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Address for correspondence:

Prof. Abdul Aziz, Executive Editor JSP
College of Physicians and Surgeons Pakistan,
7th Central Street, DHA, Karachi-75500
Ph: 5881222, 5892801. Ext: 301
E-mail: jspinternational@hotmail.com
jspinternational@yahoo.com

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#### EDITORIAL:

# SURGICAL TRAINING AT SECONDARY CARE HOSPITALS

With the advent of newer technologies the medical profession is also very rapidly advancing. These advancement and innovation are very help full and supporting in providing medical care to the society; but there limitation to this development of these technologies and one should not forget the value and importance of manpower of training.

For the development of medical human resource the need for identification of additional slots for training especially in surgery is the need of today filled by providing training. This void can be at secondary level teaching institution. To achieve the objective this will need upgradation of such identified units and posting of qualified Supervisors approved by relevant authorities. This can be done in the public as well as private sector hospitals and these institutes can be affiliated with medical schools and colleges. The trainers may be designated as tutors, assistant, associate or full professors according to their experience and laiddown criteria. If a six months or a year rotational program is made for the trainees in and trainee nearby secondary care centers, it will further improve patient care and training there measures towards teaching & training will create more job for the qualified consultants better and supervisors training, teaching material and better opportunities required hand on learning.

Private sector can also take the extra workload training if they fulfill the requirements and the criteria laid down for the training purpose, Trainees will benefit both by improved educational environment availability of patients.

In short secondary level medical institutions can provide extra slots for training, more appropriate job facilities for consultants' trainees and patients with little help from the authorities much can be achieved if serious efforts are made in this endeavor.

PROF. ABDUL AZIZ

### LAPAROSCOPIC EVALUATION OF **ENDOMETRIOSIS**

MUNAWAR HUSSAIN, MAIMOONA ASHRAF, TAHIRA JABEEN, AYESHA KAMAL NASIR,

#### HALEEMA YASMIN AND KHURSHID NOORANI.

#### ABSTRACT **Objective**

To find out number of cases with endometriosis. its relationship with age, parity and socioeconomic condition and to document its different stages.

#### Design

An observational study.

#### Place & Duration

Study was conducted in the Department of Obstetrics and Gynaecology, Jinnah Postgraduate Medical Centre Karachi, over four years period from 1st January 2000 to 31st December 2003.

#### Subject And Methods

Three hundred diagnostic laparoscopies were performed in patients with various clinical presentations such as chronic pelvic pain, dysmenorrhea, dyspareunia, infertility and menstrual irregularities to find out those due to endometriosis.

#### Results

Forty cases of endometriosis were diagnosed at laparoscopy. Majority (75%) of the patients with endometriosis were between 20-30 years of age. Endometriosis was more common in infertile as compared to fertile ladies. As JPMC is a tertiary care public sector hospital providing services to relatively poor class of patients, all the cases of endometriosis were found in lower socio economic class. Ten cases (25%) of endometriosis were in stage-I, fifteen cases (37.5%) in stage-II while there were 5 and 10 cases in stage III & IV respectively.

#### Conclusion

Endometriosis is not an uncommon gynecological problem and is commonly found in young and reproductive age group, of patients. Laparoscopy being a minimally invasive procedure requiring minimum time of hospitalization and minor post-operative discomfort is invaluable in diagnosis of endometriosis.

**KEY WORDS:** Endometriosis, Laparoscopy, Chronic pelvic pain and Infertility, Dysmenorrhoea.

Correspondence: Dr. Maimoona Ashraf, Assistant Professor, Department Obstetrics & Gynecology, Ward 8, J.P.M.C., Karachi.

#### INTRODUCTION

Endometriosis is a chronic and progressive disease that affects 10% of the women of reproductive age. Its etiology remains unknown however, factors such as retrograde menstruation, heredity, impaired immune functions and \_environmental toxins implicated.1 have been

Endometriosis have variable incidence and between 10-25% of women presenting with gynaecological symptoms in UK and USA have endometriosis. These figures are based on the findings of patients who had undergone laparotomy or laparoscopy for diagnostic indications e.g. pelvic pain or infertility.<sup>2</sup> Endometriosis was diagnosed at laparoscopy as the principal cause of pain in women presented with chronic pelvic pain.<sup>3</sup> Of the women having endometriosis, 90% are between the age of 20-50 years and the diagnosis of endometriosis in teenagers is increasing with the demand for investigation of pelvic pain. The youngest recorded case is of a 10 years old girl and oldest of a 76 years old women.<sup>4</sup>

The prevalence of endometriosis may be much higher than expected due to unpredictable clinical nature of the disease. Women may be completely asymptomatic though they may be affected from minimal to severe form of the disease, as reported by Asma et al.5 There is no specific geographical or social class distribution of the disease. It was found to be equally prevalent among all social classes and equally occurring in women of UK and USA.<sup>6,7</sup> Laparoscopy is used not only to diagnose the disease but also plays a significant role in its management and is the mainstay of diagnosing endometriosis and infertility with a small number of complications however. transvaginal ultrasound and magnetic resonance imaging (MRI) can be supplementry. 1.8.9 The past two decades have witnessed rapid progress and technological advances in laparoscopy. The use of high resolution, lightweight video cameras in operative laparoscope has facilitated the visibility of pelvis.10

This study was conducted to determine the frequency, relation to age, parity, socioeconomic class and to document the stages of endometriosis.

#### **PATIENTS AND METHODS**

This was an observational study, conducted over four years period from 1st January 2000 to 31st December 2003 at Jinnah Postgraduate Medical Centre (JPMC) Karachi Pakistan. A total of 300 laparoscopies were performed during this period. JPMC being a public sector tertiary care hospital mostly providing services to patients belonging to poor socioeconomic class who come here for treatment from different parts of country. Patients included in the study were between 20-40 years of age, with complains of chronic pelvic pain, dysmenorrhea, dyspareunia, primary or secondary infertility, menorrhagia or other menstrual problems. Diagnosed cases of endometriosis, patients of acute pelvic inflammatory disease and patients not willing or not fit for laparoscopy were excluded.

For the quantitative data the descriptive statistics of mean and standard deviation were calculated and represented as mean  $\pm$  S.D. The percentages of various pathologies were also represented by their 95% confidence interval.

All the patients were fully evaluated before laparoscopy by taking detailed history inquiring about the presenting history, medical, surgical and socioeconomic history. Economic status of the patients was determined by inquiring their monthly income. The Hb%, urine analysis, blood group and Rh factor and blood sugar random were checked. Additional investigations' like husband's semen analysis, serum FSH, LH and progesterone were checked in infertile patients.

Laparoscopy (Karl Storz 10 mm diameter) was performed in lithotomy position after observing all aseptic measures. During laparoscopy biopsies were taken from areas suspected of endometriosis. Characteristically endometriotic lesions look like "powder burn" which results from tissue bleeding and retention of blood pigment producing a brown / black discoloration of the tissues. Early lesions may appear pink, red and hemorrhagic. A chocolate cyst of the ovary was suspected when there was an ovarian cyst adherent to pelvic side walls and/or to posterior broad ligament and a characteristic tarry, thick chocolate colored fluid content.

On histopathology, characteristic findings of endometriosis were noted which consist of endometrial glands and stroma with or without haemosiderin-laden macrophages.

Staging of endometriosis was done according to the revised guidelines of American Fertility Society. Disease was staged as mild, moderate and severe by checking site, size and number of endometriotic lesions and also by checking the presence or absence of pelvic adhesions.

#### **RESULTS**

Three hundred laparoscopies were performed due to various clinical presentations. Endometriosis was found in 40 patients, (13.3%). Results in relation to parity of the patients and endometriosis revealed that it was more common in infertile as compared to fertile ladies. Out of forty cases of endometriosis. 15 (37.5%) were found in nulliparous (patients of primary infertility) followed by 10 cases (25%) in Para 1-2 group (these patients presented with complaint of secondary infertility), and the remaining 15 (37.5%) cases were found in Para 3-4 group of ladies. Clinically, 15 (37.5%) out of forty cases of endometriosis presented with history of chronic pelvic pain and the remaining 25 (65.5%) patients presented either with history of primary infertility (37.5%) or secondary infertility (25%). Table number I shows relation of endometriosis with age of patients.

| TABLE-I      | FREQUENCY OF ENDOMETRIOSIS AMONG      |
|--------------|---------------------------------------|
|              | DIFFERENT AGE GROUPS                  |
| Age in Years | No. Of Cases Of Cumulative            |
|              | Endometriosis frequency               |
| 20-25        | (n=40) (%)                            |
|              | 3/.3<br>                              |
| 26-30        | · · · · · · · · · · · · · · · · · · · |
| 31-35        | 5                                     |
|              |                                       |

All the cases of endometriosis were found in poor class of patients. Staging of endometriosis was done according to the revised guidelines of American Fertility Society and 10 (25%) patients were in stage I, 15 (37.5%) in stage II, 5 (12.55%) in stage III and remaining 10 (25.5%) patients were in stage IV.

There were no major intraoperative and postoperative laparoscopic complications except, minor postoperative pyrexia and pain in 20 patients and laparoscopic trocar site infection in 10 patients.

#### DISCUSSION

Endometriosis is called as medical enigma. The disease has very unpredictable clinical behavior. Therefore, diagnosis of endometriosis requires careful interpretation of objective surgical and pathological findings in context of patient's clinical presentation. Diagnosis is confirmed or refuted by laparoscopy, preferably performed in conjunction with histological evaluation of exercised lesions."

In the present study the frequency of the disease was found to be 13.3%, which is comparable with other studies conducted locally and internationally. Endometriosis was found in 12.5% laparoscopies in a study conducted by Mehmood Aleem in Faisalabad¹² while it was found in 10% women of UK and 25% to 38% in USA.²¹³ All patients in this study were in reproductive years of age with mean age of 27.75  $\pm$  5.13 years. The results in relation to age confirmed the fact that endometriosis is a disease of young and reproductive age, confirming hormonal responsiveness of the disease.

Among 40 cases of endometriosis, 15 (37.5%) patients presented with complaint of chronic pelvic pain and remaining 25 (63.5%) presented with history of infertility (fifteen patients of primary and 10 of secondary infertility). These results are comparable with results of different national and international studies that showed that disease is more prevalent in patients who presented with complaint of infertility or chronic pelvic pain. 13,14 This also showed that infertility and chronic pelvic pain were common problems for which women seeked medical advice and were subjected to laparoscopy and there are more chances of diagnosing the disease. However results of present study can not be generalized due to small number of study sample and moreover only those patients were studied who were suspected to have endometriosis on clinical presentation. As endometriosis has unpredictable clinical behavior, this fact may have introduced an element of bias in present study.

Analysis of endometriosis in relation to parity revealed that it was more common in infertile as compared to the parous ladies. Results of present study regarding relationship of endometriosis to parity are comparable with the study conducted by Sangi etal<sup>15</sup>, which revealed higher incidence of endometriosis in infertile and lower in fertile women.

Contrary to the previously held belief that endometriosis is more common in rich as compared to the poor ladies, studies conducted in Asia and in western countries have shown that it is equally prevalent in both classes of the patients<sup>6,7</sup> and the results of present study also demonstrated the above mentioned fact. In the present study laparoscopy was performed to stage the extent of endometriosis as well, by adding points for different findings like, presence of adhesions and obliteration of pouch of Douglas.

#### Conclusion

In conclusion, results of present study showed that endometriosis is a common gynaecological problem and is commonly found in young and reproductive age group of patients. Laparoscopy being a minimally invasive procedure requiring minimum time of hospitalization and minor post-operative discomfort is invaluable in diagnosis of endometriosis.

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## LEVELING WITH CONTINUOUS ARCHWIRES AND ITS EFFECT ON MANDIBULAR ARCH LENGTH IN EXTRACTION AND NON-EXTRACTION CASES

AMBREEN AFZAL, IMTIAZ AHMED AND S.A RAUF SHAH

ABSTRACT **Objective** 

> To compare the mandibular arch length changes during leveling of curve of Spee in extraction and non-extraction cases.

Study Design

Quasi-experimental, interventional.

Setting

Orthodontic department, Karachi Medical & Dental College

Subjects

Forty cases were divided into extraction and non-extraction group.

Methods

Depth of curve of Spee and arch length were measured on 40 pretreatment and post-treatment plaster models with the help of sharpened Boley gauge.

Results

The arch length proved to be significantly different (P< .022) between

extraction and non-extraction cases.

Conclusion

During leveling of curve of Spee the mandibular arch length in nonextraction cases significantly increased than in extraction cases.

KEY WORDS:-

Arch length; Curve of Spee and Leveling.

#### INTRODUCTION

Correction of deep bite is a major task of orthodontic treatment. The decision to proper cant and level of the occlusal plane should not be determined as an accident of mechanics but should be carefully evaluated at the beginning of treatment. It is still common in orthodontic

Correspondence: Dr. Ambreen Afzal, Associate professor, Orthodontics Department, Karachi Medical And Dental College, Karachi.

practice that correction of deep bite is determined by the use of different type of mechanics, rather than the nature of discrepancy.1

The curve of Spee was first described by F. Graf Von Spee in 1890.2 Clinically, the curve of Spee is determined by the distal marginal ridges of the most posterior teeth in the arch and the incisal edges of the central incisors.3

When a flat round or rectangular arch wire, or one with an incorporated reverse curve of Spee, is placed on the lower arch, the usual response is that the lower bicuspids are extruded, the lower molars uprighted (tipped back)

and the lower incisors tipped forward. In orthodontic offices leveling the curve of Spee is an everyday practice. Many authors have suggested that leveling requires additional arch length. Braun et al<sup>4</sup> and Baldrige<sup>5</sup>, each found a linear relationship between arch circumference and the amount of leveling. They concluded a ratio somewhat less than 1:1 between the depth of the curve of Spee and the amount of arch circumference needed to level the curve. In contrast, Germane et al<sup>6</sup> accepted a nonlinear relationship between the both variables. Woods<sup>7</sup> considered the lower incisors a separate segment that can be intruded or extruded independently of buccal segments. Therefore, arch length is not necessarily increased during leveling of the curve of Spee as long as the leveling is achieved through anterior teeth intrusion.

AlQabandi<sup>8</sup> compared the effect of rectangular and round arch wires (continuous arch wires) in leveling the curve of Spee and he concluded that in both the wires, the lower incisors proclined with uncontrolled tipping that can probably be attributed to the intrusive force introduced by the arch wire being labial to the center of resistance of the lower incisors.

Leveling out the curve of Spee always requires more space. According to Proffit and Ackerman<sup>9</sup>, "Without extraction, the incisors will be thrown forward as the arch is leveled; with extraction, some of the extraction space will be closed as the arch is leveled out. A guide for planning purposes is that approximately 0.75 mm of additional arch length is required for each millimeter of vertical leveling if the total arch including the second molars is leveled; 0.25 mm is needed for each millimeter if the second molars are not leveled."

Woods<sup>7</sup> suggested, if lower incisors must not be tipped forward and extractions are not required for other reasons, then the lower incisors should not be included in a continuous archwire as long as deep curve of Spee remains. In such cases leveling can be achieved with segmented arch mechanics. If teeth must be extracted because of severe crowding, then the mechanics should encourage significant molar and premolar extrusion. This may only compensate for the loss of vertical dimension because of the forward movement of the posterior teeth.

#### **PATIENTS AND METHODS**

This research work conducted in the department of orthodontics at Karachi Medical and Dental college, Karachi. The study was completed in 2 years. Forty patients were selected for this research. Sample included 23 female and 17 male patients. The patients were divided into two groups on the basis of treatment. The 24 cases were in extraction group and 16 cases in non-extraction group. Non-probability, convenient sampling technique was used.

#### Inclusion Criteria:

· Deep bite patients.

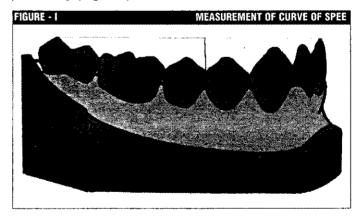
- · Patient with minimal crowding.
- · No previous orthodontic treatment.
- All the permanent teeth should be erupted except third molars.

#### Exclusion criteria:

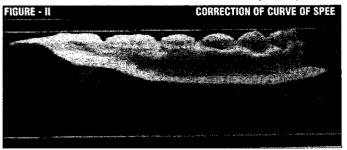
- · Young patients with deciduous teeth.
- Patient with asymmetrical arch form.
- Patients with multiple extractions.
- Patient with any systemic diseases or developmental defects.

Cast measurement was made directly on the dental cast by a single examiner with a sharpened Boley gauge and metric scale. The pretreatment (before leveling) and post-treatment (after leveling) differences in the arch length were measured in extraction and non-extraction cases.

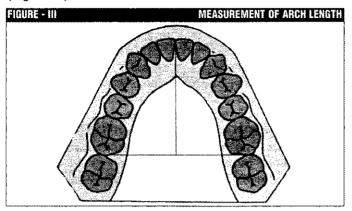
The treatment of the selected patient was started with the nickel- titanium 0.016 to 0.20 arch wires for alignment. The first impression of the arches for the study was taken with alginate after alignment and poured with orthodontic plaster. A custom made reverse curve of Spee was given in a 0.016 / 0.018 stainless steel round wire for the leveling of mandibular arch. After the completion of the leveling procedure, the second impression was taken by the same method given above. The curve of Spee was recorded by summing the right and left side maximum depths from a flat plane formed by the tips of mandibular incisors anteriorly and distal cusp tips of the second molar posteriorly (Figure I).



The correction of curve of Spee was measured as the distance from the tip of the buccal cusps of first premolar to a line connecting the tip of the distobuccal cusp of mandibular molar with the incisal edge of the lower central incisors and that line should be almost straight (Figure II).



The arch length was measured as the shortest distance from a line connecting the distal surface of the first molars to the labial surface of the most anterior tooth in the arch (Figure III).



Using the Student's t-test the hypothesis was tested. Windows SPSS 10.0 software was used for data analysis. The P-value was to be significant at less than 0.05.

#### **RESULTS**

This study included pre treatment and post treatment dental cast of 40 patients. The mean age was 18.4 years, with a range of 12 to 30 years. The sample consists of 24 extraction and 16 non-extraction cases.

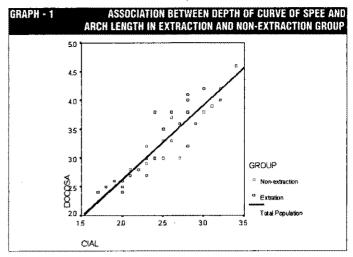
Table I and Table II respectively show the descriptives of two groups on age, depth of curve of Spee right side, depth of curve of Spee left side, arch length before leveling and arch length after leveling.

| TABLE-I       | DESCRIPT           | IVE STATISTICS ( | OF EXTRACTION<br>SAMPLE (N=24). |
|---------------|--------------------|------------------|---------------------------------|
| Variables     | Mean               | Std.Error        | Std.<br>Deviation               |
| Age 🖭 🗤 🖖     | 19.0000            | - 8702 is 1      | र्की क <b>ं 4.2631</b> • ः      |
| Docost Docost | 3.1208<br>3.2250   | ,1451            | 7108<br>6930                    |
| Albi<br>Alai  | 29.3750<br>31.7583 | 6162<br>5996     | 3.0190<br>2.9373                |

| TABLE-II                        | DESCRIPTIVE S                                     | TATISTICS OF N                             | ON-EXTRACTION                                |
|---------------------------------|---|--|--|
|                                 |   |  | SAMPLE (N=16)                                |
| Variables                       | Mean  | Std.Error                                  | Std.<br>Deviation                            |
| Age<br>Docost<br>Docost<br>Albi | 17.5625<br>3.3188<br>3.6438<br>29.3125<br>32.5125 | 1.0487<br>.1552<br>.1405<br>.6799<br>.8297 | 4.1947<br>.6210<br>.5621<br>2.7195<br>3.3186 |

It was established that there was a positive correlation between DOCOSR / CIAL, DOCOSL / CIAL and DOCOSA / CIAL as shown in Table III and scatter diagram (Graph 1).

| TABLE-III                                       | CORRELAT       | TION BETWEEN      | CHANGE IN ARCH       |
|---|----------------|-------------------|----------------------|
|   |                | LENGTH AND        | OTHER VARIABLES      |
| Variables                                       | N              | Correlation       | Sig.                 |
| Docost & Cial<br>Docost & Cial<br>Docost & Cial | 40<br>40<br>40 | 809<br>827<br>916 | .000<br>.000<br>.000 |



In comparison of different variables of extraction and non-extraction groups, CIAL proved to be significantly different (P < .022) between the two groups, while DOCOSL had marginal significance (P < .051) in this regard (Table IV).

| TABLE-I   | V          | COI              |   |                       | WEEN CH                             |                                 |                   |                    |
|---|------------|------------------|---|-----------------------|-------------------------------------|---------------------------------|-------------------|--------------------|
| Variables   | Group      | N                | Mean                                    | Std.<br>Error<br>Mean | Std.<br>Deviation                   |                                 |                   | Sig.<br>(2 tailed) |
| Docosr  | Extraction | 24               | 3.1208                                  | .1451                 | .7108                               | .906                            | 38                | .371               |
| 1984度門  | Non-       | 16               | 3.3188                                  | .1552                 | .6210                               |                                 |                   |                    |
|   | extraction |                  | Sara, A                                 |                       |                                     |                                 |                   |                    |
| Docosl  | Extraction | 24               | 3.2250                                  | .1415                 | .6930                               | -2.013                          | 38                | .051               |
| komusahintala   | Non-       | 16               | 6.6438                                  | .1405                 | .5621                               | Miserdo, EG<br>Forest and Salar |                   |                    |
|   | extraction |                  |   |                       | Salan i diga permita.<br>Kanadara   |                                 |                   |                    |
| Docosa  | Extraction | 24               | 3.1708                                  | .1272                 | 6231                                | -1.637                          | 38                | .110               |
|   | Non-       | 16               | 3.4812                                  | .1320                 | .5282                               |                                 |                   |                    |
| Cial  | Extraction | 24               | 2.3917                                  | .8468E                | .4149                               | -2.381                          | 38                | .022               |
|   | Non-       | 16               | 2.7000                                  | - 1 T 75 4            | 3795                                |                                 | 25                |                    |
|   | extraction |                  | <b>用书的</b> 证书                           | 2 477 377             |                                     |                                 | ¥                 |                    |
| 1 - 6 2 - 1 - | Taken      | naris<br>Bushawa | 1 2 3 1 3 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 | 02                    |                                     |                                 | garyaya<br>Mewiki | As Sta             |
| 1   | Extraction | 71 3.6           | to of the transfer                      | The address of the    | with the task with the first terms. | 1.051                           | 38                | .300               |
| 1.0   | Non-       | 16               | 17.5625                                 | <b>_1.0487</b>        | 4.1947                              |                                 |                   |                    |
| 100   | extraction |                  |   |                       | And processing the second           | 7. Ž.Ž                          | 网络河               |                    |

#### DISCUSSION

The shape of the curve for males and females seemed to be identical and no significant differences could be found among class I, class II division 1, or class II division 2 patients by many researchers. On Since no differences seemed to exist between the curve of Spee for male and female subjects, no distinction was made between the male and female subjects, and the data was pooled together during the statistical analysis of the results.

In current study the change in arch length proved to be significantly different (P < .022) between extraction and non-extraction groups. This study supported the statement of Proffit and Ackerman<sup>9</sup> that "Without extraction, the incisors will be thrown forward as the arch is leveled; with extraction, some of the extraction space will be closed as the arch is leveled out". The authors also agreed with the Woods' findings that, if lower incisors must not be tipped forward and extractions are not required for other reasons, then the lower incisors should

not be included in a continuous archwire. In such cases leveling can be achieved with segmented arch mechanics. If teeth must be extracted because of severe crowding, then the mechanics should encourage significant molar and premolar extrusion. This may only compensate for the loss of vertical dimension because of the forward movement of the posterior teeth.

Shannon and Nanda<sup>12</sup> conducted a study to evaluate changes in the curve of Spee with treatment and its effects on dentofacial structure. They found that extraction and non-extraction treatment had significantly different effects on the anterior segment of the curve. In the extraction group, the mandibular incisors were uprighted. the interincisal angle increased, and the intercanine width increased. In the non-extraction group, the mandibular incisors flared, the interincisal angle decreased, and the intercanine width increased, although less than in extraction group. In current study the change in arch length proved to be significantly different between extraction and non-extraction groups. In this study though following measurements were not included but it was obvious that flaring of incisors in non-extraction group increased the arch length up to some extent than in extraction group where the incisors became upright.

#### CONCLUSION

Following conclusion could be derived from the study;

- There was highly significant correlation found between the depth of curve of Spee and arch length.
- The arch length was proved to be significantly different (P < 0.022) between extraction and nonextraction cases.
- The amount of space required for arch leveling was usually small, but it was nevertheless critical to an accurate diagnosis and treatment plan.
- If the lower incisors must not be tipped forward and extractions are not required for other reasons, then the lower incisors should not be included in a continuous archwire.

 Further broad-based studies are required with larger number of samples, for more appropriate results.

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# SCREENING FOR HEPATITIS B & C IN SURGICAL PATIENTS

#### SHIRAZI B, JAFFERY AH, KISHWAR M AND SHAHID SHAMIM M

#### ABSTRACT Objective

Screening for hepatitis in pre-operative assessment of patients is not the usual practice. The aim of this study was to evaluate the frequency of hepatitis B & C disease in patients coming to hospital for elective surgery.

#### Design

Descriptive study.

#### Place & Duration

Study was conducted at Ziauddin Medical University Hospital between January 2001 to December 2002.

#### Patients And Methods

All patients admitted electively for surgical procedure were screened for Hepatitis B and C before surgery. Latex method was first applied for immediate results and later reconfirmation by the ELISA technique in seropositive patients.

#### Results

In our study a total of 411 patients were screened for hepatitis. There were 179 males and 232 females. Out of 46 seropositive males, 27 were hepatitis B positive and 19 were hepatitis C positive and out of 28 seropositive females, 9 were hepatitis B and 19 were hepatitis C positive.

#### Conclusion

Frequency of hepatitis B & C is high in elective surgical patients.

KEY WORDS:-

Hepatitis, Elective surgery, Screening and Risk factors.

#### INTRODUCTION

The world Health Organization (WHO) has developed a health system performance assessment framework, which is a comprehensive, and an overall positive contributor to the available menu of tools and methods for assisting countries in developing their health systems.¹ The theme of this system is "health for all". To achieve this theme, geographical and epidemiological causes of Correspondence:

Dr. Bushra Shirazi,
Senior Registrar,
Department of Surgery,
Ziauddin Medical University,
Karachi.

diseases need to be assessed for the formation of protocols for assessment of patients.

Collected data pertaining to the prevalence of hepatitis B and C in South Asia is far from crossing its first milestone. Representative surveys regarding the prevalence and identification of risk factors are required. Surgeons and paramedics form a group known to have documented occupational hazards, and are at high risk to the exposure to hepatitis. Screening for hepatitis prior to blood transfusion did lead to prevention of infection through transfusions. At present the transmission of hepatitis C by blood transfusion is reduced to approximately 1.5%.<sup>2</sup>

Preventive measures are also required for the transmission of hepatitis B & C to health workers and through them to other patients.

Pre operative assessment of patients does not include investigating for hepatitis status as a routine practice in many centers. Overall sero prevalence of the disease has been documented in Pakistan from 0.7% to 20%.<sup>3,4,5,6</sup> Not much has been documented on patients coming in for elective procedures. In different studies prevalence rates varied, up to 20.89% in blood donors,<sup>7</sup> 16.3% in patients with surgical ailments, 62% in patients undergoing hemodialysis and 25% in patient with chronic liver disease.

#### PATIENTS AND METHODS

All patients admitted for elective surgical procedure in our unit, between January 2001 and December 2002 were screened for hepatitis B and C after taking informed consent. Patients who were known cases of hepatitis and those less than 18 years of age were excluded from this study. Initially the screening was done by latex method, which on being positive was rechecked by enzyme linked immunosorbent assays (ELISA) technique.

The patients found to be positive were further analyzed for risk factors. The risk factors taken into account were socio-economic status, blood transfusion, history of intravenous drugs usage, abnormality in liver function test and spouse's history of similar disease were recorded. Patients were classified into poor, moderate and affluent socioeconomic groups on the basis of their monthly income, less than or equal to Rs. 5000, between Rs. 5001 and Rs. 10000, and more than Rs. 10000 respectively.

#### RESULTS

Total numbers of patients were 411 out of which 179 were males and 232 females (male female ratio 1:1.3). Hepatitis B was positive in 27 males and 9 females and hepatitis C was positive in 19 males and 19 females. None of the patients in the study had both forms of hepatitis simultaneously.

The risk factors documented that 75% belonged to the low socio-economic status. 1% gave a history of blood transfusion, less than 1% gave a history of intravenous drug abuse. Only 3 of the spouses were found to be positive of which all were female patients whose spouses were positive (two were hepatitis B and one was hepatitis C). The liver function test of 37 patients showed a raised serum alanine transaminase (ALT). All of them had history of multiple injections by general practitioners for various common illnesses.

#### DISCUSSION

Surgery and surgical techniques have revolved on protective barriers for patient protection. Not till recent years that emphasis regarding patient to doctors

transmission of blood borne diseases has been looked into.11,12 The exposure to blood borne diseases, the stigmata attached, the financial burden is reason enough to increase awareness of high risk people. In 1996, the Centre for Disease control and Prevention reported 52 health care workers with documented human immunodefiency virus (HIV) sero conversion after occupational exposure.13 It has also been seen that the risk of acquiring a virus from needle stick injury is 0.3% to 0.4% for HIV patients, 6-30% for HBV patients and 2.7-10% for Hepatitis C patients.14,15 The incidence of needle stick injury varies from 5.3% to 12.8% depending on the surgical specialty, experience and duration of surgery.16 With high prevalence of hepatitis in third world country exposure for the high risk group is much more. In our local literature the antibodies to hepatitis C virus was found to be 20 folds higher than in developed countries.17 WHO estimates that about 170 million people, 3% of the world's population, are infected with HCV with prevalence of infection in countries like Africa, Eastern Mediterranean, South-East Asia and Western Pacific. The rates are high compared to North America and Europe. 18,19 This brings countries like Pakistan and India to the region of high prevalence.

Prevalence of hepatitis C in France was 1.15 %.20 In an Italian study it was seen that blood donors had a prevalence of 1%.21 Local studies have looked into groups like college blood donors versus paid donors where the levels for HCV antibodies was 3% in the former and 30% in the latter.22 In our study of analyzing patients coming for elective surgeries a frequency of 18% was observed. This would mean a higher prevalence is expected in a population based study.

In this study the diagnosis of hepatitis was initially by Latex method, then reconfirmation by the ELISA. It is known that Enzyme immunosorbant assays (EIA) is used for the detection of HCV specific antibodies. EIAs can detect more than 95% of chronically infected patients and detect only 50% to 70% of acute infections. Jean Michel<sup>23</sup> made a conclusion that one single ELISA determination is necessary for diagnosis of hepatitis C infections and HCV-RNA detection by PCR helps to resolve weakly positive or negative ELISA results when clinical context is compatible with hepatitis C. PCR was not a routine test in our study and the patients that were sero positive for hepatitis were than referred to the gastroenterologist for further evaluation and management.

Taking into account the risk factors already mentioned, it was evident that poor socioeconomic status was the most prevalent identity. In a multivariate analyses 3 variables were significant regarding the prevalence of the disease, namely intravenous drug abuse, transfusion and low socio-economic status. This last criterion is more of a risk indicator than a risk factor.<sup>20</sup> This risk indicator was compatible to our study which documented 75% of

patients belonging to the low socioeconomic group. However, less than 1% had history of transfusion in our study.

Intravenous drug abuse is not only meant in terms of addiction to intravenous drugs in contrast the history of medical illnesses for which patients visit general practioners and during treatment they have received intravenous injections. It has been reasonably well documented that the re-use of disposable or glass syringes with out proper sterilization is a common practice, and it initiates a chain of transfer of blood borne infections. In a local study 62.7% patients had exposure to multiple injections for minor ailments.<sup>24</sup> This feature was also concomitant with our patients who had been visiting general practitioners and quacks for minor illness.

The Liver function tests have been used for screening purposes and analyzing acute and chronic infections. Different subgroups of patients have been assessed for serum alanine transaminase (ALT) levels as a marker to monitor patients on dialysis. Here the conclusion was that it was a good investigation for acute infection, but excluded those with chronic infection.<sup>25</sup> ALT levels have been found to be a good indicator in acute stage of the disease that is 80-90% but was not significant in chronic illness for on going liver disease.<sup>25,26</sup> In our study the serum tansaminase level were equivocal that is 50% of our patients had raised levels signifying that it was not a test that could be used for screening.

In order to prevent hepatitis as an epidemic in our country, prevention and counseling measures should be specified in general, the awareness of its presence and the magnitude of risk should be known to patients as well as to health care providers. Assessing the risk is based on the epidemiologic characteristics, including mode of transmission, which persons are at increased risk and areas or regions that have high prevalence.<sup>27</sup>

#### CONCLUSION

We recommend that till the risk factor for the prevalence of hepatitis are identified, one should make screening a routine practice in all patients admitted for elective surgery and have a performa filled relating to the risk factors.

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# HYPOSPADIAS: EXPERIENCE WITH MATHIEU'S REPAIR

#### SIKANDAR ALI MUGHAL AND SIRAJUDDIN SOOMRO

#### ABSTRACT Objective

To determine the effectiveness of Mathieu's urethroplasty for anterior hypospadias.

#### Design

Descriptive Study.

#### Place & Duration

Department of Paediatric Surgery, Chandka medical College Hospital, Larkana, from January 2003 to December 2003.

#### Patients And Methods

A Total of 30 boys who presented with sub coronal and distal penile hypospadias without chordee were included in the study. The neourethra was constructed by utilizing the flap of skin proximal to the meatus. Urethral catheter was used as stent and for diversion of urine.

#### Results

The age at presentation ranged between 1 and 12 years with a mean of 4.86 years. Twenty Three (76.66%) patients presented with distal penile hypospadias while the meatus was subcoronal in 7(23%) patients. The only complication encountered was minute urethrocutanems fistula in 2(6.66%) cases. The cosmetic results were satisfactory.

#### Conclusion

The well established Mathieu's urethroplasty provides excellent result in terms of having minimal complication rate and excellent cosmetic and functional result.

#### KEY WORDS:-

Hypospadias, Urethroplasty and Mathieu's procedure.

#### INTRODUCTION

Numerous surgical procedures have been attempted for the correction of distal hypospadias. Any technique to repair distal hypospadias should be simple, easy and give satisfactory functional and cosmetic outcomes with few complications. 12 The technique chosen for the repair of anterior hypospadias will depend on the anatomy of the hypospadiac penis. The most common accepted procedures are the MAGPI (meatal advancement

Correspondence:

Dr. Sikandar Ali Mughal, Department of Paediatric Surgery, Chandka Medical College Hospital, Larkana. glanuloplasty) GAP (glans approximation procedure), Mathieu or flip flap and the tubularized incised plate urethroplasty.<sup>3</sup> Mathieu's repair is a perimeatal-based urethroplasty and is commonly used for primary repair. Mathieu reported his procedure for repair of hypospadias in 1932 and it is considered as a reference operation for the treatment of anterior hypospadias.<sup>45</sup>

#### PATIENTS AND METHODS

All patients with subcoronal or anterior hypospadias, without chordee, with good urethral plate and mobile perimeatal skin were included in this study. Standard Mathieu's hypospadias repair was done in all cases. After

introducing the Foley's catheter the flap of skin, equal in length as the distance from the meatus to the tip of glans was marked, a flap with good blood supply was incised. Same incision on either side of urethral plate upto the tip of glans penis made. The flap was flipped from the shaft of penis and sutured with the margins of flap made from urethral plate in glans penis. Finally the glans flaps and skin were approximated over the neourethra. Foley's catheter was used in all cases as stent and for diversion of the urine. The catheter was removed on 8th postoperative day and patient discharged with advise to come for follow up.

#### **RESULTS**

Thirty patients were operated with Mathieu's urethroplasty technique. The youngest patient was 6 months of age and the oldest was 12 years with a mean age of 4.86 years. Twenty three patients (77%) presented with distal penile hypospadias and in 7 patients (23%) the hypospadiac meatus was subcoronal. The catheter was removed on 8th post operative day in 28 patients while in two patients the catheter was accidentally pulled out on 5th and 6th day respectively. All the patients voided normally without any complaint after removing the catheter. The only complication which occurred in this series of patients was minute pinhead urethrocutaneous fistula in two patients (6.66%). The cosmetic results were satisfactory.

#### **DISCUSSION**

Hypospadias is one of the most common congenital anomalies occurring in approximately 1:250-1:300 live births.3 Left uncorrected, patients with hypospadias may need to sit down to void and tend to shun intimal relationships because of fears related to normal sexuality. The only treatment for hypospadias is surgical repair of the anatomical defect. Numerous surgical procedures have been devised for the correction of distal hypospadias. Mathieu's urethroplasty is considered to be the reference operation for the treatment of anterior hypospadias.5 Since the surgery is elective, the optimum time for repair as recommended by the American Academy of Paediatric Consensus Panel on genital surgery is between 6 and 18 months of age.6 The age of our patients range between 6 months and 12 years with a mean of 4.86 years. This is comparable with an international study.7 Various complications of hypospadias repair have been reported ranging from acute infection, flap/graft failure, edema and erection trauma, to chronic fistulae, urethral diverticulum, stricture, hairy urethra and meatal stenosis.89 The other reported complications include split glans, skin dehiscence and complete breakdown of the repair. 10 We did not encounter any acute complication in our series of patients. This is comparable published9 studies. We encountered urethrocutaneous fistula in two of the cases (6.66%) This is less in number as compared with an international study and is comparable with the study of Rickwood."

One of the criticisms of the Mathieu procedure is fish mouth appearance of the meatus.<sup>4</sup> The other opinion which is against the Mathieu is based on the fact that the Mathieu repair is based on a random flap, which is not as reliable as a vascularized pedicle graft and long term complications from meatal stenosis secondary to ischemia have been more common.<sup>12</sup> The results are satisfactory in terms of functional and cosmetic appearance. The two patients who developed urethrocutaneous fistula were repaired successfully after 4 and 6 months of the primary operation.

From the above discussion we conclude that the well established Mathieu's repair provides excellent cosmetic and functional results. It has an overall success rate of 93% with minimum complications. We believe that in the era of newly reported techniques the well established Mathieu procedure should be the standard by which distal hypospadias repair is judged.

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# TREATMENT OF BREAST ABSCESS WITH ULTRASOUND GUIDED PERCUTANEOUS NEEDLE DRAINAGE

UZMA JALALI, SHAHID RASUL, TEHMINA SHAH\*, M. AKHLAQ HUSSAIN\* AND ASADULLAH KHAN.

#### ABSTRACT

A study was conducted from August 2003 to July 2004 on 22 consecutive females with uncomplicated breast abscess in the breast clinical of ward-03 JPMC. Percutaneous aspiration of the abscesses was done under ultrasound control instead of more traditional incision and drainage. The highest number of patients had abscess in the lower outer quadrant. Minimum age was 14 and maximum 44 years. Out of 22 patients 11 were cured on first aspiration, 7 responded on re-aspiration and 4 had incision drainage and tissue biopsy to exclude malignancy. Ultrasound guided needle aspiration is a good method to treat small breast abscess with no skin changes.

**KEY WORDS:-** Breast abscess, Percutaneous aspiration, Ultrasound guided needle aspiration.

#### INTRODUCTION

An abscess is localized collection of pus within a pyogenic membrane and may form anywhere in the body.¹ Breast abscesses are common and rarely harbour an underlying malignancy and if drainage is done, then biopsy of the abscess cavity is essential.² Treatment of breast abscess is a difficult clinical problem.³ Traditional treatments of breast abscess involve incision and drainage, with or without ultrasound guidance.⁴ The abscess cavity is left open and packed with gauze, and there are subsequent dressing changes for up to 6 weeks during wound granulation.⁵ These procedures cause considerable discomfort and morbidity for the patient.⁴ Cosmetic results are often disappointing owing to scar formation.³ Even with this aggressive approach, the abscess recurrence rate is reported to be between 10% and 38%.⁵

Reuvers et al. produced one of the earlier reports on ultrasound-guided abscess drainage in 1983.7 The authors reported their experience with 24 abdominal abscesses drained under ultrasound guidance. The authors concluded that ultrasound guidance was the

Correspondence: Dr. Uźma Jalali, Post Graduate, Surgery ward-03, Jinnah Post Graduate Medical Centre, Karachi.

\* Department of Radiology J.P.M.C

method of choice and often prevented the need for surgical exploration. Ultrasonography (US) has been shown to be useful in depicting abscesses in patients with mastitis<sup>8,9</sup> and subsequently has been used to guide abscess drainage<sup>3</sup>.

A number of reports on breast abscess drainage under ultrasound guidance have also been published. In 1993 Karstrup et al10 reported their experience with 19 patients who were scheduled to undergo surgical drainage of a breast abscess under general anesthesia. Eighteen of the 19 patients were treated successfully with ultrasoundguided needle aspiration instead. In 1997 Garg etal" reported 25 consecutive cases of breast abscess drained under ultrasound guidance. The authors noted a success rate of 84% and believed the technique was highly efficacious and helped avoid more extensive surgical procedures. Although percutaneous drainage of abscess under ultrasound guidance is a well established modality, its use in breast abscess has still not found wide application." Aspiration of breast abscess without sonographic guidance is also reported effective4.

Purpose of the study was to determine the efficacy of ultrasound guided percutaneous aspiration of breast abscesses as an alternative to surgical incision and drainage.

#### PATIENTS AND METHODS

The descriptive study was conducted in the breast clinical Surgery ward 03-Jinnah Postgraduate Medical Centre Karachi from August 2003 to July 2004, on twenty-two consecutive females above 12 years of age who presented with acute onset of symptoms with apparently healthy skin and non pointing abscesses or discharging sinuses. Non motivated, patients prolonged history, apparently necrosed skin, pointing abscess or discharging sinus were not included in the study.

Patients were diagnosed on the basis of history, clinical examination and ultrasonography. Treatment was done by percutaneous drainage under sonographic guidance, after instilling the skin with injection xylocain as a local anaesthetist agent. Needle aspiration was done for abscess smaller than 3cm and for larger abscess 14 and 16 gauge cannulae were used. Full aspiration of the cavity done with no residual fluid left. Patients were initially kept on empirical antibiotics and later on antibiotic changed according to culture and sensitivity and continued for 10 to 14 days. Follow up of patients was done by history, examination and ultrasounds on third and seventh day with re aspiration of re accumulated fluid and later on weekly for first month and once monthly from second to sixth month of aspiration. Patients found symptom less with normal ultrasound on twenty forth week of aspiration were considered cured. Those who did not respond on re aspiration with continuous re accumulation of pus. increase of size of abscess or discharging sinus underwent incision drainage and incisional biopsy of the breast tissue to exclude malignancy.

#### **RESULTS**

Twenty two patients underwent ultrasound guided aspiration of breast abscesses. Mean age of the patients were 30.14 ± 1.58 years. Minimum age was 18 and maximum 44 years. Nine of them were lactating making 40.9% of the total. Right of breast was involved in 12 cases. Involvement of the Lower outer quadrant was the commonest (Table-I).

| TABLE-I              | LOCATION OF ABSCESS |
|----------------------|---------------------|
| Position             | Number Percent      |
| Lower outer Quadrant | 10 45.5%            |
| Lower outer Quadrant | 45.5%               |
| Retro areolar        | 05 22.7%            |
| Upper outer Quadrant | 05 22.7%            |
| Upper inner Quadrant | 02 9.1%             |

Ultrasound demonstrated hypo echoic breast lesions in all cases. The cavities were well defined, oval in six (27.3%). rounded in nine (40.9%) and irregular in shape in seven (31.8%) cases. Mean area of the abscess involved were 10.9 ± 9.8cm.2 Altogether 0.6ml to 100ml pus (median value = 2.65 ml) aspirated till no residual fluid left in cavity. We observed that all those patients (n=11) with abscess size less than or equal to 3cm achieved complete

resolution with single aspiration covered with antibiotics according to culture and sensitivity. Repeat aspiration was done in patients (n=7) with abscess more than 3cm showing re-accumulation of pus on follow up ultrasound with complete response to antibiotics. Four patients required incision and drainage with tissue biopsy after failure of percutaneous aspiration. Two were due to increase in size and pointing of pus and two due to continuous discharging sinus. These patients were kept on antibiotics for two weeks according to culture and sensitivity and they responded well on it. None of them were found to be malignant on histopathology.

#### **DISCUSSION**

Out of twenty two patients who underwent percutaneous aspiration we found seventeen (77%) of age less than 40 years, favoring strong association of illness with lactation and pregnancy. In his studies Samir13 mentioned that 66.6% of the patients of breast abscess and mastitis were less than 36 years of age, reflecting the association of this lesion with lactation and pregnancy.

Although breast abscess is associated more with lactation state,4 in our and other12 studies, non lactating group of patients was more commonly affected.

We observed right side of the breast involved more than left where as Hook<sup>a</sup> reported involvement of left breast more than right. Hook observed 9 of the 13 patients had retroareolar abscesses, where as we noted 5 of the 22 patients (22,7%) having retroareolar abscess, we observed the most common site was lower outer quadrant i.e. 45% followed by upper outer guadrant (22.7%).

According to Hook abscess 2.5cm or less are suitable for aspiration procedure and in abscesses larger than 3cm. aspiration was used to make a diagnosis and obtain material for culture and sensitivity analyses, but it was not always successful in abscess drainage and treatment. In our study abscess sized 3cm or less responded excellent on single aspiration and antibiotic cover with out recurrence making this size an ideal size for aspiration. In abscess of more than 3cm size reaccumulation of pashas seen on follow up ultrasound and 5 out of 7 responded well on second and 2 on third attempt.

It was observed that in those patients whose initial aspiration yielded less than or equal to 3ml of pus responded well on first aspiration as compare to those whom aspirate were more than 3ml i.e. 3-100ml. Schwaz<sup>4</sup> observed that those patients in whom needle aspiration was successful had a significantly smaller volume of pus on initial aspiration (4 versus 21.5ml).

Garq" achieved 84% success in his 25 patient's studies of needle aspiration under sonography. Schwarz' yielded 82% success rate. O'Hara' had 86% success rate, Karstrup achieved 95%10 and 100%15 success in his two different studies. We observed 81% success rate with 18 out of 22 patients cured through this approach. Thus making Breast abscess Aspiration combined with ultrasonographic imaging is an effective alternative to incision and drainage.<sup>14</sup>

#### **CONCLUSION:**

Ultrasound guided percutaneous needle aspiration with local anaesthetic injection is a convenient method with cosmetically excellent results especially for smaller abscess. It is cheaper and should be consider as an alternative to incision and drainage in small and uncomplicated abscess.

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### DIABETIC FOOT: MAJOR CAUSE OF LOWER LIMB AMPUTATIONS

#### SYED MUJAID HUMAIL, SHAHID ILYAS AND F.U BAQAI

#### ABSTRACT

#### **Objectives**

To find out major cause of amputations in tertiary care hospital in Karachi and to see if it is preventable.

#### **Objectives**

Case review study of 65 lower limb amputations.

#### Patients And Methods

An audit of 65 lower limb amputations done in four years i.e. 2000-2004 at Department Of Orthopedics Baqai university hospital Karachi and Baqai Institute of Diabetology & Endocrinology. All 65 Patients who had lower limb amputations at different levels were either referred from Diabetic Institute for surgical intervention or admitted in Orthopedic Department.

#### Results

Major cause of lower limb amputations was diabetic foot(70.76%) followed by trauma(15.38%), gas gangrene(6.15%), tumor(4.6%), Medura foot and neurological involvement 1.53% each. Most of the patients in diabetic group were of low socio economic status.

#### Conclusion

70.76% amputations were because of diabetes comparing to other causes contrary to western world data. Proper diabetic foot care could reduce this incidence.

**KEY WORDS:-** Diabetes, Foot care and Amputation.

#### INTRODUCTION

Amputation is defined as the surgical removal of part or whole of limb. Amputation of the limb is one of the oldest surgical procedures. Archeological studies indicate that among prehistoric period amputations were found. Till recently the main aim of amputation was to save life by removal of damaged or diseased limb (gangrene or malignancy),1 In last fifty years phenomenal increase in the road traffic accident all over the world has also enormously increased the number of amoutations of limbs.2 Vascular diseases have been reported as major cause of amputations in some Western studies.34

Correspondence: Syed Mujaid Humail, Associate Professor Orthopedics, Baqai Medical University, Karachi.

In recent years foot infections in diabetics have emerged as major cause of amputation. Purpose of this study was to evaluate the causes of lower limb amoutations. rationale behind was to asses from scenario if this could be treated properly & limb could be saved.

#### PATIENTS AND METHODS

This case review study was conducted at Department of Orthopedics and Baqai Institute of Diabetology and Endocrinology from Feb 2000 to Feb 2004. Total of 65 patients having lower limb amputations at different levels were included in this study. All were admitted through accident and emergency of Bagai University Hospital or referred from Institute of Diabetology and Endocrinology.

Demographic data was taken from records. Most of the diabetic group patients were referred in very late stages where salvage of limb was not possible. In addition to proximal limb amputation some of them have more than one operations. Mortality and morbidity was high in gas gangrene and in diabetics.

The decision of performing amputation was taken on clinical judgment by at least two surgeons of the surgical team. The nature of disease, which made the part of limb unsalvageable or could increase the magnitude of illness was fully described to the patients and relatives, so in all cases informed consent was obtained.

#### RESULTS

During the study period from 2000—2004, 65 patients had lower limb amputations at different levels. Major cause was diabetic foot, 46(70.76%) followed by trauma 10(15.38%). Level of amputation is shown in table I.

|                               | ELS OF AMPUTATIONS |
|-------------------------------|--------------------|
| Total 65                      | Percentage         |
| Disarticul hip 03             | 4.61%              |
| Above knee 11                 | 16.92%             |
| Below knee amputation 29      | 44.61%             |
| Syme's amputation 03          | 4.61%              |
| Transmetatarsal amputation 08 | 12.3%              |
| Toe amputation 11             | 16.92%             |

The age of patients varied between 16 years to 82 years. The youngest patient had disarticulation of hip because of osteosarcoma in proximal femur. Other younger patient had amputation because of trauma and tumor. Most of the patients who had diabetic involvement were in their fifth to eighth decade. Male to Female ratio was 3.6:1; this highlights the active life style of male in our society. Diabetics of lower socio-economic status had higher amputation rate i-e 58.69% followed by middle class 32.6% and high class 8.69% reflecting easy and early access of affluent class to experts. Mortality was 50% in gas gangrene while 17.39% in diabetic group (table II).

| TABLE-II         |                         | MORTAL      | ITY DISTRIBUTION |
|------------------|-------------------------|-------------|------------------|
|                  | No of pts               | No of death | ns Percentage    |
| Total amputation | 65                      | 10          | 15.38%           |
| Diabetic Group   | 46                      | . 8         | 17.39%           |
| Gas Gangrene     | 4                       | 2           | 50%              |
| Trauma           | 10                      | 0           | 0%               |
| Turnor           | 3                       | ** <b>0</b> | 0%               |
| Medura Foot      | erse <b>f f</b> orsøyen | 0           | 0%               |
| Neurological     | 1                       | 0           | 0%               |

#### DISCUSSION

Lower limb amputation had been performed in different ages for different reasons. Before the turn of century it was done mostly for war injuries along with other causes like trauma. Vascular disease are common cause in western countries in last fifty years.<sup>3,4</sup> Recently diabetic foot infection has become leading cause of amputation.<sup>5,6</sup>

Foot ulcers are common and significant complication of

diabetes mellitus, as healing is problem in this due to infection and poor tissue perfusion. The world wide increase in type2 diabetes has resulted in increase in diabetic foot ulcer.<sup>7</sup> Approximately 15% of all diabetics will develop foot ulcers during course of disease<sup>8,9</sup> ultimately 20-40% of patients with diabetic foot will require amputations.<sup>10</sup>

Diabetic foot Infection was leading cause of amputations in our study (70.76%). Higher amputation rate in diabetic foot in our study matches with other studies.<sup>5,6,11</sup> Most of the patients were in grade 3 or 4 of Meggit Wegner classification of diabetic foot, similar to the study of Munnawar and Jamil et al.<sup>12</sup> The age distribution in diabetic group (50 to 80 years) and male to female ratio were similar to other studies done in Pakistan.<sup>11,12</sup> Higher mortality rate (13.2%) was reported by Gurlek A et al<sup>13</sup> in Turkish patients, comparing to our mortality figure of 17.39% in diabetic amputee.

Late referrals of foot infections in diabetics, to specialized surgeon make limbs salvage impossible in most cases. Importance of early referrals is concluded by other authors as well.<sup>11,14</sup> On the other hand awareness of foot care in diabetics regarding prevention of foot infection is also very important. <sup>15,16</sup>

Our study concluded that public health education and training of the people who treat these diabetic feet at primary level is important. Further more as indicated in the study most affected lower socio economic class seeks for help to these general practioner, quacks at primary level. Early referrals by this primary care prodviders at earlier stage could save the limb by smaller procedures like incision drainage of abscess and simple debridement. Management of diabetic foot is a team work which should necessarily include physician, surgeon, nutritionist, and orthotist.

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# FISTULAE IN ANO FOLLOWING ANORECTAL ABSCESSES

NUR SAEED, MUNIR KHAN, ZAFAR I. MALIK AND HAROON K. PASHA

#### ABSTRACT

This study was carried out to determine whether primary fistulotomy should be performed at the time of incision and drainage of anorectal abscesses and what percentage of patients would develop fistula-in-ano or recurrent abscess. The record of 77 patients was reviewed who underwent incision and drainage of anorectal abscesses. Out of 77 patients, thirteen (16 percent) developed recurrent abscesses and 26 (34 percent) developed persistent fistula-in-ano, with combined recurrence rate of 51 percent. This supports the policy of fistulotomy in the second sitting especially to prevent any complications and also of the fact that 59 percent would not need it.

KEY WORDS:- Fistula-in-ano, Fistulotomy, Anorectal suppuration.

#### INTRODUCTION

Fistula-in-ano may develop at any time during anorectal sepsis and recurrence of anorectal abscesses is probably due to underlying fistula. Although this entity exists for hundreds of years, it still poses a difficult surgical problem. Lockhart-Mummery noted in1929 that probably more reputations had been damaged by unsuccessful treatment of cases of fistula than by excision of rectum. A great deal remains uncertain and debates continue to exist whether immediate fistulotomy should be employed in treatment of anorectal abscesses. Some authorities favor a one-stage procedure in which incision and drainage is combined with fistulotomy. Doing so, they believe, will eradicate infectious process, thereby eliminating development of recurrent abscesses and fistula that they consider is inevitable.

Supporters of two stage procedure, where they perform incision and drainage initially, followed by fistulotomy at a later stage if necessary especially when incision and drainage can be performed under local anaesthesia.<sup>2</sup> They stress the point that the need for operation is not certain to occur and some patients would have needless division of sphincter with potential risk of continence disturbance.

Treatment failure rates may be decreased by a good appreciation of normal anorectal anatomy and fistula pathoanatomy, as well as wide and practical knowledge of the possible treatment regimens.<sup>3</sup>

Correspondence: Dr. Nur Saeed, Nishtar Hospital, Multan.

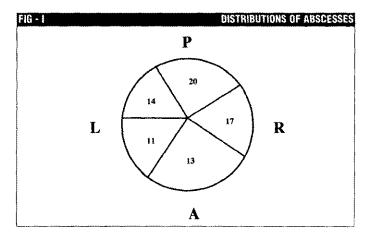
#### PATIENTS AND METHOD

The record 77 patients with anorectal suppuration were reviewed. Most patients were treated as day case procedure. Using local anaesthesia of 0.5% xylocaine and 1:200,000 adrenaline, a cruciate incision was made, allowing free drainage of pus. Skin edges were excised. Antibiotics were used in patients who were diabetics, with heart disease or patients who had extensive cellulitis. Patients with complicated abscesses or doubtful diagnosis were admitted in hospital and explored under general anaesthesia. Patients with intersphincteric abscess underwent internal sphincterotomy as far as abscess.

Postoperatively patients were advised to take sitz bath, laxatives and to return, should the condition not improve. All patients were reviewed in 10 to 14 days time with rectal and proctoscopic examination. Subsequently all patients were seen after two weeks until there was no drainage or fistulae in ano developed.

#### **RESULTS**

Follow up was available on 75 patients (97 percent) of the total 77 patients. Age range was from 12 to 80 years, majority being in fourth decade in both sexes. Out of 77 patients 57 were men (74%) and 20 females (26%). Abscesses were categorized in terms of location (Fig.1). Most of them were located posteriorly followed by left and right sides. Three abscesses were intersphincteric (4%) and two horseshoe type (2.5%). Most common symptom was pain in 70 patients (91%) and swelling in 50 patients (65%). Anal discharge, diarrhea, fever and blood per rectum were other presentations in four patients.



Examination revealed tenderness in 76 patients (98%), swelling in 45 patients (58%), increased local temperature with erythema in 30 patients (39%). Associated hemorrhoids and anal fissure were present in 5 patients (6%) each. One patient had associated pilonidal sinus. Associated illnesses were found in 25 patients (32%) with anemia, diabetes mellitus and hypertension being most common.

Incision and drainage was done under local anesthesia in 55 patients (71%), while 22 patients had their abscess drained under general anesthesia. Patients who underwent general anesthesia either had intersphincteric / horseshoe abscess or there was suspicion of complexity of abscess. Thus, 90% of ischiorectal or perianal abscesses were drained under local anesthesia. Antibiotics when used were penicillin or cephalosporin along with metranidazole. Pyodine soaked gauze was used as pack for first 12 hours to stop any bleeding from edges followed by advice for sitz bath twice daily.

Recurrent abscesses occurred in thirteen patients (16%) during the follow up period of one to sixty months. Fistula in ano developed in 26 patients (34%). In this group 71 percent had previous ischiorectal abscess, while 29 percent had two or more episodes of abscesses.

#### DISCUSSION

Management/surgery should aim to relieve symptoms, minimize time of work, be associated with as low an incidence of recurrence as possible, and identify any underlying disease. Treatment of anal fistula is a double challenge: healing the suppuration, and preserving anal incontinence. Findings in our review are similar to those reported in other studies e.g. presenting signs and symptoms, high male to female ratio 3:1, most patients in fourth decade.

Combined recurrence of abscesses and fistula in ano occurred in 51 percent of cases in this study. Buchan and Grace, in analyzing the reasons responsible for high recurrence rate, questioned whether abscess type might play a role and pointed to a study by Wilson who found more recurrences in ischiorectal abscesses which

corelates with our data in which 71 percent had ischiorectal abscesses. It appears that patients who develop ischiorectal abscess have greater chance of developing fistula in ano than perianal abscesses.

Bevans et al believe that patients who had previous anorectal surgery or prior pathology are more prone to suppurative problems since natural barriers to infection are destroyed. Buchan and Grace report a significant increase in recurrence rate in patients with previous history of abscess. In our study 22 patients had two or more episodes of abscesses.

Main issue of discussion is whether primary fistulotomy is indicated at time of incision and drainage of anorectal abscesses. Many authorities<sup>5,6</sup> support this for they believe it will prevent recurrence as fistula formation is inevitable. Abcarian support this.<sup>7</sup> However, it is not always possible to find internal opening. Read and Abcarian failed to identify an opening in 66 percent of their patients. McElwain et al who support primary fistulotomy, recorded a recurrence rate of 3.6 percent and reoperation rate of 5.5 percent.

Authorities who are more conservative<sup>2,8</sup> believe performing fistulotomy in presence of acute inflammation is hazardous. Since internal opening may not be seen and over enthusiastic attempts may damage sphincter or create false passage thus resulting in persistent suppuration.

Hanley and Scomaet al had similar results demonstrating that 34% of patients will not develop fistula who had incision and drainage. 9.10 This supports our study in which 59 percent of patients had no problems following incision and drainage.

#### CONCLUSION

Our data suggests that fistula is not the outcome of all anorectal abscesses. In our study 16% developed recurrent abscess and 34% had persistent fistula with combined recurrence of 51%. Since 59% had no further problems, perianal and ischiorectal abscesses can be safely and adequately drained under local anaesthesia. Fistulotomy can be performed as second stage procedure as and when required.

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# IS OPEN PNEUMOPERITONEUM SAFE FOR LAPAROSCOPIC SURGERY

#### SALEEM KHAN AND ZAKIUDDIN G. OONWALA

#### ABSTRACT

Objective

To find out complications associated with open pneumoperitoneum technique of laparoscopy.

#### Patients And Methods

The study included patients managed at Hamdard University Hospital and Saifee Hospital Karachi from April 1997 till April 2004. The laparoscopic procedures included were laparoscopic cholecystectomy, laparoscopic appendicectomy, diagnostic laparoscopy and laparoscopic orcheidopexy.

#### Results

In our study of 1018 cases, we only had a single major complication. Our complications mainly were port site bleeding, infection- of umbilical port and inscisional hernia.

#### Conclusion

Laparoscopic procedures using blunt trocar with open method is a safe procedure with no major complications.

**KEY WORDS:-**

Open pneumoperitoneum, Veress needle, Laparoscopic surgery.

#### INTRODUCTION

Laparoscopic surgery is now in practice for more than two decades. The most established surgical procedure is laparoscopic cholecystectomy. Other procedures which are also common in surgical practice are laparoscopic appendicectomy, laparoscopic hernia repair, laparoscopic ligation of gonadal veins for varicocele. In specialized centers procedures like fundoplicatin for hiatus hernia, nephrectomies, adrenalectomies; orcheidopexy for undescended testes using Fowler Stephen's technique, anterior resection for rectal carcinoma are frequently performed.

The most favoured method of establishing pneumoperitoneum in laparoscopic surgery is the closed technique. This involves insufflation of the peritoneal cavity through a spring loaded Veress¹ needle which is placed blindly in the peritoneal cavity. Subsequently a 10mm trocar is inserted blindly to allow introduction of the laparoscope. Nevertheless several reports from gynecological centres pointed out, that direct insertion of Correspondence:

Dr. Saleem Khan, Associate Professor General Surgery, Hamdard University Hospital, Karachi. trocar without previous pneumoperitonium is a safe alternative to Veress needle insertion.<sup>23</sup> In this study we report our experience of open technique of pneumoperitoneum for laparoscopy.

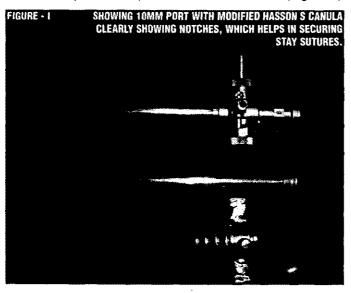
#### **PATIENTS AND METHODS**

This study was carried out at Hamdard University Hospital and Saifee Hospital Karachi. We have used open technique for inducing pneumoperitoneum. The patients with multiple laparotomies were excluded from the study where as patient with previous appendicectomy and lower midline incisions were included. The study spanned from April 1997 till April 2004. Our mean follow up was 12 months with a range from six months to 18 months. The mean age was 45 years, range from 21 years to 78 years The female to male ratio was 20:02. The most common procedure was cholecystectomy. Our conversion to open cholecystectomy rate was 7%. The main indication for conversion was dense adhesions and congenital anomalies of vessels & duct.

#### TECHNIQUE

The patient was placed in supine position. A 1.5cm subumbilical incision was made. All fat cleaned using a

swab on stick till linea alba visualized. Linea alba was held using tissue holding forceps. Two stay sutures were applied at the two ends longitudinally. A small incision in the linea alba was then made and dissection with the help of little finger done. Peritoneum was breached. The 10 mm blunt trocar introduced under direct vision and kept in place by using stay sutures. We never had any difficulty even in obese patients. The pneumoperitoneum induced and further ports were place under direct vision. (Figure 1).



#### RESULTS

Open laparoscopy was used in 1018 cases. The procedures performed were laparoscopic cholecystectomy, laparoscopic appendicectomy, laparoscopic orcheidopexy, diagnostic laparocscopy and removal of ovarian cyst using laparoscopic tenchnique (table I).

| TABLE-I                                |                  | LAPAROSC                     | OPIC P   | ROCEDUR | ES     |
|--|------------------|------------------------------|----------|---------|--------|
| <ul> <li>Laparoscopic chole</li> </ul> | cystectomy       |                              |          | 885     | 1. 91. |
| Laparoscopic apper                     | ndectomy         | Michigan .                   | Darkery. | 20      | 200    |
| Laparoscopic orche                     |                  |                              | • '      | 18      |        |
| Diagnostic Laparos                     |                  | Allen<br>Valtitude och state |          | 90      |        |
| Laparoscopic remo                      |                  | cvst                         |          | 05      |        |
| Total                                  | and the Majorite |                              |          | 1018    |        |

In our series of 1018 cases we had minimal complications. The commonest complications in this series was port site bleeding as well as minor wound infection at the umbilical port, (table II).

| TABLE-II                             | COMPLICATIONS                              |
|--------------------------------------|--|
| Bleeding from port site              | 28   |
| Slippage of stone from gall bladder  | 27   |
| Wound infection at umbilical port    | 44   |
| Omental laceration                   | 第4章 12 12 12 12 12 12 12 12 12 12 12 12 12 |
| * Incisional hemia at umbilical port |  |
| Visceral injuries                    | 1  |

#### DISCUSSION

Open laparoscopy was first described by Hasson's in 1971.4 Inspite of simple procedure with no complications still closed method of inducing pneumoperitonem is

favoured by most of the surgeons. In a survey in 1982 by Ameriacn Association of Gynaecological Laparoscopist only 4% of laparoscopic procedures were performed using open pneumoperitoneum. Prospective randomized studies of open versus closed establishment of pneumoparitoneum have not been performed. The available comparative studies involve retrospective analysis of small number of patients. As the incidence of visceral & vascular injuries due to Veress needle is low, therefore a prospective study comparing open & closed pneumoperitoneum would require quite a significant number of patients to allow statistically significant conclusion to be made.

Surgeons who prefer closed technique over open technique believe that open method is time consuming and it is compromised by leakage of carbon dioxide from umbilical port. In fact our experience to induce open pneumoperitoneum requires less than 5 minutes in most of the cases. More over using Modified Hasson's blunt cannula which has anchorage for stay sutures also prevent further escape of carbon dioxide.

Closed laparoscopy in obese patients some times can be difficult for various reasons. Lifting up of skin before insertion of Veress needle increases the distance between fascia and the skin. In certain cases peritoneum is pushed forward in front of the needle because of excessive preperitoneal fat. We did not face these problems in open laparoscopy as fasciae & peritoneum are lifted individually and incised.

#### CONCLUSION

In conclusion use of open method for inducing pneumoperitoneum in laparoscopic surgery is advocated as it is safe simple and can be performed with a reusable trocar which is very useful and cost effective specially in a developing countries like Pakistan.

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# COMPARISON OF TRUCUT BIOPSY WITH FINE NEEDLE ASPIRATION CYTOLOGY IN DIAGNOSIS OF PALPABLE BREAST LESIONS

UZMA JALALI, SHAHID RASUL AND ASADULLAH KHAN

#### ABSTRACT

A comparative study was conducted on 25 consecutive female patients with clinically palpable breast lumps from July 2003 to April 2004 in the barest clinical of Surgery ward-03 JPMC. All the patients underwent fine needle aspiration cytology and trucut biopsy simultaneously. Mean age was 45.28 years with minimum age of 32 and maximum 66 years. Most frequent site involved was upper outer quadrant (32%). The most common lesion diagnosed on FNAC was malignancy in 60% of cases, whereas on trucut 64% of the lumps were diagnosed as malignant. Trucut biopsy defined the type of lesions more accurately than FNAC. The sensitivity of FNAC and trucut was 88% & 96%. Trucut biopsy is a valuable tool for breast lumps diagnosis and provides better characterization of benign and malignant lesions.

**KEY WORDS:** Breast lumps, Fine needle aspiration cytology and Trucut biopsy.

#### INTRODUCTION

Early detection of Breast carcinoma is crucial to improve the therapeutic effect and to increase the survival rate.1 The process of assessment of significant breast lesions involves the correlation of clinical imaging and the cytological / histological findings. The highest levels of diagnostic accuracy are achieved if such a "triple approach" of imaging, clinical diagnosis and fine needle aspiration cytology is used.2 Fine needle aspiration cytology is a sensitive and specific procedure, is more acceptable to the patient then trucut or frozen section examination and open biopsy can be avoided in 83% benign breast disease in whom where all the three assessment modalities support the diagnosis of benign disease.3 Fine needle aspiration cytology is an important procedure to use in the out patients because it can reduce patient's anxiety, lead to earlier diagnosis and lower health care costs. A disadvantage of FNAC is that there may be complications such as haematoma or pneumothorax, which is rare and occurs mainly in women with small breasts.2 The main problem with FNAC of the breast however is the inadequate rate that is a function of the size and palpability of the lesion and on the

Correspondence:
Dr. Uzma Jalali,
Post Graduate, Surgery ward-03,
Jinnah Post Graduate Medical Centre,
Karachi.

histological type. Lamb and Anderson<sup>4</sup> found that inadequate rates were higher in lobular invasive carcinoma and ductal cancers whilst Hitchcock et al<sup>3</sup> noted that it was more difficult to obtain satisfactory aspirate in pure insitu carcinoma and invasive lobular carcinoma. There is a great inadequate rate with FNAC of impalpable lesions where their smaller size and fibrous nature makes sampling more difficult.<sup>2</sup> A definite diagnosis of specific conditions such as fibroadenoma, fat necrosis, Granulomatous mastitis or reactive lymphadenitis may be given if sufficient features are present for a confident diagnosis. Frable<sup>5</sup> noted that some authors state that it is not possible to differentiate between histological types of breast cancer. The use of FNAC has resulted in a reduction in the number of Trucut and frozen section biopsies performed. When the mass is clinically and mammographically suspicious, the sensitivity of FNA is 80-98%. The false negative rate of FNA is 2 to 10%.6

Breast cancer tumor sampling by core needle biopsy (CNB) is widely used in many centers and has proved to be up to 97% accurate at confirming the presence of malignant tissue within a suspicious lesion. The Tru-cut needle is the most commonly used cutting needle for biopsy of breast masses. False positive diagnostic rates are lower than with FNAC specimen because more tissue is submitted for analysis. It is an increasingly used technique in the pre-operative diagnosis of breast carcinoma, as it provides useful prognostic information

with respect to tumor type and grade. Rare complications occur with trucut biopsy e.g. bruising in 2% cases while pain during FNAC and trucut biopsy is almost equal. Pretreatment core biopsy histology accurately predicts residual tumor histology following primary chemotherapy and surgery in patients with breast cancer. Some studies have found sensitivity of trucut biopsy to be equal to that of surgical excisional biopsy. Trucut biopsy before surgical excision can facilitate planning and reduce the need of numerous surgical procedures. It is concluded from different studies that FNAC is a valuable method, although moderately less sensitive than Core biopsy for diagnosing breast lesions. The sensitivity of FNAC, Core needle and frozen section reaches 75%, 92-94% and 100% respectively in another study.

#### **PATIENTS AND METHODS**

The comparative study was conducted on 25 consecutive females presented with clinically palpable breast lump to Breast clinic of ward 03 of Jinnah Postgraduate Medical Centre, from July 2003 to April 2004. They underwent Fine needle aspiration cytology and tru cut biopsy simultaneously. FNA was done with 21-23 gauge needles where as 14-16 gauges tru-cut needle used for biopsy after infiltrating local anaesthesia around the lesion. Excision biopsy of the lump was done later on for confirmation of diagnosis.

Fine needle aspiration cytology and tru-cut biopsy were considered true positive when both cytology and histopathology showed similar results in FNAC and the histopathology result on tru-cut and excision biopsy were similar. It was false positive when histopathology did not confirm the positive cytology/ tru-cut biopsy report. It was false negative when cytology / tru-cut results were negative where as the histology report showed either a positive result, malignant or a different benign condition.

#### **INCLUSION CRITERIA**

Motivated female patients with age more than 12 years and clinically palpable breast lump of size not less than 3cm.

#### **EXCLUSION CRITERIA**

Males, non motivated females, age less than 12 years, lump less than 3cm in size and impalpable breast lumps were excluded from the study.

#### **RESULTS**

The mean age of patients was  $45.28 \pm 9.02$  years. Mininumum age was 32 where as maximum 66 years. Left breast was involved in 14 and right in 11 cases respectively. The most frequent site involved was upper outer quadrant in 8 (32%) patients, retroareolar and whole breast involved in 5 (20%) cases each. Other sites are mentioned in Table I.

| TABL<br>NO | E-I<br>SITE INVOLVED | TOTAL ( N≃25) | PERCENTAGE |
|------------|----------------------|---------------|------------|
| 1.         | Upper outer q        | - 80          | 32%        |
| 2.         | Retroareolar         | 05            | 20%        |
| 3.         | Whole breast         | <b>0</b> 5    | 20%        |
| 4.         | Lower outer q        | 03            | 12%        |
| 5.         | Lower inner q        | 02            | 08%        |
| 6.         | Upper inner q        | 02            | 08%        |

The most common lesion diagnosed on FNAC is Malignancy (n=15), making 60% of the total cases. Type of malignancy was not defined accurately in 11 cases and single case of benign phylloides tumor was reported false positively. Six cases were diagnosed as benign lesions; on histopathology two of these were Fibroadenomas, two Phylloides tumors, one epithelial hyperplasia, and single case of Invasive ductal Carcinomas was reported false negatively. Fibroadenomas were diagnosed in three cases, two confirmed on biopsy and one found out to be tuberculous (false negative). Another case of tuberculosis was diagnosed correctly on FNAC. Twenty two out of twenty five lesions were diagnosed correctly on FNAC, with 88% sensitivity. (Table II).

| TABLE-II<br>FNAC<br>DIAGNOSIS | NO.<br>n=25 | FINAL<br>DIAGNOSIS     | FALS | E FALSI<br>VE NEGATI |                 |
|-------------------------------|-------------|------------------------|------|----------------------|-----------------|
| Tuberculosis                  | 01          | Tuberculosis- 01       |      | • . da               |                 |
| Benign                        | 06          | Fibroadenoma-02        |      | 01                   |                 |
|                               |             | phylloides tumor-02    |      |                      | À,              |
|                               |             | Epith. Hyperplasia-01  |      |                      | \$ .            |
|                               |             | Invasive ductal Ca-01- |      |                      | V. By           |
| Fibroadenoma                  | 03          | Fibroadenoma-02        | 01   |                      | ٠.              |
|                               |             | Tuberculosis-01        |      | - Table 1 24         | ";              |
| Ductal Ca                     | 03          | Invasive ductal Ca-03  |      | an as migra.         | #43.5           |
| Malignant                     | 10          | Invasive ductal Ca-10  |      | origija erro 🕳 rej   | 75.7            |
| Colloid Ca                    | 02          | Phylloides tumor-01    | . 01 |                      |                 |
|                               |             | Invasive ductal Ca-01  |      |                      | , in the second |

On Trucut biopsy the most common diagnosed lesion was Carcinoma in patients 16 (64%). Exact type of Invasive ductal carcinoma was diagnosed correctly in eleven cases where as four cases of similar lesion were only reported as malignant and single case of benign phylloides tumor was false positively reported. Four cases of fibroadenomas diagnosed on tru cut confirmed accurate on biopsy. One case of epithelial hyperplasia and phylloides tumor each reported as benign lesion. Two cases of tuberculosis and single of phylloides tumor were also diagnosed accurately on trucut biopsy. Sensitivity calculated is 96% with twenty four out of twenty five lesions were reported accurately. (Table III.)

| TABLE-III    |    |                                       |     |        |         |
|--------------|----|---------------------------------------|-----|--------|---------|
|              |    | FINAL DIAGNOSIS<br>(HISTOPATHOLOGY) P |     |        |         |
| Tuberculosis | 02 | Tuberculosis-02                       | -   | ٠. ـ   |         |
| Fibroadenoma | 04 | Fibroadenoma-04                       | -   | -      |         |
| Benign       | 02 | Phylloides tumor-01                   |     |        |         |
|              |    | Epith. Hyperplasia-01                 | 100 | 11.0   | 211     |
| Phylloides   | 01 | Phylloides-01                         | *   | -      |         |
| Malignant    | 05 | Invasive ductal Ca-04                 | 01  | -      |         |
|              |    | Phylloides tumor-01                   |     | or due | 4.05    |
| Ductal Ca    | 11 | Invasive ductal Ca-11                 | -   |        | Yo yali |

#### DISCUSSION

A palpable breast lump is a common diagnostic problem both presenting to the General practitioner and the surgeon. In view of the high proportion of malignancy in older age group and also of sporadic occurrence of cancer in young women, triple assessment should be done in order to exclude or demonstrate malignancy and select suitable patients for surgery.<sup>15</sup>

Ductal Carcinoma was the most common histopathological diagnosis and comprised 60% Of the total cases (n=15). This high percentage is due to patient's selection criteria based on the age, size of the palpable lump and also on the tumor type as Ductal carcinoma is the commonest cancer of breast and comprise of 81% of the breast neoplasms.16 FNAC diagnosed 14 carcinoma accurately, but not able to describe the exact lesion type. The colloid carcinoma was not taken as false positive in our study as the lesion was not reported as benign. Phylloides tumor was falsely reported as malignant. Trucut biopsy has accurately diagnosed 11 lesions as ductal Carcinoma. Where as the remaining 4 were reported as being malignant. McIntosh® mentioned that trucut provides useful information regarding tumor type. In our study we found that 73% (n=11) of carcinoma were diagnosed with tumor type by

Fibroadenoma is a benign tumor and second most common solid tumor in breast after carcinoma and is the most common tumor in women younger than age 30 years. People used to undergo excision biopsy of fibroadenoma to remove the tumor and establish diagnosis. Now tru cut biopsy is widely used and lesion is left undisturbed in the breast if the diagnosis is fibroadenoma. Fibroadenoma is not associated with an increased risk of breast cancer. However, DuPont et al. boserved in a case-control study that complex fibroadenomas (those with cysts greater than 3mm in diameter, sclerosing adenosis, epithelial calcifications or papillary changes) increased the relative risk for breast cancer to 3.1.

In our study four fibroadenomas were reported on histopathologies which were accurately diagnosed on tru-cut biopsy, where as on FNA three of these were diagnosed and one reported as a benign lesion. Reflecting the efficacy of tru cut in characterizing the lump.

Phylloides tumor is a rare fibroepithelial neoplasia which corresponds to 0.5% of the reported breast tumors. Its biological behavior is distinct from that of fibroadenoma, since it shows between 20 and 40% of local recurrence, and if malignant may cause metastasis. <sup>19</sup> Core needle histologic examination of phylloides tumor allows the physician to preoperatively plan the definitive management at one surgical procedure, reducing the

need for reoperations.<sup>20</sup> Aspiration cytology is unreliable because of the in homogeneity of the tumor.<sup>21</sup>

One out of three phylloides tumors in our study was diagnosed accurately on Tru-cut biopsy. The other two were reported as a benign and malignant each. FNAC failed to diagnose any of the phylloides tumors and reported two as benign lesions and one as colloid carcinoma.

Breast tuberculosis is an uncommon disease.<sup>22</sup> The main problem is to differentiate it from mammary carcinoma when it presents as a lump.<sup>23</sup> FNAC in Tuberculosis is helpful in differentiating on inflammatory lesion from malignant one but cannot differentiate the various granulomatous lesions of the breast.<sup>24</sup> The diagnostic proof is the presence of caseating granuloma on histopathology.<sup>22</sup> We found tru-cut biopsy a very helpful tool for diagnosing the lesion accurately while FNAC has suggested Tuberculosis in one case while the other was reported as a benign lesion.

Epithelial hyperplasia was diagnosed as a benign lesion both on FNA and Tru cut biopsy. Although it is a benign condition but in women with palpable cysts, complex fibroadenomas, duct papillomas, sclerosis adenosis, and moderate or florid epithelial hyperplasia have a slightly higher risk of breast cancer (1.5-3 times) than women without these changes.<sup>25</sup> Our patient had moderate hyperplasia without atypia and was kept on three monthly follow ups.

#### CONCLUSION

Although FNAC is a valuable diagnostic tool for breast lesions. Tru-cut biopsy is preferred because of its better characterization of benign and malignant lesions.

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### WILSON'S DISEASE

#### YASMIN HASAN, KARIMULLAH MAKKI, SHEHLA AHMED AND MUHAMMAD ABDULLAH

#### ABSTRACT **Objectives**

To study the various pattern of clinical manifestations leading to late diagnosis, the biochemical and radiologic abnormalities and the response to treatment in patients with Wilson's disease.

#### Design

Observational case series study.

#### Place And Duration

Department of Neurology, Dow University of Health sciences, Karachi from January 1993 to December 2003.

#### Patients And Methods

Record of patients with Wilson's disease was analyzed with particular reference to clinical features, investigations and family screening at the time of presentation. The treatment received and the clinical profile on follow up with respect to side effects and whether the patient improved deteriorated or remained the same.

#### Results

Nineteen patients were diagnosed as having Wilson's disease over a period of 10 years. There were 6 males and 13 females with an age range of 8 to 40 years. Three patients had pure neurological features, 1 hepatic and a combination of hepatic, neurologic or psychiatric features were seen in 15 patients. Ten cases had a positive family history. Patients were started on penicillamine and zinc sulphate. Thirteen patients were followed over a period of 2 months to 7 years. 10 improved, 3 deteriorated and 7 developed side effects of penicillamine.

#### Conclusion

A strong suspicion of Wilson's disease should be raised in patients with unexplained neurological or hepatic disorder.

KEY WORDS:-

Wilson's disease, Penicillamine and Zinc sulphate.

#### INTRODUCTION

Wilson's disease was first described by Kinner Wilson's in 1912 as progressive lenticular degeneration.1 It is transmitted as an autosomal recessive disorder. The abnormal gene is located on the long arm of chromosome

Correspondence:

Dr. Karim Ullah Makki, Medical Unit II,

Dow University of Health Sciences,

Karachi.

13, which codes for a copper transport P- type adenosine triphosphatase.2

The gene ATP7B is expressed mainly in hepatocytes and functions in the trans-membrane transport of copper.34.5 Absence or reduced functions in the ATP7B leads to decreased excretion of copper in bile resulting in excess accumulation of copper in the liver and other organs like the brain, kidney cornea etc.6

Wilson's disease occurs worldwide with an incidence of 30 affected individual per million populations. It can present clinically as liver disease, a progressive neurologic disorder or a psychiatric illness, usually between the ages of 4 to 40 years.

In this study we reviewed the clinical profile of 19 patients admitted in the Department of Neurology, Dow University Health Sciences, Karachi.

#### **PATIENTS & METHOD**

Nineteen patients with Wilson's disease were diagnosed over a period of 10 years in the Department of Neurology, Dow University of Health Sciences, Karachi. Records were analyzed with particular reference to age of onset of symptoms, time lag between onset of symptoms and diagnosis, family history suggestive of Wilson's disease, clinical features suggestive of hepatic, neurologic and psychiatric involvement or a combination of features. Slit lamp examination for the presence of Kayser Fleischer Ring (K.F. Ring), urinary copper and serum ceruloplasmin level. Liver function test and neuroimaging in the form of C.T. scan and magnetic resonance imaging (MRI) Brain.

Patients were started on penicillamine and zinc and advised to take a diet low in copper. They were followed to look for the effects of treatment whether they improved, deteriorated or remained unchanged.

#### **RESULTS**

Nineteen patients were diagnosed as having Wilson's disease (WD) over a period of 10 years from 1993 to 2003. There were six males and thirteen females with an age range of 8 to 40 years, maximum between 12 to 20 years. The clinical features were divided into five groups. One patient presented with hepatic feature. She had jaundice, ascites with hepaticsplenomegaly. One patient had a combination of hepatic and neurologic feature. He had fulminant hepatic failure with dystonic posturing of limbs. Three patients had pure neurologic features. Five patients had a combination of neurologic and psychiatric features where as a combination of hepatic, neurologic and psychiatric features were seen in nine patients.

Jaundice was the commonest hepatic feature, hepatosplenomegaly was seen in one patient and two patients had only spleenomegaly. Altered mentation was seen in three patients, two had ascites and one had gastrointestinal hemorrhage.

Dysarthria, dystonia and gait difficulty were the commonest neurological features. Six patients exhibited tremors and three had seizures. Two patients were ataxic whereas one had titubation. There were four patients who had a history of headache. Eight patients exhibited emotional liability. Two were psychotic and aggressive. One patient inflicted self-injury and one had anxiety. Family history suggestive of Wilson's disease was seen in

ten cases, two were symptomatic, two patients had neurologic features, four cases had hepatic involvement and a combination of hepatic and neurologic involvement was seen in two patients.

K.F.ring was present in seventeen patients. It was not carried out in two patients. One had fulminant hepatic failure and the second had titubation. Serum copper was carried out in first seven patients. It was decreased in six patients and normal in one patient. Serum ceruloplasmin was decreased in seventeen patients, normal in one patient and not done in one patient. Twenty four hours urinary copper was increased in ten cases, normal in two and not done in seven cases.

Liver function test and prothrombin time were abnormal in seven patients. Four patients had thrombocytopenia, two had leucopenia and decreased hemoglobin. Ultrasound evidence of chronic liver disease was present in twelve patients. MRI was done in eleven patients, majority of them showed abnormal signals in the basal ganglia. In some the lesions were seen in the pons, midbrain and cerebellum. Brain atrophy was also present. Seventeen patients were treated with Penicillamine and zinc sulphate and two with only zinc sulphate. One patient with fulminant hepatic failure died during his stay in the hospital.

Patients were followed over a period of seven years. Minimum duration of follow up was two months. Total number of patients who turned for follow up was thirteen. Ten improved, three deteriorated and five did not turn for a follow up. In seven patients Penicillamine had to be stopped due to leukopenia and thrombocytopenia.

#### DISCUSSION

Wilson's disease (WD) is a rare disorder of copper metabolism. It occurs in about one in four thousand people. 8.9.10 In our study only nineteen indexed cases were collected over a period of ten years, however larger series have been reported having 283 patients of Wilson's disease. 11 Majority of patients with Wilson's disease present between ages 5 to 35 years. The youngest patient reported with cirrhosis due to Wilson's disease was of 3 years. 12.13 In one series the lowest age for Wilson's disease was 10 years8. In our study the age range was 8 to 40 years.

Wilson's disease has protean manifestations and is sufficiently rare. Physicians often fail to recognize the possibility of this disease and this element is responsible for the time lag of onset of this disease and its diagnosis. In an Indian study the time lag between onset of symptoms and diagnosis was 2 months to 6 years, whereas in an Italian study mean delay to diagnosis was 5.9 years, the mean delay to diagnosis in our study was 4.5 years.

A combination of hepatic, neurologic and psychiatric features dominated our study. Out of 19 indexed cases 15 presented with a combination of features as was seen in the Indian study.13 Dysarthria, dystonia and gait difficulty were the commonest neurological features in our study as seen in other case series.<sup>15,16</sup> The psychiatric feature we most commonly encountered was emotional liability. though psychosis, aggressive behavior, anxiety and selfinjury were also seen. In a series of 195 cases of Wilson's disease 99 patients displayed some evidence of psychopathologic features. The most common were abnormal behavior and personality change, although depression and cognitive impairment were also noted frequently. Schizophrenia like psychosis was rare.17 In an Indian series of 31 cases 18 patients showed psychopathologic features, cognitive impairment (45.2%), affective symptomatology (41.9%) and behavior abnormality (29%). Only one patient had schizophrenia like psychosis.18

The hepatic involvement ranged from self resolving hepatitis to chronic hepatitis and cirrhosis. We had one patient with fulminant hepatic failure, which is consistent with the Indian and Italian study. 13,14 However there are centers where only hepatic manifestations of Wilson's disease were studied. A large number of cases presented with fulminant hepatic failure. Out of thirty four patients eight had fulminant hepatic failure.19 In another study from a transplant center out of 17 patients with Wilson's disease 11 had fulminant hepatic failure, rest had the presentation of chronic hepatits20. In a study of Wilson's disease spread over three decades, thirty patients with Wilson's disease were reviewed, 22 patients presented with liver manifestations, 8 with fulminant hepatic failure and 14 with chronic liver disease.21 The reason for this high incidence of serious forms of Wilson's disease such as cirrhosis and fulminant hepatic failure may be due to the fact that these studies are being presented from a tertiary center dealing with liver transplant.

The importance of a family history cannot be over emphasized. A family history of jaundice or cirrhosis in a child with unexplained jaundice or movement disorder should make one strongly consider Wilson's disease. Family screening in a WD patient with estimation of 24hrs urinary copper or serum ceruloplasmin should be carried out.

In our study 10 indexed cases had a family history strongly suggestive of Wilson's disease as compared to an Italian study where out of 30 cases 10 had a strong family history. In an Indian study out of 25 cases 5 had a family history strongly suggestive of Wilson's disease.<sup>13</sup>

Kayser Fleischer rings (K.F.Ring) present deposition of copper in the Decemet's membrane of cornea. A large series of patients with WD showed that K.F.Ring is present in only 50-62% of patients with mainly hepatic disease at

the time of diagnosis.<sup>20,21,22,23,24</sup> In children presenting with liver disease K.F.Rings are usually absent.<sup>25,26,27</sup> K.F. Rings are almost invariably present in patients with neurological presentations, but even in these patients they may not be found in 5%.<sup>22,28</sup> In our study K.F.Ring was seen in 17 cases. In 2 of them it was not carried out. Sunflower cataract also seen by slit lamp examination represents deposition of copper in the lens<sup>29</sup>, was not present in any of our cases.

Serum ceruloplasmin is usually abnormally low in Wilson's disease.<sup>8,9,10</sup> A level less than 200mg/l has been considered consistent with WD and diagnostic if associated with K.F. ring although there are different laboratory references6. In our study 17 patients had low serum ceruloplasmin level.1. Normal levels of serum ceruloplasmin have been reported in the literature. In one series 12 of 55 patients had normal serum ceruloplasmin and no K.F.Ring.<sup>21</sup> In another series 6 of 22 WD patients had serum ceruloplasmin greater than 170 mg/l and 4 of these had no K.F.ring.<sup>22</sup>

WD is a disease of copper overload but the total serum copper is usually decreased in proportion to the decreased ceruloplasmin in the circulation.

In patients with severe liver injury serum copper may be within the normal range despite a decreased serum ceruloplasmin level. In acute fulminant hepatic failure due to the WD levels of serum copper may be markedly elevated due to the sudden release of metal from tissue stores6. In our study free copper was decreased in 6 patients, normal in 1 and not carried out in 12 patients.

The 24 hours urinary excretion of copper reflects the amount of non-ceruloplasmin bound copper in the circulation. Basal measurements provide useful diagnostic information. Basal 24 hours urinary excretion of copper in WD is typically greater than 100 microgram in symptomatic patients but a finding greater than 40 microgram may indicate WD and requires further investigation.<sup>6</sup>

Out of 19 patients, 24 hours urinary copper was estimated in 12 patients, not carried out in 7 patients. They are those 7 cases in whom serum free copper was carried out. In them the diagnosis was based on the presence of K.F.Ring, decreased ceruloplasmin level and decreased free serum copper.

Cranial magnetic resonance imaging was abnormal in 11 patients in the rest it was not carried out. Most of the patients showed abnormal signal intensity in the basal ganglia particularly putamen and globus pallidus. Thalamus, pons, midbrain and cerebellar involvement were also seen. Lesions in the white matter and brain atrophy were also present in some of the cases. In one study atrophy was present in majority of the cases and frequently involved sites were putamen and pons.

Involvement of midbrain, thalamus and caudate nucleus were also encountered.<sup>30</sup> In another study the commonest abnormality was seen in the basal ganglia (74%) followed by white matter changes (59%) and brainstem changes (20.5%).

D-Penicillamine, the first effective drug was introduced by Walsh for the treatment of WD in 1956.<sup>31,32</sup> It is fully effective in the treatment of WD in terms of constantly producing a negative copper balance, but it has become controversial because of the long list of toxicities and initial neurological worsening.<sup>33</sup> As much safer alternatives are emerging like tetrathiomolybdate and trientine.<sup>34, 35,36, 37,30</sup> The use of Penicillamine is no longer recommended in WD.<sup>39</sup> Long term studies showed that Penicillamine when used by an experienced physician is safe and effective in the treatment of WD. Initial deterioration of neurological symptoms if it occurs does not alter the final outcome unfavorably.<sup>14, 40, 41</sup>

In a series of 300 cases Walsh reported only 3 patients who showed rapid deterioration which could not be reversed.<sup>39</sup> In our study initial neurological deterioration with Penicillamine was noted in one patient, which could not be reversed. One patient with fulminant hepatic failure died during his stay in hospital as liver transplant facility is not available in our part of the world, which is a treatment of choice in fulminant hepatic failure.<sup>5</sup>

One patient initially improved on penicillamine and zinc sulphate later deteriorated because of drug noncompliance. In 7 patients penicillamine had to be stopped because leucopenia and thrombocytopenia. Along with penicillamine zinc sulphate was started in all patients as a maintenance therapy. No toxic side effects were noted as mentioned in the literature.<sup>42</sup>

WD without treatment is fatal. It should strongly be considered in patients with liver and neurological disease of unknown origin. Early diagnosis and treatment are essential to prevent severe complications and screening of the family members will lead to detection of asymptomatic patients.

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# FREQUENCY OF HEPATITIS-C VIRUS IN THE SPOUSES OF HCV POSITIVE PATIENTS AND RISK FACTORS OF THE TWO GROUPS

NARESH KUMAR, RUKHSANA A.SATTAR AND JAMAL ARA

# ABSTRACT Objective

To find out frequency of HCV in the spouses of HCV positive cases and risk factors of the two groups.

# Study Design

Descriptive study.

# Place & Duration

Ward 5 JPMC Karachi from August 2003 to January 2004.

### Patients And Methods

Fifty patients infected with HCV, aged 18 year and above of both sexes and their spouses were included through structured questionnaire while others suffering from HBV, HIV and other etiologies were excluded. Samples were collected from the spouses for anti-HCV using micro particle enzyme immunoassay (MEIA) method. Data was analyzed using SPSS.

# Results

Anti-HCV detected in 9 (18%) spouses of positive cases. The risk factors were unsterlized injections by GP's (58%), previous surgery and dental procedure in 48% patients, blood transfusion and sharing of shaving razors equally figured in 19 (38%) patients, sharing of towels 40% and toothbrush was 28%. Duration of marriage contributed a major role; average duration was  $17.86 \pm 8.91$  years.

# Conclusion

There was high frequency of HCV in the spouses of positive cases and major risk factors were blood transfusion, I/V drug abuse, unsterlized injections, previous surgery, dental procedures and longer duration of marriages.

**KEY WORDS:-**

Hepatitis C Virus, Spouse and Chronic infection.

# INTRODUCTION

HCV induced chronic liver disease is one of the two most common causes of chronic liver disease in Pakistan. It is estimated that over 100 million people world wide are infected with HCV. The routes of transmission for HCV include blood transfusion, parenteral drug abuse, blood contaminated needles, haemodialysis, tattooing, acupunctures, ear piercing, barbers, dental therapy and surgery. However studies from USA and Europe show that only 50% of Hepatitis C positive cases can be related to the above-mentioned routes.<sup>2</sup> So there are reasons to believe that non-parenteral transmission is important mode of transmission of hepatitis virus infection.<sup>3</sup>

Correspondence: Dr. Jamal Ara, Medical Unit-1Ward (5), JPMC,

Many studies have been done and have somewhat

Karachi.

conflicting results. One study conducted in Japan, showed the high prevalence of HCV in prostitutes.<sup>4</sup> In Europe it was in male homosexuals.<sup>5,6,7</sup> while other studies showed that sex partners of patient infected with both HCV and human immunodeficiency virus<sup>8</sup> and patients attending sexually transmitted diseases clinics.<sup>9,10</sup> suggest that sexual transmission may occur. Other study, which was conducted in Austria, showed anti-HCV antibodies in 5% of spouses.<sup>11</sup>

One study conducted in Japan on 96 patients, revealed interfamilial other than heterosexual transmission. This study revealed 5% of children vs.9% of persons other than spouses living in same household to be anti-HCV positive. In other study11.3% off springs and 48.8% of their siblings who were household contacts were anti-HCV positive. However Al Nasser et al from Saudi Arabia concluded interfamilial transmission of HCV as a major mode of spread in Saudi Arabia and overall prevalence was 3.6% in males and 3.15 in females.

In our country, all types of hepatitis viruses are prevalent; hepatitis A virus (HAV) infection occurs mainly in children and HBV and HCV infections mainly in adults. <sup>15</sup> A few preliminary studies have revealed the gravity of the problem in our setup. General population based studies have reported HBs Ag prevalence rate of up to 18.66% <sup>16</sup> and that of anti-HCV up to 25.7%. <sup>17</sup> Correspondingly high prevalence rates of HBs Ag and anti-HCV in healthy blood donors have been reported. <sup>18,19</sup>

A study done in central Punjab, showed the prevalence of anti-HCV positivity is about 4%.20 while Umar from Rawalpindi revealed that 23% had anti-HCV positive family contacts.21 All theses figures are alarming when compared with the international studies. This study is the first of series to determine whether sexual exposure is a potential risk factor in the spouses of chronically infected patients with HCV.

# **PATIENTS AND METHODS**

This descriptive study was conducted at Ward-5, Jinnah Postgraduate Medical Centre Karachi from August 2003 to January 2004. Consecutive patients aged > 18 years of both sexes and their spouses attending inpatients / outpatients and who were anti-HCV antibody positive were identified. All study subjects (patients and their spouses) were interviewed on a structured questionnaire which covered demographic and clinical profile of the patient and spouse.

Informed consents were taken from patients and their spouses. Questionnaires were filled after assessment for possible exposure to a number of risk factors and physical examination of both partners. After initial information, 5ml of blood samples were collected from the spouses. These samples were taken in 5cc disposable, sterile syringes and immediately transported to laboratory where tests

were performed. The method used for these test was Micro particle Enzyme Immunoassay (MEIA) according to the manufacture's specifications (Abbott Diagnostics).

Descriptive statistics; frequency, percentage, average etc. were computed for data presentation by using SPSS version-10.

# **RESULTS**

Fifty patients with HCV positive were analyzed and their spouses were also observed to assess possible contribution of HCV positive in the patients. There were 34 (68%) males and 16 (32%) females in the study. Average age of the patients was  $41.2 \pm 11.5$  (ranging from 22 to 75) years. Average duration of the marriage was  $17.86 \pm 8.91$  (ranging from 4 to 40) years.

In the first stage of the study, the history of the risk factors associated with HCV positive patients was analyzed. Patients were found with single, combined or multiple risk factors. The presence of risk factors is shown in Table-I.

| TABLE-I                                      | RISK F   | ACTORS IN                    | HCV P    | OSITIVE PAT                 |           |
|--|--|------------------------------|----------|-----------------------------|-----------|
| Risk Factors                                 |  | Patient<br>n=50<br>Frequency | \$<br>%  | Spouse<br>n=50<br>Frequency |           |
| Injection from GP's                          |  | 33                           | 66       | 29                          | 58        |
| previous Surgery<br>Dental procedure         |  | 24<br>24                     | 48<br>48 | 17<br>18                    | 34<br>36  |
| Sharing of towel                             |  | 20<br>19                     | 40<br>38 |                             | 22<br>34  |
| Sharing of shaving                           |  | 19                           | 38       | 17                          | 34        |
| Sharing of tooth bru<br>Tattooing            | usn  | 14<br>10                     | 28<br>20 | 13<br>8-                    | 26<br>16  |
| Intravenous drug al<br>Extramarital relation | and the same of th | 3                            | 6<br>2   | 0                           | 0<br>0    |
| Note: Key: GP's = G                          | eneral pra   | nctitioners, %=              | Percent  | age                         | 4030002#w |

According to the second stage of the study, blood samples from the spouses of HCV positive patients were collected and different risk factors were assessed. A total 9 (18%) spouses were diagnosed HCV positive. The sex distribution in these 9 positive spouses was 3, males and 6 females, The common risk factors in patients and their spouses were unsterlized injections (78%, 100%), (Table-II).

| TABLE-II                      | ASSOCIATED                                  |        |           |               |
|-------------------------------|---|--------|-----------|---------------|
| Risk Factors                  | POSITIVE COUPLES.  Patients Spouses n=9 n=9 |        |           |               |
| :                             | Frequency                                   | %      | Frequency | %             |
| Injection from GP's           | 7 - 6                                       | 78     | 4: 9 T    | 100           |
| Extramarital relations        | 0   | 0      | 0         | <b>0</b>      |
| Previous Surgery              | 7   | 78     | 6         | 67            |
| Dental procedure              | 7   | 78     | 8         | 89            |
| Sharing of towel              | 7   | 78     | 6         | 67            |
| Blood transfusion             | 8   | 89     | 6         | 67            |
| Sharing of shaving razors     | 8   | 89     | 6.2%      | 67            |
| Sharing of tooth brush        | -6  | 67     | 7         | - 78 ·        |
| Intravenous drug abuse        |   | 11     | 0.5       | . 0           |
| Tattooing                     | 1   | 11     | 2         | *** <b>22</b> |
| Note: Key: GP's = General pra | ctitioners, %= Pe                           | rcenta | ige -     |               |

# DISCUSSION

We found 18% sero-positivity of anti HCV antibody in the spouses of chronically infected HCV patients. This is higher rate for partners of the infected patients. Our study is in contrast to the studies from Western countries, which has placed HCV prevalence 0 to 5%<sup>22,23</sup> in the monogamous partners of infected patients. However our rates are comparable to those reported by studies from East Asian countries. They have reported spouse prevalence rates of up to 14%.<sup>24,25</sup> This similarity can possibly be attributed to somewhat similar socioeconomic conditions and practices in the Asian people, which are different from those in the West.

The sample size in studies, that reported high prevalence in study partners, varied from 21 to 168. The highest rate of 14% being associated with the smallest sample of 21. One of the highest rates (11%) was observed in one of the largest samples (n=143).24 However, this result was based on screening with a first generation ELISA without Immunoblot confirmation. The sample size of our study is of course small and this may have affected the actual outcome. This is one limitation of our study. Hence, to avoid this bias, large-scale studies are needed to reveal the facts. We cannot assess directly the extent to which our findings may have been affected by limitations of assay sensitivity and specificity. We could not confirm the sero-status of the positive spouses with more sensitive and specific tests i.e. Recombinant Immunoblot Assay (RIBA) or HCV RNA by PCR in HCV positive spouses. Nonetheless, our study has indicated high frequency rates of infections in the spouses of chronically infected HCV patients in our country and it appears that longer duration of partnership with an infected patient plays an important role in acquisition of these infections. Besides, we assessed parenteral risks factors in our study. The most frequent risk factor observed was unsterlized injections 33 (66%) by general practitioners.

# CONCLUSION

From our study, it is concluded that there is a high frequency of HCV in the spouses of chronically infected patients in our population. These high rates suggest that precautions are necessary for the regular partners of chronically infected HCV for the spouses of HCV positive patients.

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# A STUDY OF 30 CASES OF RENAL AMYLOIDOSIS

# A. MANAN JUNEJO, S. FAROOQUI AND M. H. OSMANI

# **ABSTRACT**

# **Objectives**

To determine the clinicopathological features of renal amyloidosis.

# Patients And Methods

A total number of thirty cases were included in two year study. Diagnosis was based on renal biopsy and Congo red staining. There was 18 (60%) male and 12 (40%) female patients. Age range was 20 - 70 years and maximum number was found between 40 - 50 years.

### Results

Out of 30 cases tuberculosis was present in 10 (33.3%), leprosy in 6 (20%), bronchiectasis and rheumatoid arthritis in 4 (13.3%), chronic osteomyelitis in 3 (10%), ankylosing spondylitis in 2 (6.7%) and multiple myleoma in 1 (3.3%) case. Proteinuria was present in all cases. Generalised edems found in 26 (86.6%), hypertension in 17 (56.6%), hematuria in 10 (33.3%), hepatosplemngely in 5 (16.6%) patients.

# Conclusion

Tuberculosis was the commonest cause of secondary renal amyloidosis.

KEY WORDS:-

Renal amyloidosis, Tuberculosis, Etiology.

# INTRODUCTION

Amyloidosis is a systemic disease, characterised by deposition of abnormal fibrillary proteins in the extracellular spaces of multiple organs. The kidneys are involved in almost all cases of secondary amyloidosis. The renal manifestations vary with site of involvement. Most patients have predominant glomerular deposition and present with proteinuria accompanied by oedema. Majority of patients may present with impaired renal function. In this report we share our experience of the condition.

# **PATIENTS AND METHODS**

This study was conducted at the Department of Nephrology, Jinnah Postgraduat Medical Centre, Karachi. Thirty cases of renal amyloidosis confirmed on renal biopsy and Congo red staining, were included in this study. Various investigations like haemoglobin, ESR, total leucocyte count, differential and platelets count. blood urea nitrogen, serum creatinine, serum electrolytes, serum calcium, phosphorus, serum uric acid, alkaline phosphatase, and A/G ratio were done.

Correspondence:

Dr. A. Manan Juneio, Department of Nephrology, Jinnah Postgraduate Medical Centre, Karachi. Urine analysis, 24 hours urinary protein, and creatinine clearance, x-ray chest, x-ray of long bone were done for pulmonary Koch's, bronchiectasis, chronic osteomyelitis, and renal osteodystrophy. Ultrasound abdomen, KUB and renal biopsy were done for detailed histopathology including Congo red staining.

# RESULTS

On the basis of renal biopsy with Congo red staining. 30 patients of renal amylodosis found. Out of these patients, 18 (60%) were males and 12 (40%) females. The age ranged between 20-70 years, mean age of males was  $46.22\pm10.73$  and of females  $46.17\pm12.44$ . The duration between the primary diagnosis and appearance of secondary amyloidosis varied from 5-10 years with mean of  $7.57\pm0.26$  years.

Out of 30 patients with renal amyloidosis, the primary diagnosis was tuberculosis, in 10, leprosy 6 (20%), bronchiectasis 4 (13.3%), rheumatoid arthritis 4 (13.3%), chronic osteomyelitis 3 (10%), ankylosing spondylitis 2 (6.7%), and multiple myeloma in 1 (3.3%).

In clinical presentation, protinuria was most common finding present in all these 30 (100%) patients followed by generalized oedema in 26 (86.67%) patients. Hypertension was noted in 17 (56.67%) patients,

haematuria in 10 (33.3%), anemia 6 (20%), weight loss 5 (16.67%), hepatosplenomegaly in 5 (16.67%). JVP raised in 2 (6.67%).

Urine for albumin was done in all patients, that showed 4+ albumin in 15 patients, 3 + in 11 patients and 2+ in 4 patients. Twenty Fours hours urinary proteins in all patients showed non-nephrotic range proteinuria in 4 (13.33%) patients, nephrotic range proteinuria in 18 (60%) patients, and massive proteinuria in 8 (26.71%) patients. The overall mean value of 24 hours urinary protein was mean 4.76±2.12.

Twenty Fours hours creatinine clearance in all patients showed variable degree of impairment. In renal function BUN mean  $\pm$  SD was (48.17  $\pm$  19.63) and creatinine mean  $\pm$  SD was (3.12  $\pm$  1.25), Ultrasound of both kidneys was done to see the renal size that showed normal size in 22 (73.3%) patients A/G ratio was normal in 15 (50%) altered in 13 (43.3%) and reversed in 2 (6.7%) patients.

# DISCUSSION

Amyloidosis was first described by Rokitensky in 1842 as a waxy substance, but the name amyloid was given by Virchow in 1954 as he found that it is cellulose or starch like in nature. Its major component is non branching fibril which is composed of polypeptide chain arranged in  $\beta$  sheet formation. These fibrils can be identified on electron microscopy and by their ability to bind congo red leading to apple green birefergence under polarised light and thioflavin-T producing an intense yellow green fluroscence.  $^5$ 

According to clinical and biochemical features it has been classified into following types.

- Primary amyloidosis.<sup>6</sup>
- II) Secondary amyloidosis.10
- III) Heredo familial amyloidosis.7
- IV) Senile amyloidosis.8
- V) Dialysis related amyloidosis.9

Renal involvement is common and serious manifestation in systemic amyloidosis. In our study 18 (60%) patients were males and 12 (40%) were females indicating male preponderance. Urban et el in 1993 have also observed male preponderance in patients with amyloidosis. In this study maximum number was found in 40 – 50 years. Urban et al had shown that maximum incidence between 55 – 60 years of age which is higher than our study. It could be due to a more prevalence of chronic infection in our young population than the westeren world.

In our study the duration between the primary disease and appearance of symptoms of renal amyloidosis varied from 5-10 years. Chugh et al from India observed interval of 1-30 years. In this study, tuberculosis was the commonest primary diagnosis and was present in 10 (33.3%) patients In a study conducted by Chugh et al

comprising 233 cases tuberculosis found in 59.1%, bronchiectasis in 24.1%. Mody et al in 1984 published that tuberculosis and other chronic suppurative lung diseases were found to be predisposing factor in 88% of patients proved to be suffering from secondary amyloidosis. Tuberculosis was noted as main cause of secondary amyloidosis by Metha et al in 72.4% of the patients.

Proteinuria was found as the main presenting feature in our study. In study of Chugh et al proteinuria was also present in all 233 (100%) cases. In the study of Mody et al, proteinuria was detected in 36 (70%) cases. In another study by Mehta et al, proteinuria was the presenting feature in all cases.

# CONCLUSION

Tubeculosis is still the major cause of secondary amyloidosis and needs to be detected early and treated in order to prevent development of renal amyloidosis. There is no satisfactory treatment for renal amyloidosis, so it is important to treat the primary disease and keep strict watch for destabilizing factors that can deteriorate the renal functions.

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# SHORT BOWEL SYNDROME: AN UPDATE

# **REVIEW ARTICLE**

# HASSAN MAHMOOD TABASSUM AND MUHAMMAD ANWAR CH.

# ABSTRACT

With the advent of anesthesia and better operative facilities, many patients suffering from dangerous gut diseases that were not likely to survive in near past are saved now. Non availability of parenteral nutrition was another factor in their early mortality. The advent of parenteral nutrition and its better availability has prolonged the misery of this killer disease. On the other hand development of rh-GH, IGF-I, short bowel lengthening, short bowel transplantation and better immunosuppressants have a ray of hope for the better survival of these patients. Some of the patients are saved and enjoying independent life, a lot are handicap of parenteral nutrition while majority is prey to this killer disease. Yet it is challenging era for the whole universe of medicine.

**KEY WORDS:** Short bowel syndrome, Intestinal failure, Short bowel transplantation, Parenteral nutrition.

Short bowel syndrome (SBS) is an uncommon disease that results from extensive intestinal resection.1 Intestinal failure prevails when parenteral support is necessary to maintain nutritional equilibrium.2 Congenital and perinatal conditions, for example, intestinal atresia, necrotizing enterocolitis (NEC) and volvulus are the most important causes in children.3 Tight abdominal closure for gastoschisis or omphalocele may cause bowel necrosis and SBS.4 In adults most frequent causes are mesenteric infarction, radiation enteritis and Crohn's disease.3 In a study of 95 cases, causes of intestinal failure included mesenteric venous thrombosis (n=12), necrotizing enterocolitis (n=11), gastroschisis (n=11), midgut volvulus (n=09), desmoid tumour (n=8), intestinal atresia (n=6), trauma (n=5), Hirschsprving's disease (n=5), Crohn's disease (n=5), intestinal pseudo obstrution (n=4), and others (N=19).5

# **PATHOGENESIS**

Short bowel patients develop severe malabsorption of macronutrients, micronutrients, electrolytes & water and pose difficult management problems. Short bowel patients are at risk of developing gall stones, oxalate kidney stones and rarely, d-lactic acidosis.<sup>6</sup> Correspondence:

Dr. Hassan Mahmood Tabassum,
Department of Surgery,
Sh. Zayed Medical College Hospital
Rahim Yar Khan

Malabsorption of both non-essential and essential nutrients, fluid and electrolytes, if not compensated for by increase intake, leads to diminish body stores and sub clinical and eventually clinical deficiencies. After intestinal resection, adaptation i.e. progressive recovery from the malabsorptive disorder may be seen.<sup>6</sup>

Besides nutritional deficiencies, some other consequences of extensive resections of the small intestine (gastric acid hypersecretion, d-lactic acidosis, nephrolithiasis, cholelithiasis), must be diagnosed, treated, an if possible, prevented. Nutritional outcome after intestinal resection depends on the extent and location of resection, presence of ileocecal valve and colon, functional status of the residual intestine and their adaptation.

Bifidobacterium lactis<sup>8</sup> and glucagons like peptide-2<sup>9</sup> have beneficial effect on intestinal adaptation. Endotoxemia<sup>10</sup>, liver dysfunction and portal hypertension<sup>11</sup> have deleterious effects. Role of erythopoiten and pentoxyfylline<sup>12</sup> are being investigated.

# **CLINICAL FEATURES & DIAGNOSIS**

Disease manifestation is based on etiological and anatomical characteristics such as remaining intestinal length and the presence of a functionally intact colon.<sup>3</sup> Short bowel syndrome presents as malabsorption leading to diarrhea and weight loss following an extensive resection of small bowel.<sup>13</sup> History of massive resection

followed by diarrhea and weight loss is important in the diagnosis of short bowel syndrome. Laboratory has to play very little role but Breath H test may be performed routinely in patients with SBS to diagnose elevated intestinal fermentation and treat eventual associated gastrointestinal symptoms<sup>14</sup>.

# **MANAGEMENT**

In the light of the data in our possession, it can be understood that nutritional therapy is the main treatment for SBS; parenteral administration has to be abandoned during the post operative period to give way to enteral nutrition, in order to create a physiological stimulus able to make the digestive system rapidly adapt to the new situation.<sup>15</sup>

Rehabilitation therapy for the short bowel syndrome can improve patient's nutritional status effectively and promote intestinal adaptation, providing a new hope for these patients. Early initiation promotes intestinal adaptation and increases patient's ability to wean from total parenteral nutrition. Therapeutic effects are related to the length of the residual small intestine, patients' age and duration between massive intestinal resection and start of the treatment. The rehabilitation therapy include enteral or parenteral nutrition, glutamine, recombinant human growth hormone and rehabilitative diet.

Quality of life was low both in the home parenteral nutrition group (HPN) and the non-HPN group. Fear of being a burden was the most frequently expressed concern. 16,17 Small and hourly oral feedings composed of food items high in complex carbohydrates and low in fat are started when appropriate and the diet is gradually increased as intestinal adaptation occurs. The goal during this process is to prevent diarrhea and allow the formation of semi formed stools. 18

A program of optimal diet plus growth hormone (0.1 mg/kg) and oral glutamine (30g/day) enhances the adaptive process and allow many patients independence from PN. However, those with extremely short segments of jejuno-ileum (<50cm) and no colon have excessive fluid and electrolyte losses, and intestinal transplantation may be the only therapy which allows some patients to be independent of PN.<sup>19</sup>

Recombinant GH improves anabolism dramatically. Glutamine has less dramatic effect. They do not have synergistic effect. Low dose GH significantly improves intestinal absorption in HPN-dependant SBS patients who were on a hyperphagic western diet. <sup>20</sup> IGF-1 has important growth promoting effect of rh-GH. <sup>21</sup> Treatment with growth hormone and glutamine may increase nutrients absorption but the effects are not sustained beyond the treatment periods. <sup>22</sup> IGF-1 facilitate weaning from parenteral to enteral nutrition. <sup>23</sup>

The functional adaptation encompass modifications of the brush border membrane fluidity and permeability as well

as up or down regulation of carrier –mediated transport.<sup>24</sup> Regaining enteral autonomy after extensive small bowel resection is dependant on intestinal adaptation.<sup>25</sup>

Parenteral nutrition associated cholestasis is a major clinical problem in pediatrics.<sup>26</sup> In patients with midgut volvulus parenteral nutrition associated cholestasis was treated with ursodeoxycholic acid.<sup>27</sup>

# SURGICAL PROCEDURES

Lillehei in 196428 introduced human intestinal transplantation. In a study of 95 cases of transplantations, procedures performed included 27 isolated intestine transplants, 28 combine live and intestine transplants, and 40 multi visceral transplants.5 Surgical procedures facilitate nutrients absorption by improving motility. prolonging intestinal transit and /or increasing mucosal contact time.29 Intestinal transplantation can be a lifesaving alternative for patients with intestinal failure.30 Intestinal transplant in appropriate for infants who would otherwise die from liver disease, recurrent sepsis, or lack of venous access.31 Liver complications in pediatric patients on home parenteral nutrition is another indication for intestinal or combine liver-intestinal transplantation.32 Transplantation has been carried out even at an age of four years.33

Since 1988, the one year patient and graft survival rates for isolated intestinal transplants have been 84% and 72% respectively. The causes of death were as follows: sepsis after rejection (N=14), respiratory failure (n=8), sepsis (n=6), multiple organ failures (n=4), arterial graft infection (n=2), intracranial hemorrhage (n=2), and fungemia, chronic rejection, graft vs host disease, necrotizing enterocolitis, pancreatitis, pulmonary embolism, and viral encephalitis (n=1) case of each. The prognosis after intestinal transplantation is better when it is performed before the onset of liver failure. Rejection monitoring with zoom video-endoscopy and new immunosuppressive therapy with sirolimus, daclizumab, and campath-I H have contributed to the improvement in patient survival.<sup>34</sup>

Forty two patients, each with <100cm of small bowel, were divided into three groups according to the length of remnant: group I patients (n=18), colon plus 50 cm to 100 cm of small bowel (SB); group II patients (n=14); colon plus 50cm of SB; Group III patients (n=10), had less than 50cm of SB without colon. One year mortality rates for group I, II and III were 50%, 72% and 100% respectively. All group I survivors developed intestinal adaptation returning to regular oral feedings at one year. Interestingly, three of four surviving patients in group II developed adaptation and were fed on oral short bowel diet (SBD) at one year. None of the group III survived more than one year. Deaths in the early postoperative period were due to multiple organ failure or from sepsis

later in the year. The authors conclude that patients with a very short bowel are candidate for intestinal transplantation when stable. If the colon is intact, however, regardless of small bowel remnant length, the patient should be given a chance to develop small bowel adaptation before making decision for permanent PN or IT.<sup>35</sup> Tarcolimus can be used as first line immunosuppressant in patients with SBS.<sup>36</sup>

# RESEARCH

L-Arg treatment increases villus height and crypt cell mitosis.<sup>36</sup> Sandostatin decreases cell proliferation and inhibits structural intestinal adaptation.<sup>37</sup> Conjugated bile therapy reduces urinary oxalate excretion in short bowel syndrome.<sup>38</sup>

# **OPERATIVE RESEARCH**

Ileal resections,<sup>39</sup> serial transverse enteroplasty<sup>40</sup> improves patients' nutritional status but body composition, femoral bone mineral densities and intestinal absorption had not completely reversed in short bowel syndrome after four years.<sup>41</sup>

The specific nursing care and step by step techniques to deliver enteral feeding through the mucous fistula are provided along with implications for the clinical practice, education and research.<sup>42</sup>

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# HYPERTROPHIC PYLORIC STENOSIS IN A PREMATURE

# A CASE REPORT

FARHAT MIRZA, YAQOOT JEHAN, JAMSHED AKHTAR, NASIR SALEEM, M. ALI, TAYYABA BATOOL AND RAEES TAQVI

# **ABSTRACT**

Infantile hypertrophic pyloric stenosis in a premature baby is a rare event. In this case report we describe our experience of one such case.

**KEY WORDS:-** Infantile pyloric stenosis, Premature and Vomiting

# INTRODUCTION

Infantile hypertrophic pyloric stenosis usually presents in full term male neonates at 3-4 weeks of gestation with projectile vomiting. Although it is described in newborns but its presence in premature is a rare occurrence. Pre-operative diagnosis is usually not possible until the condition is suspected. In one of the studies out of 212 patients with infantile hypertrophic yloric stenosis 10% were premature and most of them (< 33 weeks gestation) presented later after birth (40 vs 25 days).

# **CASE REPORT**

A four day old baby girl weighing 1.3 kg admitted with respiratory distress. She was delivered by Caesarean section prematurely at 30th week of gestation due to early rupture of membrane without labor pains. There was no birth asphyxia. She was provided incubator care. As baby was vomiting NG tube was placed. She had non bilious vomiting whenever trial feed given. Surgical opinion was the sought. X ray abdomen showed large gastric shadow with paucity of gas in rest of the abdomen (Figure I). A diagnosis of malrotation was made. Baby was thus explored. At laparotomy gut was found normally placed with normal caliber of the duodenum. Pylorus was found thickened with dilated stomach. Its appearance was not very classical. Pyloromyotomy was attempted. During the procedure perforation occurred at duodenal end that

Correspondence:
Dr. Jamshed Akhtar,
Assistant Professor,
Paediatric Surgical Unit B,
National Institute of Child Health,
Karachi.

was closed. Post-operative recovery was uneventful. Baby was put on TPN for 4 days. Trial feed started which was tolerated and then beast feed allowed. She was later discharged.

# DISCUSSION

Pyloric stenosis in premature babies have been reported previously especially those who had received transpyloric nasogastric tube feeding. It has also been reported in those prematures who did not receive trans-pyloric feeding.<sup>2</sup> The presentation in these



babies is usually delayed and as most of these babies are sick and projectile vomiting is not the feature.

Ultrasound in these babies does not show classical findings. In one of the studies the result of ultrasound examination showed that the pyloric length in infants with HPS was significantly greater in those born at term compared to those born prematurely (18.6 mm [SD 2.2] vs 17.3 mm [SD 3.1], P = 0.043); this was explainable by body weight, with length increasing by 1.13 mm (SE 0.35) per kilogram (P = 0.002). There was no significant relationship with measured muscle thickness.<sup>3</sup>

A high degree of suspicion needs to be exercised to arrive at diagnosis. Our patient differs as the baby developed

early vomiting which is not usually described in other prematures with pyloric stenosis. This is the reason why we suspected malrotation in our patient. Plain x ray abdomen in our patient showed persistent dilated gastric shadow which is a feature described in other reports as well. The message that we would like to convey is to consider idiopathic hypertrophic pyloric stenosis in the differential diagnosis of premature infants with upper gastrointestinal tract symptoms.

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# SALMONELLA SPONDYLITIS A CASE REPORT

FAIQ SHAFAHAT, HISHAM AMIN UL HAQ, FARID ULLAH ZIMRI, MUHAMMAD HUSSAIN, GULRAIZ AHMED CHEEMA, MUHAMMAD SAEED MINHAS, ANISUDDIN BHATTI AND GHULAM MEHBOOB

# **ABSTRACT**

Salmonella infection is common in the tropics, but osteomyelitis of the spine due to salmonella is rare. We are reporting a case of 23 years old house wife, who presented with fever and backache and was subsequently diagnosed to have salmonella spondylitis.

KEY WORDS:- Salmonella, Spine, Osteomyelitis.

# INTRODUCTION

Salmonella infection of spine usually presents with back pain with, or without constitutional symptoms. Diagnosis requires a high index of suspicion and appropriate radiological and laboratory studies. Vertebral osteomyelitis can be caused by a variety of microorganisms. The hematogenous, pyogenic form is characteristically a disease of people over 50 years, predominantly in the male population. Osteomyelitis of the spine caused by salmonella is rare Osteomyelitis due to salmonella infection is known to be associated with sickle cell anemia, various haemoglobinopathies and immune suppressive state, It may also occur in normal host. The conclusive diagnosis of osteomyelitis requires isolation of pathogen in the aspirate from bony lesion, and blood culture.

### **CASE REPORT**

A 23 years house wife presented with the complaint of pain in the lower back with radiation to both lower limbs for the last three months. The backache had gradually increased in intensity and was not associated with fever, weight loss or any gastrointestinal symptoms. History of contact with any tuberculous patient was negative. Local examination revealed loss of lumbar lordosis, point tenderness and pain on terminal flexion and extension. Thoracolumbar spine movement and straight leg raising (SLR) were grossly restricted. Motor and sensory assessments were unremarkable with her sphincters functioning normally. ESR was 70mm / 1st hour, with a total leucocyte count of 11,000 / cm.³ A peripheral blood Correspondence:

Prof: Ghulam Mehboob,
Department of Orthopaedic Surgery,
Jinnah Postgraduate Medical Centre,
Karachi.

film revealed normocytic picture, with a test for sickle cell anemia being negative.

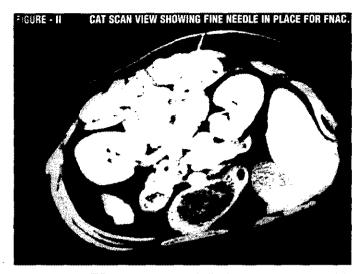
MRI revealed discitis at the L2, L3 level involving both the adjacent vertebrae. Small epidural and anterior spinal collection was noticed with modest amount of neural compression (Figure I).

Correlation with the above features, a tentative diagnosis of infective spondylitis at L2 L3 level was made. Tc-99 bone scan reveled increase up take at L2 L3 level, CAT scan guided biopsy was performed (Figure II). The specimen was submitted for AFB smear and culture



as well culture for aerobic and anaerobic bacteria. The ZN staining and culture studies were negative for AFB, however they revealed modest growth of salmonella typhi, sensitive to 3<sup>rd</sup> generation cephalosporin and quinolones.

The patient was started on parenteral ciproxin 100mg for three weeks along with analgesics and orthotic support while under admission. The patient condition and her pain improved after two days of treatment. She was discharged after three weeks with advice to continue with the orthotic support, analgesia, oral ciproxin 500mg for further three weeks and follow up weekly in the out patient



department. ESR at the time of discharge was 10mm / 1\* hour. Follow up Tc-99 scan at 6 month and one year were negative for any activity Patient remained fully mobile with no residual sensory or motor loss.

# **DISCUSSION**

Typhoid fever is a major problem affecting millions of people all over the world specially in the developing countries.<sup>7</sup> The route of spine infection includes hematogenous spread, postoperative infection, and direct implantation during spinal puncture, laser discectomy and spread from contagious foci.<sup>5</sup> In one study a primary focus was identified in 46% of cases, urinary tract infections being the commonest.<sup>6</sup> Osteomyelitis due to salmonella, however is known to be associated with sickle cell anemia, various heamoglobinopathies and immune suppressive state and as in this case it may also occur in normal hosts.<sup>7</sup>

Diagnosis of this condition requires a high degree of suspicion even though there may be a varied clinical presentation. Simultaneous involvement of the adjacent vertebrae endplate and the intervening disc is the general rule. The posterior elements of the spine are involved infrequently. It involves lumbar, thoracic and cervical spine in descending order. In our setting tuberculosis of the spine was the major differential of osteomyelitis of the spine. Clinical features regarding spinal salmonella osteomyelitis can be varied according to the stage of presentation. Infection of the spine usually presents with back pain which begins insidiously in the absences of constitutional symptoms,1 and can progress gradually, increasing in severity and also with movements.8 Gastrointestinal symptoms however as prodromal symptoms are rare.

Spinal salmonella osteomyelitis is uaually treated conservatively with intravenous antibiotics in high dose, immobilization, bed rest and analgesia. Treatment period ranging from six to twelve weeks with high dose antibiotics have been described. Culture and sensitivity results should dictate choice of antimicrobials used with single broad spectrum antibiotic shown to be as good as combination therapy and with less toxicity. Salmonella in fact has been shown to be developing increased resistance. Ampicillin, chloramphenical and co-trimoxazle, the first line of drugs for the treatment of infection are losing their efficacy and most of the organisms have developed resistance against these drugs.

Newer modalities of treatment include continuous antibiotic irrigation with gravity control outflow system, antibiotic beads and micro vascular grafts which may offer improved management if used judiciously.<sup>4</sup> The overall prognosis for this condition on conservative management alone has been described as very good to excellent.<sup>9,10</sup>

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