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Editorial

Hepatitis "C" in Pakistan and its Treatment Facilities

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In the previous days, it was discussed in the Senate of Pakistan that around 8.8 million people in Pakistan are suffering from deadly hepatitis C while another 5.6 million are affected by hepatitis B.

In a written reply to this, Minister for Health said the figures have been compiled by a recent seroprevalence study conducted by Pakistan Medical Research Council, "The quantum of hepatitis C and B are 4.9 percent and 2.5 percent respectively, "the minister added.

He said the availability of diagnostic facilities and awareness campaigns have un-earthed the hidden burden of the disease.

The Prime Minister Programme for Prevention and Control of Hepatitis was launched in August 2005 with a total cost of Rs.2.594 billion for a period of five years. The number of patients with the disease since then have increased manifold as the government started to provide free treatment, though on a limited scale.

When the programme was launched in 2005-06, the number of patients, most of them poor, who were registered and treated at government hospitals were 10,815 and 1,000 for hepatitis C and B respectively

For the year 2008-09 the figure is 84,773 and 7,204 respectively for the two categories of the disease. Free treatment is restricted only to the poor patients through financial support provided by Pakistan Bait-ul-Mal and Zakat and Ushr departments.

The Race

The race among all pharmaceutical companies to beat one another out in finding a vaccine or a lasting cure for this disease continues till to date.

Recently a team of medical researchers, while trying to get to the bottom of the rapid spread of hepatitis C all over the world, came across a strange discovery. They found striking similarity between the symptoms experienced by the hepatitis C patients and the side-effects of the antibiotics. They dug out a strong link between the extensive usage of antibiotics and the spread of hepatitis C.

They also observed that patients with a history of constant use of antibiotics for a long time are more prone to develop the chronic form of the disease.

Antibiotics are drugs used to treat infections caused mainly by bacteria. Even when properly administered, antibiotics weaken the immune system by altering the body's natural bacterial balance.

The first antibiotics were prescribed in the late 1930s. They were hailed as the magic bullet that would put an end to the threat of infectious diseases. In 1969 the U.S. Surgeon General said. "The war against infectious diseases has been won. "This impression was, however, proved erroneous as in the last few decades we faced an alarming increase in cases of bacterial infections that do not respond to antibiotics. This is because bacteria acquire resistance to antibiotics, so there is a continuous search for new and effective antibacterial agents.

The hepatitis C virus is spread by contact with an infected person's blood. But not all who get the infected blood develop chronic hepatitis. Most of the young, healthy and strong, successfully resist the virus. This means that a weak defence mechanism along with other factors contributes to the development of the chronic form of this disease.

People are now gradually becoming aware of the dangerous side-effects of the antibiotics.

Only those who have a strong defence mechanism are, by the grace of Allah, safe from hepatitis C in the real sense.

The Cure

A new treatment for hepatitis C could soon be on the market if the Food and Drug Administration takes the advice of an advisory committee.

The committee unanimously approved the first of two new drugs to treat chronic hepatitis C genotype-1 infection. Hepatitis C is a chronic viral disease that causes inflammation and swelling of the liver.

The drug, Boceprevir, is a new class of protease inhibitor and would be used in combination with ribavirin and peginterferon – the current standard of care, Boceprevir prevents the virus from replicating, and studies show the three-drug cocktail is more effective than the two drug regimen. In the study, about 66 percent patients that hadn't been treated or did not respond well to current treatment responded well to Boceprevir. The FDA's outside panel of experts considered the risks and benefits of the drug and determined the benefits far outweigh the risks.

"The benefit for the people who do achieve sustained virologic response is fantastic, "said Dr. Elizabeth Connick, University of Colorado Denver. "This is a miraculous advance." "The risks are not trivial, but we do know how to manage these risks. Still, there is a lot to learn about using these drugs appropriately," said Dr.

Thomas Giordano of Baylor College of Medicine. “This is going to be a real game changer for our hepatitis C practices, “said Dr. Barbara McGovern, Tufts University School of Medicine. “I can’t wait to get back and talk to my patients about it.”

Even hard-to-treat patients like African Americans, and people with HIV and diabetes responded extremely well to the Boceprevir combination therapy. Dr. Nizar Zein, section head of hepatology at the Cleveland Clinic says the disease is of epidemic proportions and quite costly. Zein say the new medication will usher in a very important new era for treating the disease. “We can now say for the first time that we can cure hepatitis C, “Zein said. “We are talking about complete cure, cure for life. Several studies have shown that once you achieve that endpoint, the sustained virological response, you will not get hepatitis C ever again and the risk of getting cirrhosis, needing liver transplant will go down substantially.”

But this is a powerful drug and a major concern is that drug resistance can develop in patients very quickly if the medication is not taken properly. The proposed dosage is 800 g three times a day with food. Treatment can be individualized but Zein says both doctors and patients need to be educated and clear about when and how this drug is to be taken. “If used inappropriately, the virus will rapidly develop resistance to these medications – rapidly, I mean 24 to 48 hours.”

Close attention was paid to the drug’s side effects. The most common, included anemia, abnormally low white blood cell count, fatigue, nausea, headache, hair loss and an impaired sense of taste.

According to FDA’s Dr. Poonam Mishra, the most notable safety concern is the additional decrease in hemoglobin the protein in red blood cells that carries oxygen. Hemoglobin levels lower than normal could mean anemia, bleeding or a number of other conditions.

Original Article

Female Genital Tract-Reproductive Performance With Its Variable Anomalies

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ABSTRACT

Objective: To observe the different presentation and reproductive performance of women with congenital anomalies detected by ultrasound, hysterosalpingography and on laparotomy.

Study Design: Prospective observational study.

Place and Duration of Study: This study was conducted in the Department of Obstetrics & Gynaecology at Peoples Medical College Hospital Nawabshah from January 2004 to December 2009.

Materials and Methods: All the women with congenital anomalies of genital tract detected clinically, by ultrasound and hysterosalpingography, attended the outpatient department or presented with a complication and operated; and or those who were incidentally diagnosed during cesarean section or on laparotomy were included in this study.

Results: 48 patients with different mullerian duct anomalies were detected during the study period. Their age varied from 15 to 40 years. Mullerian agenesis with absent vagina was found in 6 cases, transverse vaginal septum was found in an other 6 patients. These patients presented with primary amenorrhoea, haematometra and haematocolpos. Imperforated hymen was found in 10 patients. They also present with a primary amenorrhoea, mass in lower abdomen and cyclical pain, few patients presented with acute retention of urine. Longitudinal vaginal septum was found in 3 cases. They presented with dyspareunia and difficult labour. Bicornuate uterus was found in 9 cases. They presented with malpresentations, recurrent abortion and preterm labour. Unicornuate uterus was found in 3 cases. Who were presented with ectopic pregnancy. Uterus didelphys was found in 3 cases, 5 patients had arcuate uterus, 3 patients presented with congenital second degree uterovaginal prolapse.

Conclusion: Uterine abnormalities are not uncommon, although not all the types of uterine anomalies can affect the fertility but most of the time they have bad impact on fertility. Early diagnosis and treatment of these conditions may improve the fertility prospectus and also prevents various obstetrical complications.

Key Words: Genital tract abnormalities, Hysterosalpingography, Ultrasound Scan, Reproductive performance.

INTRODUCTION

Developmental anomalies of the mullerian duct represent some of the most fascinating disorders that obstetricians and gynaecologistists encounter[1]. The range of mullerian duct anomalies varies from minor uterine anomalies, duplication of uterus and vagina to agenesis of the mullerian duct.

Mullerian malformations are frequently associated with abnormalities of renal and axial skeletal system[1]. Due to wide variation in clinical presentation, mullerian duct anomalies may be difficult to diagnose clinically but because of the better availability of the recent diagnostic modalities such as transvaginal sonography, 3D ultrasound, hysterosalpingography, MRI and laparoscopy, detection of such anomalies could be possible. The imaging will help to diagnose and distinguish surgically correctable from inoperable conditions[2,3,4,5,6,7,8].

The reproductive outcome can be improved with early diagnosis and better treatment but generally poor reproductive performance prevail[9,10].

Incidence and prevalence

The actual incidence of mullerian duct anomalies in general population are not accurately known. Frequency varies widely and depends on various diagnostic methods implied during the studies. Most authors reported the incidence of mullerian duct anomalies varies from 0.1 – 3.5 %[11,12,13,14]. In women with infertility problem, the incidence is slightly higher (3 – 6 %)[1], women with recurrent abortion have an incidence of 5 – 10 %[15,16]. The most commonly reported anomalies are septate uterus, arcuate uterus, uterus didelphys, unicornuate uterus and hypoplastic uterus. The exact distribution depends on diagnostic tools, expertise and geographic location[17].

The aim of this study is to observe the mullerian duct anomalies found in our setup and its impact on reproductive performance and to share the experience regarding the diagnosis, complications and management.

MATERIALS AND METHODS

A prospective hospital based observational study was conducted in the Department of Obstetrics & Gynaecology at Peoples University of Medical and

Health Sciences Nawabshah from January 2004 to December 2009.

All the women with congenital anomalies diagnosed clinically by ultrasound, hysterosalpingography or presented with complication and those who were incidentally diagnosed during cesarean section and laparotomy were included in the study. All the women underwent clinical examination, most of them required anaesthesia for proper evaluation.

Ultrasonic screening of the associated renal tract anomalies was also done in all the patients. Treatment was carried out according to the facilities and expertise available. Some patients were referred to special centres for reconstructive surgery.

RESULTS

Forty Eight (48) patients with different congenital malformation were detected during the study period. Their age varied from 15 to 40 years, including the married and unmarried women. Mullerian agenesis with absent vagina was found in 6 patients. All these have well developed secondary sex characteristics and presented with a primary amenorrhoea, chromosomal analysis confirmed XX female. 4 patients were unmarried and 2 patients were married. One patient presented with apareunia and one patient presented with postcoital bleeding and tearing of vagina. Transverse vaginal septum was found in 6 patients, among them 2 patients had high vaginal septum while 4 patients had low vaginal septum. They presented with mass in lower abdomen and cyclical pain, concomitant urinary retention was detected in few cases. 4 were unmarried, 2 patients were married. All these presented with primary amenorrhoea, haematocolpos and haematometra. One patient had small hole in the septum, she menstruate regularly but complaining of severe dysparunia.

Imperforate hymen was found in 10 young girls. All had primary amenorrhoea, 2 of them presented with mass in the abdomen and 2 presented with acute retention of the urine. Bicornuate uterus was found in 9 cases, 3 of them presented with second trimester abortion, 2 patients came with preterm labour and 4 patients were diagnosed during cesarean section, performed for breech presentation and transverse lie. Arcuate uterus was found in 5 patients, among them one presented with breech presentation and 4 patients were incidentally diagnosed during cesarean section performed for other obstetrical conditions. 3 patients had unicornuate uterus, 2 patients were presented in shock, because of severe haemorrhage, laparotomy revealed ruptured ectopic pregnancy in accessory horn. One patient presented with history of recurrent dilatation and evacuation for missed abortion, examination revealed an adenexal mass and laparotomy confirmed haematometra in non-communicating horn which was then excised.

Uterus didelyphus was found in 3 patients, one patient was diagnosed during cesarean section performed for transverse lie; one patient presented with missed abortion and diagnosed with ultrasound, one patient presented with primary infertility, double uterus with double cervix was detected on hysterosalpingography.

Table No. 1:Congenital anomalies and their clinical presentation

Abnormalities	No. of Patients	Presentation
Mullerian agenesis with absent vagina	06	Primary amenorrhoea, infertility, postcoital bleeding
Transverse vaginal septum	06	Primary amenorrhoea
Longitudinal vaginal septum	03	Dyspareunia, difficult labour
Bicornuate uterus	09	Malpresentation, abortion, premature labour
Unicornuate uterus	03	Ectopic pregnancy
Imperforated hymen	10	Haematometra, haematocolpos
Uterus didelphys	03	Incidental diagnosis during laparotomy and hysterosalpingography
Arcuate uterus	05	Incidental diagnosis at LSCS
Second degree uterovaginal prolapse	03	Primary infertility, disturb marital relationship

Table No. 2:Reproductive performance of different types of uterine malformation

	Unicor-nuate	Bicor-nuate	Uterus didelphys	Arcuate
Total pregnancy	03	09	03	05
Early abortion	00	00	00	00
Late abortion	00	03	00	00
Ectopic pregnancy	03	00	00	00
Preterm delivery	00	02	00	00
Term delivery	00	00	00	04
Malpresentation	00	04	03	01

Congenital second degree uterovaginal prolapse was present in 3 patients. One patient was unmarried and ended up in vaginal hysterectomy, other 2 patients were married and both had disturbed marital relationship.

Associated renal tract anomalies were found in 3 patients, one patient had fused kidney (Horse shoe) found in the pelvis. In 2 patients, one kidney was absent.

DISCUSSION

The association of uterine anomalies with obstetrical complications has long been recognized, however a large proportion of the women with uterine malformation have no obstetrical problems. There are controversies regarding the surgical treatment in asymptomatic patients. In mullerian agenesis with absent vagina, vaginoplasty is only required when the prospectus of marriage and sexual activity are concerned.

Hossan Ara in her study also used to do the vaginoplasty and creation of neovagina when there is prospectus of marriage and sexual activity[7,8,9,10,11,12,13,14,15].

As we do not have the expertise for such a treatment, so these patients were referred to the special centres for reconstructive surgery.

Excision of the transverse vaginal septum was done with vaginal reconstruction. 2 of them have high vaginal septum with small atrophic cervix and they ultimately ended up in hysterectomy. Remaining 4 patients had successful surgery and were advised to have a regular vaginal dilatation to prevent the vaginal stenosis. One patient had a small hole in the septum and the septum was excised after the insertion of the Foley's catheter through that hole and inflated with 30 ml of water. The septum was excised on that balloon of the catheter. Postoperative dilatation was done for one week and patient was discharged with an advice to practice normal marital relationship.

Imperforated hymen with haematocolpos and haematomatra was quite common in young pubertal girl in our population. Hymentectomy with drainage of collected blood was a preferred treatment.

Ali A. et al in her studies shows the insertion of foley's catheter through the hymenal hole without damaging hymen structures as they consider that this new technique is less invasive and prevents many social problems by preventing destruction of the architecture of hymen and providing annular intact of hymenal ring[16].

Another study was performed at Agha Khan Hospital Karachi by Zafar Nazir et al, they used abdominal, perineal and abdominoperineal approach for reconstructive surgery of vagina in different age groups of the patients according to level of the septum[17]. Patients with urogenital sinus and cloacal malformations had stretch reconstruction[10,17].

Patients with bicornuate uterus, those who are diagnosed incidentally during cesarean section do not require any surgical correction. They advised to have antenatal checkup in next pregnancy and hospital delivery, those patients with recurrent abortion referred to special centres for further management.

Unicornuate uterus with rudimentary horn required the excision of accessory horn as a rupture of the rudimentary horn may occur in 90 % of the cases[11,12].

Arcuate uterus were diagnosed incidentally producing no symptoms and needed no treatment. Uterus didelphys as one patient has term pregnancy, so she required no treatment and 2 other patients, one patient had missed abortion and other patient had primary infertility as these problems could be because of other reasons not because of uterine anomaly. So, they were referred to special centres with proper counseling.

Second degree uterovaginal prolapse was found in 3 patients, one patient had Manchester repair with successful full term pregnancy afterwards, one patient had a sacrohysteropexy and one patient had a vaginal hysterectomy. They had the improvement of the symptom in the postoperative period but they did not come for long term follow up.

CONCLUSION

Uterine abnormalities are not uncommon, for defining their actual prevalence in population. It needs a well designed study including all the segments of reproductive age group women. Congenital anomalies of genital tract mostly hamper the sexual and fertility aspect of women, their early diagnosis and treatment may improve the fertility prospectus and also prevent the occurrence of various complications.

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Original Article

Evaluation of Reasons of Failure of Trial of Labor for Better Prognosis of VBAC

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ABSTRACT

Objectives The present study was conducted to determine the reasons of failure of VBAC after previous one caesarean section.

Study Design: Descriptive type of study.

Place and Duration of Study: This study was carried out in the department of obstetrics and gynecology Ayub Teaching Hospital Abbott Abad from 21 October, 2007 to 20 April,2008.

Materials and Methods: The study population included 201 cases that were declared eligible for TOL having only one previous CS for non recurrent cause, a low transverse uterine scar, and adequate pelvis. All the findings were noted and recorded on predesigned proformas. Data was analyzed on SPSS version 10.Discriptive statistics were used to calculate Mean and standard Deviation for age, frequencies for abnormal lie, fetal distress, failure to progress, placeta previa, and other maternal or fetal causes of failed trial. Chi square test was used to test for significant difference of frequencies between groups; the student T test was used for significant

Result A total of 201 patients with previous one caesarean section were admitted. VBAC was successful in 60 patients, the rest i.e. 77 patients were given trial of labor but failed. Among them 20(26%) failure was due to scar tenderness in the prospective pregnancy, 15(19.5 %) patients had emergency lower segment CS for failure to progress, 8(10.4%) patients had another CS for fetal distress, 6(7.8%) had CS for impending rupture, 1(1.3%) had failed trial of labor due to rupture of uterus and 4(5.2%) had scar dehiscence.

Conclusion: Results show that trial of labor in patients with previous one caesarean section due to non-recurrent causes is safe and has a success rate of 43.7%, which brings a hope to check the existing rate of CS.

Key Word: Cesarean section CS, trial of labor TOL, Vaginal birth after cesarean section.

INTRODUCTION

The incidence of CS varies between 10% and 20% in most developed countries. The incidence of Caesarean section in tertiary care hospitals of Pakistan is very rightly higher than this (30-35%) because a very high number of unbooked cases land in emergency after having been mismanaged outside

Provided there are no contraindications, a woman with previous one transverse lower segment cesarean section should be offered a trial of labor (TOL) with appropriate discussion of risks and benefits.[3] The risk factors for failure of TOL are increased maternal age, obesity, fetal macrosomia and uterine rupture The risk factors for uterine rupture are increased maternal age, postpartum fever after the previous cesarean; short inter delivery interval, history of at least two previous cesarean deliveries, unicornuate, bicornuate, didelphic and septate uterine malformations and a history of classical incision.[4] .

There is a 2.7 fold increase risk of placenta previa. Placenta accreta and placenta increta are associated with significant maternal morbidity including post partum hemorrhage and peri partum hysterectomy, complication of blood transfusion, infection, damage to bladder and bowel, deep vein thrombosis, transient tachypnoea difficulty in conceiving a further child.

Indications of previous CS, operative technique for CS, incisions both abdominal & uterine, complication of CS related to anesthesia, hemorrhage, urinary tract injuries, post operative complications like transient ileus, urinary tract infection, thromboembolism, wound infections, psychological complication, anesthesia complication and the risk of uterine rupture are the guidelines for decision of TOL.

Peri natal mortality and morbidity associated with vaginal delivery after CS is attributable to uterine rupture.[104,] The fear of uterine rupture dates back to time when classical uterine incision was used. [44] Now a days transverse incision in lower uterine segment is used which is a stretchy and fibrous part of the uterus so there are less chances of rupture and hemorrhage.

On the other hand previous vaginal delivery is the most favorable prognostic factor for a successful VBAC

The American college of obstetricians and Gynecology issued a consensus statement supporting vaginal birth after caesarean section as a safe and acceptable care option.

Recommendations of the American College of Obstetricians and Gynecologists for (1999) for selection of candidates for vaginal birth after cesarean delivery are:

1. One or two prior low transverse cesarean delivers
2. Clinically adequate pelvis
3. Physician immediately available throughout active labour capable of monitoring labor and performing and emergency cesarean delivery.
4. Availability of anesthesia and personnel for emergency cesarean delivery.[6]

MATERIALS AND METHODS

This descriptive study was conducted in department of Gynecology and Obstetrics of Ayub Teaching Hospital Abbott Abad from 21st October 2007to April 20, 2008 . A total of 201 cases of previous one C S were admitted during the study period and 137 were given TOL .Patients with only one previous C S for a non recurrent cause, a low transverse uterine scar, adequate pelvis, single fetus with vertex presentation, estimated weight of the baby less than 3.8 kg and no contraindication for TOL, or medical or obstetrical complications were included in the study. The data was collected through proforma.

Data was analysed using SPSS version 11 and descriptive statistics were used to calculate Mean and Standard Deviation for age, Frequencies for fetal distress, failure to progress and other maternal or fetal causes of failure of trial. Data was presented as tables. Chi square test was used to test for significant difference of frequencies between groups; the students T test was used for significant difference of means between groups .P value of ≤ 0.5 was considered significant.

RESULT

Out of 201 patients, 60 patients delivered vaginally and VBAC was successful. 43 patients had elective lower segment caesarean section, whereas 21 patients were not given trial of labor due to additional medical disorders/obstetrical emergencies. The rest i.e. 77 patients were given trial of labor but failed. So N=77

Ages of patients ranged from 18-40 years, with a mean $\pm$ standard deviation (SD) age of 24.83 $\pm$ 4.99 years, with 95% confidence interval (CI) of 1.42-2.11. Seven (9.1%) cases were below 20 years of age, 57(74%) between 21-30 years, and 13(16.9%) case sin 31-40 years age group.

Table No.1 Patients by Age Group:

Age Group	Number	%
Below 20	7	9.1
21-30	57	74.0
31-40	13	16.9
Total	77	100.0
Mean$\pm$SD	27.83$\pm$4.99	
95% CI	1.42-2.11	

In this context, 70(90.9%) patients had no history of previous vaginal births. Three (3.9%) patients had previous one vaginal birth, 2 (2.6%) patients had history of previous 2 vaginal births and 2 (2.6%) patients had a history of more than 2 vaginal births after one CS.

Table No.2: Number of Previous Vaginal Deliveries

Previous Vaginal Deliveries	Number	%
One	3	3.9
Two	2	2.6
More	2	2.6
None	70	90.9
Total	77	100.0

A total of 20(26%) patients had failed trial of labor due to scar tenderness in the prospective pregnancy, 15(19.5 %) patients had emergency lower segment CS for failure to progress, 8(10.4%) patients had another CS for fetal distress, 6(7.8%) had CS for impending rupture, 1(1.3%) had failed trial of labor due to rupture of uterus and 4(5.2%) had scar dehiscence.

Table.3. Patients by Reasons of Failure

Reasons for Failure	Number	%
Borderline pelvis	3	3.9
Intrauterine growth restriction	1	1.3
Oblique lie	1	1.3
Obstructed labour	4	5.2
Ruptured uterus	1	1.3
Scar dehiscence	4	5.2
Scar tenderness	20	26.0
Pre-eclampsia	1	1.3
Twin pregnancy	1	1.3
Breech presentation	2	2.6
Brow presentation	2	2.6
Decreased fetal movements	2	2.6
Failed induction	1	1.3
Failure to progress	15	19.5
Fetal distress	8	10.4
Fetal macrosomia	5	6.5
Impending rupture	6	7.8
Total	77	100.0

Table-4. Reasons for Failure versus Type of Previous Caesarean Section

		Type of previous Caesarian Section		
		Emergency	Elective	Total
Reasons for Failure	Borderline pelvis	3	0	3
	Intrauterine growth restriction	0	1	1
	Oblique lie	1	0	1
	Obstructed labor	4	0	4
	Ruptured uterus	0	1	1
	Scar dehisence	3	1	4
	Scar tenderness	15	5	20
	Pre-eclampsia	0	1	1
	Twin pregnancy	0	1	1
	Breech presentation	1	1	2
	Brow presentation	1	1	2
	Decreased fetal movements	2	0	2
	Failed induction	1	0	1
	Failure to progress	13	2	15
	Fetal distress	7	1	8
	Fetal macrosomia	5	0	5
	Impending rupture	6	0	6
Total		62	15	77

Chi-Square Tests			
	Value	DF	Asymp. Sig. (2-sided)
Pearson Chi-Square	25.307[a]	16	.065
Likelihood Ratio	25.594	16	.060
N of Valid Cases	77		

Effects of previous CS indications on reasons of failure of VBAC are summarized in table A total of 62 (80.51%) patients had emergency CS previously, while 15 (19.48%) patients had elective CS previously. In this study 15 (75%) of patients had failed trial of labor due to scar tenderness having emergency CS previously while 5 (25%) had failed trial of labor having elective CS previously. Similarly, 13 (86.66%) patients had failed trial due to failure to progress having emergency CS previously and 2 (13.33%) patients had failed trial having elective CS previously. These 7 (87.5%) patients had failed trial due to fetal distress having emergency CS previously and 1 (12.5%) patient had failed trial due to fetal distress having elective CS. There is no significant difference at 5% level between previous CS and reasons of failure in this regard.

DISCUSSION

The objective of this study was to determine the reasons of failure of vaginal birth after previous one CS.

It was observed in the study that 20 (26%) of patients had failed trial due to scar tenderness, 15 (19%) patients due to failure to progress, 8 (10.4%) due to fetal distress followed by impending uterine rupture, and scar dehiscence respectively. Only 1 (1.3%) patient, the TOL failed due to uterine rupture, which was repaired successfully. Similarly there was no adverse outcome in patients with scar dehiscence as well as scar tenderness. This observation is similar to two studies conducted in Nishter Medical College Multan in 2005 and in department of Gynecology, Ayub Teaching Hospital Abbottabad regarding the reasons of failure to achieve VBAC

Other factors observed were the indications of previous CS and their effects on failure of VBAC. In this study, maximum patients (18.2%) had previous CS due to fetal distress, 15.6% had previous CS for breech presentation followed by failure to progress respectively. Taj et al also found the same indications of previous CS in their study in 2008, where the trial of vaginal delivery was carried out on 100 patients. The same reasons were also observed in another study conducted by Hassan[1].

In our study 90.9% of patients failed to deliver vaginally who had no previous vaginal births, which indicates that the more the number of previous vaginal births, more are the chances of successful vaginal delivery after previous one CS[53].

No maternal death was recorded in this study. Only one (1.29%) patient had ruptured uterus while 4 (5.19%) had scar dehiscence. The observation of no maternal mortality in our study is because majority of the patients selected in this study had spontaneous onset of labor, which is a good prognostic sign for successful vaginal birth.

The rising rate of CS has been a problem for the obstetrician and this can be dealt in two ways for reduction. Firstly, by reducing the primary CS rate and secondly by attacking the repeat CS incidence. The risks, which are more threatening to the obstetrician when permitting TOL in patients, are fear of uterine rupture with threat of damage to mother and fetus, and possible subsequent litigation. Secondly many obstetricians consider CS safe as compared to vaginal delivery[116]. A number of studies have been conducted with highly successful outcome of vaginal delivery but still reports are there about uterine rupture and scar dehiscence.

Enkin et al analyzed some studies that qualified according to their criteria, revealed in their work a uterine rupture/dehiscence rate of 1.5% for elective repeat CS and 1.7%for overall women undergoing TOL[116].

It is also observed in this study that patients who had been operated upon previously for breech presentation, fetal distress or other mal-presentations had more chances of successful vaginal delivery, compared to those with dystocia, cephalo-pelvic disproportion. This observation is comparable to global literature[52].

CONCLUSION

Results show that trial of labor in patients with previous one caesarean section due to non-recurrent causes is safe and has a success rate of 43.7%, which can be further increased by encouraging the patients to make decisions about VBAC. Therefore, properly selected patients of vaginal birth after cesarean section should be offered facilities of Operation Theater, anesthesiologist, pediatrician, and blood transfusion services in the hospital.

In the management of patients with previous CS, regular and intensive antenatal care is required to reduce maternal and fetal, morbidity and mortality.

It was also concluded from this study that risk of repeat CS arises because of an increased rate in the previous CS in non-booked obstetric patients. In this way growing rate of cesarean section will be decreased, which is one of the most important issues in modern obstetrics.

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Original Article

An Outcome Review of Conventional Surgical Treatment of Angiofibroma

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ABSTRACT

Objective: To determine the efficacy of conventional surgical treatment for juvenile nasopharyngeal angiofibroma, in terms of morbidity and recurrence.

Study Design: A descriptive study

Place and Duration of Study: This study was conducted at ENT Unit I, Allama Iqbal Medical College/Jinnah Hospital, Lahore, from September 2007 to September 2010.

Patients and Methods: Fifty patients with juvenile nasopharyngeal angiofibroma treated surgically were analyzed. For each patient, data were obtained regarding the symptoms, extension of the lesion, various surgical approaches and rate of recurrence. Preoperatively, all the patients were evaluated with detailed history, endoscopic nasal cavity and nasopharyngeal examination and computed tomography. Age, gender, main symptom leading to consultation, any previous surgical treatment performed, various surgical approaches, duration of hospital stay and recurrence were evaluated. Follow-up examinations were performed in the first, three and six months postoperatively. All patients had CT scan after 6 months interval to rule out any recurrence.

Results: All the 50 patients were male either adults or adolescents. The age of the patients ranged from seventeen years.

The most common symptom was nasal obstruction with repeated episodes of epistaxis, seen in all the patients. The other associated symptoms seen were nasal discharge snoring in 20 %, headache in 10%, speech defects (rhinolalia clausa) in 20%, facial asymmetry in 40 %, deafness unilateral (on the side of disease) in 10%, bilateral in 10% and orbital pain in 10% of the patients. The clinical examination demonstrated mass in the nasopharynx in all patients (100%), and nasal fossa in 30 patients (60%). The other less common signs included external nasal deformity in 10%, palatal displacement in 20%, cheek swelling in 40%, proptosis in 20% and conductive deafness in 20%.

Lateral rhinotomy Transmaxiliary via midfacial degloving and Lateral rhinotomy and Subtemporal preauricular infratemporal fossa approach was used in 22%, 60% and 18% patients respectively. In 6 patients tracheotomy was done per operatively and all of them were decanulated after removal of pack. Per operative exposure and temporary closure of external carolid artery was done in 8 patients who had extensive disease and bleeding pre-operatively.

Five units of whole blood were arranged for each patient pre-operatively. Hypotensive anesthesia was used in all patients to minimize the blood loss. The blood loss ranged from 150 ml to 2.3 liters with an average loss of 400 ml. The average duration of hospital stay was 15 days, with shortest stay of 8 days with the maximum stay of 32 days. All patients had a minimum follow up for six months. 8 patients had recurrence for which they were operated again.

Conclusion: Conventional surgical procedures still have their place in the treatment of the JNF.

Key Words: Juvenile, Nasopharynx, Angiofibroma.

INTRODUCTION

Juvenile nasopharyngeal angiofibroma (JNA) is histologically benign yet locally aggressive vascular head and neck tumor. It affects almost exclusively adolescent males. JNA is an uncommon tumor, with reported incidence between 1 in 5000 and 1 in 60,000 otolaryngology patients.[1] It is estimated to account for only 0.5% of all head and neck neoplasms, but is nevertheless considered the most common benign neoplasm of the nasopharynx.[2] The histogenesis and pathogenesis of JNA are unclear. The site of origin of JNA is usually broad, on the postrolateral wall of the nasal cavity. This area forms the superior aspect of the sphenopalatine foramen at the posterior end of the middle turbinate.[3]

The diagnosis of nasopharyngeal angiofibroma is based on history, physical examination and radiographic studies. Biopsy of these tumors is hazardous.[4] The most common presenting symptoms are nasal obstruction and episodes of spontaneous epistaxis. Symptoms have usually been present for several months before the patient is seen. Other less common symptoms include diplopia, blindness, hearing loss, otitis media, rhinorrhoea, anosmia, nasal speech, mouth breathing, eye pain, and headache. On examination, virtually all patients have a nasopharyngeal pinkish to purple mass.[5] Juvenile nasopharyngeal angiofibroma has several characteristic radiographic features. CT scan, MRI,

MRA and angiography are currently the mainstay of diagnosis of nasopharyngeal angiofibroma. MRI is considered superior to CT scan in delineating the margins of tumor and revealing tumor vascularity.[1] The predominant blood supply of most nasopharyngeal angiofibromas is the ipsilateral internal maxillary artery. As the tumor grows, it may get bilateral arterial supply from the nearby vessels. Arterial embolization has been shown both to decrease intraoperative hemorrhage and to lower rate of tumor recurrence.[6]

The two primary therapeutic modalities for nasopharyngeal angiofibroma are surgery and radiotherapy. Several adjuvant measures have been tried, including hormonal therapy and chemotherapy. Surgical treatment is preferred in all patients with extracranial disease, and radiation is reserved usually for unresectable intracranial tumors. Many surgical approaches like transantral approach, lateral rhinotomy approach, transmaxillary via midfacial degloving approach, and the subtemporal preauricular infratemporal fossa approach have been used for nasopharyngeal angiofibroma. The decision regarding approach is made after reviewing radiographic studies to assess tumor extent, blood supply, and presence or absence of intracranial extension.[5]

PATIENTS AND METHODS

This is a prospective descriptive study of fifty cases of nasopharyngeal angiofibroma (JNA) treated surgically in ENT-I unit of Jinnah Hospital, Lahore from September 2007 to September 2010. Most of the patients presented in outpatients department while five patients were admitted through emergency with recent episode of epistaxis, which was controlled by conservative measures and later examination revealed a nasopharyngeal mass. Preoperatively, all the patients were evaluated with detailed history and clinical examination. The diagnosis was confirmed by endoscopic nasal cavity and nasopharyngeal examination and computed tomography was done to see the extent of the tumor and staging was done. MRI and Angiography were done in patients with intracranial extension. All patients had routine hematological investigations (blood complete & clotting profile) and underwent surgical removal of JNA. None of the patient had pre-operative embolization due to lack of facility in our set up. Per operative exposure and temporary closure of external carotid artery was done in 8 patients who had extensive disease and bleeding pre-operatively. The factors like age, gender, main symptom leading to consultation, previous surgical treatment performed, duration of hospital stay and recurrence were evaluated. The patients were discharged on fourth day after the removal of nasal pack (which was done on third post operative day). Patient was given oral first generation cephalosporin for five days, analgesics as per requirement and nasal douching for seven days. Follow-up examinations were performed in the first, three and six months postoperatively. All patients had CT scan on their last visit to rule out recurrence.

RESULTS

All the 50 patients were male either adults or adolescents. The age of the patients ranged from 10 years to 22 years with peak incidence between 13-18 years. The average age incidence as calculated in our patients was seventeen years. The age distribution of the patients is given in Table No.1

Table No.1: Age

Age	No. of Patients	Percentage
10 – 14	14	28%
15 – 18	25	50%
19 – 22	11	22%

The most common symptom was partial to complete unilateral and sometime bilateral nasal obstruction with repeated episodes of epistaxis, seen in all the patients. The other associated symptoms included nasal discharge in 10 (20 %), nocturnal snoring in 10 (20%), headache in 5 (10%), speech defects (rhinolalia clausa) in 10 (20%), facial asymmetry in 20 (40 %), deafness unilateral (on the side of disease) in 5 (10%), bilateral in 5 (10%) and pain deep to eyes in 5 patients (10%). The important signs on clinical examination demonstrated mass in the nasopharynx in all patients (100%), and nasal fossa in 30 patients (60%). The other less common signs included external nasal deformity in 5(10 %), palatal displacement in 10 (20%), cheek swelling in 20(40%), proptosis in 10 (20%) and conductive deafness in 10 (20%) patients. Temporal fossa fullness, reduced visual acuity, mild optic atrophy and papilloedema were noted in 5 (10%) patient suspected of having intracranial extension.

Table No.2: Surgical Approaches

Approach	No. of patients	Percentage
Lateral rhinotomy	11	22%
Transmaxillary via midfacial degloving	30	60%
Lateral rhinotomy & Subtemporal preauricular infratemporal fossa	9	18%

Different approaches used are summarized in Table No.2. In 6 (12%) patients tracheotomy was done per operatively and all of them were decannulated after removal of pack. Per operative exposure and temporary closure of external carotid artery was done in 8 (16%) patients who had extensive disease and bleeding pre-operatively.

Five units of whole blood were arranged for each patient pre-operatively. Hypotensive anesthesia was used in all patients to minimize the blood loss. The blood loss ranged from 150 ml to 2.3 liters with an average loss of 600 ml. The average duration of hospital stay was 10 days. After the removal of nasal pack on third post operative day, patients stayed for another 4 days to make sure that there was no bleeding. The average hospital stay of patients was 15 days, with shortest stay of 8 days with the maximum stay of 32 days. Nasal splints were placed in all patients to avoid synechia formation which were removed on tenth post operative day in outpatient. All patients had a minimum follow up for six months. 8(16%) patients had recurrence for which they were operated again.

DISCUSSION

JNF is the most common benign tumor of nasopharynx. Although it is a benign, but is biologically quite aggressive tumor. It originates almost exclusively in adolescent males or young adults. In our study of 50 patients, all were male, and the majority of them were around the age of puberty with mean age of 15 years, the peak incidence between 13-17 years and total age range of 10-22 years. Although cases have been reported in female patients as well, none of the female patient was encountered in this study. [7]

The most common mode of presentation of this tumor is recurrent epistaxis and nasal obstruction. In this study, 100% of the cases presented with recurrent nasal bleeding. This figure is near to the result of *93.9%* in another study.[5] Economou et al have presented a figure of *73%* patients who suffered from epistaxis.[8] This difference from other studies may be due to the fact that most of patients come late to the hospital. The other less common features are speech problems, snoring at night, deafness, cheek swellings, proptosis and rarely visual defects.

A fairly reasonable diagnosis of the tumor is made on the basis of history and clinical examination. Investigations are employed only to confirm the diagnosis and to determine the possible extensions. None of the study patients were biopsied pre operatively in our unit to confirm diagnosis. However, 4 of the patients who presented in emergency were biopsied in other hospitals and sent with complaint of profuse bleeding. MRI and angiography are certainly very helpful in determination of feeding vessels and collateral supply, localization of the site of the lesion and its relations to large vessels in the vicinity. But due to limited facilities and long waiting time for these procedures, they were performed only in the patients with aggressive disease and those with suspected intra cranial extension. 14 (28%) patients had MRI to rule out intracranial extension. 3(6%) patients had intracranial extrameningeal disease.

An appropriate management is based on precise diagnosis of the tumor and its extensions, correction of any pre-operative deficiency and with procedures for reducing intra-operative blood loss. Anemia is the most important preoperative deficiency that needs correction.[2] Most of our patients were anemic to whom 1-2 pints were transfused preoperatively. The cut off value of hemoglobin before taking the patient to operation room was 10 G %. On an average four pints of blood were arranged for surgery. Since most of these tumors bleed profusely at time of surgery and due to the non availability of the facility of pre operative embolization, the technique of hypotensive anesthesia along with rapid removal of the tumor were employed to reduce the blood loss. Average blood loss was 600ml.

The primary mode of treatment is mainly surgical intervention. Surgery provides more radical and safe clearance of the disease as evident from various reports e.g., 15 % by Zaidi and Jaffery.[9] Since most of the patients suffering from the disease are very young radiotherapy is only reserved for the cases with intra meningeal extension, since it may hamper the normal growth of facial skeleton or may induce secondary malignancy in later life.[10] Six patients during the study time were referred for radiotherapy due the advanced stage of the disease at the time of presentation. The average hospital stay was 15 days, which is slightly more than reported in other studies. This was because quite a significant number of patients came to hospital without an investigations and time was consumed in their pre operative investigations. 8 (16%) patients had second surgery for their recurrence. This incidence of recurrence is slightly higher as compared to the recent studies. Due to the non availability of the facility of pre operative embolization, once the patient started to bleed profusely and more than usual, we were left with only option of packing the area and abandon the procedure to avoid severe complications.

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Original Article

The Effect of Abietic Acid (Cedrus Deodara Compound) on the Histopathology of Rat Stomach in Comparison with Ulcer Healing Drugs

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ABSTRACT

Purpose of study: The aim of this study is to observe the anti-ulcer effects of Abietic acid (a compound of Cedrus deodara) on the histopathology of rat's stomach in comparison with standard anti-ulcer drugs such as Femotidine (H_2 receptor blocker) and Protonix (a proton pump inhibitor).

Design of study: Experimental study.

Place and Duration of Study: This study was conducted in the department of Pharmacology, Institute of Pharmaceutical Sciences, Baqai Medical University, Karachi.

Materials and Methods: This study was carried out on 50 albino rats of Wistar Strain for experimental purpose. The animals were divided into five groups and each group comprised of 10 rats (i.e. 5 male and 5 female). The experimental procedure was repeated for three times. The compound of abietic acid was provided by the chemistry department of Karachi University. The ulcer was induced in the animals by giving 1ml of 100% ethanol after 48 hrs of fasting. The induction of ulcer in animal was then treated with abietic acid (25 mg/kg for 2 weeks) orally through feeding tube. The ulcer healing effects of this compound were then compared with the effect of known anti-ulcer drugs.

Results: Abietic acid used in this study showed the healing effects on the mucosal epithelium of stomach, decreased inflammatory cells and formation of granulation tissues on the sub mucosal layer during histopathological examination.

Conclusion: It is thus concluded that abietic acid has an anti-ulcerative effects when given in the required dose and may be adapted in the management of gastrointestinal disorders particularly in peptic ulcer.

Key Words: Histopathology, Abietic acid, Stomach, Anti-ulcer drugs, Albino rats.

INTRODUCTION

Abietic acid which is one of the terpenoids found in many dietary and herbal related plants[1], producing many functional and biological activities such as anti-tumor proliferation, antihypercholestrolemia and antidiabeties[2-3]. Abietic acid an abietane diterpenoids has also shown some other biological roles in various ailments like anti-allergic[4], anti-inflammatory[5], phytoalexin effects[6] and anti-convulsant activities[7]. A study indicated that abietic acid exerts *in vitro anti-inflammatory* activity after oral or topical administration and also having partial ability to prevent the production of some inflammatory mediators[8]. It has also been reported that abietic acid which is the main component of rosin fraction of oleoresin synthesized by confier species also have anti-inflammatory effect. It is also indicated that one of the compound 12- sulfo dehydroabietic acid mono sodium salt exhibit potent anti-pepsin and anti-ulcer activity with low toxicities[10]. Another compound of abietic acid, Ecabet sodium which is an anti-ulcer agent may cause epigastric fullness in patients with dysmotility - like function dyspepsia. Catechols derived from abietic acid were also evaluated for several biological activities mainly antifungal, antitumoral, antimutagenic, antiviral, antiproliferative and inhibition of nitric oxide[12]. Studies have shown that much work have been done on different lines of investigation in relation to the effects of abietic acid but no such studies have been conducted so far in Pakistan and other countries in relation to its histopathological effects of abietic acid on animal tissues. Therefore, present study has been carried out to observe the anti-ulcer effects of abietic acid histopathologically on stomach tissues of albino rats in comparison with known anti-ulcer drugs Femotidine (H_2- receptor blockers) and Protonix (a proton-pimp inhibitor).

MATERIALS AND METHODS

The compound of Abietic acid was collected from Chemistry department of Karachi University and was used to investigate its pharmacological and

therapeutical characteristics. The animals used for this experimental study were adult albino rats (Wistar strain) weighing 200-250 gms. They were housed in cages (i.e., 2 rats per cage) in the animal house of Baqai Medical University, Karachi, Pakistan. They were maintained on a well balanced laboratory diet in the form of biscuits prepared in Hussain Ebrahim Jamal (HEJ) Research Institute of Chemistry, University of Karachi. They were kept in a 12 hrs light / 12 hrs dark cycles and water was given freely.

Experimental Design

A total of 50 albino rats weighing 200~250grms were taken in this study and divided into five groups. Each group comprised of 10 rats (i.e., 5 male and 5 female rats). The animals were fasted except group 'A' for 48 hrs before oral administration of 1 ml of 100 % ethanol with metallic feeding tube for induction of gastric ulcer. All the animals were fed with special diet and water was given freely before sacrificed the animals.

Group'A' (Control): The animals in this group only received 1 ml of normal saline orally for two weeks.

Group 'B' : In this group 1 ml of 100 % ethanol was given after 48 hrs of fasting for the induction of ulcer. The animals were anaesthetized by the chloroform. The rats were sacrificed and stomach was removed out for histopathological study to observe for gastric ulceration.

Group 'C' (Check): After induction of ulcer with 1 ml of 100% ethanol, 1 ml of Pea-nuts oil was given for 02 weeks to observe its effect on the stomach in comparison with test groups (i.e., D & E groups)

Group 'D': After induction of ulcer Abietic acid was given (25-100mg/kg) accordingly[7]. Dose of abietic acid i.e. 25 mg / kg was dissolved in 1 ml of distilled water and given for two weeks to see its anti-ulcer effects with comparison of known anti-ulcer drugs i.e. Femotidine (20 mg) and protonix tablet (40 mg).

Group 'E': After induction of ulcer by 1 ml of 100 % ethanol, known anti ulcer drugs i.e. Femotidine (20 mg) and protonix tablet (40 mg) was given orally and the dose was also calculated according to the weight of rat.

The approval for conducting the experimental procedures on animals was taken by the Broad of Advance Studies and Research (BASR) and Ethics Committee of Baqai Medical University, Karachi – Pakistan.

Routine Tissue Processing

All the groups of animals were fasted over-night prior to being sacrificed. The animals were anesthetized with chloroform and placed on a dissection board. A midline incision was given on abdomen to expose out the abdominal organs. The stomach tissue was taken out and preserved in 10 % formalin before microscopic examination. The tissues were then fixed in normal saline for 24-48 hrs and processed through a series of ethyl alcohol of ascending strength (70, 80 and 95%) for the period of 1 hrs, twice in absolute alcohol (for 1 hr each) and twice in xylene (for 1 hr) in order to render the tissue elements transparent. The tissues were then infiltrated with molten paraplast at 58 ^{0}C. This was done for two times (1 hr on each occasion). The transparent tissues after clearing all elements from it were embedded in a solid mass of paraplast. The blocks were labeled, allowed to cool and the metal blocks were removed. The solid mass was then trimmed free of excess paraplast, leaving some free margins around the embedded tissues.

Five microns thick longitudinal sections were cut with a rotary microtome. The sections were mounted on thoroughly cleaned gelatinized slides and were placed on hot plates at 37 ^{0}C for 24 hrs for proper fixation. The slides were then stained by Hematoxylin and Eosin (H & E) stain according to the prescribed staining method[8]. The stain was prepared by dissolving hematoxylin and absolute alcohol. The mixture was boiled rapidly and mercuric oxide was then added. The stain was cooled rapidly in cold water bath; glacial acetic acid was then added and the stain was ready for immediate use. Several slides were prepared accordingly. The stained slides, after drying and labeling were preserved and stored for histopathological studies before microscopic examination for comparative morphological and pathological changes in the gastric tissues of the animal Abietic acid to observe the anti-ulcer effects on rat stomach (Fig 4). Animals of group 'E' were given known anti-ulcer drugs i.e. Femotidine 20 mg (H_2 – receptor blocker) and protonix 40 mg (Proton Inhibitor) to observe their anti-ulcer effects on rat stomach (Fig 5) Therefore, during the present study, anti-ulcer effects of drugs and samples were observed as compared to the protective effect used by some other authors[7,10].

RESULTS

The general characteristic features of the stomach tissue section of the animals examined microscopically are presented in Table-1.

Normal stomach tissues of control group 'A' (i.e. not treated with drugs) were observed as normal mucosa, sub-mucosa, muscularis and adventitia (Fig 1). The tissues also showed normal gastro-duodenal junction

and normal gastric glands. The animals of remaining groups were induced for ulcer by giving 1 ml of 100% ethanol after keeping them for 48 hrs fasting. Ulceration was confirmed in group 'B' both macroscopically and microscopically during histopathological studies(Fig 2). Animals of group 'C' was given peanuts oil as check to note the changes in the histopathology of the stomach tissue. (Fig 3). Animals of group 'D' after the induction of ulcer by giving 1 ml of 100% ethanol were treated with Abietic acid i.e., 25 mg dissolved in 1 ml of distilled water to observe the anti-ulcer effects on rat stomach (Fig 4), where as animals of group 'E' were given known anti-ulcer drugs i.e. Femotidine 20mg (H_2 – receptor blocker) and Protonix 40 mg (Proton-pump Inhibitor) to observe their anti-ulcer effects on rat stomach (Fig 5).

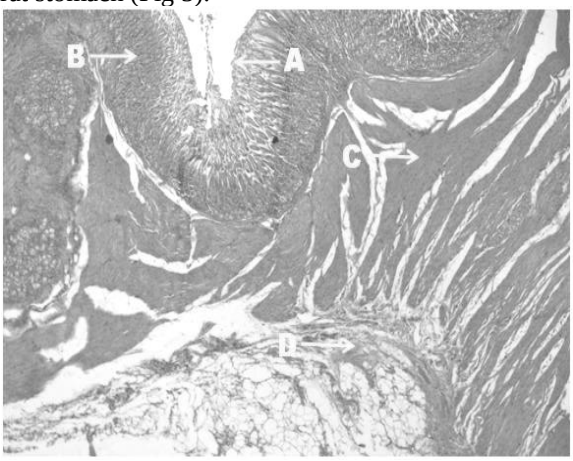

Figure No. 1: Photomicrograph of a 5 micron thick H & E stained paraffin section from the stomach of normal untreated rat (group A) showing normal mucosa (A), sub mucosa (B), muscularis (C) and adventitia (D). X 100 magnification.

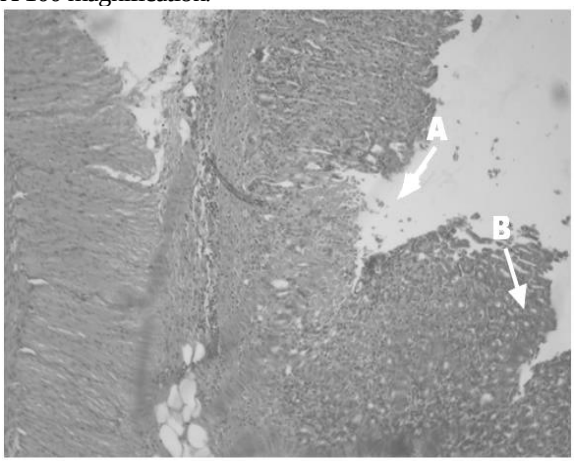

Figure No. 2: Photomicrograph of a 5 micron thick (H & E) stained paraffin section from the stomach of treated rats with 100% ethanol (dose 1 ml) showing superficial ulceration and erosion on mucosa (A) and inflammatory cells (B). X 100 magnification.

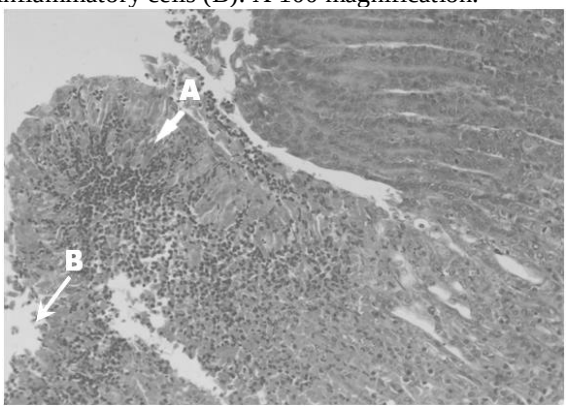

Figure No. 3: Photomicrograph of a 5 micron thick (H & E) stained paraffin section from the stomach of treated rats with 100% ethanol and 1 ml pea-nut oil showing inflammation of mucosal layer with inflammatory cells (A). Disruption of luminal epithelium (B). X 100 magnification.

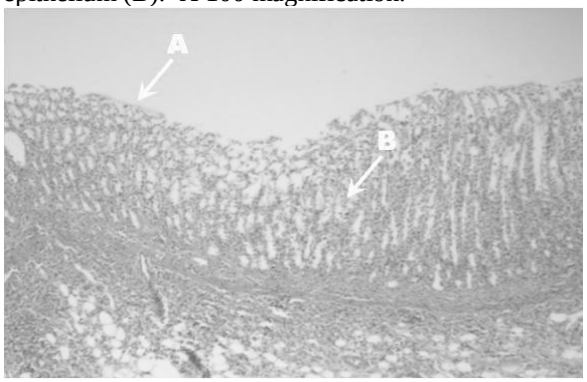

Figure No. 4: Photomicrograph of a 5 micron thick (H & E) stained paraffin section from the stomach of treated rats with 1 ml of 100% ethanol and abietic acid. (Group D). Showing healing of mucosal ulcer i.e. re-epithelization (A) and decreased inflammmatory cells (B). X 100 magnificati

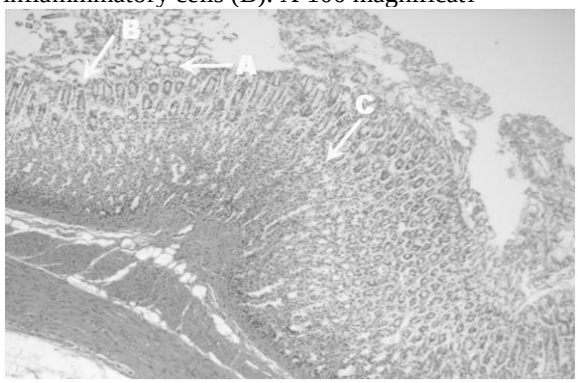

Figure No. 5: Photomicrograph of a 5 micron thick (H & E) stained paraffin section from the stomach of treated rats with 100% ethanol and Femotidine (H_2 receptor blocker) (Group E). Showing healing of gastric mucosa with re-epithilization (A). Formation

of gastric pits (B). Decreased inflammatory cells (C).
X 100 magnification.

Table No.1: Gross features of un-treated and treated stomach tissues of albino rat

TISSUE TYPE	ASSESS	UN-TREATED CONTROL GROUP	TREATED GROUPS			
		A	B	C	D	E
Stomach	Macroscopic	1 ml Normal Saline	1 ml of 100% Ethanol	1 ml of 100% Ethanol + 1 ml peanut oil	1 ml of 100% Ethanol + 25 mg / kg of Abietic acid	1 ml of 100% Ethanol + Anti-ulcer drugs
		♦ Dilated part of gastro-intestinal tract. ♦ consists of cardia, fundus, body, pylorus	♦ Multiple hemorrhagic red patches seen on greater curvature	♦ Multiple hemorrhagic spots also seen on the mucosal surface.	No hemorrhagic spots were noticed	♦ No hemorrhagic spots were seen
	Microscopic	♦ Showed normal architecture i.e. Normal gastric mucosa (A), Sub-mucosa(B), Muscularis mucosae(C), Adventitia(D) … Fig 1.	♦ Superficial ulceration and erosion seen on mucosal surface ♦ Inflammatory cells also seen Fig 2	♦ Inflammation seen on mucosal and sub-mucosal layer ♦ Few inflammatory cells (A) ♦ Disruption of luminal epithelium Fig 3.	♦ Re-epithelization of mucosal layer (A) ♦ Decreased inflammatory cells (B). ♦ Formation of granulation tissue Fig. 4	♦ Re-epithelization of mucosal surface (A) ♦ Formation of gastric pits (B) ♦ Decreased inflammatory (C) cells Fig 5.

DISCUSSION

In the present study anti-ulcer effects were seen on the rats' stomach, when 25 mg / kg Abietic acid was given orally in comparison with anti-ulcer drugs i.e. Femotidine and Protonix. The findings were observed histopathologically and was reconfirmed by using scanning electron microscopic method (submitted somewhere else).

The effects of Abietic acid were noted on stomach tissues with anti-ulcer drugs e.g, Femotidine 20 mg (H_2 – receptor blocker) and Protonix 40 mg (a proton inhibitor). The dose 25-100 mg / kg of Abietic acid was calculated[7] and was dissolved in 1 ml of distilled water. Abietic acid was then given to the rats after producing ulcer with 1 ml of 100% ethanol by keeping them on fasting to 48 hrs. Histopathological changes were observed in the rat stomach tissues i.e. healing effects on the mucosal epithelium of stomach, decreased inflammatory cells and the formation of granulation tissue seen in the sub-mucosal layer (Fig 4) In relation to the anti-ulcerative effect of the Abietic acid, only few references have been found in the scientific literature, however, some researchers have worked on the activity of Abietic acid but on different lines of investigations[10]. Abietic acid when given orally at the doses of 25-100 mg / kg body weight reported significant reduction of pepsin as well as prostaglandin mediated process[7,10]. The present work is also found more closely to the clinical approach in which anti-ulcer activity of Abietic acid was studied when given at the doses of 25 mg dissolved in 1 ml of distilled water orally to albino rats and significant healing effects on the mucosal surface of rats' stomach were noted. As very little work or investigation has been done on abietic acid to observe

its protective effects, so more research is needed in relation to the scientific and medicinal use of this compound.

CONCLUSION

Gastric ulcer is a serious gastro – intestinal disorder that requires a well targeted therapeutic strategy. As number of drugs like H_2 – receptor blocker and Proton-pump inhibitor are available commercially for the treatment and healing of gastric ulcer but showing incidence of relapses, side effects and drug interactions. To overcome this problem, drugs of plant origin are gaining popularity. On this basis Abietic acid is used in this study in order to assess the anti-ulcerative and healing effects when intorduced with the dose of 25 ml / kg orally to the albino rats. Therefore through this study it is suggested and recommended to medical personals that obietic acid can be used as a drug with appropriate doses for the management of peplic ulcer therapeutically.

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Original Article

Postoperative Outcome of Minicholecystectomy and Conventional Cholecystectomy

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ABSTRACT

Objective: To investigate the effects of different incision lengths following elective Cholecystectomy

Study Design: Prospective cross sectional, comparative study

Place and Duration of Study: This study was conducted at Surgical Unit II Peoples Medical University of Health Sciences Nawabshah from January 2009 to December 2010.

Patients and Methods: In this study, 100 patients were taken as a sample size. In this study, sampling technique was Purposive, non probability. Main Outcome Measures were postoperative pain, Length of hospital stay, Cost of treatment, Time until return to work, Complications. Most surgeons still prefer the open approach when dealing with common bile duct stone. The technique of open Cholecystectomy might compete with laparoscopic Cholecystectomy in avoiding prolonged operating time and major expenses. Mini-Cholecystectomy requires less operating time, less postoperative pain, and early return to work than standard conventional open Cholecystectomy

Results; There were 37 female and 13 male in MC group, and 42 female and 8 male in CC group. Median age was 55 (range 20-80 years) median BMI was 23 (range 17-30). 15 patients in MC and 18 patients in CC group were with acutely inflamed gall bladder and remaining were with chronic gall stone disease. In MC group of 50 patients the mean hospital stay was 2.5 days with shortest 1 day and longest 5 days. 35 (70%) patients were discharged within 2 days 10(20%) on 3rd and 5 patients remained fro 5 days.

Conclusion Minicholecystectomy offers less pain, earlier recovery and better cosmetic results than conventional open Cholecystectomy.

Key Words; Minicholecystectomy, Conventional Cholecystectomy, hospital stay,

INTRODUCTION

Today the removal of gall bladder is the safest, the most effective and widely recommended treatment for gall bladder disease. It is the second most common abdominal problem after acute appendicitis.[1] Three essential methods are used for the removal of gall bladder, Standard open Conventional Cholecystectomy (CC), Mini-Cholecystectomy (MC), and Laparoscopic Cholecystectomy (LC).

The first to describe Cholecystectomy through minilaparotomy incision was Dubios in 1982 and it appears that the term minicholecystectomy was coined by Gocco and Chambers in 1983.[2] There is a rise in the conversion rate from laparoscopic to open surgery, that reflects to adapt an all corners policy for laparoscopic Cholecystectomy and may be willing to undertake the operation in those with acute cholecystitis and previous abdominal surgery or alternatively that they have a more mature and suitable approach to conversion.[3] The most surgeons still prefer the open approach when dealing with common bile duct stone.[4] The technique of open Cholecystectomy might compete with laparoscopic Cholecystectomy in avoiding prolonged operating time and major expenses.[5] Open Cholecystectomy is still the gold standard by itself or in candidates contraindicating laparoscopy or as a sequel of laparoscopy during conversion.[6] Symptomatic gall stone disease has been treated for a century, Carl Langebuch performed first Cholecystectomy through a "T" shaped incision which was perfected by Theodor Kocher incision, it starts from the Xiphoid process to the right costal margin for about 10 to 30 cm, depending upon the surgeons to do Cholecystectomy through a small incision. Cholecystectomy and nearly all biliary surgeries can be performed in adults through a right transverse or oblique incision which varies from 3 to 6 cm in minicholecystectomy, and 10 to 16 cm in conventional Cholecystectomy.

Mini-Cholecystectomy requires less operating time, less postoperative pain, and early return to work than standard conventional open Cholecystectomy.[7] The aim of the work is to determine whether the patient comfort and hospital stay can further be improved if the wound is painful by shorter incision or not.

PATIENTS AND METHODS

About 100 patients were selected 50 patients in each group for Minicholecystectomy (MC) and conventional Cholecystectomy (CC) from January 2008 to December 2009 at Surgical Unit II of Peoples Medical College & Hospital Nawabshah. Patients with symptoms of gall

stone disease of either sex above the age of 20 years upto 80 years were included in our study. Patient excluded from study were, below 20 and above 80 years and patients with mass in right hypochondrium suspected to malignant, HCV positive with disturbed prothrombin time, and cirrhotic patients.

Each Cholecystectomy was prospectively recorded according to a protocol that involves patient's characteristics, surgical details, hospital stay, postoperative pain, intra and postoperative complications. Patients under going elective Cholecystectomy were given verbal and written information concerning the operation, expected hospital stay and convalescence. We operated on both acute and chronic cholecystitis on list. Every patient was given prophylactic antibiotic dose of Ceftriaxone and metronidazole 8 hours before surgery and at the time of induction of anaesthesia. Thrombosis prophylaxis was administered as tinzaparin subcutaneously the evening before surgery and five hours after surgery.

A personal standardized technique for MC as established after a 4 year experience of performing the operation with chronic gall stone disease. A small cushion was placed under the caudal portion of the right thoracic cage in order to raise the gall bladder region. The incision was started approximately 3 cm right to the midline ran obliquely parallel to and 3 cm below the right costal margin. The initial length of the incision was 4-5 cm depending upon the size of the patient was extended if necessary but did not more than 7 cm.

Data were presented as median, mean and range, comparisons of operative time, postoperative analgesia, and length of hospital stay were done by Student t test, and U-test. Difference between start of oral diet and complications rate were evaluated by the X^2-test and were considered significant when probability value was <0.05.

RESULTS

This prospective comparative cross sectional study was conducted at Surgical unit II PMCH Nawabshah. A total of 100 patients were included in the study 50 in MC group and 50 in CC group. There were 37 female and 13 male in MC group, and 42 female and 8 male in CC group. Median age was 55 (range 20-80 years) (Table 1) median BMI was 23 (range 17-30). 15 patients in MC and 18 patients in CC group were with acutely inflamed gall bladder and remaining were with chronic gall stone disease.

In CC group the incision adopted was Kocher's incision about 13 to 16 cm length. The average hospital stay was 6.5 days, shortest stay was 4 days and longest stay was 9 days. Out of 50 patients 15 (30%) were discharged on 4th postoperative day, 20(40%) on 5th day and 2 (4%) on 9th day (Table 2) there was no any operative difficulty, there were 8 patients with dilated CBD and Obstructive jaundice due to gall stone disease, which were explored T tube was placed. Recovery was smooth in all patients 6 developed wound haematoma and seroma formation wounds were opened and patients discharged on 7 to 9th postoperative day, 3 patients developed wound infection which was controlled by proper antibiotics and dressings. There was no operative mortality; mean operation time was 75 minutes (range 55-105 min)

Table No 1:Age and sex distribution (CI=95)

No	Age / years	Conventional cholecy-stectomy	Mini cholecy-stectomy	Total
1	20-35	15 (f-12, m-3)	20 (f-17, m-3)	35 =29+6 p= 0.002
2	36-50	20 (f-18, m-2)	15 (f-11, m-4)	35= 29+6 p= 0.005
3	51-65	10 (f-8, m-2)	12 (f-9, m-3)	22= 17+5 p= 0.002
4	66-80	5 (f-4, m-1)	3 (f-3, m-0)	08= 7+1 p= 0.001
	Total	50 (f-42, m-8)	50 (f-37, m-13)	100= 82+18

F= Female, M= Male, CI= Confident interval,

Table No 2: Postoperative Hospital Stay

Discharged on post operative day	Conventional Cholecystectomy	Mini Cholecystectomy
1st	0	4
2nd	0	16
3rd	0	15
4th	15	10
5th	20	2
6th	8	3
7th	5	0
8th	2	0
9th	0	0

In MC group of 50 patients the mean hospital stay was 2.5 days with shortest 1 day and longest 5 days. 35 (70%) patients were discharged within 2 days 10(20%) on 3rd and 5 patients remained fro 5 days. Three patients operated for acute cholecystitis developed operative bile leakage and which was stopped spontaneously in 5 to 6 days. Six patients were found with dilated Common Bile Duct with stone which were explored after removal of gall bladder without extending the incision. There was wound infection in three patients which was controlled by antibiotics and daily dressings. There was no operative mortality,

median operative time was 60 minutes range (45-84 min)

All patients remained in followup for one year. No one in MC group developed incisional hernia but 6 patients in CC group developed incisional hernia which were repaired by proline mesh. Cost of treatment was almost same in both groups, linear and small incision scar was acceptable and postoperative pain was more in CC with visual analogue scale of 10, in MC group 4.5 and in CC group 6.8, and diclofenac sodium was the drug used for pain control.

DISCUSSION

The incidence of gall stone disease is increasing in our society probably due to various factors, like use of oral contraceptive pills, oral estrogen replacement therapy, climacteric symptoms and change in dietary habits.

In this study the female to male ratio was 4:1 of gall stone disease which correlates with a study conducted at Chandka Medical College Pakistan.[8]

More than 2000 cases of MC have been reported world wide without any death or major CBD injuries since first reported in 1982.[9] by decreasing the incision size to 4-7 cm preserving the rectus muscle and using headlights, we have reduced operative morbidity and no increased risk to the patient. A study was conducted at Karachi Vlika Social Security hospital and discussed 10 years experience on MC and CC. In this study MC was performed through 3.5 cm average incision and main outcome measures were, operative time, postoperative pain, hospital stay and resumption to daily life and concluded that MC is superior than CC.[10]

In a study in Israel shows that mean postoperative analgesia requirements in MC and CC group (no of doses of 10mg morphine) were 4.0 to 5.8 respectively (p=0.002). Mean duration of hospitalization was 3 and 4.7 days respectively in MC and CC groups. Mean satisfaction of patient on 1-10 analogue scale was 8.6 and 6 (p=0.002) and was concluded that MC offers less pain, earlier recovery and better cosmetic results than CC.[11] This study is comparable to our study regarding postoperative stay of 2.5 to 6.5 days which is slight longer in CC group.

An other study conducted at Mayo Hospital Lahore showed that less postoperative pain and early return to work is seen in MC than CC patients.[12] and is same as in our study which shows less pain in MC than CC with analogue scale of 10 5.5 and 6.8 respectively.

A study conducted in Budapest, Hungry to elaborate the true value of MC as compared to laparoscopic and CC procedures and concluded that "Cholecystectomy performed by modern minilaparotomy is a realistic alternative to conventional and laparoscopic Cholecystectomy.[13] This study has same results regarding incision length of 4 to 6 cm and cosmesis.

The postoperative complications were more in CC than MC in our study, which is comparable to a study conducted at Lautaro Clinic Africa Chilli which showed that incidence of postoperative complications is much higher in CC than in MC patients.[14] Our study indicates small open Cholecystectomy incision is an alternative treatment for patients with their high incidence of acute cholecystitis and common bile duct stones which is same as done in 2000 by Jorgensen[15] median operative time for MC in our study was 60 minutes (45-84min) and is almost equal to previous studies (40-74min)[16] where as in our study operation time was measured between "knife to skin and last stitch" Post operative hospital stay was about two days in our study which is same as mentioned in the previous studies of MC [17,18,19].

MC is now performed as a day case or ambulatory surgery[20].The results of MC for chronic and acute cholecystitis in our study are comparable with those reported by LC [21] but at lower cost. Avoiding the need for special instruments improves the cost effectiveness of MC.

CONCLUSION

Minicholecystectomy offers less pain, earlier recovery and better cosmetic results than conventional open Cholecystectomy.

Conventional Cholecystectomy should be reserved for problematic and malignant and difficult adherent gall bladders.

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Original Article

Frequency of Endoscopic Gastric Neoplasms in Five Years at JPMC

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ABSTRACT

Objectives: Gastric cancer is among the most common malignancies in Pakistan. The aim of our study are i) to document different histological types of gastric malignancies as per age and sex ii) discuss its possible association in patients who underwent endoscopy and iii) compare our data with local and abroad studies.
Study Design: Retrospective study.
Place and Duration of Study: This study was conducted in the Department of Pathology, Basic Medical Science Institute, Jinnah Postgraduate Medical Centre, Karachi, Pakistan, from 1st January2003 to 31st December 2007.
Materials and Methods: A total of 740 cases of gastric endoscopic biopsies were received for histopathological evaluation at the Department of Pathology, Basic Medical Science Institute, JPMC, Karachi. Out of these cases, a total of 70 gastric neoplasms were separated, analyzed and classified according to the WHO classification system and their relative frequencies were recorded.
Results: Gastric adenocarcinoma was the commonest neoplasm with male predominance in 5th to 7th decade of life, account for 88.57% (62/70) of all gastric neoplasms. Gastric lymphoma was the second common with 8.57%(06/70) and gastric carcinoid was least common with 1.43%(1/70) of all gastric neoplasms.
Conclusion: This study highlights that adenocarcinoma is the most common gastric malignancy seen in most high risk group includes elderly males followed by lymphoma with no gender difference. So we advise regular endoscopic biopsies surveillance at least in high risk age group for the early detection of cancer.
Key Words: Gastric carcinoma, adenocarcinoma, lymphoma

INTRODUCTION

Cancer is still one of the major health problems worldwide with increasing frequency, especially with increased modernization, increased exposure to radiation and predisposition to large number of carcinogenic agents.[1] In 2004, cancers accounted for over 7 millions deaths (13% of total mortality) and there were more than 10 million new cases worldwide. More than 60% of cancer deaths and approximately half of new cases occurred in developing regions.[2,3] There is a significant variation in the distribution of site-specific cancer mortality and incidence by region.[3] Gastrointestinal cancers account for a large fraction of human neoplasms. They are almost without exception incurable when gross metastases exist.[4]Gastric carcinoma is a worldwide disease. In 1990, it was the second most common cancer in the world with an estimated 800,000 new cases every year, 60% of them being in developing countries[6]. The areas of highest incidence include Eastern Asia, South America and Eastern Europe and those of lower incidence include North America, North Europe, most parts of Africa and South Eastern Asia.[7,8]. Its incidence has markedly decreased in developed countries but remains high in countries like Japan and Chile; Japan having the highest incidence worldwide[9].In 2008, it has come down to become the 6th commonest cancer worldwide. Interestingly, 74% of all global cases are from Asia, where gastric carcinoma is the 2nd commonest cancer in males and the 4th in females[10]. The gastric antrum is the most common location.[11]Endoscopic biopsy is widely regarded as the most sensitive and specific diagnostic tool for gastric cancer[7]. Identifying the environmental risk factors may possibly shed more light on effective treatment and the prevention of gastric cancer but exact prevalence rate in Pakistan is unknown due to the lack of a population based cancer registry.

The aim of our study was to document different histologic types of gastric cancer as per age and sex groups in the patients and to know the frequency of microscopic subtypes of gastric malignancies seen in the Department of Pathology, Basic Medical Sciences Institute , Jinnah Postgraduate Karachi over a five year period and to classify them using the Classification Scheme proposed by the World Health

Organization (WHO)[12] for gastric malignancies, analyze the cases using simple statistical methods, and to compare the data obtained with those of other workers in other parts of country and rest of the world.

MATERIALS AND METHODS

Seven hundred and forty consecutive endoscopic gastric biopsies received during 1st January 2003 to 31st December 2007, were studied in the department of Pathology, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre,Karachi. This is a retrospective study. The specimens were mostly received from the Medical unit VII of JPMC Karachi. The relevant clinical information and demographic data were retrieved from record. The gastrointestinal symptoms included were abdominal pain, dyspepsia, and vomiting and weight loss. Patients above 12 years of all ages and both sexes having undergone gastric biopsy were included in the study.The endoscopic gastric biopsy tissue was fixed in 10% formaldehyde, routinely processed in an automatic tissue processor for 17 hours and then embedded in paraffin wax. Three to five sections of 4 micron thickness were cut on rotary microtome and routinely stained with Haematoxylin and Eosin (H&E). The tissue blocks were serially sectioned. In selected cases Periodic-acid Schiff (PAS) staining was also performed to detect signet ring cancer cells. The tumours were classified according to the WHO classification of gastric tumours. Majority of the biopsies were taken form antral part of gastric mucosa. Cases excluded from the study were tumors with extensive areas of necrosis and no viable or normal looking tissues, cases where the site of biopsy is unclear, not mentioned by endoscopist or could not be identified histologically and other types of gastric malignancies like gastrointestinal stromal tumors. The author and his senior pathologist examined the sections independently and diagnosis was made in the light of final histological findings.

RESULT

Out of the 740 cases reviewed, a total of 70 gastric malignant neoplasms were observed 48(68.57%) males versus 22(31.43%) females. The mean age at the time of diagnosis was 56 years. Median age was 60 years (range 22–85). Out of total gastric malignant neoplasms, adenocarcinoma found as a commonest malignant tumor with high frequency of 88.57% and second common tumor was lymphoma with 8.57%. A least percentage (1.43%) of carcinoid tumor and infiltrating squamous cell carcinoma were also found (Table No. 1).Maximum biopsies (70%) sended from antrum and 30% of the endoscopic biopsies received from body (corpus) of the stomach. (Table No.2). Gastric neoplasms were found more than double in males with 68.57% as compare to female(31.43%) reflects male predominance.Out of a total 70 malignant gastric neoplasms,a large number of tumors 60(85.71%) were found in 4th to 7th decades of life. Maximum number of cases, 19(27.14%) were found in 5th decade and minimum number of cases, 01(1.42%) was found in 9th decade of life. (Table No.3).

Table No.1: Frequency of neoplastic lesions in gastric biopsies

Gastric Neoplastic lesions	Frequency	Percentage
Adenocarcinoma	62	88.57
Lymphoma	06	8.57
Carcinoid	01	1.43
Squamous cell carcinoma(Infiltrating)	01	1.43
Total	70	100

Table No.2: Frequency of sites of gastric neoplastic lesions

Site	Frequency	Percentage
Antrum	49	70
Body	21	30
Total	70	100

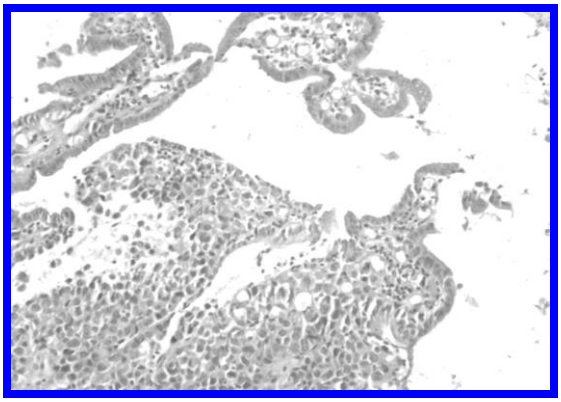
Table No.3: Age and sex distribution of different gastric malignancies

Age Group	Gastric Malignant Lesions								Total
	Adenocarcinoma		Lymphoma		Carcinoid		Squamous cell carcinoma		
	M	F	M	F	M	F	M	F	
10-20	-	-	-	-	-	-	-	-	
21-30	1	3	-	-	-	-	-	-	4
31-40	8	2	1	-	1	-	-	1	13
41-50	11	4	2	2	-	-	-	-	19
51-60	11	2	-	-	-	-	-	-	13
61-70	8	6	-	1	-	-	-	-	15
71-80	4	1	-	-	-	-	-	-	5
81-90	1	-	-	-	-	-	-	-	1
Total	44	18	3	3	1	-	-	1	70

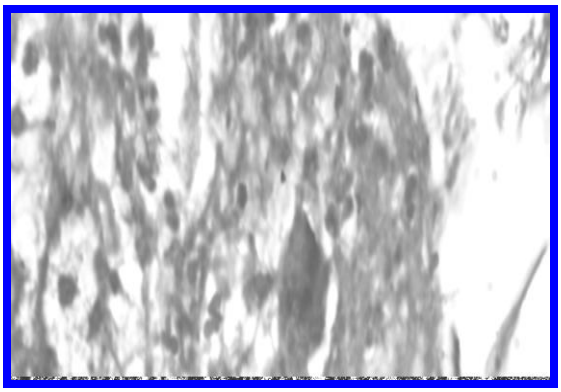
Gastric neoplasms were significantly high in males as compare to females with Chi-square 19.31 (P<0.001).Frequency and different subtypes of gastric adenocarcinoma analysed according to WHO classification. In a total of 62 cases of adenocarcinoma, maximum number of cases 20 (32.25%) were found to be adenocarcinoma (intestinal type), 19 (30.64%) cases were found to be signet ring cell carcinoma, 16 (25.81%) cases were found to be adenocarcinoma (diffuse type) and 07 (11.3%) cases of mucinous carcinoma were also found. (Table No.4).

Table No.4: Frequency and types of adenocarcinoma

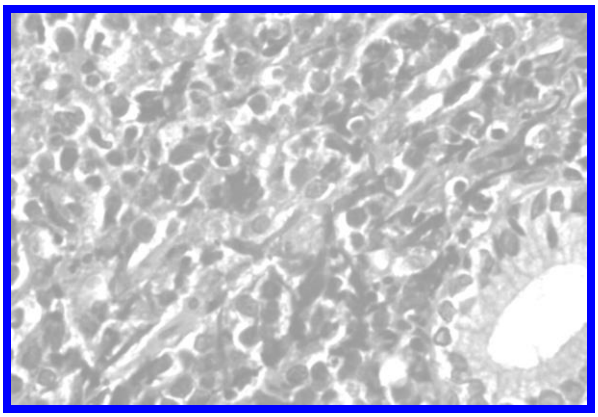
Type	Frequency	Percentage
Intestinal	20	32.25
Diffuse	16	25.81
Signet ring cell carcinoma	19	30.64
Mucinous	07	11.30
Total:	62	100



Photomicrograph: Gastric adenocarcinoma showing gastric mucosa with discohesive signet ring cells. H&E X 100.



Photomicrograph: Adenocarcinoma showing groups of discohesive cells with pleomorphic nuclei. PAS X 400.



Photomicrograph: Gastric lymphoma. H&E X 400.

DISCUSSION

Gastric carcinoma is one of the most common malignancies worldwide [13]. It is the fourth most common type of cancer and the second most common among cancer deaths worldwide.[14]We have reported a total of 70 cases of endoscopic gastric malignancies in the study period. Gastric carcinoma is extremely rare before the age of 30 years and most patients are above 50 years of age [15,16]. Though a steady decline in the incidence and mortality rates of gastric carcinoma has been observed worldwide over the past several decades, the absolute number of new cases per year is increasing mainly because of the aging of the population[17]. In our study, majority of the patients 60 cases (85.7%) were in the age range of 41 to 70 years. This finding corroborates well with international trends. However, cases of gastric carcinoma in young and even in children are recorded in world literature [18,19]is in agreement of our study and we found 04 cases (5.7%) and 13cases (18.57%) in the age groups of 21-30 and 31-40 years. As seen in other international studies, males were clearly affected more commonly, nearly two times more than females[15]. These findings were also in agreement with our findings where gastric neoplasms were found more than double in males with 68.57% as compare to female (31.43%) reflects male predominance.

The most frequent site of stomach cancer is the distal stomach i.e., the antro-pyloric region[15]. Carcinomas of the body or the corpus are located mostly along the greater or lesser curvature [15,16] . In our study, the distal stomach (antrum) was also seen to be the primary site in 70% of cases followed by the body or corpus (30%).

A study done in Nepal[20], who found adenocarcinoma to be the most common malignancy constituting 40% of 82 cases. In other studies Afzal et al[21] who

reported 42 (87.5%) of adenocarcinoma, Arif and Syed [22] reported 35 (70%) adenocarcinomas and Kim[23] reported 332 (97%) cases of adenocarcinoma all were inagreement with our study showed 62(88.57%) of adenocarcinoma as commonest malignancy. But our study showed disagreement with Hsu et al[24] who reported only 7 (1.13%) cases of adenocarcinoma in their neoplastic subjects. Primary malignant lymphoma of stomach makes up only a small percentage of all malignant tumors of this organ but there is evidence that its incidence is increasing [25]. In our study lymphomas were 6 (8.57%) out of a total 70 malignant tumors with 1:1 male female ratio (Table 1). Mehdi[26] reported 21 (6%) gastric lymphomas in a large series of 352 cases with male:female ratio 2:1 is comparable. Our study was comparable with Afzal [21] and Hsu et al[23]who reported 1 (2.2%) case and 1 (0.16%) case of lymphoma in their studies respectively.In our study 1 (1.4%) case of carcinoid was found out of a total of 70 malignant neoplasms. In our series 1 (1.4%) case of infiltrating squamous cell carcinoma was also observed.

H. pylori has been implicated as an etiologic factor in gastric carcinoma[27]. A prospective study in Korean population and found strong association of smoking and alcohol consumption[28]. Despite a high incidence in many Asian nations, patients have improved gastric cancer survival compared with other races[29-32]. These observations highlight the need to carefully examine gastric cancer outcomes among the different pakistani ethnicities. Among risk factors, salt intake, smoked meat, smoked fish, pickled vegetables, chili peppers, alcohol and tobacco are found to incur high risk[16]. Our study invites research in Pakistan to find out the incidence of gastric carcinoma in different castes and age groups and also correlate with above risk factors.

CONCLUSION

Gastric carcinoma is a common malignancy in this part of world. This study highlights that adenocarcinoma is the most common gastric malignancy seen in most high risk group includes elderly males followed by lymphoma with no gender difference. However, we advise that regular endoscopic biopsies surveillance should be done at least in the high risk group for the early detection of cancer.There is obvious scope of further studies on gastric carcinoma to assess the clinical correlation and also risk factors.

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Original Article

Extra Pulmonary Tuberculosis, Clinical and Imaging Overview

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ABSTRACT

Objective: Extrapulmonary tuberculosis is the tuberculosis of the organs other than lungs,caused by mycobacterium tuberculosis. It is endemic in Kingdom of Saudi Arabia (KSA), especially in Makkah as Asian / Southeast people are more here.
Design of Study: Experimental study.
Place and Duration of Study: This study was conducted at King Abdul Aziz Hospital, Makkah during 1st Jan.2007 to 31 Dec. 2008.
Patients and Methods: In our study 13 cases where examined, diagnosed (by both imaging and laboratory work up) and treated for extra pulmonary tuberculosis in King Abdul Aziz Hospital, Makkah. Diagnosis of extra pulmonary tuberculosis is often difficult, especially where lungs are not involved. Radiological findings,especially C.T. were of great help in the diagnosis of extra pulmonary tuberculosis. Final diagnosis was made by histopathological examination and culture for most of the patients. Predominantly (82 %) two systems were involved. 44 % lymphadenopathy, mainly cervical and mediastinal while musculoskeletal system was involved (with involvement of vertebrae and paraspinal muscles) in 38 %. Diagnosis of extra pulmonary tuberculosis requires high clinical suspicion, different imaging work up and special staining / culture media for diagnosis of mycobacterium tuberculosis bacilli (acid-fast bacilli). Patient's delay (average 2 months) and Doctor's delay time (average 7 days) was also observed in individual cases. Various patterns of extra pulmonary tuberculosis (EPT) in Makkah in Saudi and Non-Saudi patients also compared with other parts of KSA by reviewing the literature.
Results: The results showed that disease pattern has changed along with increase incidence rate of EPT in KSA over the last few years. True rates may be higher as there may be incomplete reporting or the patients may be referred to other areas of Kingdom.
Conclusion: The clinical and radiological features of extra-pulmonary tuberculosis may clue to the diagnosis as many other diseases can mimic the imaging. The patterns of extrapulmonary tuberculosis may vary due to extent of disease involvement otherwise inclination of region involvement is same everywhere. Extrapulmonary tuberculosis is relatively less in Saudi patients (from 1:2 to 1:3 depending upon regions) as compared to non Saudi patients.
Key Words: Anti tuberculous treatment, Extra pulmonary Tuberculosis, Human Immune deficiency Virus, Kingdom of Saudi Arabia, Tuberculosis.

INTRODUCTION

There is world wide continuous steady, increase in the incidence of Extrapulmonary tuberculosis (EPT) and decrease in pulmonary tuberculosis from the last one and half decade. In KSA, In 1993, reported EPT has annual incidence rate of 1.7 cases per 100,000 population[1]. In 1997, it was 4.7 cases per 100,000 population. During same period, pulmonary T.B. rates decreased[2]. In U.S.A., EPT percentage of all cases of T.B. was 15% in 1981 which increased to 18% in 1990 without a clear explanation [(3)]. However there was a resurgence of tuberculosis from 1985 to 1992, that considered with epidemic of acquired immune-deficiency syndrome[4]. A recent (2001) study in Riyadh also showed about 66%. cultured confirmed EPT of all tuberculous patients identified at KFSHRC[5]. The possible factors that have contributed to this increase are, the rising number of people with suppression of immune system, the development of drug resistant strains of mycobacterium tuberculosis, aging population demographics and an increase in the number of health care workers exposed to disease[6]. Diagnosis of EPT is often difficult. A negative smear of acid fast bacillus, a lack of granulomas on histopathology and failure to culture mycobacterium tuberculosis do not exclude the diagnosis[7]. Novel diagnostic procedures such as adenosine deaminase levels and polymerase chain reaction can be useful in certain forms of extra pulmonary tuberculosis but these facilities are not available in all centres, so sometimes antituberculous therapy may need to be initiated empirically to reduce

the morbidity and mortality. Although the incidence of tuberculosis is decreasing in U.S.A., it remain a major global problem with a prevalence rate of 32%[8]. It is increasing in foreign born persons (53% in 2003)[9]. Extra pulmonary involvement may be seen in more than 50% of patients with concurrent AIDS. The risk of EPT and mycobacteremia increases with advancing immunosupression. The features of AIDS associated tuberculosis may include extra pulmonary disease, disseminated disease, rapid progression,visceral lymphadenopathy, tissue abscess and negative tuberculin skin test. Response to ATT is usually similar to that of patients without HIV infection. Initial therapy (6 to 12 months) is same for all forms of EPT. Extended therapy may be required for bone / joint tuberculosis, delayed response or drug resistance. Adjunctive steroids may be useful in patients who have tuberculous meningitis, tuberculous pericarditis or miliary T.B. with refratory hypoxemia[10]. Directly observed therapy is strongly recommended to encourage medication compliance[11].

PATIENTS AND METHODS

The study consist of 13 patients who presented in different departments (according to region involved) of King Abdul Aziz Hospital, Makkah during 1st January to 31st December 2007. The patients of all ages (average 22 years) and of both sexes (M : F 10 : 3) were included who have the clinical suspicion of extra pulmonary tuberculosis after thorough clinical assessment.

Mixed tuberculosis (EPT + Pulmonary T.B.) and patients who have past H/O pulmonary T.B. were included in study. Isolated pulmonary tuberculosis patients were not included. Along with routine tests as that of CBC, ESR and tuberculin test, special laboratory investigations were also conducted in most of patients. These included the culture, staining and histopathological examination along with PCR (In some patients). In the mean time radiological investigations, x-rays and computed tomography were also done for different regions. C.T. was performed without and with I.V. contrast enhancement on single slice G.E. C.T. scan (CT/e – 2002), having spiral mode. In few cases, especially musculoskeletal and lymph node T.B., U/S or C.T. guided aspiration, both diagnostic and therapeutic, was done.

Most of the cases were followed by both laboratory and imaging work up. Regarding imaging, x-ray, U/S (G.E Logic 500) and C.T. follow up was done depending upon the requirement and region involved. Most of cases (11) responded well to treatment, two patients died due to poor response and other complications especially of brain and spine. 4 patients lost contact though they has responded well to treatment initially. During study it was tried to minimize the Doctors delay time (average 7 days) by starting ATT early even before the final reports came so as to minimize morbidity and mortality.

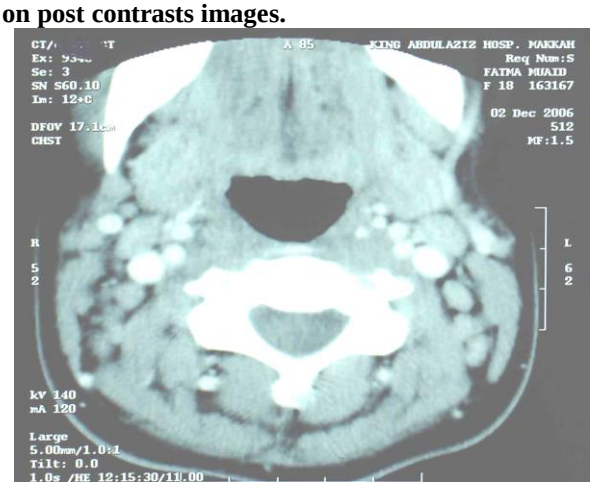
DISCUSSION

Ratio of pulmonary and extrapulmonary tuberculosis varied from region to region and in different times but most of studies (in Riyadh and Jeddah), showed values between 1 : 1 and 1 : 2 respectively. In our study, of 13 total patients. No clinical and radiological evidence of pulmonary tuberculosis seen in 10 (77 %) of cases while only 03 patients had mixed lesions (both pulmonary and extrapulmonary). Five patients (38 %) had isolated lesions either in spine or bones. 62 % had other organs involvement including 6 patients (44%) of cervical or mediastinal lymphadenopathy. We will discuss the patterns of involvement of different organs by tuberculosis in this study.

1. Tuberculosis Lymphadenitis:

No doubt, most common (44% in our study) form of extra pulmonary T.B. is tuberculosis lymphadenitis, mainly involving cervical region in almost all studies in / outside KSA. In one study of South west area of KSA, 45% of cervical lymphadenopathy was due to tuberculosis, more involvement of children and females with mean age of 31-32 years.Other regions like inguinal, axillary, mesenteric, mediastinal and intramammary, also have been mentioned in the literature[13,14]. Patients without H.I.V. infection, present with non tendor, chronic lymphadenopathy while patients with H.I.V. infection usually present with night sweats, fever and weight loss[15].Lymph nodes are firm and discrete, with time, may become matted together as

Figure No.1: Tuberculous Lymphadenopathy: Enhanced C.T. of neck showed extensive bilateral, variable sized, relatively solid looking (no necrosis) lymph nodes with mild homogeneous enhancement on post contrasts images.



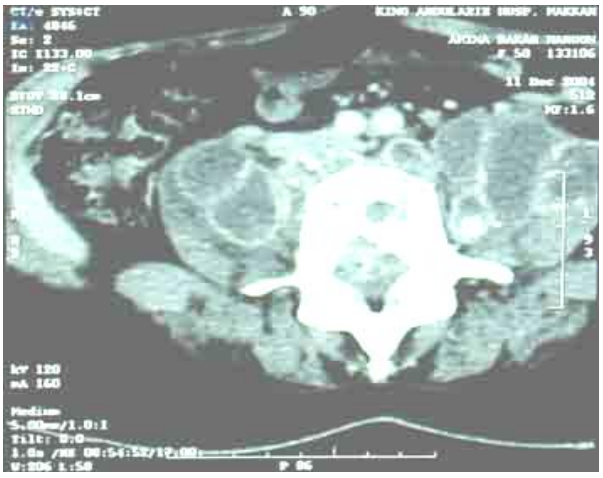
mass. If untreated, the nodes become fluctuant and drain spontaneously with sinus formation. Most patients have positive tuberculin test while chest x-ray is negative. Excisional biopsy of lymph node with histology, AFB stain and mycobacterium culture is diagnostic procedures of choice[16] On C.T. lymph nodes usually demonstrated peripheral enhancement with central low attenuation but not pathognomonic as this pattern can be seen in metastasis, lymphoma and other inflammatory conditions. Few may contain tiny calcification. Some may show homogeneous texture and enhancement (Figure No. 1).

2. Skeletal Tuberculosis:

Bone and joint tuberculosis account for about 35% of extrapulmonary tuberculosis and 3% of tuberculosis as a whole. Skeletal tuberculosis, most often involves spine, mainly dorso lumbar junction.Then comes tuberculous arthritis in weight bearing joints and then extra spinal tuberculous osteomylitis[17]. In middle aged or elderly patients, with active bone / joint T.B., miliary T.B. is sometimes caused by bacillemia originated from infected bone / joint lesions[18].

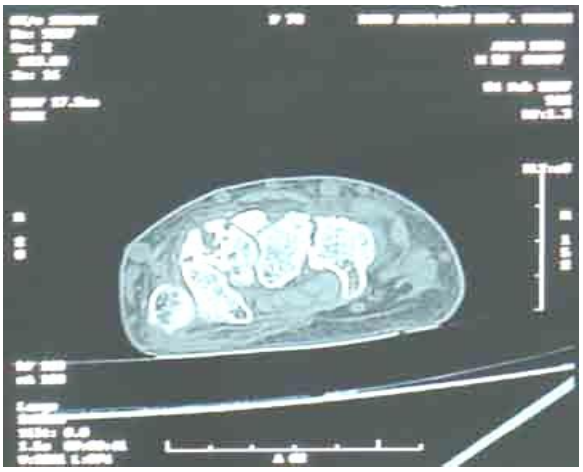
Tuberculous Spondylitis: Most common (50% of skeletal tuberculosis) typically involving more than one vertebra. Usually anterior / inferior part of vertebra is involved with involvement of disc. Later on anterior wedging may lead to classical kyphosis (gibbus), pain and cord compression. Paraspinal and psoas abscesses can develop which can extend upto groin. Calcification in abscess is pathognomonic of T.B. (Figure No. 2).

Figure No. 2: TuberculousSpine: Enhanced C.T. dorsolumbar spine showed extensive vertebral destruction with extension into canal and loculated paraspinal collections, involving both psoas muscles. Calcific foci seen in left psoas abscess.



Tuberculous Arthritis: It is slowly progressive , usually mono arthritis of hip, knee, S.I. joint or elbow. Usual presentation is pain, swelling and reduced movement. Draining sinuses are seen in chronic cases Radiographic changes are non specific however soft tissue swelling and phemister triad (Figure No.3), juxtra articular osteopenia, gradual joint space narrowing and peripheral subchondral erosions, may be characteristic. Fibrous ankylosis is end result. Bony ankylosis frequently seen in pyogenic arthritis.

Figure No. 3: Tuberculous Arthritis: Non enhanced C.T. of right wrist showed soft tissue swelling and lytic, destructive lesions in trapezoid and capitate in right wrist. The radial end was also involved (not shown) in this case.



Tuberculous osteomylitis:

Femur, tibia and small bones of hand and feet are usually involved with local pain and swelling usually metaphysis is involved. Involvement of adjacent structures may result in complications such as carpel tunnel syndrome, tenosynovitis and facial palsy. C.T. / MRI may be helpful to assess degree of bony destruction and to see soft tissue extension and encroachment on adjacent structures (Figure No. 4).

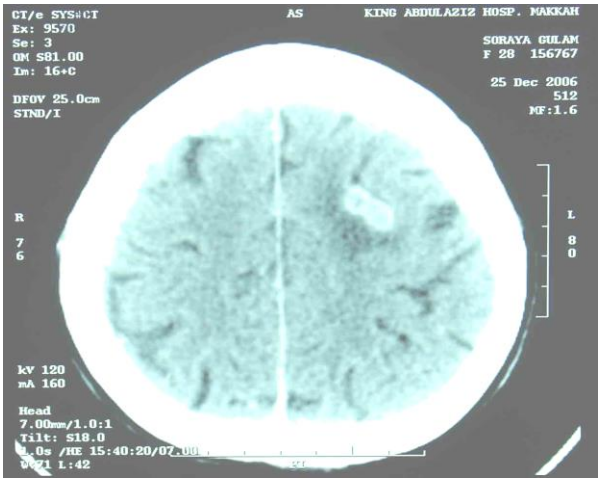
Figure No. 4: Tuberculous Osteomylitis: X-ray of left elbow showed minimally expansile, lytic lesion of upper part of ulna with break of articular surface and cortex as well. Mild soft tissue swelling also seen.

After clinical and radiological evaluation, arthocentesis (culture positive in 80% patients), Synovial and bone biopsy may be required. Small bones may be involved, especially in children,called tuberculous dactylitis. Later on cystic expansile cavity develops giving the appearance of wind filled sail, Spina Ventosa. A well defined cystic tuberculosis also exists with minimal sclerosis. The radiographic features of cystic tuberculosis may resemble with eosinophilic granuloma, sarcoidosis, cystic angiomatosis, plasma cell myeloma, chordoma, fungal infection and metastasis[19].

3. Central nervous system tuberculosis:
May be located in meninges, brain or spinal cord in the form of meningitis (commonest form), tuberculoma, abscess, cerebritis and miliary tuberculosis.

Meningitis:
It results from intense inflammation following rupture of subependymal tubercle (Rich focus) into subarachnoid space leading to arachnoiditis resulting in cranial nerve palsies, vasculitis and communicating hydrocephalus[20]. Tuberculoprotein hypersensitivity may cause meningism and typical CSF picture. Cerebral oedema causes impairment of consciousness, seizures and raised intracranial pressure. C.T. and M.R.I. imaging may show typical enhancement of basal cisterns due to gelatinous exudate.

Figure No. 5: Tuberculoma: Enhanced C.T. brain, axial images showed left subcortical lobulated tuberculoma with moderate surrounding oedema in precentral area causing occasional fits.

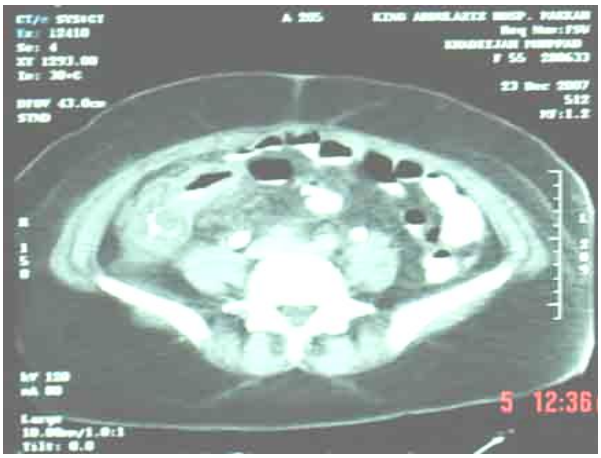


Most commonly communicating hydrocephalus is seen however obstructive hydrocephalus can be seen. Ischemic infarcts may be seen in basal ganglia and internal capsule. Tuberculomas may be seen on C.T. as variable sized, homogeneous or ring enhancing lesions with surrounding oedema (Figure No.5). M.R.I. appearance will depend whether tuberculoma is caseating or non caseating. Non caseating tuberculomas are often hyperintense on T_2 weighted images with homogeneous enhancement while caseating tuberculomas isointense to markedly hypointense on T_2 W images and exhibit ring enhancement[21].
This patient also had vertebral T.B.

Miliary tuberculosis:
It may appear as numerous rounded, homogeneously enhancing lesions less than 2 mm in diameter. Rare forms of parenchymal T.B. are cerebritis and abscess (sequelae of cerebritis). Contrast enhanced spinal meningitis may reveal nodular, thick, linear intradural enhancement. Syringomyelia can occur as complication of arachnoiditis and is seen as cord cavitation that typically demonstrates CSF fluid signal intensity on both T_1 and T_2 weighted images and does not enhance. CSF chemistry, AFB smears and culture are certainly helpful in diagnosis. CSF, PCR examination should not be done to exclude tuberculous meningitis as it has sensitivity of only about 56%[22].

4. Abdominal Tuberculosis:
Abdominal tuberculosis may involve gastrointestinal tract, peritoneum, mesenteric lymph nodes. Other organs like liver, spleen and adrenals usually are effected by miliary T.B.

Figure No. 6: Ileocecal Tuberculosis: C.T. abdomen with oral and I.V. contrast showed significant thickening of ileocecal region with relatively patulus ileocecal valve and peri ileocecal strandings. Few lymph nodes, not seen in this image, were also present.



Gastrointestinal Tuberculosis:
Tuberculous enteritis may result from swallowing of infected sputum or food. Hematogenous spread and extension from adjacent organs also seen. G.I. lesions are mainly ulcerative, however hypertrophic and ulcerohypertrophic types also seen. Pain, diarrhea, weight loss and malena is seen. Right lower quadrant mass with tenderness seen in 25-50% of patients.

Ileocecal and jejunoileal regions (90%) usually involved. Ultrasound, Barium studies and C.T. scan can delineate the lesions well. Thickening of the valve lips or wide gaping of the valve with narrowing of terminal ilium (The Fleischner sign) characteristically seen in tuberculosis. Greater thickening of wall and relatively larger ulcers are seen in T.B. rather than Crohn's disease. In advanced disease, characteristic deformities include symmetric annular "napkin ring" stenosis, obstruction, shortening, retraction and pouch formation. The caecum classically amputated. C.T. show thickening (circumferential or medial wall) of caecum and terminal ileum, enlargement of ileocecal value and mesenteric lymphadenopathy. Differential diagnosis of tuberculous enteritis includes Crohn's disease, Amoebiasis, Neoplasm, Yersinia infection and adinomycosis. Surgery is reserved for patients with complications.

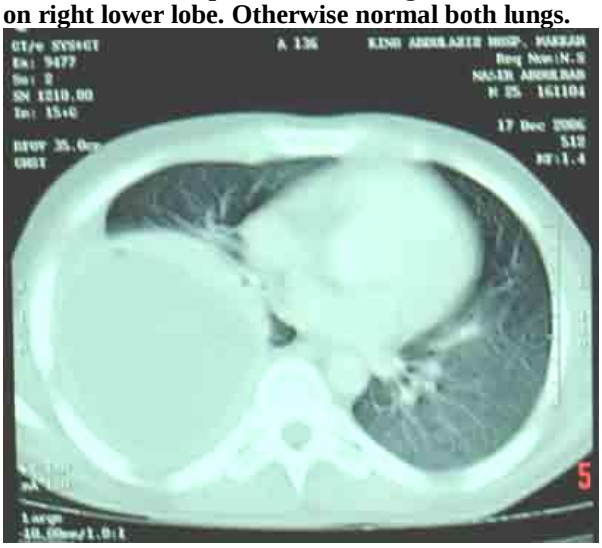
5. Genito-Urinary Tuberculosis:

Virtually all genitourinary organs can be involved by hematogeneous spread of tuberculous bacilli except testes which may be involved by direct spread from epididymis. Renal tuberculosis usually present with dysurea, hematuria or flank pain. More than 90% asymptomatic patients have sterile pyuria with or without microscopic hematuria. Intravenous urography may show moth eaten calyx due to erosion, followed by papilliary necrosis. Poor renal function, dilatation of pelvicalyceal system due to ureteropelvic junction stricture or focal dilatation due to infundibular stenosis can be seen. Cavitation / Cicatization may lead to calyceal or renal pelvic traction. C.T. may reveal renal calcification, calculi, scarring, hydronephrosis or evidence of extra renal disease. Culture of three morning specimens is about 90% diagnostic. Renal function is usually preserved except in tuberculous interstitial nephritis. End result may be autonephrectomy. Surgery may be reserved for persistant flank pain or hypertension[10]. Similar lesions can be found in acute focal bacterial nephritis, xanthogranulomatous pyelonephritis or with small benign and malignant lesions. Renal assessment is best achieved with I.V.U, U/S, C.T. or MR imaging[25]. Urethral or urinary bladder tuberculosis also seen with reduced bladder capacity. Calcified tuberculous cystitis may be differentiated from schistosomiasis, cyclophosphamide therapy, radiation induced changes and calcified urinary bladder carcinoma.

Male Genital Tuberculosis: May involved prostate, seminal vesicles, epididymis and testes. No specific radiological feature however MR may show diffuse, radiating, streaky areas of low signal intensity in prostatic T.B. (Water melon skin sign) on T_2 W images So diagnosis is usually made by biopsy / surgery.

Female genital tuberculosis: may involve fallopian tubes (94%), spreading to peritoneum, endometrium, ovaries, cervix and vagina. Response to chemotherapy is excellent for all form of genital tuberculosis. Surgery is necessary for large tubo ovarian abscesses.

Figure No. 7: Pleural Tuberculosis: C.T. chest, lung window revealed large loculated collection in right hemi thorax with pleural thickening and mass effect on right lower lobe. Otherwise normal both lungs.



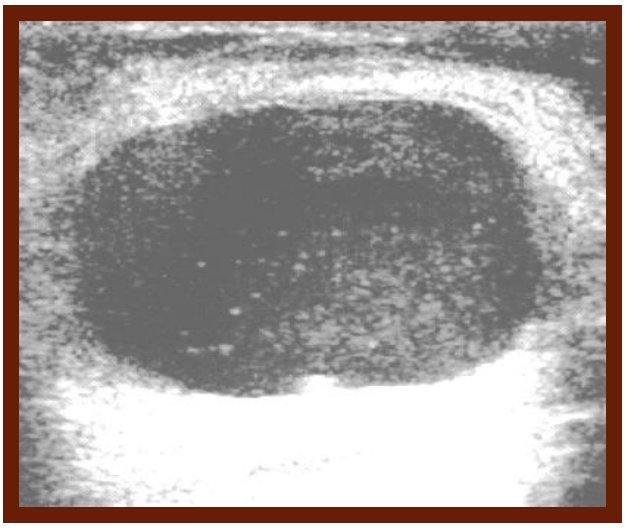
6. Pleural Tuberculosis:

More common in Eastern provinces and in non Saudi patients (only 34% Saudi patients). Usually presented with pleural effusion and diagnosed by pleural biopsy and pleural fluid analysis. On C.T. pleural effusion with non specific pleural enhancement and mild thickening is seen.

7. Breast Tuberculosis:

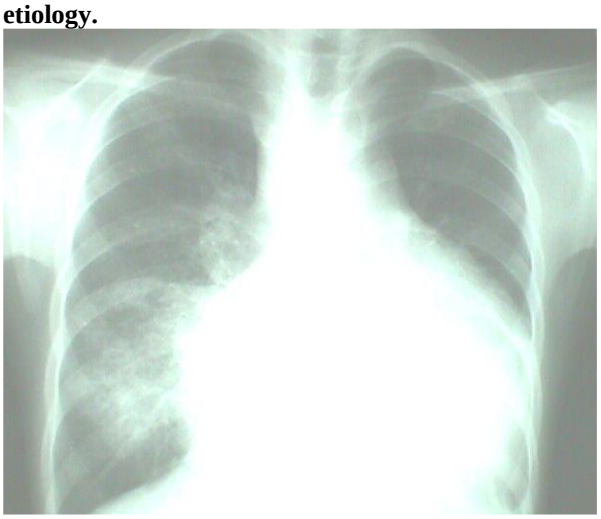
Is extremely rare, young, multiparous, lactating women are commonly affected. U/S reveals complex cyst / mass with sinus and abscess formation. Minimal debris and tiny calcification are pathognomonic (Figure No.8). Mammography is non specific.On MRI, parenchymal asymmetry with enhancement, microabscesses and peripherally enhanced mass can be seen.

Figure No. 8: Breast tuberculosis: 35 years female, a well defined, thick walled hypoechoic lesion with debris, peripheral tiny calcification and posterior acoustic enhancement.



8. Pericardial Tuberculosis:
Most common cause (80-85%) of constrictive pericarditis, though rare may be found in adolescent to young patients (Figure No. 9). In studies from Riyadh and Jeddah, it was found to be 3% and 1% of pericardial diseases respectively.
Other regions like parotids, pancreas and sternum have also been reported for tuberculous involvement.

Figure No. 9: Tuberculous Pericarditis: 13 years old male with right mediastinal distortion, lower lobe consolidation (non tuberculosis) and cardiomegaly. Aspiration cytology proved to be of tuberculosis etiology.



CONCLUSION

The clinical and radiological features of extra-pulmonary tuberculosis may clue to the diagnosis as many other diseases can mimic the imaging. So a high index of suspicion is required, especially in high risk population and some times in patients who are not responding to conventional antibiotic therapy. Routine laboratory investigations like ESR and tuberculin test may support the diagnosis. A positive culture, PCR, Deaminase test and histopathological analysis of biopsy specimen may still be required in many patients to yield the definitive diagnosis. Recognition and under standing of spectrum of imaging features of extrapulmonary tuberculosis can aid in diagnosis, especially with experience as some regional involvement may have classical imaging findings. Radiological imaging not only helps in diagnosis of the extrapulmonary disease, it can be used as follow up analysis with full confidence to see the progress of disease after proper chemotherapy. The patterns of extrapulmonary tuberculosis may vary due to extent of disease involvement otherwise inclination of region involvement is same everywhere. Extrapulmonary tuberculosis is relatively less in Saudi patients (from 1:2 to 1:3 depending upon regions) as compared to non Saudi patients.

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Original Article

Comparison of biochemical and ultrasonographic features in hirsute females with polycystic ovarian Syndrome and other causes of hirsutism

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ABSTRACT

Background: Polycystic ovarian syndrome is a heterogeneous disorder and one of the commonest endocrine disorders of women. One of its common presentations is hirsutism.

Objective: The aim of this study was to evaluate the biochemical and ultrasonographic features of PCOS in patients with hirsutism and to compare these features with other etiologies of hirsutism in our setup.

Study Design: Comparative study.

Place and Duration of Study: This study was conducted between 1st September 2007 to 31st December 2008 in the department of Obstetrics and Gynecology, Fauji Foundation Hospital Rawalpindi.

Materials and Methods: All the female patients who presented to gynae and dermatology clinics with hirsutism were included in the study. A detailed history, clinical examination with special reference to Ferriman-Gallwey scoring system, endocrinological workup and abdominopelvic ultrasonography (USG) was done in all patients. We divided the patients into two groups, one labeled as PCOS group (i.e. treatment group) and the other control group including idiopathic hirsutism and other etiologies. Data was analyzed using STATA 11. Multivariant test and logit model was used for statistical analysis.

Results: A total of 74 patients were included in the study, 44 had PCOS and 30 were in the control group with other etiologies of hirsutism.

Regarding the biochemical tests, only serum FSH, LH and progesterone levels showed statistically significant difference between the two groups (p-value ≤ 0.05). The comparison of ovarian volume (>10 ml) between the two groups was also statistically significant (i.e. p-value ≤ 0.05).

Conclusion: It was concluded that out of the long list of biochemical test for diagnosis of PCOS in hirsute females only serum FSH, LH and progesterone are statistically significant. Patients who present with hirsutism should be evaluated systematically and initial investigations must not include a long list of endocrine test. Abdominopelvic USG for polycystic ovaries has a definite role in diagnosis and must be done at initial visit.

Key Words: hirsutism, polycystic ovaries, polycystic ovarian syndrome..

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a heterogeneous disorder and is first described by Stein and Leventhal in 1935[1]. It is one of the commonest endocrine disorders of women[2] and a frequent cause of hirsutism[3]. It affects 5-10% of women of reproductive age[4].

The diagnosis of PCOS remains controversial. It is recognized that a uniform characteristic of PCOS is hyperandrogenism[5] detected either by clinical examination or laboratory analysis. Other features fundamental to diagnosis include ovulatory dysfunction and polycystic ovarian morphology detected by ultrasonography (USG). Features not included in diagnostic criteria but have been reported to be present in PCOS patients are obesity (in 30-60% of patients[6, 7]), insulin resistance and hyperinsulinism (present in 50-70%) [8, 9], and an LH: FSH ratio of >2 or 3 (in 30-50%) [10, 11].

PCOS is a diagnosis of exclusion and other etiologies causing hirsutism or ovulatory disorders are to be excluded.

We conducted this study to evaluate the biochemical and ultrasonographic features of PCOS in patients with hirsutism and to compare these features with other etiologies of hirsutism in our setup.

MATERIALS AND METHODS

It was a comparative study performed between 1st September 2007 to 31st December 2008 in the department of Obstetrics and Gynecology FFH Rawalpindi.

All the female patients who presented to gynae and dermatology clinics with chief complaint of hirsutism were enrolled for the study after informed consent. A

detailed history including the onset and progression of hirsutism, menstrual history, dietary history and family history of hirsutism was taken. Clinical examination included an assessment of amount, distribution and severity of hirsutism by Ferriman-Gallwey scoring system[12]. It is a quantitative method of measuring hair growth which allows for the determination of severity of hirsutism by assessing the extent of hair growth in nine key anatomical sites i.e. face (particularly moustache, beard and temple areas), chest, linea alba, inner thigh, external genitalia, inner surface of upper arm, upper back, lower back and buttocks. A score of 7-9 was considered to represent mild hirsutism, 10-14 as moderate hirsutism and 15 or more as severe hirsutism.

Height, weight and a calculation of body mass index (BMI) was obtained because many women with PCOS are obese (BMI>30kg/m2). Breast examination for galactorrhoea and abdominopelvic examination to detect mass lesion that may indicate an androgen secreting ovarian tumor was also done. Endocrinological work up included day 2 serum follicle stimulating hormone(FSH), luteinizing hormone(LH) levels, serum prolactin, testosterone, estradiol, mid luteal progesterone, fasting insulin, dehydroe-piandrosterone(DHEAS), 17-hydroxyprogesterone, and thyroid function tests. All these tests were done free of cost in our laboratory. Abdominopelvic USG was done for adrenal tumors, ovarian tumors and polycystic ovaries. A total of three visits were done for this workup. The detailed history, clinical examination and results of all investigations were recorded in proformas for analysis later on.

The data was analyzed and etiology of hirsutism was ascertained. After excluding other etiologies of hirsutism, we labeled our patients as having PCOS using the criteria proposed by European Society for Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM) in 2003[13,14]. According to this criterion two out of the following three must be present to label the patient as PCOS: 1) oligomenorrhoea and or anovulation, 2) hyperandrogenism (clinical or biochemical) and 3) polycystic ovaries on ultrasonography (USG). Criteria for labeling PCOS on USG was an ovarian volume of more than or equal to 10 ml[15]. Clinical features of PCOS included menstrual irregularity, obesity, hirsutism[16, 17], BMI[18] more than or equal to 30kg/m^2. Biochemical criteria was high serum LH level with normal or low FSH, elevated testosterone level [19] and insulin resistance, evidenced by raised fasting insulin levels [16]. The patients who had normal ovulatory function and androgen levels were labelled as idiopathic.

We divided the patients into two groups, one labeled as PCOS group and the other control group including idiopathic hirsutism and other etiologies. Data was analyzed using STATA 11. Multivariant test and logit model was used for statistical analysis. *P*- value less than 0.05 was considered statistically significant i.e. all the statistical tests are conducted at 5% level of significance.

RESULTS

A total of 74 patients were included in the study, 44 had PCOS and 30 were in the control group with other etiologies of hirsutism including idiopathic, late onset CAH, hyperprolactinemia and thyroid disorders. We analyzed that mean age (Table I) and FG scoring (Table No.2) showed a statistically significant difference between the two groups while mean BMI (Table No.1), although slightly raised in PCOS group, but difference was not statistically significant at any significance level.

Regarding the biochemical tests, only serum FSH, LH and progesterone levels showed statistically significant difference between the two groups (p-value ≤ 0.05).

Table No.1: Demographic Variables of PCOS and Control group

Demographic Variables	PCOS (n=44) Mean (range)	Control (n=30) Mean (range)	p-value
Age	22.0 (15-42)	25.0 (13-46)	0.01
Body Mass Index	25.8 (1.6-36.9)	25.4 (16.8-39.8)	0.738

Table No.2: FG Scoring of PCOS and Control group

	PCOS (n=44) Mean (range)	Control (n=30) Mean (range)	p-value
FG Scoring	17.6 (6-32)	17.0 (8-31)	0.03

Table No.3: Biochemical features in PCOS and Control group

Hormones	PCOS (n=44) Mean (range)	Control (n=30) Mean (range)	p value
FSH (IU/L)	4.1 (1.07-26.4)	4.2 (1.1-10.6)	0.038
LH (IU/L)	11.49 (1.9-44)	3.7 (0.7-10)	0.001
Prolactin(mIU/ml)	331 (91-856)	349 (120-1540)	0.224
Oestradiol(pg/ml)	99.1 (0.005-419)	137 (0.05-500)	0.752
Basal insulin	16.5 (0.75-143)	9.6 (3.0-42)	0.342
Testosterone(ng/ml)	1.36 (0.1-7.8)	1.5 (0.03-14.4)	0.32
DHEAS(ug/dl)	185.6 (3.7-403)	230 (40.1-530)	0.456
Progesterone(ng/ml)	4.8 (0.1-37)	6.9 (1.0-37)	0.006

When we analyzed the ultrasonographic features, in PCOS group 22.7% of the patients have both ovaries enlarged (volume > 10ml) while in 29.6% either right or left ovary was enlarged. So overall in 52.3% patients of treatment group at least one ovary was enlarged while this overall number was only 20% in the control group. In control group, both ovaries were enlarged in 3.3% and single ovary was enlarged in 16.7% of the patients. This difference was statistically significant (p-value ≤ 0.05).

Table No.4: Ovarian Volume of PCOS and Control group

Ovarian Volume	PCOS (n=44	Control (n=30)	p-value
>10 ml (both ovaries	22.7%	3.3%	< 0.05
>10 ml (single ovary)	29.6%	16.7%	

DISCUSSION

Polycystic ovarian morphology is considered fundamental to diagnosis of PCOS. We used ASRM/ESHRE criteria i.e. ovarian volume > $10ml^3$ to label the patient as PCOS. More than 50% of our patients had either single or both ovaries enlarged (>10 ml^3) in PCOS group while in the control group only 20% had this finding. The difference was statistically significant. Ovarian volume of > 10 ml in PCOS patients is also quoted in other studies[20].

A number of biochemical tests have been reported for diagnosis of PCOS. These include serum FSH, LH, testosterone, oestradiol, progesterone, prolactin, fasting insulin and sex hormone binding globulin. In our study only serum FSH, LH and progesterone were (statistically) significantly different between two groups at 5% level of significance. An elevated serum LH >10 IU/L in early to midfollicular phase of cycle is commonly seen in patients with PCOS and is always included in diagnostic criteria[21]. An Italian study also quoted significantly raised LH level in PCOS group as compared to control[22]. Anovulation which is commonly seen in PCOS patients is confirmed by serum progesterone (<30 nmol/l) [21]. Our results showed that PCOS group had significantly lower levels of progesterone than the control group suggesting chronic anovulation associated with PCOS.

Regarding the serum testosterone level if it is < 5nmol/l, the diagnosis of PCOS or idiopathic hirsutism is made otherwise; other etiologies of hyperandrogenism should be sought[23]. In our study, none of such causes were seen so the difference between two groups regarding this biochemical test was not statistically significant. Dehydroepiandrosterone (DHEAS) and sex-hormone binding globulin (SHBG) are not routinely recommended in patients with PCOS[24]. Our study failed to find any significant difference in levels of DHEAS and SHBG in the two groups. This might be explained by the fact that measurement of biochemical androgens in PCOS is limited by poor accuracy and reproducibility of assays, which are designed for significantly higher male androgen levels.

It is also noteworthy that despite the role of insulin resistance hypothesis in PCOS, serum insulin level is not included in diagnostic criteria of PCOS[25]. Fasting insulin levels were also not significantly raised in PCOS patients in our study. One reason for this might be that obesity exacerbates the underlying insulin resistance in patients with PCOS and in our treatment group significant obesity was not observed.

Hyperprolactinemia is seen in 17-43% patients with PCOS in different studies[26, 27]. We were also not able to find significantly raised levels of serum prolactin in our patients.

The mean age in the PCOS group was 22.045years (range 15-42 years) and in the control group was 25.067 (range 13-46 years). The difference was statistically significant (*p-value* = 0.01). The mean FG scoring in PCOS and control group was 17.6 and 17.03 respectively showing statistically significant difference (*p-value* = 0.03). A recent Mexican study also showed statistically significant difference in FG scoring in PCOS and control group[28]. This finding is explained by the fact that patients with PCOS present with greater degree of hyperandrogenism than patients without PCOS.

Obesity is not always associated with PCOS, only 40-50% of patients with PCOS are obese[29]. The mean BMI in the PCOS group was 25.8 (range, 16.2-36.9) and in the control group was 25.4 (range, 16.8-39.8) that was not statistically significant. A study conducted in Iran also showed no significant difference in BMI between PCOS and control group[30].

CONCLUSION

It was concluded that out of the list of biochemical test for diagnosis of PCOS in hirsute females only serum FSH, LH and progesterone are statistically significant. Patients who present with hirsutism should be evaluated systematically and initial investigations must not include a long list of endocrine test. Abdominopelvic USG for polycystic ovaries has a definite role in diagnosis and must be done at initial visit.

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Original Article

Streptokinase Study on ST Segment Resolution in Patients age Less Than 40 Years with Myocardial Infarction

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ABSTRACT

Background: Thrombolytic therapy for Acute Myocardial Infarction has been one of the most potent treatment ever developed for condition that kill more patients worldwide than any other.

Objective: To evaluate the benefit and efficacy or observational studies of streptokinase therapy on ST-segment elevation resolution in different types of myocardial infarction that focus especially on the younger age group less than forty years.

Study design: To observe the streptokinase therapy, in ST-segment elevation resolution, in age less than 40 years and in different types of myocardial infarction.

Place and Duration of Study: The study was conducted at national institute of cardiovascular diseases (NICVD) of Pakistan, Karachi.

Materials and Methods: All patients fulfilling the inclusion criteria for thrombolytic therapy were included. Baseline ECG recorded before streptokinase infusion and repeated at completion of infusion i.e. 90 minutes, day 1 and day 2.

Results: Streptokinase therapy on blood pressure, CKMB, and ST-segment resolution at 90 minutes, day 1, and Day2 in less than 40-year of age patient. The mean systolic blood pressure was 124$\pm$ 3.32 and 112$\pm$3.00 pre and post SK therapy reflecting a percentage decrease of 6.67 and highly significant ($P<0.001$). The Diastolic blood pressure was decrease to 6.25% with a mean value of 76.80$\pm$ 2.70 and 72$\pm$1.91 before and after the Streptokinase therapy's, segment resolution at 90 minutes was decreased to 52.01 percent from the baseline and continued to decrease at Day-1 and Day-2 with a percentage reduction of 70.65 and 83.69 % respectively. The P values were highly significant ($P<0.001$).

Conclusion: Thrombolysis improves survival when given within 12 hours of the onset of symptoms. The magnitude of benefit is greatest when reperfusion is established early. Age itself should not be considered a contraindication for fibronolysis

Key Words: Streptokinase, ECG, ST-Elevation, Myocardial infarction.

INTRODUCTION

Cardiovascular diseases (VCD) are the leading cause of death and disability in developed nations and are increasing rapidly in the developing world.

Coronary atherosclerosis is by far the most frequent cause of ischemic heart disease and plaque disruption with superimposed thrombosis is the main cause of acute coronary syndrome of unstable angina, myocardial infarction and sudden death[1, 2].The true frequency of atherosclerosis is difficult, if not possible to accurately determine because it is a predominantly asymptomatic condition. More advanced lesions begin to develop when individuals are aged approximately 25 years.

Plaque rupture is probably the most important mechanism underlying the unpredictable rapid progression of coronary lesions[3].The role of platelets in acute coronary syndromes begins with the exposure of the sub-endothelium after plaque rapture. Thrombosis develops on a plaque either because the plaque tear open (rupture) exposing the highly thrombogenic core to blood in arterial lumen [4].

ST-segment elevation is an excellent marker of acute coronary occlusion in which reperfusion therapy is needed. Patient with non ST elevation of myocardial infarction have a thrombotic stenosis in the affected artery but the artery is usually patent ,in contrast ST-elevation myocardial infarction the artery is occluded and at base line flow cannot be worsen, it can only improve [5].

The most frequently use electrocardiographic criteria for identifying acute myocardial infarction is ST-segment elevation where ST-segments are (re) emerging as a clinical tool of great importance. Evaluating the response to thrombolytic therapy that early resolution of ST-segment elevation is a useful mean of assessing perfusion [6].

Thrombolytic therapy is that early and sustained recanalization prevents cell death, reduces infarct size, preserves myocardial function, and reduces early and late mortality [7]

Purpose of study: The current evidences indicate that early thrombolytic therapy can limit extent of myocardial necrosis in evolving myocardial infarction may be early restoration of coronary blood flow, preserve left ventricular function and reduce mortality in patients with acute myocardial infarction (AMI)

Primary Objective: To observe the streptokinase therapy, in ST-segment elevation resolution, in age less than 40 years and in different types of myocardial infarction.

Secondary Objective: To observe the toxicity of streptokinase.

MATERIALS AND METHODS

The study was conducted in the Department of Pharmacology and therapeutics, Basic Medical Sciences Institute Jinnah Post-graduate Medical Centre in collaboration with National Institute of Cardiovascular diseases (NICVD) of Pakistan, Karachi. The study was approved by the postgraduate committee at NICVD. Informed consent for administration of thrombolytic drug was obtained from each patient.

Inclusion criteria: Less than 40 years.
Chest pain suggestive of myocardial infarction
ECG findings of ST-Segments elevations.

Exclusion Criteria: Active internal bleeding
Cerebro-vascular accident
Blood pressure>200/100 mmHg
Pregnancy
Allergic reaction to streptokinase
Previous Coronary Artery bypass Graft

Materials: Streptokinase (Streptofactor, Hakimsons/ Eskinase, Medinet), 1500000 units.
Sphygmomanometers, Cardiac monitor,
Electrocardiograph,

Methods:

Criteria of ST-segment resolution: A positive ST-marker was defined as a reduction in ST-segment elevation of more than 50% within 90 minutes after the start of thrombolytic therapy.

Treatment of Plan:

- All patients fulfilling the inclusion criteria for thrombolytic therapy were included and admitted to either coronary care unit or place in the ward with and continuously monitored for arrhythmias.
- Baseline 12 lead electrocardiogram was taken
- Two intravenous lines were maintained, one in each arm. One I/V line used for medication and another for collection of blood samples.
- Blood sample for complete blood count, erythrocyte sedimentation rate, urea creatinine, blood glucose, cardiac enzymes and lipid profile, activated partial thromboplatin time.
- Tablet aspirin 150 mg was given once for 24 hours.
- Isosorbide dinitrate I/V infusion 10-20 ug/min followed by oral nitrates
- Streptokinase 1.5 million units dissolved in 100 ml 5% dextrose water infused in 60 minutes.
- Vital signs 10 minutes during the infusion.
- The 12 lead electrocardiograms were recorded
- Baseline ECG recorded before streptokinase infusion and repeated at completion of infusion i.e. 90 minutes, day 1 and day 2.

RESULTS

During the four months study period 50 patients were included in the study after fulfilling the inclusion criteria for thrombolytic therapy.

Demography of patients with acute myocardial infarction exhibits that there were 46 (92%) males and 4 (8%) females, of these 50 patients 30 (60%) had an anterior wall infarction, while 20 (40%) suffered from an inferior wall infarction. No patient had a lateral wall acute myocardial infarction. Two patients died and cause of death was ventricular fibrillation in this patient.

Table-1 shows the effects of streptokinase therapy on blood pressure, CKMB, and ST-segment resolution at 90 minutes, day-1, and Day-2 in less than 40-year of age patient. The mean systolic blood pressure was 124$\pm$ 3.32 and 112$\pm$3.00 pre and post SK therapy reflecting a percentage decrease of 6.67 and high significant ($P<0.001$). The Diastolic blood pressure was decrease to 6.25% with a mean value of 76.80$\pm$ 2.70 and 72$\pm$1.91 before and after the Streptokinsae therapy. ST-segment resolution at 90 minutes was decreased to 52.01 percent from the baseline and continued to decrease at Day-1 and Day-2 with a percentage reduction of 70.65 and 83.69 % respectively. The P values were highly significant ($P<0.001$).

Table-2 shows the effects of Streptokinase therapy according to the site of Myocardial Infarction in less than 40-years of age. There were 30 patients out of 50 with anterior wall Myocardial Infarction. The mean value of Systolic Blood Pressure (SBP) before therapy was 120.67$\pm$ 4.08 and was decreased to 108.67$\pm$3.22 after therapy with Streptokinase. The Diastolic Blood Pressure (DBP) was decreased to 4.47 percent post Streptokinase therapy. The ST segment shows a resolution of 51.6% 72.3% and 83.07% at 90 minutes, day-1 and day-2 respectively. The P value for SBP, DBP and ST-segment resolution was highly significant ($P<0.001$).

Table-3 includes patients with inferior wall infarction in less than 40-years. Twenty patients present with this type of infarction. Two patients died because of

ventricular fibrillation within one hour of infusion. There was highly significant value of for SBP, DBP and ST-segment resolution. The mean Systolic Blood Pressure value was 129.00 ±5.47 before therapy and decrease to 117.00± 5.59 post Streptokinase therapy which shows a percentage decrease of 9.30.

Table No.1: Myocardial infarction patients of less than 40-years of age Percentage changes from Pre to Post Streptokinase therapy

Variables	No of observation	(Mean ± SEM) Pre SK Therapy	(Mean ± SEM) Post SK Therapy	% change Pre to Post	p-Value
SBP (mmHg)	48	124.00 ± 3.32	112.00 ± 3.00	(-) 9.67	0.001***
DBP (mmHg)	48	76.80 ± 2.70	72.00 ± 1.91	(-) 6.25	0.001***
CKMB (IU)	48	52.64 ± 2.49	150.52 ± 6.69	185.94	0.001***
ST Resolution 90 min	48	1.92 ± 0.15	0.92 ± 0.20	(-) 52.01	0.001***
ST Resolution day 1	48	1.92 ± 0.15	0.56 ± 0.08	(-) 70.65	0.001***
ST Resolution day 2	48	1.92 ± 0.15	0.31 ± 0.08	(-) 83.69	0.001***

Pharmacological action of Streptokinase therapy on blood pressure, CKMB and ST-Segment elevation resolution
*** Highly Significant
(-) Shows decrease from pre to post streptokinase therapy

Table No.2: The effects of Streptokinase therapy according to the site of Anterior wall Myocardial Infarction in >40 year of age

There were 30 patients out of 50 with anterior wall MI.

Variables	No of observation	(Mean ± SEM) Pre SK Therapy	(Mean ± SEM) Post SK Therapy	% change Pre to Post	p-Value
SBP (mmHg)	30	120.67 ± 4.08	108.67 ± 3.22	(-) 9.94	0.001 ***
DBP (mmHg)	30	74.67 ± 1.65	71.33 ± 1.92	(-) 4.47	0.001 ***
CKMB (IU)	30	52.13 ± 2.90	152.6 ± 9.00	192.86	0.001 ***
ST Resolution 90 min	30	2.17 ± 0.19	1.05 ± 0.29	(-) 51.6	0.001 ***
ST Resolution day 1	30	2.17 ± 0.19	0.60 ± 0.01	(-) 72.3	0.001 ***
ST Resolution day 2	30	2.17 ± 0.19	0.37 ± 0.11	(-) 83.07	0.001 ***

Pharmacological action of Streptokinase therapy on blood pressure, CKMB and ST-Segment elevation resolution
*** Highly Significant
(-) Shows decrease from pre to post streptokinase therapy.

Table No.3: The effects of Streptokinase therapy according to the site of Inferior wall Myocardial Infarction in >40 year of age

There were 20 patients out of 50 with inferior wall MI.
Two patients died because of ventricular fibrillation within one hour of infusion

Variables	No of observation	(Mean ± SEM) Pre SK Therapy	(Mean ± SEM) Post SK Therapy	% change Pre to Post	p-Value
SBP (mmHg)	18	129.00 ± 5.47	117.67 ± 5.59	(-) 9.30	0.001 ***
DBP (mmHg)	18	80.00 ± 3.33	73.00 ± 3.96	(-) 8.75	0.001 ***
CKMB (IU)	18	53.40 ± 4.64	147.30 ± 11.52	175.84	0.001 ***
ST Resolution 90 min	18	1.50 ± 0.17	0.59 ± 0.12	(-) 60.44	0.001 ***
ST Resolution day 1	18	1.50 ± 0.17	0.50 ± 0.14	(-) 66.66	0.001 ***
ST Resolution day 2	18	1.50 ± 0.17	0.22 ± 0.09	(-) 85.18	0.001 ***

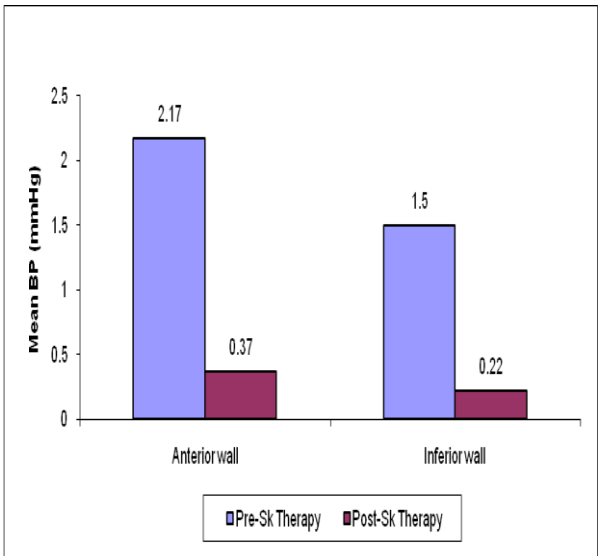
Pharmacological action of Streptokinase therapy on blood pressure, CKMB and ST-Segment elevation resolution
*** Highly Significant
(-) Shows decrease from pre to post streptokinase therapy

Table No.4: Duration of chest pain, Cholesterol, Random blood sugar and duration of patients stay at hospital

Group		Duration Chest Pain	Cholesterol	RBS	Hospital stay
		Hours	(mg/dl)	(mg/dl)	Days
Less than 40 years	n	50	50	50	48
	Mean ± SEM	4.56±0.54	218.84±8.67	132.16±13.82	5.29±0.47
	Range	2-12	132-290	59-392	4-15

Figure No.1:

	Pre-SK Therapy	Post-SK Therapy
Anterior wall	2.17	0.37
Inferior wall	1.5	0.22



ST- Resolution according to site of myocardial infarction in less than 40 years age Patients

The Diastolic Blood Pressure showed a percentage decrease of 8.75. The ST elevation before therapy was 1.50± 0.17, which was resolved to 0.59± 0.12, 0.50 ± 0.14 and 0.22± 0.09 at 90-minutes, day-1 and day-2, showing a percentage decrease of 60.44, 66.66 and 85.18 respectively. The P value was also highly significant (P<0.001).

Table-3 shows the comparative percentage change in the <40 age according to the site if myocardial Infarction group with anterior wall infarction there was a percentage change of 9.94, 4.47, 72.3 and 83.07 of SBP, DBP and ST-segment resolution at 90 minutes, day1, and day2, as compared to a percentage decrease of 9.30, 8.75, 60.4, 66.6, and 85.18 in patients with inferior wall myocardial Infarction

Table-4 shows the mean value of other variables in the less than 40 years age patient. The mean duration of chest pain was 4.56± 0.54 hours. The minimum chest pain duration was 2 hours and maximum it was 12 hour. The mean stay at hospitals was at hospital was 5.29 ± 0.47from a period of 5-days to 15-days.

The complications of Streptokinase therapy in less than 40 years age patients was, that out of 50 patients two died because of ventricular fibrillation, which could have been due to reperfusion arrhythmias or the arrhythmias as a normal cardiac event in Myocardial Infarction.

DISCUSSION

The best reperfusion treatment is one that achieves the highest rate of early, complete, and sustained infract-related artery patency in the largest number of patients, but with the lowest rate of undesirable effects.

Emergency management of acute myocardial infarction is evolving at an extremely rapid pace. What nearly all mortality reducing strategies have in common is, prompt restoration of blood flow to ischemic myocardium that has been compromised by intra-coronary thrombosis. Three clinical criteria have been proposed as markers for myocardial perfusion is reduction of chest discomfort (pain), improvement of electrocardiographic ST-segment elevation, and reperfusion arrhythmias. These clinical signs have been shown to be related to coronary artery recanalization and prognosis. Resolution of chest pain is very subjective and may frequently be related to analgesic medicine, cardiac arrhythmia could be a part of arrhythmias complicating acute myocardial infarction Resolution of ST-segment elevation has been shown to be a simple and useful predictor of final infarct size, left ventricular function and clinical outcome after thrombolytic therapy.

Though the use of thrombolytic therapy decrease with increased age, but should not be considered a contraindication [8]. This study was conducted to observe the efficacy and complication of streptokinase therapy in young less than 40 years age patient.

The results of the present study suggest that streptokinase is effective and reduces the percentage resolution of ST-segment elevation. It is also suggested this therapy should be offered to all patients presenting with ST-segment elevation of acute myocardial infarction.

Our study matches with the study of Laurie.A.Otto [9] which provided careful and detailed analysis of trial with specific regard to beneficial-to risk ratio for patients.

Our study matches with the GISSI-study [10] in hospital mortality was 2 to 9 percent for patients 61 to 70 years old as compared with younger patients. In our study the in hospital mortality was 4 percent in patients younger than 40 years.

Present study has demonstrated rapid restoration of coronary blood flow in patients with evolving myocardial infarction. Our study matches with the study of Schroder R[11] .who performed short term infusion of streptokinase in 93 patients within six hours after the onset of acute myocardial infarction.

Our study matches with Fibrinolytic Therapy Trials Collaborative (FTT) group study[12]. The data of the study do not provide evidence from withholding fibrinolytic therapy from patients on the basis of age. The excess of death in this study on day 0 to 1 increased with age but so did the reduction in death during days 2 to 35. The absolute mortality reduction seems much the same among younger and older patients. We do have early death in our study, two patients died within twelve hours of the start of therapy, whereas the patients discharged continue to do well

Our study did match with the study of Thiemann et al [13]. This study reported an analysis of 7864 patients treated with thrombolytic therapy. After thrombolysis there was survival benefit in younger patients. The complications rates were up to 16 percent in old age but were of minor nature.

CONCLUSION

The present study has demonstrated rapid restoration of coronary blood flow in patients with evolving myocardial infarction. Although intra-coronary application may be somewhat more effective, the advantage of intravenous administration is striking.

Considering the experience of others we concluded that I/V short term infusion of streptokinase can be performed safely in patients with evolving myocardial infarction.

One limitation of the administration of an intravenous infusion of streptokinase is that it can cause a significant fall in systemic blood pressure and rapid infusion of high dose intravenous streptokinase frequently causes transient and sometimes severe fall in blood pressure, the magnitude of which is directly related to the rate of infusion of streptokinase.

The clinical results are encouraging. Yet, to ascertain the true impact on short and long term morbidity and mortality from acute myocardial infarction.

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Original Article

Effect of Decoction of Camellia Sinensis on Blood Pressure and Heart Rate

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ABSTRACT

Objective: Camellia sinensis as a tea (hot decoction) is so widely used throughout the Asia. Therefore to find out, their effects on all the body functions are the need of hour. In the current study the effect of Camellia sinensis on human (females) blood pressure has been evaluated.

Study Design: Observational study.

Place of Study: This study was conducted at Pharmacy Department, University of Malakand.

Materials and Methods: The blood pressure before and after giving the decoction of Camellia sinensis to seventy six individuals was evaluated by using sphygmomanometer and stethoscope.

Results: A moderate increase in the blood pressure had been noted. Also a great decrease in the heart rate of individuals has been identified after taking the decoction.

Conclusion: From the current study it can be concluded that green tea have an effect of increasing blood pressure in the females, so the heart patients have to take care while using green tea in excess quantity.

Key words*:* Camellia sinensis, Decoction, Blood pressure, Heart rate

INTRODUCTION

Nature has been a source of medicinal agents and a large number of drugs are isolated from natural sources. Medicinal plants have a great value in the field of health. From the very past the use of herbal medicine have been very important, and fulfills the primary health care needs of about 80% of the world population[1].

The leaves of Camellia sinensis is used as green tea, which have undergone minimal oxidation during processing. Green tea originates from China[2] and has become associated with many cultures in Asia. According to a survey released by the United States Department of Agriculture in 2007[3], the mean content of flavonoids in a cup of green tea is higher than that in the same volume of other food and drink items that are traditionally considered of health contributing nature, including fresh fruits, vegetable juices or wine. Flavonoids are a group of phytochemicals in most plant products that are responsible for such health effects as anti-oxidative and anticarcinogenic functions[3].

Green tea contains salubrious polyphenols, particularly catechins, the most abundant of which isepigallocatechin gallate, carotenoids, tocopherols, ascorbic acid (vitamin C) minerals such as chromium, manganese, selenium or zinc, and certain phytochemical compounds. It is a more potent antioxidant than black tea[4]. Types of tea are commonly graded depending on the quality, parts of the plant used and how they are processed[5]. After water, tea is the most widely consumed beverage in the world[6]. In a study of the eating habits of 2,018 women, consumption of mushrooms and green tea was linked to a 90% lower occurrence of breast cancer[7]. The green tea extract may play a role in the control of body composition via sympathetic activation of thermogenesis, fat oxidation, or both[8]. It has also been presented that epigallocatechin-3-gallate (a component of green tea) can be used in prevention or treatment of inflammatory processes[9]. However, pharmacological and toxicological evidence does indicate that green tea polyphenols can in fact cause oxidative stress and liver toxicity[10]. Other evidence presented in the review cautions against the drinking of green tea by pregnant women[11].It "suggested that the oral intake of L-Theanine (a chemical found in green tea) could cause anti-stress effects via the inhibition of cortical neuron excitation[12]. Daily consumption of tea containing 690 mg catechins for 12 wk reduced body fat, may be useful in obesity[13]. Green tea also has a role in the treatment and prevention of cancer[14] and to treat multiple sclerosis[15].

As Camellia sinensis is mostly used as a tea in the form of hot decoction, throughout the Asia. Therefore the current study was designed with a view to confirm and explore the effects of green tea on the blood pressure according to gender. Whether it is beneficial for high

blood pressure in females or it may lead to high blood pressure, to stop drinking by volunteers' have routine high blood pressure.

MATERIALS AND METHODS

Plant Material

The fresh dried and processed leaves of Camellia sinensis plant were purchased from local market Abbottabad, Pakistan. The specimen pack, marked with a number 1320 has been deposited in Pharmacy Museum, University of Malakand Pakistan.

Preparation of Decoction

Each sachet contained 02 grams of dried plant material were soaked in each cup of 150ml boiling water for three minutes. 10 grams of sugar were added as a sweetening agent to each cup.

Experimental protocol

The basis for this investigation was blood pressure and heart rate of 3rd year students of Frontier medical College Abbottabad Pakistan. Subjects were selected on the basis of four primary criteria. These include age, sex, health and Physical body status. The research specifically targets individuals between 21 and 23 years of age. Seventy six female students, who fulfilled the above criteria, were selected for the study. They were first provided a thorough explanation of the research effort, its benefits and the potential risks to subjects.

Blood pressure and heart rate were noted in all the volunteers by using aneroid sphygmomanometer with stethoscope before and after the drinking of one cup of decoction. I.e. Before, at 0min and after 30 &60 minutes of taking the decoction. Cumulative results were calculated by using formula;

Cumulative (systolic/ diastolic/ Heart rate) =

$$\frac{Sum\ of\ all\ systolic\ /\ diastolic\ /\ heart\ rate}{total\ number\ (76)}$$

RESULTS

A total seventy six individual were selected in the current study, and a cumulative result was shown in table 1.

Table.No.1: cumulative result of eighteen female subjects for B.P & HR

Sex	Timing	Systolic Blood Pressure	Diastolic Blood Pressure	Heart Rate
Female	Initial Reading	105 mmHg	68 mmHg	75/min
	After 30 minutes	107 mmHg	69 mmHg	71/min
	After 60 minutes	114 mmHg	72 mmHg	60/min

A decrease in the heart rate was observed as; in the first half hour a little decrease in the heart rate had been noted, while in the next half hour a great decrease in the heart rate had been observed. From this it has been confirmed that Camellia sinensis has a strong effect on heart rate, i.e. it decreases the heart rate in normotensive female individuals. It was also noted a little increase in the systolic blood pressure in the first half hour which further increased in the next half hour. As far as the diastolic blood pressure is concerned, the decoction of Camellia sinensis was found to have a little increase in the diastolic blood pressure too.

DISCUSSION

The current study reveals that, drinking of Green tea by the females individuals may have a high risk of increase blood pressure. For each heartbeat, BP varies between systolic and diastolic pressures. Systolic pressure is peak pressure in the arteries, which occurs near the end of the cardiac cycle, when the ventricles are contracting. Diastolic pressure is minimum pressure in the arteries, which occurs near the beginning of the cardiac cycle when the ventricles are filled with blood. An example of normal measured values for a resting, healthy adult human is 120 mmHg systolic and 80 mmHg diastolic.

As Hodgson et al[16] reported that drinking of green tea leads to acute increase in systolic and diastolic blood pressure at 30 min after drinking. Same result was noted in the current study, but no significant increase were noted at 30 minutes but after 60 minutes more significant increase in the systolic blood pressure were recorded. And also a notable increase in the diastolic blood pressure was confirmed, may be dependant on gender.

Seifert et al[17] reported that, Green tea extract in a short-term dosing schedule similar to that commonly used with dietary supplements did not result in alterations in heart rate or blood pressure, while in the current study it was found that each cup of green tea have a significant increase in systolic and minor increase in diastolic blood pressure. Also a great fall in heart rate had been noted i.e. from 75 heart beat to 60 heart beat. So it is recommended for heart patients to take care of drinking green tea.

There is some evidence suggesting that regular green tea drinkers have lower chances of heart disease[18] and of developing certain types of cancer[19]. Although green tea does not raise the metabolic rate enough to produce immediate weight loss, a green tea extract containing polyphenols and caffeine has been shown to induce thermo genesis and stimulate fat oxidation, boosting the metabolic rate 4% without increasing the heart rate[8]. Same was the finding that it couldn't increase heart rate but we can say that it decreases the heart rate.

CONCLUSION

From the current study it can be concluded that, Green tea have an effect of increasing blood pressure in the females, so the heart patients who have proven to high blood pressure must, have to take care while using green tea in excess quantity.

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Original Article

The Impact of Renal Lower Pole Radiographic Anatomy on the clearance of Stone fragments after Extracorporeal Shock wave Lithotripsy

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ABSTRACT

Objectives: 1. To determine the frequency of clearance of stone fragments after extracorporeal shock wave lithotripsy (ESWL) for isolated lower pole renal calculi. **2**. To compare the average Lower Infundibular diameter and lower infundibulo-pelvic angle (L-IPA) between patients with residual stone fragments and those who become stone free after extracorporeal lithotripsy (ESWL) for isolated lower pole renal calculi.

Study design: Descriptive Study.

Place and Duration of Study: This study was conducted at Department of Urology, Liaquat National Postgraduate Medical Centre, Karachi from June 2006 to June 2010.

Materials and Methods: One Hundred patients of either sex, aged > 14 years with isolated lower pole calculi (LPC) of <20mm undergoing ESWL were included in the study, while patients with lower pole calculi > 20mm, multiple renal calculi, congenitally distorted pelvi-calyceal anatomy, with concomitant Ureteric calculi, with decreased urine output due to renal insufficiency, with Hydronephrosis, with previous pyelo-uretral surgery, who required ancillary procedures e.g. Ureteroscopy, DJ Stent insertion were excluded from the study. The confirmation of stone in lower pole and LPC anatomy (width of the infundibulum and lower infundibulo-pelvic angle) were viewed on the IVU. The Infundibular width was measured as the narrowest point of the infundibulum. The L-IPA was determined in two axes, the ureteropelvic axis and the infundibulo-pelvic axis.

Results: Frequency of clearance of stone fragments after ESWL for lower pole renal calculi was 82%. Average L-IPA was significantly higher in those who become stone free after ESWL than patients with residual stone fragments (79.34 ± 8.33 vs. 64.56 ± 5.53, $p<0.001$). Average Lower Infundibular diameter was slightly higher in stone free patients after ESWL but not statistically significant (5.02 ± 0.76 vs. 4.89 ± 0.78, $p=0.631$).

Conclusion: Successful ESWL is sensitive to lower pole anatomical variables especially lower Infundibulo-pelvic angle and preferably first line treatment in patient with a lower pole stone has L-IPA >80 degrees and lower infundibular diameter of >5mm.

Key words: ESWL, Renal Calculi, Lower Infundibulo-pelvic angle.

INTRODUCTION

Renal stone disease is a significant and worldwide health problem. This disease affects about 8% to 15% of the population in Europe and North America.[1] Its prevalence is next to malaria and Schistosomiasis. Morbidity rate due to urinary calculi is 2% to 4%, which is similar to that of diabetes.[2] Pakistan is located within the geographical distribution of stone disease. Urolithiasis is the commonest urological problem in Pakistan. The effected populations mean age group in Pakistan is 40 years.[3] Most of stones are composed primarily of calcium oxalate or, less often, calcium phosphate [4]. Only available medical therapy for stones, which is non invasive, is chemotherapy for uric acid calculi. Alkalization of urine may dissolve and cure the stones. However, there is association of surgery with anesthesia, prolonged hospitalization, long incisions, significant blood loss, post operative pain, wound dehiscence, ugly scars and incisional hernias.

Open surgery has been replaced by effective outpatient treatment, which has revolutionized the management of stone disease.[5] Open surgery is still performed especially for large complicated staghorn calculi[6].

The management of Lower pole Calculi (LPC) has always been controversial. Prior to development of Endourology, open stone surgery was the only modality of treatment. Lower pole nephrectomy was common operative procedure performed for LPC in those days to remove poor functioning lower pole and potential

source of recurrent calculi. Since the introduction of ESWL and Percutaneous Nephrolithotomy (PNL), the management of LPC stones has changed.

There is a general consensus that the treatment of lower pole calyceal stones has a poor success rate with ESWL due to various factors, these include stone burden, type of lithotripter, LPC anatomy and body habitus[7]. The anatomy of lower pole of kidney is found to be the most important predictive factor in determining the clearance of fragments.

Various variables of the lower pole anatomical dimensions were proposed to have an affect on the outcome of ESWL. Amongst these variables important are the lower pole Infundibulo-pelvic angle and the Lower Infundibular width. There is other variables also e.g. Stone size, Infundibular length, Infundibular height and number of lower pole minor calyces and these were also analyzed in different studies. In different studies, Stone size is found to have a significant impact on the stone clearance, while there is controversy on the effects of other variables on the clearance.

This theory of anatomical variables of lower pole was initially given by Sampaio and Aragao in 1990, indicated that the stone clearance was greater in patients with a lower Infundibulo-pelvic angel of greater that 90 degrees and the lower Infundibular diameter more than 5 mm but their method did not strictly define which segment of the proximal ureter was used when measuring the angle.[8,9] Later on Elbansay et al[10] determined fixed landmarks for to ensure proper measurement of infundibulo-pelvic angle in IVU and described spatial anatomy of lower pole as a possible factor in stone clearance.

Observation in a Meta analysis by Lingmen[11] and other reports showed lower stone free rate of ESWL for LPC when compared to results of stones in other calyces.

The lower pole infundibulo-pelvic angle was the most significant factor followed by infundibular width in a study by Gupta et al. However, infundibular length was not a statistically significant factor in stone clearance in their study[12].

So by taking measurements of the lower infundibulo-pelvic angle as well as Infundibular width and length, several authors have concluded that an acute infundibulo-pelvic angle and a narrow infundibulum has negative influence on fragment clearance[13]. In other studies however, no such relationship has been demonstrated.[14]

It is less difficult for the lower pole calculi to pass in to the renal pelvis after ESWL in the presence of a wider lower infundibular diameter and wide angle. In the presence of these favorable anatomical factors, the stone fragments will be passed from lower pole by flow of urine as well as by change in the direction of gravity by change in position of the patient.

MATERIALS AND METHODS

Study design: Descriptive Study.

Place of Study: Department of Urology, Liaquat National Postgraduate Medical Centre, Karachi.

Duration of Study: June 2006 to June 2010.

Sample Size: Total 100 patients with isolated lower pole calculi will be included in study.

Sampling technique: Non-probability, convenience sampling.

Sample Selection:

Inclusion criteria: Patients of either sex, aged > 14years, with isolated lower pole calyceal calculi of up to 20mm size undergoing ESWL.

Exclusion criteria: Patients with lower pole calculi more than 20mm. Patients with multiple renal calculi, Distorted pelvi-calyceal anatomy congenitally, Patients with concomitant Ureteric calculi, Patients with decreased urine output due to Renal Insufficiency, Patients with Hydronephrosis, Patients with previous pyelo-ureteral surgery, Patients who required ancillary procedures e.g. Ureteroscopy, DJ Stent insertion.

Data Collection Procedure: Patients of either sex aged ≥ 14 years, with isolated lower polar calyceal calculi up to 20mm, from both indoor and OPD will be included in the study. The confirmation of stone in lower pole and LPC anatomy (width of the infundibulum and lower infundibulo-pelvic angle) will be viewed on the Intravenous Urograms (IVU)[15]. The Infundibular width will be measured as the narrowest point of the infundibulum. The lower infundibulo-pelvic angle will be determined in two axes, the ureteropelvic axis and the infundibulo-pelvic axis. Former is an axis connecting the central point of the pelvis opposite the margins of superior and inferior renal sinuses to the central point of ureter opposite the lower pole of the kidney. Latter is the central axis of the lower pole infundibulum. **(Figures No. 1, 2 & 3).**

The procedure of ESWL was explained to all patients and a written consent was taken from patient or his/her attendants. All patients underwent ESWL on Alpha Compact Dornier echo guided lithotripter. Post procedural follow up will be done after every 15 days by plain X-ray or/and ultrasound. All patients with radio-opaque stones will be followed with plain x-rays; ultrasound will be used for patients with radiolucent stones. After the follow-up period of three months, patients will be divided into two groups depending upon stone clearance status: Group I will consist of stone free patients (or with residual fragments up to 03mm) and Group II of those with residual fragments of more than 3mm. All the related variables like age, sex, stone size, lower infundibulo-pelvic angle, lower Infundibular diameter, will be recorded on Performa.

Statistical Analysis: Statistical analysis was preformed through SPSS version-11.0. Ratio (M: F) was computed to present gender distribution. Continuous response variables like age, stone size, lower Infundibulo-pelvic angle and lower infundibular diameter were presented

by Mean ± SD. Frequencies and percentages were computed to present qualitative response variables including co-morbid factors, presenting complaints, site of kidney ultrasound/ IVU, clearance of stone fragments after ESWL. Student's t-test (Unpaired) was applied to compare the average lower infundibular diameter and lower infundibulo-pelvic angle between patients with residual stone fragments and those who become stone free after ESWL.

Figure No. 1: Two axes in measurement of L-IPA

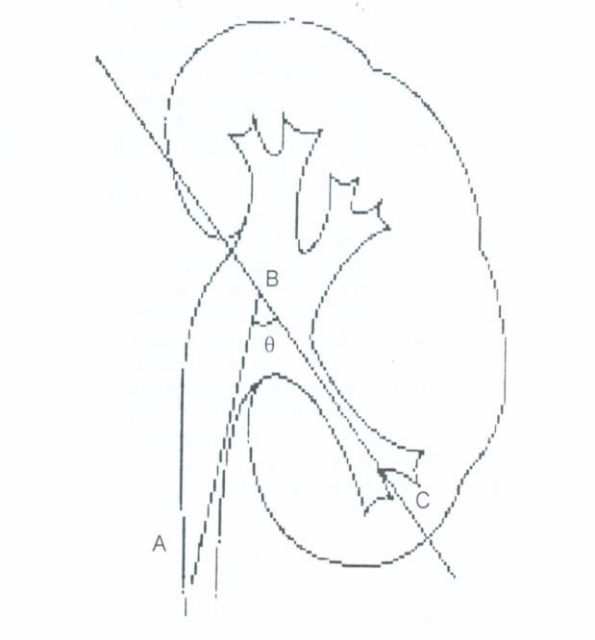


Figure No. 2: Lower Infundibular Diameter

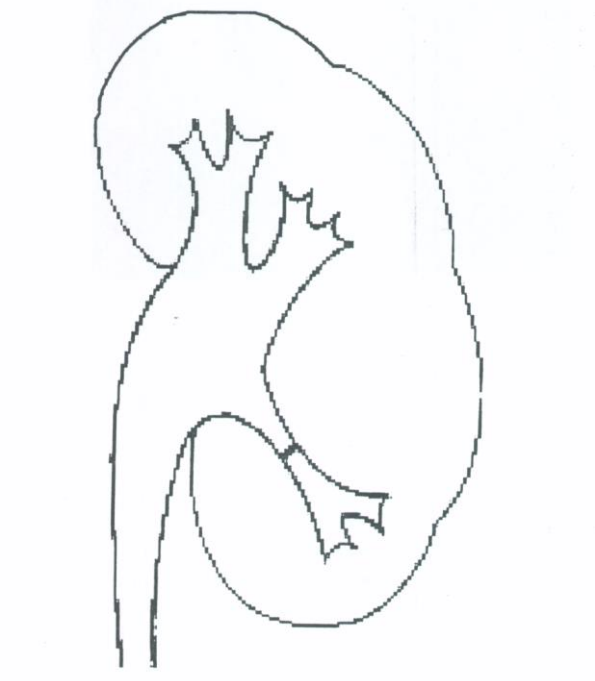


Figure No. 3: IVU measurement of L-IPA

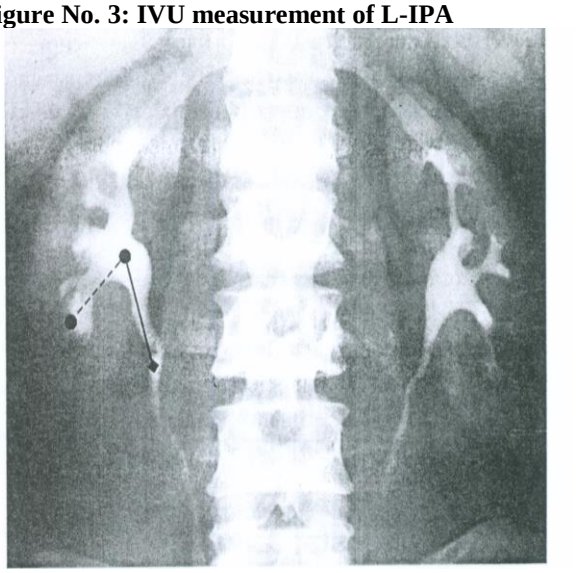


Figure No. 4: Gender distribution: n = 100 Male, Female = 1.8: 1

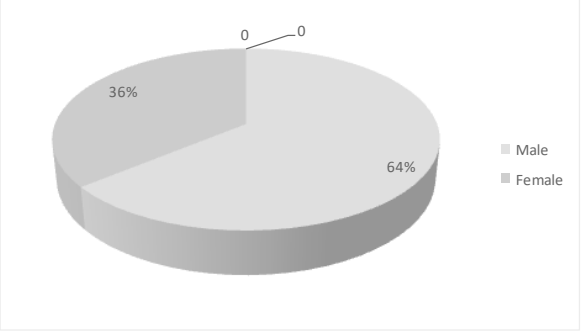
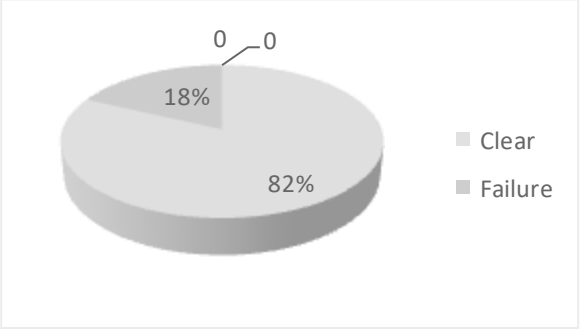


Figure No. 5: Frequency of clearance of stone fragments after Extracorporeal Shock wave Lithotripsy (ESWL) for isolated lower pole renal calculi: n = 100



RESULTS

Out of 100 patients of with isolated lower pole calculi, 64 (64%) were males and 36 (36%) females (M: F = 1.8: 1) as shown in Figure No. 4.

Average age of the patients was 40.46 ± 15.23 (ranging from 15 to 77) years. Fifty percent patients were old between 21 – 40 years.

Figure No. 6: Clearance of Stone fragments on different follow ups: n = 100

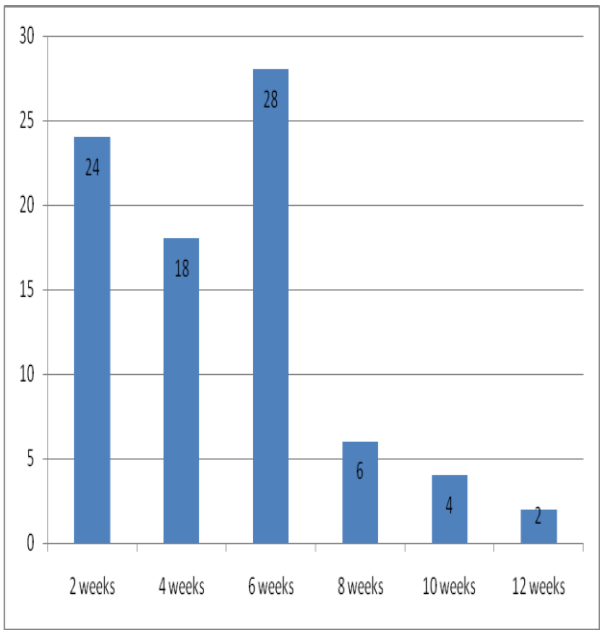
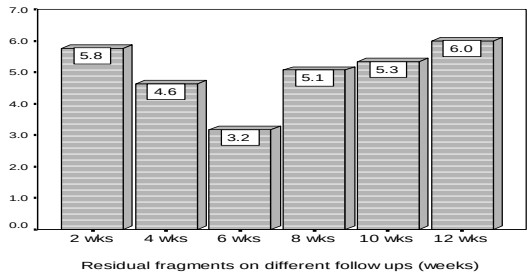


Figure No. 7: Clearance of residual fragments on different follow-ups: n = 100



Total 28 (28%) patients out of 100 were observed having co-morbids. Hypertension was the commonest co-morbid factor that was found in 14 (50%) patients, diabetes mellitus in 12 (42.9%), BPE in 6 (21.4%) and IHD was observed in only 2 (7.1%) patients. (Table No. 1.)

Table No. 1: Co-Morbid Factors: n = 14

Co-morbid factor^	Frequency	Percentage
Hypertension	14	50.0
Diabetes mellitus	12	42.9
BPE	6	21.4
Ischemic heart disease	2	7.1

^ 06 (21.4%) patients had more than one co-morbid factor

Pain was the commonest presenting complaint that was reported by 88 (88%) patients followed by headache in 4 (4%) patients. No complaint was reported by 8 patients. (Table No. 2)

Table No. 2: Presenting complaints: n = 100

Presenting complaint	Frequency
Pain	88%
Headache	4%
No complaint	8%

Ultrasound of right kidney and left kidney were done respectively in 40 (40%) patients and 42 (42%) patients while ultrasound was not done in 18 (18%) patients. Hydronephrosis was not found in any case on ultrasound. The mean stone size on ultrasound was 12.68±4.62. (Table No. 3)

Table No. 3: Ultrasound Findings: n = 100

Investigation	Number of pts
Ultrasound kidney ▪ Right ▪ Left ▪ Not done	 40 42 18
Hydronephrosis on ultrasound ▪ Yes ▪ No	 0 100
Stone size on U/S	12.68±4.62

IVU of right kidney was done in 25 patients and of left kidney also in 25 patients. Hydronephrosis was not found in any case on IVU. The mean stone size on IVU was 12.88±4.39. The mean lower Infundibulo-pelvic angle was 76.68±9.72 and the mean lower infundibular diameter 5.00±0.76. (Table No. 4).

Table No. 4: IVU Findings n= 100

Investigation	Number of patients
IVU kidney done ▪ Right ▪ Left	 50 50
Hydronephrosis on IVU ▪ Yes ▪ No	 0 100
Stone size on IVU	12.88±4.39
Lower Infundibulo-pelvic angle	76.68±9.72
Lower Infundibular diameter	5.00±0.76

Out of 100 patients, frequency of clearance of stone fragments after extracorporeal shock wave lithotripsy (ESWL) for isolated lower pole renal calculi was 82 (82%) while failure of stone fragments was observed in 18 (18%) patients. (Figure No. 5)

Frequency of clearance of stone fragments 2 weeks after ESWL was 24 (24%). Four weeks after ESWL,18 (18%) patients were observed with clearance of stone fragments. After 6 weeks of ESWL, 28 (28%) patients were observed with clearance of stone fragments. After 8 weeks of ESWL, 06 (6%) patients were observed with clearance of stone fragments. Later on, 04 (4%) patients after 10 weeks and 02 (2%) patient after 12 weeks of ESWL were observed stone free. (Figure No. 6)

Table No. 5: Comparison of the average Lower Infundibular Diameter and Lower Infundibulo-pelvic angle between patients with residual stone fragments and those who become stone free after Extracorporeal Lithotripsy (ESWL): n = 100

Variables	Clearance of stone		p-value
	Clearance n = 82	Failure n = 18	
Lower Infundibulo-pelvic angle	79.34 ± 8.33*	64.56 ± 5.53	<0.001
Lower infundibular diameter	5.02 ± 0.76	4.89 ± 0.78	0.631

Key: Values given in columns 2 & 3 are Mean ± SD

Mean residual fragments, two weeks after ESWL was 5.8 ± 3.9, four weeks after ESWL was 4.6 ± 2.9, six weeks after ESWL was 3.2 ± 3.3, eight weeks after ESWL was 5.1 ± 3.1, ten weeks after ESWL was 5.3 ± 3.03 and twelve weeks after ESWL the mean residual fragments was 6 ± 2.7. (Figure No. 7)

Average lower Infundibulo-pelvic angle was significantly higher in those who become stone free after ESWL than patients with residual stone fragments (79.34 ± 8.33 vs. 64.56 ± 5.53, p<0.001). Average lower infundibular diameter was slightly higher in those who become stone free after ESWL than patients with residual stone fragments but not statistically significant (5.02 ± 0.76 vs. 4.89 ± 0.78, p=0.631). (Table No. 5)

DISCUSSION

The principal finding of my study shows that the frequency of stone clearance from lower pole after ESWL was in 82 % of patients. The failure was in 18% of patients. The average L-IPA was significantly higher in those who become stone free than patients with residual stone fragments (79.34 ± 8.33 vs. 64.56 ± 5.53, p<0.001). Average lower infundibular diameter was slightly higher in those who become stone free after ESWL than patients with residual stone fragments but not statistically significant (5.02 ± 0.76 vs. 4.89 ± 0.78, p=0.631).

After the original idea of L-IPA in the resin cast of collecting system given by Sampaio and Aragao, Sabins et al subsequently applied this method to IVU but due to ill defined radiological landmarks, there results did not become reproducible.

Elbansay et al reported residual stones in 64% of the patients with an L-IPA of <90 degrees, lower infundibular width <5mm and lower Infundibular length >25mm; and only 12% in those with IPA of >90%, infundibular width of >5mm and lower Infundibular length of <25mm.

Keely et al [16] showed that if L-IPA is >100 degrees stone clearance rate was 66% while in <100 degrees it is 34%, concluding the significant effect of L-IPA.

In my study, I used the method of Elbansay et al because it depends on the fixed points and hence provides more consequent landmarks for measurement, easily reproducible and it holds valid for both intra-renal as well as extra-renal pelves. I found comparable results of stone clearance of 82 with average L-IPA of around 80 degrees and infundibular diameter of 5mm.

Gupta et al[17] demonstrated L-IPA of greater than 90 degrees was predictive of successful SWL, demonstrating 75% clearance rates compared with 23% for angles less than 90 degrees.

On the other hand some authors don't found a significant impact of L-IPA and infundibular diameter on stone clearance even after three months follow up[18].

Ather MH et al [19] did not find significant effect of L-IPA and infundibular width on the fragment clearance. They concluded that there may be increased shock wave requirement in patients with acute L-IPA and narrow infundibulum, but this was also not statistically significant.

In almost all studies, no demographic or gender distribution is described and in my study, majority were male patients between 21 to 40 years of age. No significant demographic impact on stone clearance was noted.

In my study I found the L-IPA, a significant variable in determining the outcome of ESWL while lower infundibular diameter does not. But because of small number of patients in this study it is difficult to obtain statistically significant results due to small variations in the measurements of lower pole anatomy especially the infundibular diameter. So a large sample study is recommended for more precise results.

The lower infundibulo-pelvic angle is one of the most important variables of lower pole anatomy that can predict the outcome of ESWL and in patients with L-IPA less than 80 degrees or calculi of more than 2cm, other treatment options should be considered e.g. PNL or Pyelolithotomy.

As far as other lower pole anatomical variables are concerned, the stone burden and lower infundibular length are found significant in different studies. In my study I found some short comings and difficulties e.g.:

- After each session of ESWL the follow up after two weeks was often missed by the patient side.
- While measuring the L-IPA and infundibular diameter, the exposure of IVU film should be nearly 100% because if the X-ray size is concise, as generally done to fit four exposures in one film, it is difficult to measure the variable especially the infundibular diameter. So I the radiologists are always required for a full film of 20 minutes

duration in IVU (or if sometimes it was not possible), I measured the variables directly from the monitor screen showing the full exposure.

- Now a day there is trend of un-enhanced CT KUB instead of IVU for the evaluation of Renal Calculi especially in patients with radiolucent calculi and Azotemia. So patients with LPC undergoing ESWL, in whom CT KUB was done, could not include in the study.

Some corporations that are providing medical facilities to their employees may not approve ESWL expenditure at our institute – offering them open surgical procedures.

CONCLUSION

Results of my study demonstrate that:

- The frequency of stone clearance was 82 % (41 patients), while failure was in 18 % (09 patients)
- Male predominance was observed.
- Higher average L-IPA was in stone free patients.

Insignificant difference in lower infundibular diameter in stone free and in patients with residual stones.

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Original Article

The Pattern of Ventricular Septal Defects and the Severity of Associated Pulmonary Hypertension in Our Set-Up

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ABSTRACT

Background*:* Ventricular Septal Defect (VSD) is commonest of all the congenital heart diseases. This is found as an isolated lesion as well as in association with other congenital cardiac lesions. The management and outcome of isolated VSD is not only dependent upon the size but also depends on the associated complications of ventricular septal defect (VSD). Pulmonary hypertension is not only the most common complication but also the most important indication of surgery in our setup.

Objectives*:* To study the pattern of various types of ventricular septal defects (VSDs) and assessment of severity of associated pulmonary hypertension in our population.

Study Design*:* Cross sectional descriptive study.

Patients and Methods: The study was conducted at the paediatric cardiology department of The Children Hospital & The Institute of Child Health Multan, from October 2009 to March 2011. All patients with ages between 1 day to 15 years presenting with isolated VSD during the study period were studied using 2-D, continuous wave Doppler and color Doppler transthoracic echocardiography.

Results: Out of 403 patients with isolated VSD, 288 were of perimembranous type (71.4%), 57 were of muscular type (14.2%), 19 were of doubly committed sub arterial (DCSA) type (4.7%) and 39 patients were having inlet VSD (9.7%). The mean age was 2.4 years. Females were 137 (34.0%) and males were 266 (66.0%). Pulmonary hypertension was present in 210 patients (52.1%). Amongst these mild pulmonary hypertension was present in 86 (40.9%), moderate in 65 (30.9%) and severe pulmonary hypertension was present in 59 (28.1%).

Conclusion: Perimembranous (PM) VSD is the commonest type of ventricular septal defect presenting to our hospital. The incidence of pulmonary hypertension is very high (52.1%) and even severe pulmonary hypertension was found in about a quarter of the patients. This shows the degree of delay in surgery and the major reason is non availability of pediatric cardiac surgery centers in government setups.

Key Words: Ventricular Septal Defect (VSD), pulmonary hypertension,

INTRODUCTION

Ventricular septal defect (VSD) is the most common congenital cardiac malformation[1]. VSD can be classified in many ways but the most popular and practical classification is dividing VSD's into perimembranous, muscular and doubly committed sub arterial (DCSA). It was described by Soto et al[2]. Perimembranous defects account for 80% of surgical and autopsy series. Muscular VSD's account for 5 – 20% of the defects and generally have a better prognosis[3]. They tend to close spontaneously earlier than perimembranous VSD[4]. Doubly committed sub arterial VSD's account for 5 – 7% of surgical and autopsy series but they are much more common in Asia, especially in Far East where incidence is about 29% [5].

Un operated VSD is associated with many complications. These include failure to thrive, repeated chest infections, development of pulmonary hypertension, prolapse of aortic valve cusps along with aortic regurgitation, right or left ventricular outflow tract obstruction, pulmonary vascular obstructive disease and even Eisenmenger syndrome. Pulmonary hypertension is of special consideration in our setup because it will develop in almost all the cases of moderate to large sized VSDs if left un operated. Furthermore, if it is severe then it may lead to pulmonary vascular obstructive disease and Eisenmenger syndrome and then the patient will be declared inoperable. Prolapse of aortic valve cusp is another important complication. It occurs mainly with doubly committed sub arterial and less commonly with perimembranous outlet type VSDs. The reported incidence varies between 0.7–5percent depending upon the type of age group studied. The prevalence of this complication increases with age but can occur before 6 year of age[6]. Aortic regurgitation can occur in these patients and varies in severity in different individuals. The anatomic and hemodynamic features in doubly committed sub arterial VSD have a great impact on the development of aortic valve leaflet deformity and subsequent aortic regurgitation[7]. Cusp deformity may

predict possible progressive deterioration of aortic regurgitation[8].

Perimembranous outlet VSDs are also associated with infundibular hypertrophy and right ventricular outflow tract obstruction can progress in severity and may lead to right ventricular hypertrophy[9].

The purpose of the present study was to identify the relative incidence of type of ventricular septal defect (VSD) in patients with isolated VSD and to assess the severity of associated pulmonary hypertension.

PATIENTS AND METHODS

This is a cross-sectional descriptive study conducted at pediatric cardiology department of Children Hospital Multan from October 2009 to March 2011. It included all isolated VSD cases seen during this period of one and a half years.

Inclusion Criteria:

A) All the patients with ages between 1 day and 15 years.
B) All the patients with isolated VSDs

Exclusion Criteria:

A) Patients with associated congenital cardiac defects other than VSD.
B) Post Op patients with pulmonary artery banding or VSD closure and residual shunt.

Toshiba Pnemio XG machine was used for echocardiography. All echocardiographic studies were performed by pediatric cardiologist experienced in echocardiography for congenital heart diseases. Transthoracic echocardiography was performed in all cases using 2D, continuous wave Doppler and color Doppler techniques. VSDs were classified as perimembranous, doubly committed sub arterial, muscular & inlet VSDs using Soto's classification[2]. Records of these selected patients were reviewed to assess the relative incidence of various types of VSD with special reference to pulmonary hypertension. Pulmonary hypertension was assessed by using CW and color Doppler by measuring tricuspid regurgitation and pulmonary regurgitation jets and by calculating the right ventricular pressure. Systemic blood pressure (LV pressure) was also taken at the same time. Severity was graded in three categories as mild moderate and severe.

Mild PH= RV pressure in between 1/3rd to 1/2 of systemic pressure

Moderate PH=RV pressure in between 1/2 to 2/3rd of systemic pressure

Severe PH= RV pressure more than 2/3rd of systemic pressure

Severity of aortic regurgitation was assessed by using parameters like left ventricular end–diastolic & systolic dimensions, Doppler flow velocity measurement[10] and assessment of length, width and area of regurgitant jet[11]. Sub pulmonary obstruction or any other complication was also noted. The severity of sub pulmonary obstruction was assessed by Doppler peak flow velocity measurement across right ventricular outflow tract[12].

RESULTS

1. Types of VSDs:

Out of 3754 patients who underwent echocardiography during the study period, 403 had isolated VSDs (10.7%). Females were 137 (34%) and males were 266 (66%). Of these 71.4% were perimembranous type, 14.2% were muscular type, 4.7% were DCSA type and 9.7% were inlet type.

Table No. I: Types of VSDs n = 403

Type	Subtype	Number	Percentage
PM VSD		288	71.4%
Muscular VSD		57	14.2%
	Apical	18	31%
	Mid	24	42%
	Upper	15	26%
DCSA		19	4.7%
Inlet		39	9.7%
Total		403	100%

Pulmonary Hypertension in VSD:

A total of 210 (52.7%) cases with pulmonary hypertension were seen. It was mainly associated with larger size defects. The mean age of these patients was 1.8 years. 101 were females and 109 were males.

Table No.2: Pulmonary Hypertension n = 210

Severity	Number	Percentage
Mild	86	40.9%
Moderate	65	30.9%
Severe	59	29.1%

DISCUSSION

VSD is the most common congenital cardiac malformation. Its fate not only depends upon the size of the VSD but also on its type. Larger VSDs tend to have more complications like failure to thrive, repeated chest infections, and development of pulmonary hypertension. Similarly DCSA VSDs and PM VSDs have less chances of spontaneous closure than the muscular VSDs. As regards the overall pattern of types of VSD's, the commonest type was of perimembranous VSD (71.4% cases of total VSD). The second in order of frequency were muscular VSD (14.2% of total VSD) and least frequent were DCSA type, which accounted for 4.7% of the total. These results were similar to those what is found in Western literature, where the largest group of VSD consists of PM type, followed by

muscular and DCSA type in decreasing order of frequency[6].

Locally very little work has been done on this aspect of the disease. In a study at NICVD, Karachi, Aziz et al found that PM VSD were 92% of total VSD, DCSA were 7% and the least common were muscular i.e. 1.7%[10]. Whereas, in Southeast Asian children the studies done on VSD types showed that DCSA was quite common reaching up to 29 to 30% of total VSDs[7]. Among the South Asian countries, there were very few studies done on the incidence of the types of congenital heart disease. In one study, done in Sri Lanka VSD was 27.5% of total congenital heart diseases[11]. In another study done in Lahore, Pakistan by Sadiq M. et al the incidence of VSD was 32% of all congenital heart diseases[12].

In our study, 52% of the patients had some degree of pulmonary hypertension. Amongst these 52% patients, 40.9% had mild, 30.9% had moderate and 28.1% had severe pulmonary hypertension. While overall incidence of severe pulmonary hypertension was found to be 14.6%. This is a very high percentage as compared to western studies where incidence of severe pulmonary hypertension in VSD cases is less than 5%[13]. Moreover 52% incidence of overall pulmonary hypertension is again a very high and alarming figure as compared to the studies done in South East Asia. In our study, incidence of pulmonary hypertension was very high even among the patients of less than I year of age. 11% of the patients presenting under I year of age had severe pulmonary hypertension while this incidence is found to be very low in study done by Levi DS et al[14].

To detect aortic valve prolapse is critical in patients with PM and DCSA VSDs because this complication may cause permanent aortic regurgitation[15]. In our study, 4.2% of the patients had aortic valve prolapse. Patients with clinically important aortic regurgitation or RVOT obstruction are candidates for surgery[16]. Early repair may prevent progression of aortic valve damage and regurgitation. Right ventricular outflow tract obstruction was found in 3 out of 288 patients with perimembranous type VSD of our study. Glenn et al found that 5.8% patients of VSD developed infundibular stenosis while AV prolapse was found in 3.6% of their patients[17].

All this shows that pulmonary hypertension is the most alarming complication of VSD in our setup. This is because of lack of freely available pediatric cardiac consultation facilities in Pakistan. Moreover delay in surgery even after the diagnosis and proper medical management is another important factor. This shows that how much it is necessary to develop new pediatric cardiac surgery centers in this country.

CONCLUSION

Amongst the types of VSDs, perimembranous VSD is the most common type and DCSA VSD is the least common type. The incidence of pulmonary hypertension is very high. This signifies that to develop new pediatric cardiac surgery centers in Pakistan is the need of the day. We need this because to have early VSD closure is the best way to avoid life threatening complication of pulmonary hypertension.

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Original Article

Attitude and Analysis of Using Computers by the Medical Students in Karachi

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ABSTRACT

Background: Computers provide the wealth of information and the means of communication, education and patient management. Although several studies in different countries have explored the extent to which health science students use the computer and the internet, a few researches are available on this subject in Pakistan, where the Internet culture is cultivating rapidly. Hence this study was conducted to assess the knowledge, skills, proficiency of using computers and browsing internet by the medical students and their implement of this knowledge in the medical field for the purpose of study and research.

Objectives: To assess the frequency and purposes of computer and subsequent internet usage among medical students.

Study Design: A Descriptive cross-sectional study.

Place and Duration of Study: This study was conducted during 1st.September – 1st.November 2008 amongst the Medical Students enrolled in public and private Medical Colleges of Karachi.

Materials and Methods: The sample size was 450. A well designed structured questionnaire was used to collect responses in a voluntarily and confidential manner.

Result: 91% medical students were computer literate. The main reason for lack of computer knowledge was lack of time and lack of access to a computer. 88% agreed that computer has revolutionized and better off the world. 93.3% use internet for research, chatting, health information and medical news, emails, music and entertainment.86.3% students use Google as the main search engine. 83.7% have used internet for the research purpose. 77% use internet for latest medical news. 68.5% students use it for the diagnosis, prognosis and treatment of diseases. Only 17% are the members of Medical Journals.

Conclusion: The medical students using computers have a positive attitude towards its use in the medical field, which not only has made a significant impact but also encourages them in study, research and keep them updated in this fast developing world. Use of computers enhances decision-making, management planning and medical research among the students.

Key words: Medical students, Karachi, computer, medical education. Internet users.

INTRODUCTION

In our fast developing world, the emerging need of computer knowledge has made an impact in every field, including the medical world. There is rampant use of computer technology in patient management, therapeutics, pharmaceutical products, education, conference and many other tenets of the health-care industry. It has a lower cost as compared to paper based dissemination of information and also has an added advantage of being available worldwide instantly on demand[1]. This makes it almost mandatory for the healthcare professionals to be well versed with this technology.

The internet, one of the important scientific developments of today, provides vast information in relation to diseases, therapeutic procedures and pharmaceutical products just within few clicks of mouse. Therefore, there is a need not only to equip medical fraternity with adequate skills in ICT but also to make internet facility available in institutions providing medical education and health care.[2]

In the last decade, advances in computer technology have occurred at a very rapid pace. These developments have impacted greatly on developments in medicine. A large amount of medical literature and information is now available electronically and even medical teaching is becoming electronically based in some developed countries. In resource poor settings, however, computer technology may not be widely utilized by medical students[3,4] because only limited courses for basic computer skills are taught to them. Students acquire their competence from sources outside the university. Therefore, ascertaining the opinions of students is necessary to correct deficiencies and address negative attitudes[5].

MATERIALS AND METHOD

This population- based cross-sectional study was carried out using disproportionate stratified sampling technique. The study was conducted in various medical colleges of Karachi including Dow medical college, Sindh medical college, Ziauddin Medical University &

Baqai Medical University. Only MBBS undergraduate students were covered in it. An initial validation survey was conducted on 25 medical students to test the questionnaires and the required changes were inducted in the questionnaire. The questionnaire was bereft of any technical details and was designed to be simple and easy to understand. The respondents were given a choice of answers and were only expected to mark the answers with a tick. The language used in the questionnaire was English and it was consist of 22 questions. Information was collected regarding age, sex, use of computer and internet service and basic knowledge of computer skills and programming. 450 forms were distributed among students with their verbal consent, out of which 416 forms were filled and given back in hand. Data was fed in SPSS version 10 and analysis was carried out using frequency chart and, pie chart and graph.

RESULTS

Total 450 forms were distributed among the students of Sindh Medical College, Dow Medical College, Baqai Medical College and Ziauddin Medical University. The (Figure 01) shows the graph of the students from each university. The response rate was 93%. Majority of the students were females (65%). Demographic data shows the mean age to be 22.5 years, ranging from 17 to 25 years. 91% students were computer literate. The rest 9% excused of having lack of time and interest or to have no access to use it. 68% students have access to computers at home while rest have been using it at library (26%), at acquaintances' s place (5%) and only 1% go to internet café. 50% medical students felt that working with computer gave them a lot of self-confidence. 88% agreed that computer has revolutionized and better off the world. 51% medical students felt that they would prefer spending evening with family and friends rather than working on computer. 94% students think computers are valuable and necessary for present era. 52% Students enjoy working on computer and believe that it has built lots of self-confidence in them. 70.7% students use computer whenever needed, while 12.3% students use it many times a day and 17% have used it hardly ever. The proficiency of using basic computer programmes has been evaluated in (Table No.01)

The use of internet among medical students is 93.3%. (Figure 02) indicates the main purposes of using internet. The most popular search engines among medical students are found to be Google (86.3%), followed by Yahoo (31.5%), Msn (30.3%), Wikipedia (20%), Others (5.8%). 83.7% have used internet for the research purpose. 77% use internet for latest medical news. 68.5% students use it for the diagnosis, prognosis and treatment of diseases. Around 58% students sometime in life have downloaded free medical books on internet.

Table No.1: Basic computer knowledge of medical students

Basic Computer Programs	Good (%)	Poor (%)	Average (%)
Keyboard Skills	56.3	7.0	36.8
MS Office	35.8	25.2	38.9
Power Point	43.8	22.1	34.1
Operating System	29.8	22.4	47.8
Setting database & management data	17.8	43.3	38.9
Online searching & downloading information	67.8	10.3	21.9
Installing software on computers	41.8	28.8	29.3
Troubleshooting problems	19	41.6	39.4

Figure No.1: The % of the Medical Students Participated in the Survey

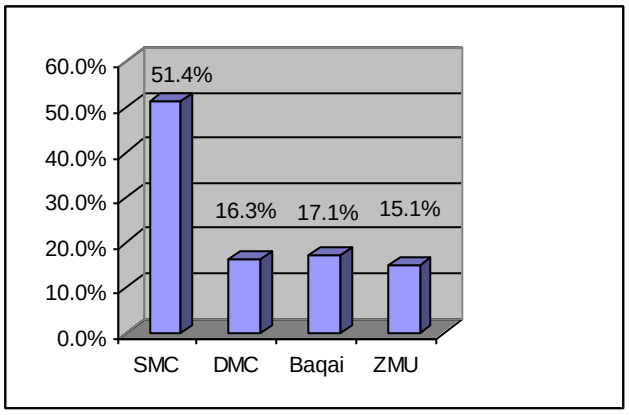
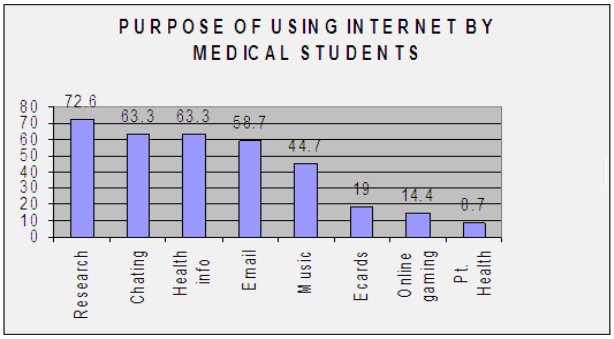


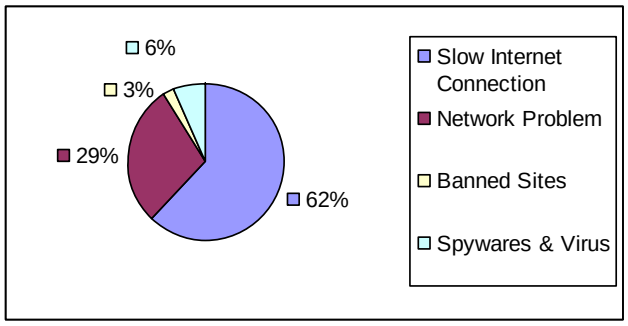
Figure No.2: Purpose of Using Internet By Medical Students in percentage



The major problems faced by the students while working on the internet is illustrated in (Figure 03). The percentage of the medical students who have done courses in computers is 24%. Others learned computer

by self-learning or using manuals. Only 17% students are member of Medical journals.

Figure No.3: The Problems Faced by Students while working on Computer



DISCUSSION

The aim of this study was to investigate the current knowledge, skills, and opinions of undergraduate medical students regarding use of computer and internet in a technology-savvy city, like Karachi, in Pakistan. 91% of the entire sample in this study was computer literate, and have fair competency in downloading, e-mail, browsing internet. Majority (93%) uses Internet regularly. A similar survey was conducted in 2007 in Army Medical College, Rawalpindi where 89% computer literacy rate was indicated[6] and in another survey of final year medical students of Allama Iqbal Medical College, Lahore where the computer literacy rate was 19%[7]. This figure is quite better than the findings from similar studies in Malaysia, where 67% of Medical students surveyed reported adequate skills in browsing the Internet[8]. Similarly, in Lagos, Nigeria, the computer and Internet were used by 61% of medical students[9] and 83% medical students in the UK[10]. Research and E-mail was the most popular of the Internet services (73% & 59% respectively) used by the students. This is comparable to previous studies where e-mail use was high (78%) among medical students in Malaysia[11]. 68% of students in our sample have computer at home. This figure is pretty close with the 71.7% of first year medical students that do have access to a computer at home in Aarhus, Denmark[3], 73% of medical students in Hadhramount, Yemen[12] and 86% in California, USA[13].

Despite the fact the computer is being used widely among medical students in Karachi, their proficiency in Keyboard skills, using MS Office and Power Point, Operating system, Troubleshooting and Setting database is inadequate at national level which explains training to the medical students can enhance their skills making its use mandatory not just in their professional life but for general purposes also. From the survey it was found that 94% of students agreed that computers are need of today's world and 52% of them said, they enjoyed working with computers.

The attitude is defined as a learned, global evaluation of an object (person, place or issue) that influences thought and action[14]. The earliest research that examined attitudes toward computers was conducted by Lee in 1970. He identified two dimensions of attitude: (1) the beliefs in the computer as a beneficial tool and (2) beliefs that the computers are autonomous entities[15]. In our survey, it is remarkable the medical students posses a positive attitude towards computers and internet technology. This attitude acts as facilitator in the learning process and inculcation of ICT in not just medicine but all fields of science, arts and commerce.

Hence if computer- assisted technology is introduced into traditional teaching methodologies it would greatly enhance the understanding of several concepts in anatomy, pathophysiology, biochemistry and pharmacology. It would also help the doctors to develop indigenous interactive computer programmes for the caring, the diagnosis and the management of the patients[16]. More surveys need to be carried out in other big and smaller cities to look at the overall computer scenario in Pakistan. Furthermore computers should be a part of curriculum of medical universities, and access to computer library catalogue should be available.

CONCLUSION

The medical students using computers have a positive attitude towards its use in the medical field, which not only has made a significant impact but also encourages them in study, research and keep them updated in this fast developing world. Use of computers enhances decision-making, management planning and medical research among the student.

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