum ferritin was 11.26 ± 2.88 ug/l. The rise in serum ferritin was statistically significant (p=0.00) by one sample t-test. The pre and post-treatment serum ferritin in group B was 8.25 ± 2.7ug/l and 30.5 ± 7.6 ug/l respectively. The rise in the serum ferritin was statistically significant, p=0.00 by one sample t-test The mean rise in the serum ferritin levels in group A was 2.95 ± 0.875ug/l while it was 21.7± 5.97 ug/l in group B. The mean increment in serum ferritin after the treatment was significantly higher in intravenous group; p=0.00.Therefore,intravenous iron therapy group achieved higher levels of hemoglobin and serum ferritin levels as compared to oral iron therapy.

Table No.I: Descriptive Statistics of Group A

	Minimum	Maximum	Mean	Std.Deviation
Age (years)	20.0	45.0	32.38	5.934
Weight(kg)	46.0	85.0	61.06	8.034
Gestational age(weeks)	18.0	35.0	27.06	4.181
Pre treatment hemoglobin (g/dl)	7.50	10.0	9.32	0.630
post-treatment hemoglobin (g/dl)	8.10	11.20	10.32	0.629
Pre treatment Ferritin in ug/l	3.39	11.80	8.34	2.713
Post treatment Ferritin in ug/l	3.40	18.55	11.26	2.881

Table No.2: Descriptive Statistics of Group B

	Minimum	Maximum	Mean	Std. Deviation
Age (years)	24.0	40.0	33.64	4.202
Weight (kg)	20.0	72.0	53.16	14.445
Gestational age (weeks)	20.0	34.0	29.46	2.977
Pre treatment hemoglobin (g/dl)	6.7	10.0	8.82	1.018
Post treatment hemoglobin (g/dl)	9.0	14.0	10.91	1.201
Pre treatment Ferritin (ug/l)	3.0	11.90	8.25	2.730
Post treatment Ferritin (ug/l)	18.0	60.42	30.53	7.684

DISCUSSION

Mothers in developing countries embark on pregnancy with low iron and other nutritional stores. Anemia occur in 10 to 30% of pregnant women[7].In countries with sub-optimal anemia management maternal mortality can reach 450/100,000 pregnancies, a similar figure in Europe 200 yrs ago[8].Oral iron therapy is has been shown to be effective in correcting iron deficiency anemia in most of the cases[9].Its efficacy is however limited in many cases due to dose dependent side effects, lack of compliance and insufficient duodenal absorption [10, 11]. By using IV iron rather than oral iron it is possible to increase Hb concentration to ideal threshold. IV iron is used increasingly in obstetrics[5, 12, 13,14,15.] In our study the mean rise in hemoglobin of oral therapy group was 1.00 ± 0.36 g/dl while it was 2.09 ± 0.51 g/dl in intravenous group. Surriaya also quoted an average increase of 1.85±0.28 g/dl in oral iron therapy and 3.45 ± 1.06g/dl in intravenous group[16]. The change in hemoglobin from baseline was significantly higher in the intravenous group than the oral group in the study by Aira[17]. Bayoumeu showed no advantage of IV sucrose over oral iron with regard to Hb increase [5].Professor Breymann reported that in 200 pregnancies the average increase in Hb over 25 days was 1.8 g/dl with use of iron sucrose. This is quite considerable and corresponds to two to three blood transfusion[18].The mean rise in serum ferritin in oral iron therapy was 2.95 ± 0.875 ug/l while the mean increment in intravenous therapy group was 21.76 ± 5.97ug/l which was highly significant as in studies by Bayoumeu and Aira[5,17] .Currently ,it has been shown that single dose of up to 200mg iron sucrose are safe and cumulative doses of up to 1600mg are sufficient to treat anemia. Side effects such as warmth, flushing, dizziness and some local reaction occurred in 0.4% of the patients .There have been no serious side effects, no severe tissue reaction and no deaths reported due to IV iron sucrose. Local data showed favorable results on safety, clinical and laboratory response of intravenous iron sucrose complex in iron deficiency anemia[19].Anemia in pregnancy is common in our part of world especially in pregnant women of low socio-economic class and in majority of them it is caused by nutritional deficiency of iron, folic acid or vit B12 [20] .It was also found that serum ferritin levels are raised more in intravenous therapy as compared to oral therapy[4].It was concluded that intravenous sucrose complex is safe, effective treatment for iron deficiency anemia of pregnancy; which can successfully be used as a day care without hospitalization[6].

Therefore, the available data show that iron sucrose is effective, safe and easy to handle in managing iron deficiency anemia during pregnancy and the postpartum; in addition it is associated with good acceptance and compliance.

CONCLUSION

Iron deficiency anemia during pregnancy is common and deserves special attention because of its potential consequences. Moreover, some pathological situations increase the risk of hemorrhage and require a rapid restoration of iron reserves. In practice physicians are often faced with poor compliance justified by digestive side effects that can lead to worsening anemia. In these cases the parenteral form of iron administration is the treatment of choice. Intravenous iron therapy is also very effective in cases where oral treatment is ineffective. It was concluded from our results that intravenous iron therapy is more effective than oral iron therapy in raising the hemoglobin and serum ferritin levels in pregnant patients with iron deficiency anemia. Intravenous iron sucrose should be used as valid first line therapy for the safe and rapid reversal of iron deficiency anemia during pregnancy.

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Original Article

Etiological Aspects of Penicillin-Failure in the Treatment of Tonsillitis and Pharyngitis Caused by Group A, Beta-Hemolytic Streptococci (GABHS)

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ABSTRACT

Objective: To observe and study the cause of penicillin-failure and to see the therapeutic effects of other drugs and find out more effective and better remedy.

Study Design: A Retrospective study

Place and Duration of Study: This study was conducted in Microbiology Department, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, National institute of Child Health from April 2004 – June 2005.

Materials and Methods: A total of 300 children attending OPD's and admitted (250 suspected and 50 Normal as control cases) of age group 5 – 15 years were included in this study.

Result: Drug sensitivity pattern of *streptococcus pyogenes* isolated in infected and control children was observed. Antibiotic discs used were Penicillin (10) units and Erythromycin(15 micrograms). The organism isolated GABHS shows 100% sensitivity to penicillin, while in case of erythromycin, it was sensitive in 24(85.7%) infected cases and resistant to 4(14.3%) cases.

Conclusion: Pharyngotonsillitis is a disease of poor community, the therapy with penicillin is economical compared with Cephalosporin group. Penicillin therapy is helpful in preventing the supportive and n supportive complications caused by GABHs.

Key Words: Penicillin Group A, beta hemolytic streptococci Beta-lactamase.

INTRODUCTION

Apart from its excellent in vitro efficacy, the repeated reports of the inability of penicillin to eradicate group-A, beta hemolytic streptococci (GABHS) from patients with acute and relapsing tonsillitis was concerned cause. Over the past 50 years, the rate of penicillin failure had constantly increased from about 7% in 1950 to almost 40% in 2000.[1]

Several explanations exist for the failure of penicillin to eradicate GABHS tonsillitis. One explanation was the poor penetration of penicillin into the tonsillar tissues as well as into the epithelial cells[2].

Other explanation relates to the bacterial interactions between GABHS and the other members of the pharyngo-tonsillar-bacterial flora. It was hypothesized that the enzyme beta-lactamase which was secreted by beta-lactamase producing aerobic and anaerobic bacteria, that colonize the pharynx and tonsils, may "shield" GABHS from pencillins[3].

These organisms include S.aureus, H.influenzae, and provetella, porphyromonas and Fusobacterium spp[4].

A recent increase was noted in the recovery of MRSA which was isolated from 16% of tonsils, making it more difficult to eradicate this and other beta-lactamase producing organisms. [5]

Another possibility was the co-aggregation between Moraxella catarrhalis and GABHS, which could facilitate colonization by GABHS.[6]

Increased recovery of Moraxella catarrhalis and Haemophilus influenza in association with group A beta haemolytic streptococci in healthy children and those with pharyngo-tonsillitis.[7]

Normal bacterial flora could interfere with the growth of GABHS.[8,9]

The absence of such competitive bacteria made it easier for GABHS to colonize and invade the pharyngo-tonsillar area.[10]

GABHS could also be reacquired from a contact or an object (i.e, toothbrush or dental braces)[11]

Bacteriologic and clinical treatment failures occur with penicillin, as with all antibiotics. Bacteriologic failure was failure to eradicate the streptococcal organism responsible for the original infection. Patients with this type of treatment failure might present with symptoms or be symptomatic. Some infected but asymptomatic patients might be carriers. Patients who remained symptomatic despite treatment were considered clinical failures and must be retreated. Study conducted over the past 40 years had reported penicillin bacteriologic failure rates ranging from 10 to 30 percent and clinical failure rates ranging from 5 to 10 percent.[12]

Penicillin had been the agents of choice for the therapy of a variety of bacterial infections. However, within the past sixty years, an increased resistance to these drugs had been noted. In addition to bacteria long known to resistant penicillin, such as Staphylococcus aureus and Enterobacteriaceae, other previously susceptible organisms became increasingly resistant due to several mechanisms including the production of the enzyme beta-lactamase(BL), these include aerobic and facultative bacteria such as Haemophilus influenza, Moraxella catarrhalis, as well as anaerobic gram-

negative bacilli(AGNB, i.e, Bacteroides fragilis group, pigmented Prevotella and Porphyromonas, Prevotella bivia, and Prevotelladisiens) and Fusobacterium SPP.[13]

Beta-lactamase- producing bacteria (BLPB) had a important clinical role in infections. These organisms can be pathogenic in causing the infection as well as had a indirect effect through their ability to produce the enzyme BL into their environment. BLPB might not only survive penicillin therapy but also might protect other penicillin-susceptible bacteria from penicillin by releasing the free enzyme into their environment.[14]

Animal studies demonstrated the ability of the enzyme BL to influence poly- microbial infections. BL producing of AGNB protected a penicillin-sensitive Fusobacterium necrophorum and group A beta hemolytic streptococci(GABHS) from penicillin therapy in mice. Clindamycin or the combination of penicillin and clavulanate (a BL inhibitor), which were active against both GABHS and AGNB,(Anaerobic Gram-Negative-Bacilli) were effective in eradicating the infection. An increase in resistance of GABHS to penicillin was found when it was co-inoculated with S.aureus, Haemophilus parainfluenzae, or B.fragilis.[15]

Aerobic and anaerobic BLPB(Beta-Lactamase Producing Bacteria) might play a role in penicillin failure to eradicate GABHS tonsillitis. It was plausible that these BLPB could protect GABHS from penicillin by inactivation of the antibiotic. BLPB was recoverd in 37 of 50 tonsils (74%) removed from children who failed penicillin therapy.[16]

Strains of GABHS had been demonstrated to internalize within epithelial cells both in vitro and in vivo in recent studied.[17]

The internalization-associated gene, prtF1/stbI, had been identified more from patients with eradication failure of GABHS than had been recovered from patients with successful eradication.[18]

Since penicillin penetrate mammalian cells poorly, intracellular survival of GABHS possibly allowed the pathogens to persist despite antibiotic treatment.[19]

The intracellular spaces might therefore protect GABHS strains from penicillin that was not in high intracellular concentration. In support of this hypothesis, GABHS strains were shown to survive 4-7 days within cultured epithelial cells. Thus, internalization and intracellular survival represented a novel explanation for penicillin eradication failure.[20]

Marouni et al, compared the survival of GABHS strains from cases of eradication failure and eradication success, using an epithelial cell culture model."Eradication failure" strains showed significantly increased intracellular survival, compared to the' eradication success' strains. These results demonstrated how an intracellular reservoir of GABHS may play a role in the etiology of antibiotic eradication failure.

Kaplan et al., recently examined the viability of intracellular GABHS in a human laryngeal epithelial cell line(HEp-2epithelial cell) after exposure to antibiotics (penicillin, erythromycin, azithromycin, cephalothin, and clindamycin) that were commonly recommended for GABHS. Three techniques were used to study antibiotic killing of ingested GABHS: 1) electron microscopy examination of ultra- thin sections of internalized GABHS; 2) qualitative determination of intra-epithelial cell antibiotic; and 3) special stain evaluation of intracellular GABHS viability within antibiotic-treated epithelial cells. Group A beta-hemolytic streptococci survived intracellularly despite exposure of the GABHS-infected epithelial cells to penicillin. Cephalothin (a cephalosporin) and clindamycin were more effective than penicillin in killing ingested GABHS. However, erythromycin and azithromycin, agents known to accumulate to high levels in cells, were more effective than cephalothin and clindamycin in killing ingested GABHS. These observations strongly suggest that the upper respiratory tract carrier state of GABHS results from intra-epithelial cell survival, and the failure of penicillin to kill internalized GABHS. Penicillin's failure to eradicate GABHS from pharyngo-tonsillar tissue might be impacted by its inability to eradicate intracellular GABHS as well as its inability to maintain sufficient concentration within the tonsillar fluid. The stage of the GABHS PT (Pharyngo-Tonsillitis) inflammation determines the concentration of penicillin in tonsillar surface fluid. Stjernquist-Desatnik et al, investigated the concentration of penicillin in serum, as well as penetration to tonsillar surface fluid and saliva. Among the nine healthy subjects, despite high serum penicillin concentrations (mean, 2.04 µg/ml), there was no penetration to tonsillar surface fluid or to saliva. Of the nine patients with acute GABHS tonsillitis, eight manifested high concentrations of penicillin in tonsillar surface fluid (mean, 0.34 µg/ml) on the first day of treatment, but only two patients had penetration to the saliva. On the tenth day of treatment, penicillin was present in the tonsillar surface fluid of only one patient and was not present in the saliva of any patients. Furthermore, orrling et al., demonstrated that the cephalosporins loracarbef and clindamycin maintained higher concentration in tonsillar surface fluid for longer duration than penicillin.[21-23]

Causes of Penicillin Failure in Therapy of Gabhs Tonsillitis:

1. the presence of beta-lactamase-producing that ''protect''GABHS from pencillines.[19]
2. coaggregation between GABHS and M. catarrhalis.[20]
3. absence of members of the oral bacterial flora capable of interfering with the growth of GABHS(through production of bacteriocins and/or competition on nutrients)[21-22]
4. poor penetration of penicillin into the tonsillar cells and tonsillar surface fluid (allowjng intracellular survival of GABHS.[23]
5. resistance(ie, erythromycin) or tolerance(ie, penicillin) to the antibiotic used.

6. inappropriate dose, duration of therapy, or choice of antibiotic.
7. poor compliance.
8. Reacquisition of GABHS from a contact or an object(ie, toothbrush or dental braces)[24]
9. Carrier state, not disease.[25]

MATERIALS AND METHODS

This study was conducted in the department of Microbiology, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Center, Karachi, from April 2004 to June 2005.

Inclusion Criteria: Patients of age group 5-15 years were included in this study.
Patients from government schools, OPD of National Institute of Child Health (NICH) and OPDs of JPMC and Civil hospitals of Karachi.
Children with history of sore-throat with fever were included in this study.

Exclusion Criteria: Patients with history of antibiotics since last two weeks. Patients above 15 years of age and below 5 years of age. Patients with metabolic disorders and chronic disease. Patients with history of malignancy.
250 children with suspected pharyngitis and tonsillitis and with the complain of sore throat and temperature etc attending OPDs of JPMC, Civil hospital, NICH and different govt. schools, were included in this study.
After taking all the aseptic measures, the throat swab was taken from the patients with the special care that the swab was taken from the posterior part of the pharynx and the tonsils, care was taken that the swab should not touch the tongue or cheeks, and for that purpose a tongue depressor was used. The information was recorded on a prescribed Performa. It was transported in the Amies and BHI broth.
In the laboratory the specimen was cultured and sensitivity was observed according to standard laboratory procedure.

RESULTS

Table 1: Distribution of group A, beta haemolytic streptococci in OPDs of JPMC, Civil Hospital, NICH and 20 different schools of Karachi. (n=24)

Institutions	N0. of cases	Percent
Jinnah Postgraduate Medical Centre (n=93)	12	12.9%
Civil Hospital Karachi (n=72)	06	8.4%
National Institute of Child Health (n=48)	04	8.4%
20 different schools of Karachi (n=37)	02	5.4%
Total (n=250)	**24**	**35.1%**

Table 1 shows the distribution of the GABHS in the outpatient departments of JPMC (ENT OPD) out of 93 cases 12(12.9%) were positive for GABH. In Civil hospital(ENT OPD) and in NICH from 72cases 6 cases were positive(8.4% each), in 20 different schools of Karachi out 0f 37 cases only 2 (5.4%) were positive for GABHS.

Table 2: Drug sensitivity pattern of group A beta haemolytic streptococci isolated in infected and carrier children. (n=28)

Antibiotics used	Organism isolated (Streptococcus pyogenes)			
	Sensitive		Resistant	
	No of cases	Percent	No of cases	percent
Pencillin (10units)	28	100%	0	0%
Erythromycin (15µg)	24	85.7%	04	14.3%

Table 2 shows the drug sensitivity pattern of streptococcus pyogenes isolated in infected and carrier children(28). Antibiotic discs used were Penicillin(10) units and Erythromycin(15 micrograms). The organism isolated GABHS shows 100% sensitivity to penicillin, while in case of erythromycin, it was sensitive in 24(85.7%) infected cases and resistant to 4(14.3%) cases.

DISCUSSION

Pharyngo-tonsillitis occupy a prominent place among the young children ranging from 5-15 years of age and also a most important cause of morbidity due to the post-infectious complications(suppurative and non-suppurative) produced by the Streptococcus pyogenes i.e, Aute rheumatic fever and Acute glomerulonephritis as non-suppurative and Cervical lymphadenitis, Peritonsillar or Retropharyngeal abscess, Sinusitis, Mastoiditis, Otitis media, Meningitis, Bacteremia, Endocarditis, Pneumonia as suppurative complications. And when tonsils get enlarged, they occupy and obliterate the respiratory passages.
Our way of living, over-crowding at residential places, public places and of course, at schools, the infected children cough, sneeze, laugh and handle the things and infect the other normal children. In this way the infection spreads from ill to normal.
A recent study demonstrated that over 30% of children with group A, beta hemolytic streptococci associated acute pharyngitis continued to have persistent presence of organisms in upper respiratory tract, despite the appropriate oral or intra-muscular penicillin therapy, this could be co-habitation of beta-lactamase producing normal oral flora, which "shield" Group A, beta hemolytic from penicillin, intra-cellular invasion of group A, beta hemolytic streptococci and consequent "escape" from penicillin. (shet and Kaplan, 2004)
In our study,as for as the sensitivity pattern of the organism (GABHS)is concerned, we have used two

drugs i.e, penicillin and erythromycin. And it was observed that the organism is 100% sensitive to penicillin, which was according to the other studies. As in Sao Paulo, Brazil, the group A, beta hemolytic streptococcus isolates from the infection were all susceptible to the penicillin.(data not shown) (cited by santos et al.,2003)

In another recent study carried out in Ankara, Turkey, says that because eradication of GABHS is necessary to prevent non-suppurative and suppurative sequelae, the primary outcome and antibiotic treatment goal of interest should be eradication of the bacteria(Delmar C, Bisno AL). Among the antibiotics that have been used in the treatment of GABHS tonsillitis, oral penicillin has been the firsrtline drug, and oral cephalosporinsm, macrolides and beta lactam/beta-lactamase inhibitor combinations were the alternatives. Although some reports suggested that oral cephalosporins had produced superior bacteriologic cures when compared with oral penicillin for treatment of GABHS tonsillitis, three important problems have not been resolved yet:(1) some authors believed that the difference in the cure rates might have resulted from the presence of carriers in the study groups in whom penicillin is not very effective in eradicating the streptococci from the pharynx; (2) while oral penicillin is the drug of choice in developed countries, one dose intramuscular penicillin G is the drug used most often in developing countries, the effect of which on eradication of GABHS and throat flora is not fully known;(3) Although penicillin and an alternative drug have been compared for efficacy, all of the antibiotics used for GABHS tonsillitis have rarely been evaluated in the same study.

This study further says that, the existence of BULB (beta-lactamase producing bacterias) in the throat has been mentioned as one of the reasons for treatment failure in GABHS tonsillitis treated with penicillin. some authors demonstrated a higher treatment failure if S. aureus was present in throat cultures (Simon HJ, Sakai W and Tunevail G.) The presence of BLPS (S, aureus and M.catarrhalis) was not different among the antibiotic groups in our study. they further say that, despite the low subject number in our study, it can be postulated that BL production is not as important as AHS(alpha hemolytic streptococci) in the resistance of GABHS to antibacterial therapy with oral penicillin or penicillin G.(Yildirim I, Ceyhan M, Gur D, Kaymakoglu I.)

An other study carried out by Nazgul A Omurzakova et al in Kawasaki, Japan and Bishkek, Kyrgyzstan in 2010,states that all discovered GABHS was studied for susceptibility to antibiotics, only 12.5% of GABHS positive samples out of total 80 samples were positive to penicillin. This pathogenic microbe was more sensitive to ampicillin 36.2% and to ceftriaxon 38.7% (cephalosporin). The most sensitive streptococcus pyogenes has appeared to amoxicillin 45.0%. low sensitivity has appeared to macrolids: roxitromycin 26.2% and erythromycin 23.7%.

Further more they states that, considering the recognized streptococcal etiology of rheumatic fever at present the penicillin is the drug of choice for eradication of GABHS in its initial clinical displays and for prevention of recurrence of infection. It has been established, that the treatment by phenoxymethyl penicillin during 10 days is optimum for achievement and full eradication of GABHS from throat.

In their study they further says that, in comparative randomized research it has been shown that prescription of amoxicillin/clavulanate potassium allows to amount to 100% eradication of GABHS in comparison with 70% eradication at use of penicillin ($p<0,001$). In cases of allergy to penicillin, macrolide or cephalosporin is recommended.(Nazgul A. Omurzakova et al)

An other study carried out by Michael E, Pichichero, MD et al says that there is increased acquisition of antibody to streptococcal antigens with a longer illness prior to treatment.(Bass JW, and Shvartzman P et al) This immunity has been suggested as one possible explanation for the higher success rate with penicillin in patients ill longer before therapy is started.(Pichichero ME et al) It may also be that penicillin treatment is more often successful in patients who have been ill longer prior to treatment because such patients have a greater degree of tonsillo-pharyngeal inflammation, which permits better penetration of penicillin. (Stjernquist-Desatnik A et al)

They further say that, our results and those of others (Breese BB and Spitzer TQ et al) consistently suggest that penicillin is equally effective weather administered 2,3 or 4 times daily. Although not an important factor under study conditions, poor compliance with the 3 or 4 times daily administration of penicillin may account for treatment failures in clinical practice. Less-frequent dosing improves compliance.Cockburn J and Eisen SA).

Most patients treated with penicillin for GABHS tonsillopharyngitis will experience bacteriologic eradication and a clinical cure.(Pichichero ME,Kaplan EL, Markowitz M,Shulman ST) [28].

CONCLUSION

Pharyngotonsillitis is a disease of poor community, the therapy with penicillin is economical compared with Cephalosporin group. penicillin therapy is helpful in preventing the supporative and n supporative complications caused by GABHs.

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CORRIGENDUM

It is to clarify that the Designation of Aftab Ahmed Soomro was wrongly published as Asstt. Prof. of Hematology, GMMC, Sukkur instead of his correct Designation i.e. Asstt. Prof. of Pathology, DMC, Karachi, appeared in our Journal Medical Forum Monthly, April, 2012 in Articles “Significance of Gram’s stain in the diagnosis and management of Lower respiratory tract infections” (page 22) and “Cutaneous Leishmaniasis in Karachi” (page 44) (Med.Forum.Vol.23 No.4).

It is, therefore, proclaimed that the Designation of Aftab Ahmad Soomro will be read as Asstt. Prof. of Pathology, DMC, Karachi.

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Original Article

Significance of Bone Marrow Biopsy in Diagnosis of Pediatric Diseases; One Year Experience at a Single Pediatric Hematology/Oncology Center

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ABSTRACT

Background: Despite the recent advances in the field of hematology in the form of molecular studies and immunophenotyphing, morphological study of bone marrow remains a corner stone in the diagnosis of pediatric hematological diseases. It is also helpful in the diagnosis of many non-hematological diseases. This study is unique in a sense that bone marrow biopsy procedure and morphology reporting were done by a pediatrician trained in clinical hematology.

Objective: To describe the indications of bone marrow biopsy and frequency of pediatric hematological and non-hematological diseases on morphological basis.

Study Design: Descriptive Case Series

Place & Duration of the Study: This study was conducted at the Pediatric Hematology/Oncology Department, The Children Hospital & the Institute of Child Health Multan from January 2010 to December 2010.

Materials and Methods: This study was conducted on children whether admitted in hematology / oncology ward or referred from various departments of this hospital. A Performa was filled for each patient including detailed history, clinical examination, base line investigation reports and provisional diagnosis. All bone marrow biopsies were performed from posterior iliac spines according to standard protocol for this procedure. Biopsy samples were stained with Leishman stain for morphological study. Bone marrow biopsy report was issued with detailed morphology, morphological diagnosis and suggestion for further investigations e.g. immunophenotyping.

Results: Patients age range was 3 months to 13 years with Male: Female = 1:1. Out of 100 bone marrow biopsy reports , disease distribution was acute lymphoblast leukemia (ALL) 30%, acute myeloid leukemia (AML) 7%, lymphoma infiltration 3%, aplastic anemia 18%, idiopathic thrombocytopenic purpra (ITP) 7%, storage disorders 11%, hemolytic anemia 5%, congenital dyserythropoitic anemia (CDA) 2%, red cell aplasia (RCA) 2%, refractory anemia with excessive blasts (RAEB) 2%, nutritional anemia 3%, malaria 3%, reactive changes 5% and normal morphology 2%.

Conclusion: In children, acute leukemia is a leading hematological disease on bone marrow morphology followed by aplastic anemia and various non-hematological diseases. Despite availability of advanced diagnostic facilities, bone marrow biopsy is still a useful diagnostic test in many childhood diseases.

Key Words: Bone Marrow Biopsy, hematological diseases, Leukemia.

INTRODUCTION

Bone marrow examination is a very important investigation for the diagnosis of various hematological and non hematological diseases. Bone marrow sampling is the process of obtaining marrow tissue smear for analysis and diagnosis. First bone marrow examination was performed by Ghedini of Genoal[1] Initially bone marrow examination was based on smear histology but in 1927, examination of curetted tibia marrow section was introduced[2]. In 1933, an account of sternal marrow biopsy and touch preparation had been demonstrated[3]. During the late 1950, bone marrow core biopsies were introduced to overcome the difficulties of dry tap or when insufficient material was obtained during aspiration.[4] Absolute indications for bone marrow biopsy include evaluation of Leucopenia, anemia, Leucoerthroblastic picture, leukemia, storage disorders and post chemotherapy monitoring.[5,6] Relative indication include pyrexia of unknown origin, splenomegaly, iron metabolism and sampling for immunophenotyping or culture. The preferred sites for bone marrow aspiration and biopsy in both adults & children are posterior iliac Spine, sternum and vertebral spinous process. Tibia is proffered site for infants under 18 months of age.[5,6,8] Contraindications are Hemophilia and other coagulation disorders[9] Complications include vessel laceration, marrow embolization, perforation of bone , retroperitoneal hemorrhage , local infection and pain at biopsy site. Premedications and sedation are helpful measures before performing biopsy especially in children. It is a safe and simple procedure if performed by an expert and can be repeated many times if needed.[9] However, It should be performed with clear clinical indication[10].

This study shows experience of a pediatrician trained in clinical hematology and ascertaining the role of bone marrow examination in diagnosis of hematological and

non hematological diseases. It will also be helpful in deciding the appropriate indications of this invasive procedure.

MATERIALS AND METHODS

We carried out bone marrow biopsy in 100 Children with clear indications for this procedure. Patients whether admitted in hematology ward or referred from other departments were included. Patients with inadequate marrow material, inconclusive reports and incomplete History were excluded from the study. A Performa was filled for each patient containing history, examination and provisional diagnosis.

Standard protocol for bone marrow biopsy procedure was followed .Hemogram along with finger prick morphology and retics slide was evaluated at first. Hemogram was obtained from a hematology analyzer, Sysmex. Procedures were carried out under aseptic measures. Children were sedated with midazolam or diazepam in calculated doses. Medication was given intravenously. Lumbar puncture needle of gauge 16-18 were used to get the aspirate from posterior iliac spine. After infiltration of local anesthesia like lignocain ,concentrated marrow particles were Obtained and Smear Prepared . Air dried smear were stained with leishman .Marrow histochemical stains were used when needed.

Trephine biopsy was performed in selected cases like lymphoma, aplastic anemia or dry tap. Trephine was processed for decalcification, printing and staining at histopathology / hematology department, Combined Military Hospital Multan. Immunophenotyping was sent to tertiary research center on bone marrow Aspirate or Peripheral blood containing blast cells more than 30% in cases of leukemia.

Bone marrow biopsy report was issued Containing morphological findings, diagnosis and Suggestion for further investigations.

RESULTS

Out of 100 patients selected for bone marrow biopsies, Male Female = 1:1. Age of children ranged from 3 months to 13 years. In 45% children, age was less than 2 years while in 55% children were more than 2 years. Indications for bone marrow biopsy in descending order of frequency were 1) fever , pallor and evidence of bleeding (Petechiae , bruises, epistaxis) in 27 patients, fever in 19, Hepatosplenomegaly in 18, Anemia in 17, bleeding in 07 Hepatosplenomegaly with Lymphadenopathy in 07 and Splenomegly in 05 (Table – 1). On morphological study malignant diseases were found in 40 % cases with ALL being most common (30%) followed by AML(7%) and lymphoma infiltration(3%). Among non – malignant diseases, aplastic anemia was most common (18%) followed by storage disorders(11%), ITP(7%) hemolytic anemia(5%), malaria (3%), nutritional anemia(3%), red cell aplasia(2%), congenital dyserythropoitic anemia(2%) and RAEB(2%).Reactive changes were noted in 5% cases and normal bone marrow morphology in 2% (Table 2).

Table No.1: Indications of bone marrow biopsy

Clinical features	No of cases
Fever Pallor,Bleeding	27
Fever	19
Hepatoslenomegaly	18
Pallor	17
Bleeding	07
Hepatoslenomegaly,lymphadeopathy	07
Slenomegaly	05

Table No.2: Disease distribution on bone marrow morphology study

Diseases	No. of cases	Age < 2years	Age > 2 year
ALL	30	7	23
AML	07	4	3
Lymphoma	03	0	3
Aplastic anemia	18	6	12
Storage diseases	11	11	0
ITP	07	3	4
Malaria	03	0	3
Hemolytic anemia	05	3	2
Redcell aplasia	02	1	1
Congenital dyserythro-poietic Anemia	02	1	1
RAEB	02	1	1
Nutritional anemia	03	3	0
Reactive changes	05	3	2
Normal	02	2	0
Total number	100	45	55

DISCUSSION

Bone marrow biopsy is helpful test in approaching the final diagnosis of many pediatric diseases both malignant and non-malignant. It is one of the most common & safe procedure done in children, but its role and contribution has been questioned in recent years.[11] Rarely infection or embolism has been reported after bone marrow biopsy[12].

This study shows that ALL is the most common disorder (30%) in children among malignant and non-malignant diseases on bone marrow morphology and results are comparable to a study conducted by Layla A. and Bashawri which showed 33 % children having ALL on bone marrow biopsy.[13] collectively malignant disease including ALL, AML & Lymphoma account for 40 % cases which is comparable to a study conducted by Nina S and Kadan L, which showed incidence of malignant Neoplasm 40 % too.[14] Another study conducted by Fazlur Rahim, showed 24 % cases having malignant disease on bone marrow morphology.[15] Aplastic anemia was the 2nd most common and lethal non- malignant disease in our

patients (18 %) which is comparable to 14 . 6 %[15]. in a study conducted by Fazlur Rahim.

Epidemiologically, aplastic anemia has a pattern of geographic variation opposite to that of leukemias, with higher frequency in the developing world than in the industrialized West[16,17]. Although not a common disease worldwide, aplastic anemia has a social impact disproportionate to its incidence[18]. Large prospective studies indicate an annual incidence of two new cases per million populations in Europe and Israel[19]. Its exact incidence in Pakistan is unknown due to lack of reliable population based studies. The rate is much higher in the developing world. This has been shown from the studies in Thailand[12] and China[13], where the incidence has been determined to be about threefold that in the West.

Storage disorders being 11% is the third most common non-hematological disorder found on bone marrow examination. All children of storage disorder were less than two years of age. Gaucher and Neiman pick disease were found among them. Naveen Naz study[22] was showing 11% of storage disorder and it is accurately comparable with our study. Nutritional anemia was at the lowest number in this study, the possible explanation being that majority of the cases of iron deficiency anemia and mixed anemia are diagnosed on smear examination on blood test. Hence bone marrow biopsy is usually not performed in these patients. Idiopathic thrombocytopenic purpra was also found on bone marrow examination in 7% cases, although its frequency in literature varies between 32 % to 48%. Fever with bleeding and anemia was the most common indication for bone marrow biopsy. hepatosplenomegaly was also an indication particularly in children having storage disorders, leukemia and malaria later on bone marrow morphology.

CONCLUSION

This study is in favor that bone marrow biopsy is an important investigation for the diagnosis of common hematological and various non-hematological diseases in children. Fever, pallor, hepatosplenomegaly and bleeding are the common indications of bone marrow biopsy.

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Original Article

Lethality of Suicidal Organophosphorous Poisoning in Karachi in 2010

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ABSTRACT

Objective: The study was aimed to evaluate the cases of suicide using organophosphorous compounds as intoxicant with the objective to bring up possible preventive measures based upon modifiable factors associated with lethality.
Design: Cross-sectional analytical Study.
Materials and Methods: This retrospective study was based upon 66 patients of poisoning treated at intensive care unit of Ward No.5, JPMC Karachi during a period of one year from January 2010 to December 2010.
Results: Out of total 66 cases of poisoning 38 were of organophosphorous compounds (OPC) poisoning, 20 males and 18 females. Most of the cases (63%) of OPC poisoning were in age range of 20-40 years, 33 (86.84 %) were of suicidal poisoning while 5 (13.16%) had accidental poisoning and 57 % reported to treatment facility within 6 hours.
Conclusions & recommendations: All the cases of OPC poisoning had severe symptoms with fatal out come. Suicidal ratio was quite high. The period between the ingestion of poison and initiation of treatment plays vital role. In order to reduce fatality rate urgent intervention is required by government by improving the treatment facilities at local level hospitals i.e. primary health care centres and banning of highly toxic organophosphorous compounds. Additional measures which can help include improving the public awareness regarding recognition of toxic symptoms & importance of prompt referral to an appropriate facility.
Key words: organophosphorous compounds, poisoning, suicide.

INTRODUCTION

The organophosphorous compounds (OPC) are widely used in agriculture as pesticides and as chemical warfare. They are easily accessible, thus they are commonly associated with deliberate self poisoning. OPC poisoning is a major clinical health problem across much of the rural Asia & account for an estimated 500,000 deaths from self harm each year. These are common suicidal agents in Pakistan, India, Turkey, Sri Lanka and other South Asian countries.[1] Accidental poisoning may also occur especially when they are kept within the reach of children & farmers could get exposed while spraying crops if they are not well protected with masks or gloves.

Poisoning is a common method of suicide especially in developing countries.[5] In many reports the rates of poisoning with OPC as suicidal method range from 20.6%-56.3%.[6,7,8] It has remained so for almost a century, 44.2% in 1872-76 and 49.2% in1972.[9] The reported poisoning rates in the suicide attempters who reached hospital varies from 40%- 80%.[10-12] OPC available as pesticides are amongst the most common poisons used.[13-14] In hospital based studies mortality rates associated with pesticides have been reported as high as 50%-70%.

In order to understand the mechanism of action of OPC recall that the nervous system is made up of a large number of nerves & which are meant for transmission of signals. When a signal reaches the end of a nerve, it releases a substance called neurotransmitter that carries the signal to adjacent nerves of an organ such as muscle or gland. Many nerves release acetylcholine as the neurotransmitter. Once the signal passes to the next nerve an enzyme called cholinesterase destroys the acetylcholine. OPC blocks this enzyme thus preventing the breakdown of acetylcholine & which acts for an excessively long time causing symptoms like increased secretions of glands, muscles twitches and the muscles after sometime get fatigued leading to paralysis.

The mode of exposure of OPC insecticides varies including dermal, GIT, inhalation and intravenous routes.[2, 3, 4] The mortality rate of OPC is very high, fatality is often related to a delay in diagnosis or an improper management.

MATERIALS AND METHODS

It was a retrospective study based upon 66 patients of poisoning treated at intensive care unit of Ward No. 5 of JPMC Karachi during a period of one year from January 2010 to December 2010. The initial diagnosis was made from the history taken from the patient's relatives regarding exposure to poisoning agent and was confirmed from serum and red blood cell cholinesterase levels. Blood gases, electrolytes, pH, LFT, LDH and PT were also assessed. The outcome of patients was assessed after applying a standard protocol of management. This includes use of intravenous atropine and pralidoxime as soon as possible, along with other measures like gastric lavage and administration of activated charcoal via nasogastric tube and cleansing of the patient's body with soap and water. Ventilator

support was provided if they had excessive salivation, respiratory failure or a depressed level of consciousness or unresponsive to oxygen treatment.

RESULTS

During the study period total 66 cases of poisoning were admitted in the unit. Out of these 38 were of organophosphorous compounds poisoning (used Typhon), 8 were of alcohol intoxication, 6 of heroin intoxication, 3 of corrosive acid ingestion and 11 of undetermined poisoning. (Table 1)

Table No.1: Distribution of cases of poisoning (n=66)

Sr. No.	Type of poisoning	No. of cases	Percentage
1	Organophosphorous poisoning	38	57.58
2	Alcohol poisoning	08	12.12
3	Heroin poisoning	06	9.09
4	Acid ingestion	03	4.54
5	Unknown poisoning	11	16.67
	Total	66	100.00

Table No.2: Gender distribution of cases of organophosphorous poisoning (n= 66)

Sr. No.	Sex	No. of cases	Percentage
1	Males	20	52.63
2	Females	18	47.37
	Total	38	100.00

Gender distribution revealed 52.63% males and 47.37% females (Table 2). Most of the cases were between the ages of 20-40 years. All cases proved fatal. Regarding manner 33 cases were of suicide and 5 were intoxicated accidentally. In suicidal cases the route of administration of poison was through GIT while in others it was inhaled accidentally.

All of the patients received atropine which was administered during 2-5 days as a continuous infusion or intermittent dosing. Mechanical ventilatory support was needed for 25 patients. The mean arterial blood gas values of these patients were, PCO_2 ranged between 17-48.3mmHg with mean 32.64+15.65, PO_2 ranged between 56 – 90 mm Hg with mean 73 $\pm$ 17mm Hg, HCO_3 ranged between11 – 25 mmol/l with mean 18 $\pm$ 7, SaO_2 ranged between 78 – 95% with mean 86.5 $\pm$ 8.5 & pH ranged between 78 – 95% with mean 7.23$\pm$0.29.

The duration of mechanical ventilation was 4-7 days. The mortality rate for the mechanically ventilated patients was not statistically different from patients not mechanically ventilated.

Liver function profile of these patients showed Total bilirubin 0.9-1.6mg/dl with mean 1.25$\pm$0.35 (Normal = 0.1-1), direct bilirubin 0.5-0.6mg/dl with mean 0.55 $\pm$ 0.05 (Normal = upto 0.3mg/dl), indirect bilirubin 0.8-0.9 with mean 0.85 $\pm$ 0.05mg/dl(Normal = upto0.7mg/dl), alkaline phophatase 102-107u/l with mean 104.5 $\pm$ 2.5 (Normal =50-135),Gamma GT 28-50u/l with mean 39$\pm$11 (Normal =10-50).

The other biochemical tests showed Lactic dehydrogenase (LDH) ranged between 321-325 u/l with mean 323$\pm$2 (Normal = 100-190 u/l), Prothrombin time ranged between 14-18 with mean 6$\pm$2 (Normal = 12-14), Serum Electrolytes, Na ranged between 146-149mEq/l with mean 147.5 $\pm$ 1.5 (Normal = 136-146), K ranged between 2.6-3.2 mEq/l with mean 2.9$\pm$0.3 , (Normal = 3.5-5.5), Cl ranged between 108-118mEq/l with mean 113 $\pm$ 5 (Normal = 98-106), blood urea nitrogen ranged between 7-9mg /dl with mean 8 $\pm$1 (Normal = 10-20), creatinine ranged between 0.6-1.3mg /dl with mean 0.95$\pm$0.35, serum cholinesterase level ranged between 0.2-6.5u/ml with mean 3.35 $\pm$ 3.15 (Normal = 7.0-190).

Intermediate syndrome was observed in most of the patients. The most frequent signs were meiosis, change in mental status, hyper-salivation, abdominal pain, diarrhea, respiratory distress, fasciculations & depressed level of consciousness.

Fatal outcome was significantly associated with higher mean age, lower mean pseudocholinesterase level, longer duration between organophosphorous compound ingestion and specific intervention.

Table No.3: Interval between OPC ingestion and specific intervention

Sr. No.	Interval	No. of cases
1	1 – 6 hours	22
2	7 – 12 hours	03
3	13 – 18 hours	03
4	18 – 24 hours	09

Table No.4: Blood chemistry in OPC poisoning cases.

Parameter	Range	Mean
PH	7.43 – 7.52	7.23$\pm$0.29
PCO_2	17 – 48.3 mm Hg	32.65$\pm$15.65
PO_2	55 – 72.2 mm Hg	73.0$\pm$17.0
SaO_2	89% - 97%	86.5$\pm$ 8.5
HCO_3	11.2 – 25 mmol / l	18.0$\pm$ 7.0
Sodium	146 – 149 mEq/L	147.5 $\pm$ 1.5
Potassium	2.6 – 3.2 mEq/L	2.9$\pm$ 0.3
Chloride	108 – 118 mEq/L	113$\pm$ 5
Blood urea nitrogen	7 – 9 mg/dl	8$\pm$1
Creatinine	0.6 mg/dl- 1.3 mp /04	0.95$\pm$0.35
Serum cholinesterase level	0.2 – 6.5 u/ML	3.35$\pm$3.15
Total bilirubin	0.9 – 1.6 mg/dl	1.25$\pm$0.35
Direct bilirubin	0.5 – 0.6 mg/dl	0.55$\pm$0.05
Indirect bilirubin	0.8 – 0.9 mg/dl	0.85$\pm$0.05
Alkaline phosphatase	102 – 107 u/l	104.5$\pm$2.5
Gamma GT	28 – 50 u/l	39.0$\pm$11.0
Lactate dehydrogenase	321 – 325 u/l	323$\pm$2.0
Prothrombin time	14 – 18	16$\pm$2.0

DISCUSSION

0rganophosphorous compounds are used worldwide in agriculture as well as in household gardens.[16] The easy availability of these compounds has resulted into a gradual increase in suicidal poisoning mainly in developing countries.[17]

In our study of 66 patients of poisoning, 38 patients were of OPC poisoning, among them 33 cases were suicidal and 5 cases were reported as accidental. Majority of cases in this study died due to delay in admission but some were misdiagnosed. They presented with history of headache for 3-4 days along with recent history of inhaling pesticides during spray over fields. Before ruling out the ruptured brain aneurysm by CT scan they were given atropine with fatal outcome.

In our study the rate of suicidal poisoning was 90%, probably because of uncontrolled sale and use of these agents all over the country. Most of the patients died due to intermediate syndrome, despite of endotracheal intubation deaths were due to respiratory failure. The intermediate syndrome is a state of muscle paralysis that occurs after recovery from cholinergic crisis but before the expected onset of the delayed polyneuropathy and it probably results from post-synaptic junction dysfunction.[18]

The increase in respiratory rate (24-46/min) is an obvious sign of respiratory failure which is the most troublesome complication which was observed in almost all patients. Respiratory failure may be due to many other reasons like aspiration of gastric contents, excessive secretions, pneumonia and septicemia complicating acute respiratory distress syndrome. Exposure to OPC will interfere with synaptic transmission peripherally at muscarinic and nicotinic receptors which cause decreased muscle power, skeletal muscle fasciculations and excessive salivary secretions, meiosis, diarrhea, abdominal pain, depressed level of consciousness and respiratory distress [17] which was observed in almost all patients in our study.

In the present study we observed that mortality rate was not significantly different whether or not the patients were treated with pralidoxime sulphate. This observation is in consensus with that of De Silva.[19]

Our mortality rate is higher compared with other reported series of OPC poisoning and intensive care management.[19,20] The reason for this is that our patients were admitted to the hospital quite late after exposure as they were referred from small rural hospitals where the facilities were not sufficient. The lethality can be reduced by improving treatment facilities at periphery i.e. primary health care centres. This will save the time which is presently being wasted in moving the patient to a distantly placed tertiary care hospital.

Lethality is an important clinical variable for both medical and psychiatric evaluation and management. In contrast to intent-to-die which is subjective measure lethality is objective, more descriptive of the behavior and often co-relate with the degree of intent. [21]

Banning of extremely toxic pesticides and the restriction of their use have been urged by WHO.[15]

CONCLUSION

All the cases of OPC poisoning had severe symptoms with fatal out come. Suicidal ratio was significant. The period between the ingestion of poison and initiation of treatment plays vital role in survival. In order to reduce fatality rate, urgent intervention is required from government by improving the treatment facilities at local level hospitals i.e. primary health care centres and banning of highly toxic compounds. Additional measures which can help include improving the public awareness regarding recognition of toxic symptoms & importance of prompt referral to an appropriate facility.

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Original Article

Comparison of High Sensitivity C-Reactive Protein Level Between Obese and Non-Obese Pregnant Women

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ABSTRACT

Objective: To find out whether obesity is associated with low grade systemic inflammation as measured by serum c-reactive proteins (CRP) levels.

Study Design: Cooperative Observational Study

Place and Duration of Study: This was conducted in the department of Physiology BMSI, JPMC with the collaboration of gynecology & obstetric department of JPMC Karachi from October 2008 to May 2009.

Materials and Methods: This study includes thirty obese pregnant women and thirty normal weight pregnant women as a control group of similar age, sex, height and gestational age. Subjects were randomly selected from gynae OPD of JPMC Karachi.

Results: The mean values of C – reactive protein concentration was higher in obese pregnant women as compared with control group (4.3±0.16 mg/L vs 9.0±12 mg/L). It showed statistically significant positive correlation with body mass index (BMI).

Conclusion: Higher BMI was associated with higher C-Reactive proteins concentration. These findings suggest a state of low-grade systemic inflammation in obese pregnant women.

Key Words: Obesity, C-reactive proteins, Pregnancy, Adipose tissue, Inflammation.

INTRODUCTION

Adipose tissues primarily was considered a reservoir for excess calories that were stored in the adipocyte as triglycerides, in times of caloric deprivation these stored lipids were mobilized as free fatty acids. It is now clear that in humans the expansion of adipose tissues seen in the obesity results in more blood vessels and more connective tissue fibroblast and especially more macrophages. There is an enhancement in the secretion of some interleukins and inflammatory cytokines in adipose tissue of obese which produce inflammation[1]. Among the recently discovered compound expressed in human adipose tissue is the pro-inflammatory cytokine interleukin 6(IL6) [2,3] Moreover, IL -6 produce in the adipose tissue of healthy humans is released in to the circulation[4]. Because of the inflammatory properties of IL – 6, including the stimulation of acute phase protein production in the liver [5,6], the release of IL - 6 from adipose tissue may induce low - grade systemic inflammation in persons with excess body fat.

A sensitive marker for systemic inflammation is acute phase C - reactive protein (CRP). Elevated C-reactive protein concentration was shown to predict future risk of coronary heart disease[7]. The purpose of present study was to find out whether obesity is associated with low-grade systemic inflammation as measured by C - reactive protein.

MATERIALS AND METHODS

This study was carried out in department of Physiology, basic medical science institute, Jinnah post graduate medical centre, Karachi. This was a cooperative and observational study performed during the period of October 2008 to May 2009. Patients were selected for the study with the collaboration of gynae/ obs: department JPMC Karachi. A total number of 60 subjects in the age range of 20 – 40 years and gestational age was third trimester were included in the study. Subjects were divided into two groups: A - non obese pregnant women (n = 30) and B - obese pregnant women, (n = 30).

Venous blood of 5ml was drawn under all aseptic measures then transferred to a gel centrifuge tube. After 30-60 minutes the blood was centrifuge for 5-10 minutes at a speed of 2500-3000 rpm. Serum obtained was transferred to clean and dry plastic cups, then cups were properly covered and stored at -50Ċ till analyzed. Before analyzing serum was thawed and allowed to attain room temperature. Weight and height of all subjects were measured in kilograms and centimeters respectively, using weighing with height - scale machine (MIC health scale machine made in china) height in centimeter was converted into meters for calculation of body mass index (BMI). BMI was calculated by applying following formula

Body mass index = $\frac{\text{weight in kilograms}}{(\text{Height in meter})^2}$

Serum C - reactive protein was estimated by enzyme linked immunosorbant assay (ELISA) using kit – Cat No. BC – 1119 manufactured by Biocheck, Inc USA. Data was analyzed on SPSS version to mean and standard divisions (SD) were used to describe the numeric variables like age and inflammatory markers. Person's co-relation co-efficient (r) values were calculated to check the linear co-relation between C-Reactive proteins and BMI. Only P-value (<0.05) are considered Significant. P-value (<0.001) are considered highly significant.

RESULTS

The mean weight in obese was75.1± 0.44 percent, while in control it was 57.9 ± 0.40 percent. Mean BMI in obese was 31.4± 0.15, while in control it was 24.2 ± 0.11. The mean C-Reactive proteins level in obese was 9.0 ±0.12 percent, while in control it was 4.3 ± 0.16 percent.

Table No.1: Comparison of the Age and Gestational Age Between Group A And Group B

Parameter	Group A Normal weight pregnant women (n=30)	Group B Obese pregnant women (n=30)	P-Value
Age	22.6 ± 0.29	22.6 ± 0.26	0.405
Gestational Age	31.2 ± 0.18	31.2 ±0.18	1.00

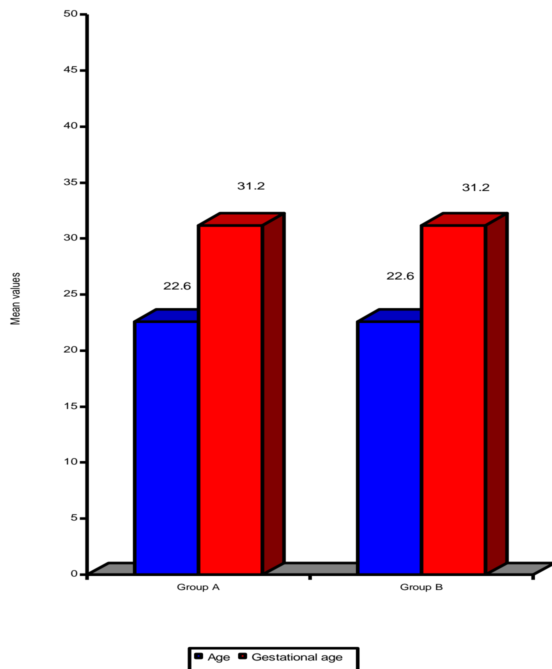

Table No.2: Comparison of the Height Weight and Body Mass Index Between Group A and Group B

Parameter	Group A Normal Weight Pregnant Women	Group B Obese Pregnant Women	P-Value
Height (m)	1.5 ± 0.01	1.5 0. ± 62	0.62
Weight (Kg)	57.9 ± 0.40	75.1± 0.4 4	0.001
BMI (kg/m²)	24.2 ± 0.11	31.4 ± 0.15	0.001

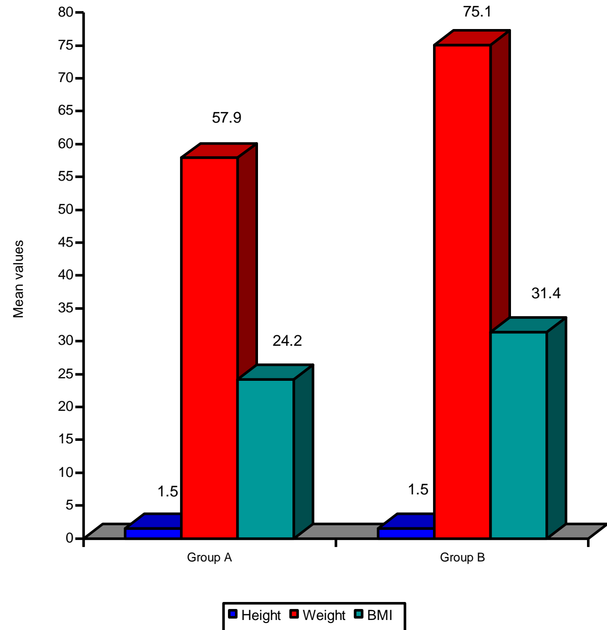

Table No.3: Comparison of the C - Reactive Protein between Group A and Group B

Parameter	Group A Normal Weight Pregnant Women (n=30)	Group B Obese Pregnant Women (n=30)	P-Value
C - reactive protein	4.3 ± 0.16	9.0 ± 0.12	0.001

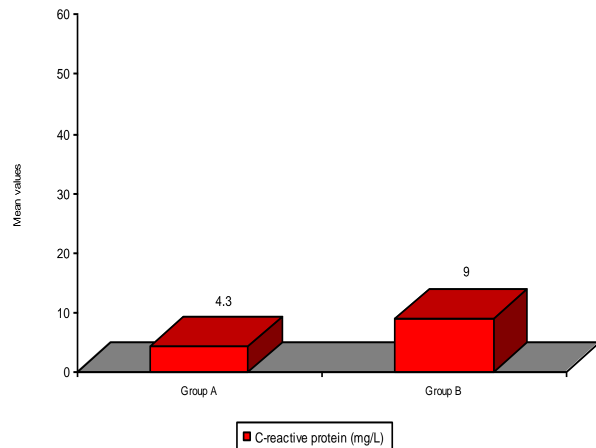

Table No.4: Correlation Coefficient of Serum C - Reactive Protein Versus BMI

Parameter	Group A	Group B	P-Value
Serum CRP versus BMI	0.39	0.42**	0.001

DISCUSSION

Koening et al[7], Mendall et al[8], and Tracy et al[9] studied in middle aged and elderly persons have reported a positive association between BMI and CRP concentration. In present study we demonstrate that maternal serum CRP levels were higher in obese pregnant women than non-obese pregnant women in the third trimester of pregnancy. However the association may have been confound by diseases like Diabetes Mellitus and Cardio Vascular disease, as these prevalent diseases are associated with obesity and increased CRP concentration[10,11]. A higher prevalence of low grade systemic inflammation was observed in obese pregnant women compared with normal weight pregnant women. Marjolein et al [12] observed that higher body mass index is associated with higher C-Reactive protein concentration that could not be explained by inflammatory disease or other factor known to increase C-Reactive protein concentration. The data of above study suggest that state of low grade systemic inflammation is present in over weight and obese persons. The results of our study are similar to this study. Verhaeghe et al [13] has been recently reported that plasma concentration of C-Reactive protein measured in gravidas, measured at 24-29 weeks, of gestational age were strongly related to body mass index . The results of our study are in agreement with this study. In the study of Rexrode et al[14] that body mass index was the strongest predictor of elevated inflammatory markers. The associations with BMI were dramatic. Women in the highest BMI quartile (BMI=28.9kg/m^2) have more their twelve fold increase risk of having elevated CRP levels. Our results are in total agreement with this study.

CONCLUSION

The result of our study shows that higher BMI is associated with higher C - reactive protein levels that could not be explained by inflammatory disease or other factor or disease known to increase C - reactive protein concentrations.

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Original Article

A Morphological Study of Renal Arteries in Atherosclerosis – A Human Autopsy Study

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ABSTRACT

Objective: To assess the different morphological changes in atherosclerotic lesions in renal arteries in relation to age and sex

Study design: Prospective descriptive observational study

Place and Duration of Study: Mortuary of King Edward medical University and mayo hospital, Lahore, Pakistan. Duration of study was one and a half year

Materials and Methods: A total of one hundred and thirty human autopsies were carried out during this study. Ninety were males and forty females. The age range was between 8 and 85 years. The autopsies were done left renal arteries were taken out artery for histological examination. Tissue processing was done. On the average 7-8 slides were prepared from each block by taking ribbons of tissues. The paraffin sections were stained using Haematoxylin and Eosin stain, Curtis's picro-ponceau stain, verhoeff's elastic tissue stain, von kossa's staining technique, periodic acid Schiff (PAS) reaction, Toludine blue stain and peral's Prussian blue stain.

Results: The fibrolipid plaques were seen in 32 of the 39 cases seen on gross appearance in the right renal artery and 20 of the 24 cases seen on gross appearance in the renal artery. The complicated lesions were present in 15 cases in the right renal artery and 11 cases in the left renal artery. In the right 12 cases showed ulceration, 3 cases showed intimal vascularization and haemorrhage, whereas 2 of these cases also showed thrombus formation. In the left renal artery there were 8 cases showing ulceration, 3 cases showed intimal vascularization and haemorrhage and one of theses also showed thrombus formation. The calcified lesions were seen in 9 case in the right renal artery and 7 cases in the left artery. The morphological changes in the media and elastic were in 11 cases in right renal artery and 7 cases in left renal artery.

Conclusion: Incidence of fibro-lipid plaques complicated and calcified lesion are quite high in both renal arteries. The relative high incidence of raised lesions in Right renal arteries may be due to more length, lower position and its position across the inferior vanacava.

Key Words: Marphological, atherosclerosis, renal arteries.

INTRODUCTION

Depolymerisation of acid-mucopolysaccharides involved in the plaque formation results in the loss of metachormasia of the ground substance[1]. After that the visible fibers crumble and dissolve completely and it is replaced by lipid droplets and cholesterol[2]. In ulcerated atheroma extensive foma cell are formed that are connected by fibrin- mesh[3]. Intimal thickening causes hypoxia of mis-zone of media .this provides the stimulus for the ingrowth of capillaries from the adventitial vessels into the thickened intima[4]. Thrombosis may occur on an ulcerating atheroma[5]. In atherosclerosis fine granules of Calcium appear in the ground substance and the necrotic tissues at the marginal layer of ulcers. The relative attenuation of the media is due to the disintegration of the elastic fiber system in the inner layer of the medial coat[6].

MATERIALS AND METHODS

A total of one hundred and thirty human autopsies were carried out during this study . Ninety were Males and forty females. The age range was between 8 and 85 years. The autopsies were done in the Mortuary of the King Edward Medical College, Lahore. Right and left renal arteries were taken out and opened lengthwise. One to four sections were taken from each renal artery for histological examination. Tissue processing was done. On the average 7-8 slides were prepared from each block by taking ribbons of tissues . The paraffin sections were stained using Haematoxylin and Eosin stain, Curtis's Picro-ponceau stain, Verhoeff's elastic tissue stain, von kossa's staining technique, periodic acid Schiff (PAS) reaction, Toludine blue stain and Peral's Prussian blue stain.

RESULTS

Gross Appearances: The fatty streaks were seen in 41 of 130 cases in the right renal artery, and 41 of the 130 cases in the left renal artery. They were present along the long axis of the vessel wall. The fibrolipid plaques were seen in 39 cases in the right renal artery and 24 cases in the left renal artery. The complicated lesions were present in 8 cases in the right renal artery and 7 cases in the left renal artery. Out of these complicated cases in right renal artery the ulceration was seen in 6 cases, intimal vascularization and haemorrhage in one case and thrombus formation in one. In the left renal

artery the ulceration was present in 5 cases, intimal vascularization and haemorrhage in one case and thrombus formation in one case. The calcified lesions were seen in 9 cases in the right renal artery and 7 cases in the left renal artery. The number of the raised lesions in these cases was 2-3. The size of the largest raised lesion in the right renal artery was 3x6 mm and the left renal artery 3 x 5mm. Size of the smallest raised lesion in both the branches was 3x3 mm. The colour of the fatty streaks was yellow, whereas that of the fibrolipid plaques was yellow to yellowish white. The complicated lesions were yellowish grey and the calcified lesions were yellowish black. All the raised lesions were seen within 0.5 cm of the ostia in these cases (Table No.1).

Table No.1: Atherosclerotic Lesions in Renal Arteries in Relation to Age and Sex (Gross Findings) (130 cases)

Age in years	Fatty Streaks		Fibrolipid Plaques		Complicated Lesions		Calcified Lesions	
	R	L	R	L	R	L	R	L
	M:F	M:F	M:F	M:F	M:F	M:F	M:F	M:F
6-15	-	-	-	-	-	-	-	-
16-25	5:0	5:0	1:0	1:0	-	-	-	-
26-35	14:9	14:9	8:1	2:0	-	-	-	-
36-45	8:5	8:5	6:3	5:1	1:0	1:0	-	-
46-55	-	-	6:4	5:3	2:1	2:0	2:1	2:0
56-65	-	-	8:1	5:0	2:1	2:0	4:1	3:0
66-75	-	-	0:1	1:1	0:1	1:1	0:1	1:1
Total	27:14	27:14	29:10	19:5	5:3	6:1	6:3	6:1
%age	20.76: 10.76	20.76: 10.76	22.30: 7.69	14.61: 3.84	3.84: 2.30	4.61: 0.77	4.61: 2.30	4.61: 0.77

Table No. 2: Atherosclerotic Lesions in the Renal Arteries in Relation to Age and Sex (microscopic findings) (130 Cases)

Age in years	Fatty Streaks		Fibrolipid Plagues		Complicated lesions		Calcified Lesions	
	R	L	R	L	R	L	R	L
	M:F	M:F	M:F	M:F	M:F	M:F	M:F	M:F
6-15	-	-	-	-	-	-	-	-
16-25	5:0	5:0	1:0	1:0	-	-	-	-
26-35	14:9	14:9	8:1	2:0	-	-	-	-
36-45	8:5	8:5	5:2	4:1	2:1	2:0	-	-
46-55	-	-	4:3	4:2	4:2	3:1	2:1	2:0
56-65	-	-	6:1	4:0	4:1	3:0	4:1	3:0
66-75	-	-	0:1	1:1	0:1	1:1	0:1	1:1
Total	27:14	27:14	24:8	16.4	10:5	9:2	6:3	6:1
%age	20.76: 10.76	20.76: 10.76	18.46: 6.15	12.30: 3.07	7.69: 3.84	6.92: 1.53	4.61: 2.30	4.61: 0.77

R= Right, L = Left

Microscopical changes: The fatty streaks were present in 41 cases in the right renal artery and 41 cases in the left renal artery. The fibrolipid plaques were seen in 32 of the 39 cases seen on gross appearance in the right renal artery and 20 of the 24 cases seen on gross appearance in the left renal artery. The complicated lesions were present in 15 cases in the right renal artery and 11 cases in the left renal artery. In the right renal artery 12 cases showed ulceration, 3 cases showed intimal vascularization and haemorrhage, whereas 2 of these cases also showed thrombus formation. In the left renal artery there were 8 cases showing ulceration, 3 cases shwoed intimal vascularization and haemorrhage and one of these also showed thrombus formation. The calcified lesions were seen in 9 cases in the right renal artery and 7 cases in left renal artery. The morphological changes in media and elastic were seen in 11 cases in right renal artery and 7 cases in left renal artery.

On histological examination of the fatty streaks the foam cells alongwith the increaseof fluid was present in the intima. Lipid was present both intracellularly and extracellularly alongwith the connective tissue changes. The fibrolipid plaques showed fibrous degeneration and regeneration with mucoid changes. There was a metachromatic change and hyalinization in the atherosclerotic lesion. Number of foam cells was prominent and the number of fibrocytes was also increase. The fat was present in the form of fatty pool and the needle-shaped cholesterol crystal clefts were also demonstrated. Variable number of foam cells was present with the necrotic areas at the base of the lesion. In ulcerated lesions the lipid contents were less in amount. Foam cells with fibrin was present abundantly.

Lymphocytic reaction with fibrin was present abundantly. In cases showing intimal vascularization and haemorrhage, there was neovascularization in the intima. In addition to that the red blood cells and haemosiderin deposits were also present at the junction of media and atherosclerotic lesions. In atherosclerotic lesions showing thrombus formation the fibrin strands were present at the peripheryand in between the platelet aggregates. The calcified masses were deposited in the degenerated debris and hyalinized collagen tissue in the intima. Deposite of calcium were particicularly present around the necrotic areas, lipid pool and marginal layers of the ulcers in atherosclerotic lesions. The medial coat was relatively attenuated below the sclerotic plaque and was one half or less of the thickness of the media in the adjacent part of the artery. The fibres on the inner third of media were severely degenerated. The fragmented internal elastic lamina was separated apart and was totally deficient over wide areas at the base of large plaques (Table No.2).

DISCUSSION

Gross morphology of Atherosclerotic lesions: The fatty streaks were present along the long axis of the vessel wall. The number of the raised lesions in these cases was 2-3. The size of the largest raised lesion in the right renal artery was 3x6 mm and the left renal artery 3 x 5mm. Size of the smallest raised lesion in both the branches was 3x3 mm. The colour of the fatty streaks was yellow, whereas that of the fibrolipid plaques was yellow to yellowish white. The complicated lesions were yellowish grey and the calcified lesions were yellowish black. All the raised lesions were seen within 0.5 cm of the ostia in these cases (Table No.1)

Microscopic Appearance of Atherosclerotic Lesions
On the light microscopy, the fatty streaks showed the presence of foam cells beneath the endothelial lining. There was increase of fluid in the ground substance. In addition to these changes, the connective tissue was arranged in the form of loose mesh with some fibrin deposition[7]. It seems likely that lipoproteins are transported across intact endothelial cells by micro-pinocytosis[8]. Lipid was present both intra- cellularly and extra-cellularly. Foam cells are smooth muscle cells containing lipids[9]. Probably local adherence of the platelets at the endothelium releases Mitogenic platelets to the endothelium releases Mitogenic Platelet factors into the arterial wall and causes some intimal smooth muscle cells proliferation[10]. In fibro-liqid plaques both connective tissue and lipid changes were prominent. These changes were visible as mucoid swelling due to the presence of protein molecules and acid-mucopolysaccharides. In addition there was a metachromatic change in the ground substance alongwith hyalinization . This change has previously been related to the increased amount of the ground substance[2]. Alteration in intrinsic composition and molecular size of proteoglycans occurs in atherosclerotic lesion[11]. The increase in the number of foam cells in fibrolipid plaques was probably due to increase in the smooth muscle cell proliferation and vacuolated forms[12-13]. In such vacuolated cells the lipid containing inclusions have been associated with the structural elements of smooth muscle cells[14]. Foam cells accumulation have been demonstrated in experimentally induced atherosclerosis[15]. The number of fibrocytes is increased during plaque formation. It is associated with increased formation of collagen and elastic fibres. These connective tissue components are probably derived from the proliferating smooth muscle cells in the intima. There was high concentration of fibrin in developing atherosclerotic lesion[11]. It was established that there is an association between accumulation of fibrin and binding of low density lipoproteins (LDL)[16]. On the other hand it was proposed that the process of smooth muscle cell proliferation is related to the tumour formation initiated by mutation[17]. The lipids were seen in the form of fatty pool and needle-shaped cholesterol Crystal clefts[18,19]. LDL is important to the initiation and probably the progression of atherosclerotic lesions[20,21]. In the ulcerated lesions the lipid contents were markedly less in amount . On the other hand foam cells were extensively present at the base and fibrin was seen intervening these cells[3]. The blood vessels were found in the intima. RBCs and haemosiderin deposits were present at the junction of media and atherosclerotic lesion[22]. It was also explained that neo-vascularization in the intima may lead to haemorrhage because they run the tissue that does not support them adequately[6]. In thrombus formation Platelet aggregation at the exposed sub endothelial tissue was seen. The fibrin strands were present at the periphery and in between the platelet aggregates. The collagen rich atherosclerotic lesion initiates thrombosis, because it exposes the blood to powerful platelet aggrating (collagen), and coagulation activating (traumatic surface and lipids) factors that are not found in normal vessel wall[23]. Fibrinogen leads to the Platelet aggregation associated with release of vasoconstrictor, thromboxane A2. This hypercoagu-libility of platelets again is associated with hyperfibrinogenaemia and thrombosis[24]. Lack of PG12 due to endothelial injury may lead to thrombus formation[23], because PG12 is powerful anti-aggregating vasodilator[22]. Contrary to above mentioned observations it was described that Fibrous plaque is fibrinoid or organized thrombus(6,25) This study was supported by the observations that calcified granules were presented around the degenerated debris and hyalinized collagen tissue in the intima [9,26]. They also observed that deposits of calcium were particularly present at the periphery of necrotic areas, lipid pool and marginal layer of ulcers in atherosclerosis. The fibres on the inner third of media were severely degenerated. Internal elastic lamina was fragmented and was totally deficient over wide areas at the base of large plaques due to rigid pressure[2,9].

CONCLUSION

Incidence of fibro-lipid plaques complicated and calcified lesion are quite high in both renal arteries. The relative high incidence of raised lesions in Right renal arteries may be due to more length, lower position and its position across the inferior vanacava.

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