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EDITORIAL

CONTINUING PROFESSIONAL DEVELOPMENT: A MANDATORY REQUIREMENT FOR HEALTH CARE PROFESSIONALS

Waris Qidwai

Health care professionals are duty bound to keep their knowledge and skills up to date. The tradition of obtaining a licence to practice for life after graduating from a training program, without any further ongoing continuing medical education (CME) seems unacceptable in the present era. The quality of care provided is so dependent on the efforts to keep up to date that ongoing continuous learning should be considered mandatory.1

Continuing professional development (CPD) allows health professionals to keep up to date in order to meet the needs of patients, the health service, and their own professional development. It includes continuous acquisition of new knowledge, skills, and attitudes to enable competent clinical practice. CME and CPD are different. The former now includes managerial, social, and personal skills while topics beyond the traditional clinical medical subjects, necessitate to call it CPD and not just CME. The term CPD acknowledges the wide ranging competences needed to practice high quality medicine in addition to the multidisciplinary context of patient care.2

CPD programs are based on an hours related credit system, in which one hour of educational activity equates to one credit. The advantage of this system is that time devoted to CPD activities can be measured and recorded. The disadvantage is that it focuses on quantity and not on quality. It should be the quality and relevance of the activities that is important, not the quantity.3 The undifferentiated pursuit of credits provides a false security blanket that may bear little or no relation to the real outcomes of activities aimed at professional development.4

Educational activities can be divided into three categories. Live or external activities includes courses, seminars, meetings, conferences, audio and video presentations. Internal activities includes practice based activities, case conferences, grand rounds, journal clubs, teaching, consultation with peers and colleagues, and enduring materials such as print, CD Rom, or web based materials.5 There is a sizeable literature on the proven effectiveness of CPD interventions rendering CME and CPD programs as norms in the developed countries but their high costs are raising concerns even in countries with enough resources.5,7

CME and CPD have acquired more importance today because they are being linked to recertification and revalidation of credentials. The objectives of periodic revalidation are to encourage doctors to respect changes in societal values and integrate into their practices innovations that are shown to enhance patient care and also to give recognition to doctors who meet national standards of competence and performance. Delays in establishing such systems are occurring even in developed countries, but eventually.1

Health care provision in Pakistan has improved over the years but is still far from optimum. Approximately 74,000 physicians were practicing in Pakistan in 2005 that required regular CME/CPD activities to keep their knowledge and skills up to date and evidence-based.8

In Pakistan, annually, local medical schools and international medical graduate certification provide 6,800 physicians; 1,150 physicians emigrate; and an estimated 570 physicians stop practicing for various reasons. The current ratio (0.473) of physicians to 1,000 populations is inadequate to maintain the nation’s health. Future Physician Workforce Shortages (PWSs) for Pakistan range between 57,900 and 451,102 physicians in 2020, depending on assumptions about future need.8

This situation changes focus from ensuring CME/CPD activities for practicing physicians to concentrate and focus attention on producing more and more physicians. It is indeed a challenge to increase the number of well trained healthcare providers and to provide CME/CPD programs of high quality to practicing healthcare providers at the same time.

The CME/CPD activities in Pakistan are far and few with varying quality. Knowledge of those attending such
activities is found to be deficient, offering a challenge to CME/CPD program organizers to reverse the situation.9

Time has come to promote CME/CPD activities for health care professionals at the local and national level. It will ensure availability of quality services for patients across the country. There is marked need for our medical, dental, nursing and allied health institutions to develop comprehensive CME/CPD programs in their areas. Relevant material has to be developed and regularly updated. Monitoring of these programs will also be required.

Healthcare professionals today are keen to learn and want to be updated with the latest developments in medicine. It is the responsibility of educators and leaders in academic medicine to come forward, develop, implement and monitor CME/CPD programs for healthcare professionals. Such programs will have an impact only if they are relevant, practical and cost-effective. Academic institutions will have to play a major role in developing high impact CME/CPD programs.

CME/CPD programs are considered essential in the professional lives of healthcare professionals in the developing countries. In order to ensure delivery of high quality and evidence-based care to the masses, time has come to make CME/CPD mandatory for practicing healthcare providers in the country.

REFERENCES


ORIGINAL ARTICLE

MODES OF PRESENTATION AND REASONS OF HOSPITALIZATION FOR PATIENTS WITH DECOMPENSATED CHRONIC LIVER DISEASE AT CIVIL HOSPITAL KARACHI

Dileep K. Rohra¹, Jaipal², Ameer A. Khowaja¹, Khalid Mahmood², Kanya Lal Ahuja³

ABSTRACT
OBJECTIVE: To determine different modes of presentation and reasons that need hospitalization of patients with established chronic liver disease (CLD) and associate the presenting features with age, and severity of disease with the co-morbidity.
Design: Cross sectional, observational study
Patients And Methods: The study was conducted at Medical Wards of Civil Hospital, Karachi from July, 2006 to December, 2006. Patients who were admitted to the Medical Wards of Civil Hospital, Karachi and who already had established diagnosis of chronic liver disease were included in the study. Patient’s charts were reviewed. Demographic information was noted from the charts and for more clarification, patients or their attendants were interviewed. The reason of hospitalization was noted. Different modes of presentations of chronic liver disease were analyzed and were compared with different demographic and clinical characteristics, using chi-square test.
Results: A total of 427 patients’ charts were reviewed. Average ages of patients was 48.7 years. Hepatitis C was most common cause of CLD (64.6%). Other causes included Hepatitis B (23.7%), both Hepatitis B and C (3%) and others (8.7%). Majority of patients with CLD were hospitalized due to more than one signs and/or symptoms (63.5%). Common reasons of hospitalization in decreasing order were altered sensorium, hematemesis, abdominal distension, fever, abdominal pain and melena. More signs and symptoms of decompensation were seen in age groups 45-70 years (p=0.032). Patients with any co-morbidity presented with greater number of signs and symptoms of decompensation when compared to patients without any co-morbidity (p=0.002). No statistically significant association was found when presenting features of CLD were compared with duration of CLD and different co-morbidities.
Conclusion: Hepatitis C was the common cause of CLD in this study. The reasons of hospitalization were a combination of neurological and gastrointestinal clinical features. These features did not associate with the duration of CLD or the cause of CLD.
Key words: Chronic liver disease, Hepatitis, Hospitalization.

INTRODUCTION

Chronic liver disease is a slow process persisting over a long period of time, resulting in a progressive destruction of the liver. Patients with chronic liver disease (CLD) present special challenges to the clinicians. The quality of life is very poor in advanced liver disease.¹ Moreover, patients with CLD constitute a significant burden on the economy of the country.

Hepatitis B and C are the most common cause of chronic liver disease in this part of the world.²,³ Chronic hepatitis B virus afflicts 400 million people worldwide.³ The spectrum of chronic hepatitis B infection ranges from an asymptomatic hepatitis B surface antigen carrier state to chronic hepatitis with progression to cirrhosis and end stage liver disease.⁴,⁵ It is estimated that 15-40% of patients with chronic hepatitis B infection will progress to cirrhosis.⁶ Approximately 3% of global population are estimated to be chronically infected with Hepatitis C virus
with an annual incidence of 3 to 4 million new cases globally.7

Chronic liver disease is a grave consequence of HBV and HCV, eventually leading to cirrhosis and/or hepatocellular carcinoma.7 and decompensated CLD presents with wide spectrum of clinical signs and symptoms. Diagnosis and management of chronic liver disease in timely manner is very crucial for prolonging life expectancy as well as to improve the quality of life of the patients. Diagnosis of decompensated CLD is an integration of clinical acumen and laboratory tests as reflected by Child-Turcotte-Pugh scores for CLD.8

Study of the patterns of clinical presentations of decompensated CLD facilitate health care providers to readily suspect and diagnose CLD and intervene accordingly. This may have significant influence on the life of patients both quantitatively and qualitatively. The aim of this study was to determine the different modes of presentation and reasons for hospitalization of patients with established/decompensated chronic liver disease at Civil Hospital, Karachi, and to compare presenting features with different demographic and clinical characteristics.

PATIENTS AND METHODS

It was a descriptive study. Patients admitted with the diagnosis of CLD to Medical ward Unit IV (formerly Unit V) at Civil Hospital, Karachi from July to December, 2006 were included. Inclusion criteria comprised of those patients who already had the established diagnosis of CLD on the basis of history, physical examination (presence of ascites, varices, splenomegaly), laboratory profile (low serum albumin, increased prothrombin time, altered liver function tests), and sonology (portal hypertension, splenomegaly, varices, ascites), presenting to the hospital with signs and symptoms of decompensation of CLD. There was no exclusion criterion.

Patients’ charts were reviewed. Each patient was assigned study code for identification and confidentiality was maintained. Demographic data including age, marital status, address, first language, occupation and educational status were obtained. Second part of questionnaire aimed at collecting clinical information including presenting complaints, reason for current hospitalization, co-morbidities, duration of chronic liver disease, cause of chronic liver disease, history of previous hospitalizations, duration of current hospitalization and other complaints.

Data was entered in epidata version 3.1 and analyzed in SPSS version 11.0. Frequencies and cross tabulations were calculated. Chi-square test was used to compare the association of presenting features of CLD with age, presence of any co-morbidity and the duration of CLD with confidence interval set at 95% and p-value <0.05 was considered as statistically significant.

RESULTS

A total numbers of 427 patient’s charts were reviewed. Demographic data showed average age of patients as 48.7 (ranging from 13-85) years. Majority of subjects were married (82.9%). Individuals with Sindhi as first language contributed the largest study population (41.5%). Marked numbers of patients were housewives (40.5%). Majority of subjects were illiterate (74.9%). Table I summarizes the demographic data of the study subjects.

<table>
<thead>
<tr>
<th>Marital Status</th>
<th>n (%)</th>
<th>First Language</th>
<th>n (%)</th>
<th>Occupation</th>
<th>n (%)</th>
<th>Educational Status</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Married</td>
<td>354 (82.9)</td>
<td>Sindi</td>
<td>177 (41.5)</td>
<td>Students</td>
<td>17 (4%)</td>
<td>Illiterate</td>
<td>320 (74.9)</td>
</tr>
<tr>
<td>Single</td>
<td>38 (8.9)</td>
<td>Urdu</td>
<td>139 (32.8)</td>
<td>Housewives</td>
<td>173 (40.5)</td>
<td>Can read and write</td>
<td>12 (2.8)</td>
</tr>
<tr>
<td>Widowed</td>
<td>29 (6.8)</td>
<td>Punjabi</td>
<td>9 (2.1)</td>
<td>Farmers</td>
<td>48 (11.2)</td>
<td>Primary</td>
<td>25 (5.9)</td>
</tr>
<tr>
<td>Not Known</td>
<td>6 (1.9)</td>
<td>Balochi</td>
<td>59 (13.8)</td>
<td>Laborers</td>
<td>66 (15.5)</td>
<td>Middle</td>
<td>15 (3.5)</td>
</tr>
<tr>
<td>Total</td>
<td>427</td>
<td>Pashto</td>
<td>22 (5.2)</td>
<td>Professionals</td>
<td>8 (1.9)</td>
<td>Matric</td>
<td>31 (7.3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Serali</td>
<td>3 (0.7)</td>
<td>Unemployed</td>
<td>29 (6.8)</td>
<td>Intermediate</td>
<td>15 (3.5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Brahi</td>
<td>7 (1.6)</td>
<td>Servants</td>
<td>12 (2.8)</td>
<td>Graduates</td>
<td>6 (1.4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hindko</td>
<td>3 (0.7)</td>
<td>Shopkeepers</td>
<td>30 (7.0)</td>
<td>Not known</td>
<td>3 (0.7)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other</td>
<td>5 (1.2)</td>
<td>Drivers</td>
<td>14 (3.3)</td>
<td>Total</td>
<td>427</td>
</tr>
<tr>
<td></td>
<td>Not known</td>
<td></td>
<td>3 (0.7)</td>
<td>Hawkers</td>
<td>9 (2.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>427</td>
<td>Accountants</td>
<td>2 (0.5)</td>
<td>Clerical jobs</td>
<td>13 (3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Teachers</td>
<td>1 (0.2)</td>
<td>Not known</td>
<td>5 (1.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total</td>
<td></td>
<td>Total</td>
<td>427</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Analysis of clinical information showed that the mean duration of chronic liver disease since the time of diagnosis in our patient sample was 20.4 months (ranging from 1-42 months). Hepatitis C was the most common cause of chronic liver disease (64.6%). Other causes included Hepatitis B (23.7%), both Hepatitis B and C (3.0%) and others (8.7%). However, there was no significant association between ages of patients and cause of chronic liver disease found (p= 0.192). Fifty six percent patients had previous history of hospitalization. Mean duration of current hospitalization was found to be 8.92 days (ranging from 1-60 days). The duration of hospitalization was not associated with the cause or presenting feature of CLD.

Presenting features of decompensated CLD were analyzed as single clinical sign and symptom or combination. Patients presenting with single clinical sign and symptom included fever (2.1%), altered sensorium (12.9%), hematemesis (9.1%), melena (1.6%), abdominal distension (6.6%), abdominal pain (3%) or others (1.2%). Majority of patients presented with more than one sign and symptom (63.46%) as depicted in Table 2.

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>9 (2.1%)</td>
</tr>
<tr>
<td>Fever, hematemesis, abdominal distension, abdominal pain, altered sensorium</td>
<td>161 (37.7%)</td>
</tr>
<tr>
<td>Altered sensorium</td>
<td>55 (12.9%)</td>
</tr>
<tr>
<td>Altered sensorium, melena, abdominal distension, hematemesis</td>
<td>17 (3.98%)</td>
</tr>
<tr>
<td>Hematemesis</td>
<td>39 (9.1%)</td>
</tr>
<tr>
<td>Hematemesis, altered sensorium, melena</td>
<td>47 (11.0%)</td>
</tr>
<tr>
<td>Melena</td>
<td>7 (1.6%)</td>
</tr>
<tr>
<td>Melena, abdominal distension</td>
<td>4 (0.9%)</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>28 (6.6%)</td>
</tr>
<tr>
<td>Abdominal distension, abdominal pain</td>
<td>42 (9.8%)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>13 (3.0%)</td>
</tr>
<tr>
<td>Others</td>
<td>5 (1.2%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>427</td>
</tr>
</tbody>
</table>

Majority of the patients in this study did not have any co-morbidity (68.9%). When present, Diabetes mellitus (17.1%) and hypertension (11.2%) were the most frequent co-morbidities. Patients with any co-morbidity presented with greater number of signs and symptoms of decompensation when compared to patients without any co-morbidity (p=0.002). However, when number of signs and symptoms were compared among different co-morbidities like Diabetes mellitus, hypertension, chronic obstructive pulmonary disease (COPD), and ischemic heart disease, no significant association was found between these and presenting features of decompensated chronic liver disease (p= 0.117). Greater number of signs and symptoms of decompensation were seen between age groups 45-70 years (p= 0.032). No statistically significant association was found when presenting features of CLD were compared with duration of CLD (p= 0.245).

**DISCUSSION**

CLD is marked by the gradual destruction of liver tissue. It has been recognized as one of the most common cause of morbidity and mortality in both developed as well as under developed countries differing by their etiologies. CLD is the 10 leading cause of mortality in the United States and is responsible for deaths of more than 25,000 Americans each year.9 Although CLD can not be cured, earliest possible diagnosis and timely intervention is the core of management and prevention of progression of CLD.10 There is wide spectrum of CLD presentations varying with respect to emergency medical and demographic factors. Major cause of CLD in developed world is attributed to alcoholism. On the other hand, infectious agents are mainly responsible for CLD in developing countries especially South Asia including Pakistan.11 However, etiology of infectious causes varies even within Southeast Asian countries.12 This study aimed at exploring common clinical presentations among different strata of patients with respect to their clinical as well as demographic characteristics.

In the present study, Hepatitis C followed by hepatitis B were the most frequent causes of CLD which is consistent with another study that is the only one on this subject in Pakistan that could be found.12

This study found that patients between age group of 45-70 years had greater number of signs and symptoms, mostly more than one, that made their presentation complicated. Increased number of signs and symptoms can also be extrapolated as greater severity of CLD, that is, patient presenting with one sign or symptom indicate less severe decompensation versus patient with multiple signs and symptoms, a predictor of more severe decompensation. Therefore, early detection of infections leading to CLD is important in elderly since mode of presentation of CLD is more severe in this age group as found in this study. Furthermore, elderly patients have
Hospitalization in patients with decompensated liver disease

worse treatment response.14

It was found that majority of patients presented with more than one clinical sign and symptoms, a feature that is not generally observed. Among those who presented with only one clinical feature, altered sensorium secondary to hepatic encephalopathy was found to be most common which is consistent with an Indian study.11 However, gastrointestinal hemorrhage and other signs of portal hypertension have also been observed as the most common presenting feature of CLD in other studies.12,13 One study in Nepal has reported bacterial infections as the most common cause of hospitalization for CLD patients.15 Mean age of presentation in this study population was 48.67 years much less than seen in other studies that is 58.72 years.16,17 One plausible explanation for this could be the acquisition of disease at a later stage of life in Pakistan. Since acquisition in relatively older age is associated with faster progression of chronic liver disease and hence earlier presentation with decompensation compared with acquisition at a younger age appears to be due to slower pace of progression.18,19 Most of the patients in the current study presented with more than one clinical feature of CLD, mainly combination of fever, hematemesis, abdominal distension, abdominal pain, constipation and altered sensorium. This multiple presentation of CLD has not been studied so far. This is one of the earliest local studies that explored mode of presentation and co-morbidity. Though majority of patients in this study did not have any co-morbidity, but some patients with co-morbidity present with more signs and symptoms of CLD. However, patients with different co-morbidities did not show any difference in their mode of presentation.

The study showed that Hepatitis C was by far the most common cause of CLD in all population strata. Hepatitis C virus, as a major cause of CLD has also been reported from other South Asian country; Bangladesh.20 Housewives formed interestingly largest subgroup of occupation in the present sample. We strongly feel the need to further study transmission of causative agent resulting in CLD in different population subgroups. No difference in number of clinical features severity and duration of CLD was found. This finding is be supported by above mentioned of evidence of rapid progression of CLD when acquired later in life. This reflects a potential reciprocal relationship between mode of presentation and duration of CLD. Since CLD acquired early in life is more likely to progress slowly, thus lesser severity of presenting features and vice versa. Nevertheless, this dimension of clinical features of CLD needs to be elucidated by a systematic study.

The limitations of this study are, relatively smaller sample size, data derived from a single centre; and the design being a cross-sectional observational one.

CONCLUSION

Hepatitis C was the commonest cause of CLD in patients presenting to the medical wards of Civil Hospital, Karachi. The reasons of hospitalization were combination of neurological and gastrointestinal clinical features. The features did not show significant association with the duration or the cause of CLD. However, the presence of co-morbidity increased the number of presenting features.

REFERENCES


ORIGINAL ARTICLE

FREQUENCY OF ABNORMAL PAP SMEAR AND ASSESSMENT OF RISK FACTORS FOR CERVICAL CANCER IN AN OUT-PATIENT CLINIC

Firdous Jahan¹, Naheed Nabi¹, Waris Qidwai¹, Tasneem Borhany¹, Samina Hossein¹, Iqbal Azam²

ABSTRACT

Objective: To estimate the frequency of abnormal Pap smear and assessment of risk factors for cervical cancer in an out-patient clinic of a tertiary care hospital

Study Design: A cross sectional study

Patients and Methods: All married female patients attending the preventive health check up (family medicine) clinics, The Aga Khan University Hospital, Karachi from December 2004 to April 2005 for general checkups and had Pap smear after informed consent, were included. Data were collected through a structured questionnaire administered to all participants and double entered in EPIDATA and analyzed in SPSS. Frequencies of all variables were generated. Means with standard deviations and ranges were also calculated for quantitative variables.

Results: A total of 103 patients were enrolled. The mean age was 45.8 ± 10.7 years. Half of the study population were menstruating at the time of interview. Mean age at marriage was 21.4 ± 4.57 years. Mean age at first pregnancy was 22.6 ± 4.4 years. A minority of husbands (2.9%) were uncircumcised. About one third (30.8%) of patients had at least four full term deliveries while the mean number of deliveries were 3.3 ± 2.0 years. More than one third (36.9%) were practicing contraception, with 5% using oral contraceptive pills and the rest using barrier methods. About one third of the women complained about vaginal discharge with foul smell, dysuria and dyspareunia in most patients. About two-third (63.1%) had at least one Pap smear in the past. None had any dysplasia or cancer. Reports of Pap smear findings showed that 16.5% patients had atrophic vaginitis, 37.9% had infective bacillary background diagnosed on histo pathology and the rest were reported normal.

Conclusion: The most frequent abnormality found in Pap smear study was infective bacillary background. None of the patients had any pre-cancerous or active cervical cancer. The study was limited by small sample size and choice of Pap smear by the elite class population with self referral for general health checkup.

Key Words: Pap smear, Cervical carcinoma, Screening.

INTRODUCTION

Cervical cancer is the leading killer of all cancers for women in the developing world. In 1990, at least 371,000 new cases of cervical cancer were identified, with 290,000 of these cases were estimated to have occurred in developing countries.¹ In Pakistan, hospital based data shows that cervical cancer is the third most common cancer in the country after breast and oral cancer.² Cervical cancer can be prevented through screening by routine Papanicolaou (Pap) smears and treating women at risk.³ However, such screening services are not always feasible in developing countries because cytology facility are largely unavailable and are often costly at private hospitals.³,⁴ Risk factor assessment is also necessary along with Pap
smear. Risk factors for cervical cancer are infection with the Human Papilloma virus (HPV) that also causes genital warts, other chronic infections, nutritional imbalance, hormonal and psychological factors, along with other immune suppressive factors. Certain sexual behaviors increase the risk of getting HPV like sex at an early age, having many sexual partners and having sex with uncircumcised males. Some of the other known factors are smoking and infection with Human immunodeficiency virus (HIV) and Chlamydia. There is evidence that long-term oral contraceptive (OC) use, multiparity and low socioeconomic status also increases the risk of cancer of the cervix. Women with diets low in fruits and vegetables may be at increased risk for cervical cancer. Also overweight women are more likely to develop this cancer. Many women with low income do not have ready access to adequate health care services, including Pap tests and treatment of precancerous cervical disease.

Screening for cervical cancer is justified as natural history of disease is chronic, and detectable in preclinical phase. A significant proportion of pre-clinical lesions progresses to clinical disease. Screening test as a rule should be valid, acceptable to the patient and physician, and should be affordable. HPV is a known risk factor but HPV DNA test is not available in Pakistan.

Pap smear has its own limitation like high costs in private hospitals, difficulty in preserving cell samples and transporting slides, lack of trained laboratory technicians to analyze the results, and difficulties in getting women back for follow-up tests and for treatment and referral, when necessary.

This study was conducted to determine the frequency of abnormal Pap smear and distribution of risk factors in healthy females having Pap smear as a part of their routine general health checkups.

RESULTS

A total of one hundred and three married female patients were included in the study. Mean age of the participants was 45.8±10.7 years ranging from 25 to 69 years. Majority of them were housewives. All of them reported first sexual contact at their marriage. The mean age at first marriage was 21.4±4.6 years ranging from 13 to 40 years. Mean age at first pregnancy and mean age at menarche were reported as 22.6±4.4 years, ranging form 15 to 35 years and 13.19±1.3 years ranging from 10 to 17 years respectively. The mean number of deliveries was 3.3±2.0 per woman ranging from 0 to 11.

More than half (61.2%) of the patients had received education matriculation and above. Sixteen (15.5%) patients were working for pay or profit and out of those majority were either teacher or businesswomen. Only two (1.9%) patients were married more than once at the
time of interview. Three patients (2.9%) reported as being either current or past smokers. Out of these smokers two were regular current smokers and one was occasional past smoker. All of them were self-referred except one patient who was referred by general practitioner (Table I).

Table 1: Percentage distribution of patients by their age, age at first marriage, level of education and occupational status

<table>
<thead>
<tr>
<th>Factor</th>
<th>Infective smear/Bacillary background % (n)</th>
<th>Atrophic Vaginitis % (n)</th>
<th>Normal % (n)</th>
<th>Total Percent (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of the patient (in years)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30 years</td>
<td>10.3 (4)</td>
<td>0.0 (0)</td>
<td>8.5 (4)</td>
<td>8.5 (4)</td>
</tr>
<tr>
<td>30-39 years</td>
<td>20.5 (8)</td>
<td>0.0 (0)</td>
<td>25.5 (12)</td>
<td>25.5 (12)</td>
</tr>
<tr>
<td>40-49 years</td>
<td>26.6 (10)</td>
<td>34.0 (16)</td>
<td>16.7 (8)</td>
<td>16.7 (8)</td>
</tr>
<tr>
<td>50-59 years</td>
<td>21.4 (6)</td>
<td>10.5 (5)</td>
<td>34.0 (16)</td>
<td>34.0 (16)</td>
</tr>
<tr>
<td>60 years and above</td>
<td>10.3 (4)</td>
<td>25.0 (9)</td>
<td>8.5 (4)</td>
<td>8.5 (4)</td>
</tr>
<tr>
<td>Mean age in years (SD)</td>
<td>44.8 (10.53)</td>
<td>53.6 (7.75)</td>
<td>44.0 (10.74)</td>
<td>44.0 (10.74)</td>
</tr>
</tbody>
</table>

| Age at first marriage (in years)    |                                          |                          |              |                   |
| <18 years                           | 17.9 (7)                                  | 17.0 (8)                 | 17.0 (8)     |                   |
| 18-21 years                         | 35.9 (14)                                 | 36.2 (17)                | 36.2 (17)    |                   |
| 22 – 25 years                      | 30.8 (12)                                 | 36.2 (17)                | 36.2 (17)    |                   |
| 26 years and above                  | 15.4 (6)                                  | 10.6 (5)                 | 10.6 (5)     |                   |
| Mean age at first marriage (SD)     | 21.2 (4.26)                               | 21.4 (5.03)              | 21.4 (5.03)  |                   |

| Level of education                  |                                          |                          |              |                   |
| Illiterate                          | 5.1 (2)                                   | 8.5 (4)                  | 8.5 (4)      |                   |
| Can read and write                  | 7.7 (3)                                   | 6.4 (3)                  | 6.4 (3)      |                   |
| Below Matric                        | 7.7 (3)                                   | 17.0 (8)                 | 17.0 (8)     |                   |
| Matric                              | 7.7 (3)                                   | 11.8 (2)                 | 12.8 (6)     |                   |
| Intermediate                        | 23.1 (9)                                  | 8.5 (4)                  | 8.5 (4)      |                   |
| Graduate                            | 28.2 (11)                                 | 34.0 (16)                | 34.0 (16)    |                   |
| Post graduate                       | 20.5 (8)                                  | 12.8 (6)                 | 12.8 (6)     |                   |

| Occupation                          |                                          |                          |              |                   |
| Housewife                           | 76.9 (30)                                 | 93.6 (44)                | 93.6 (44)    |                   |
| Teacher                             | 7.7 (3)                                   | 0.0 (0)                  | 0.0 (0)      |                   |
| Business women/                     | 7.7 (3)                                   | 6.4 (3)                  | 6.4 (3)      |                   |
| Manager                             | 0.0 (0)                                   | 0.0 (0)                  | 0.0 (0)      |                   |
| Gynecologist                        | 7.7 (3)                                   | 5.9 (1)                  | 0.0 (0)      |                   |
| Other                               | 7.7 (3)                                   | 5.9 (1)                  | 0.0 (0)      |                   |
| Total                               | 39                                        | 17                       | 47           | 103               |

*One missing information

Approximately two third (63.1%; n=65) patients reported having Pap smear in past. Forty Six (44.7%) of them had normal Pap smear, eleven (10.7%) had abnormal Pap smear, while eight of them did not know the result of those had abnormal Pap smear, six had infective bacillary background, and one had chronic endometritis.

According to the current Pap smear findings more than half (54.4%; n=56) had abnormal Pap smear. In patients with abnormal Pap smear findings, 37.9% (n = 39) patients had infective bacillary background, and 16.5% (n=17) patients had atrophic vaginitis. None had dysplasia or carcinoma-in-situ in Pap smear examination.

**DISCUSSION**

Cervical cancer generally develops slowly and has a readily detectable and treatable pre cancerous condition; it can be detected through screening. Pap smear screening is the best screening program world wide recommended for sexually active women. In this study majority of subjects were housewives presented by self referral. Those females had Pap smear as one of the essential component of their routine general health checkups. Mean age of marriage of the study population was 21.40 years which was also the age of first sexual contact. Only 3 male partners / husbands were non circumcised. It is a documented fact that carcinoma cervix is more common in those females whose male partners are non circumcised. Clinically, sexually transmitted disease (Herpes, gonorrhea and Chlamydia infection) were absent in the study population which is another risk for cancer, although one third patients had abnormal vaginal discharge. Other risk factor associated with cervical cancer is poor socio-economic conditions, early marriage and multi parity.

In a Muslim country, extra marital sex practice is not as common as in Western countries and all Muslim males...
are circumcised. Moreover, poor socio-economic group who are at high risk do not come for screening by Pap smear. It is recommended that an effective screening program should be introduced at national level and awareness regarding risk factors must be created in local women.

According to Ahmed’s study done on recent trends in diagnosis and management of cervical cancer, 59.50% showed normal Pap smear while 33.22% were inflammatory smears; only 2.47% showed mild dyskaryosis.11 None of the subjects in the study had dysplasia on carcinoma-in-situ in Pap smear examination.

Another hospital-based study done in an out patient clinic at Karachi showed 30.55% normal smear while 60.44% had inflammatory and 4.16% had dysplasia. In contrast, none of the present study population had any grade of pre cancerous condition.12 However, more than one third of the current Pap smear showed inflammatory bacillary back ground.

A cervical cancer screening study was done in Northern Pakistan which showed 37% dysplasia/malignant cells in retrospective group while 2% dysplasia was seen in prospective group.13 More than half of the present study population had Pap smear in the past but none of them had pre cancerous changes or dysplasia which was reconfirmed on the repeat Pap smear with an average interval duration of 2 years. Efficient and cost effective screening programme will substantially reduce the burden of cervical cancer.14 Khan and colleagues conducted a study on Pap smear screening for pre cancerous condition of cervical cancer and found 55.3% inflammatory, 22.7% normal, 7.33% atrophic and 3.12% dysplastic smear.15 Bhatti evaluated prospective application of cervical screening program in local setting and found normal finding in 75% of cases, in inflammatory changes 17% and 8% had intraepithelial neoplasia.16

The Western recommendations are screening in three years after the last negative smear in women 30 - 64 years who had three or more consecutive negative smear.17-19 It is recommended that an effective screening program should be introduced at national level and awareness must be created in women regarding screening of cervical cancer.20 A high number of this study group had Pap smear in past but again none of them had any pre cancerous cellular changes in histopathology reports.21 Most of the standardized guidelines for cervical cancer screening have been developed in Western countries as per own high risk population as well as mass screening.22,23

According to American Cancer Society guideline for the early detection of cervical neoplasia and cancer, the screening should be started approximately three years after the onset of sexual intercourse but not later than age 21 years.2,23

This study population mainly comprised of elite group of women who wanted to screen themselves yearly without having any medical or gynecological problems. Utilization of Pap smear will be more effective if it is used according to standard guidelines.

Further studies at different socioeconomic levels are needed for the assessment of risk factor. The burden of cancer in developing countries is becoming higher which needs better awareness program and feasible screening. This study had limited sample size and a large sample size is needed to make some kind of recommendation or to make local guide lines.

CONCLUSION

None of the subjects had cervical dysplasia or carcinoma-in-situ in this Pap smear based study. Infective bacillary background and atrophic vaginitis were the most frequently seen abnormalities. This study was limited by sample size and population with self referral. Further studies are needed on a wider scale to assess risk factors as well as abnormal Pap smear to detect cervical carcinoma at an early stage.

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ROLE OF TUTORS’ TRAINING IN DELIVERING EFFECTIVE MEDICAL EDUCATION

Zeba Haque¹, Zeenat Ayoob², Fauzia Intiaz¹

Objective: To determine the effectiveness of training of the tutors to conduct small group tutorial sessions.

Study Design: A descriptive study

Methodology: One hundred and thirty nine students of first till fourth year of MBBS course, were introduced to the subject/topic and the learning objectives. In the following week, they attended small group sessions arranged for their respective subjects. Trained tutors were identified on the basis of having taken the tutor training course/workshops arranged by College of Physician and Surgeons, Pakistan. The tutors conducted the small group tutorial sessions as per their assignment. At the end of tutorial sessions the students were asked to complete a questionnaire encompassing the learning outcomes of the students and behaviors of the tutor during the tutorial classes. Learning outcomes were compared using Pearson test.

Results: The motivation of the students and their clarification of concepts increased significantly by attending the tutorial sessions with trained tutors (trained 77.7% vs. un-trained 21.58% p<0.005 and trained 80.58% vs. un-trained 19.42% p<0.005 respectively).

Conclusion: Trained tutors facilitated the sessions in such a way that students discussed themselves and found their own queries help in the clarification of the concepts more efficiently. Effective faculty development program should be designed and implemented to enhance the learning process of the students by trained facilitators.

Key words: Small group tutorials, Tutor Training, Learning, Facilitators.

INTRODUCTION

The curriculum in most of the medical colleges in Pakistan is discipline based using lectures as main instructional method. Lecture is the best strategy to transfer a new concept or information to a large number of students at a time. A lecture is usually thought of as mechanism for imparting factual information and provides an opportunity to “paint the big picture” of the topic to the whole class. Unfortunately in public sector medical colleges of Pakistan the student population is large enough to limit the interactive nature of the lecture. According to O’Donnell, lecture is a process by which the notes of teacher become the notes of a student without passing through the minds of either.¹ With undergraduate medical education currently carrying a health warning because of the stress and anxiety exhibited by students and young graduates, any educational process that promotes enjoyment of learning without loss of basic knowledge is likely to be a better idea.²

Undergraduate students are assumed to be capable of creative and critical thinking, and problem-solving skills. With large classes of over a few hundred and over-crowded syllabi, explicit teaching of thinking skills during lectures is not considered a practical choice. Small group work is characterized by student participation and interaction.³ Small group tutorials sessions are an innovative technique of information transfer which allows the tutor to develop the student more effectively as good listener, speaker, manager, life long learner and researcher.⁴ When adults teach and learn in one another’s company, they find themselves engaging in a challenging, passionate and creative activity.⁵

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Tutor’s training effect on conducting small group tutorials

On the other hand, one of the problems, which is commonly seen, is unavailability of experienced facilitators to conduct sessions in the appropriate way. There are several schools of thoughts regarding the benefits of problem based learning and small group tutorial for the knowledge provision to the students. Some private medical institutions are following a problem based learning system (PBLS), whereas many public medical institutions follow a conventional lecture based curriculum. Pakistan Medical and Dental Council has policies regarding the standard of teaching in medical schools, however there is no such policy to force any institution for opting small group session strategy. Therefore different institutes implement tutorials and lectures based system in different ways. The role of tutorial support by the tutor/facilitator is to assist students and encourage a learning environment that empowers students. A trained tutor is capable of facilitating the tutorial sessions in a coherent way, so that the students clarify their concepts without the involvement of the tutor. While the untrained tutor may not be able to facilitate the discussion rather he/she starts leading the discussion and give all the answers him/herself turning small group tutorial session into a mini lecture again a didactic one. The leading role of tutor also supresses the inquisitive nature of the students limiting them to become a life long learner.

The objective of this study was to determine the effectiveness of training programs for the tutors to conduct small group tutorial sessions.

METHODOLOGY

It was a descriptive study conducted at Jinnah Medical and Dental College Karachi, during the academic year 2006-7. The College observes the conventional type of MBBS curriculum with two years of basic and three years of clinical sciences education. One hundred and thirty nine students from MBBS first year till MBBS fourth year were identified by a randomly stratified method for the study. The students were introduced to the topic and its key concepts in didactic lectures. The learning objectives regarding the topic were given at the end of the week. In the following week, they attended small group sessions arranged for their respective subjects. Tutors of the respective department facilitated the tutorial sessions. The trained tutors were identified as the one who had taken the teacher-training courses regarding conduction of small group tutorials arranged by the College of Physician and Surgeons of Pakistan (CPSP). Trained and un-trained tutors conducted the small group tutorial sessions according to their assignments. At the end of tutorial sessions the students were asked to complete a questionnaire addressing the learning outcomes (motivation towards study and clarification of concepts) of the students and behaviors of the tutor (lecture based, minimal interference, keeping discussion on track, bouncing the question back to the students) during the tutorial classes. Statistical analysis was done through SPSS version 15.0 and Pearson chi-square test was applied to calculate the association among various responses with significance at p<0.05.

RESULTS

The sessions facilitated by untrained tutors were mostly teacher centered and were unable to clarify concepts of students and they were not motivated towards their studies (Table -I). The sessions conducted by the trained tutors were mostly student centered and the discussion was kept on a track that resulted in significantly higher motivation towards studies and clarification of concepts compared to the sessions led by untrained teachers (77.7% vs. 21.58% p<0.05 and 80.58% vs. 19.42% p<0.05 respectively). Figure I depicts the students response towards the method of facilitation by a trained tutor. Keeping the discussion on track, making the students discuss among themselves and bouncing the question back to the students, significantly increased the motivation of the students towards their studies and helped them clarify their concepts (p<0.05). Figure-2 is the graphical representation of the responses of the students towards the tutorial sessions conducted by the un-trained tutors. It shows that delivering the lecture in tutorials was not helpful in motivating the students towards their studies. Moreover the qualities of the tutor that is keeping the discussion on track (p<0.05), making it more student centered (p<0.05), and bouncing the question back (p<0.005) to the student group highly correlated with the motivation and understanding of the students regarding their subject clarifying their concepts (Table-I).

DISCUSSION

In this paper outcome-based approaches are described in which competence in teaching was defined in terms of learning outcomes. There have been many calls to decrease the use of didactic lectures methods in medical education and to increase student centered learning. Small group works is a powerful educational tool and group learning is the variety of
Table 1: Responses of the students on the items in the questionnaire (N=139)

<table>
<thead>
<tr>
<th></th>
<th>Descriptive output</th>
<th>P - Value</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Trained Tutor</td>
<td>Untrained Tutor</td>
<td>Trained Tutor</td>
</tr>
<tr>
<td></td>
<td>Frequency</td>
<td>Mode</td>
<td>%</td>
</tr>
<tr>
<td>Teacher centered</td>
<td>75</td>
<td>2</td>
<td>54.0</td>
</tr>
<tr>
<td>(Lecture based)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Student Centered</td>
<td>92</td>
<td>1</td>
<td>66.2</td>
</tr>
<tr>
<td>(minimal interference)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Keeps the discussion on</td>
<td>93</td>
<td>1</td>
<td>66.9</td>
</tr>
<tr>
<td>track</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bounces the question</td>
<td>78</td>
<td>1</td>
<td>56.1</td>
</tr>
<tr>
<td>back</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motivation toward studies</td>
<td>108</td>
<td>1</td>
<td>77.7*</td>
</tr>
<tr>
<td>Clarification of concepts</td>
<td>112</td>
<td>1</td>
<td>80.6*</td>
</tr>
</tbody>
</table>

* p<0.05, **p<0.005. 1= always, 2= sometimes, 3= never

Educational sessions designed to enhance the learning capabilities of the student. Personal understanding of an educational issue can be attained in a number of ways but small group make it possible to turn such understanding into a coherent, rational and professionally defensible position that can be clearly articulated. Group is defined as the set of people gathered together to discuss the topic of similar interest. The optimum size of the group in these sessions is 18 – 20 students. Trained tutors can actually play the role of true leaders, who direct the discussion onto the right tract in such a way that at the end of discussion the participants are convinced that they themselves have reached to the right decision. Leaders can model manual, intellectual and communication skills, and learners can safely rehearse and refine these capabilities. Preston-Whyte et al. in their study declared that over two-thirds of academic and clinical staff had received no formal training in teaching skills. It is quite possible that sessions are arranged with a small number of students and a tutor yet the discussion is one sided and the participation of the students is minimal. This is better called mini-lecture. The role of tutor during the session is more of the facilitator rather than a resource person. The trained facilitator keeps the discussion on the right track and directs it to the achievement of task with minimal his/her interference.

Optimally effective small group work is done when there is more interaction of students which makes
them more expressive, encouraging them into a good 
listener and speaker; that are the qualities of a good 
doctor. In case of traditional tutorial sessions, the tutor 
normally states the objectives, initiates the process, 
invites learning input, promotes discussion and brings 
the session to an appropriate close. Throughout the 
session the tutor “leads from the front” often literally. 14 
During all this process the discussion revolves around 
the tutor him/herself and a few outspoken students 
among the group. This clearly does not elicit the 
motivation of all of the students and the aim of the 
small group session is not achieved. The success of 
these sessions depends upon the tutor’s role. 15 This 
study confirmed that the training of teacher influences 
significantly (p<0.05) the motivation of the students 
towards their studies. The authors surveyed forty-eight 
distinguished teachers from clinical departments 
regarding the role of instructional successes in learning 
to teach. Using qualitative content analysis of 
comments, the authors identified nine common 
successes in clinical teaching associated with planning, 
teaching, and reflection. In anticipatory reflection used 
for planning, common successes occurred by involving 
learners, continuously innovating, creating a positive 
atmosphere for learning, considering the learners, 
engaging the learners, preparing adequately, and 
limiting content. 16

In addition to the participation, small group sessions 
are also characterized by group work on task and 
reflection on the work completed. This is reflected by 
the achievement of the learning objectives with the 
clarification of the concepts. The training of the tutors 
as the facilitators of group discussion has a vital role 
in this aspect. The ability of the tutor to keep the 
discussion on the right track and bouncing the question 
back to the students is positively and significantly 
correlated with the clarification of the concepts by the 
students themselves (p<0.05 and p<0.005 respectively). 
A fundamental feature of effective facilitation is to 
make the participants feel that they are valued as 
separate, unique individuals deserving of respect. 5 If 
the tutors are new to small group learning, then they 
need to be trained and acquire some basic knowledge 
of adult learning. Appropriate faculty development 
programs should be developed to meet these 
requirements. These may take the form of specific 
courses or “on the job” training and may include the 
opportunity to join experienced tutors at work. 17 
Faculty development and evaluation program were 
found to have contributed significantly to the process 
of curricular change. 18 Successful small group 
sessions are based on development of trust, fostering 
of collaboration and achievement of task. As with 
all teaching instruments its benefits are maximized 
when it is used skillfully by a well trained tutor with 
structured with well defined objectives.

CONCLUSION

Trained tutors were able to manage small group 
tutorials in a way that students could obtain maximum 
learning benefits. Students’ satisfaction and motivation 
become high after attending tutorial session conducted 
by trained tutors. Therefore the authors strongly 
recommend that the teaching staff of medical college 
should be trained through short courses/series of 
workshops to be well acquainted with the teaching 
skills and learning methodologies so as to conduct 
tutorial session effectively.

ACKNOWLEDGMENT

The authors thank the management of Jinnah Medical 
and Dental College, Karachi for providing the 
opportunity to study the effects of trained tutor on 
the learning process of the students, during the first 
author’s tenure in the college.

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ORIGINAL ARTICLE

ESTIMATION OF GLOMERULAR FILTRATION RATE BY USING TC-99M DTPA PLASMA 1 SAMPLE METHOD, GATES METHOD, COCKCROFT-GAULT METHOD AND PREDICTED CREATININE CLEARANCE METHOD: A PROSPECTIVE COMPARATIVE ANALYSIS WITH PLASMA 2 - SAMPLE CLEARANCE METHOD.

Nosheen Fatima, Maseeh-Uz-Zaman, Khalid Niaz, Salman Habib, Sharjeel Usmani, Shahid Kamal, Abid Hameed

Study Objective: To compare diagnostic accuracy of predicted clearance method, Gates method, Cockcroft-Gault method and plasma 1-sample clearance method with plasma 2-samples clearance method with Te-99m DTPA for the estimation of glomerular filtration rate (GFR).

Study Design: Comparative study.

Materials and Methods: This study included 91 consecutive patients who were referred for evaluation of renal function to the Nuclear Medicine section of Karachi Institute of Radiotherapy and Nuclear Medicine (KIRAN) from September 2004 to September 2005. The GFR was determined simultaneously by 5 methods including Plasma two-Sample Clearance method after Te-99m DTPA injection (PSC 2); Plasma one-Sample Clearance method after Te-99m DTPA injection (PSC 1); Gamma camera uptake method after Te-99m DTPA injection (Gates method); Predicted Creatinine Clearance by Modification of Diet and Renal Diseases (MDRD); and Cockcroft-Gault’s equation for GFR estimation (CG). PSC 2 was chosen as a reference.

Results: Out of the 91 patients, 71 were males and 20 females with age ranging from 16-68 years. The regression equation of the PSC 1, Gates, MDRD and CG method against the PSC 2 was Y = 1.884 +0.970X (r=0.90, p<0.001, SEE value=10.23 ml/min/1.73m2), Y = 9.944 + 1.083X (r=0.82, p<0.001, SEE value=11.02 ml/min/1.73m2), Y =25.606+ 0.640X (r=0.71, p=0.002, SEE value=15.56 ml/min/1.73m2), and Y =14.981+ 0.714X (r=0.77, p=0.002, SEE value=14.44 ml/min/1.73m2) respectively. In comparison with the GFR by PSC 2, the PSC 1 and Gates tended to overestimate by 1% (p=0.359) and 2% (p=0.265) respectively, MDRD and CG tended to underestimate GFR by 11% and 14% respectively (p<0.001).

Conclusions: PSC 1 correlate well with PSC 2 and either can be substituted for the other as ideal GFR markers. The Gates method shows good correlation with PSC 2 however it is less precise than PSC 1. MDRD and CG methods due to significant underestimation are not considered as ideal GFR marker.

Keywords: Glomerular filtration rate, Plasma Sample Clearance, Gates method, Cockcroft-Gault’s equation, Radionuclide scan.

INTRODUCTION

The glomerular filtration rate (GFR) is considered to be a representative parameter for evaluating the functional state of the kidney. Inulin clearance is the gold standard for GFR estimation. However, this method is not performed in clinical practice, because of technical complexity and limited availability.

Measurements of GFR are based on the renal clearance of a marker in plasma, expressed as the volume of plasma completely cleared of the marker per unit time. Plasma sample method following a single-injection after Te-99m DTPA (Diethylene Triamine Penta-acetic acid) injection has been proved effective as an alternative to the continuous infusion method with inulin for the determination of GFR in clinical practice. In view of the accuracy and technical simplicity, the single-sample method (sample at 180 minutes) is the first choice in routine
practice. The two-sample method (sample at 60 and 180 minutes) is essential for patients in whom the GFR is expected to be below 30 ml/min/1.73 m².

In Tc-99m DTPA renography, the GFR is calculated without blood or urine sampling. The method introduced by Gates has been most common in the routine setting, although the diagnostic accuracy of the gamma camera methods is debatable.

Serum creatinine is a useful marker of stable renal function, but it is unreliable when GFR is rapidly changing. Numerous formulae have been developed to estimate GFR or creatinine clearance from serum creatinine and other variables including the “Modification of Diet in Renal Disease” (MDRD) Study and Cockcroft-Gault (CG) equations in adults. The intrinsic creatinine clearance (CrCl) has been widely performed as only alternative to inulin clearance in routine practice. This method, however, is not accurate compared to inulin clearance. Therefore, simple and accurate determination of the GFR is still a clinical challenge.

The aim of this study was to estimate GFR using predicted clearance method, Gates method, Cockcroft-Gault method and plasma 1 sample clearance method and compare these with plasma 2 samples clearance method considering it as the gold standard to find a reliable and precise test in routine clinical practice.

PATIENTS AND METHODS

The study included 91 consecutive patients who were referred for evaluation of renal function to the Nuclear Medicine section of Karachi Institute of Radiotherapy and Nuclear Medicine (KIRAN) from September 2004 to September 2005. Informed consent was taken from all the subjects. The demographics, body surface area in m² and reasons for referral were noted. Those with hypertension/ diabetes, taking potentially nephrotoxic agents and with previous history of renal disease were excluded.

The radiopharmaceutical used for the study was 99mTc-DTPA. The kit for preparing 99mTc-DTPA was provided by Isotope Production Division, PINSTECH Islamabad, Pakistan, under the name of “PINSCAN-DTPA”. The labeling and quality control tests were carried out according to instructions of manufacture. The radiochemical purity was ensured to be more than 90 % before injection. The GFR of each subject was measured simultaneously by PSC2, PSC1, Gates method, MDRD and CG method.

Plasma Sample Clearance Methods

Tc-99m DTPA was prepared by following the package insert directions, aseptically two or more 5-mCi aliquots with a 3-cc syringe having 22-gauge needle were drawn. One of the aliquots was set, aside as the standard and the remaining were used for patients doses. The standard and the doses were calibrated carefully in a way that the percent difference between standard and dose did not exceed 5% under any circumstance.

The patient was injected under the gamma camera the renogram was also acquired and the time of injection was recorded. The empty syringe was also recorded in the same way as full syringe both with camera and with counter, being less than 3% of the dose. In two- samples method, the samples were drawn first at 60 minutes and then at 180 minutes from the contalateral arm in a collection bottle containing EDTA (Ethylene Diamine Tri Acetic acid), mixed well and centrifuged for 10 minutes. The sample was removed as soon as the centrifuge stopped. The 0.1 ml of filtrate was pipetted out by using micropipette into labeled test tube. The standard and sample test tubes were counted in a gamma scintillation counter set for 140 KeV 99mTc photopake with a 20% window, background, correction was done and sample was counted for one minute to ensure good counting statistics. PSC 2 and PSC 1 methods were automatically calculated by Biodex Medical System Atomlab 950 version 3.08 by Russell method.

Gamma Camera Uptake Method (Gates Method)

The patient was hydrated with 300 ml of water 20 minutes prior to the examination. The patient was laid down in supine position. 5 mCi of Tc-99m-DTPA was given through an indwelling butterfly needle in an antecubital vein under the gamma camera and was followed by infusion of 20 ml of normal saline. Frames of 64× 64 matrix were recorded with an online-computer, initially at one second for one minute and then at 10 seconds for 20 minutes. The post-injection syringe was again counted by the two devices in the same way as pre-injection. The GFR was automatically calculated by Gates method in ml/min/1.73 m².

Predicted Creatinine Clearance by MDRD method

In this method simply blood sample of the patients was
required for serum creatinine (Scr), serum albumin (Alb) and blood urea nitrogen (BUN) the GFR was calculated in ml/min/1.73m² by putting the age and gender in the following formula:

\[ \text{GFR (ml/min/1.73m²)} = 170 \times (\text{Scr})^{-0.999} \times (\text{Age})^{-0.175} \times (\text{BUN})^{0.130} \times (\text{Alb})^{0.318} \times (0.762 \text{ if female}) \times (1.180 \text{ if male}) \]

where Scr= serum creatinine, BUN= blood Urea Nitrogen and Alb= serum albumin.

**Cockcroft-Gault Method**

By putting the serum creatinine, age, height and gender factors in the following formula the GFR in ml/min was calculated:

\[ \text{GFR (ml/min) } = (140 - \text{ Age}) \times \text{Weight} \times (0.85 \text{ if female}) \div 72 \times \text{Scr} \]

The GFR (ml/min) values as obtained by the 5 methods were normalized for a body surface area (BSA) of 1.73 m² in order to interpret the result and compare it with the reference range. Values of BSA were estimated from patient’s height and weight using the following Haycock formula:

\[ \text{BSA (m²) } = 0.024265 \times \text{Wt} \times 0.5378 \times \text{Ht} \times 0.3964 \]

where Wt = patient’s body weight in kilograms (Kg) and Ht = patient’s height in centimeters (cm).

For method of comparison, standard linear least-squares regression analysis was used. p-value of 0.001 or less were considered significant. Bland and Altman’s analysis was referred agreement between the two methods.

**RESULTS**

Out of the 91 patients, 71 were males and 20 females with age ranging from 16 - 68 years (mean age, 46.05 years ± 13.71; median age 48 years) and average body surface area was 1.62 ± 0.14 m² (ranging from 1.17 to 1.92 m²). There was a range of renal function including 53 cancer patients with normal renal status as a baseline GFR for chemotherapy, 10 patients were hypothyroids, 10 hypertensive, 11 diabetics and had chronic renal failure.

The regression equation and correlation coefficient of PSC 1 and Gates methods against PSC 2 was \( Y = 1.884 + 0.970X \) (r= 0.90, p<0.001, SEE value=10.23 ml/min/1.73m²) and \( Y = -9.944 + 1.108X \) (r= 0.82, p<0.001, SEE value=11.02 ml/min/1.73m²) respectively as illustrated in Figures 1 and 2. The correlation coefficient of MDRD and CG’s method against PSC 2 was least significant and regression equation was \( Y = 26.752 + 0.631X \) (r= 0.72, p= 0.002, SEE value= 15.56ml/min/1.73m²), and \( Y = 18.694 + 0.678X \) (r= 0.77, p= 0.002, SEE value=14.44 ml/min/1.73m²) respectively as demonstrated in Figures 3 and 4.

The average difference of GFR between PSC 2 method and other methods was calculated as shown in Table 1. It was found that PSC 1 method overestimated by 1% (-1.06ml/min/1.73m², p= 0.359), Gates method overestimated by 2% (-1.71 ml/min/1.73m², p= 0.265), Predicted Creatinine Clearance by MDRD method underestimated by 11% (9.19 ml/min/1.73m², p<0.001) and CG’s method underestimated by 13% (12.39 ml/min/1.73m², p<0.001) of PSC 2 method. The values of difference indicated the bias or deviations of individual method from PSC 2. The PSC 1 and Gates tended to overestimate the GFR as shown in figures 5 and 6. The mean difference PSC 2 - PSC 1 method was small as compared to the PSC 2 - Gates methods. The difference of PSC 2-MDRD and PSC2-CG methods showed that both significantly underestimated the GFR.

**Table 1: Results on agreement of differences in GFR between the PSC 1, Gates, MDRD or CG’s method against the PSC 2 method.**

<table>
<thead>
<tr>
<th>Methods of GFR Estimation</th>
<th>Mean difference in GFR ± Standard Deviation (SD) (ml/min/1.73m²)</th>
<th>Standard Error Mean (ml/min/1.73m²)</th>
<th>95% Confidence Interval of Difference (CID) lower</th>
<th>95% Confidence Interval of Difference (CID) upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>GFRPSC2 - GFRPSC1</td>
<td>-1.06 ± 10.97</td>
<td>1.15</td>
<td>-3.34</td>
<td>1.23</td>
</tr>
<tr>
<td>GFRPSC2 - GFRGates</td>
<td>-1.71 ± 14.57</td>
<td>1.15</td>
<td>-4.75</td>
<td>1.32</td>
</tr>
<tr>
<td>GFRPSC2 - GFRMDRD</td>
<td>9.18 ± 18.08</td>
<td>1.89</td>
<td>5.42</td>
<td>12.95</td>
</tr>
<tr>
<td>GFRPSC2 - GFRCG</td>
<td>12.39 ± 16.52</td>
<td>1.73</td>
<td>8.96</td>
<td>15.84</td>
</tr>
</tbody>
</table>

*Significantly higher (p-value<0.001)

**Figure 1: Scatter plot of Plasma one sample clearance (PSC 1) against Plasma two sample clearance (PSC 2) method and the solid line indicates the regression line.**
Various methods are available for determination of GFR. Inulin clearance, the gold standard for estimation of GFR is usually cumbersome and inconvenient for routine use. Measurement of the plasma clearance of Chromium-51 Ethylene Diamine Tetra-Acetic acid (Cr-EDTA) and ⁹⁹mTc-DTPA after a single intra venous injection is widely used for estimation of overall GFR due to its simplicity and accuracy. The plasma clearance of ⁹⁹mTc-DTPA generally correlates well with the plasma clearance of ⁵¹Cr-EDTA. Multiple plasma sample technique
using $^{99m}$Tc labeled DTPA correlates well with inulin clearance and is considered reliable.
Barbour et al. reported that the plasma clearance of $^{99m}$Tc-DTPA overestimate GFR by 3.5 ml/min in average as compared to the renal clearance of inulin as a golden GFR marker.
A simplified method such as Russell two-sample method is sufficiently accurate as suggested by Biggi et al. for routine clinical use particularly in patients with variable renal function and in patients who require multiple GFR estimations.
The formulae of Russell can be adopted for both $^{99m}$Tc-DTPA and $^{51}$Cr-EDTA. On the basis of these studies, PSC 2 was considered as the gold standard as compared to other methods of GFR estimation. PSC 2 measure average GFR of 97.31 ± 25.29 ml/min/1.73m$^2$ with the range of 33.78-156.42 ml/min/1.73m$^2$. The reason for using $^{99m}$Tc-DTPA instead of $^{51}$Cr-EDTA in the study was its low cost, easy availability, low radiation hazard, and shorter half-life.

Comparison of this study with those in the published literature, the first observation was that the PSC 1 method and Gates techniques of GFR estimation seem to be highly correlated with PSC 2 method and the difference of correlation coefficients between PSC 1 method and Gates method is not significant ($p=0.109$), while other methods showed less significant correlation coefficients ($r$).
The correlation coefficient of PSC 1 method was 0.90 ($p<0.001$) and measured average GFR of 98.37 ± 23.51 ml/min/1.73m$^2$ with the range of 43.78-145.66 ml/min/1.73m$^2$. On the basis of best correlation and least non-significant negative bias (mean difference between PSC 2 and PSC 1 i.e. Bias = PSC 2-PSC 1 of -1.06 ml/min/1.73m$^2$ of PSC 1) method they can be substituted for each other. The reason of 1% over estimation of PSC 1 method in comparison with PSC 2 method is the effect of protein binding of DTPA. Biggi et al. observed that the protein binding increases with time from a mean of 3% at 60 minute after DTPA to a mean of 6% at 180 minutes after injection.
According to Russell et al., simplified methods have been proposed that require only one or two plasma samples in lieu of a more complete clearance curve but the error was introduced by this simplification. The error resulting from replacement of complete clearance curve by a single 3-hour sample was about 8 ml/minute and by using two samples (at 1 and 3 hours), it could be reduced to 4 ml/minute.

The Gates correlated well with the plasma sample method.
In this study, the Gates measured average GFR of 99.02 ± 19.15 ml/min/1.73m$^2$ (range =40-125 ml/min/1.73m$^2$). On comparison with PSC 2 correlation coefficient of Gates was 0.82 (p<0.001) and tended to overestimate by 2% (-1.71 ml/min/1.73m$^2$). The bias for overestimation by the Gates may be attributed to insufficient correction of background count in the kidney.
Mitral et al. reported that the Gates technique, which calculates GFR by the renal uptake of $^{99m}$Tc-DTPA, has been recommended but with rising levels of serum creatinine (> 4 mg/dl), it loses its value as the GFR estimation may not be accurate.
In the present study the reason for very good correlation was probably due to the fact that serum creatinine level of about all patients did not exceed beyond 4 mg/dl with the exception of five patients of chronic renal failure in whom serum creatinine was more than 4 mg/dl at which the accuracy of Gates method become debatable according to Mitral et al.

MDRD and CG’s methods measure average GFR of 88.13 ± 22.23 ml/min/1.73m$^2$ (range =41-133.13 ml/min/1.73m$^2$) and 84.19 ± 22.36 ml/min/1.73m$^2$ (range =40.2-125.9 ml/min/1.73m$^2$) respectively. The CG’s method underestimated by 14% and Predicted Creatinine Clearance by MDRD method underestimated by 11% of PSC 2 method. Lin and colleagues described the sources of errors in CG’s equation when compared with MDRD equations due to the inaccuracies of the formulas Multiple sources for measurement of error (including intra-assay serum creatinine = Scr variability, intra-individual Scr variability, lack of calibration of Scr assays across different laboratories, intra-assay GFR variability, intra-individual GFR variability, and measurement error of other variables in the prediction equations) can affect the precision and accuracy of renal clearance prediction equations.

There are few limitations and possible biases in this study. Personal error could be due to incorrect dose calculation and injection of DTPA. The bias may affect the results if the sample is not drawn at the correct time and from the correct arm.

CONCLUSION

On the basis of the best correlation of PSC 1 method with PSC 2 method, both methods can substitute for each other in the assessment of GFR. Gates correlates well with PSC 2 method but less precisely with PSC 1 method. Due to significant underestimation, MDRD and CG’s methods are not considered suitable for the accurate determination of GFR.

REFERENCES


ORIGINAL ARTICLE

RELATIONSHIP BETWEEN CENTRAL CORNEAL THICKNESS (CCT) AND INTRA OCULAR PRESSURE

Mashooduzzafar¹, Ziauddin A. Shaikh²

Objective: To determine relationship between central corneal thickness (CCT) and intra ocular pressure (IOP).

Design: Cross-sectional analytical study.

Methodology: The study subject were recruited from Ophthalmology Outpatient Department, Dow University of Health Sciences and Civil Hospital Karachi, from January to July 2006. Patients above 40 years of age of either gender having no history of ocular trauma, disease or surgery, neither suffering from systemic disorder nor taking medicine for any disease were studied for CCT and IOP. Goldmann applanation tonometry and pachymetry were performed in a single session. IOP was measured by Goldmann Applanation Tonometer (GAT). Pachymetry was performed with ultrasonic pachymeter. Regression analysis was conducted to determine relationship.

Result: Six hundred eyes of 300 patients (male 53%, female 47%), were analyzed. Average IOP was 14.83 mmHg. Average CCT was 548 microns. A significant association was found between CCT and IOP (r=0.63, p<0.001). CCT was found to be correlated linearly with increased IOP values (p<0.000).

Conclusions: A positive relationship exists between CCT and IOP.

Key words: Corneal thickness, Intraocular pressure, Pachymetry.

INTRODUCTION

Intraocular pressure (IOP) is an important parameter for screening, diagnosis and progression monitoring, response to treatment and control of glaucoma. The diagnosis of glaucoma is straightforward when classical triad of increased IOP, visual field defects and glaucomatous optic nerve damage is present. Glaucoma may still develop with normal IOP termed normal-tension glaucoma (NTG). If glaucoma does not develop despite the IOP range being above normal, The condition is termed ocular hypertension (OHT).¹ Normal IOP is one that does not result in optic nerve damage.²

Measurement of IOP with Goldmann applanation tonometer (GAT) is considered to be most accurate because of its reliability and reproducibility.³,⁴ Central corneal thickness (CCT) has been identified as an important variable for accurate assessment of IOP.⁵ Accurate measurements of IOP by GAT are most likely in eyes with CCT of 0.52mm and values above or below may produce error in measurements.⁶ IOP is found to be positively related to CCT.⁵,⁷ The IOP measured by GAT is underestimated if cornea is thin and overestimated with thick corneas.⁸ Laser refractive surgery changes the thickness of the cornea and affects the accuracy of measurement of IOP by GAT. The cornea becomes thin after refractive correction by excimer laser. The work by Faucher et al. demonstrated change in accuracy of GAT causing underestimation of IOP after photorefractive keratectomy.⁹ A significant decrease in IOP was found in eyes after refractive correction of myopia, hypermetropia and astigmatism by laser in-situ keratomileusis.¹⁰ Since CCT and IOP measurements correlate positively, monitoring of the CCT has served as a basis for adjustments of reading of IOP.⁸ Misdiagnosis may occur when CCT
is not considered.

In view of the importance of relationship between these two parameters, this study was conducted to determine a relationship between CCT and IOP in an out patient population.

**METHODOLOGY**

This cross sectional study was conducted at Ophthalmology Outpatients Department, Dow University of Health Sciences and Civil Hospital, Karachi from January to July 2006. Six hundred eyes of 300 patients were analyzed with non-probability purposive sampling from attending outpatients, of 40 years or above irrespective of gender. Patients having history of ocular trauma/disease/surgery, suffering from or taking medicine for any systemic disorder, having corneal/ocular pathology/disease and having vision below 6/6 after full correction were excluded. Informed consent was taken. A detailed history and examination was carried out. Refraction was performed to attain a corrected vision of 6/6 where it was found below this level. The IOP and CCT were measured in a single session.

IOP was measured according to standard protocol, with a calibrated GAT from the central area of the cornea with eyes in primary position of gaze. A drop of proparacaine hydrochloride 0.5% was instilled into the lower conjunctival cul-de-sac for topical anaesthesia and fluorescein impregnated paper strip was touched to the tear film. The patient's head and the microscope were positioned so that the bar was against the patient's forehead, well above the eyebrows, allowing maximal separation of the patient's eyelids. The outer canthus of eye was aligned with the mark on the side rod of the slit lamp by rotating the chin rest. The GAT was mounted on the end of the lever hinged on the slit-lamp. The patient was asked to keep gaze in the primary position. With the cornea and tonometer biprism maximally illuminated by the cobalt blue light from slit-lamp, the biprism was brought into gentle contact with the apex of the cornea. The semicircular patterns were observed through the left ocular of the slit-lamp. The tension dial was adjusted so that the inner edges of the upper and lower semicircles became aligned. The reading on the dial was multiplied by 10 to obtain IOP in mmHg.

DGH400/JEDMED ultrasonic pachymeter was used to measure CCT with frequency set at 1640m/s. A drop of proparacaine hydrochloride 0.5% was instilled into the lower conjunctival cul-de-sac of the eye for topical anaesthesia. Before taking measurement, the patient was asked to blink to avoid corneal drying. The patient was then asked to look straight ahead and the probe was placed perpendicular to the center of the cornea. Five measurements were taken rapidly. The pachymeter is programmed to take measurements only when the probe is positioned perpendicular to corneal surface. The lowest CCT reading was used for analysis as this represented the most accurate measurement from the centre of the cornea.

The IOP and CCT measurements were taken between 9 am to 12 noon to avoid any effect of diurnal variation of CCT and IOP. The data was entered on a proforma including the name, age, gender, registration number of the patient including IOP and CCT measurements. Both eyes of the patients were analyzed and used for the study.

The collected data was analyzed by SPSS version 10.0. Relevant descriptive statistics, frequency and percentages were computed for presentation of qualitative variables like gender and ocular findings. Quantitative variables like IOP, CCT and age were presented by mean and standard deviation. Scattergram for IOP as the independent variable and CCT as dependent variable was drawn. Test of linear correlation (Pearson’s correlation) was applied to test the hypothesis at p value below 0.05 level of significance.

**RESULTS**

The sample included 600 eyes of 300 patients. There were 53% males and 47% females. Average IOP was 14.83 mmHg with ranging from 11-19 mmHg. Individuals were also divided into 14 subgroups according to measured CCT with 10 microns increment steps. Mean CCT was 548 microns ranging from 445-655 microns. Mean IOP of each subgroup was also calculated as well as the difference of mean according to increment in CCT presented in Table I. Mean of difference of IOP according to 10 micron of CCT increase was 0.27 mmHg. Average age was 48.04 years ranging from 41-68 years presented in Figure I and 49.3 % individuals were between the ages of 41-45 years. The age showed no association with CCT (p=0.929). A significant association was found between CCT and IOP (Pearson correlation coefficient r=0.63, p<0.001 (Figure II). In linear regression analysis, the CCT was found to be correlated linearly with increased IOP values (p<0.001).
Table 1: IOP Relationship to CCT

<table>
<thead>
<tr>
<th>CCT in microns</th>
<th>Mean IOP</th>
<th>Difference of IOP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group: I</td>
<td>(441-450)</td>
<td>12.04</td>
</tr>
<tr>
<td>Group: II</td>
<td>(451-460)</td>
<td>12.33</td>
</tr>
<tr>
<td>Group: III</td>
<td>(461-470)</td>
<td>12.60</td>
</tr>
<tr>
<td>Group: IV</td>
<td>(471-480)</td>
<td>12.95</td>
</tr>
<tr>
<td>Group: V</td>
<td>(481-490)</td>
<td>13.12</td>
</tr>
<tr>
<td>Group: VI</td>
<td>(491-500)</td>
<td>13.43</td>
</tr>
<tr>
<td>Group: VII</td>
<td>(501-510)</td>
<td>13.72</td>
</tr>
<tr>
<td>Group: VIII</td>
<td>(511-520)</td>
<td>14.00</td>
</tr>
<tr>
<td>Group: IX</td>
<td>(521-530)</td>
<td>14.32</td>
</tr>
<tr>
<td>Group: X</td>
<td>(531-540)</td>
<td>14.68</td>
</tr>
<tr>
<td>Group: XI</td>
<td>(541-550)</td>
<td>14.89</td>
</tr>
<tr>
<td>Group: XII</td>
<td>(551-560)</td>
<td>15.17</td>
</tr>
<tr>
<td>Group: XIII</td>
<td>(561-570)</td>
<td>15.50</td>
</tr>
<tr>
<td>Group: XIV</td>
<td>(571-580)</td>
<td>15.88</td>
</tr>
<tr>
<td>Group: XV</td>
<td>(581-590)</td>
<td>16.05</td>
</tr>
<tr>
<td>Group: XVI</td>
<td>(591-600)</td>
<td>16.44</td>
</tr>
<tr>
<td>Group: XVII</td>
<td>(601-610)</td>
<td>16.64</td>
</tr>
<tr>
<td>Group: XVIII</td>
<td>(611-620)</td>
<td>16.93</td>
</tr>
</tbody>
</table>

Figure 2: Correlation of CCT and IOP

DISCUSSION

Glucoma is one of the leading causes of blindness worldwide. Glaucoma is defined as an optic neuropathy with characteristic appearance of optic disc and specific pattern of field defects that is associated frequently but not invariably with raised IOP.

GAT is the gold standard of measuring IOP. Goldmann and Schmidt presented their applanation tonometer in 1957 and also cautioned about the possible sources of error in measurements by the instrument with CCT as one of them. The IOP measurements with GAT assume a corneal thickness of 520 microns. When it is greater, IOP is recorded as high and when it is lower, the IOP is recorded low due to the effect of corneal rigidity and corneal thickness. The present study have shown a positive relationship between CCT and IOP as has been described in other studies. IOP measurements by pneumotonometer, non-contact tonometer, Tono-Pen, ocular blood flow and GAT have all shown positive relationship with CCT. Variations in CCT and its relationship to IOP have been worked out and it is estimated that for every 10 microns change in CCT produce an error in the measurement of IOP. Patients having OHT have demonstrated thicker CCT as compared to normal subjects and patients with Primary open angle glaucoma (POAG) while patients having NTG have shown to have thin cornea compared to normal subjects and patients with POAG. Based on positive correlation between CCT and IOP, true IOP was calculated with the result that many patients diagnosed as OHT were reclassified as normal and many patients diagnosed as having NTG were...
The cornea becomes thin after refractive correction by excimer laser resulting in lower IOP values postoperatively.9-10 This may lead to subsequent mismanagement of glaucoma due to underestimation of IOP if CCT is not considered especially in patients who underwent refractive surgery while having glaucoma and in myopic individuals who are at increased risk of developing glaucoma.

Variation in CCT and its relationship to IOP have been worked out. It is estimated that every 10 microns of change in CCT produce error in the measurement of IOP.17-19 Underestimation and overestimation of IOP based on CCT range to about 16 mmHg.17 Results of the present study have demonstrated mean IOP change of 0.27 mmHg for every 10 microns change in CCT.

Population based studies have demonstrated the pattern of CCT and it’s implication on IOP has been determined for proper diagnosis and management of glaucoma.8,15,16,26-27 Uncorrected underestimation of IOP due to thin CCT may lead to delay in diagnosis, inadequate treatment target setting and high morbidity.

In the present study, 49.3% individuals were between the ages of 41-45 years and only 0.7% were between 66-70 years presented in Figure I. Although the study has demonstrated a positive relationship between CCT and IOP, further large population-based studies are required to determine this relationship including all age groups because it is difficult to find large number of healthy individuals of different age groups in hospital patient population.

The authors would like to recommend that CCT measurement should be included as a baseline evaluation for glaucoma assessment for proper classification and management of patients.

CCT and IOP measurements should be performed and documented both preoperatively and postoperatively in all patients undergoing corneal refractive surgery to be used as reference for future glaucoma assessment especially in myopic individuals and patients having glaucoma.

CONCLUSIONS
A positive relationship was found between CCT and measured IOP in the studied subjects.

REFERENCES


HOW FREQUENT ARE CONSANGUINEOUS MARRIAGES?

D.S.Akram, Fehmina Arif, Jabeen Fayyaz

Objective: To determine the frequency of consanguineous marriages in parents and grand parents of all admitted children in a pediatric unit

Design: An observational study.

Methodology: All patients admitted over one year period from January to December 2001 in Unit 1 of Pediatric Department were included. Information was obtained regarding consanguinity of parents and grandparents of the children. Clinically evident inherited disorders were also noted.

Results: Consanguinity was found in 72.7% of marriages. First cousin marriages were seen in 87% while second cousin marriages were seen in 12%. Consanguinity was also seen in the grandparents. It was found in 64.15% of maternal and 60.3% of paternal grandparents.

Conclusion: Cousin-marriages are a norm in the population studied. Its effect on inherited disorders deserves further studies.

KEY WORDS: Consanguinity, Inherited disorder, Social norms.

INTRODUCTION

Consanguineous marriages are frequent in developing countries but their frequency has declined in the developed countries. Studies from various countries and communities in South East Asia show a prevalence of cousin marriages ranging from 20-70% or higher. There is an association of consanguinity with increased incidence of inherited malformations and autosomal recessive disorders. The chances of inheriting biological weaknesses in consanguineous marriages are higher. This exposes the child at a relatively younger age to illnesses and increased chances of succumbing to various inherited disorders.

Consanguinity is considered to be the single most important cause of genetically related mortality in developing societies. There has been a decline in consanguineous marriages due to above concerns, in certain countries like Cyprus where there are laws restricting marriages among blood relations while in China there have been reports of arranged marriages being annulled. In Turkey there has been a steady decline from one marriage cohort to the next. Factors attributable may be related to increase in literacy of woman, mobility from rural to urban and an increase in women labour force. Socioeconomic status also has an impact on the pattern of consanguinity. Improvement it showed a decline in consanguinity rates.

Pakistan is a country where consanguineous marriages are a societal norm and are widely practiced. Strengthening family relationships and keeping wealth within the family are some of the reasons for intermarriages. Previous studies have shown that in Pakistan consanguinity was seen in 60% of marriages out of which 80% were between first cousins.

Inherited disorders have been found to be twice as common in consanguineous marriages versus non consanguineous marriages. Relative risks between 1.3 and 2.7 for congenital anomalies had been demonstrated by Khlat and Khoury for offspring of consanguineous versus non-consanguineous marriages.
of Pakistan and the high fertility rate with the cultural background of consanguineous marriages, the problem of inherited disorders and congenital malformations may be significant. This would add to the high infant mortality rates of the country. It is imperative that more data should be available on consanguineous marriages and the prevalence of inherited disorders to address the issues of antenatal screening and genetic counseling. This study was therefore undertaken to determine the frequency of cousin marriages in the parents and grandparents of children admitted in Paediatric Unit 1 of Civil Hospital Karachi over a period of one year.

METHODOLOGY

All patients admitted in the Paediatric ward over one year period were included in the study. Children were admitted with problems ranging from infection to chronic illnesses and malignancies

Parents were informed about the study and their consent was taken. Information was obtained from the parents of children about the blood relationship between each other and whether it was a first cousin marriage or a second cousin marriage. Similar information was sought about consanguinity in both the maternal and paternal grandparents and also the degree of blood relation. A complete history and physical examination was then performed to establish clinical diagnosis. All patients who had clinical evidence of inherited disorders including autosomal recessive, dominant, X-linked, chromosomal, multifactorial disorders and dysmorphism were documented. Frequencies were calculated and the results were expressed in percentages.

RESULTS

A total of 650 patients were admitted over a one year period. There were 354 (55%) males and 296 (45%) females. Consanguinity among parents was positive in 473 (72.7%) admitted children. Among them 412 (87%) parents were first cousin marriages, while 61 (12.0%) were 2nd cousin marriages. Forty two percent were Sindhi and 33% were Balochi. The age ranged from 1 month to 12 years.

Consanguinity was common in maternal and paternal grandparents. It was found in 64.15% of maternal and 60.3% of paternal grandparents.

Seventy seven percent of maternal grandparents were 1st cousin while 22% were second cousins. Similar results were obtained in paternal grandparents, eighty three (83%) being first cousins while 16.8% were second cousins. Sixty patients out of seventy (85.7%) had double consanguinity.

Inherited disorders were found in 70 patients (14.79%) in whom consanguinity was present and 15 patients (8.47%) were with no consanguinity. The male: female ratio was 1.8:1. Autosomal dominant, recessive and chromosomal disorders were found in 5.7%, 17% and 4.2% of patients respectively (Table-I). The lists of disorders are given in tables 2 and 3.

| Table 1: Frequency of inherited disorders in the studied children n=70 |
|-------------------------|-------------------|---------|
|                         | NUMBER | PERCENTAGE |
| Autosomal recessive (AR) | 12     | 17       |
| Autosomal dominant (AD)  | 4      | 5.7      |
| Chromosomal             | 3      | 4.2      |
| Sex linked              | 2      | 2.8      |
| Dysmorphism             | 9      | 12.8     |
| Multifactorial (MF)     | 40     | 57.1     |

| Table 2: Inherited disorders seen in the studied children with positive consanguinity |
|---------------------------------|-------------------|---------|
| INHERITED DISORDERS         | NUMBER | PERCENTAGE | CATEGORY |
| Thalassemia major           | 6      | 8.57       | AR       |
| Aplastic anemia             | 6      | 8.57       | AR/AD    |
| Hereditary spherocytosis    | 1      | 1.42       | AD       |
| Sickle cell anemia          | 1      | 1.42       | AR       |
| Fanconi’s anemia            | 1      | 1.42       | AR/AD    |
| Wilson’s disease            | 1      | 1.42       | AR       |
| Glycogen storage disorders  | 1      | 1.42       | AR       |
| Congenital heart diseases   | 7      | 10         | MF       |
| Congenital adrenal hyperplasia | 1     | 1.42     | AR       |
| Epidermolysis bullosa       | 1      | 1.42       | AD/AR    |
| Insulin dependent Diabetes mellitus | 3  | 4.28       | MF       |
| CP child                    | 9      | 12.85      | AR/AD/MF |
| Aperts syndrome             | 1      | 1.42       | MF       |
| Leish-Nyhan syndrome        | 1      | 1.42       | MF       |
| Diastrophic Nanism syndrome | 1      | 1.42       | AR       |
| Cleft palate                | 1      | 1.42       | MF       |
| Cruzon syndrome             | 1      | 1.42       | AD       |
| Trisomy 21                  | 2      | 2.85       | Chromosomal |
| Ichthiosis                  | 2      | 2.85       | AD/AR    |
| Others                      | 23     | 32.85      | AR/AD/MF |
| Total                       | 70     | 100        |

* CP = Cerebral palsy, AR = autosomal recessive, AD = autosomal dominant, MF = multifactorial
Table 3: Inherited disorders seen in the studied children with negative consanguinity

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Number</th>
<th>Percentage</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thalassemia major</td>
<td>3</td>
<td>20</td>
<td>AR</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>2</td>
<td>13.33</td>
<td>Multifactorial</td>
</tr>
<tr>
<td>Neural tube defect</td>
<td>2</td>
<td>13.33</td>
<td>Multifactorial</td>
</tr>
<tr>
<td>CNS malformation</td>
<td>1</td>
<td>6.66</td>
<td>Multifactorial</td>
</tr>
<tr>
<td>Insulin dependent Diabetes mellitus</td>
<td>2</td>
<td>13.33</td>
<td>Multifactorial</td>
</tr>
<tr>
<td>Dysmorphism</td>
<td>4</td>
<td>26.66</td>
<td></td>
</tr>
<tr>
<td>Muscular dystrophy</td>
<td>1</td>
<td>6.66</td>
<td>X-linked</td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

*AR= Autosomal recessive

DISCUSSION

The results indicate that in the admitted patients the frequency of consanguinity was 72.7%. Data from Pakistan Demographic and Health Survey 1990-1991 shows a consanguinity rate of 58.1%. Similar results have been quoted by Bittles. He reported that 50.3% of all marriages in urban Punjab were between 1st and 2nd cousin with prevalence higher in rural areas. The frequency documented in this study was much higher.

First cousin marriages are the most prevalent form of cousin marriage and was also reflected in the present study. Consanguinity rate had shown increase in certain countries. In UAE it had increased from 39% to 50.5%. The reasons stated were primarily socio cultural. Religious beliefs and traditions too may have an effect on the practice of consanguineous marriage, although they were the least cited reason in a study on thalassemia.

Consanguinity in marriages not only has sociological but also health implications. Such marriages result in transference of recessive gene with a greater chance of congenital malformations and inherited disorders. In this study 14.79%, 12.68% and 8.47% of children had inherited disorders with positive single consangunuity, positive double consangunuity and non-consangunuous marriages respectively. Hashmi found an overall highly significant prevalence of congenital malformations in children of related parents it was 40% vs. 26% in non-related parents. Similar results have been reported from a study done at Ganga Ram hospital Lahore. Razzaq found that offsprings of consanguineous marriages had a significantly higher incidence of illnesses (37.1%) than non-consanguineous marriages (29%). A study done at Islamabad showed a strong association of offspring of close relative marriages with cardiovascular diseases compared to controls. In the present study, congenital heart disease was most common among the consangunuous off-springs followed by cerebral palsy, thalasemia and aplastic anemia. In the non-consangunuous children, thalasemia was the commonest.

In this study out of 70 children with inherited disorders, 17% children had autosomal recessive disorders, 5.7% had autosomal dominant while 4.2% had chromosomal abnormalities.

Hoodfar and Teebi found the incidence of autosomal recessive disorders to be twice as common in consangunuous unions versus the non consangunuous. These results can be used for advocacy to discourage cousin marriages especially in families known to have inherited problems as well as for genetic testing of extended families.

CONCLUSION

Consangunuity is an important issue in the local population. There is a need to conduct community studies on its effect on increase in frequency of inherited disorders. This can be further studied by comparing the frequency with a population without a history of consangunuity for two generations.

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CASE REPORT

LACTIFEROUS FISTULA IN THE AXILLARY BREAST

Saba Sohail

ABSTRACT

Lactiferous fistulae are uncommon post inflammatory conditions usually occurring around the areola of nipple. A young nursing mother presented with milk discharge from the site of a previous infection in left anterior axillary discharge whenever baby suckled. Ultrasound of right breast and axilla showed a fistulous track coursing between skin and a lactiferous duct in the axillary tail of breast. Due to the nursing state, local care was advised deferring surgery to post lactation period. The fistula remained quiescent after the nursing period ended. Follow up ultrasound and examination 18 months later showed complete healing.

Key words: Breast, Lactiferous fistula, Axilla.

INTRODUCTION

A lactiferous or mammary duct fistula is an uncommon entity first described by Hertz in 1952.1,2 Common causes include post-abscess rupture and discharge to surface, mammary duct ectasia, periductal mastitis, granulomatous mastitis, nipple abnormalities, post-operative infection with a strong relationship with heavy smoking.2,4 Majority occur around the areola of nipple.2,3 Axillary tail is an uncommon place.

This case report describes a young lady who developed a milk-discharging fistula located in the axillary tail of breast which ‘erupted’ only during active nursing.

CASE REPORT

A 30 years old lactating lady presented with history of milk discharge from the right anterior axillary fold. She was mother of three children presently nursing the youngest aged eight months. Two years ago when her second child, aged one year at that time, was getting weaned off the breast feed, she developed a painful swelling in front of the right axilla which turned red, tender and then exuded pusy discharge over a period of one week. When the condition did not respond to oral medication, a general surgeon drained it by giving an incision under local anesthesia. Antibiotics were then given according to the culture report and the lesion healed with minimal scarring and a small depression of overlying skin. No mass or tenderness remained.

During the third trimester of the last pregnancy, she noticed a focal swelling with a tense feeling under the scar. After the delivery as she nursed the child, the swelling increased in size, became painful and from the 2nd post-natal week onwards, there was milk discharge from the site every time the baby suckled. The pain and size of the swelling abated but the condition was uncomfortable for the lady. So she consulted her gynecologist. There was no co morbidity, smoking history or any other remarkable feature in the personal, menstrual or family history.

On local examination, there was a small punctum around pin-head size, in the line of a thin irregular scar near the anterior axillary fold. It was not tender to touch, was wet-looking but not inflamed or excoriated. Glandular tissue of similar texture as breast was palpable underneath. No other abnormality was noted on local or general physical examination. Lymph nodes were not palpable.

Due to the nursing state, she was subjected to high frequency ultrasound of right breast and axilla as first line investigation. Probe was covered with sterile glove and sterile gel was used for imaging the discharge site. Ultrasound showed a hypo echoic track of 1.37 cm length and 5 mm width which was leading to a dilated (3 mm) lactiferous duct in the axillary tail of breast. It was filled with fluid as well as echogenic material. As soon as she started to feed the baby, the duct dilated (to 4.5 mm) and clear milky fluid exuded from the opening (figure 1). This confirmed the...
clinical diagnosis of lactiferous or mammillary duct fistula. The rest of the right breast, the left breast and the axilla were normal. As the lady was lactating, galactogram/fistulogram was not performed. Surgery was deferred till the nursing period would get over. She was advised local care with alcohol swabs three times a day, salcosaryl™ application twice a day between longer gaps of nursing to promote epithelialization, and use of pressure with nursing pads at the fistula site during active nursing. She was also instructed about the symptoms and signs of possible infection with advice to report back should this occur.

She returned after 19 months in January 2008 seeking permanent contraception. The discharge had ceased about a year ago as the child was weaned off the breast feed. Local examination did not show the previous punctum; the overlying skin had healed leaving a tiny scar. Complimentary ultrasound with high frequency probe also did not show the previously visualized tract indicating complete healing.

**DISCUSSION**

Lactiferous or mammillary duct fistula is an uncommon condition. Nipple abnormalities, long standing infection with coagulase-negative Staphylococci, age (median of 32 years), smoking habit, previous biopsies, Hadfeild procedure for duct ectasia, periductal mastitis etc. are the usual associated factors that predispose to this complication. It has also been described in male breast following senescent gynecostasia, and in an infant following incision of infantile breast swelling. A true fistula should be differentiated from superficial fistula resulting from an infection of sub-epidermal gland(s). The usual histology is periductal mastitis and duct ectasia although idiopathic granulomatous mastitis and tuberculous mastitis are also described.

The condition usually presents as sub-areolar abscess or peri-areolar discharging sinus. The present case had an unusual location in this regard.

For management purpose, these fistulas are divided into a simple and a complex type. Over half of the simple fistulae can be managed medically.

Burdred et al. described a series of 40 fistulae. Only two were associated with lactation state and both healed spontaneously without resorting to surgery as in this case. Surgical procedures range from total duct excision (recommended for complex fistula), and fistulectomy with saucerization. About 23% recur particularly if there is post-operatively infection. Maier et al. recommend demonstrating and removing/un-roofing the sinus tract for prevention of recurrence.

The presently described case had the preceding history of surgical drainage of an inflammatory mass (which could have been an infected galactocoele) in the axillary tail. However none of the other described associated factors were there. The self remission and closure with local care alone also corresponds with the observations of Bundred et al.

**ACKNOWLEDGEMENT**

The authoress would like to acknowledge Dr Fouzia Nasir, consultant gynecologist, Bismillah Taqee Hospital, Karachi for referring the case and providing management detail.

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CASE REPORT

ABDOMINAL WALL COMPLICATIONS OF MISSED GALL STONES IN LAPAROSCOPIC CHOLECYSTECTOMY.

Muhammad Zubair¹, Lubna Habib², Masoom Mirza²

ABSTRACT
Port site complications due to lost gall stones in anterior abdominal wall are recently reported complications of laparoscopic cholecystectomy. Two cases are hereby reported who had underwent laparoscopic cholecystectomy and later on one presented with discharging sinus and the other with anterior abdominal wall mass. On exploration both the problems were found related to stones lodged in the anterior abdominal wall.

Key words: Laparoscopy, Cholecystectomy, Missed stones, Port site, sinus, Abdominal wall.

INTRODUCTION
Laparoscopic surgery revolutionized the treatment of symptomatic cholelithiasis and gained acceptance worldwide over a very short period of time. Port site complications are newer procedure related events and require notification to update the literature and design protocols to prevent these complications.¹² Many of these complications such as abscess formation, recurrent sinuses and abdominal wall mass are the result of stone slipped in abdominal wall during extraction of gall bladder.¹³⁻⁵ Here are two reported cases who presented with the consequences of missed stones lodged in the anterior abdominal wall.

CASE REPORT

Case 1

A 32 years old woman presented in out patient department with a discharging sinus at the site of epigastric port. She had elective laparoscopic cholecystectomy two and half months ago for chronic calculus cholecystitis in another hospital. The epigastric wound got infected in the immediate post operative period. It was treated by several courses of antibiotics but with partial response. On examination, there was local induration, erythema and seropurulent discharge from the sinus at epigastric port site. Systemic signs of sepsis were absent. Ultrasound scan was normal. Sinus was explored under general anaesthesia. The sinus was limited to abdominal wall. At the depth of sinus two small, dark brown, facetted gall stones were retrieved. Wound was irrigated thoroughly and left open. It healed in three weeks time.

Case 2

A 45 years old woman was admitted with pain and lump in epigastrium for three months. She had laparoscopic cholecystectomy for acute calculus cholecystitis four months ago. There was no history of fever or vomiting. On examination, there was an ill defined, non tender lump just below the epigastric port site scar. On ultrasound scan there was a mass of mixed echogenecity in upper abdomen. Contrast enhanced computed tomography of the upper abdomen showed a 5 x 3 cms, soft tissue mass adherent to the anterior abdominal wall in midline with low attenuation in the centre (Figures 1 and 2). On exploration under general anaesthesia there was a necrotic mass attached to and deep to the linea alba. A single gall stone was retrieved from this mass, area was irrigated and primarily closed with suction drain. Postoperative recovery was unremarkable.

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frequency of 32% and spillage of stone around 6%.\textsuperscript{1,5,7,8} Perforation can occur during retraction and dissection of gall bladder from the liver bed especially in acute cholecystitis or during its forceful extraction through port-site.\textsuperscript{1,3,8} Up till now gall bladder perforation is considered as a benign event and many surgeons leave these stones because of limited access or difficulty,\textsuperscript{3} but follow up with this technique complications of retained stones have been described in isolated case reports or small case series. These include intra abdominal abscesses, cutaneous fistulae, gastric outlet obstruction, small bowel obstruction, erosion into sigmoid colon and gall stones in femoral canal mimicking incarcerated hernia.\textsuperscript{3} The estimated incidence of these complications is low, stated to be about 0.6 to 0.8%.\textsuperscript{3} Most of these present between 12 days to 12 months after surgery but complication is also reported after 20 years of original operation.\textsuperscript{6,7}

Perforation of gall bladder during extraction may result in spillage of stones in the anterior abdominal wall which presents as abscess formation, chronic sinus and abdominal wall mass mimicking a neoplasm.\textsuperscript{1,5,9} As compared to intraperitoneal spillage these complications have not been reported frequently. Presentation of the first case of this report was similar to those reported by Pavlidis, Bour and Chowbey from India.\textsuperscript{4,5} All those cases presented with sinus formation and ultimately required second operative procedure for healing. The second patient presented with a vague lump in anterior abdominal wall. Similar presentation is described by Donna nine years after laparoscopic cholecystectomy which was initially interpreted as desmoid tumor.\textsuperscript{1} The complications caused by these unretrieved stones usually do not respond to conservative measures and require some operative procedure for recovery.\textsuperscript{3,8}

Different techniques have been described in literature to minimize the risk of spillage of gallstones as applications of clips, endoloops, sutures and placement of gall bladder in endoscopic bag immediately upon completion of dissection.\textsuperscript{2,3,6} If spillage does occur, these slipped stones should be retrieved but up till now spillage alone is not considered as indication for conversion.\textsuperscript{3,8,10} It is suggested that if spillage occurs it should be properly recorded and patient counselled to avoid clinical misinterpretation of neoplasm and waste of health resources.\textsuperscript{1} We recommend that some form of endobag should always be used to deliver the gall bladder to prevent this complication.

**DISCUSSION**

Laparoscopic cholecystectomy has become the standard treatment for symptomatic cholelithiasis since its introduction in 1987 by the French surgeon Phillipe Mouret.\textsuperscript{6} Its advantages over conventional open cholecystectomy have been discussed extensively. This technique has introduced newer complications not known in era of open surgery for example complications of creating pneumoperitoneum like vascular and bowel injuries and port site related complications including port site hernias.\textsuperscript{1,2,6} Perforation of gall bladder has been observed and experienced as the most common intraoperative complication with estimated
REFERENCES:


LETTER TO THE EDITOR

IMPORTANCE OF DIGITAL RECTAL EXAMINATION IN DIAGNOSING SACROCOCCYGEAL TERATOMA

Muhammad Talat Mehmood, Farhan Shahzad, Muhammad Sajjad Ashraf, Shero Moti Muhammad Shahab Athar.

A 6 years old girl presented with a recurrent discharging sinus in the natal cleft since the age of 6 months. The baby had first developed a small swelling between the buttocks at the age of 6 month which was surgically drained elsewhere. After 6 months the swelling recurred and later started discharging. Since then, she had gone through multiple surgical procedures at different hospitals of the city.

Inspection revealed discharging sinus at the level of coccyx just to the left of midline and scars of previous operation (Figure 1). Discharge was mucopurulent. Digital rectal examination revealed two cystic swellings behind the rectum with well defined margins. Upper limit was reachable with mobile overlying rectal mucosa. Pressure on the cyst led to mucopurulent discharge from the sinus. General examination was unremarkable.

Ultrasound examination and computed tomography of pelvis revealed two cystic masses behind the rectum (Figure 2). No intra-abdominal extension or lymphadenopathy was seen. Sinogram showed a pre sacral cyst filling with contrast which was draining through the sinus tract (Figure 3). Serum alpha fetoprotein level was within normal range. Provisional diagnosis of presacral teratoma was made. Excision of cystic swelling along with coccyx and sinus tract was performed through posterior sagittal approach. Postoperative recovery was uneventful. Histopathology revealed a benign teratoma containing salivary tissue.

Figure 1: Photograph showing sinus and scars of previous surgery.

Figure 2: CT scan showing two retro-rectal cysts.

Figure 3: Sinogram showing the sinus communicating with retro rectal cyst.

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Sacroccocygeal teratoma is the most common neonatal tumor.\textsuperscript{1} The incidence of sacroccocygeal teratoma is 1 in 40,000 live births. It is more common in females (75\%) than the male child (25\%).\textsuperscript{1,3} It is important to recognize and treat it early to prevent complications particularly malignant transformation. The risk of malignant transformation increases with increasing age. In neonates the frequency of malignant transformation is 7\% whereas above 2 years it rises to above 50\%.\textsuperscript{3}

Sacroccocygeal teratomas are of 4 types according to presentation. Type I is predominantly external with minimal presacral component (47\%). Type 2 is external with significant but minimal intrapelvic extension (34\%). Type 3 is predominantly intrapelvic with minimal external component (09\%). Type 4 has no external component and there is a presacral component only (10\%).\textsuperscript{2}

Most of these can be diagnosed in the antenatal period by antenatal sonography.\textsuperscript{4} Majority of sacroccocygeal teratomas (> 81\%, types 1 and 2) present as bulging over the sacroccocygeal region, however types 3 and 4 are difficult to diagnose due to lack of external component and may present late usually with complications.\textsuperscript{5} It is usually the constipation, abdominal mass or urinary symptoms that bring the infant to medical attention in such cases. Rectal examination shows retro rectal mass pushing the rectum forwards. Anterior meningocele, rectal duplication cysts, dermoid cysts, chordoma and haemangioma must be considered in differential diagnosis.\textsuperscript{6}

Radiography of the lumbosacral region may demonstrate tumor calcification. Ultrasound, CT scan and MRI are useful in diagnosing and assessing the extent of sacroccocygeal teratoma.\textsuperscript{4} Raised alpha fetoprotein level differentiates between benign and malignant tumor and is used as a prognostic factor as well as a sign of recurrence.\textsuperscript{3,6}

Delay in diagnosis and surgical treatment may be associated with malignant transformation, pressure necrosis, infection or haemorrhage.\textsuperscript{1} Omission of rectal examination in this case led to delayed diagnosis although she presented at the age of 6 months and was operated multiple times at different hospitals. It is therefore important to perform a thorough physical examination including digital rectal examination in every child who presents with a swelling or sinus in sacroccocygeal region.

REFERENCES


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