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Review Article

PHARMACOLOGICAL EFFECTS OF CORIANDER (CORIANDRUM SATIVUM)

Hina Pasha and Hamid Javaid Qureshi

Abstract : Coriander (coriandrum sativum) is widely cultivated in Pakistan and other countries. The whole plant is used in preparation of sauces while its leaves give taste to soups, curries and bakery products. Its fruits are widely used as condiments. Coriander possesses extensive pharmacological actions. Coriander has hypoglycemic and antihyperlipidemic effects. It decreases levels of total cholesterol, triglycerides, low density lipoproteins while it increases high density lipoproteins. Hepatoprotective effect of coriander has also been reported. It possesses antioxidant and sedative effects. Coriander also protects gastric mucosal damage. Because of its multiple effects coriander should be included in the diet and its medicinal use is recommended.

Keywords: Coriander, corianderum sativum, hypoglycemic antihyperlipidemic.

Introduction

Use of herbs and plants in medicine is increasing because these are cheap and have relatively few side effects. Coriander is one of these plants. The word coriander was derived from old French "coriandre" which came from Latin coriandrum , in turn from greek κορίαννον (koriannon).[1] Coriandrum sativum is widely cultivated in India, Pakistan, Russia, Central Europe, Asia and Middle East.[2] It is very important spice and has a prime position to flavor the substances. Whole of the plant (stem, leaves and fruits) has a very pleasant aromatic odour. The whole plant is used in preparation of chutneys and sauces when it is young while leaves give taste to soups and curries. The fruits are widely used as condiments in seasoning curry powder, pickling spice and sausages. It is also used to add flavor to bakery products.[3]

Common Name of Plant:

Coriander has different names in different languages. In Hindi, it is called dhania, dhanya; in English: coriander, Chinese parsley; in Spanish: coriandro; in German: koriander; in Japanese: koendoro and in Greek: koriannon, korion.[4]

History of Plant:

It is one of the oldest herbs described in the history because of its use for more than 5000 years ago. Coriander seems to have been cultivated in Greece since second mellinium B.C.[5] In Egypt, people used to call it Herb of Happiness. The Chinese used coriander in their medical practice 207 B.C and had faith that coriander could entrust immortality.[6]

Plant morphology:

Coriander consists of dried ripe fruits of coriandrum sativum, a thin long soft hairless and branched annual and a perennial herb, growing upto 50cm, giving a characteristic aroma when rubbed. Its crop matures in 2-3 months after sowing then, herb is pulled out with roots after drying and fuits are threshed out and dried in sun. These seeds have a lemony citrus flavor when crushed.[7] **(Fig 1, 2)**

Whole of the plant is edible, but the fresh leaves and the dried seeds are the most commonly used parts of plant in cooking.[8]

Fig-1: Fresh coriander

Fig-2: Coriandrum sativum seeds (fruits)

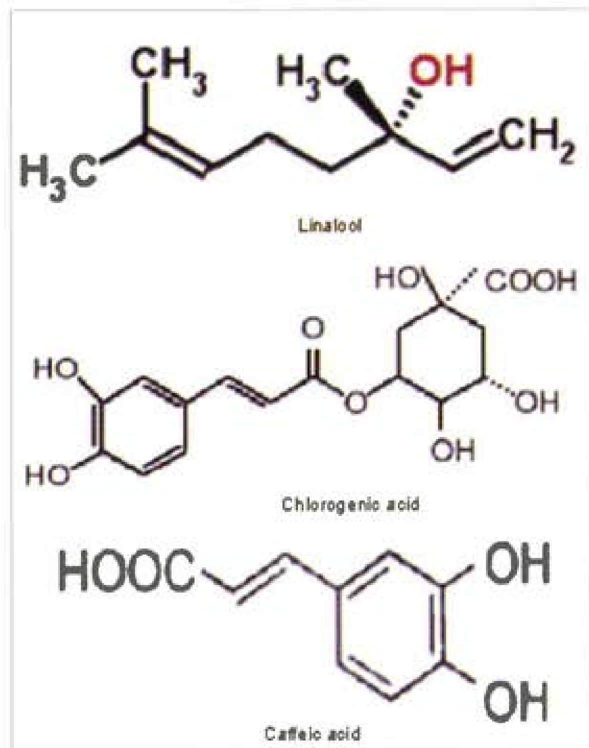

Fig-3: Active components of coriandrum sativum.

Phytochemistry of Coriandrum Sativum:

Because of medicinal use of *coriandrum sativum*, a lot of studies have been done to identify its active chemical constituents. Mostly studies have been done on its seeds. Phytochemical studies have been conducted on its volatile oil[9], ethanolic extract, aqueous extract[10] and methanolic extract.[11]

The major constituents of coriander are essential oils and lipids (rich in petroselinic acid).[12] Among essential oils, linalool is the major component (65-79%)[13] (Fig. 3). Others important constituents are camphor, alpha pinene and gamma terpinene. The main components of fatty acids are petroselinic acid (68.8%), linoleic acid, oleic acid and palmitic acid. Coriander also contains other phytochemicals which include flavinoids, polyphenolic compounds and sterols.[14] Rajeshwari et al (2011) carried reversed-phase high performance liquid chromatography (RP-HPLC) method to separate and identify the flavinoids in ethanolic and methanolic extract of coriander seeds. They separated rutin, quercetin, chlorogenic acid and caffeic acid and reported that chlorigenic acid is predominantly found in methanolic extract followed by others while ethanolic extract contains more rutin than other constituents.[11]

Pharmacological effects of coriandrum satiuvm:

Coriandrum sativum has extensive pharmacological actions and many studies have been conducted so far to reveal its effects.

Hypoglycemic effect:

The hypoglycemic effect of Coriandrum sativum was investigated in streptozotocin induced diabetic rats. Significant decrease in blood glucose level with increased activity of pancreatic beta Cells and insulin were observed After treatment with ethanolic extract of seeds of Coriandrum sativum Given in Traperitoneally.[16] Aissoui et al, in 2011 conducted a study on diabetic and normal rats and reported that blood glucose of diabetic rats decreased after treatment even with a single dose of aqueous extract of coriandrum sativum.[17] In another study, the antidiabetic activity of aqueous extract of coriandrum sativum was investigated in streptozotocin induced diabetic rats. The dose of 250mg/kg and 500mg/kg of extract showed decrease in blood glucose level.[18] Antihyperglycemic effect of coriander seeds was studied by using its powder, alcoholic extract and aqueous extract in type 2 diabetic humans. These seeds in high dose (4.5g t.i.d) showed hypoglycemic effects more markedly in those subjects who were taking oral hypoglycemic agents already but with a history of poor control.[19] Coriandrum sativum essential oil was analysed by using gas chromatography and was administered to a group of streptozotocin induced diabetic rats. The essential oil showed decreased blood glucose level besides improving kidney and pancreas pathological changes occurred as a result of induction of diabetes.[20,21] Antihyperglycemic action of coriander is associated with stimulation of insulin secretion and enhancement of glucose uptake and metabolism by muscle. In a study conducted by Gray (2012), actions of aqueous extracts of coriander on glucose metabolism in isolated murine abdominal muscle and on insulin secretion by a clonal β-cell line were investigated. The effect of coriander, not only as hypoglycemic agent was studied but also the presence of natural constituents and products in coriander was investigated which exhibited insulin releasing and insulin like actions.[22]

Antihyperlipidemic effect:

The antihyperlipidemic activity of coriandrum sativum was observed in diabetic as well as in normal animals. The oral administration of aqueous extract of coriander and ginger showed synergetic effects with glibenclamide in lowering the lipid profile of diabetic animals.[23] In a study conducted on the patients having metabolic syndrome with disturbed levels of lipids and

glucose, thirty drops of plant mixture (3 times daily for 6 weeks) containing the ethanolic extracts of olive leaves, bilberry leaves, elder flowers, coriander fruits and the aerial parts of centaury were given, the levels of serum triglycerides and cholesterol were decreased. [24] Sreelatha et al (2012). Determined that coriander contained some bioactive compounds like phenolics, flavonoids, steroids, and tannins. The extract treated diabetic (allaxon induced) rats showed decreased level of total cholesterol, triglycerides and serum low density lipoprotein (LDL) while high level of high density lipoprotein (HDL).[25] The coriander seeds incorporated into the diet of rats fed with high fat diet and added cholesterol. The effect on the metabolism of lipids was determined by Dhanapakiam et al. They concluded that it had a significant hypolipidemic action. In the tissues of experimental rats, the level of total cholesterol and triglycerides increased significantly. A significant increase in β-hydroxy, β-methyl glutaryl CoA reductase and plasma lecithin cholesterol acyl. Transferase activity (LCAT) was noted. The increased activity of plasma LCAT, enhanced degradation of cholesterol to fecal bile acids and neutral sterols appeared to account for its hypocholesterolemic effect.[26]

Hepatoprotective effect:

KUmar et al (2011), Showed the hepatoprotective effects of coriander seeds In organophosphate induced Intoxicated lIver Of albino mice. An elevated level of liver enzymes was observed in intoxicated mice in comparison to the control. COriander exract was given to those mice and DecreasEd levelS of liver enzymes wEre observed.[27]

Diuretric effect:

The aqueous extract of coriander seed possesses diuretic and saluretic activity. The crude aqueous extract of coriander seeds increased diuresis, excretion of electrolytes, and glomerular filtration rate. The mechanism of action of the plant extract appears to be similar to that of furosemide.[28]

Antioxidant action:

Antioxidants are of interest to biologists and clinicians because these protect the body from hazards induced by free radicals generated in atherosclerosis, ischemic heart disease, Alzheimer's disease and even in aging process.[29] This activity was attributed due to the presence of total phenolic contents of extract.[30]

Anxiolytic and sedative effects:

The aqueous extract of coriandrum sativum seed has anxiolytic effect and may have potential sedative and muscle relaxant effects. The aqueous and hydroalcoholic extracts and essential oil of coriander seeds possess sedative-hypnotic effect. They increased the phenobarbitol induced sleeping time. [31]

Anti-microbial action:

Coriandrum. sativum essential oil has been reported to inhibit a broad spectrum of micro-organisms. The primary mechanism of action of coriander oil is membrane damage, which leads to cell death.[32]

Anthelmentic action:

The aqueous and hydro-alcoholic extracts of coriandrum sativum have anthelmintic activity.[33]

Gastrointestinal effects:

The gastric mucosal injuries caused by NaCl, NAOH, ethanol, indomethacin and pylorus ligation accumulated gastric acid secretions and effect of coriander pretreatment on these injuries was investigated in rats by Al-Mofleh et al. The protective effect against ethanol-induced damage of the gastric tissue might be related to the free-radical scavenging property of different antioxidant constituents (linanool, flavonoids, coumarins, catechins, terpenes and polyphenolic compounds) present in coriander. The inhibition of ulcers might be due to the formation of a protective layer of either one or more than one of these compounds by hydrophobic interactions.[34]

Coriander possesses gut stimulatory and inhibitory effects mediating through cholinergic and Ca2+ antagonist mechanisms respectively.[35]

Antimutagenic action:

Cortes-Eslava et al, investigated the antimutagenic activity of coriander juice. They showed that the aqueous crude coriander juice significantly decreased the mutagenicity of metabolised aromatic amines and the chlorophyll content in vegetable juice.[36]

Metal detoxification:

Chemical compounds present in the coriander get attached to the toxic metals and remove them from the body. Arunasagar et al, observed that coriander is very effective to remove inorganic (Hg+2) and methyl mercury from aqueous solution. This effect was due to the binding effect of carboxylic group to mercury.[37,38]

Conclusion

Because of its hypoglycemic, antihyperlipidemic, antioxidant and other pharmacological effects, coriander should be a part and parcel in our daily diet. Its medicinal use is also recommended.

Department of Physiology
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Original Article

HEEL PAIN AND ITS ASSOCIATIONS

Muhammad Azhar Iqbal, Amber Hussain, Maria Imran, Muhammad Usman Azhar and Shazia Azhar

Objective: Heel pain is an everyday increasing problem in young people more commonly in females. It is estimated that about one million people with complaint of heel pain seek medical advice per year. Therefore, it was needed to highlight its clinical associations.

Methods: One hundred and thirty-eight cases with heel pain were registered. For comparison, 134 subjects were registered as control. All subjects were segregated into gender groups. Each gender group was further subdivided into young (age < 40) and old (age > 40) groups. Three parameters were considered, i) blood pressure, ii) body mass index (BMI) and iii) serum uric acid level.

Results: The overall male to female ratio was 1:3. There was significant difference (p < .05) in the means of systolic and diastolic blood pressure of old (> 40) cases of both gender groups. The Odds ratio showed association between DBP and heel pain in female group only. There was significant difference (p < .05) in the means of BMI of cases from those of age and gender matched controls. The Odds ratios also showed strong association between increased BMI and heel pain. There was significant difference (p < .05) in the means of uric acid levels of cases from those of controls in female groups only. Similarly, the Odds ratio in this group showed association between hyperuricemia and heel pain. When above parameters were analysed for anindependentrisk factor, increased BMI and hyperuricemia were found to be associated with heel pain as isolated and independent risk factors.

Conclusion: In our study, the female cases outnumbered the male cases by 1:3.The results showing the association between heel pain and increased BMI were well consistent with the international studies. For hyperuricemia, the association with heel pain was also consistent with international studies. Similarly, the hypertension was also found in the cases with heel pain in old groups only. The obesity and hyperuricemia were found to beisolated and independent risk factors associated with the heel pain.

Keywords: Heel pain, BMI, Hyperuricemia, Hypertension.

Introduction

Heel pain is defined as pain at the bottom of heel and/or at the site of insertion of Achilles tendon, worsening on walking after rest or prolonged sitting.1 Planter fascists and heel spurs are the most common pathological causes of heel pain.[1,2] It is an everyday increasing medical problem commonly seen in young females. In a study in the USA, it was estimated that about one million people with heel pain (planter fascists) visit hospitals per year.[3]There are many factors associated with heel pain such as congenital deformities, excessive running, chronic arthritis, pronated gait, ill-fitting footwear, etc. Certain medical conditions are also attributed as risk factors with heel pain; these include obesity, hyperuricemia and hypertension.[4,5] Therefore, in this study, three risk factors, body mass index, serum uric acid level and blood pressure were included. These parameters in cases with heel pain were compared with those of the age and gender matched controls.

Methods

It was a case-control study. The cases were selected solely upon clinical basis; fulfilling the above definition of heel pain. The subjects with congenital deformities of foot, diabetes mellitus and with acute or chronic arthropathy were excluded from the study. There was no age or gender restriction. Any subject fulfilling the above definition criteria was included in the study. All cases and controls were segregated into male and female groups. Each gender group was then further divided into two subgroups, *i.e.,* young group, age less than 40 years and old group, age more than 40 years. All subjects were selected at the Out-door Patient Department, Sheikh Zayed Medical College Hospital, Rahim Yar Khan from 22-09-2015 to 16-05-2016. Five parameters were recorded in all subjects in the study. These were age, gender, blood pressure, body mass Index and serum uric acid. Blood pressure was taken with mercury sphygmomanometer. The upper limit of systolic blood pressure ≤ 140 mmHg and that of diastolic

pressure ≤ 90 mmHg was taken as normal. Weight and height were recorded on standard weight and height machine. Weight was recorded in kilograms nearest to the whole digit in ordinary clothes and height in centimetres nearest to 0.5 without shoes and DUPTA/CHADAR. The body mass index was computed using Quetelet ratio, weight (Kg)/height (meter)^2. Queteletratio 20-25 was taken as normal in both genders.[6,7] Serum uric acid of all subjects was assayed incomputerised Serum Analyser Machine. Normal upper limit of serum uric acid was ≤ 7 mg/dL in males and that of ≤ 6mg/dL in females. For statistics, the 'p' value was calculated using t-distribution using 95% confidence interval. The association with the risk factors was established using Odds ratio. The confidence interval for Odds ratio was calculated at the level of 95%. The Odd ratio or confidence interval containing 1.0 or zero was considered as "no association" between the heel pain and the parameter under consideration.

Results

Total 272 subjects were finally selected in the study. Among these, 138 subjects were cases and 134 were controls. The distribution of cases and controls in gender and age groups is summarised in the **(Table-1).** The above results showed that prevalence of heel pain in females was higher as compared to age matched males.

(Table-2). In young age groups, more females (1:4) were involved with heel pain as compared to old female group (1:1.5). The overall male to female ratio was found to be 1:3.

(Table-3). It is evident that there was no statistical difference in means of ages of cases and controls in both gender groups. The statistics of blood pressure revealed that the means of blood pressure were significantly higher in cases than those of controls in old groups (age > 40) of both genders. For body mass index, the means in cases were significantly higher than those of controls in all age and gender matched groups. The means of uric acid levels in female cases (both young and old groups) were significantly higher than those of age and gender matched controls. While, in both young and old groups of male cases, the means of the serum uric acid levels were statistically insignificant from those of age matched controls. **(Table-4).**

The Odds ratios of BMI in both gender groups revealed that the risk factor wass trongly associated with heel pain. This result was well consistent with that of found in the t-distribution ($p < .05$, in all age and gender groups). For hypertension, the Odds ratioshowed relationship between diastolic blood pressure and heel pain in females only. In males, no association was found between blood pressure and heel pain. While, the results of t-distribution revealed significant difference ($p < .05$) in the means of blood pressure in old male and female groups. For serum uric acid levels, the Odds showed strong association with heel pain in females only. The Odds ratio in males showed no relationship with heel pain. This is well consistent with the result of t-distribution that showed the significant difference in means of uric acid in female cases of young and old age groups from those of age matched controls($p < .05$). While, in males, the results of uric acid were insignificant($p > .05$)in both age groups.

The parameters under consideration, i.e., hypertension, obesity and hyperuricemia were analysed for an isolated and independent risk factor associated with the heel pain using Odds ratio. The combined (all subjects) data analysis revealed that obesity was associated as an isolated and independent risk factor with the heel pain, (OR 5.02; 95% CI = 2.78 9.05). The hyperuricemia was also associated as an isolated and independent risk factor with the heel pain (OR 2.19; 95% CI = 0.051 9.41). While, the Odds ratio evaluation for blood pressure as an isolated and independent risk factor for heel pain revealed nil results.

Discussion

In this study, the overall male-to-female ratio was 1:3. In a study in the USA, this ratio was found to be 1:2.[3] In another study in the USA, the females had

Table-1: Distribution of cases and controls in gender, age groups.

	Age<40		Age>40		Total		Grand Total
Gender	Cases	Controls	Cases	Controls	Cases	Controls	
Females	69	68	33	33	102	101	203
Males	16	16	20	17	36	33	69
Grand Total	85	84	53	50	138	143	272

Table-2: Summary of cases.(Male-to-Female Ratios)

Age	Males	Females	Grand Total	M:F Ratios
Age<40	16	69	85	1:4
Age>40	20	33	53	1:1.5
Grand Total	36	102	138	1:3

Table-3: The results of t-distribution.

Parameters	Females		Males	
Age	Age< 40 p>0.05 insignificant	Age< 40 p>0.05 insignificant	Age< 40 p>0.05 insignificant	Age>40 p>0.05 insignificant
Systolic BP	p>0.05 insignificant	P<0.05 significant	p>0.05 insignificant	p<0.05 significant
Diastolic BP	p>0.05 insignificant	P<0.05 significant	p>0.05 insignificant	p<0.05 significant
BMI	P<0.05 significant	p<0.05 significant	P<0.05 significant	p<0.05 significant
Uric Acid	P<0.05 significant	P<0.05 significant	p>0.05 insignificant	p>0.05 insignificant

Table-4: Results of Odds ratio.

Parameters	Females			Males		
Systolic BP	OR=0	AD/BC= 0	No association	OR=0	AD/BC= 0	No association
Diastolic BP	OR=6.60	CI=2.02 - 21.50	Associated RF	OR=0	AD/BC= 0	No association
BMI	OR=8.62	CI=4.20 - 17.67	*Associated RF	OR=6.93	CI=2.41 - 19.98	*Associated RF
Uric Acid	OR=11.76	CI=3.44 - 40.24	*Associated RF	OR=5.17	CI=1.03 - 26.02	*Associated RF

increased rate of incidence than males OR 1.95 (95% CI = 1.93-1.98).[8] In our study, the male-to-female ratio was increased most probably because of the fact that in female cases three risk factors were Bprevailing,*i.e.,* hypertension, increased BMI and hyperuricemia in comparison to male where only one risk factor,*i.e.,* increased BMI was found **[Table 3c].**

The means of the BMI of cases of both young and old age groups of males and females had significant difference (p < .05) from those of age and gender matched controls. Similarly, the results of Odds ratio also showed strong relationship between increased BMI and heel pain in both gender groups. In our study, the Odds ratio in males was 6.93 (95% CI = 2.41 19.98); and for females it was 8.62 (95% CI = 4.20 17.67). The statistical analysis also showed that increased BMI was an isolated and independent risk factor for heel pain. The results were similar to a study carried out in the USA where the Odds ratio in subjects with heel pain having BMI > 30 was 5.6 (95% CI = 1.9 16.6; P < .05).[8] In another study carried out in Netherland, the Odds ratio in subjects with heel pain having raised BMI (> 27) was 3.7 (95% CI = 2.93 5.62).[9] In another study by David M Pizzano, showed that 40% of obese, 23.4% of overweight and 11.4% of normal weight subject had heel pain.[10] In another study in the USA, study concluded a moderate correlation between increased BMI and planter fascia thickness.[11] Thus, the results regarding BMI in this study were well comparable with those of international studies.

The means of serum uric acid levels in young and oldfemale age groups with heel pain had significant difference (p < .05) from those of age matched controls. Similarly, the Odds ratio also showed strong association (OR 11.76; 95% CI = 3.44- 40.24) between hyperuricemia and heel pain in this gender group. The statistical analysis also showed that hyperuricemia was an isolated and independent risk factor for heel pain. In a study by Taniguchi Y, revealed that uric acid crystals were found from the aspirates of heel enthesitis.[12] In another article by Christian Nordqvist, higher levels of uric acid were associated with heel pain.[13]The attacks of acute gouty arthritis occur in joints of various locations including heels.[14] So, our results were consistent with the international researches. But, in 5.17; 95% CI = 1.03 26.02). Thus, in our study, there was disparity in results of male and female cases with regards to hyperuricemia. This parity can be explained on the fact that in female cases, hypertension (DBP) was associated with the heel pain. While in male cases, hypertension did not show any association with heel

pain (see below). It is fact that hypertension itself has strong associated with hyperuricemia.[15] In our study, the Odds ratio in female cases, showed strong association between high blood pressure (DBP) and hyperuricemia while in male cases, the same did not show such association. Therefore, hypertension could be a contributory factor of hyperuricemia in female cases.

Male cases of both age groups, the means of serum uric acid levels had insignificant difference ($p > .05$) from those of age matched control groups. Similarly, the Odds ratio did not show any association between hyperuricemia and heel pain in male cases as the confidence interval contained 1.0 (OR 5.17; 95% CI = 1.03 26.02). Thus, in our study, there was disparity in results of male and female cases with regards to hyperuricemia. This parity can be explained on the fact that in female cases, hypertension (DBP) was associated with the heel pain. While in male cases, hypertension did not show any association with heel pain (see below). It is fact that hypertension itself has strong associated with hyperuricemia.[15] In our study, the Odds ratio in female cases, showed strong association between high blood pressure (DBP) and hyperuricemia while in male cases, the same did not show such association. Therefore, hypertension could be a contributory factor of hyperuricemia in female cases.

For hypertension, there was significant difference ($p < .05$) in the means of blood pressure in cases of old age groups of both gender groups from those of age and gender matched controls. For Odds ratios, the female gender group with heel pain showed strong association with high diastolic pressure (OR 6.60; 95% CI=2.02-21.58). While in male groups, the Odds ratio was found to be zero. This disparity can be explained on the facts that in female cases there were three risk factors found, *i.e.,* increased BMI, hyperuricemia and high blood pressure. While, in male cases of both young and old groups, only one risk factor *i.e.,* increased BMI was found to be strongly associated with heel pain. This is another reason that number of female cases was three times of the male cases. As the high blood pressure had been found in both the old groups of male and female cases, most probably it could be age related. But it is fact that hypertension and hyperuricemia are inter-linked.[16]

Conclusion

In our study, increased BMI found to be the strong risk factor for heel pain in all age and gender groups of cases. In female cases of both young and old age groups, all three parameters, increased BMI, hyperuricemia, and hypertension were found to be associated with heel pain. The cases of old male group showed the relationship between hypertension and heel pain. The statistical analysis of combined data of all subjects revealed that increased BMI and hyperuricemia were isolated and independent risk factors for heel pain.

Department of Medicine
SIMS/Services Hospital, Lahore
www.esculapio.pk

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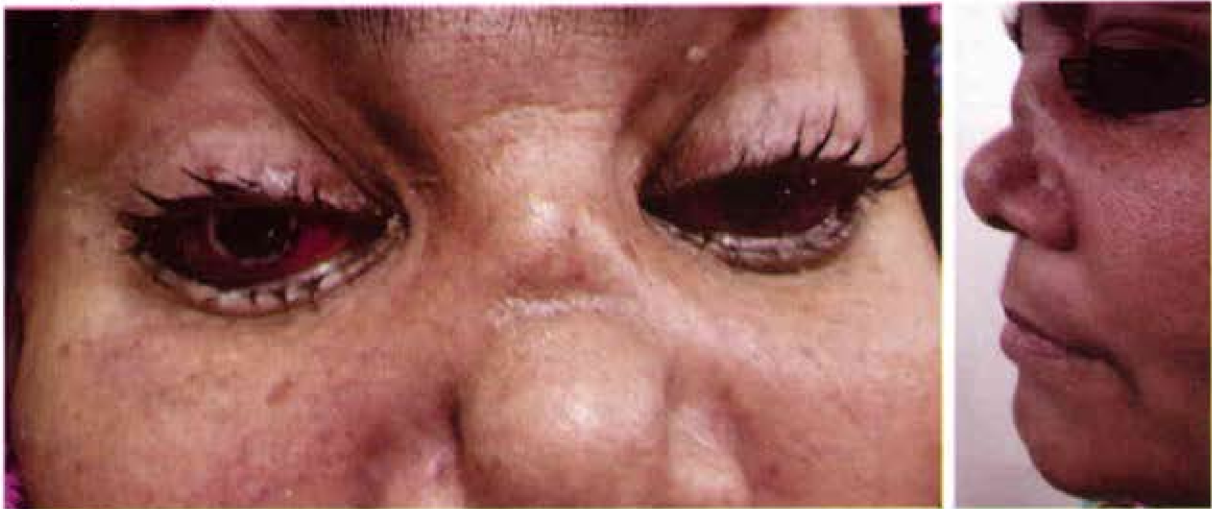
Picture Quiz

WHAT IS THE DIAGNOSIS?

A 45 years female patient with four month history of joint pain, fever, cough and ear discharge.



Courtesy: Dr. Muhammad Shahzad Hafeez

See answer at page #37

Original Article

SURGICAL EXCISION WITH SECONDARY HEALING VERSUS LIMBERG TRANSPOSITION FLAP IN THE MANAGEMENT OF SACROCOCCYGEAL PILONIDAL DISEASE

Muzaffar Aziz, Tariq Jamil Choudhary, Jamil Zahid and Khalid Hussain Qureshi

Objective: To compare the outcome of Open excision and secondary healing with rhomboid excision and Limberg flap in the management of sacrococcygeal pilonidal sinus disease.

Methods: A comparative study using randomized controlled trial (RCT) was conducted at Nishtar Hospital Multan & Ghazi Khan teaching Hospital DG khan from November 2012 to July 2016. In total 49 patients, who either underwent open excision and secondary healing (group A: 25 patients out of which 4 patients did not reported during follow up so actual figure of 21 was included in this group) or rhomboid excision and Limberg flap (group B: 24 patients), were enrolled in the study. Duration of operation, postoperative pain, duration of hospital stay, postoperative complications, and time to recurrence were noted. The inclusion criteria were all patients with primary or recurrent Disease. Diabetics, patients with other co morbid condition, patients with poor follow up and patients with incomplete record were excluded from study.

Results: Duration of operation was longer in group B patients (p=0.004) but pain perception was markedly reduced in this group (p=0.003). Total hospitalization period was shorter in patients in group B (p=0.002) and so was the time for complete healing of the wound (p=0.002). The recurrence rate was also significantly lower in patients who underwent Limberg rotation flap (p=0.005).

Conclusion: Limberg flap is advantageous over simple excision and secondary healing in the management of pilonidal disease.

Keywords: Pilonidal disease, Limberg Flap, Excision and Secondary healin

Introduction

Pilonidal disease was first reported in 1833. This process was first described by Anderson in 1847 and later named pilonidal sinus by Hodges in 1880.[1] The word pilonidal derives from the Latin words *pilus* ("hair") and *nidus* ("nest"). Sacrococcygeal pilonidal sinus is a common disorder among young adults. Observed most commonly in people aged 15-30 years, with a 3:1 male-to-female ratio, it occurs after puberty, when sex hormones are known to affect the pilosebaceous gland and change healthy body hair growth. The onset of pilonidal disease is rare in people older than 40 years.[2] One of the simplest medical treatments of pilonidal sinuses is to shave the sacral area free of hair and to pluck all visible imbedded hair in the sinus,[3] phenol injections into sinus track.[4,5] Another newer medical therapy that is applied after simple curetting of the sinus tract is fibrin glue.[6] Radio frequency ablation techniques have also been studied in an attempt to reduce the pain associated with the procedures.[7] Primary wound closure and wound healing by secondary intention are the two principal surgical options for a chronic pilonidal sinus.[8,3] Primary closure is considered better then healing by secondary intension.[9] Bascom and Edwards described a procedure in which pilonidal disease was treated with only removal of the hair and the follicles.[10,11] Karydakis procedure,[12,13] begins with excision of the wound and en-bloc removal of the sinuses with an elliptical specimen of overlying skin. Flap procedures (rhomboid flap/Limberg flap, V-Y advancement flap and Rotational flap[14-18] are performed for complex and recurrent disease. Simple excision techniques are associated with high morbidity and recurrence due to presence of natal cleft. Different studies have reported recurrence rates of 0-5 %.[19-21] these high recurrence rates are attributable to a persistence natal cleft in the midline, which provides a portal for hair entry. Once the hair is inside, the vicious circle of abscess formation and discharging sinuses begins.[22] The experience with rhomboid excision and Limberg transposition flap versus open excision and secondary healing in the management of primary and recurrent SPD is presented.

Methods

This study was conducted simultaneously at Nishtar Hospital Multan and Ghazi Khan teaching Hospital

DG Khan, from Nov 2012 to July 2016.

It was a prospective, analytical, comparative study using randomized controlled trial (RCT). Blocked randomization was used for allocation of patients in 2 groups (A and B). The patients are divided in blocks of two, and within each block the first patient was allocated in group A and the second patient in group B.

A total of 49 patients were enrolled in the study. Group A, comprised of 25 patients. 14 patients have primary disease while 11 patients have recurrent pilonidal sinus. Open excision and secondary healing was the procedure performed in these patients. 4 patients did not reported for follow up so they were excluded from study so in Group A, 21 patients were included in study. Group B had 24 patients, subjected to rhomboid excision and Limberg transposition flap. 12 patients in this group had primary disease and others have recurrent pilonidal disease.

Inclusion criteria were all patients with primary and recurrent disease. Diabetic and patients with co morbid disease (cardiac, renal disease, asthmatic) were excluded from study. Patients those were lost to follow-up and incomplete records were also excluded from study. An informed consent was taken and patients were counseled about the merits and demerits of both the procedures. Duration of operation, postoperative pain, duration of hospital stay, postoperative complications and time to recurrence were noted. The average period of follow up was 18 months (12-24 months).

Operative technique:

All the patients were operated under general anesthesia. Antibiotic prophylaxis was done, using 1gm of intravenous Ceftezidime were given to all the patients. Patients were placed in Jack-knife position with hips strapped apart. Methylene blue was injected in the sinus tract. Patients in group A underwent excision of all the diseases area as lined by Methylene blue. The wound was packed with pyodine soaked dressing. Postoperatively, the dressing was changed daily after washing the wound with normal saline. Patients were discharged on 4-6th postoperative day.[23] The patients were followed up in ward on weekly basis till complete healing of wound. They were then followed at monthly basis for 18 months. Patients were advised to keep the area hair free.

In group B patients, the proposed flap was marked on the skin. Rhomboid excision of the tissue was done incorporating the whole sinus tract and extending deep into pre-sacral fascia (Figure 1).[36] The Limberg flap was then rotated from the gluteal fascia to the area excised. Subcutaneous tissue was sutured using polyglactin 2/0 suture and skin by prolene 3/0 suture. Homeostasis was secured and no drain was used for drainage purpose.[28] The patients were discharged from the hospital usually on 2-3 day. Skin sutures were removed on 14th post-operative day. Patients were advised to maintain good hygiene and to keep the area hair free. The follow-up schedule included a monthly follow up for 3 months and a quarterly follow-up for at least 18 months.

Operative time was defined as the time between the placements of incision to the last suture applied. Severity of pain was defined using visual analogue score and need and type of analgesia. Return to the normal routine was considered as the period of first day of admission to hospital until the patient resumed work. Statistical analysis was done using SPSS.

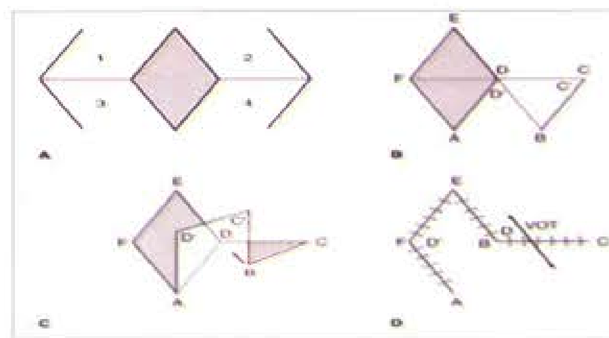


Fig-1: Diagrametic Presentation.[36]

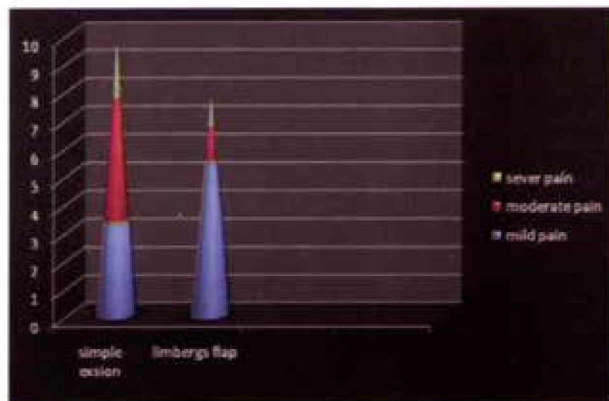


Fig-2: Pain response and need of painkillers.

Discussion

After surgery for pilonidal sinus wounds healed more quickly when primary closure (Limberg Flap) was used as compared to excision of the sinus. Significant difference was found in rate of complications between the two approaches. A careful assessment of the harms

and benefits of each should be made when considering surgical treatment. A clear benefit was, however, found with Primary closure (Limberg Flap) compared with excision only is assessment of variables (pain, hospital stay, return to routine activity and recurrence of disease). In present study, the pain perception in group A was significantly high as compared to Group B where proper skin coverage was provided by Flap. When compared to the literature, similar results were found by Akmal Jamal et al.[24] Faisal Bilal Lodhi et al[27] Urhan et al[25] and Bozkurt & Tezel[26] reported a mean hospital stay of 3 days, 3.7 days and 4.1 days respectively similar to what we have observed in our study (mean hospital stay in Group B being 4 days). In contrast to that, patients who underwent simple excision of the sinus tract had to stay for a longer time in hospital due to presence of open wound. The longer hospital stay results in delay in return to routine activity resulting in social and financial impacts. One main problem recognized with flap construction is early development of seroma/haematoma formation resulting in wound infection and flap failure. To prevent this, insertion of suction drainage has been advocated by many centers. However we did not placed darin in any patient, a study published by Erdem et al,[28] suggested no considerable difference in complication rates between two groups who underwent Limberg flap rotation with or without suction drainage. Different series have reported wound infection rates of 1.5-7 %.[21,29] in the present study, it was 4.1% with Limberg flap (group B) whereas in those patients who underwent open excision (group A) it was increased to 24%. Akmal Jamal et al[24] reported the similar results. If the disease recurs, it commonly presents in first 2-3 years. In our study the recurrence rate observed was 4.1% with Limberg flap. Recurrence rate remained quite high in Group A. Akmal Jamal et all[24] reported the similar results. Our results are close to results reported by Mentes et al (3.1%),[30] Hizbullah Jan et al.[31] & Akin et al (2.91%).[29] Hence, with all the controversies about best surgical technique for the treatment of pilonidal sinus, an ideal operation should be simple and with low complication rate. Less hospital stay and early return to activity must be considered. The Limberg flap has proven efficacy in the management of both primary and recurrent disease.[12,34] Quick healing time, short hospital stay, early return to daily life, low complication and recurrence rate are the important advantages of the Limberg flap procedure.[29,30,33,34,35]

Conclusion

We conclude that the excess terminal hair growth is more common in overweight women having less hirsutism score.

Department of Surgery
Nishtar Medical college Multan
www.esculapio.pk

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Original Article

Correlation Between Transglutaminase Antibody (TGA) Ratio and Histological Findings of Villous Atrophy in Celiac Disease By Marsh Grading

Aafrinish Amanat, Tahmina Gul, Rabia Naseer Khan, Usman Nasir and Romaisa Amanat

Objective: To assess the correlation between TGA ratio and degree of duodenal damage by using histologic Marsh grading in patients with CD.

Methods: This present study was conducted in the Department of Histopathology, Shaikh Zayed hospital, Lahore. After taking informed consent (from the patients and guardians in case of minors), endoscopic biopsy from the distal duodenum was taken routinely. Data was computerized with window SPSS version 22. P value ≤ 0.05 was considered significant.

Results: In our study, the mean age of the patients was 32.23±16.37 years and male to female ratio was 1.08:1. The mean TGA ratio of the patients was 16.51±7.37. A strongly positive correlation was found between the Marsh grading of CD and TGA ratio of the patients i.e. r=0.872. Statistically, a highly significant difference was found between Marsh grading and TGA ratio.i.e. p-value=0.006

Conclusion: The results of our study concluded that the titer of TGA ratio is strongly correlated with duodenal histologic Marsh grading in patients of CD.

Keywords: Marsh grading, TGA ratio, CD, correlation, small Intestine

Introduction

Celiac Celiac disease has now emerged as the most common genetically based food intolerance. Celiac disease was initially considered to be a disease of western society. However, it has now been detected in many other parts of the world including Africa, Middle East and Asia with the highest prevalence in Saharawi population living in Algeria.[1] Regarding Pakistan, no specific figure has been documented for its prevalence.[2] In 1940's, the association between the dietary wheat component (gluten) and CD was described by the Dutch paediatrician Dicke.[3] The features characteristic of Celiac disease are villous atrophy of the duodenal mucosa, intraepithelial lymphocytosis and crypt hyperplasia.[4] The result is decrease in the mucosal surface area of absorption. It ultimately leads to malabsorption, diarrhea and growth failure.[5]

There are multiple complications of untreated Celiac disease. Some of these include growth failure in children, anaemia, osteoporosis, infertility and development of lymphoma in the small intestine.[6]

Diagnosis

The diagnosis of Celiac disease should comprise of: history, clinical symptoms, serology & histopathology of the proximal duodenum[7]. However, a definite diagnosis relies on the histological findings. The grading of these changes is done by a classification system proposed by Marsh[8].

The best serological test used to screen patients of Celiac disease is considered to be anti-TGA assay. Anti-TTG assay has a high sensitivity and positive predictive value as compared to anti-endomysium antibodies. However, the gold standard for diagnosis is biopsy of the proximal duodenum, although it has many limitations due to patchy distribution of mucosal changes.[9]

The researchers are currently trying to discover non-invasive and economical methods for the diagnosis of CD, especially in children. It has encouraged them to find if any correlation exists between TGA levels and mucosal damage and whether it has a PPV sufficient to be used for the diagnosis of CD. Recent evidence has suggested that the duodenal changes correlate with the TTG titers. Accordingly, duodenal biopsy can be ignored in strongly positive TTG levels provided additional symptoms and history are suggestive of CD.[10]

It has been claimed that high level of TGA has a positive predictive value of almost 100% for diagnosing Celiac disease and in such cases a duodenal biopsy can be avoided. Hence, a gluten free diet can be prescribed based on confirmed greatly positive TGA result.[11] The TGA level five times the upper limit of normal is 100% specific for villous atrophy. By using a this cut-off value, biopsy can be

avoided in 1/3 of patients.[12]

It was a cross sectional analytical study, conducted in the Department of Pathology, Shaikh Zayed hospital, Lahore.Study was completed in one year after approval of research synopsis.The estimated sample size was 100. It was calculated by using 95% confidence interval, 8% precision level with expected sensitivity and specificity of anti-tissue transglutaminase antibody, 91% with expected frequency of positive cases 50%.

A designed proforma was used to collect the consent and data of patients.Patients of both genders with malabsorption, diarrhea and/or risk factors suggestive of CD were included.

Patients with other autoimmune disease, viral or parasitic infection, drugs, gastro-intestinal malignancy were excluded.

Study Protocol: The study was carried out in one year. Patients were selected from the Department of Gastroenterology and Paediatric Medicine, ShaikhZayed Hospital Lahore, who had been advised anti-tissue transglutaminase antibody level or had already got serology report and were suspected of having biopsy positive CD.Informed consent regarding the inclusion of the endoscopic biopsy in this study was obtained from the patients & the parents/guardians (in case of minor patient) before entering into the study. Endoscopic biopsy was taken routinely (which was free of cost for admitted patients).

Data analysis plan:

\Data was computerized with window SPSS version 22. The strength of association of both parameters was seen by Pearson's correlation curve. P value ≤ 0.05 was considered significant.

Results& Discussion:

In this present study, a total of 100 random patients from either gender were enrolled with age range from 17 months to 80 years.

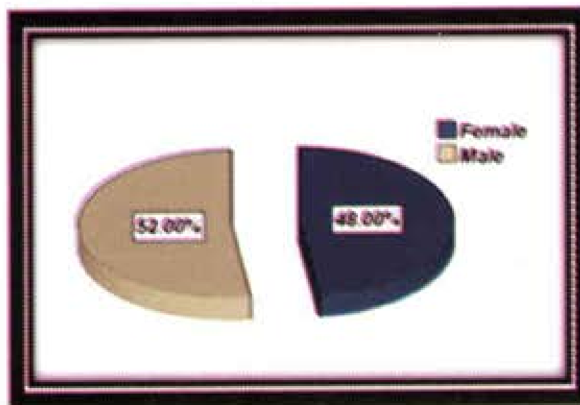

Fig-1: Male to female ratio.

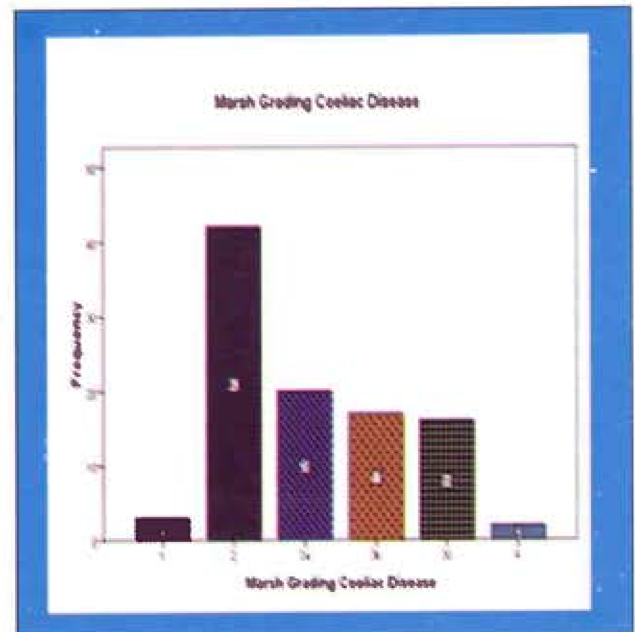

Fig-2: Frequency of various Marsh grades.

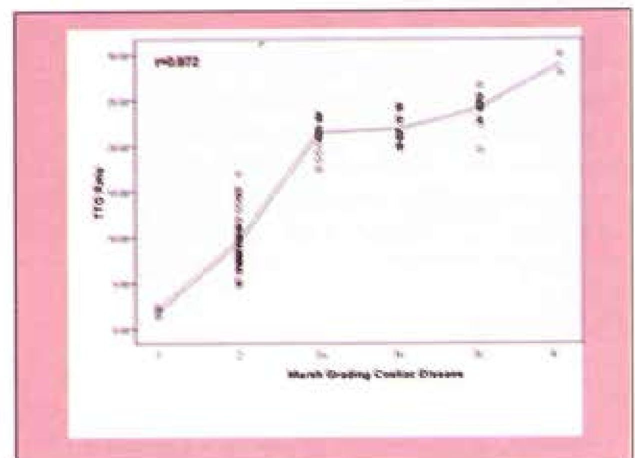

Fig-3: TTG ratio in various Marsh Grades.

In our study, 52% of the patients were males and 48% of the patients were females. The male to female ratio of the patients was 1.08:1. **(Fig-1)**

Frequency of various Marsh Grades is shown in **(Fig-2).** A positive correlation was found between the Marsh grading of Celiac disease and TGA ratio of the patients. i.e $r=0.872$ **(Fig-3).**

Statistically, a highly significant difference was found between Marsh grading and TGA ratio of the patients i.e. p-value<0.05.

In our study, the mean age of the patients was 32.23±16.37 years and the male to female ratio of the patients was 1.08:1. A weakly negative correlation was found in our study between the TGA ratio and age of the patients ($r= -0.030$). On the other hand, a highly

positive correlation was observed between the TGA ratio and Marsh grading of Celiac disease i.e. r=0.872. Some of the studies which support the findings of our study are as follows.

Rahmati et al showed in their study that the mean TGA titers were considerably higher in patients with Marsh grade 3 (p=0.003). They found that a correlation exists between TGA titers and degrees of duodenal damage in patients of Celiac disease.[13]

In another study, Vivas et al concluded that the levels of TGA correlate with the Marsh grades (r = 0.661, p< 0.0001). Furthermore, in children, the diagnosis of Celiac disease might be considered when the TGA titer is very high.[14] In another study, it was suggested by Diamanti et al that in symptomatic patients, a strong correlation is present between TGA levels and degree of mucosal injury, and further demonstrated that TGA value ≥20 U/mL can predict mucosal atrophy.[15] Alessio et al carried out a study and investigated an almost complete correspondence (99.8%) between TGA ratio >20 with atrophic lesions (Marsh 3) and 100% positive predictive value for Celiac disease.[16] A study carried out by Zulfiqar et al at the Histopathology laboratory, Karachi concluded that a strong correlation exists between the serological TGA levels and histological findings as graded by Modified Marsh classification.[17] Another study by Parizade et al conducted in the paediatric age group found that in high risk population, high level of antibody can predict villous atrophy with high sensitivity.[18]

However, few studies which showed contradicted findings to this study are as follows:

A study by Evans et al demonstrated that the serology cannot entirely replace histology. Therefore, definite diagnosis should be based on positive antibodies in the presence of villous atrophy[19]. Sweis Rami et al have also reported in their study that a small but significant number of cases of Celiac disease will be missed if only serology is considered.[2] A study conducted by Arevalo et al showed that the frequency of positive serology is low in patients who have had biopsy compatible with Celiac disease[21]. It was shown in another study conducted by Emami et al that the sensitivity of TGA is lower in patients with lesser degree of villous atrophy. Therefore, cases with low Marsh grades can be missed if serology is used as a sole source of diagnosis.[22]

Conclusion

The results of our study concluded that the levels of TGA ratio are strongly correlated with duodenal histologic Marsh grading in patients of Celiac disease.

Department of Histopathology,
Shaikh Zayed Hospital. Lahore
www.esculapio.pk

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Original Article

CORRELATION BETWEEN SERUM CALCIUM LEVEL WITH BLOOD PRESSURE LEVEL IN PATIENTS PRESENTING WITH TYPE 2 DIABETES MELLITUS

Dur Muhammad Khan , Imran Mahfooz Khan,Fawad Ahmad Randhawa and Muhammad Shahid

Objective: To study the relationship between serum calcium level and blood pressure level in patients presenting with type 2 diabetes mellitus.

Methods: This cross sectional study was conducted at East Medical Ward, Department of Medicine Mayo Hospital Lahore. This study was done in six months period from March 10, 2015-Sep 10, 2015. The non-probability consecutive sampling technique was used in this study. Informed consent and demographic information like name, age and address was recorded. Systolic and Diastolic Blood pressure was measured by using standard and absolute sphygmomanometer. 3ml Blood sample of each patient was taken with informed consent and was sent to the laboratory of the hospital to assess serum calcium level (as per operational definition). Reports were assessed and calcium level was recorded. Pearson correlation coefficient was calculated to measure the relationship between serum calcium level and systolic & diastolic blood pressure. pvalue ≤0.05 was considered statistically significant.

Results: In our study the mean age of the patients was 59.42±11.02 years, 30% patients were males and 70% patients were females. The mean SBP value of the patients was 140.56±11.35 mmHg and mean DBP value was 87.98±6.11 mmHg. In this study the mean value of calcium level of the patients was 8.22±1.24 mg/dl. The negative correlation was observed in our study between the calcium level and SBP, DBP of the DM patients i.e. r= -0.665 & -0.401 respectively

Conclusion: The study concluded that negative correlation was observed between the serum calcium level and the blood pressure level in patients presenting with type 2 diabetes mellitus.

Keywords: Serum Calcium, Type 2 diabetes mellitus, blood pressure.

Introduction

Hypertension is up to three times more common in patients with diabetes contributing its major effect in development of macro vascular complications.[1] Hypertension affects 34%of US adults and African American adults have among the highest rates of hypertension in the world at 44%.[2] At present, it is estimated that about 1 billion people worldwide have hypertension (>140/90 mmHg), and this number is expected to increase to 1.56 billion by 2025.[3] According to WHO, the total prevalence of diabetes in 2011 in Pakistan was 12.9 million (10% of total population) . It has been estimated that Pakistan is known as the 7th largest country in terms of highest prevalence of diabetes and will be 4th largest by the year 2030.[4] In a report, it was shown that 18% of people in Pakistan suffer from hypertension with every third person over the age of 40 becoming increasingly vulnerable to a wide range of diseases. It was also mentioned that only 50% of the people with hypertension were diagnosed and that only half of those diagnosed were ever treated. Thus, only 12.5% of hypertension cases were adequately controlled.[5] Cardiovascular and kidney functions have a significant dependency on serum calcium levels and calcium homeostasis is an integral part in carrying out the physiologic functions of these systems.[6] Studies have concluded that there is a significant difference in serum levels of calcium in hypertensive and normotensive individuals. Amongst the different forms of serum calcium that are present in the serum, it's the ionized form that is physiologically active .[7,8] extracellular calcium levels are in strict check under the effects of different endocrine systems and any alterations in its normal values may affect the intracellular calcium levels too and possibly can contribute towards development of hypertension.[9] Behradmanesh S et al inferred a significant inverse correlation between serum calcium and diastolic blood pressure (DBP) (r= -0.261, p=0.046). Interestingly, the statistically insignificant reverse relationship was observed with systolic blood pressure (SBP) and serum calcium levels (r= -0.232, p=0.080).[10] to make the matters more intriguing and

interesting, Phillips A at al reported way back in early 1990s a significant correlation between serum calcium and both SBP and DBP (r = 0.15 and 0.11, respectively; P<0.0001).[11] In order to make these associations more clear this research idea was launched on this relationship of both variables with a rationale to measure the relationship between calcium level and blood pressure (BP) in diabetic patients as hypertension control is of prime importance in diabetics and carries equal weightage as glycemic control to control microvascular and macrovascular complications. Previously mixed results have been noted and different criteria have been employed and the results of those studies few of them are already mentioned provided us with different results of the relationship of these variables. Very weak relationship has been observed which showed that decrease in calcium may cause elevation in BP (negative correlation), while other reported positive correlation (i.e. decrease in calcium may cause decrease in blood pressure). So to resolve this controversy, this study was conducted to study the relationship between BP and serum calcium in diabetic patients. This will help us to plan management option for such cases to prevent them from hazardous events like stroke or MI, as these are very common in diabetic patients.

Methods

A sample size of 150 cases were calculated with5% type I error, 10% type II error and taking value of correlation coefficient i.e. r = -0.232 between serum calcium level and blood pressure of diabetic patients with non-probability consecutive sampling. Patients of age between 40-80 years of either gender with diabetes mellitus (as per operational definition) for at least 1 year were included in the study. Current smokers (>1pack year), patients taking calcium or vitaminD supplements (on medical record), patients taking antihypertensive medicines (on medical record), patients with CKD patients stages 3 and 4 not taking calcium or vitamin D supplements.[12]were excluded. A total of 150 patients fulfilling the inclusion and exclusion criteria were included in the study from Outpatients Department of Medicine, Mayo hospital, Lahore. Informed consent was obtained. The demographic information like name, age and address was recorded. Systolic and Diastolic Blood pressure was measured by using standard and absolute sphygmomanometer. 3ml Blood sample of each patient was taken with informed consent and was sent to the laboratory of the hospital to assess serum calcium level. Reports were assessed and calcium levels were recorded. Data was collected in a predesigned proforma.Data was analyzed in SPSS version 20. Mean ± SD was calculated for age, systolic & diastolic blood pressure and serum calcium level. Frequency and percentage were measured for gender. Pearson correlation coefficient was calculated to measure the relationship between serum calcium level and systolic & diastolic blood pressure. *P* value ≤0.05 was considered statistically significant.

Results

In this study a total of 150 cases were enrolled.

Table-1: Descriptive statistics.

	SBP	DBP	Serum Calcium
Mean	140.56	87.98	8.22
SD	11.35	6.11	1.24
Minimum	120.00	80.00	6.00
Maximum	160.00	100.00	10.20

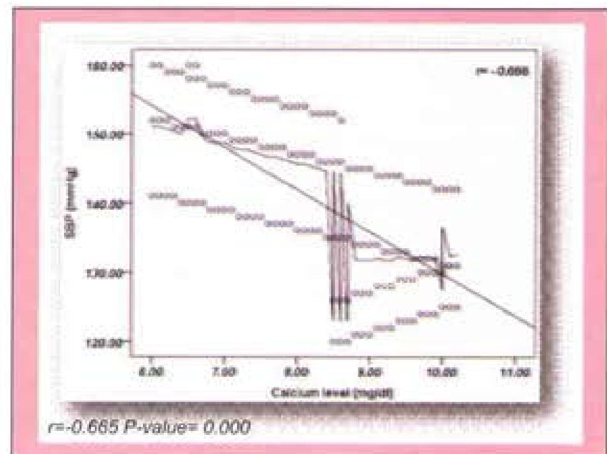

Fig-1: Correlation between the calcium level & SBP.

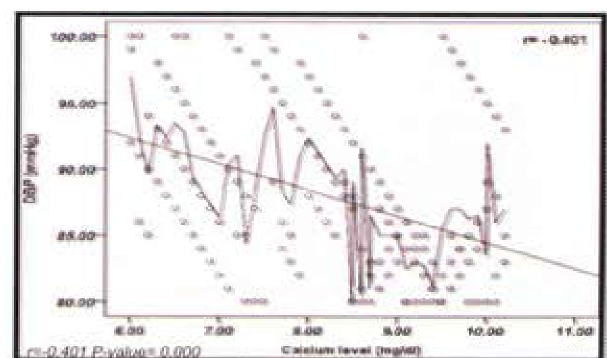

Fig-2: Correlation between the calcium level & DBP.

The mean age of the patients was 59.42±11.02 years with minimum and maximum ages of 41 & 80 years respectively. Out of 150 cases, 70% patients were males and 30% patients were females. The male to female ratio of the patients was 2.3:1. In our study the mean duration of DM of the patients was 2.44±0.92 years with minimum and maximum duration of 1 & 4 years respectively. The study results showed that76% patients were on treatment of DM and 24% were treatment naive. Furthermore, the mean SBP value of the patients was 140.56±11.35 mmHg with minimum and maximum SBP values of 120 & 160 mmHg respectively. The study results showed that the mean DBP value of the patients was 87.98±6.11 mmHg with minimum and maximum DBP values of 80 & 100 mmHg respectively .In this study, the mean value of calcium level of the patients was 8.22±1.24 mg/dl with minimum and maximum levels of 6 & 10.20 mg/dl respectively. (Table#1)The negative correlation was observed in our study between the calcium level and SBP of the DM patientsi.e. r=-0.665.(Fig-1)The week negative correlation was observed in our study between the calcium level and DBP of the DM patientsi.e. r=-0.401. **(Fig-2)**

Discussion

This present cross sectional study was conducted at East Medical Ward, Department of Medicine, Mayo Hospital, Lahore to assess the correlation coefficient between serum calcium level and blood pressure level in patients presenting with type 2 diabetes mellitus. Diabetes mellitus is a systemic disease that adversely affects the quality and length of life by exerting its deleterious impact on cardiovascular events and sudden death. The prevalence of diabetes increases with age, with over 25% of the elderly having type 2 diabetes. Epidemiological studies have stated that interestingly there are up to 6 times more Non-Caucasians that are type 2 diabetics than Caucasians.[13]In this study, the mean value of calcium level of the patients was 8.22±1.24 mg/dl , the mean value of SBP & DBP were 140.56±11.35 mmHg & 87.98±6.11 mmHg respectively. There was an inverse relationship observed between the calcium level and systolic as well as diastolic blood pressures in diabetics i.e. r=-0.665, -0.401 respectively. Studies conducted around the globe have mixed results. A number of epidemiological studies suggested an inverse relationship between serum calcium and blood pressure level.[14-16] Kesteloot et al inferred positive correlation between total serum calcium positively and blood pressure in male subjects, while 24-h urinary excreted calcium positively correlates with blood pressure. In a subgroup of 297 male subjects no correlation was found between the serum ionized calcium level and blood pressure.[17]to make the things more controversial and at the same times intriguing, Folsom reported an inverse association between serum ionized calcium and hypertension though the sample size was small.[18]One recent study found that a significant inverse correlation of serum calcium with level of DBP (r= -0.261, p=0.046) was seen. In addition, a negative correlation of SBP with level of serum calcium was observed, however, this correlation was not significant(r= -0.232, p=0.080). Vargas and coworkers, in a previous study using NHANES III data, reported an inverse association between serum ionized calcium and hypertension in the subgroup of younger Mexican-American men only.[19] Hunt et alstudied 875 normotensive patients and described a positive association between ionized calcium and BP among the high renin group and an inverse association between ionized calcium and BP among the low renin group.[20] On the contrary, some studies showed positive relationship between the serum calcium level and hypertension. A cross sectional study conducted by Philips and colleagues involving 7735 healthy middle-aged men, reported that higher serum total calcium was associated with hypertension. They demonstrated a small but significant correlation between serum calcium and both SBP and DBP (r = 0.15 and 0.11, respectively) after adjusting for age. This association was diminished after adjustment for serum albumin, but remained significant (r = 0.10 and 0.07; P less than 0.0001).[11] Rinner and coworkers, in a small sample of 182 Dutch adults, reported that higher serum total calcium was positively associated with hypertension after adjusting for age, BMI, and albumin and in the subgroup analysis stratified by sex, the association was found to be stronger in women than in men.[21] Gruchow et al showed in their study that the associations of age, BMI, gender, and alcohol with blood pressure were not affected by calcium levels.[22] So it was worth an effort conducting this study to determine the reasons for these different results. May be gender, race and environments and genetic factors all play there part in this association.

Conclusion

The study results concluded that the negative correlation was observed between the serum calcium

Levels and the blood pressure level in patients presenting with type 2 diabetes mellitus. Further cohort studies need to be conducted to observe whether calcium replacement in hypocalcemic normotensive type 2 diabetic patients can prevent the development of hypertension and the study should expand and should include non-diabetics as well to see the pattern.

Department of Medicine
King Edward Medical University
www.esculapio.pk

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Original Article

VISUAL HYGIENE IN ADULT MYOPES

Rabia Mobeen, Ammara Faiz and Faisal Rashid

Objective: The purpose of this study was to evaluate. 1. The importance of visual hygiene in adult myopes. 2. To find out the association of myopia with posture and visual environment. Main outcome measures were to evaluate role of visual hygiene, to evaluate the effects of posture in developing myopia and to evaluate the effects of visual environment in developing myopia.
Methods: This was an institutional based cross sectional study conducted at College of Ophthalmology and Allied Vision Sciences in the main OPD of Eye Department, Mayo Hospital, Lahore, during the months of July to September 2016. Total of 100 subjects of both genders aged between 5-15 years, having Myopia of -1D to -5D were included in the study by using non-probability convenient sampling technique. All the subjects were asked to fill the questionnaire containing questions regarding academic performance with and without spectacles. Data was collected through a self designed questionnaire and analyzed on SPSS software (Version 20.00) and p value was calculated by one sample t-test and ANOVA.
Results: A total of 100 subjects were checked having myopia of varying degree (1.00-5.00diopters).The results showed that there was greater degree of myopia in subjects having poor visual hygiene. The results showed that out of 100 subjects, 98 were into the habit of cleaning their glasses before wearing them. Positive relationship between myopia development and reading distance was found. Those who watched TV on daily basis for 3 hours had myopia in the range of -4.25 to -5.0 D. It was also found that most of the subjects study under bright light. Higher degree of myopia was found in subjects who were also computer users. Positive association between posture and myopia development was also found.
Conclusion: The results concludes that poor posture, dim light while studying & excessive use of computer is significantly related to the degradation of naked vision. This data and whole study support the assumption that visual hygiene improvement could be useful in minimizing the myopia development.
Keywords: Visual Hygiene, Myopia, Adults, Posture, Near work.

Introduction

Myopia occurs when distant object focused in front of retina due to eyeball elongation. As a result, the light entering the eye isn't focused correctly and distant objects look blurred it is mostly developed in early adulthood.[1,2]

Generally, nearsightedness first occurs in school-age children. Because the eye continues to grow during childhood, it typically progresses until about age 20. However, nearsightedness may also develop in adults due to visual stress or health conditions.[3]

Myopia can be classified based on cause or degree of severity or age of onset. The exact cause of myopia is still undetermined but two contributing factors are myopic parents and excessive near work. The excessive amount of reading and other close work that we do in our modern society is the REAL cause of acquired myopia.

Lighting while studying play important role in developing myopia, low lighting cause dilation of pupil allowing more light to pass and entire lens receive excessive amount of light rays. Also, lesser accommodation is needed during near work in the presence of brighter illumination. Educated people of modern society use their vision more for near work while studying, office workbooks reading and using computer as compared to illiterate people. Near work Induce Transient Myopia (NITM) is a type of short-term myopia when the far point shifts immediately following a sustained near visual task.[4]

Essentially, the individual's far point of eyes varies with illumination level. Night myopia is mainly caused by dilation of pupils allowing more light to pass resulting in aberration and it finely leads to more myopia. Night myopia has greater effects on younger myopes than elderly. Form deprivation myopia is the type of myopia which occurs when there is limited vision range and illumination or with the use of artificial contact lenses. This type of myopia is considered reversible within short duration of time.

A study in 2008 reveals the relation between myopia and intelligence level. Near work is considered as common cause for myopia so myopic child is more adapted for readings and studies which enhanced intelligence.[5] Authors Parssinen and Lyyra also reveal more myopic progression in subjects using more accommodation than subjects needing less accommodation[6].

Adults use computers almost exclusively. Today, millions of children are using computers every day, at school and at home, for education and recreation. Computer viewing is complicating how children use their eyes in school because these visual skills are not yet fully developed in children, making any near-point activities that much more difficult.[7]

This study examined the posture of young subjects while studying and its relation to the degradation of naked vision. The posture while studying was quantitatively analyzed, along with a comparison made with visual functions. The parameters were:

1. Viewing distance (cm)
2. Neck angle
3. Vertical gaze direction
4. Viewing angle.

A significant relationship arose between the viewing distance and eye accommodation (diopter), near point (cm), viewing angle and neck angle. Based on the results, author concluded that poor posture, particularly decreased neck angle, is significantly related to the degradation of naked vision.[8]

A study was conducted on a large population reading, writing, working on a computer or watching television might be associated with the occurrence of myopia. The obtained results indicate that reading, writing, working on a computer might be associated with the occurrence of myopia among schoolchildren.[9] The prevalence of myopia is higher in the city than in the countryside. One possible explanation for these different rates could be that schoolchildren in the city spends more time reading and writing outside of school compared with children in the countryside. Myopic children in both the city and the countryside spent more time reading and writing compared with non-myopic children. This increased near-work activity may contribute to the prevalence of myopia.[10]

Nearsightedness is a very common vision condition affecting nearly 30 percent of the U.S. population. Some research supports the theory that nearsightedness is hereditary. There is also growing evidence that it is influenced by the visual stress of too much close work.[11]

In Australia, subjects who performed high levels of near work but low levels of outdoor activity had the least hyperopic mean refraction. Furthermore, in an analysis combining the amount of outdoor activity and near work activity spent, children with low outdoor time and high near work were two to three times more likely to be myopic compared to those performing low near work and high outdoor activities.[12]

Children who read continuously for more than 30 min were more likely to develop myopia compared to those who read for <30 min continuously. Meanwhile, children who performed near-work at a distance of <30 cm were 2.5 times more likely to have myopia than those who worked at a longer distance. Similarly, children who spent a longer time reading for pleasure and those who read at a distance closer than 30 cm were more likely have higher myopic refractions.[13]

The purpose of this study was to evaluate the importance of visual hygiene in people aged between 10-15 years. Usually subjects might not be aware of their problem related to poor visual hygiene. This study will help to prevent development of myopia related to bad posture, dim illumination and unawareness of visual hygiene. So, purpose was to find difference in degree of myopia in subjects using good hygienic environment and those who does not care about the importance of visual hygiene.

Methods

This was an institutional based cross section study conducted at College of Ophthalmology and Allied Vision Sciences in the main OPD of Eye Department, Mayo Hospital, Lahore, during the months of July to September 2016. It included selection of research type, target population, sample size, study design of survey, proforma, questionnaire, dummy tables, sampling method, research methodology, organizational issues, pilot study and work plan. Total of 100 subjects of both genders aged between 10-15 years, having Myopia of -1D to -5D were included in the study by using non-probability convenient sampling technique. All the subjects were asked to fill the questionnaire containing questions regarding academic performance with and without spectacles. Data was collected through a self designed questionnaire and analyzed on SPSSS software.

Results

Figure 1 Relationship between cleanliness of spectacles and myopia.

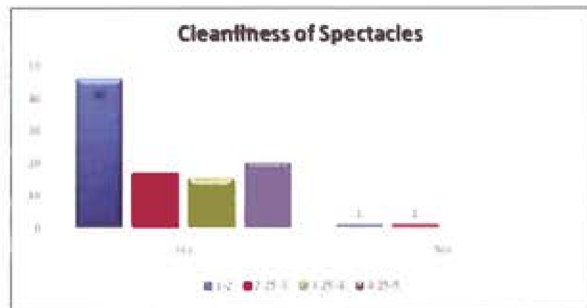

Fig-1: shows that out of 100 subjects, 98(98%) subjects were cleaning spectacles while 2(2%) were not cleaning their spectacles. This also shows that there were 46(46.93%) subjects having myopia 1-2diopters, 17(17.35%) subjects having 2.25-3diopters, 15(15.31%) subjects shows myopia of 3.25-4 and 20(20.49%) subjects were in the range of 4.25-5 diopters.

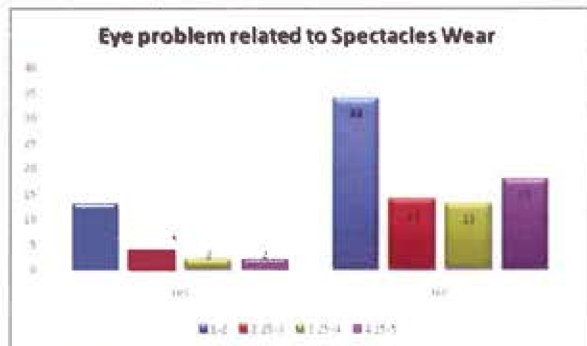

Fig-2: Relationship between eye problems and spectacle wear.

Figure-2 shows that out of total 100 subjects, 21(21%) were having problem (Headache, eyeache, blurring, discomfort) in wearing of spectacles while 79(79%) were not having problem in wearing spectacles. This also shows that there is no significant relationship between the degree of myopia and spectacles wearing problem. ($p>0.05$)

Fig-3: Relationship between reading distance and myopia.

Fig-3 shows that there is positive relationship between myopia development and working distance. This shows that there is greater degree of myopia (4.25-5diopters) in subjects using studying distance <arm length or arm length as compared to those who studied at distance greater than arm length. ($p<0.05$)

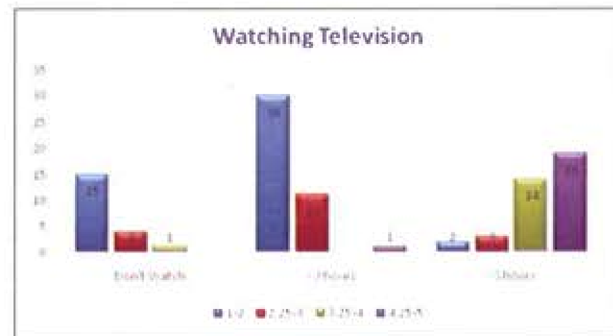

Fig-4: Relationship between watching television and myopia.

Fig-4 shows that out of total 38 subjects having myopia of 4.25-5 diopters, 19 were watching TV more than 3 hours. Greater degree of myopia was present in subjects watching TV more than 3 hours. ($p<0.05$)

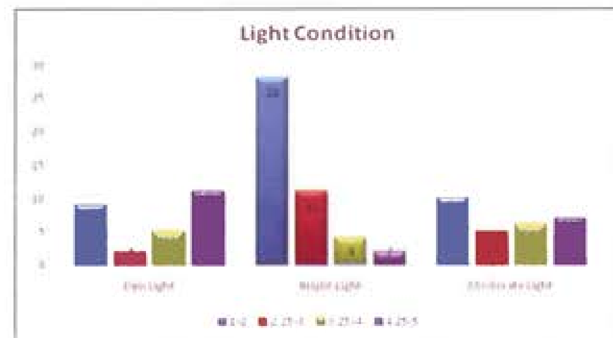

Fig-5: Relationship between light condition and myopia.

Fig-5 shows that the subjects using bright light while studying have low degree of myopia as compared to those subjects using moderate and dim light. ($p<0.05$)

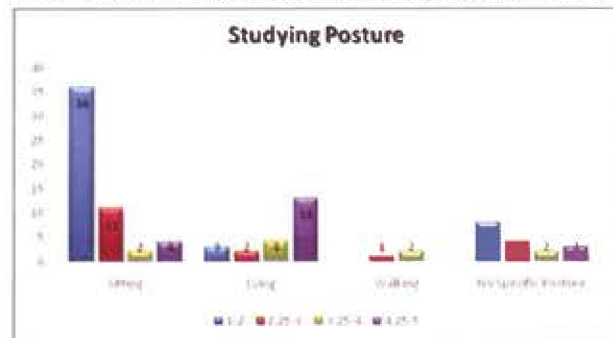

Fig-6: Relationship between study posture and myopia.

Fig-6 shows that out of 19 subjects there were 13

subjects having myopia of 4.25-5diopters using lying posture while studying as compared to those studying with sitting posture, walking and non-specific posture. So the results showed positive association between posture and myopia development. ($p<0.05$)

Discussion

In this study, different variables were included like spectacle cleaning, spectacles wearing eye related problems (headache, eyeache, blurring, Asthenopic sysmptoms), duration of computer and television exposure, illumination level while performing near work, posture adaptation during studying and regular follow ups to ophthalmologist/optometrist after starting spectacles wearing to evaluate the role of visual hygiene in developing myopia.

A total of 100 subjects were checked having myopia of varying degree (1.00-5.00diopters).The results showed that there was greater degree of myopia in subjects having poor visual hygiene. The results showed that out of total 100 subjects, 98(98%) were into the habit of cleaning their glasses before wearing them, positive relationship between myopia development and reading distance was found. Those who watched TV on daily basis for 3 hours had myopia in the range of -4.25 to -5.0 D. It was also found that most of the subjects study under bright light. Higher degree of myopia was found in subjects who were also computer users. Positive association between posture and myopia development was also found.

It is recommended that sitting posture should be erect and comfortable. Avoid reading while lying on your stomach on the floor. Do not sit any closer to TV than 6 to 8 feet, and be sure to sit upright. Maintain good posture. A sloping surface of 20-23 degree tilted from horizontal that makes an optimum angle should be used. Provide for adequate general illumination, as well as good central illumination, at the near task. Long study hours or prolonged use of computer screens can have adverse effect on our eyes so care must be taken in this context. Avoid continuous work for too long time without giving rest to eyes. There should be regular follow ups to know about refractive status and progression of disease.

Conclusion

The study concluded that the significant association of myopia development with posture adaptation in doing near work is because there was greater degree of myopia in subjects having bad posture like lying as compared to those having sitting posture. Similarly the subjects studying in dim light and used computer more than 3 hours were seemed to have high degree of myopia as compared to those subjects using bright/moderate light.

College of Ophthalmology & Allied Vision Sciences,
K E M/Mayo Hospital ,Lahore.
www.esculapio.pk

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Original Article

ANALYSIS OF MATERNAL MORTALITY AT DISTRICT HEADQUARTER, SAHIWAL

Safia Perveen and Hina Ilyas

Objective: The objective of the study was to find the incidence of maternal mortality, and causes of maternal mortality in females presenting in a tertiary care hospital of Sahiwal.
Methods: It is prospective study on 94 females delivered in a tertiary care hospital. All the women admitted in ward and designed proforma filled, which include scrutiny for age, parity, antenatal care, education, residential area and cause of death. Data was entered and analyzed through SPSS version 21.
Results: During the study period, there were 94 maternal deaths out of 3223 live births giving an MMR of 1766-4655/100,000 live births as shown in the table. About 78% cases were un-booked, 92% belongs to rural area, 57% illiterate, 77% were multi -gravidae and 30% deaths were in 30-35 year age group. Hemorrhage was major cause of maternal mortality after eclampsia and then sepsis following hemorrhage.
Conclusion: There is need to stress the importance of good antenatal care in reducing MMR. Focusing on special groups of women with targeted program, such as training, monitoring and supervision of birth attendants.
Key words: Maternal mortality, pregnancy, parity, causes.

Introduction

World health organization defines maternal death as death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the site of pregnancy, from any cause related to or aggravated by pregnancy or its management. Approximately half million woman die every year due to pregnancy and child birth complications. More than three quarter of these women are from Africa, Asia and other developing countries.[1] Millennium declaration, September 2000,outlined the targets to be achieved by 2015.Major sub goals were: reduction of maternal mortality by three quarter between 1990 and 2015 and provision of universal health for women.[2] Measuring maternal mortality is the only way to ensure that its reduction remains at top priority.[3] A woman die due to complications of pregnancy and child birth in 2 minutes. It put the family in disaster and continual of sufferings. Pregnancy and child birth is a normal physiological process. But physiological process always does not culminate in safe delivery.[4] There may be maternal or fetal morbidity or even mortality. Death of the mother is basically results in a 'motherless, family. All that leads to serious consequences for children. There care, education and grooming effected which results in useless and criminal persons for society.[5] Largely the complication which arise during labour and delivery, which cannot be accurately predicted may lead to maternal mortality and morbidity. In developing countries the causes of maternal mortality are haemorrhage, sepsis, hypertensive disorders, obstructed labour and induced abortion. Most of these are caused by avoidable factors. It was men duty to protect women during pregnancy and intervention aimed at increasing male involvement.[6] Major limitation to accessing antenatal care and delivery services are lack of knowledge about ANC , long distance and high transport cost.[7] We can reduce maternal mortality through health education, better understanding, diagnosis and management of pregnancy and labor complication.[8]

Methods

It is prospective analysis of maternal mortality in Obstetrics and Gynaecology department of District headquarter/Teaching hospital from 1st January 2011 to 31st December 2013. All the women admitted in ward and designed proforma filled, which include scrutiny for age, parity, antenatal care, education, residential area and cause of death. Death defined and classified according to WHO international classification of disease, 10th revision (ICD-10). Deaths were classified as direct, indirect or fortuitous. MMR is defined as number of direct and indirect maternal deaths/100,000 live births up to 42days after the termination of pregnancy. Data was entered and analyzed through SPSS version 21. Descriptive statistics was presented for age, mean and SD were calculated and for parity, booking status,

SD were calculated and for parity, booking status, residence education and cause of death were presented as frequency and percentage.

Results

During the study period, there were 94 maternal deaths out of 3223 live births giving an MMR of 1766-4655/100,000 live births as shown in the table. About 78% cases were un-booked, 92% belongs to rural area, 57% illiterate, 77% were multi -gravidae and 30% deaths were in 30-35 year age group. As seen from table 3 analysis of causes of death revealed that Eclampsia is the leading cause, on 2nd number was haemorrhage and sepsis, obstructed labour, ruptured uterus, ruptured ectopic pregnancy and anemia respectively 83% deaths were due to direct causes and 17% deaths were due to indirect causes which were anemia, cardiovascular disorder, tetanus, renal failure, diabetes mellitus and dengue fever. Majority of above mentioned death were due to preventable causes of death provided the treatment instituted in time. Training of medical, nurses, Lady health visitors, health workers and birth attendants working in rural areas by programme like basic emergency obstetric care and gives ray of hope in reducing maternal mortality.

Table-1: Years wise distribution of maternal deaths and live births

Year	Maternal Deaths	Live Births	MMR
2011	46	988	4655.87
2012	25	933	2679.53
2013	23	1302	1761.51

Table-2: Maternal deaths and its Socio-demographic characteristics.

Variable	Characteristic	No of Pts.	Percentage
Age	< 20 Years	07	7.4
	20 - 24 Years	23	24.5
	25 - 29 Years	19	20.2
	30 - 34 Years	29	30.9
	35 of Above	16	17.0
Parity	Primigravida	21	22.3
	Multigravida	73	77.7
Antenatal	Booked	20	21.3
	Unbooked	74	78.7
Residence	Urban	07	7.4
	Rural	87	92.6
Education	Literate	37	39.4
	Illiterate	57	60.6

Table-3: Maternal deaths and its Socio-demographic characteristics.

	Causes	Deaths	Percentage
Direct	Eclampsia	29	30.9
	Hemorrhage	26	27.7
	Sepsis	16	17.0
	Obstructed Labor	03	3.2
	Rapture Uterus	03	3.2
	Ectopic	01	1.1
	Pragnancy	03	3.2
	Anemia	03	3.2
	Jaundice	02	2.1
	Heart Disease	02	2.1
	Tetanus	01	1.1
	Renal Failure	02	2.1
Indirect	CCF	01	1.1
	DM (diabetes mellitus)	02	2.1
	Drug Reaction	01	1.1
	Blood Reaction	01	1.1
	Dengue Fever	01	1.1

Discussion

The MMR in our study is 1766-4655/100,000 live births.It is in accordance with studies from tertiary care hospital, that was371-4268/100,000 live birth. The reason is large number of referred cases. Same situation in our hospital, single facility for referral of critical obstetrical emergencies from Tehsil headquarter, Rural health centre, Basic health units and private sector. About 83% deaths were due to direct causes and 17% were due to indirect causes. Most deaths were observed in multipara with age of 25-35 years and 21-35years in other studies. Most maternal deaths reported in women from rural area (92.4%), unbooked cases (78.7%) illiterate (60.6%) women. All our findings similar to study of Jain M that was (87%), (74%) and (57%) respectively.[9] Nisar N showed high ratio of maternal mortality in women of age 29-39 years.[10] The reason was same in both studies that was rural background, illiteracy and lack of slandered health care.[7] Regarding haemorrhage (27.7%), eclampsia (30.9%), and sepsis (17.0%), our findings were consistent with findings of Bhasker K and colleagues, Jain M, Rehman TT .[9,12] Anisa F found eclampsia and its complications as main cause of maternal death that is consistant with our findings.[13] Most maternal deaths reported in women of rural area (92.4%) in our study. The rural societies need

to address: problems of ignorance, traditional myths and family restrictions on seeking better treatment.[14] MMR dropped from 4655 to 1706/100.000 over three years periods, reasons are up-gradation of hospital as teaching, arrival of highly qualified trained doctors and EMOC training by district government to staff at urban and rural area. The analysis of causes of maternal deaths enables us to formulate strategy for reduction of MMR in our area.[15]

Conclusion

There is need to stress the importance of good antenatal care in reducing MMR. Focusing on special groups of women with targeted program, such training, monitoring and supervision of birth attendants. Adequate training of obstetrical life-saving skills, rising community awareness along with intervention program for improving timely referral and up-gradation of hospitals are suggested.

Department of Obst & Gayne
DHQ/Teaching Hospital, Sahiwal
www.esculapio.pk

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Original Article

GROSS AND FINE MOTORS FUNCTIONAL IMPAIRMENTS IN CHILDREN WITH CEREBRAL PALSY: A CROSS-SECTIONAL STUDY

Ramma Inam, Ehsan Ullah, Naeem Liaqat, Shazia Maqbool, Fouzia Rashid and Saba Aziz

Objective: To assess prevalence of gross and fine motor functional impairments in children with CP.

Methods: This cross sectional study was conducted at Department of Developmental & Behavioural Paediatrics, The Children's Hospital and Institute of Child Health, Lahore from October, 2014 to September, 2015. A total of 100 CP patients were taken to assess for gross and fine motor functional impairment, using Gross Motor Functional Classification System (GMFCS) and Bimanual Fine Motor Function (BFMF) scales. All data were analyzed using SPSS version 20.

Results: In this hospital-based study comprised 100 children with a diagnosis of CP with 2 to 8 years of age were ascertained. The mean age of patients was found as 4.090 ± 1.672 years. Study group included 32 females and 68 males. GMFCS was found at level I in 5% patients, level II in 18% patients, level III in 16% patients, level IV in 15% patients and level V in 46% patients. The corresponding percentages for BFMF were 21.7% patients, 18% patients, 15% patients, 13% patients and 33% respectively. Among oral musculature problems, drooling was the most common problem (68 %). Larger proportion of gross motor functional impairment were associated with the spastic type of cerebral palsy (p=0.03), more specifically quadriplegic cerebral palsy (p=0.000). Also a larger number of patients with fine motor functional impairments were associated with spastic type of cerebral palsy (p=0.009), more precisely quadriplegic cerebral palsy (p=0.000).

Conclusion: It is concluded that quadriplegic spastic CP was the most frequent type that had the worst motor impairment hence making patients functionally dependant in activities of daily livings.

Keywords: cerebral palsy; gross motor; fine motor; impairment.

Introduction

Cerebral Palsy (CP) is a non-progressive movement disorder, which has different types. CP is caused by an abnormality or disruption in brain development, in perinatal, natal or postnatal period.[1,2] Classification of CP depends on movement impairments; topographical and according to severity.[3] CP children along with other problems also usually have motor disturbances.[4] There are two types of motor movements; fine and gross motor movements. To assess functional motor impairments in CP children Gross Motor Functional Classification System (GMFCS)[5] and Bimanual Fine Motor Function (BFMF) have been used, both of these scales use a five-level system that corresponds to the extent of ability and impairment limitation. A higher grade indicates a higher degree of the severity.[6,7] In Pakistan, prevalence data on motor impairments and activity limitations in children with CP has not been available until now. So we planned this study with the objective to find prevalence of fine and gross motor functional impairments in children with CP.

Methods

After obtaining approval from our hospital's ethics committee, we conducted this cross sectional study at Developmental and Behavioral Paediatrics, The Children's Hospital and The Institute of Child Health, Lahore. It was one year study spanning from October, 2014 to September, 2015. We included all the diagnosed cases of CP with age range from 2 year to 8 years presenting to our hospital. Our exclusion criteria included: patients with co-morbidity; patients with other developmental disorders and syndromes for example autism; patients having attention deficient hyperactivity disorder. A total of 100 patients fulfilling these criteria were included in the study. All patients were assessed using GMFCS and BFMF for motor functions among CP patients. Statistical analysis of data was done on Statistical Package for Social Sciences (SPSS) version 20. Mean

and standard deviation were determined for all quantitative variables. Frequency and percentages were used to describe qualitative variables like age, types of CP. GMFCS and BFMF Chi square test was used to determine the relationship of demographic data and motor impairments (gross and fine) among types of cerebral palsy. P-value of ≤ 0.05 was considered statistically significant.

Results

The mean age of patients was found to be 4.090 ± 1.672 years. Of total 100 patients, 68 were males while 32 were females. The most common type of CP was found to be spastic type (79%) followed by athetoid and ataxic types. In spastic type of CP, according to the topographical classification, hemiplegic variety was 13.9% and quadriplegic were 68% of patients. **(Table:-1).** Also we found that the most common type of spinal deformity in patients with CP was lumber lordosis (17%), most common oral musculature problem was drooling of saliva in 39% of children and most common contracture was of hip joint. All these data were summarized in **(Table-2).** When assessed for GMFCS, most of patients were at level V (46%), followed by level II (18%) and level III (16%). Similarly according to BFMF, most of patients were at level V (33%) followed by level I (22%) and level II (18 %). **(Figure: 1).** The association of CP categories with GMFCS and BFMF was also determined. It had been found that larger proportion of gross motor functional impairment were significantly associated with the spastic type of cerebral palsy (p=0.038), more specifically quadriplegic cerebral palsy (p=0.000). Larger ratio of fine motor functional impairments were significantly associated with spastic type of cerebral palsy (p=0.009), more precisely quadriplegic cerebral palsy (p=0.000). **(Table: 3, 4)**

Table-1: Frequency of classification of CP based on movement impairment and topographical classification of cerebral palsy.

Classification of CP based on movement Impairment	
Spastic	79 (79%)
Athetoid	8 (8%)
Ataxic	8 (8%)
Mixed	5 (5%)
Total	100 (100%)
Topographical Classification of Cerebral Palsy	
Hemiplegic	11 (13.9%)
Diplegic	10 (12.7%)
Quadriplegic	54 (68.4%)
Monoplegic	4 (5.1%)
Total	79 (100%)

Table-1: Frequency of classification of CP based on movement impairment and topographical classification of cerebral palsy.

Spinal Deformities in Cerebral Palsy	
No Spinal Deformity	81 (81%)
Scoliosis	1 (1%)
Lumber lordosis	17 (17%)
Both	1(1%)
Total	100
Oral Musculature Problem in Cerebral Palsy	
Having no Problem	25 (25%)
Drooling	39 (39%)
Swallowing Difficulty	7(7%)
Both	29 (29%)
Total	100
Contractures in Cerebral Palsy	
Contracture of elbow flexor	22%
Contracture of knee hip adductors	26%
Contracture of knee flexor	20%
Contracture of flexor of hip	20%
Most Common Deformities in Cerebral Palsy	
Wrist drop/wrist flexion deformity	37%
Elbow flexion deformity	21%
Finger felxion deformity	10%

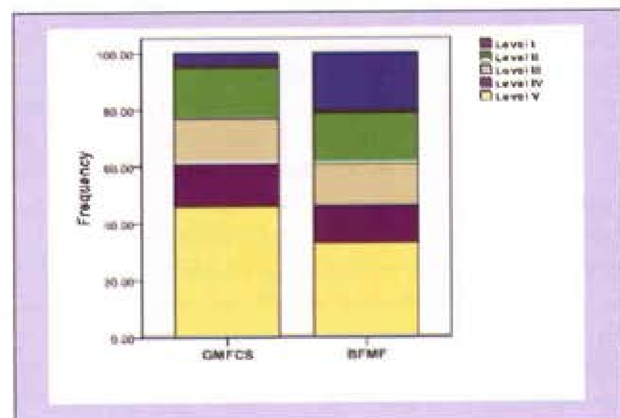

Fig-1: Frequency of GMFCS and BFM levels in CP Pts

Table-3: Relationship of GMFCS levels with classification of cerebral palsy and topographical classification of cerebral palsy.

GMFCS Levels	Classification of CP based on movement impairment				P-value
	Spastic	Athetoid	Ataxic	Mixed	
Level I	3	1	1	0	
Level II	12	2	4	0	
Level III	12	3	1	0	0.038
Level IV	12	1	2	0	
Level V	40	1	0	5	
Total	79	8	8	5	
	Topographical Classification Of Cerebral Palsy				
	Hemiplegic	Diplegic	Quadriplegic	Monoplegic	
Level I	0	0	3	1	
Level II	6	1	5	0	
Level III	5	2	3	2	0.000
Level IV	0	3	8	1	
Level V	0	4	36	0	
Total	11	10	54	5	

Table-4: Relationship of BFMF levels with classification of cerebral palsy and topographical classification of cerebral palsy.

GMFCS Levels	Classification of CP based on movement impairment				P-value
	Spastic	Athetoid	Ataxic	Mixed	
Level I	10	1	6	2	
Level II	15	2	1	0	
Level III	13	3	1	0	0.009
Level IV	10	1	0	2	
Level V	31	1	0	1	
Total	79	8	8	5	
	Topographical Classification Of Cerebral Palsy				
	Hemiplegic	Diplegic	Quadriplegic	Monoplegic	
Level I	0	3	5	2	
Level II	5	5	3	2	
Level III	6	2	5	0	0.000
Level IV	0	0	10	0	
Level V	0	0	31	0	
Total	11	10	54	4	

Discussion

In the present study, GMFCS and BFMF classification levels were documented in 100 CP children. Higher frequency of spastic quadriplegic CP had worst motor functional impairments based on GMFCS & BFMF Levels. These results are closely related to another study which stated that the classification of CP should be based on CP type and motor function, as the two combine to produce an indicator of total impairment load.[8]

The present study in contrast with another study conducted in which the distribution by Gross Motor

Function Classification System (GMFCS) level was: Level I, 50.6%; Level II, 18.2%; Level III, 9.3%; Level IV, 9.7%; Level V, 12.1%. The most common topographical classification was spastic diplegia (38.5%), followed by spastic hemiplegia (34.8%) and spastic quadriplegia (14.6%). Significant difference was that quadriplegic CP was most common spastic type of CP in the present study.[9]

This study reveals that quadriplegic CP was the most frequent type that had worst motor impairment using GMFCS and BFMF levels. Same results were found in another study which states that spastic CP was most common type (80.5%), more specifically bilateral CP (62.5%) was more common than unilateral CP (18%) with respect to Manual Ability Classification System (MACS) and GMFCS levels it was concluded that bilateral spastic CP was the most frequent type that had the worst motor impairment.[10]

In present study, among oral musculature problems, drooling was found to be the most common problem and it was most common in the spastic type of quadriplegic CP. Among spinal deformities, lumber lordosis was found to be highest in frequency. Other deformities were also found to be present mostly among Spastic CP more specifically in quadriplegic CP. Contracture of elbow flexor, hip adductors, knee flexor and flexor of hip were also frequent in spastic type of quadriplegic CP in children.

Conclusion

In our series of paediatrics patients with CP, most of the patients were spastic (79 of 100). Frequency of male patient affected with CP was higher than female patients. More severe GMFCS and BFMF levels correlated with larger proportions of accompanying fine and gross motor impairment. Fine and gross motor functional impairments were more frequently associated with spastic type of CP, more specifically quadriplegic spastic type of CP as compared to any other type of CP with respect to the GMFCS and BFMF Scales.

Depptt. of Developmental & Behavioural Paediatrics, The Children's Hospital and Institute of Child Health, Lahore

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Original Article

POTENTIAL RISK FACTORS FOR CONGENITAL MALFORMATIONS IN NEONATES: A CASE SERIES STUDY IN TWO TERTIARY CARE HOSPITALS OF LAHORE CITY

Najam ud Din, Shahbano Ishfaq, Muhammad Naeem, Malik Shahid Shaukat, Zaheer Iqbal and Zain Safdar

Objective: 1.To Study the potential risk factors for congenital malformations in neonates admitted at two tertiary care hospitals of public sector in Lahore city. 2.To find out the frequency of systems affected in congenital anomalies.

Methods: It was a "case series" study conducted at Children hospital and Services hospital Lahore. All the congenital malformations from 1st April to 30th April, 2013, in neonates admitted in these institutions were included in the study. Mothers of 40 cases of congenital malformations were interviewed after taking verbal consent, using self-administered, pre-tested questionnaire. Data was analyzed by using SPSS version 14.

Results: The frequency of cousin marriages in parents with congenitally malformed children was considerably high i.e. 65%. Majority of mothers i.e. 62.5% were below metric, 87.5% belonged to low income group, 62.5% did not made an increase in diet during pregnancy, 35% suffered from stress during pregnancy and 30% had previous abortion. The number of anomalies of urogenital system and GIT were higher with frequency of 45% and 30% respectively with a cumulative frequency of 75%.

Conclusion: The frequency of congenital malformations was considerably higher among parents with consanguinity, in low income groups, mother's education less than metric and paternal age greater than 30 years. The number of anomalies of urogenital system and GIT were higher in our subjects with frequency of 45% and 30% respectively with a cumulative frequency of 75%.

Keywords: Public hospitals, congenital malformation, congenital anomalies, cousin marriage, stress during pregnancy, diet during pregnancy.

Introduction

Congenital anomaly is a defect at birth and occurs in approximately 5% of babies. Congenital anomalies are categorized in to two groups.[1] First group: Malformations is a primary defect of organ or tissue development in the embryo or fetus. Second group: Deformation is damage caused by external factors influencing previously normal structure. Malformation & deformations occur in a ratio of 3:2.These conditions are important cause in neonatal & prenatal mortality accounting for about 40% of deaths.[2] Congenital malformations affect 2.5% of infants at birth and are responsible for about 15% of perinatal mortality in India.[3,4] In United States in 2013, infant mortality rate was 5.96 infant deaths per 1000 live births and the leading cause of infant death was congenital malformations accounting for 20% of all infant deaths.[5] Birth defects account for 1530% of all pediatric hospitalizations. They exert a proportionately higher health care cost than other hospitalizations and impact a significant burden to families and society.[6] Children with congenital malformations in Egypt, male were more affected than female (1.8:1). According to ICD-10 classification of congenital malformations the system involved in descending order of frequency were nervous system ,chromosomal abnormalities, genital organ anomalies, musculoskeletal system, urinary system, circulatory system, eye ear face and neck anomalies, other congenital malformations, digestive system ,cleft lip and cleft palate anomalies,respiratory System.[7] Congenital Malformations are not rare in Pakistan, studies show that 2.9 to 7% of newborns had various congenital anomalies in Pakistan .[8,9] According to the latest WHO data published in May 2014; congenital anomalies deaths in Pakistan reach 26,353 or 2.34% of total deaths and ranks Pakistan #5 in the world. [10] In many cases, the cause of congenital anomalies is unknown, however, several factors are known to be associated with congenital anomalies including genetic factors i.e. achondroplasia, cystic fibrosis, hemophilia, neural tube defects. Socioeconomic and demographic factors i.e. Low-income may be an indirect determinant of congenital anomalies, with a higher

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frequency among resource-constrained families and countries. It is estimated that about 94% of severe congenital anomalies occur in low- and middle-income countries.[11] Factors often associated with lower-income may induce or increase the incidence of abnormal prenatal development. Dietary factors (Folate insufficiency and excessive vitamin A intake) and poorer access to healthcare may also be indirect determinants of congenital anomalies. Advanced maternal age increases the risk of chromosomal abnormalities, including Down syndrome. Environmental factors i.e. Maternal exposure to certain pesticides and other chemicals, as well as certain medications (thalidomide, streptomycin, tetracycline, phenytoin), alcohol, tobacco and radiation during pregnancy, may increase the risk of having a fetus or neonate affected by congenital anomalies. Maternal infections (rubella, cytomegalovirus, toxoplasmosis, syphilis & exposure to Zika virus) may affect the normal development of an embryo or fetus.[11] Recently, it is assumed that the health effects of maternal stress may include increased risk of certain birth defects.[12] A large number of malformations are incompatible with life and they involve one system or multiple systems of the fetus. Congenital malformations cause mental trauma to the parents since it puts the entire life of child with congenital malformations into jeopardy. The congenital malformations are collectively major health problem and leads to lifelong disabilities in children that compromises the quality of life from the very beginning. In Pakistan very few studies have been conducted so far, the data of this study will contribute to explore the risk factors of congenital malformations and some hypothesis can be generated by this descriptive data.

Methods

The Study Design was a "Case Series" conducted at Neonatal Intensive Care Unit, Surgical Neonatal Intensive Care Unit, Cardiac Intensive Care Unit of Children hospital Lahore and pediatrics department of Services hospital, Lahore, after obtaining written permission from higher authorities of these settings. All neonates with congenital malformations admitted in these institutions during 1st April to 30th April, 2013, were included in the study. Mothers of malformed neonates were interviewed after taking informed consent using self-administered, pre-tested questionnaire. Mothers too sick to give interview were excluded from the study. SPSS computer software version 14 was used for entry, compilation, analysis of the data. The outcome variables were listed as frequencies and proportions.

Results

The results shows that out of 40 subjects, 23(57.5%) mothers having anomalies in their babies, were below 30 years of age while 17(42.5%) were 30 years and above. Overwhelming majority i.e. 37(92.5%) mothers were housewives while only 3(7.5%) were workers. Out of 40 mothers, 25(62.5%) were under matriculation while 15(37.5%) were metric and above. Regarding the age of the fathers, 13(32.5%) fathers were 30 years and below while 27(67.5%) were above 30 years. The frequency is considerable high in age above 30year.Regarding the monthly family income, 35(87.5%) families were up to 3000 and 5(12.5%) were above 3000 rupees. The frequency is considerably high in low income group i.e. rupees 3000 and below and constitutes 87.5 %.Regarding the mode of delivery, out of 40 subjects, 30(75%) mothers had SVD while 10(25%) had C-section. As for as the parity is concern, 14(35%) were prime-para and 26(65%) were multiparous. **Table-1** shows that out of 40 subjects, 14(35%) mothers married outside the family while 15(37.5%) married with paternal relatives and 11(27.5%) married with maternal relatives. The frequency is considerably high for cousin marriage i.e. 65%. Out of 40 subjects in our research, 4(10%) of the siblings of the malformed babies were also congenitally malformed. Out of 40, not a single of mother or father suffered from any congenital malformation and not a single mother was drug addict. Out of 40 subjects, 2(5%) of mothers took anti-allergic, 2(5%) took anti-hypertensive, 7(17.5%) took other drugs and 29(72.5%) did not take any drug at all during pregnancy. Out of 40 mothers, 14(35%) suffered from Psychological stress during pregnancy. Out of 40 subjects, 25(62.5%) of mothers didn't make any increase in diet while just 15(37.5%) made an increase in different sort of diets. Out of 40 mothers, 12(30%) had previous abortion while 28(70%) did not have any abortion previously. Only 1(2.5%) of mother had radiation exposure to X-rays, 4(10%) had other types of radiation exposure and 35(87.5%) did not have any kind of radiation exposure. Out of 40, only 1(2.5%) mother gave the history suggestive of rubella infection during pregnancy while remaining mothers i.e. 39(97.5%) did not give any history suggestive of rubella infection during pregnancy.

Table-1: Frequency distribution of potential risk factors for congenital malformations

Risk Factors	Frequency (n=40)	Percentage
Relation with spouse		
Married outside family	14	35.0
Married with paternal relative	15	37.5
Married with maternal relative	11	27.5
Anomaly in siblings		
Yes	04	10.0
No	36	90.0
Congenital anomaly in parents		
Mother No anomaly	40	100.0
Father no anomaly	40	100.0
Mother's illness		
Diabetes	02	5.0
Hypertension	01	2.5
Any other	07	17.5
None	30	75.0
Addiction in mothers		
None	40	100.0
Drugs taken during pregnancy		
Anti-allergic	02	5.0
Anti-Hypertensive	02	5.0
Any Other	07	17.5
None	29	72.5
Psychological stress during pregnancy		
Yes	14	35.0
No	26	65.0
Diet during pregnancy		
No increase in diet	25	62.5
Yes in meat	03	7.5
Yes in fruits and vegetable	10	25.0
Yes in milk	01	2.5
Yes in vitamins and iron supplements	01	2.5
H/O of previous abortion		
Yes	12	30.0
No	28	70.0
Rediation exposure		
X-ray	01	2.5
Any other	04	10.0
History suggestive of Rubella infection		
Yes	01	2.5
No	39	97.5

Table-2: Frequency of Systems affected in congenital anomalies.

Systemic involment of congenital anomalites	Frequency (n=40)	Percentage
Urogenital anomaly	18	45.4
GIT	12	30.0
CVT	03	7.5
CNS	02	5.0
Facial	05	12.5
Total	04	100.0

Table-2 reveals that out of 40 subjects in our research, 18(45%) of the children showed urogenital anomalies, 12(30%) showed GIT anomalies, 3(7.5%) showed CVS anomalies, 2(5%) showed CNS anomalies and 5(12.5%) showed facial anomalies.

Discussion

In our research women less than 30 years of age have highest prevalence of anomalies i.e. 57.55% which is in contrary to research done by Crone and Shaw in California [13] in which it was stated that, the overall prevalence of all congenital anomalies across the age distribution was shown as a J shape, with pregnant women aged 20-29 years having the lowest prevalence, teenage pregnant women having an intermediate prevalence and pregnant women more than 40 years old having the highest prevalence. Findings of another research done by Seda Ates et al with topic of "Pregnancy Outcome of Multiparous Women Aged over 40 years [14] in which it was found that, less than one tenth of the mothers were adolescence and also less than one tenth were old mothers and the infants of the older mothers showed a higher incidence of stillbirth (5.1% versus 0%), admission to the neonatal intensive care unit (5.1% versus 1.03%), and fetal malformation (3.09% versus 0.8%) than younger mother. The reason may be the difference of sample size, place and socioeconomic status of the populations.

Regarding the paternal age, in our research it was found that fathers with age more than 30 years have higher frequency of abnormal babies i.e. 67.5% which goes in accordance with the research conducted at Cairo University, Tehran[15] which showed that overall there were no differences in the prevalence of malformations as a function of paternal age. However, the prevalence of malformations of extremities and syndromes of multiple systems, as well as Down's syndrome, increased with increasing paternal age which is in accordance. In our study population 62.5% women did not make an increase in diet during

pregnancy which is in accordance with research conducted in Haryana on Prevalence of multiple micronutrient deficiencies amongst pregnant women in a rural area of Haryana[16] in which dietary intake data revealed an inadequate nutrient intake. Over 19% Pregnant women were consuming less than 50% of the recommended calories. The consumption of food groups rich in micronutrients (pulses, vegetables, fruits, nuts and oil seeds, animal foods) was infrequent. In our study 65% of all cases with anomalies have parents with consanguinity which indicates a much higher prevalence of congenital malformations in consanguineous marriage which is in accordance with the research conducted in Kashan[15] shows that among the consanguineous group, 7.0% births had congenital anomalies. Congenital malformations in the non-consanguineous group were 2.0%. Therefore congenital malformations were 3.5 times more common in consanguineous versus non-consanguineous marriages. In our studies it is found that only 5% of mothers having babies with congenital malformations used anti-hypertensive drugs which is in contrast with the research conducted in England by Cooper et al[17] on congenital malformations after first trimester exposure to medicines which shows that Infants with only first-trimester exposure to ACE inhibitors had an increased risk of major congenital malformations (risk ratio, 2.71; 95 percent confidence interval, 1.72 to 4.27) as compared with infants who had no exposure to antihypertensive medications. Among infants with exposure to ACE inhibitors in the first trimester alone, the adjusted proportion with any major congenital malformation was 7.1 %. In comparison with children with no fetal exposure to antihypertensive medications, the risk of major congenital malformations in this group was increased by a factor of more than 2 (risk ratio, 2.71; 95 percent confidence interval, 1.72 to 4.27).

Only 2.5% of the subjects of our study population had history suggestive of rubella infection during pregnancy. Literature shows that Congenital Rubella Syndrome (Congenital defects)) can occur in a developing fetus of a pregnant woman who has contracted rubella, usually in the first trimester. If infection occurs 028 days before conception, the infant has a 43% risk of being affected. If the infection occurs 012 weeks after conception, the risk increases to 51%. If the infection occurs 1326 weeks after conception, the risk is 23% of the infant being affected by the disease. If infection occurs 2640 weeks after conception, Infants are not generally affected.[18]

In our research, 18(45%) of the children showed urogenital anomalies, 12(30%) GIT anomalies, 3(7.5%) CVS anomalies, 2(5%) CNS anomalies and 5(12.5%) facial anomalies, however this finding differs from what was observed in a study done in neonatal unit of Combined Military Hospital, Kharian Cantt Pakistan9 ,where it was found that anomalies related to the central nervous system were 46(20.35%), musculoskeletal 42(18.58%), genitourinary 34 (15.04%), cardiovascular system 30 (13.27%), ear, eye, face, neck 27(11.94%), digestive system 19 (8.40%), syndromes and skin 14 (6.19%) each. This difference may be due to many factors like difference in place of study, nature and size of sample and socioeco- nomic status.

Conclusion

The frequency of congenital malformations was considerably higher among parents with consanguinity, in low income group, under matric mothers, multiparity, paternal age greater than 30 years. Moreover, the frequency of congenital malformation was considerably high among mothers who did not make an increase in diet during pregnancy. The number of anomalies of urogenital system and GIT were considerably higher in our subjects with frequency of 45% and 30% respectively with a cumulative frequency of 75%.It is recommended that cousin marriages should be avoided. Balanced diet should be maintained throughout pregnancy including macronutrients as well as micronutrients. Awareness should be created among target groups through media and High school curricula should include a chapter on congenital anomalies emphasizing on primordial prevention of risk factors to reduce the burden of diseases related to such defects.

Department of Community Medicine
SIMS/Service Hospital, Lahore
www.esculapio.pk

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Answer Picture Quiz

Granulomatosis with polyangitis (wegener's Granulomatosis)

Original Article

SONOGRAPHIC JOURNEY FOR THE DETECTION OF GASTROINTESTINAL MASSES FROM DISTAL ESOPHAGUS TO RECTUM WITH HISTOLOGICAL CORRELATION

Khalid Rehman Yousaf, Salman Atiq, M. Ismail Khalid Yousaf, Qamar Sardar Sheikh, Saleem Shehzad Cheema, Adeela Iqbal, Shazia Muzammil and Zahid Mansoor

Objective: To demonstrate the sonographic features of gut masses detected either incidentally or purposely through the gastrointestinal tract sonography with histological correlation to compare the detected abnormalities for their benign and malignant nature.

Material and Methods: The study was conducted between September 2009 and February 2013. Ultrasound scanning was performed on 72 patients (20-75 years, mean age 46 years) presenting with clinical suspicion of underlying primary gastrointestinal pathology due to abdominal symptoms. The histological confirmation was done either through surgically resected specimen, trucut biopsy, flexible endoscopic biopsy or fine needle aspiration.

Results: Out of 72 patients, upper GI tract masses included 2 distal esophageal and 7gastric cancers. Mid gut included 9 cases of primary small bowel lymphoma. Intussusception was found in 6 patients. Ileoceacal masses were found in 13 patients with one case of jejunal mass. 18 patients were diagnosed as acute appendicitis, 3 patients demonstrated appendicular mass. Large intestine revealed a single case of diverticulitis besides 15 cases of colorectal cancer. The masses were either lobulated or revealed a segmental wall thickening simulating appearance of kidney (Pseudokidney sign), or diffused wall thickening (Target sign).

Conclusion: In our experience, ultrasonography of the gastrointestinal tract is an extremely useful modality for evaluating gut masses from distal esophagus up to rectum. Sonographic appearance ofgut related masses helps to evaluate the clinical differential diagnosis. However, additional work-up may be needed in the form of contrast study, cross-sectional imaging or endoscopy for specifying the diagnosis with histological confirmation.

Keywords: Ultrasonography, gastrointestinal tract, bowel related masses, histology.

Introduction

Transabdominal ultrasound is often the initial imaging modality performed in most of the patients with abdominal pain or vague symptoms related to the gastrointestinal tract. An awareness of the sonographic appearances of intestinal pathology is essential to reach proper diagnosis and to proceed for an appropriate management plan. Pathological processes affecting the gastrointestinal tract generally cause decreased peristaltic activity and gut wall thickening. A commonly held belief is that bowel gas and peristalsis interfere with sonographic evaluation of the intestine.[1] Although this may be true in the normal state, the diseased intestine typically has a thickened wall, a narrowed lumen, and decreased peristalsis, allowing evaluation of the diseased intestine in most patients. Abnormal lesions may appear as fungating mass with eccentrically located bowel lumen (pseudokidney sign) or symmetrical or asymmetrical, encircling thickening of the colonic wall (target sign).[2]

Transabdominal and transpelvicsonography is useful in diagnosing infectious and inflammatory conditions, i.e. acute appendicitis, diverticulitis, inflammatory bowel disease, pseudomembranous colitis, small and large bowel obstruction, bowel related vasculitis, and is particularly helpful for detecting tumors, such as gastric carcinoma, primary bowel lymphoma, and colorectal cancer. Familiarity with sonographic appearances of the above mentioned diseases affecting intestine allows specific diagnosis based on the degree and distribution of bowel wall thickening and associated changes of the surrounding tissues.[3] The purpose of this article was to demonstrate the sonographic features of gut masses detected either incidentally or purposely through the gastrointestinal tract with histological correlation for the confirmation of sonographic diagnosis and to compare the sonographic appearance of different abnormalities of the gut masses to evaluate the role of sonography in their differential diagnosis.

Methods

This cross sectional study was conducted in

Department of Radiology in collaboration with Department of Pathology between September 2009 and February 2013. Ultrasound scanning was performed in the patients with abdominal pain or vague symptoms related to the gastrointestinal tract, referred from the indoors & Out Patient Department of Services Hospital Lahore, with clinical suspicion of underlying primary gastrointestinal pathology. The patients' medical records were reviewed. The study population consisted of 72patients,including 45 men and 27 women, who were 20-75 years old (mean, 46 years old). The diagnosis was confirmed either by histology through surgically ressected specimen, trucut biopsy, flexible endoscopic biopsy or fine needle aspiration.

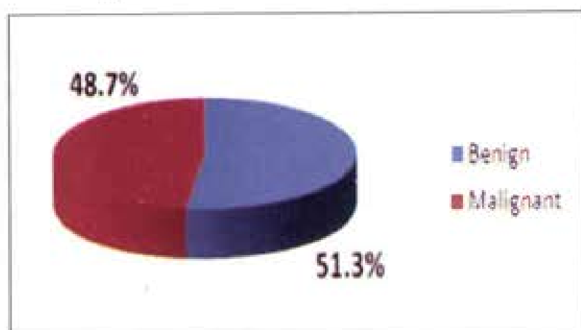

Fig-1: Gut masses percentage distribution according to the benign and malignant histologic features.

Ultrasound Technique and applied parameters:

We performed transabdominalsonography using Toshiba Xario (SSA 660A; Tokyo, Japan). Sonographic scans of the abdomen were usually performed after the clinical examination. The selection of transducer was based on the patient's built; 3.5 MHz curvilinear transducer was used for heavy patients. A high-frequency linear array transducer was used for superficial abnormalities. The large intestine was examined by starting in the right upper quadrant with identification of the ascending colon, recognized by its constancy of position and the presence of haustra, proceeded along the ascending colon to the right lower quadrant, where the cecum was identified as a blind-ending loop of large intestine. The terminal ileum was then identified, and the region of the appendix was examined. Once the right lower quadrant had been adequately assessed, the ascending portion of the colon was followed along the transverse and descending portions of the colon. The sigmoid colon was followed into the pelvis, and the rectum was visualized through the distended urinary bladder. The potential location of small bowel loops was then scanned. Small bowel loops were recognized by the presence of valvulaeconniventes when the lumen was filled with fluid. During ultrasound examination, repositioning of the patient and compression was often performed to optimally visualize the region of interest. Color Doppler was applied to assess flow in the abnormally detected part of gut. The perienteric soft tissues were assessed for the presence of enlarged lymph nodes and for inflammation or infiltration of the perienteric fat by the gut masses.

Normal intestine has a layered appearance and is compressible. It shows intermittent peristalsis. The normal large intestine has a wall thickness of 4 mm or less, whereas the small intestine has a thinner wall 1. The abnormal intestine demonstrated one or more of the following features: increased thickness (>4 mm), loss of the layered appearance, and lack of compressibility 2. Assessment of the degree and distribution of wall thickening was important in determining the underlying cause. When a focal mass was noted, its location relative to the bowel wall was determined and classified in one of the following categories: intraluminal, mural, or exophytic. The perienteric fat, when either inflamed or infiltrated, became hyperechoic and produced a mass effect. Enlarged mesenteric lymph nodes were found more in association with infectious or inflammatory than neoplastic processes.

Table-3: Relationship of GMFCS levels with classification of cerebral palsy and topographical classification of cerebral palsy.

Sonographic detected pathology	No. of Patients (n=72) Male	Female	Total
Distal esophgeal cancers	2	0	2 (2.7%)
Gastric cancers	5	2	7 (9.7%)
Small bowel lymphoma	4	5	9 (12.5%)
Jejunail / Ileoceacal masses	8	6	14 (19.4%)
Intussusception	2	4	6 (8.3%)
Acute appendicitis / appendicular masses	12	6	18 (25%)
Diverticulitis	1	0	1 (2.0%)
Colorectal cancers	11	4	15 (20.8%)

Results

Out of 72 patients, there were 9 patients with upper GI tract masses including 2 cases of distal end esophageal cancer and 7cases of gastric cancer. Small bowel masses included 9 cases of primary small

bowel lymphoma. Intussusception was found in 6 patients. Ileoceacal masses were found in 13 patients with one case of jejunal mass. 18 patients were diagnosed as acute appendicitis out of which 3 patients Demonstrated appendicular mass. Large intestine revealed a single case with diverticulitis besides 15 cases of colorectal cancer detected sonographically. The small and large masses with either bulky lobulations or segmental wall thickening possessed an echogenic center due to air and bowel contents in the lumen or ulcer simulating appearance of kidney demonstrated as "Pseudokidney sign". The diffused wall thickening in uniform pattern with an echogenic center demonstrated "Target sign". The central echogenic clusters were rather small because of narrow lumen. Esophageal tumors involving distal esophageal end, which is intrabdominal part, appeared hypoechoic eccentric or circumferential mural thickening. Esophageal distension proximal to an obstructing tumor was also demonstrated. On histological correlation, 1 out of the 2 cases turned out to be adenocarcinoma of esophagus, while the other was diagnosed as squamous call carcinoma histologically.

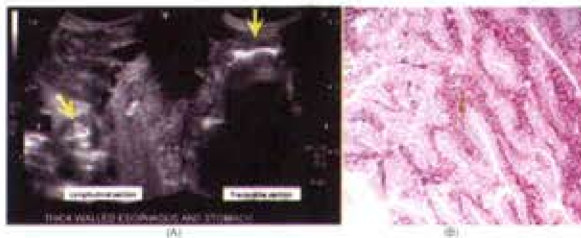

Fig-2:(a)Distal esophageal tumors with hypoechoic eccentric lumen and circumferential mural thickening (longitudinal sonogram) and extension of the tumor in the stomach (transverse sonogram). (b) Histology: Stratified squamous epithelium with underlying stroma glandular structures lined by pleomorphic, hyperchromatic cells consistent with well differentiated adenocarcinoma.

Seven patients with gastric cancer were diagnosed who presented for ultrasound examination due to nonspecific upper abdominal symptoms. Gastric cancer produced a localized or diffuse hypoechoic mass with destruction of the normal layered appearance of the bowel wall. The histological correlation revealed 2 out of 9 cases were of primary stomach lymphoma while all the other cases were adenocarcinoma of the stomach.

We detected 6 cases of intussception, all 6 patients belong to adult age group. 4 cases were ileocolic while 2 wereileoileal intussusceptions confirmed on histological specimen after surgical resection. Ultrasound is the modality which is close to 100% sensitive in detecting intussusceptions. The small bowel mass revealed "doughnut / target / bulls eye sign" on transverse scan with concentric rings of alternating hypoechoic and hyperechoic layers (intussuscipiens) with central hyperechoic portion (mesentery of intussusceptum).

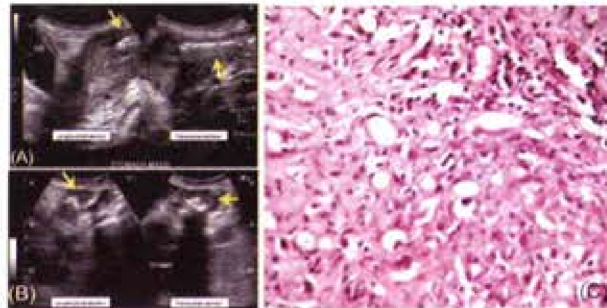

Fig-3: (a & b) Gastric cancer withlocalized/diffuse hypoechoic mass, destruction of the normal layered appearance of the bowel wall (yellow arrows) and an echogenic center due to air. (c) Histology: Poorly differentiated adenocarcinoma of signet ring type.

"Pseudokidney/sandwich/hay fork sign" was demonstrated on longitudinal scan as hypoechoic layers on each side of echogenic center of mesenteric fat peritoneal fluid trapped inside intussusception associated with irreducibility and ischemia. Color Doppler demonstrated mesenteric vessels dragged between entering + returning wall of intussusceptum with absence of blood flow suggested bowel necrosis in two cases. However, flow was demonstrated in one case within intussusceptum considering it a good predictor of reducibility.

Table-2: Gut masses percentage distribution according to the benign and malignant histologic features.

No. of sonographically detected gut masses (N=72)

Histology of Gut Masses

Benign:	*37(51.3%)*	*Malignant:*	*35 (48.7%)*

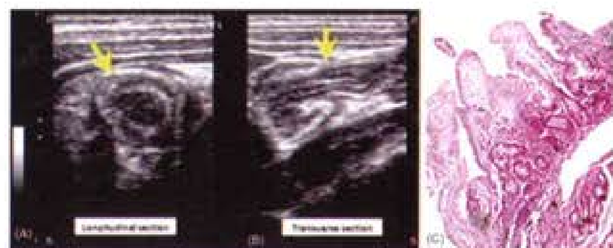

Fig.4: (a) Small bowel mass revealed "doughnut / target / bulls eye sign" with concentric rings of alternating hypoechoic and hyperechoic layers (intussuscipiens) and central hyperechoic portion (mesentery of intussusceptum). "Sandwich sign" was also demonstrated as hypoechoic layers on each side of echogenic center of mesenteric fat. (b) Histology: Small bowel mucosa with normal villous architecture. No dysplasia or malignancy seen.

While through the journey of intestine, we came across a mass at the junction of distal duodenum and proximal jejunum. The mass revealed segmental bowel wall thickening possessing an echogenic center due to air. The appearance was more in keeping with primary small bowel neoplasm, either leiomyoma or lymphoma. Upon histological correlation, it turned out to be a case of intestinal tuberculosis.We found two more cases of ileocecalmass that turned out to be intestinal tuberculosis on histology rather than primary ceacal cancer. Narrowedterminal ileum with thickened ileocecaljunction was demonstrated.

Table-3: Regional distribution of gut masses along with their histology.

Region of the gastrointestinal Tract	Sonographic Diagnosis	Histological Corelation
Distal esophagus	Esophageal cancers (n=2)	Adenocarcinoma (n=1) sequamous cell carcinoma (n=1)
Stomach	Gastric cancers (n=7)	Adenocarcinoma (n=5) Primary lymphoma (n=2)
Small intestine	Lymphoma (n=9) Jejunal /ileocealcal masses (n=14)	B-cell lymphoma (n=9) jejunal tuberculosis (n=1) Ceacaladenocarcimona (n=2) intussusception (n=6)
Large intestine	Appendicitis (n=18) Diverticulosis (n=1) cancers (n=15)	Acute appendicitis (n=15) Complicated appendicitis (n=3) Diverticulitis (n=1) Adenocarcinoma (n=13) Mucinous carcinoma (n=2)

Acute appendicitis was diagnosed in 18 patients on sonographic as well as histological appearances. The sonographic diagnosis was established when a distended (diameter >6 mm), non-compressible aperistaltic appendix was identified. Appendicoliths were present in 2 cases and were seen as echogenic, shadow producing structures within the lumen of the appendix.[4] In acute appendicitis with appendicular mass, the peri-appendiceal fat and mesentary became inflamed and echogenic. When compression was applied, the appendix and the inflamed fat moved as a relatively fixed structure. Color Doppler was useful in demonstrating a hyperemic wall.[5]

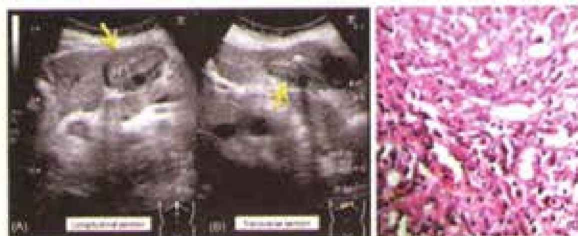

Fig-5: (a) Bulky pyloric tumors adjacent to the left lobe of liverwith segmental wall thickening possessing an echogenic center due to air in the lumen simulating appearance of kidney demonstrated as "Pseudokidney sign".(b) Histology: Poorly differentiated adenocarcinoma of signet ring type.

Diverticulitis was present in one case. Diverticulum was seen as outpouching from the bowel wall and was found in the sigmoid colon. Muscular hypertrophy, inflammation, and edema produced segmental hypoechoic bowel wall thickening.[6]

We found 9 cases of primary gut lymphoma diagnosed on abdominal ultrasound. Most gastrointestinal lymphomas were B-cell tumors on histological correlation and involved the small intestine more commonly than the large intestine.[7] At sonogram, these tumors appearedhypoechoic and showed a variety of growth patterns including circumferential wall thickening as well as nodular or bulky tumor spread. Circumferential involvement was the most common pattern demonstrated.[8] The affected lumen showed aneurysmal dilatation, which is thought to be a result of destruction of the autonomic nerve plexus by the tumor. Lymphadenopathy in the adjacent perienteric structures was also demonstrated.

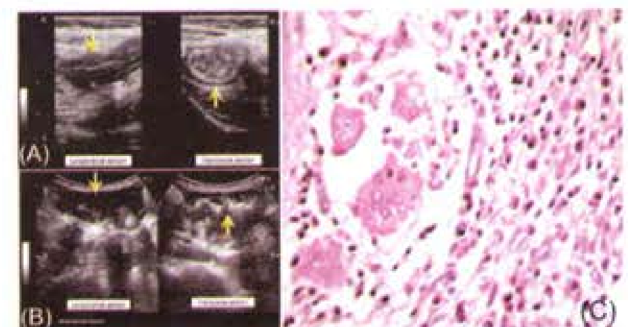

Fig.6: (a) Mass at the junction of distal duodenum

and proximal jejunum revealed segmental wall thickening possessing an echogenic center, appearance more in keeping with primary small bowel neoplasm(leiomyoma or lymphoma). Histologically it turned out to be jejunal tuberculosis. (b). Ileoceacally it turned out to be jejunal tuberculosis. (b). Ileoceacal mass with diffused wall thickening in uniform pattern demonstrating "Target sign". (c) Histology: Poorly formed granulomas with an abscess on the serosal wall of the small bowel suggestive of chronic granulomatous inflammation (intestinal tuberculosis).

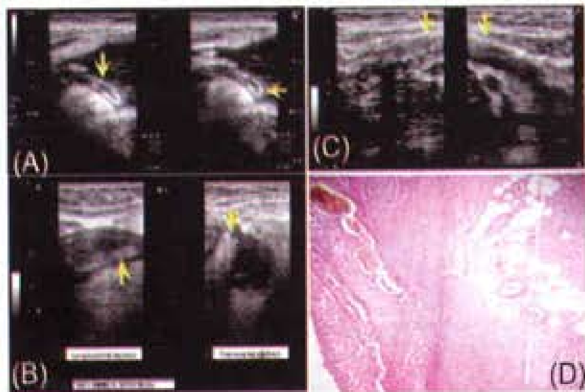

Fig.7: (a) Acutely inflamed appendixdemonstrated as a distended (diameter >6 mm), non-compressible aperistalticstructure. (b). Appendicular mass with thickening of peri-appendiceal fat and mesentary. (c).Acutely inflamed diverticulum with blind ending aperistaltic lumen.(d) Histology: Appendix with ulcerated mucosa with lumen containing inflammatory exudates, submucosa and serosa infiltrated by dense mixture of acute and chronic inflammatory cells, consistent with acute suppurative appendicitis (a) with localized peritonitis (b).

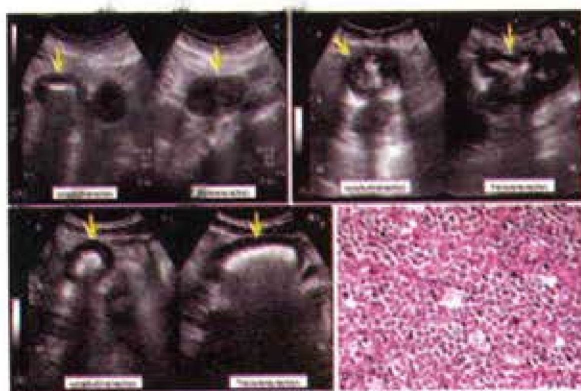

Fig-8: (a, b, c) Small and large masses with bulky lobulations and segmental wall thickening (Pseudokidney sign).(d) Histology: Diffused sheets of neoplatic lymphoid cells, consistent with high grade Non-Hodgkin's lymphoma.

There were 15 cases of colorectal cancers detected on transpelvicsonography. Adenocarcinoma was the most common malignant tumor of the colon on histology, however, 2 cases of mucinous carcinoma were also found. Morphologically, the tumor produced either an annular or polypoid colonic mass. Sonogram revealed an annular tumor that appeared as a hypoechoicmass with central linear echoes, representing the tumor and air in the residual lumen, respectively. Polypoid tumors appeared as focal, irregular colonic wall thickening. An abrupt lossof the normal layered appearance of the bowel wall was typical of a neoplastic process.

Discussion

By virtue of its lack of radiation, noninvasiveness, recent technical advances and cost-effectiveness, sonography is frequently the first examination performed in the evaluation of patients with abdominal complaints and may allow the detection of unexpected tumor within the abdominal cavity.

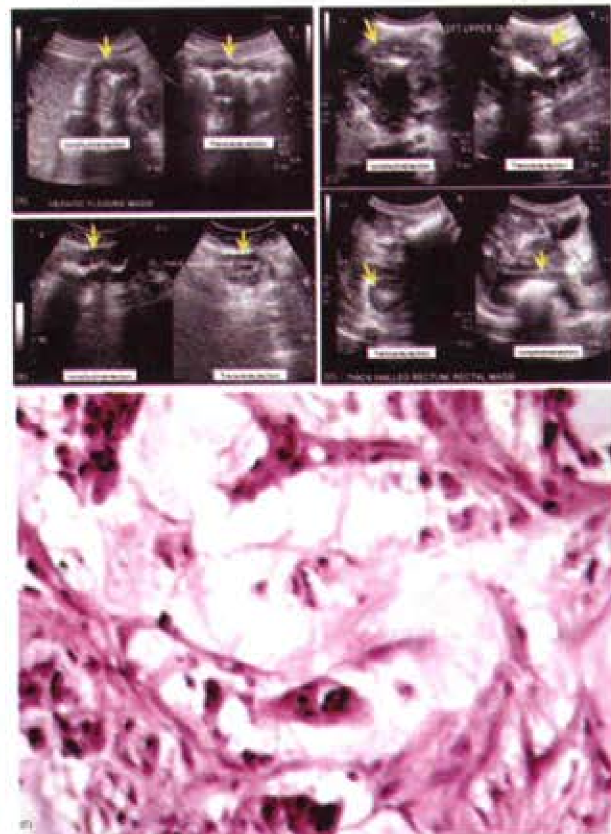

Fig-9: Large bowel including hepatic flexure (a), transverse colon (b), splenic flexure (c) and rectum (d)

revealing variable sized masses with segmental wall thickening, an echogenic center due to air trapping and bowel contents in the lumen is also seen, diffused but uniform bowel wall thickening with an echogenic center (Target sign). (e) Histology: Fragments of tissue infiltrated by malignant epithelial neoplasm composed of glands and sheets of pleomorphic malignant epithelial cells with hyperchromatic vesicular nuclei and prominent nucleoli, suggestive of moderately differentiated adenocarcinoma.

Easiness of sonographic detection of bowel pathology, purposely or unexpectedly, warrants the inclusion of bowel loops during ultrasound examination when a patient complains of symptoms indicating diseases of the bowel. Sonography has become a major diagnostic tool by directly imaging the gut and detecting any perienteric changes. Weundertook this study to systematically assessthe sonographic appearance of different gut related abnormalities to evaluate the role of sonography in their differential diagnosis.[9]

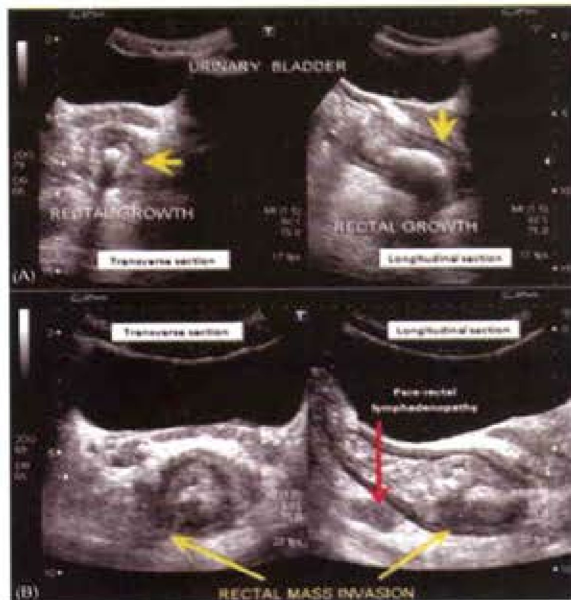

Fig-10: (a) Rectal mass with segmental wall thickening and an echogenic center. (b). Rectal mass with para-rectal invasion and lymphadenopathy suggestive of advanced stage of the disease.

The distribution of gut involvement varied among the diseases examined. Involvement of the left hemicolon in diverticulitis was found in one patient. As expected, a short diseased segment was a significant finding favoring malignant rather than benign conditions. Circumferential involvement was seen in most of the study population. Loss of stratification was found to be significantly more common in malignant conditions than in the benign entities. As shown in previous cross-sectional imaging reports,[10] asymmetric involvement aided in the differentiation of malignant from benign conditions. The association of diverticula with diverticulitis is highly significant. Therefore, diverticula shouldbe sought when evidence suggests segmental thickening of the colon. Not surprisingly, we found almost half of the gut mass related to the large intestine (47%) including appendicular masses, diverticulitis and colorectal cancer. Out of all gut masses we detected sonographically, half of the cases turned out benign histologically (acute appendicitis and complicated appendicitis, diverticulitis, jejunal and ileoceacal tuberculosis and intussusceptions respectively). Adenocarcinoma was the most common malignant tumor involving all gastrointestinal tract except small bowel, in lymphoma was predominant malignancy.

Conclusion

In our experience, ultrasonography of the gastrointestinal tract is extremely useful for evaluation of gut masses from distal esophagus up to rectum. Patients complaining of dysphagia, acute abdominal or nonspecific gastrointestinal symptoms and signs such as abdominal pain, diarrhea, hematochezia, change of bowel habit, or bowel obstruction, should undergo abdominal sonography to reveal the primary causes. Sonographic appearance of gut related masses is often of certain help to evaluate the clinical differential diagnosis. However, in patients with gut mass or bowel wall thickening detected on ultrasonography, additional work-up may be needed in the form of contrast study, cross-sectional imaging or endoscopy for reaching a specific diagnosis followed by histological confirmation.

Department of Radiology
SIMS / Services Hospital, Lahore
www.esculapio.pk

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Original Article

OUTCOME OF SHISH KABAB OSTEOTOMIES FIXED WITH SIGN NAILI IN OSTEOGENESIS IMPERFECTA. OUR EXPERIENCE AT GHURKI TRUST TEACHING HOSPITAL, LAHORE, PAKISTAN

Ashfaq Ahmed, Latif Khan, Muhammad Farrukh Bashir, Saeed Ahmad, Shahzad Javed, Naeem Ahmed, Amer Aziz

Objective: To evaluate the results of shish kabab osteotomies fixed with SIGN NAIL in long bone deformities of patients suffering from osteogenesis imperfecta.

Methods: This study was carried out on 12 patients who presented in OPD or Emergency Department with deformities of long bones. Detailed history, examination and investigations including X-ray AP and Lateral view of involved bone were done. All these cases were treated with Shish Kabab Osteotomies and SIGN NAIL under spinal or general anaesthesia. These cases were followed up for up to average of 20 months (range 06 months -6 years) and results of the nail were observed in terms of union, rehabilitation and complications.

Results: It was found that 8 (66.7%) were male and 4 (33.3%) were females with a mean age of 14.83±5.24. 5 (41.7%) patients having age 10-15 years and 7 (58.3%) were between 16-20 years. Total 21 surgeries performed. 3(25.0%) had surgery on unilateral femur,2 (16.7%) on unilateral tibia, 3(25.0%) on both unilateral tibia and femur,3 (25.0%) had surgery on bilateral tibia and 1(13.3%) with bilateral tibia and femur. The parents of all patients had a first degree consanguineous marriage. The mean hospital stay were 4.17±1.75 days. All osteotomies sites heal within 06 months, better bone densities, 1 Having recurrence of deformity and no fracture were found. Only two patients using walkers while remaining need no support for walking.

Conclusion: Sign Nail along with shish kabab osteotomies in deformities of osteogenesis imperfecta is the treatment of choice. Patient rehabilitation is early, hospitalization is short, and osteotomies site healing response is good as well as decrease risk of fracture.

Keywords: Osteogenesis imperfecta, SIGN Nail, Shish Kabab, Osteotomy.

Introduction

Osteogenesis imperfecta, also known as "brittle bone disease," is a genetic disorder that affects collagen. Worldwide, osteogenesis imperfecta affects approximately 1 of every 20,000 births. In the United States, it affects between 25,000 and 50,000 individuals and is classified as an orphan disease (ie, a disease that affects fewer than 200,000 individuals nationwide).[1] The first recorded case of osteogenesis imperfecta was in a partially mummified body discovered in ancient Egypt, but it was not until 1835 that the term was coined and the disease was truly understood. Lobstein was the first to correctly identify the pathophysiology of the disease and first termed the disorder Lobstein's disease. The name was later changed to osteogenesis imperfecta, which means "imperfect bone formation.".[2] It is a heritable disorder that is characterized by bone fragility and reduced bone mass. Severity varies widely, ranging from a lethal form with intrauterine fractures to a very mild form with no or few fractures and normal growth. Extraskeletal manifestations include blue sclera, dentinogenesis imperfecta, skin and ligament hyperlaxity, and presence of wormian bones within cranial sutures.[3] Since each person/family with OI has their own unique mutation the management of these children must be individualized. [4]Fractures are common in children, and the commonest cause is osteogenesis imperfecta (OI).[5] Diagnosis is usually clinical. History should include attention to fractures, back pain, motor development and family background. Examination should focus on the skeleton, including the spine, and on identifying other features which support the diagnosis, including scleral hue, teeth and ligamentous laxity. Other investigations including plain radiography, transiliac bone biopsy and genetic analysis which may support the diagnosis.[6] The current classification into four major subgroups (types IIV), based on clinical findings, was proposed by Sillence *et al* in 1979. This was based on clinical and radiological findings of OI.[7] Type I includes patients who have the mild form, almost normal stature, and blue sclera. Type II is considered the most severe form and is lethal in the prenatal period. Type III includes patients with the classic disease manifestation, usually with moderate deformity at birth, and progressively deforming bones. Type IV includes patients with extensive phenotypic variability, including mild to severe forms

of OI.[8] It may also be classified as; Osteogenesis Imperfecta Congenita-usually death occur in utero and Osteogenesis Imperfecta Tarda-manifest in childhood or adolescence. Patients with this disorder suffer from brittle bones that may lead to frequent recurrent fractures.[9] It also occur in two forms. The classic clinical forms of OI comprise Lobstein's type and Vrolik's type. The first has a variable symptomatology, with a greater or lesser degree of deformity and onset of fractures during growth and adulthood. The second is a severe form that is observable from birth, with frequent intrauterine fractures and a high mortality rate[10] Management of OI is multidisciplinary. The standard of care includes pain management, therapy input for muscle strength and range of movement, aids to daily living and mobility, psychologic and social support, and regular monitoring of dentition and hearing.[11]

Sofield and Millar introduced the concept of multiple osteotomies and IM rodding to realign bones for children with OI in 1959.[12] This so called 'shish kebab' technique reduced the frequency of fractures and achieved an acceptable correction of deformity of the extremities. Nonexpendable rods such as Rush nails, William's and Kuntscher's rods were used for the 'shish kebab' technique. These rods can be outgrown resulting in angulation and fracture in areas of the bone that are no longer splinted beyond the extremities of the rod.[12] In an effort to solve this problem, Bailey and Dubow designed the first expandable telescopic rod in 1963[13]. As anticipated, the time interval between the initial operation and revision has increased remarkably with the use of this device.[13]

Our goal was early mobilisation of the patient without external support. We therefore planned intramedullary fixation with a SIGN nail and upto best of our knowledge it is the first study in which the SIGN NAIL had been used.

Methods

This prospective study was carried out at Orthopaedics department of Ghurki Trust Teaching Hospital, Lahore from Jan 2009 to July 2016 after the approval by institutional medical ethics committee. A total of 12 patients of either sex and upto age of 20 years with Osteogenesis Imperfecta with lower limb deformities were included in the study while children with upper limbs, spinal, and other extra osseous deformities ,in whom other implants used were excluded from the study. After history, examination , investigations ,pre operative anesthesia fitness and written informed consent ,the patients underwent surgery. The patients were followed on regular basis with mean follow up of 20 months. The longest follow up was of 6 years and the minimum follow up of 6 months and in each follow up, they were clinically and radiologically assessed for fracture healing, joint movements and implant failure. According to the criteria the results are graded as excellent when the fractures unites within 16 weeks. without any complications, good when union occurs within 24 weeks with treatable complications like superficial infection and knee stiffness and poor when union occurs before or after 24 weeks with one or more permanent complications like infection (osteomyelitis), implant failure, non-union, limb shortening and permanent knee stiffness. Delayed union was recorded when the fracture united between three to six months while nonunion was noted when union had not occurred after eight months of treatment. All the patients were given proper regimen of bisphonates according to their weight and duration as advised by the paediatrician. The preoperative and postoperative gait ability was assessed by dividing the patients into two groups of ambulating and no ambulating. All the patients were non ambulatory preoperatively, but after the operation they were being ambulated with support like walker with full weight bearing. The surgical procedure was carried out by using the same technique as described by Sofield and Millar, which consists of exposing long bones and preserving periosteum, performing multiple bone osteotomies between proximal and distal metaphyses using an electric saw, achieving bone straightening. Proper size SIGN Nail were passed with proximal and distal static locking done. The data were initially entered on a pre formed proforma and later on SPSS 17.0 version.

Results

It was found that 8 (66.7%) were male and 4 (33.3%) were females with a mean age of 14.83±5.24. 5 (41.7%) patients having age 10 - 15 years and 7 (58.3%) were between 16-20 years. Total 21 surgeries were performed. 3(25.0%) had surgery on unilateral femur,2 (16.7%) on unilateral tibia, 3(25.0%) on both unilateral tibia and femur,3 (25.0%) had surgery on bilateral tibia and 1(13.3%) with bilateral tibia and femur. The parents of all patients had a first degree consanguineous marriage. The mean hospital stay The average follow up was 20 months (6 months 6 years).

All osteotomies sites heal within 06 months, better bone densities. Overall the results were excellent in 9 patients and good in 3 patients while considering the union. One patient having recurrence of deformity with bending of nail after 3 years but no fracture were found. Only two patients now using walkers because of having generalized weakness and at last follow up ,there ambulation without support were started at physiotherapy department. **(Table-1)** limb.

In the present study, the procedure has been shown not to interfere with physis, because we had no patient with physeal changes.

We didn't find growth disorders inherent to the adopted procedure. length discrepancy were not found in any patient. The children as well as parents were satisfied with their overall progress and improvement in ambulatory status. were 4.17±1.75 days.

Table-1: Summary of the study;

Mean Age		14.83±5.24 years
Average Follow up		20 month (6months-6 years)
Sex	Male n (%)	8 (66.7%)
	Female n (%)	4 (33.3%)
Mean Hospital stay		4.17±1.75 days
Outcome of surgery	Excellent	9 (75.0%)
In term of union	Good	3 (25.0%)
	Poor	0
Ambulatory status	Ambulatory without support	10 (83.33%)
	Ambulation with support	2 (16.67%)

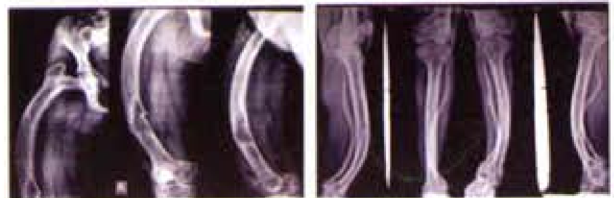

Fig-1a,b: Pre Opp xrays of young female suffering from bilateral tibia and femur deformity.

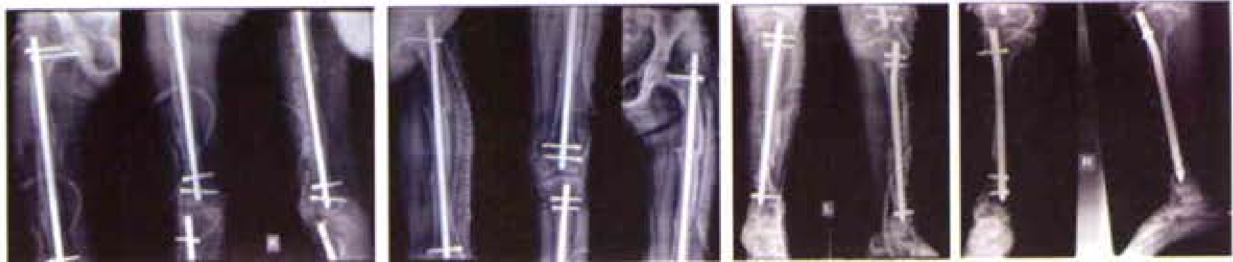

Fig-2 a,b,c; Immediate Post opp x-rays of young female with Shish kabab Osteotomies with SIGN nail in bilateral tibia and femur.

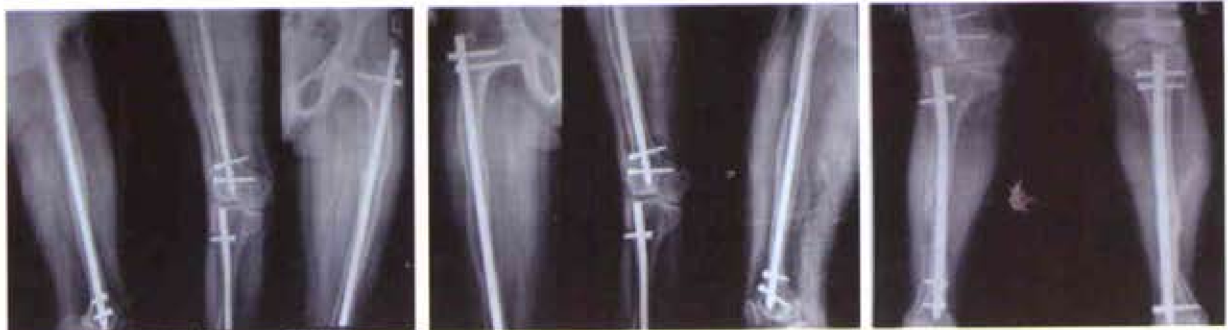

Fig 3 a,b,c; Post opp xrays after 3 months of follow up

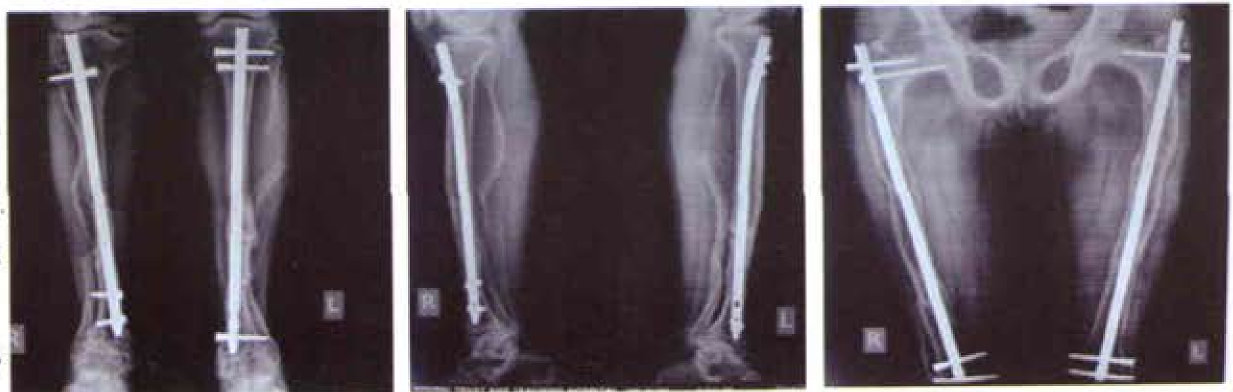

Fig 4 a,b,c: Post opp x-rays after 6 months.

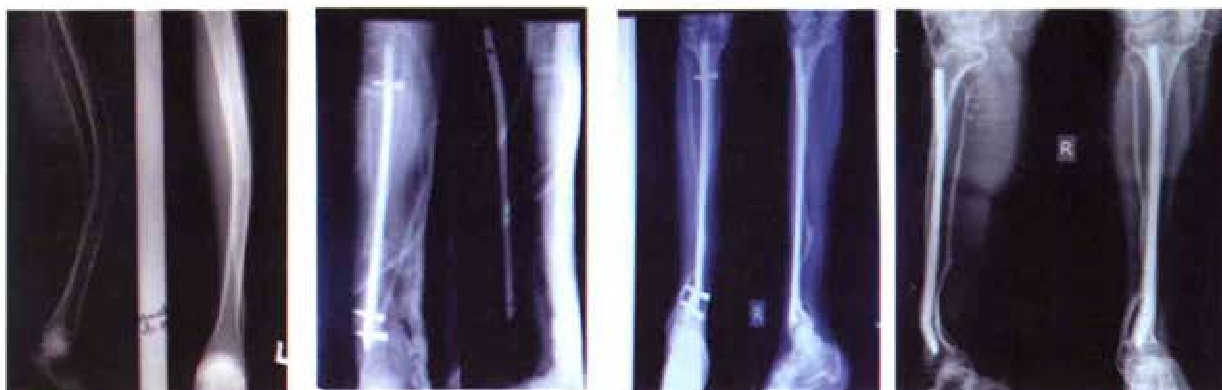

Fig 6 a,b,c ,d; 19 years old male with pre ,immediate post opp, after 3 years and after 6 years xray.Note the bending of SIGN Nail.

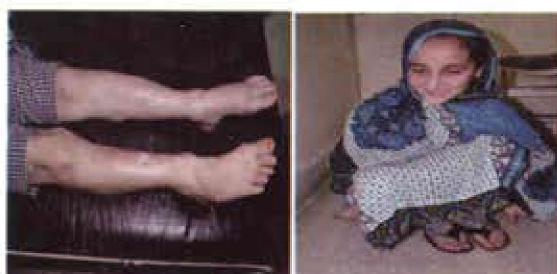

Fig-5 a,b: Post opp follow up images.

Discussion

Conventional management for patients with OI consisted of supplementation with vitamin D and minerals, or administration of bisphosphonates However, these methods did not ameliorate the symptoms of OI .Moreover, in young teenage patients the bisphosphonates cannot be used continuously, because they slow down bone turnover and as consequence child's growth and healing of eventual bone fractures .Another option of supportive treatment of OI patients is surgical and orthopedic intervention or protection with the use of braces, steel rods and other orthopedic equipment .[14] Children and adults with OI will also benefit from maintaining a healthy weight, eating a balanced diet and avoiding activities like smoking or excessive caffeine intake or alcohol consumption or steroid medication. Such things deplete the bone mass making them more fragile and thereby susceptible to fractures.[15] Regarding the surgical management,Intramedullary fixation rather than plating is preferred, and allowing early protected weight bearing and rehabilitation of children with ambulatory potential is the ideal goal.[16] The IM devices are broadly classified into two major categories: the Static rods (Williams' rods and Rush nails) and the telescoping or elongating rods (Sheffield, Baily-Dubow, and Fassier Duval). The choice of IM device is influenced by the clinical features, efficacy of the implant in preventing fractures, the frequency of complications, the technical details of surgery and the cost of the implant. Healing of fractures and osteotomies usually is satisfactory in Osteogenesis imperfecta, although the healed bone may be no stronger than the original.[17] The male to female ratio of OI in our study were 2:1 (8 male and 4 female), indicating that there is gender predilection in OI. Lin et al reported a male to female ratio of 1:2 (15 male and 33 female) [18]. Patel et al [19] showed a 1:1.3 male to female ratio and Plotkin et al [20] reported a 1:0.9 male to female ratio. 4 (33.33%)had a positive family history of a first degree relative with Osteogenesis Imperfecta. Greeley et al reported the presence of family history in 46% of patients OI [21]. Patel et al reported a family history of 40.3% across all types of OI in a 47 cross-sectional multi-centre study [19]. The reason for the reported lower percentage of a positive family history could be attributed to lower level of community awareness and community health care amongst the study population.

The only complication seen in Using SIGN NAIL was bending of nail after 3 years in 1 patient without fracture.However the patient was kept on conservative and after 6 years ,the deformity didn't increase and the nail didn't bend any more.Georgescu et all found the different complications after the implant of the Sheffield telescopic rods i-e 7 external migrations of the obdurate rod, 7 pseudarthroses, 3 fractures with the bending of the rod, 2 fractures with the breaking of the rod, 1 fracture on disengaged rod, 1 case of osteitis of the femur, 1 case of cellulitis, 1 tibia fracture below Dall-Miles plate with hematoma and 1 case with wound .dehiscence.[22] Watzl et all found the following complications with the use of non extensible nails i-e deformity (67%) and fracture (33%).[23] SATVINDER KAUR et all in their mean follow-up of 30 months Found that the using of

intramedullary rods having no recurrence of deformities and better bone densities .[24] Saldanha et all used the monolateral external fixator and illizarov frame over previously inserted intramedullary rods for lengthening and correction of angular deformity but no significant results found.[25] Nicolas Nicolaou et all used the Shieldfield telescoping rods and the complications rate was almost 50%.ten rods (15%) were exchanged because of rod disengagement due to growth, thirteen rods (20%) were exchanged because of complications, and ten rods (15%) required further surgery other than exchange because of complications.[26] G.EL.ADL et all did a comparative study of using telescoping vs non telescoping rod insertion. The reoperation rate was high with non telescoping rods as compared to telescoping group.[27] Similarly Alzahrani et all in their study found the migration of the FD rod while managing the osteogenesis Imperfecta.[28] There are some limitations in our study.First of all the number of patients are less though the follow up is sufficient.Moreover the SIGN Nail is not an extensible nail .We didn't discuss the exchange of nail needed with the growth.So,further study needed which can evaluate more .

Conclusion

The use of SIGN NAIL for the correction of deformity in Osteogenesis Imperfecta is excellent choice.It prevents the implant associated complications like displacement, breakage etc as compared to other intramedullary nailing system. It should always be considered while treating the patients with Osteogenesis Imperfecta. Patient rehabilitation is early, hospitalization is short, and osteotomies site healing response is good .

Department of Orthopaedics and Spine Centre , Ghurki Trust Teaching Hospital ,Lahore

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Original Article

BACTERIOLOGICAL STUDY OF BILE IN PATIENTS WITH CHOLELITHIASIS

Abdul Basit Qureshi, Sajid Mukhtar and Ahmad Raza

Objective: To determine the aerobic microbial flora in bile of patients having cholelithiasis.
Methods: Study included seventy patients of cholelithiasis, out of which 56 (80%) underwent open cholecystectomy, while 14 (20%) were operated by laparoscopic cholecystectomy. Bile for culture was taken per operatively in all patients.
Results: Mean age of patients was 44.17±13.20 and majority of patients were in age group 35-72. Female to male ratio was 3.4:1. Pain in right hypochondrium was major presenting feature in 65 patients (93%). Mean pain duration was 26.21±23.44 months. Bile culture was positive in 25 (36%) patients.13 (62%) culture positive patients were diabetics. Postoperatively 7 patients (10%) developed fever while 4 patients (5.7%) developed wound infection.
Conclusion: SThe frequency of positive bile culture in patients of cholelithiasis was 36%, in this series, commnest organisms being E. coli and Klebsiella. Wound infection 5.7% could have been due to endogenous or exogenous contamination. As all patients who developed wound infection were culture positive in this series, peri-operative antibiotic prophylaxis is recommended in patients undergoing biliary surgery.
Keywords: Gallstones, Open and Laparoscopic Cholecystectomy, Bile Culture.

Introduction

Gallstones are present in about 10-15% of the adult population. Between 1-4% become symptomatic each year.[1] Among the digestive diseases requiring hospitalization, gallstones are the most common.

Bile formation is one of the most sophisticated functions of liver and it is also one of the most readily disturbed. It constitutes the primary pathway for the elimination of bilirubin, excess cholesterol and xenobiotics.[2] when bile leaves the liver; it is composed of water, bile salts, bile pigments, cholesterol and fatty acids.[3]

Gallstones are the most common biliary pathology responsible for more than 95% of biliary tract diseases[4] and is the commonest indication for abdominal surgery.[5] Different factors have been implicated in the causation of gallstones amongst which infection of the bile is also important factor.[6] Inflamed gallbladder has markedly altered permeability, which permits absorption of bile acids and movement of inorganic salts into the gallbladder lumen. The role of excessive cellular debris and increased protein secretion, which occurs in response to inflammation, may be present. Most gallstones are composite in nature. Bacteria can be found in most pure stone (i.e. those whose structure consists more than 90% cholesterol).[7]

The natural history of gallstones is unknown. It is likely that brown pigment stones can evolve in their chemical composition after termination of the infection process that initiate their formation, and may further develop into either mixed or nearly pure cholesterol stones.[7] Gallstones may lead to acute calculus cholecystitis or chronic cholecystitis.[3] Acute cholecystitis is a chemical or bacterial inflammation of the gallbladder. In approximately 95% of patients with acute cholecystitis, stones are present in the gallbladder. Acute cholecystitis is caused by gallbladder outlet obstruction, almost always by a stone.[8] Chronic cholecystitis may follow an acute episode or it may occur primarily without antecedent acute cholecystitis. It is almost always associated with gallstones.[8] Treatment modalities for cholecystitis and gallstones are; laparoscopic cholecystectomy, minicholecyst- ectomy, or conventional open cholecystectomy.[9] Amongst treatment options, laparoscopic cholecyste- ctomy has rapidly become the "gold standard" for uncomplicated symptomatic gallstone disease.[10] Cholecystectomy is a clean contaminated operation according to the surgical wound classification.[3] In about 30% of the patients with cholelithiasis, bacteria can be cultured either from the bile or from the wall of the gallbladder. The biliary infection can be caused by any type of bacteria ranging from aerobic gram positive or gram negative to anaerobic organisms. Aerobic organisms cause 94% of biliary tract infection while anaerobic organisms cause the rest. Bacteria are commonly found in inflamed gallbladder and in patients with cholelithiasis, whereas evidence suggests

Than normal bile is sterile.[6] It is difficult to ascertain that whether bacterial infection of bile arose from stone formation or vice versa. Although the exact contribution of bacteria in lithogenesis is not known, it is important for the clinician to realize that most gallstones are likely to be colonized by bacterial biofilm, even though the bile may be culture negative.[7] so in the treatment of symptomatic gallstone disease (i.e. cholecystectomy) perioperative antibiotics are being given to avoid infective postoperative complications.[9] The aim of study is to determine the presence of aerobic bacteria in patients suffering from chronic cholecystitis as, to effectively treat the biliary tract infections and postoperative wound infections, a comprehensive knowledge of bacteriology of bile is essential.

Methods

This study was done in Department of Surgery Unit I, SIMS Services Hospital Lahore. Seventy admitted patients were selected from Surgical Unit I of Services Hospital Lahore. Diagnosis was made on the basis of history, clinical examination and investigations. Detailed history including recurrent attacks of pain right hypochondrium or pain eipgastrium, episodes of biliary colic, flatulence, dyspepsia, fever, nausea, vomiting, jaundice were recorded. Examination findings including, tachycardia, temperature, jaundice, tenderness in right hypochondrium, Murphy's sign were also recorded. Complete blood count, liver function tests, random blood sugar level, abdominal ultrasonography was carried out. Patients were asked to sign an informed consent. All Patients underwent cholecystectomy, during which bile sample was collected under aseptic measures and sent to Microbiology Department of SIMS Services Hospital, Lahore for aerobic bacterial culture. Wound examination was done on 2nd and 5th day for any type of infection. All that information including bile culture report (positive or negative) was recorded on a Performa.

The collected data was entered and analyzed by using computer program SPSS version 11. The variables to be analyzed were age, gender, symptoms (recurrent attacks of pain right hypochondrium or pain epigastrium, episodes of biliary colic, flatulence, dyspepsia, fever), examination findings (tachycardia, temperature, jaundice, tenderness in right hypochondrium, Murphy's sign) and investigations (complete blood count, liver function tests, random blood sugar level, abdominal ultrasonography and aerobic culture of bile).

Mean and standard deviation was calculated for age and duration of symptoms. Gender, type of symptom, bile infection (whether culture positive or negative), type of aerobic flora (in case of positive culture) were expressed as frequency and percentage. Bile infection and type of aerobic flora (Escherichia coli, Klebsiella, Streptococci, Staphylococci, Pseudomonas, and Proteus) were presented as frequency distribution table.

Results

This study included seventy patients of cholelithiasis. Out of these 56 (80%) patients underwent open cholecystectomy while 14 (20%) patients had laparoscopic cholecystectomy. This study was conducted at Services Hospital Lahore, Surgical Unit-I.

The age of the patients ranged from 12 to 72 years. The mean age of the patients was 44.17±13.20 years. Of these 9 (13%) patients were in the age group between 12-32 years, 35 (50%) patients were in age group between 33-52 years, while18 (26%) patients were in age group between 53-72 years and 8 (11%) patients were in age group 72 years or above.

There were 16 (23%) males and 54 (77%) female patients. Female to male ratio was 3.4:1. Abdominal pain was the major presenting feature which was located in right hypochondrium and/or epigastrium in 65 (93%) patients, 5 (7%) patients had no history of abdominal pain. Pain duration ranged from 1-120 months. The mean of pain duration was - 26.21±23.44 months. Of these 50 (71%) patients had pain duration between 1-30 months, 13 (19%) patients had pain duration between 31-60 months, while 4 (6%) patient had pain duration between 61-90 months and 3 (4%) patients had pain duration between 91-120 months.

Dyspepsia was the next common presenting symptom reported by 47 (67%) patients, while 23 (33%) patients had no dyspepsia. The difference was statistically significant ($p < 0.05$). The nausea was present in 42 (60%) while this complaint was absent in 28 (40%) patients. The difference was not statistically significant ($p > 0.05$). Regarding clinical signs, temperature of patients ranged from 98-101F°. The mean temperature of patients was 98.80±0.70. Of these 59 (84%) patients were in the temperature range between 98-99F°, while 11 (16%) patients were in the temperature range between 100-101F°. Deep tenderness was present in 55 (79%) patients, while 15 (21%) patients had no deep tenderness. The gall bladder was palpable in 2 (3%) patients while 68

(98%) patients had no palpable gallbladder. There were 14 (20%) patients who had single calculus in their gallbladder, while 56 (80%) patients had multiple calculi, as evident by abdominal ultrasonography. Open cholecystectomy was performed in 56 (80%) patients while laparoscopic cholecystectomy was done in 14 (20%) patients. Per operatively increase gallbladder wall thickness was found in 12 (17%) patients, while it was normal in 58 (83%) patients. Bile culture was positive in 25 (36%) of patients, of these 5 (7%) patients were male while 20 (28%) patients were female.45 (64%) patients had negative bile culture, of these 11 (16%) were male patients, while 34 (49%) were female patients.

Table-1: Age distribution of patients (n=70).

Age in years	Frequency	Percentage
12 -32	09	13.0
33 - 52	18	26.0
53 - 72	35	50.0
> 72	08	11.0
Total	70	100.0

Table-2: Distribution of Culture Sensitivity with Sex of Patients (n=70).

Culture Sensitivity	Frequency Percentage	Male Percentage	Female Percentage
Positive	25 (36%)	05 (7%)	20 (28%)
Negative	45 (64%)	11 (16%)	34 (49%)

Table-3: Frequency of Organism in Positive Culture Bile of Patients (n=25)

Culture Type	Frequency	Percentage
E.Coli	10	40.0
Klebsiela	06	24.0
Pseudomonsa	05	20.0
Proteus	02	08.0
Staphaureus	02	08.0

Table-4: Distribution of culture positivity and complications with Sex (n=25).

Culture positive and complications	Sex	
	Male Percentage	Female Percentage
Fever	2 (8%)	5 (20%)
Wound Infection	1 (4%)	3 (12%)
No complications	2 (8%)	12 (48%)

Frequency of organisms in positive bile culture patients showed 10 (40%) E. coli, 6 (24%) Klebsiella, 5 (20%) Pseudomonas, 2 (8%) Proteus and 2 (8%) Staph aureus. 7 (10%) patients suffered from postoperative fever, while 4 (6%) patients got wound infection and 59 (84%) patients had no postoperative complications.

All patients who suffered from fever had positive bile culture, among them 2 (8%) were male patients while 5 (20%) were female patients, 1 (4%) male patient got wound infection and 3 (12%) female patients got wound infection. There were 13 (52%) culture positive patients who were diabetics among them 2 (8%) were male patients and 11 (44%) were female patients, while 12 (48%) patients with positive bile cultures were non-diabetics.

Discussion

Cholecystitis and cholelithiasis are prevalent in certain regions of the world and are quite rare at other places.[13] Hence these are sometimes called South Western American diseases and has been reported in 54% of the adults above 21 years of age.[7] Normal biliary tract and bile is sterile in healthy population, however, bacteria are frequently present in biliary tract disease and may lead to septic complications.[8] A bacterial cause of cholecystitis has been proposed and positive bile cultures have been noted in 46% of patients with acute cholecystitis.[7] In one study from Germany, using molecular genetics methods, bacteria could be found in most pure cholesterol stones (i.e. those whose structure consists of more than 90% cholesterol).[14] It is suggested that bile infection by E. Coli, in addition to bile stasis, plays a crucial role in the pathogenesis of brown pigment stones.[15] Interest has continued to abound in the role of infection in cholelithiasis. Two fallacies, however, exist in this regard. Firstly, the culture of the organism from the bile at the time of the operation does not necessarily indicate a cause effect relationship between the infective micro-organism and lithogenesis, as infection may be secondary to calculous formation. Secondly, the failure to isolate organism from bile also does not indicate that the etiology is unrelated to the infection as it is well known that organisms which have initiated the stone precipitation may not persist in the viable form in the bile till surgery. This study shows that this disease is much more common in females as compared to the males. The mean age incidence in this series is 44 years. Iqbal et al[16] reported maximum number of patients with cholelithiasis between the age of 20-30 years with the highest

incidence in 61-75 years of age. In this series, the positive bile culture was 36%, which is Considerably higher than that reported by Yaqin and Sultan.[17] However, more recently Al-Abbasi et al[18] have reported an incidence of 9%. Harbi[28] reported 25% and Pokharel et al[19] reported 8%. Hazrah et al[20] reported from India that the incidence of bacteria to be very high, ranging from 20 to 80% depending on the kind of gallstone present. The frequency of positive bile culture also differ in acute and chronic calculous cholecystitis. Linhores et al[21] showed positive bile culture in 68% of patients. Karamarkovic et al have showed 79% positive culture in acute and 18% positive culture in chronic cholecystitis.[22] Chang et al[23] have showed 47% positive bile culture in acute and 17% in chronic cholecystitis. Therefore infection is likely to range from 8 to 80% which corroborates with the present finding. E. coli was found to be the commonest organism in this study as has already been reported by previous studies, however, klebsiella was reported by Sabir.[24] In one of the Saudi studies, the most common organism isolated were E. coli (28%). Pseudomonas (9.4%) klebsiella (6.3%) Staph aureus (12.4%).[12] Petakovic et al[25] showed E. Coli (55%) klebsiella and Staphylococcus (10% and 34%). The importance of the predominance of E. coli is seen by the fact that older studies have shown glucuronidase enzymatic activity of E. coli to have a role to play in calcium bilirubinate gallstone formation. The other organisms found in our study were klebsiella, Pseudomonas, Proteus and Staph aureus. These are quite consistent with other series as Ohdan et al showed E. coli, Klebsiella and pseudomonas.[11] The frequency of postoperative wound infection in this study of 5.7% is consistent with study by Sattar et al[7] in 2007 which showed postoperative wound infection of 4.9%. But in his study half of the patients who developed postoperative wound infection were culture positive while half were not. In present study all patients who developed wound infections were culture positive. The low frequency of wound infection in this series may be due to the fact that all the patients were operated electively and had perioperative prophylactic course of antibiotics. According to Rehman and Anson[26] perioperative antibacterial prophylaxis reduces surgical site infections significantly (6% in antibacterial prophylaxis group versus 15% in control group in which no antibiotics were given). The limitations of this study were that antibiotic was injected intravenously, about 10-15 minutes before the bile sample was collected, and therefore it may be argued that the bile sample could have some quantity of the antibiotic. The pus from the infected wound was minimal; therefore role of biliary bacteria in wound infection cannot be concluded. Anaerobic cultures were not included in this study because anaerobes are present in only 6 % of patients with cholelitiasis.

Conclusion

The frequency of positive bile culture in patients of cholelithiasis was 36%, in this series, commonest organisms being E. coli and Klebsiella. Wound infection 5.7% could have been due to endogenous or exogenous contamination. As all patients who developed wound infection were culture positive in this series, peri-operative antibiotic prophylaxis is recommended in patients undergoing biliary surgery.

Department of Surgery
SIMS/Services Hospital, Lahore
www.esculapio.pk

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Medical News

VACCINE CANDIDATE OFFERS PROTECTION FROM ZIKA VIRUS IN ANIMAL TESTS

A newly developed vaccine against Zika virus induces a rapid and long-lived immune response in mice and non-human primates, a Nature paper reports. Although further tests are needed to assess the vaccine's effects on pregnant animals and unborn fetuses, it remains a promising candidate for further development in the global fight against Zika virus.

Drew Weissman and colleagues devised a novel vaccine based on a modified messenger RNA that encodes two different Zika virus proteins. Mice and rhesus macaques given a single, low dose of the vaccine developed neutralizing antibodies against Zika virus within 2 weeks. Critically, the immunity persisted when vaccinated animals were challenged with Zika virus. Mice and macaques remained protected at 5 months and 5 weeks post-vaccination, respectively.

The new vaccine has several potential advantages over previously described alternatives. Delivered by lipid nanoparticles by injection just below the skin, it is easy to administer. Moreover, while some other vaccines require two immunizations with large doses, a single low dose of the new vaccine offers lasting immunity in animal models, potentially making it more cost-effective and scalable (just a single contact with healthcare workers would be needed). Made from mRNA, the vaccine is also non-replicating and cannot integrate into the host genome, easing safety concerns.

Courtesy: medicalnewstoday.com

Case Report

MISPLACED IUCD

S Shazia Haider and Ayesha Irfan

Abstract: The Copper IUCD is a type of long acting reversible contraception. It is also the most effective nonhormonal contraceptive device. These are highly effective with failurerates of less than 1 per 1000 women per year.[1] The T-shaped models with a surface area of 380mm2 of copper have the lowest failure rate. The effectiveness of copper IUCD is comparable to tubal sterilization however the effects of copper IUCD are reversible. It is the second most common method after sterlization.[2] They are suitable for lactating mothers as it has no effect on quality and components of breast milk.[3]

Key words: Failurerates ofless, sterlization.

Case Discussion

Mrs. Safoorah W/o Zabiullah, 28 year, P3+0 with previous I C/Section was admitted on 22-03-2014 through OPD with complaint of oozing from the site of pfannensteil incision scar for last 1-1/2 year. Patient was P3+0 with first 2 SVD and last C/Section 2 year ago. 4 months after C/S she had a multiload insertion from some local center. She developed oozing form the wound of c/section off and on since the surgery. For evaluation, she was admitted in services hospital 1-1/2 year ago and her sinus tract excision was done. The patient, at that time, requested for the removal of copper T and she was told that everything is fine. After excision ofthe sinus tract she was not cured and she kept on visiting doctors and was admitted again on 22-03-2014 with the complaint of discharge from the wound. Her various investigations were carried out.

Lost IUCD is a rare complication. It usually perforates the uterus and is found in the peritoneal cavity. This rare case of misplaced IUCD was in the subcutaneous tissues below the pfannensteil incision. Actually the patient presented P3+0 with (c/section 1-1/2 year back) sinus formation. She was operated one year back and the sinus tract was removed but she did not recover. Again she presented in Services Hospital Lahore with the same complaint of discharge from the wound. Her complete general and local physical examination was carried out and various investigations were carried out. Her general physical examination was unremarkable and on local examination there was purulent discharge oozing from her pfannensteil incision making a sinus tract. On local examination the thread of IUCD was missing. USG report showed that the IUCD lay in between intramural / subfacial plane in longitudinal direction from which a sinus tract was seen extending into skin. Length of sinus tract was 3.5cm. Laparotomy was done, multiload removed from the subcutaneous tissues above the rectus sheath, the sinus tract excised and BTL done. The site of perforation was near the fundus. She was kept on injectible antibiotics and discharged after two days on oral antibiotics. She was called after six days and the stitches were removed. Now there was no oozing from the wound. Actually the sinus previously formed was not healing because of the thread of multiload below the tract of the sinus which was a continuous source of irritation and was not allowing the sinus to heal. Post operatively recovery was uneventful. Investigations; HB: 11.1g/dl, WBC: 08, Platelet: 349, BSR: 115mg/dl

Discussion

Cu- IUCD is the most widely used reversible birth control method. The most recent data indicates that there are 169million IUCD users around the world. In addition to T-shape copper there is U shape copper multiload also present. Perforation of the uterus with IUCDs has been reported. They perforate the uterus and enter into the pelvic cavity. IUCD can be inserted at any time as long as patient is not pregnant and does not have pelvic infection. Usually IUCD is inserted at the 4th or 5th day of menses because the patient is not pregnant and the cervical os is dilated and insertion is easy .The Copper IUCD is a type of long acting reversible contraception. It is one of the most effective forms of contraception.[4] The primary mechanism of action of copper IUCD is to prevent fertilization. Copper acts as natural spermicide in the uterus. The presence of copper increases the level of copper ions, prostaglandings and white blood cells within the uterine tubal fluid.[5] Its primarymechanism of action is contraceptive not abortifacient. A missing string is the first sign of perforation inapproximately 80% of

cases.[6] Primary diagnoses of a "lost string" include: IUCD in situ, unrecognized expulsion, and perforation of the uterus.[7] Very rarely the IUCD can move through the wall of the uterus. Risk of perforation is mostly determined by the skill of practitioner and is 1 per 1000 insertions or less. Although the perforation is rare but it almost always occur during insertion.[8]. Lost IUCD has to be removed because of the risk of adhesions or perforation of organs (bladder or intestine). Most of time lost IUCD is removed from the peritoneal cavity either free or adherent to omentum.
IUCD should be removed if the uterus has perforation.[9] Rarepossibilities include: fragmentation of the IUCD with expulsion of the fragment bearing the string, and migration of a linear IUCD into the uterotubal junction.[10] Cases of invasion of cu-T into bladder have been reported. Very few cases of even stone formation over copper T in the bladder have also been reported. This is a very rare case in which the multiload has invaded through the rectus sheath and entered into subcutaneous tissue below the pfannensteil incision.

Department of Obst& Gayne
SIMS / Service Hospital, Lahore
www.esculapio.pk

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