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Editorial

Information Technology and Medical Education

There is no argument over the influence of information technology (IT) in medicine and education. But in context of the developing countries, there are still many areas which need to be improved before we could utilize IT to its full extent. In the meantime, it would be best for the developing countries to make a balance between the traditional education system and the new IT based education system.

However advance the technology gets, it can never replace the interaction that the doctors and students require with the patient. So, in the pursuit of modern technologies, we should be careful that the doctor patient relationship does not get overlooked in our medical education system.

Information Technology Association of America (ITAA) defines Information Technology (IT) as "the study, design, development, implementation, support or management of computer-based information systems, particularly software applications and computer hardware."[1] Today, these two terms - computers and IT - are almost synonymous. In a way, IT has brought the world to our fingertips. With the development in IT, there has been a significant change in the medical education all over the world. The changes is that majority of the medical students are computer literate these days. Instead of heavy books, the students rather carry CD-ROMs, or small drives in their pockets and these can be used anywhere and anytime. New information on medical topics is more readily accessible via the internet and handheld devices such as palmtops, PDA (Personal Digital Assistant).

Information technology can assist medical education in various ways such as in college networks and internet. Computer-assisted learning, virtual reality, human patient simulators are some options. With the help of college networks and internet, the medical students as well as the teachers may stay in contact even when they are off college. Rapid communication can be established with the help of e-mails, course details, handouts, and feedbacks can be circulated easily. Many medical schools these days use online programmers. Such programmers allow speedy access to information and quick turnaround of evaluation and messaging, and allow all tutors, assessors, and students at any site to look at the curricular context of their own particular contribution. Similarly, the internet provides opportunities to gain up-to-date information on different aspects of health and disease and to discuss with colleagues in different continents via net conferencing. Free access to Medline, various medical journals, online textbooks and the latest information on new development in medicine also encourages learning and research.

As computer assisted learning (CAL) is gaining more popularity, these days many medical schools encourage the students to purchase computers, and others are making strategies for integrating medical informatics into the curriculum[2,3]. Interactive digital materials for study of histopathology, anatomy, heart sounds are used widely. Development of anatomical three dimensional atlases of various internal organs using computed tomography and magnetic resonance imaging are very illustrative and help the students to understand the subject matter clearly. One can also have web-based learning. The learning materials are uploaded in the internet, so that anyone in any corner of the world can read them[4]. With new technology, the students can virtually go inside each and every organ and see how they actually look like from outside as well as from inside. We now have proofs that we can have virtual trainings that improves the surgical skills of young surgeons[5,6]. In more organized form, even we can have formal medical courses and training courses which students or doctors can attend online like any course in a medical college. At the end of the course, one can also get an evaluation and grades or credits accordingly[7].

The problem medical education system faces in developing countries is the access to journals. Due to limited resources, they cannot subscribe all the renowned international journals, which make a very essential part of

medical education. IT has made it possible to have online databases like HINARI, Pubmed, Cochrane etc and online journals like BMJ, Nature, Annals, and a lot others. IT has also helped a lot to promote research activities in developing countries. First, it gives access to many previous research articles on the topic, so that people can learn about the methodology previously designed. Next, they can design their own methodology so that the results can be comparable with the previous ones because non comparable findings are not of much worth. Besides, unless and until, the findings of a research are published and reach out to numerous people, it does not carry any significance. And, only with IT can we have huge number of readers because very few countries and associations subscribe journals where most of our research articles are published. So, IT has helped to put our national journals in an international arena. Had they not have an online version, many would not have heard of them. Problem based learning and evidence based medicine are supposed to be the pillars of modern medicine and education system. The essence of these systems lie in the study of researches, literatures and experiments and it requires access to vast amount of information which only internet can provide. So, IT has become indispensable in the present day medical education system.

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Original Article

Intra Coronary Bolus Dose of Eptifibatide is Effective to Prevent Early Major Adverse Cardiac Events in Patients Undergoing Elective Per-cutaneous Coronary Intervention

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ABSTRACT

Acute coronary syndromes (ACS) are caused by plaque rupture and thrombosis leading to ischemia from a new significant coronary stenosis. Per-cutaneous coronary intervention (PCI) is often a primary therapy. Before the era of glycoprotein IIb/IIIa inhibitors, PCI was associated with a major adverse cardiac events. The GP IIb/IIIa inhibitor eptifibatide has been demonstrated to improve cardiac outcomes among patients with PCI by reducing the occurrence of major adverse cardiac events (MACE). This prospective interventional study conducted in the University Cardiac Centre (UCC), Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from January 2009 to October 2010 to determine the effect of high bolus dose of intra-coronary eptifibatide in the prevention of early major adverse events - death, myocardial infarction (MI), target vessel revascularization (TVR) and severe bleeding in patients under going elective PCI. One hundred one patients were selected for elective PCI according to inclusion and exclusion criteria. Patients were divided into two groups. Group- I (n=53) with eptifibatide and Group-II (n=48) without eptifibatide. During peri-procedural period, in hospital and 30-day follow-up, we recorded major adverse cardiac events (death, MI, TVR) and bleeding in two groups. Major adverse cardiac events (MACE) were not found in Group I patients but found 8.3% in Group II patients. Only 3.8% and 2.1% of the patients had minor bleeding in Group-I and Group-II respectively. No death and major bleeding were recorded in both groups. Peri-procedural major adverse events were higher in Group-II and were statistically significant ($p<0.05$). Single bolus dose of intra-coronary eptifibatide is simple, safe, cost-effective therapy in patients under going elective PCI than conventional heparin only.

Keywords: *Eptifibatide, Per-cutaneous coronary intervention, Acute coronary syndrome.*

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INTRODUCTION

Ischemic heart disease (IHD) is a major health problem and important cause of death in affluent nations of the world. Incidence of IHD is increasing in developing countries, including Bangladesh. In 1975, the incidence of IHD in Bangladesh was reported to be 3.3 per thousand and in 1985 that was 14 per thousand[1]. There are some studies conducted among general population to see the prevalence of Ischemic Heart Disease (IHD). Limited number of data is available which are mostly based on small size population based cross-sectional survey. The average prevalence of IHD from 3 small scale population based studies in Bangladesh was 6.56/thousand[2]. Bangladeshi people, as other South

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Asians, have high susceptibility to ischemic heart disease (IHD) but population based data are lacking in Bangladesh. A prevalence of 3.4% was recorded in rural and agricultural free living population with traditional lifestyle and thin body mass index[3].

The treatment of myocardial infarction has evolved considerably over the past decades. Reported mortality rates have fallen as a result of a variety of factors, including earlier diagnosis and treatment of the acute events, improved management of complications and general availability of pharmacological treatment. Most attention however, has been focused on treatments that restore antegrade coronary blood flow in the culprit artery of the patient with evolving acute myocardial infarction. The two methods to achieve this goal are thrombolytic treatment followed by elective angioplasty if appropriate[4].

Per-cutaneous coronary interventions (PCI) have become an accepted means of treating the symptoms of ischemic heart disease for both stable and unstable variants. The major benefit of PCI is in improving patient quality of life. According to the American Heart Association over 600,000 angioplasties were performed in the United States in 2001 and approximately 1000 are performed annually at the McGill University Health Centre (MUHC), PCI is generally a safe technique with low rates of mortality and morbidity. However, this technique is not devoid of complications, particularly in certain high-risk patient groups. The most frequent complication is a peri-procedural myocardial infarction[5].

However, PCI with uncontrolled plaque rupture may expose underlying plaque debris such as von Willebrand factor and vitronectin, which then interact with the glycoprotein IIb/IIIa (GP IIb/IIIa) receptors on the platelet membrane leading to platelet aggregation. This cross-linking of activated platelets with fibrinogen is known as the final common pathway of platelet aggregation and may mediate many of the complications associated with interventional procedures, including death, myocardial infarction, or recurrent ischemia requiring repeat intervention. GP IIb/IIIa inhibitors (eptifibatide, tirofiban, abciximab) are powerful anti-platelet that have consistently improved clinical outcomes of patients with acute coronary syndrome and those undergoing PCI[6].

Eptifibatide is a competitive inhibitor of the GP llb/llIa receptor, and is a potent agent for preventing platelet aggregation. It has a rapid onset of action and a relatively short plasma half-life (90 minutes). At therapeutic levels GP llb/llIa inhibitors have generally been showed to suppress platelet aggregation >80%. A number of clinical trials have shown a beneficial effect of high single bolus dose of eptifibatide in reducing the incidence of peri-procedural major adverse cardiac events in both urgent and elective PCI[7].

Over the last decade, several randomized trials of platelet glycoprotein IIb/IIIa inhibitors during percutaneous coronary intervention (PCI) have been shown to reduce ischemic complications, death, and nonfatal myocardial infarction, and release of peri-procedural creatine kinase-MB (CK-MB). Beneficial effects of GP IIb/IIIa inhibitors during PCI are primarily due to optimal platelet inhibition (PI) as reflected by a decrease in platelet-mediated distal micro-thromboembolism[8].

Eptifibatide reduces major adverse cardiac events in patients with acute coronary syndromes undergoing percutaneous coronary intervention (PCI). Intracoronary bolus administration of eptifibatide may result in higher level of platelet glycoprotein IIb/IIIa receptor occupancy in the local coronary bed, disaggregate thrombus in the epicardial artery and microvasculature, and thereby improve coronary flow. Platelet glycoprotein IIb/IIIa receptor occupancy was significantly greater with intra-coronary than intravenous administration. Higher concentrations of a GP IIb/IIIa antagonist are necessary to effectively disaggregate stable, aged aggregates compared with newly formed thrombi. In this study, we tried to evaluate that intra-coronary high-dose single bolus eptifibatide is superior to conventional intravenous heparin therapy in reducing MACE and major bleeding in elective PCI.

MATERIALS AND METHODS

This prospective interventional study was conducted in the department of cardiology, Bangabandhu Sheikh Mujib Medical University (BSMMU) from January 2009 to October 2010. We took 150 patients with suspected ischemic heart disease (IHD). Then inclusion and exclusion criteria were applied to all patients. Finally 101 patients were included in the study. Patients were referred by their physicians, from out door and emergency department of cardiology, for assessment of chest pain, shortness of breathing and other symptoms of IHD. All patients were evaluated by their history, physical examination, 12 lead ECG, routine laboratory investigation, and exercise ECG test using Bruce protocol. Selective coronary angiography was performed for all patients in the study. There were two groups, Group-I (with eptifibatide) included 53 patients (male 50, female 3) and Group- II (without eptifibatide) included 48 patients (male 40, female 8)

with angiographycally documented significant coronary artery disease.

Inclusion Criteria: Patients undergoing elective PCI for a). Q wave myocardial infarction [QMI]; b). Non Q wave myocardial infarction; c). Unstable angina; d). Stable angina.

Exclusion Criteria: a). Recent QMI or non QMI [within 24 hours]; b). Left ventricular dysfunction [LVEF <40%]; c). Renal impairment; d). Hepatic impairment; e). Cerebrovascular accident [CVA]; f). Saphenous venous graft requiring PCI; g). Patients coronary lesions needs rotational atherectomy or brachytherapy; h). Primary PCI; I). Severe chronic illness; j). Malignancy; k). Obesity.

All patients were treated with aspirin before and after the procedure. All patients received clopidogrel loading dose before or after the intervention, unless they were already on standing dose of one of these agents prior to the stent procedure. Patients received weight-adjusted unfractionated heparin prior to the intervention. A weight adjusted heparin regimen was used to titrate and achieve an activated clotting time of 200-250 seconds before PCI. The eptifibatide bolus dose (weight adjusted) was administered before the lesion was crossed with the guide wire. All patients were treated via the femoral approach with the modified Seldinger entry technique. Seven French sheaths were used. Following anticoagulation administration stenting was performed using standard techniques. Outcome variables of study were: a) Death. b) MI. d) Target vessel revascularization [TVR]. e). Bleeding- major or minor. Data was collected on variables of interest using a predesigned structured questionnaire. Informed written consent was taken from each patient. Thirty-day follow-up data for major adverse events (death, MI, TVR) and severe bleeding were obtained by phone interview and hospital visit(s). Data was processed and analyzed using software SPSS for windows, version-12. Ethical clearance was obtained from the authority of Bangabandhu Sheikh Mujib Medical University to undertake this study.

Operational Definitions:

MACE (Major adverse cardiac events): Death, MI and TVR

Death: Death from any cause or nonfatal myocardial infarction during the first 30 days after the index PCI, whichever occurred first.

Urgent TVR (Target vessel revascularization): Urgent TVR was defined as a second PCI on the original target vessel or CABG performed on an emergency basis for recurrent myocardial ischemia or MI.

Major Bleeding[9]: a. Fatal bleeding; b. Retroperitoneal, intracranial, or intraocular bleeding; c. Bleeding that causes hemodynamic compromise requiring specific treatment; d. Bleeding that requires intervention (surgical or endoscopic) or decompression of a closed space to stop or control the event; e. Clinically overt bleeding, requiring any transfusion of ≥1 unit of packed red cells or whole blood; f. Clinically overt bleeding, causing a decrease in hemoglobin of ≥3 g/dl (or, if hemoglobin level not available, a decrease in hematocrit of ≥10%)

Minor Bleeding[9]: a. Gross hematuria not associated with trauma (e.g., from instrumentation); b. Epistaxis that is prolonged, repeated, or requires plugging or intervention; c. Gastrointestinal hemorrhage; d. Hemoptysis; e. Subconjunctival hemorrhage; f. Hematoma >5 cm or leading to prolonged or new hospitalization; g. Clinically overt bleeding, causing a decrease in hemoglobin of 2 to 3 g/dl; h. Uncontrolled bleeding requiring protamine sulfate administration.

RESULTS

Age distribution:

The maximum disease incidence was found between 41-50 years age group in both groups. The mean age was found 52.0 (±8.4) years with ranged from 39 to 72 years in Group I and 51.5 (±9.5) years with ranged from 37 to 75 years in Group II as shown in Table-I.

Table I: *Age distribution of patients (n=101)*

Age Group	Group I (n=53)	Group II (n=48)	P value
≤40 years	5 (9.4%)	8 (16.7%)	
41-50 years	23 (43.4%)	18 (37.5%)	0.754^{NS}
51-60 years	17 (32.1%)	14 (29.2%)	
>60 years	8 (15.1%)	8 (16.7%)	

NS= Not significant, p value reached from unpaired t-test

Sex distribution:

The sex distribution of the patients found male predominance in both groups. In Group I, 50 (94.3%) were male and rest 3 (5.7%) were female. In Group II, 40 (83.3%) and 8 (16.7%) were male and female respectively as shown in Table-II. The difference was not statistically significant (p>0.05).

Table II: *Sex distribution of the patients (n=101)*

Sex	Group I	Group II	p value
Male	50 (94.3%)	40 (83.3%)	
Female	3 (5.7%)	8 (16.7%)	0.076^{NS}
Total	53 (100%)	48 (100%)	

NS= Not significant, p value reached from Chi-square test

Peri-procedural events:
During peri-procedural period it was observed that TVR and MI not found in Group I patients but found in 4 (8.3%) in Group II patients which was statistically significant by Fisher's Exact Test (Table-III). Minor bleeding occurred in 2 (3.8%) and in 1 (2.1%) of the patients in Group I and Group II respectively. Periprocedural events were higher in Group II but the difference were not statistically significant (p>0.05) by Chi square test between two groups (Table-IV). Death and major bleeding were not recorded in either group.

Table III: *Peri-procedural MACE of the study patients (n=101)*

MACE	Group I (n=53)	Group II (n=48)	p value
Present	0 0.0	4 (8.3%)	0.047
Absent53	(100%)	44 (91.7%)	

P value <0.05 is significant, Fisher's Exact Test was employed to analyze the data.

Table-IV: *Peri-procedural event (minor bleeding) of the study patients (n=101)*

Minor bleeding	Group-I n=53	Group- II n=48	P value
Yes	2 (3.8%)	1 (2.4%)	0.453^{ns}
No	51 (96.2%)	47 (97.2%)	

NS= not significant, p value reached from Chi-square test

DISCUSSION
The study included 101 subjects out of which 53 patients treated with eptifibatide considered as Group I and rest 48 patients treated without eptifibatide considered as Group II. The maximum disease incidence was found between 41-50 years age group in both groups. The highest age incidence reported by different authors in the past was >50 years[10]. In this study 9.4% in Group-I and 16.7% in Group-II were below 40 years of age. This observation correlates with the report of Khandaker[11] where the study found 18.74% of the patients were under 40 years of age.
During peri-procedural period and 30 day follow-up urgent TVR and MI were not found in Group I patients but found in 4 (8.3%) in Group II patients. The finding was statistically significant (p<0.05). In our study there was no MACEs in Group-I patients who received intra-coronary single bolus dose of eptifibatide during elective PCI, which is better than the result of the ESPRIT trial where MACEs was 6.6% with higher double bolus dose of eptifibatide and infusion regimen used as adjunctive therapy during non emergency coronary stent implantation (elective PCI)[12]. In IMPACT-II trial, (the IMPACT-II investigator)[13] found that 9.1% of MACEs with single bolus dose followed by a continuous infusion of eptifibatide during peri-procedural and at 30 day follow up. In another study done by the Pursuit investigators in 1998 (PURSUIT Trial) found MACEs 14.2% with single bolus dose and infusion regimen of eftifibatide in patients with non ST- elevation ACS (Acute coronary syndrome) who under went PCI[13]. Major Adverse Cardiac Events (MACE) occured in Group-II is 8.3% (P<0.048) by Fisher's Exact Probability Test, which is statistically significant.
There was no procedure related major bleeding in Group-I of the study but severe bleeding was recorded in IMPECT-II trial with eptifibatide 135/0.5 dose: 5.1% and 135/0.75 dose: 5.2%. In ESPRIT and PURSUIT trial there were 1.3 and 10.6% severe bleeding respectively[14].
The first randomized study to compare all three available GP inhibitors during PCI revealed that a second bolus dose is needed in the tirofiban group but a single dose in the eptifibatide group[8]. Deibele et al[15] demonstrated significantly higher local platelet GPIIb/IIIa receptors occupancy by intra-coronary eptifibatide versus intravenous bolus administration. Eptifibatide reduces major adverse cardiac events in patients with acute coronary syndromes undergoing percutaneous coronary intervention (PCI). Intra-coronary bolus administration of eptifibatide may result in higher levels of platelet GP IIb/IIIa receptor occupancy (RO) in the local coronary bed, disaggregate thrombus in the epicardial artery and microvasculature, which is associated with improved microvascular perfusion demonstrated by an improved cTFC (corrected thrombolysis in myocardial infarction frame count). Local platelet GP IIb/IIIa RO was significantly higher in the intra-coronary group for both boluses: first bolus, 94±9% versus 51±15% (P<0.001); second bolus, 99±2% versus 91±4% (p =0.001). PRICE study was a randomized trial investigating economic and clinical outcomes of eptifibatide as compared to abciximab therapy during elective PCI. Eptifibatide was associated with lower in-hospital and 30-day follow-up costs compared to abciximab[13].

Limitations of the study:
We do not know the exact prevalence of coronary artery disease in our country. The sample for this single

center based study may not be representative of the general population. The higher percentage of male in the study is another limitation of the study. Involving equal ratios of both genders would have given us more representative idea.

CONCLUSION

Single high bolus dose of intra-coronary eptifibatide is simple, safe, cost-effective therapy to patients under going elective PCI than conventional heparin therapy only. Heparin is as good as eptifibatide but in this study we recorded early major adverse cardiac events in patients undergoing elective PCI without eptifibatide were more during peri-procedural period, in hospital and 30-day follow-up than in patients who received intra-coronary eptifibatide during elective PCI.

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JALALABAD MEDICAL JOURNAL

Original Article

Clinical Presentations and Histological Patterns of Lung Cancer

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ABSTRACT

Lung cancer is the leading cause of cancer-related mortality in both men and women throughout the world that is preventable and potentially curable if diagnosed in earlier stage. This descriptive and cross sectional study was conducted in the Department of Medicine, Jalalabad Ragib-Rabeya Medical College Hospital, Sylhet during the period from 1st July 2009 to June 2010. In this study clinical presentation of lung cancer and its histologic variety was observed to find out the correlation between the common clinical presentation and histologic diagnosis of lung cancer. For this purpose 50 patients were enrolled in this study after inclusion and exclusion criteria. Lung cancer is more common in elderly male with prolonged smoking. The common pulmonary symptoms of bronchial carcinoma were cough (88%), dyspnoea (60%), wheeze (54%), chest pain (50%) and haemoptysis (46%); and common extra pulmonary symptoms were anorexia (68%), weight loss (56%), fever (48%), horseness (40%) and dysphagia (2%). The common physical findings were anaemia (48%), clubbing (36%), cervical lymphadenopathy (26%), features of consolidation (40%) and pleural effusion (32%). Histologic pattern of bronchial carcinoma are squamous cell carcinoma (56%), adenocarcinoma (30%), small cell carcinoma (20%) and large cell carcinoma (4%). Clinical presentations did not correlate the histological pattern.

Key words: *Bronchial carcinoma, Consolidation, Pleural effusion.*

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INTRODUCTION

Lung cancer is one of the leading causes of cancer death in both men and women[1]. The prevalence of lung cancer is more common in male than in female[2]. Most of the lung cancer occurs between the age of 40 to 70 years and peak between 55 to 65 years of age[3]. The incidence of lung cancer in the United Kingdom has increased every year until 1985, when a decrease was noted for the first time in men than in women[4]. There is no statistical data regarding the epidemiology of lung cancer in Bangladesh. In a retrospective study by Rahim[5] in 1978 found that about 9 fold increase in the lung cancer during the period from 1960 to 1973.

Lung cancer is a devastating malignant disease. Most of the cases it keeps a very secluded course with very trivial feature initially until it is diagnosed when the disease has already been disseminated. Early detection of lung cancer by clinical presentation and histologic diagnosis of type of cancer is a predictor of patient's outcome. Correlation of clinical presentation and histologic type of lung cancers will help in predicting the prognosis and referring the patients early for surgical treatment and radiotherapy.

Lung cancer was a rare entity in the early 1900's, but, by the end of the century, lung cancer is the leading cause of cancer-related mortality in both men and women in the United States and throughout the world that is preventable[6,7,8]. The prevalence of lung cancer

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is second only to that of prostate cancer in men and breast cancer in women.

Most lung carcinomas are diagnosed at an advanced stage, conferring a poor prognosis. The need to diagnose lung cancer at an early and potentially curable stage is obvious. In addition, most patients who develop lung cancer have been smokers and have smoking-related damage to the heart and lungs, making aggressive surgical or multi-modality therapies less viable options[8]. This study was designed to detect clinical presentations of lung cancer, its histologic variety and to correlate the common clinical presentation and histologic diagnosis.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Medicine Jalalabad Ragib-Rabeya Medical College Hospital, Sylhet, Bangladesh during the period from July 2009 to June 2010 with a view to find clinical presentation and histopathologic pattern of lung cancer. For this purpose 50 patients were enrolled in this study after fulfilling inclusion and exclusion criteria. Inclusion criteria were diagnosed cases of primary lung cancer patients, age more than 20 years, both sexes. Exclusion criteria were age less than 20 years, secondary lung cancer, those who refused to participate in the study. The cases were collected from Jalalabad Ragib-Rabeya Medical College Hospital and Sylhet MAG Osmani Medical College Hospital, Sylhet. A detailed history of each patient on admission was taken by using a pre-designed questionnaire for the study and examined thoroughly. Findings were recorded and pre-testing of the research instruments done. Explanation of the purpose of the study and informed written consent were taken from the patients. The interview was held in a peaceful, non-threatening environment. Investigations like blood for TC, DC of WBC, haemoglobin level, ESR, X-ray chest P/A view and sputum for malignant cell were done in all cases. Pleural fluid study, bronchoscopy and biopsy or brushing, CT or USG guided FNAC, pleural biopsy which was appropriate for the case also was done.

RESULTS

The age of the patients was ranging from 35 to 83 years with the mean age of 58 (±11.143) years. Thirty four percent of the patients were in the age group of 61 to 70 years, 30.0% were in the age group of 51 to 60 years, 24.0% were in 41-50 years, 8.0% were above 70 years and 4.0% were in the age group of 31 to 40 years. Out of 50 patients 42 (84%) patients were male and 8 (16%) patients were female. Sixty six percent of the patients were smoker, 18% were ex-smoker and 16% were non-smoker.

Distribution of patients on pulmonary symptoms of bronchial carcinoma:

Cough (88%) was the most frequent pulmonary symptoms of bronchial carcinoma, followed by dyspnoea (60%), wheeze (54%), chest pain (50%) and haemoptysis (46%). Distribution of patients on pulmonary symptoms of bronchial carcinoma is shown in Table-I.

Table I: *Distribution of patients on pulmonary symptoms of bronchial carcinoma (n=50)*

Pulmonary symptoms	Frequency	Percentage
Cough	44	88
Dyspnoea	30	60
Wheeze	27	54
Chest pain	25	50
Haemoptysis	23	46

Distribution of patients on extrapulmonary symptoms of bronchial carcinoma:

Anorexia (68%) was the most frequent extra pulmonary symptoms of bronchial carcinoma, followed by weight loss (56%), fever (48%), hoarseness (40%) and dysphagia (2%). Distribution of patients on extrapulmonary symptoms of bronchial carcinoma is shown in Table-II.

Table II: *Distribution of patients on pulmonary symptoms of bronchial carcinoma (n=50)*

Extra-pulmonary symptoms	Frequency	Percentage
Anorexia	34	68
Weight loss	28	56
Fever	24	48
Hoarseness	02	04
Dysphagia	01	02

Distribution of patients on physical findings:

Physical findings of the patients were anaemia (48%), clubbing (36%), cervical lymphadenopathy (26%), superior venacaval obstruction (4%), features of consolidation (40%), pleural effusion (32%), hepatomegaly (4%) and ascites (2%). Distribution of patients on physical findings are shown in Table- III.

Table III: *Distribution of patients on physical findings (n=50)*

Physical findings	Frequency	Percentage
Anaemia	24	48
Consolidation	20	40
Clubbing	18	36
Pleural effusion	16	32
Lympadenopathy	13	26
Superior venacaval obstruction	02	04
Hepatomegaly	02	04
Ascites	01	02

X-ray findings of bronchial carcinoma:
X-ray findings were analyzed and found that consolidation (58%) was the most common features; others were pleural effusion (24%), collapse and consolidation (4%), consolidation and effusion (14%), mediastinal enlargement (10%) and upper lobe lesion (14%). Table-IV shows the X-ray findings of bronchial carcinoma.

Table IV: *X-ray findings of bronchial carcinoma (n=50)*

X-ray findings	Frequency	Percentage
Consolidation	29	58
Pleural effusion	12	24
Collapse and consolidation	4	8
Consolidation and effusion	7	14
Mediastinal enlargement	5	10
Upper lobe lesion	7	14

Histological pattern of bronchial carcinoma:
Squamous cell carcinoma (56%) was the most common histological pattern of bronchial carcinoma, followed by adenocarcinoma (30%), small cell carcinoma (20%) and large cell carcinoma (4%). Histological pattern of bronchial carcinoma is shown in Figure-1.

Association of clinical presentation and histopathologic type of bronchial carcinoma:
An association of clinical presentation and histopathologic type of bronchial carcinoma was calculated and found that there was no association of clinical presentation and histopathologic type of bronchial carcinoma in relation to cough (p=1.000), dyspnoea (p=0.701), wheeze (p=0.553), chest pain (p=0.735), haemoptysis (p=0.253), fever (p=0.958), anorexia (p=0.727), weight loss (p=0.635), hoarseness (p=1.000) and dysphagia (p=1.000). Association of clinical presentation and histopathologic type of bronchial carcinoma is shown in Table-V.

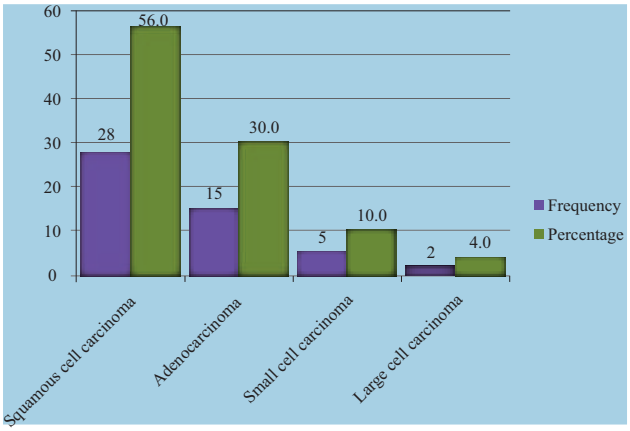

Figure 1: *Histological pattern of bronchial carcinoma (n=50)*

Association of physical findings and histopathologic type of bronchial carcinoma:
An association of physical findings and histopathologic type of bronchial carcinoma was calculated and found that there was no association of physical findings and histopathologic type of bronchial carcinoma in relation to anaemia (p=0.927), cervical lymphadenopathy (p=0.890), clubbing (p=0.143), pleural effusion (p=0.692), consolidation (p=0.102), superior venacaval obstruction (p=1.000), hepatomegaly (p=0657) and ascites (p=1.000). Association of physical findings and histopathologic type of bronchial carcinoma is shown in Table-VI.

Table V: *Association of clinical presentation and histopathologic type of bronchial carcinoma (n=50)*

Clinical presentation	Histopathologic type of bronchial carcinoma				*p value
	Squamous cell carcinoma (n=28)	Adenocarcinoma (n=15)	Small cell carcinoma (n=5)	Large cell carcinoma (n=2)	
Cough	24 (85.7)	13 (86.7)	5 (100.0)	2 (100.0)	1.000
Dyspnoea	15 (53.6)	10 (66.7)	4 (80.0)	1 (50.0)	0.701
Wheeze	13 (46.4)	9 (60.0)	4 (80.0)	1 (50.0)	0.553
Chest pain	14 (50.0)	8 (53.3)	3 (60.0)	0 (0.0)	0.735
Haemoptysis	16 (57.1)	5 (33.3)	2 (40.0)	0 (0.0)	0.253
Fever	13 (46.4)	7 (46.4)	3 (60.0)	1 (50.0)	0.958
Anorexia	19 (67.9)	9 (60.0)	4 (60.0)	2 (100.0)	0.727
Weight loss	16 (57.1)	7 (46.4)	3 (60.0)	2 (100.0)	0.635
Hoarseness	1 (3.6)	1 (6.7)	0 (0.0)	0 (0.0)	1.000
Dysphagia	1 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)	1.000

* Fisher Exact Test was applied to analyze the data; figure in the parenthesis indicates percent.

Table VI: *Association of physical findings and histopathologic type of bronchial carcinoma (n=50)*

Physical findings	Histopathologic type of bronchial carcinoma				*p value
	Squamous cell carcinoma, n=28	Adenocarcinoma n=15	Small cell carcinoma, n=5	Large cell carcinoma, n=2	
Anaemia	13 (46.4)	8 (53.3)	2 (40.0)	1 (50.0)	0.927
Lympadenopathy	7 (25.0)	4 (26.7)	2 (40.0)	0 (0.0)	0.890
Clubbing	14 (50.0)	3 (33.3)	1 (20.0)	0 (0.0)	0.143
Pleural effusion	8 (28.6)	6 (40.0)	2 (40.0)	0 (0.0)	0.692
Consolidation	15 (53.6)	3 (20.0)	2 (40.0)	0 (0.0)	0.102
SVO	1(3.6)	1 (6.7)	0 (0.0)	0 (0.0)	1.000
Hepatomegaly	2 (7.1)	0 (0.0)	0 (0.0)	0 (0.0)	0.657
Ascites	1 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)	1.000

* Fisher Exact Test was applied to analyze the data; SVO-Superior venacaval obstruction; figure in the parenthesis indicates percent.

DISCUSSION

In this study the age of the patients was ranging from 35 to 83 years with the mean age of 58 (± 11.143) years; and 34% of the patients were in the age group of 61 to 70 years, 30% were in the age group of 51 to 60 years, 24% were in 41-50 years, 8% were above 70 years and 4% were in the age group of 31 to 40 years. Frank in 1982 reported that the most of the lung cancer occurs between the age of 40 to 70 years and peak between 55 to 65 years of age. Only 2% of cases occur before the age of 40 years[3].

Le Roux[9] in 1968 studied 4000 patients with lung cancer and found that 75% of lung cancer was occurred in 6th and 7th decade, 15% below the age of 50 years and another 10% above the age of 70 years. Howard[10] in 1997 reported 2286 patients with lung cancer and found that maximum incidence of lung cancer in the 6th and 7th decade. Baum[11] et al. in 1997 reported maximum incidence of lung cancer (51%) was above the age of 50 years among the study patients of 473.

Lung cancer was more common in male than in female. But there was increasing trends of lung cancer in female due to increasing smoking habit in female[12]. In this study out of 50 patients, 84% patients were male and 16% patients were female. This result was supported by Bignal[12] that sex ratio of lung cancer was 10:1. Other studies also found male preponderance. Howard[10] found male female ratio of 6:1.

Sixty six percent of the patients were smoker, 18% were ex-smoker and 16% were non-smoker in this study. These findings were supported by the study of Howard[10]. He found that 95% of the lung cancer patients were smoker and 85% of them smoked more than 20 years.

In this study cough (88%) was the most frequent pulmonary symptoms of bronchial carcinoma. This findings were concordance with the findings of Spiro[4] that cough was the presenting features of bronchial carcinoma in 80% of the patients. Rahim[5] et al. reported about 70% of patients with lung cancer presented with cough.

Dyspnoea was present in 60% of patients with lung cancer in the current study. This finding was similar to the study of Spiro[4] that 60% patients of bronchial carcinaoma presented with dyspnoea. In this regards Hyde and Hyde[13] found 58% and [14]Ehler et al. observed only 30% patient had dyspnoea. Chest pain was present in 50% of the patients in the present series. Spiro[4] reported 40% and Ochsner[15] et al. reported 60% of patients with lung cancer presented with chest pain.

In this study, haemoptysis was present in 46% of the patients. This result was concordance with the finding of Ochsner[15] et al. that 46% of patients with lung cancer presented with chest pain, other study reported higher incidence of haemoptysis of 60% as the presenting features of lung cancer[4].

Anorexia (68%) was the most frequent extra pulmonary symptoms of bronchial carcinoma, followed by weight loss (56%), fever (48%), horseness (40%) and dysphagia (2%) in the present study.

Physical findings of the patients were anaemia (48%), clubbing (36%), cervical lymphadenopathy (26%), superior venacaval obstruction (4%), features of consolidation (40%), pleural effusion (32%), hepatomegaly (4%) and ascites (2%). Hyde and Hyde[13] in 1974 found clubbing in 20% and Spiro[4] found 50% lung cancer patients had clubbing. Hyde and Hyde[13] also found cervical and axillary lympnadenopathy in 23% of their series at presentation. [5]Rahim et al. found superior venacaval

obstruction in 4% of the patients of lung cancer.

X-ray findings were analyzed and found that consolidation (58%) was the most common features; others were pleural effusion (24%), collapse and consolidation (4%), consolidation and effusion (14%), mediastinal enlargement (10%) and upper lobe lesion (14%).

Squamous cell carcinoma (56%) was the most common histological pattern of bronchial carcinoma, followed by adenocarcinoma (30%), small cell carcinoma (20%) and large cell carcinoma (4%). In this regards [16]Ahmed et al. found squamous cell carcinoma in 52%, small cell carcinoma in 23%, adenocarcinoma in 12% and large cell carcinoma in 10% of patients of lung cancer.

A study was carried out on 1277 consecutive lung cancer patients, from January 1989 to October 2002 and showed a statistically significant association between cell type and the symptomatic pattern ($p<0.001$)[17]. In particular, incidental diagnoses were more common in adenocarcinomas (20.6%), while bloody sputum was more commonly reported with squamous cell lung cancers (13.4%). Dyspnoea (19.4%), chest pain (19.4%) and symptoms of mediastinal or distant dissemination were more frequent (13.9%) than expected in small cell carcinomas[17]. But in our study there was no association between clinical presentation and histopathologic type of bronchial carcinoma in relation to cough (p=1.000), dyspnoea (p=0.701), wheeze (p=0.553), chest pain (p=0.735), haemoptysis (p=0.253), fever (p=0.958), anorexia (p=0.727), weight loss (p=0.635), hoarseness (p=1.000) and dysphagia (1.000).

Limitation of study:

This study was conducted in tertiary hospitals in Sylhet involving a small number of patients which may not reflect the actual situation of the country.

CONCLUSION

Clinical presentations of patients in this study did not correlate the histological pattern but reflected at least some clinical and histological aspects of bronchial carcinoma in Bangladesh. This study correlated and sometimes differed with the data of studies at home and abroad. Mass screening for early detection is very helpful and antismoking campaign, motivation against smoking, legislative measures, discouraging cigarette production and marketing are the only way to prevent and reduce the load of lung cancer.

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JALALABAD MEDICAL JOURNAL

Original Article

Treatment of Incomplete Abortion in First Trimester with Misoprostol

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ABSTRACT

The objectives of this study were to find out the efficacy of misoprostol in complete evacuation of first trimester incomplete abortion and to select the more effective and safe route of administration. A total of 88 patients were treated of which 46 were in oral and 42 were in vaginal group. Both groups were treated with 400 µgm of misoprostol 4 hourly and a total of 3 doses were given. In the course of treatment 8 patients from oral group and 12 patients from vaginal group were withdrawn from the study due to various side effects like diarrhoea, fever, tachycardia and excessive per vaginal bleeding and were immediately managed by surgical evacuation. The remaining patients were evaluated after 24 hours for complete evacuation clinically and by ultrasonogram. The overall success rate irrespective of route of administration was 57.4%. Although both the routes were found equally effective, the success rate of vaginal route was 63.3% and in oral group it was 52.6% (P>0.05).

Key words: *Misoprostol, Complete evacuation, First trimester, Incomplete abortion.*
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INTRODUCTION

Pregnancy and childbirth is a natural process but 15-20% of pregnancies end in spontaneous abortions[1]. Most of these abortions occur in the first trimester and are incomplete. Management of incomplete abortion is surgical evacuation of the uterus to prevent complications[2]. But surgical evacuation themselves have a overall complication rate of 4-10%[1,2].

So all over the world there is vigorous search for alternative medical management of incomplete abortions. Research evidence indicates that medical treatment of incomplete abortion with misoprostol is an effective alternative[3]. So long there are several reports about the use of a drug named misoprostol, a prostaglandin E_1 analogue. It is widely used in prevention and treatment of postpartum haemorrhage. The use of this drug in medical management of incomplete abortion is controversial and there are arguments about the route of administration of this drug. Some are using this drug orally, some are using in vaginal route while others are using this drug sublingually. There are reports of success in all the routes. The success depends upon the dose, frequency and duration of follow up. There are also reports of complications with the use of misoprostol which predominate with the route of administration[4,5]. It is revealed from many studies that higher the dose and longer the duration of follow up the success rate is high. High dose is intimately related to the more adverse effects and longer duration of follow up is related to anxiety, fear and uncertainty which is quiet stressful for most of the patients. A recent review of misoprostol for women health indicators highlighted the variety of regimens that have been studied for medical treatment of incomplete abortions. There are insufficient evidences to recommend these regimen[4] but medical management is effective and cost saving when compared with surgical management[6,7]. In a cost minimization analysis, a multicentre randomized

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trial comparing misoprostol and curettage, had shown that misoprostol reduced the need for curettage in 53%. In a sensitivity analysis the percentage of women who needed curettage after misoprostol varied between 25 and 90% in different studies. There are many studies revealing similar complications in both the oral and vaginal application of misoprostol. However the incidence of diarrhoea was significantly higher in the oral compared to vaginal route[8]. Oral route offers easy administration at home and vaginal route requires expert personnel for application so needs hospital admission. Oral route is more related to GIT problem[8] while vaginal route is more related to uterine hyper stimulation syndrome[9]. All these complications are dose related. There is no significant difference between oral and vaginal route in success rate. In case of high dose and long follow up there are reports of higher success rate as far as 60% to 85%[8,10].

Therefore this study has been designed to evaluate the effect of multiple lower doses of misoprostol and short-term observation for the management of first trimester spontaneous incomplete abortion. Both oral and vaginal route was chosen to find out the most effective route.

MATERIALS AND METHODS

This randomized controlled clinical trial was conducted in the Obstetrics and Gynaecology department of Sylhet MAG Osmani Medical College Hospital from July 2006 to June 2008. All admitted patients during the study period fulfilling the inclusion and exclusion criteria were randomized by lottery into oral misoprostol group (Group A) and vaginal misoprostol group (Group B). In Group A 46 and Group B 42 patients were selected. Group A was treated with 400µgm misoprostol orally 4 hourly and a total of 3 doses were given. Group B was treated by 400µgm misoprostol vaginally, 4 hourly and a total of 3 doses were given in the posterior fornix of the vagina. In both the groups, drug was administered by same person. Patients pulse, temperature, respiration, blood pressure, per vaginal bleeding and other side effects were monitored routinely. Patients were instructed to report for any discomfort. Patients who developed any complications like diarrhoea, fever, tachycardia, shivering, and lower abdominal pain were immediately attended and excluded from the study and managed symptomatically and by emergency surgical evacuation. If there were no side effects then 3 doses of misoprostol were completed and after 24 hours of first dose complete evacuation were assessed clinically and was confirmed by abdominal ultrasonogram (USG) by the same sonologist. If there was any retained product or endometrial wall thickness >15 mm or both, the case was labeled as failure case and was managed by surgical evacuation. Haemoglobin level and blood grouping was done prior to use of misoprostol. Haemoglobin level was measured again after complete evacuation. Drop of haemoglobin level for every patient was compared. If haemoglobin level dropped below 2 gm/dl from initial haemoglobin level then discharge was cancelled and managed by blood transfusion. The study was approved by the ethical committee of Sylhet MAG Osmani Medical College.

RESULTS

A total of 88 (oral 46 and vaginal 42) eligible patients were counseled and briefed about the study. The mean age and mean gestational age of the respondents in both the groups were similar. Mean duration of abortion in oral and vaginal group were 6.61 (±3.2) days and 7.19 (±3.4) days respectively. The mean haemoglobin level on admission was similar in both the groups (Table-I). In oral group 38 patients and in vaginal group 30 patients completed 3 doses of misoprostol (Table-II) of whom 20 patients in oral and 19 patients vaginal group have complete evacuation of the uterus (Table-III) whereas 16 patients in oral group and 18 patients in vaginal group had haemoglobin drop by ≥1gm/dl between admission and discharge which is statistically insignificant (Table-III) Excessive per vaginal (P/V) bleeding occurred in 14 (6 oral, 8 vaginal) cases, high fever occurred in 8 (4 oral, 4

Table-I: *Base line characteristics of the respondents*

Variables	Group A (n= 46)	Group B (n= 42)	P value
Age (years) Mean (±SD)	28.13 (±6)	28.61 (±7.9)	
Gestational age (weeks) Mean (±SD)	10.5 (±1.39)	10.52 (±1.17)	
Duration of abortion (days) Mean (±SD)	6.61 (±3.2)	7.19 (±3.4)	$> 0.05^{NS}$
Haemoglobin (gm/dl) Mean (±SD) on admission	9.35 (±1.1)	9.32 (±1.2)	

SD = Standard deviation, NS= not significant, p value reached from Chi square test

Table-II: *Evacuation status and haemoglobin drop between admission and discharge*

Group three doses	Completion of evacuation	Complete evacuation	Incomplete ≥ 1 gm%	Hb drop
Group A n= 46	n= 38	20 (52.6%)	18 (47.4%)	16 (42.1%)
Group B n= 42	n= 30	19 (63.3%)	11 (36.7%)	18 (60%)
Combined (A+B) n= 88	n= 68	39 (57.4%)	29 (42.65%)	34 (50%)

P value >0.05 (Not significant), p value reached from Chi square test

vaginal) cases, and diarrhoea occurred in 4 (2 oral, 2 vaginal) cases. On the other hand tachycardia in 4 patients and shivering in 2 patients occurred only in oral group and severe lower abdominal pain occurred in 2 patients in vaginal group. It is worthwhile to mention that one patient had more than one side effect (Table-III). Eight patients in oral and twelve patients in vaginal group were withdrawn from study.

Table-III: *Shows Pattern of Complications between two groups of respondents who were withdrawn from the study*

Complications	Group A (n= 46)	Group B (n= 42)	P value
Diarrhoea	2	2	
High fever (>1020F)	4	4	
Tachycardia (heart rate >100/min)	4	0	>0.05^{NS}
Shivering	2	0	
Severe lower abdominal pain	0	2	
Excessive per vaginal bleeding	6	8	

NS= not significant, p value reached from Chi square test

DISCUSSION

In this study the demographic characteristics of both the groups are similar (Table-I) which is consistent with the study of Demetroulis et al[11]. Due to various side effects 8 patients in oral group and 12 patients in vaginal group were withdrawn from the protocol (Table-II) before completion of 3 doses and were immediately managed by evacuation and curettage. These side effects are consistent with other studies[5,8,11]. Irrespective of route of administration of misoprostol, the rate of complete evacuation of uterus was 57.4% (Table-II) which is consistent with similar study[8] where the success rate was approximately 60% with either route. The result of this study is higher than another study[12], which showed a success rate of 13% with a single dose of 400µgm oral misoprostol after 24 hours of treatment. The reason for higher success in this study may be due to the use of 400µgm triple doses 4 hourly. On the other hand the success rate of this study is lower than the study of Demetroulis et al[11], where 800 µgm single dose vaginal misoprostol was used and after 10 days follow up success rate was 82.5%. In another study with repeated doses of 800µgm misoprostol either orally or vaginally the success was approximately 60%[13]. In this index study although vaginal route shows a higher percentage of success rate (Table-II) (P>0.05) but this is insignificant. The success rate of Pang et al[8] was 65% (oral) and 61% (vaginal) after one day follow up i.e. more success in oral group which is inconsistent to the findings of another study[3], where with 600µgm of oral misoprostol with a single or double dose regimen the success rate was 66% (single dose) and 70% (double dose). Their dose was higher than this index study and duration of follow up was one week. Bagratee et al[14], used 600µgm single dose of misoprostol vaginally, their success after one day, two days and seven days follow up was 32.7%, 73.1% and 88.5% respectively. Here in this index study 400µgm multiple doses were used and after one day follow up the success rate in oral group 52.6% and vaginal group is 63.3%. These findings made us optimistic that if duration of follow up is increased same result can be expected irrespective of the route of administration i.e. longer duration of follow up may lead to higher success rate. Although statistically insignificant this study revealed the loss of haemoglobin (≥1gm/dl) is more in vaginal group which highlights the need for careful administration. This finding is consistent with another similar study but the incidence of diarrhoea in that study was significantly higher (p<0.01) in oral route[8]. This study revealed similar incidence of the side effects which were managed symptomatically and are consistent with the findings of other studies[4,5]. It is also evident that 6 (out of 46) in oral group and 8 (out of 42) in vaginal group had excessive PV bleeding which is statistically similar (Table-III).

CONCLUSION

Despite small sample, shorter duration and lack of post treatment follow up equal efficacy of misoprostol in both oral and vaginal route is obvious in the treatment of incomplete abortion. Yet as oral administration is easier and self administrable it may be recommended in selected cases in outpatient departments as an alternative to surgical management of incomplete abortion in haemodynamically stable patients.

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JALALABAD MEDICAL JOURNAL

Original Article

Outcome of Management of Patients with Post Partum Haemorrhage in A Private Teaching Hospital in Sylhet - A One Year Study

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ABSTRACT

To evaluate the outcome of different types of management of post partum haemorrhage (PPH), a prospective study was done in North East Medical College Hospital, Sylhet from July 2007 to June 2008. The study population was 80. The patients who developed PPH in hospital both after vaginal delivery and caesarean section and who admitted with PPH, all were included in this study. After resuscitation along with general measure causes of PPH was identified and were managed accordingly. Step wise management done in atonic PPH. Haemoglobin levels were 3.9-9.8 gm/dl and 1-11 units of blood transfusion were needed according to severity of anaemia and amount of blood loss. All patients were followed up to see any complications. During study period 10.64% obstetrical patients developed PPH. Among them 19.56% were after vaginal birth and 8.1% were following caesarean section. In 81.25% of cases, PPH were due to atony of uterus and 66.25% patients were multigravidae. During management 51.25% patients responded with medical measure. Inflation of condom was required in 18.75% patients and B-Lynch sutures were required in 8.75% patients, which were the alternatives of hysterectomy. Hysterectomy needed in 5% patients. Maternal death was nil. Effective management of PPH along with blood transfusion can prevent maternal death.

Key word: *PPH, B-Lynch brace suture, Atony of uterus.*

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INTRODUCTION

Still leading cause of maternal mortality is haemorrhage and among haemorrhage, post partum haemorrhage (PPH) is in the top of the list. All women who carry pregnancy beyond the age of viability are at risk of PPH and its sequelae[1]. Incidence of post partum haemorrhage varies 4-22%. In UK it is 4-11%[2]. PPH accounts 25% cause of maternal death in developing country but in developed country it accounts only 8%[1]. The definition of PPH is somewhat arbitrary. Blood loss more than 500 ml following vaginal delivery or more than 1000 ml following caesarean section is termed as PPH[3]. Another consideration is the differing capacities of individual to cope with blood loss. A healthy woman has 30-50% increase of blood volume in a normal singleton pregnancy and can tolerate much more blood loss than a woman who has preexisting anaemia, an underlying cardiac disease or a volume contracted condition secondary to dehydration or pre-eclampsia. So PPH should be diagnosed with any amount of blood loss that threatens the haemodynamic stability of a woman. A loss of these amount of blood within 24 hours of delivery is termed as primary PPH, whereas such losses are termed as secondary PPH if occur 24 hours after delivery.

The main causes of primary PPH have suggested using the '4 T's as tone, tissue, trauma and thrombosis[4]. i) Tone - Uterine atony; ii) Tissue - Retained placenta or placental bits; iii) Trauma - Genital tract trauma includes - Vulval and perineal tear, episiotomy, vaginal tear, cervical tear, vulvovaginal haematoma, broad ligament haematoma, uterine rupture, uterine inversion; iv) Thrombosis- Coagulation disorders,

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disseminated intravascular coagulation (DIC), autoimmune thrombocytopenic purpura, leukemia, von-Willebrands disease.

Uterine atony is the most common cause of postpartum haemorrhage and is reported in 80% cases[4]. Causes of uterine atony- a) Prolonged labour; b) Over distension of uterus- Multiple gestations, fetal macrosomia, fetal abnormality, polyhydramnios; c) Rapid uterine evacuation- Precipitate labour, forceps delivery, initiation and augmentation of delivery by oxytocin; d) Malnutrition and anaemia; e) Structural abnormality- Uterine fibroid, uterine malformation; f) Pharmacological factors- Magnesium sulphate, beta adrenergic agents, halothane, calcium channel blockers; g) Mismanaged third stage of labour- Too rapid delivery of baby preventing the uterine wall to adapt to the diminishing contents, premature attempt to delivery the placenta before it is separated, over manipulation of uterus, pulling the cord, manual separation of placenta during caesarean section[4].

Sepsis is the 2nd most common cause of maternal mortality. Infection due to retained placental bits, retained membranes, slough out of infected injured area of genital tract are the more common cause of secondary PPH. Most dangerous form of secondary PPH is due to slough out of infected slough from caesarean wound which needs sometimes hysterectomy, if PPH is not controlled by conservative treatment[5].

Management depends upon the causes of PPH. Repair of tear area of genital tract stops the traumatic bleeding[5]. If atonic PPH occurs, we do stepwise treatment. Step-1: Uterine massage with uterotonic drugs, evacuation of urinary bladder and examination of expelled placenta. Step-2: Exploration of uterus under anesthesia and continuation of uterotonic drugs. Misoprostol (PGE1) 600-1000µg per rectally. Step-3: Aortic compression or bi-manual compression. Step-4: Uterine tamponade. Step-5: Laparotomy followed by- a) B-Lynch brace suture. b) Bi-lateral uterine artery ligation or mass uterine artery ligation. c) Ligation of anterior division of internal iliac artery. d) Angiographic arterial embolisation. e) Hysterectomy[5].

In secondary PPH- mostly conservative treatment is done. As infection is the main cause of secondary PPH - it is treated by giving appropriate antibiotic after isolation of organism from endocervical swab or high vaginal swab and according to sensitivity to antibiotic. Evacuation and curettage for retained placental bits or membranes. Rarely hysterectomy is needed[6].

World wide 14 millions women suffer from PPH in each year and 150,000 women die annually due to PPH[7]. PPH is also associated with significant morbidity like chronic ill health, anaemia, Sheehan`s syndrome which leads to lactational failure[5]. Infant suffers from diarrhoeal diseases, poor physical and mental development due to lack of breast-feeding. Some patients need hysterectomy which leads to mental upset due to surgical menopause in early age which is sometime difficult to treat.

PPH is not 100% preventable but if we take some measures, we can save mothers life and complications. Only correction of anaemia by haematinics during antenatal period can prevent a significant number of PPH. In high risk cases where PPH may occur, mandatory hospital delivery should be done and cross matched blood should be kept in hand for transfusion in high risk cases.

MATERIALS AND METHODS

This prospective study done in Obstetrics and Gynaecology Department of North East Medical College Hospital, Sylhet from July 2007 to June 2008. Total 80 patients were included in this study according to the inclusion criteria (Primary PPH, Secondary PPH, PPH following vaginal delivery, PPH following caesarean section, PPH following delivery in the North East Medical College Hospital, patients who delivered outside the North East Medical College Hospital).

After diagnosis of PPH, first resuscitation and general treatment were given such as volume replacement, continuous catheterization with Foley's catheter, blood was sent for blood grouping, Rh-typing and cross matching. Then causes of PPH were identified and were managed according to cause. Steps wise treatments were done in atonic PPH. Who developed PPH in hospital, uterine massages were given along with oxytocic drugs (oxytocin, ergometrin, misoprostol), and evacuation of urinary bladder with continuous catheterization and then placenta was examined for any missing cotyledon or membranes. Blood clots were removed manually from uterine cavity; if fail then intra uterine tampon by inflation of condom with normal saline were done in vaginal delivery. Genital tract injuries were searched and were secured accordingly. During caesarean section, when uterus found flabby even with medical measure then B-Lynch brace suture, uterine artery ligation or hysterectomy were done. When PPH developed after caesarean section along with medical measure intrauterine inflation of condom were done.

Patients who were admitted with PPH, after resuscitation, cause of PPH were searched and were managed according to cause. Haemoglobin level

estimation was done in all patients. All patients received antibiotics (amoxycillin and metronidazole), but in secondary PPH patients received antibiotic according to culture report (ceftriaxone, gentamycin and metronidazole). Patients who were treated with condom inflation were under 20 unites oxytocin drip for 24 hours. All study patients improved within 1 to 11 days and were discharged with advice. Follow up done at 2nd week 6th week and 6th month.

RESULTS

During this study period 752 obstetric patients were admitted. Among them 276 (36.7%) patients delivered vaginally and 321 (42.69%) delivered by caesarian section. 15 patients were admitted with PPH following vaginal delivery at home and 3 patients were admitted following caesarean section in other hospitals. In this study 80 cases of PPH were included. Among them 62 (77.5%) were delivered in North East Medical College Hospital and 18 (22.5%) patients were admitted with PPH delivered at home or other hospital. PPH developed 54 (67.5%) following vaginal delivery, 26 (32.5%) following caesarean section (Table-I). Twenty seven (33.75%) patients were primigravida and 53 (66.25%) were multi gravida patients (Table-II).

The mean age of mothers was 22.39 years ranging from 16-36 years. Among them 17.5% were adolescent mothers (Table-III). All patients had haemoglobin level less than 9.8 gm/dl (3.9- 9.8gm/dl) and all patients received blood transfusion ranging from 1-11 units after proper screening and cross matching [2 patients developed disseminated intravascular coagulation (DIC), 1 patient received 11units and another patient received 9 units of fresh blood transfusion]. Sixty five percent patients received 1-3 units of blood transfusion (Table-IV). Out of 80 patients, 65 patients (81.25%) developed PPH due to atony of uterus, 7 patients (8.75%) were admitted with PPH due to retained placenta, 4 patients (5%) had traumatic PPH and 3 patients (3.75%) were admitted with secondary PPH (Table-V).

During management 41 (51.25%) patients responded to oxytocic drugs with uterine massage after removal of clots from uterine cavity manually. Fifteen (18.75%) patients needed inflation of intra uterine condom, among them 2 patients were following caesarean section. B-Lynch suture was given in 7 (8.75%) patients and bilateral uterine artery ligation was done in 1 patient during caesarean section. Hysterectomy was needed in 4 (5%) patients (Table-VI). Secondary PPH were 3 (3.75%).

Table-III: *Age distribution of patients [N=80]*

Age Group	Number of patients
16-19 years	14 (17.5%)
20-25 years	45 (56.25%)
25-30 years	17 (21.25%)
>30 years	4 (5.0%)

Table-IV: *Distribution of patients according to blood transfusion required [N=80]*

Number of blood transfusion in unit	Number of patients
1 - 3	52 (65%)
4 - 6	26 (32.5%)
7 - 9	1 (1.25%)
10 - 12	1 (1.25%)

Table-I: *Distribution of patients developed PPH following vaginal delivery and caesarean section according to place of delivery [N=80]*

Place of delivery	Vaginal delivery	Caesarean section	Total
North East Medical College Hospital	39 (48.75%)	23 (28.75%)	62 (77.5%)
Outside the hospital	15 (18.75%)	3 (3.75%)	18 (22.5%)
Total	54 (67.5%)	26 (32.5%)	80 (100%)

Table-II: *Distribution of patients of PPH according to gravidae [N=80]*

Gravidae	Vaginal delivery	Caesarean section	Total
Primi gravida	18 (22.5%)	9 (11.25%)	27 (33.75%)
Multi gravida	36 (45%)	17 (21.25%)	53 (66.25%)

Table -V: *Distribution of patients according to cause of PPH [N=80]*

Cause	Number
Atony of uterus	65 (81.25%)
Retained placenta	7 (8.75%)
Traumatic	4 (5%)
Secondary PPH	3 (3.75%)
Placenta acreata	1 (0.125%)

Table -VI: *Distribution of patients according to varieties of treatment [N=80]*

Management	Number
Removal of clot from uterus + catheterization and oxytocic drug + uterine massage	41(51.25%)
Inflation of condom	15 (18.75%)
B-Lynch suture	7 (8.75%)
Manual removal of placenta	5 (6.25%)
Subtotal hysterectomy	4 (5%)
Evacuation and curettage	2 (2.25%)
Repair of perineal tear	2 (2.5%)
Delivery of placenta by controlled cord traction (CCT)	2 (2.25%)
Bilateral uterine artery ligation	1 (1.25%)
Release of vulval haematoma	1 (1.25%)

DISCUSSION

PPH is number one cause of maternal mortality in Bangladesh. PPH accounts 18% of all birth. In this study PPH occurred in 10.64% cases. Magann et al showed 5.15% PPH after vaginal birth and 6.75% in emergency and 4.84% in elective caesarean section in King Edward Memorial Hospital, Perth, Australia[8]. In this study PPH occurred 20.69% after vaginal birth, the percentage is higher as it is a tertiary level hospital and usually patient admitted in this hospital with prolonged labour and with trial at home leads to atony of uterus and PPH, 8.18% PPH developed following caesarean section.

Adolescent pregnancies are in great risk of pregnancy associated complication. There is 11-23% adolescent pregnancy rate in USA[9]. In this study PPH occurs in 17.5% adolescent mother. Multigravida patients are at greatest risk to develop atonic PPH. Here 66.25% patients were multigravida patient. Usually atony of uterus accounts 80% causes of PPH[5]. In this study atony accounts 81.25% causes of PPH. Anderson found in western Pennsylvania Hospital, Manneville Pennsylvania, atony accounts for 70% cases of PPH, traumatic cause 20%, retained placenta 10% and coagulopathy 1%10. In this study traumatic PPH 5%, retained placenta 8.75%, placenta acreata 1.25%. Incidence of placenta acreata is 0.003-0.04% since 1950. But now a day's incidence of placenta acreata increases due to increase incidence of caesarean section[11].

Usually primary PPH due to atony of uterus responds mostly with uterine massage and oxytocic drugs. In this study, 51.25 % patient responds with uterine massage with oxytocic drugs. Hospital base descriptive and retrospective study was carried out in the department of Obsetrics and Gynaecology at Kathmandu Medical College Teaching Hospital, Nepal, in 2008 with surgical method for managing atonic PPH showed 5 cases respond with B-Lynch brace suture among 15 cases without further intervention. Among various surgical methods B-Lynch brace suture was found to be simple, effective and minimally invasive[12]. In this study B-Lynch suture controlled PPH in 8.76% of cases. This suture is an alternative to hysterectomy especially during caesarean section and less parous women.

Most common indication of post partum hysterectomy is PPH, for life saving purpose. According to survey by the UK Obstetric Surveillance System (UKOSS) the incidence of peripartum hysterectomy is 4 in 10000 births or 250 women in a year in UK. Having a history of previous caesarean birth the risk increased by 10-20 folds due to placenta praevia and placenta acreata[13]. In my study hysterectomy needed 4 (5%) patients.

O'Leary found bilateral uterine artery ligation is effective in 95% of cases but the technique failed in case of placenta praevia or placenta acreata[14]. In this study bilateral uterine artery ligation controlled PPH in 01 (1.25%) patient and condom inflation were done in 15 (18.75%) patients. Akhter et al studied 152 cases of PPH, showed 71.71% responded with medical measure, 13.16% with B-Lynch suture, 15.13% with condom inflation[15]. In developed country secondary PPH occurs 1-2% of women[16]. In this study secondary PPH accounts 3 (3.75%).

No maternal death and none patient showed signs of Sheehan's syndrome during follow up. Two (2.5%) patients developed DIC. Except hysterectomy, all patients resumed menstruation with average flow and duration.

CONCLUSION

Though PPH is a life threatening condition of women, outcome is good if managed systematically, promptly and senior doctors should attend the patient from beginning.

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JALALABAD MEDICAL JOURNAL

Original Article

Management of Subtrochanteric Fracture Femur by Intramedullary Interlocking Short SIGN Nail

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ABSTRACT

The purpose of this study was to evaluate the result of management of subtrochanteric fracture femur by intramedullary interlocking short SIGN (Surgical Implant Generation Network) nail. A prospective study was done in National Institute of Traumatology and Orthopedic Rehabilitation (NITOR) Hospital Dhaka during the period of July 2002 to June 2004. During this period a total of 18 patients were treated with intramedullary interlocking short SIGN nail. They were operated within 1-2 weeks of fracture. Follow up period was 6-18 month. Mean age was 37.33years. Right sided fracture was more than left side. And highest number (38.89%) belongs to day labourer community. Most common cause was high velocity trauma (78%). Average duration of union 19.6 weeks and union rate was 89%. Out of 18 patients, 06 (33.34%) had excellent, 10 (55.56%) had good, 01 (5.55%) had poor and 01 (5.55%) had bad result. Management of subtrochanteric fracture femur by intramedullary interlocking short SIGN nail is a better option with an excellent outcome.

Key words: *Subtrochanteric fracture femur, Interlocking short SIGN nail, Intramedullary nail.*

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INTRODUCTION

Subtrochanteric fracture femur accounts only 10% to 15% of all hip fracture[1]. It has bimodal age distribution. Fractures in older patients typically due to low velocity trauma whereas younger patient result from high velocity trauma[2]. It occurs in the highest stressed region of the body[3]. This fracture usually difficult both to achieve stabilization and subsequent union due to its muscular attachment. No satisfactory conservative treatment has yet been established except in case of children. So open reduction and internal fixation is the treatment of choice. Many internal fixation devices are available. The selection of implant depends on individual fracture anatomy and biomechanical research. Locked intramedullary nail has an advantage of achieving stability of fracture. Precise anatomical reduction always not necessary. It allows early mobilization which maintain joint motion and reduce hospital stay[4].

Short interlocking intramedullary nail has more load sharing with the medial cortex of femoral neck. Many varieties of SIGN interlocking nail are available. Short SIGN (Surgical Implant Generation Network) intramedullary interlocking nail is a solid nail having 9^0 bend proximally. It has two proximal holes and three distal holes. Among them most proximal one is round and rest are oblong. Interlocking nail maintain the length of a bone and prevent rotation[5]. In this prospective study short SIGN nail were used as it is very suitable fixator and relatively easy with less per operative difficulties and to evaluate the result of management of subtrochanteric fracture femur by intramedullary interlocking short SIGN nail.

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MATERIALS AND METHODS

This study was carried out in National Institute of Traumatology and Orthopedic Rehabilitation (NITOR) Hospital, Dhaka for a period of 2 years from July 2002

to June 2004. Total 20 patients with subtrochanteric fracture femur were included in this study. Two patients were lost during follow up, so excluded from study. Remaining 18 patients were available for follow up. Adult patients (above 18 years) and closed fracture of any type within 5 cm of lesser trochanter were included. All patients were admitted via emergency or out patient department (OPD) and diagnosed clinically and radiologically. After initial management, surface/skeletal traction was applied. All preoperative investigation were done for operative fitness. Surgery was performed on an average of 1-2 weeks after injury. The used nail size varied from 9-12 mm but the length was 190 mm.

Under spinal anaesthesia, patient kept in lateral position with affected side uppermost. Fracture ends were exposed through lateral approach. Reduction was done with manual traction and hold it by bone holding forceps. Entry point of nail was prepared at piriform fossa and femoral awl was introduced in the fossa. Progressive reaming of medullary canal was done by SIGN reamer up to 1mm larger than the selected nail. Assembling the jig and attached it to appropriate size and length of nail. Then the nail was introduced gently and was passed across the fracture into the distal fragment until proximal end of nail flushed with the greater trochanter. Locking screws were inserted at their proper holes. Jig removed and wound closed in layers keeping a drain in situ. Drain was removed on 2nd post-operative day (POD) and patient was allowed to knee mobilization exercise. Stitch off at 12-14th POD and discharged. Follow up after 6 weeks of operation. Functional scoring was done according to Merle d Audbign[6] scoring system.

RESULTS

Total 18 patients of subtrochanterirc fracture femur were treated with open reduction and internal fixation by intramedullary interlocking short SIGN nail over a period of 2 years. The range of follow up was 6 to 18 months (average 12 month). The mean age was 37.33 years (range 20-75 year). Male were 14 (77.78%) and female 04 (22.22%). Right sided 55.56% and left sided 44.44%. Motor vehicle accident was highest 10 (55.56%) while 04 (22.22%) were domestic fall. Average duration of union was 19.6 weeks and union rate was 89%. One patient ended up with non-union. Two patients developed delayed union, one developed shortening (1 cm) and varus angulation at fracture site. Functional out come were excellent in 06 (33.34%), good in 10 (55.56%), poor in 01 (5.55%) and bad in 01 (5.55%)

Follow up:

All patients were advised to come for follow up after 06 weeks, 12 weeks, 20 weeks, 24 weeks, 36 weeks, 48 weeks of operation. During each follow up, patients were examined both clinically and radiologically to ascertain union.

Table-I: *Age incidence (n=18)*

Age group	No of patient	Percentage
20-29	03	16.67%
30-39	10	55.56%
40-49	02	11.11%
50-59	02	11.11%
60-75	01	5.55%

Mean age was 37.33years

Table-II: *Mode of trauma (n=18)*

Trauma	No of patient	Percentage
Motor vehicle accident	10	55.56%
Fall from height	04	22.22%
Domestic fall from bed/chair	04	22.22%

Table-III: *Incidence of complication*

Complication	No of patients	Percentage
Nonunion	01	5.55%
Wound infection	01	5.55%
Varus angulation	01	5.55%
Delayed union	02	11.11%

Table-IV: *Duration of fracture union (n=18)*

Duration	No of patient*	Percentage
14 Weeks	02	11.11%
16 Weeks	01	5.55%
18 Weeks	10	55.56%
22 Weeks	03	16.66%
28 Weeks	01	5.55%

Average 19.6 weeks. *Non-union occurred in 1 patient.

Table-V: *Functional out come according to Merle d Audbigne scoring system (n=18)*

Output	No of patient	Percentage
Excellent	06	33.34%
Good	10	55.56%
Poor	01	5.55%
Bad	01	5.55%

Z-value>3 at p<0.001; Satisfactory (Excellent + Good) =16 (88.89%); Unsatisfactory (Poor + Bad) = 02 (11.11%)

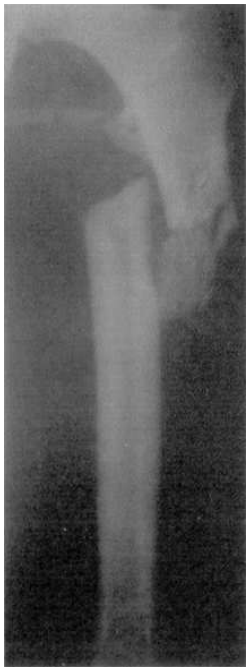

Figure 1: *Preoperative X-ray of subtrochanteric fracture.*

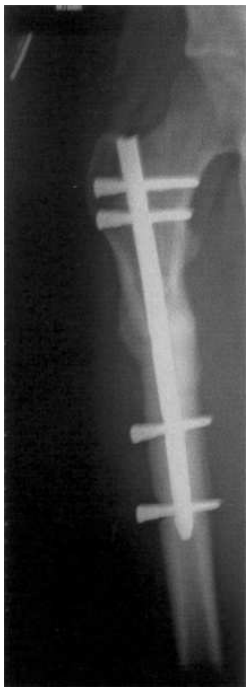

Figure 2: *Postoperative X ray of subtrochanteric fracture after fixation with short SIGN nail*

DISCUSSION

Subtrochanteric fracture femur always presents a problem in management because of opposing muscle forces. Close reduction not only difficult but yield unrewarding result like nonunion, varus, rotational deformity and shortening[7]. The optimum treatment by open reduction and internal fixation greatly simplifies the nursing care, early mobilization and subsequent union.

Intramedullary interlocking short SIGN nail can fulfill almost all these criteria. Proper placement and accurate size nail could markedly influence the functional outcome.

In our study, mean age of patient was 37.33 years (Table-I) which is close to Wiss and Brien[4] study where mean age was 32 years. The nature of trauma is high velocity 78% (Table-II), where as Wiss and Brien[4] study it was 77%. One patient developed wound infection which is 5.55% (Table-III) in contrast subtrochanteric fracture of Kinast et al[8] series it was 20.8%.

All cases in this study, fixation was done by interlocking intramedullary short SIGN nail as it was available in NITOR free of cost. Due to bending moment stress is generated at the angle of JNP (Jewett Nail Plate) and DHS (Dynamic Hip Screw) and there is possibility of implant failure. In SIGN interlocking nailing there is no chance of such type of complication. Moreover it allow early weight bearing enhance healing that could not be possible in JNP and DHS. Short SIGN interlocking nail is stable fixator which allow early weight bearing. Moreover short operative procedure with minimum tissue handling.

In this study, 89% of fracture were found united and able to full weight bearing. Time of fracture healing was 14-28 weeks average 19.6 weeks (Table-IV) in our series. Whereas the average duration of union were 25.5 weeks in Wiss and Brien[4] series, 21.6 weeks, in Kinast et al.[8] series, 18 weeks in Mohammad[9] series, 18 weeks in Momen[10] series, and 18.27 weeks in Datta[11] series. So average fracture healing time of the present series almost corresponds to the other series. Non-union in one (5.55%) patient after 12 month whereas 1 nonunion in Wiss and Brien[4] series, 3 (12%) in Datta[11] series, 2 (8.33%) in Waddell[7] series, and 1 (4%) in Mohammad[9] series. So there is no significant difference regarding nonunion with other series.

Delayed union in subtrochanteric region is common as it is mostly composed of cortical bone. Two delayed union in this series were comminuted fracture but they healed by 12 months. Functional out come was significant. Out of 18 patients 06 (33.34%) excellent and 10 (55.56%) were good. So satisfactory functional result was 89%. In Mohammad[9], Momen[10] and datta[11] series satisfactory result were 72%, 76.66% and 72% respectively. So there is no significant difference regarding functional outcome between present series and other series.

CONCLUSION

The management of subtrochanteric fracture constitutes a therapeutic dilemma due to its basic anatomic structure and biomechanical stresses. The result of present study suggest that fixation of subtrochanteric fracture femur by intramedullary interlocking short SIGN nail is satisfactory. Favourable mechanical character and locking system eliminated absolute requirement of medial cortex reconstruction. It is load sharing device and high rate of success with minimal rate of complication. So interlocking short SIGN nail is one of favoured form of treatment in the management of subtrochanteric fracture femur.

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JALALABAD MEDICAL JOURNAL

Review Article

Neonatal Sepsis: An Update

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ABSTRACT

Neonatal sepsis is still one of the major causes of neonatal morbidity and mortality in the developing countries and it accounts for about 30%-50% of total neonatal deaths in these countries. In the recent past huge improvements have been made in the diagnosis and treatments of different diseases of the neonates but mortality due to neonatal sepsis is still high. The causative organisms of neonatal sepsis also differ in the developing countries from that of the developed countries. The presenting features of neonatal sepsis are often subtle and non-specific, indeed a high index of suspicion is needed for early diagnosis and early initiation of appropriate treatment. This review article indented to summarize the recent updates of neonatal sepsis in order to initiate early treatment of the suspects and thereby help to achieve MDG-4 by 2015.

Key words: *Neonatal sepsis, Septicaemia, Blood culture.*

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INTRODUCTION

Despite huge advances in modern medical diagnosis and treatment bacterial septicaemia is still one of the commonest cause of neonatal morbidity and mortality[1,2,3]. Neonatal septicaemia is responsible for about 30-50% of total neonatal deaths in the developing countries[4,5,6]. It is estimated that up to 20% of the neonates develop septicaemia and approximately 1% die of sepsis related causes[4,7]. In the last few decades considerable progress has been made in the neonatal intensive care and reduction in neonatal deaths due to prenatal asphyxia, hyperbilirubinaemia, low birth weight has been achieved. But unfortunately morbidity and mortality due to neonatal septicaemia is still high[8]. Proper barrier nursing of neonates and proper use of antimicrobial therapy with aggressive supportive care can reduce the mortality and morbidity due to neonatal septicaemia.

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Definition:

Neonatal septicaemia also called neonatal sepsis is so far best defined by Gotoff and Behrman as a "Clinical syndrome characterized by signs of systemic infection and documented by a positive blood culture in the first four weeks of life"[9]. Neonatal septicaemia encompasses various systemic infections of the newborn such as septicaemia, meningitis, pneumonia, arthritis, osteomyelitis and urinary tract infction[4]. Superficial infections like conjunctivitis, oral thrush, and minor skin infection are not usually included under neonatal septicaemia.

Epidemiology:

The incidence of neonatal sepsis has remained fairly constant over the past few decades and it is in the developed countries 1-10 per 1000 live births, where as about three times more in the developing countries like India, Pakistan, Bangladesh[5,10,11]. The mortality in 1928 were 90% but now 3-5% in the developed countries but 30-50% in the developing countries[5,6,12] depending upon the factors like gestational age, quality of supportive care, age at onset of the disease and presence of meningitis.

During last one decade (1994-2007) there has been a substantial decline in childhood mortality in Bangladesh. The average annual rate of reduction of mortality was 9.4% for deaths among children of 1-4 years, 5.8% among 1-11 months and only 2.6% among neonate[13].

The neonatal mortality rate is 32 per 1000 live births in Bangladesh and 36% of the deaths are due to neonatal infection[11,14]. To achieve Millennium Development Goal-4 (MDG-4) by 2015 Bangladesh has to reduce this huge neonatal mortality.

Classification and Etiology:

Neonatal septicaemia is classified into three major categories depending upon the age of the neonate at the onset of signs and symptoms.

Early onset neonatal sepsis (EONS): It presents from birth to 6 days of life. It is fulminant multi-system illness usually during the first 72 hours and almost always during the first week of life. These infants have a history of one or more significant obstetric complications and many are preterm or low birth weight. The source of infection is generally maternal genital tract. Some maternal or perinatal conditions have been associated with an increased risk of EONS. Knowledge about these potential risk factors would help in early diagnosis of sepsis. Based on studies in the developing countries following risk factors seem to be associated with an increased risk of early onset sepsis[4]:

1. Low birth weight: <2500 gm.
2. Preterm: <Completed 37 weeks.
3. Febrile illness in the mother with evidence of bacterial infection within 2 weeks prior to delivery.
4. Foul smelling and/or meconium stained liquor.
5. Rapture of membrane: >24 hours.
6. Single unclean or >3 sterile vaginal examination during labour.
7. Prolonged labour (1+2 stage): > 24 hours.
8. Perinatal asphyxia.

In EONS most common organisms are: *Escherichia coli*, Group B Streptococcus, *Staphylococcus aureus*, coagulase negative Staphylococcus, *Haemophilus influenzae* and *Enterococcus*[1].

Late onset neonatal sepsis (LONS): It occurs from 7th day to 30 days of life. It is more insidious in presentation and mortality is relatively low. The source of infection in LONS is either nosocomial (hospital acquired) or community acquired and neonates usually present with speticaemia, pneumonia or meningitis. Various factors predispose to an increased risk of nosocomial sepsis include, low birth weight, prematurity, admission into intensive care unit, mechanical ventilation, invasive procedures, administration of parenteral fluids etc. Factors that might increase the risk of community acquired LONS include: poor hygiene, poor cord care, bottle feeding and prelacteal feeds. In contrast breast feeding helps in prevention of neonatal infection[4,15,16].

In LONS common organisms are: Coagulase negative staphylococcus, *E. coli,* Group B Streptococcus, *Staphylococcus aureus, Klebsiella, Enterobacter, Pseudomonus aeruginosa* etc[1].

Late-Late onset neonatal sepsis (LLONS): That occurs at more than 30 days of life but within 6 months. Other features are like that of LONS.

Clinical Features:

Non-specific features: The earliest signs of sepsis are often subtle and non-specific, indeed a high index of suspicion is needed for early diagnosis of neonatal sepsis. Neonates with septicaemia may present with any of the following symptoms or signs: reduced or stopped sucking; weak or no cry; limbs becoming limp; vomiting or abdominal distension; baby cold to touch; severe chest indrawing; umbilical infection. Simultaneous presence of any 2 of these 7 signs predicted deaths due to sepsis with sensitivity 100% and specificity 92%[17].

Specific features: related to various systems:

Central nervous system: Buldging anterior fontanelle, vacant stares, high-pitched cry, excessive irritability, stupor/coma, seizure, neck retractions.

Cardiac: Hypotension, poor perfusion, shock.

Gastrointestinal: Feed intolerance, vomiting, diarrhoea, abdominal distension, paralytic ileus, necrotizing enterocolitis (NEC).

Hepatic: Hepatomegaly, direct hyperbilirubinaemia.

Renal: Acute renal failure.

Haematological: Bleeding, petechiae, purpura

Skin: Multiple pustules, abscess, sclerema, mottling, umbilical redness and discharge.

According to the 'National Neonatal Health Strategy and Guidelines for Bangladesh'[18] presence of any one of the following signs and symptoms should be classified clinically as neonatal septicaemia and empirical treatment with antibiotic should be started:

i) Not feeding well (based on history and assessment).
ii) Convulsions (based on history and assessment).
iii) Fast breathing (≥60 breath/min on second count).
iv) Severe chest indrawing.
v) Low body temperature (< 35.5^{0}C or 95.9^{0}F).
vi) Fever (> 37.5^{0}C or 99.5^{0}F).

vii) Movements only when stimulated or no movement at all.

Investigations:

Since treatment should be initiated in a neonate suspected to have sepsis without any delay, only minimal and rapid investigations should be undertaken[4,5]. Following investigations can be done to diagnose neonatal septicaemia.

1. Blood culture: It is the gold standard for diagnosis of septicaemia and should be performed in all cases of suspected sepsis prior to starting antibiotics.
2. Septic screen[4,5,19]: The various components of septic screen includes: (a). Total leukocyte count: <5000 /mm^3; (b). Absolute neutrophil count: <1000 /mm^3; (c). Immature to total neutrophil ratio: > 0.16. (d). Micro ESR: >15 mm in 1st hour; (e). C-Reactive Protein: >1 mg/dl

If two or more parameters are abnormal it should be considered as a positive screening and neonate should be started antibiotics[5].

3. Lumbar puncture: The incidence of meningitis in neonatal sepsis has varied from 0.3-3% in various studies[4,5]. In EONS lumbar puncture is only indicated in the presence of a positive blood culture or if the clinical picture is consistent with septicaemia. In LONS lumbar puncture should be done in all infants prior to starting antibiotic.
4. Radiology: (a). Chest X Ray- in respiratory distress or apnoea. (b). Abdominal X-ray - in suspected NEC. (c). Neurosonogram or CT scan - in suspected meningitis.
5. Urine culture: In LONS urine culture is indicated. UTI may be diagnosed in the presence of one of the following: a. > 10 WBC/mm^3 in a 10 ml centrifuged sample; b. > 10 organism/ml in urine obtained from a catheter; c. Any organism in urine obtained by suprapubic puncture.

Management:

If the history and clinical signs lead the physician to suspect that a neonate is septic, proper and available investigations should be performed and following treatment should be started without delay. Afterwards, if the disease is confirmed by the results of investigations then the therapy should be continued, modified or discontinued accordingly.

A. Supportive care[4,5,19]:

i) Maintenance of temperature by incubator, wrapping or Kangaroo Mother Care (KMC).
ii) Fluid and nutrition: Fluid should be 20% less from total requirements to avoid SIADH. Choice of nutrition should be according to the age of neonate and severity of disease. These may be: I/V for very sick neonate; NG feeding; Breast feeding.
iii) O_2 inhalation if necessary.
iv) Gentle physical stimulations for apnea.
v) Control of convulsions, correction of hypoglycaemia or metabolic acidosis.
vi) Small blood transfusion in DIC, shock or sclerema.
vii) Double volume exchange transfusion if severe jaundice.

B. Antimicrobial therapy:

There can't be a single recommendation for the antibiotic regimen of neonatal sepsis for all settings. The choice of antibiotic depends on the prevailing flora in the particular unit and their antimicrobial sensitivity. Decision to start antibiotic is based upon clinical features and/or a septic screen. However duration of antibiotic therapy is dependent upon the presence of a positive blood culture and meningitis[4,5].

Indications for starting antibiotics in EONS[4,5]:

Presence of any one of the following in EONS: (a). Presence of 3 risk factors for EONS; (b). Presence of foul smelling liquor; (c). Presence of 2 antenatal risk factors and a positive septic screen; (d). Strong clinical suspicion.

Indications for starting antibiotics in LONS[4,5]: (a). Positive septic screen and (b). Strong clinical suspicion.

Empirical therapy[18]:

a. First line treatment: Inj. Gentamicin I/V or I/M, 5mg/kg/day in single dose with Inj. Ampicillin I/V or I/M, 50mg/kg/dose twice daily or Inj. Procain penicillin I/M, 50000 unit/kg as single daily dose or Inj. Benzyl penicillin I/M, 50000 unit/kg/dose 6 hourly.
b. Second line treatment: Inj. Ceftazidime/Cefotaxime I/V or I/M, 50mg/kg/dose twice daily with Inj. Amikacin I/V or I/M 7.5mg/kg/dose twice daily.

Duration of treatment[19]:

Usually 7-10 days or at least 5-7 days after a clinical response has occurred. For associated meningitis: (a). Gram negative bacteria: 21 days; (b). Gram positive bacteria: 14 days. Antibiotics should be changed according to the culture sensitivity results, if necessary.

C. Host defense modulation[4,5,19]:

i) Granulocyte transfusion may significantly improve the survival of septic newborn who is also

neutropenic and who has insufficient bone marrow reserve to replenish the granulocyte deficit.

ii) G-CSF/GM-CSF: 5 micro gm/kg/dose for 3-6 days stimulates production, modulation and activation of neutrophils.

iii) Immunotherapy (IVIG): 250mg/kg/day I/V over 2-4 hours for 4 days stimulates PMNs and potentiates actions of complements.

Prevention:

As the mortality rate in neonatal septicaemia is high so emphasis should be given more towards prevention of sepsis. Following practice can prevent neonatal septicaemia to a considerable percentage:

a. Improve maternal health and nutrition.
b. Proper antenatal care.
c. Clean, safe delivery practices and hand washing.
d. Risk based intrapartum antibiotics for pregnant women.
e. Promotion of early (within 1 hour) and exclusive breast feeding.
f. Minimal handling of a neonate.
g. Hand washing of health care providers.
h. Care of the umbilicus.

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JALALABAD MEDICAL JOURNAL

Review Article

Tuberculin Test- A Review Article

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ABSTRACT

The tuberculin test is the standard method of determining whether a person is infected with Mycobacterium tuberculosis or not. Reliable administration and reading of the tuberculin skin test requires standardization of procedures, training, supervision, and practice. Tuberculin testing mainly used for contact tracing, BCG vaccination programme. The tuberculin test is based on the fact that infection with Mycobacterium tuberculosis produces a delayed-type hypersensitivity skin reaction to certain components of the bacterium. The components of the organism are contained in extracts of culture filtrates and are the core elements of the classic tuberculin PPD (Purified Protein Derivative). Tuberculin antigen is injected intradermally and cell mediated response at 48-72 hours is recorded with the development of induration and inflammation at the site of inoculation due to infiltration with mainly T lymphocytes. A positive test indicates that the patient has been infected in the past and continues to carry viable mycobacteria in some tissue. A strong positive test probably means active infection but many of those with disseminated and rapidly progressive disease may be negative. Tuberculin test positive persons are at risk of developing disease from reactivation of the primary infection. The tuberculin test is widely used as a diagnostic test, although its usefulness is limited by its failure to distinguish active disease from quiescent infection and past BCG vaccination. In addition exposure to various mycobacteria in the environment may induce low levels of tuberculin reactivity.

Keywords: *PPD, Delayed-type hypersensitivity, Mycobacterium tuberculosis*

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INTRODUCTION

The Tuberculin test has been the traditional method for detection of infection with tubercle bacilli. Epidemiologists have used it extensively for assessment of tuberculosis situation in different communities. In clinical practice, it is used to find out the presence or absence of tuerculous infection. This aids in the differential diagnosis of tuberculosis among children and to decide about administration of chemoprophylaxis. The usefulness of the test lies not only on proper technique of administering a standard dose of a standard tuberculin and reading of the reactions by trained personnel but also in its careful interpretation. However, there is no clear understanding among some of the medical practitioners and health workers regarding the performance and interpretation of the test[1].

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The tuberculin antigens used in a tuberculin skin test are called purified protein derivative (PPD). A measured amount of PPD in a shot is put under the top layer of skin on the forearm. This is a good test for finding a tuberculous infection. It is often used when symptoms, screening, or testing, such as a chest X-ray, show that a person may have tuberculosis[2].

A tuberculin skin test cannot tell how long a person have been infected with tuberculosis. It also cannot tell if the infection is latent (inactive) or is active and can be passed to others[2].

The Mantoux test (also known as the Mantoux screening test, Tuberculin Sensitivity Test, Pirquet test, or PPD test for Purified Protein Derivative) is a diagnostic tool for tuberculosis. It is one of the two major tuberculin skin tests used in the world, largely replacing multiple-puncture tests such as the Tine test.

Until 2005, the Heaf test was used in the United Kingdom, but the Mantoux test is now used. The Mantoux test is also used in Australia, Canada, Hungary, Poland, Russia, the Netherlands, New Zealand, Spain, Portugal, South Africa and the United States and is endorsed by the American Thoracic Society and Centers for Disease Control and Prevention (CDC). It was also used in the USSR and is now prevalent in most of the former Soviet states[2].

History:

Tuberculin was discovered by German scientist and physician Robert Koch in 1890 is a glycerine extract of the tubercle bacilli and was developed as a remedy for tuberculosis, but it was ineffective in this role. Clemens von Pirquet, an Austrian physician, discovered that patients who previously received injections of horse serum or smallpox vaccine had quicker, more severe reactions to a second injection, and he coined the word "allergy" to describe this hypersensitivity reaction. Soon thereafter von Pirquet discovered the same type of reaction took place in those infected with tuberculosis, and he thus found the utility of what would become the tuberculin skin test. Individuals with active tuberculosis were usually tuberculin positive, but many of those with disseminated and rapidly progressive disease were negative. This led to the widespread but erroneous belief that tuberculin reactivity is an indicator of immunity to tuberculosis. The test used in the United States at present is referred to as the Mantoux test. An alternative test called the Heaf test was used in the United Kingdom until 2005, although the UK now uses the Mantoux test in line with the rest of the world. Both of these tests use the tuberculin derivative PPD[3].

Methods of administration and reading of tuberculin skin test (TST):[4,5]

The tuberculin skin test is performed by injecting 0.1 ml of tuberculin purified protein derivative (PPD) into the inner surface of the forearm. The tuberculin skin test is an intradermal injection. The skin area chosen should be free of scars, veins and areas of inflammation. The test site need not be sterilized before injection. It can be simply cleaned with soap and water and should be dried before injection. The injection is given with the standard one ml tuberculin syringe graduated to hundredth of a mm, fitted with 26-gauge needle of half an inch length and 20 degree bevel. When placed correctly, the injection should produce a pale elevation of the skin (a wheal) 6 to 10 mm in diameter.

The skin test reaction should be read between 48 and 72 hours after administration. A patient who does not return within 72 hours will need to be rescheduled for another skin test.

The reaction should be measured in millimeters of the induration (palpable, raised, hardened area or swelling). The reader should not measure erythema (redness). The diameter of the indurated area should be measured across the forearm (perpendicular to the long axis). The widest transverse diameter of the induration is measured in millimeters using a 10 cm transparent ruler. If there is no palpable "0"mm diameter induration is recorded.

Adverse effects:[4,5]

In some atopic individuals, an urticarial wheal may appear within minutes of injection. It usually disappears in 1-2 hours. The formation of vesicles, bullae, lymphangitis, ulceration or necrosis at the test site, which may occur in a proportion of children, indicates a high degree of tuberculin sensitivity.

Pathogenesis and indications:[6,7]

The injection of the tuberculin antigen leads to migration and proliferation of the sensitized T-cell lymphocytes to the test site. These T-cells release lymphokines, which further attract other lymphocytes and monocytes. The tuberculin skin test is not used as a general population screen but is used to screen particular populations at high-risk for tuberculosis exposure, such as:

- those with diseases or conditions that weaken their immune systems, such as those with HIV or AIDS, that make them more vulnerable to a tuberculosis infection;
- those who are in confined living conditions such as nursing homes, schools, and correctional facilities;
- healthcare workers and others whose occupations bring them in close contact with those who may have active tuberculosis;
- those who have been in close contact with someone who has an active case of tuberculosis;
- those who come from or have lived for a period of time in a foreign country where tuberculosis may be more common.

The tuberculin skin test is also used sometimes as part of a routine examination prior to starting school or a new job. Since mothers can pass tuberculosis to their unborn children, pregnant women are sometimes screened.

Interpretation of tuberculin test:

The tuberculin test is based on the principle that the

individuals who have been infected with tubercle bacilli respond with a delayed type hypersensitivity reaction at the test site. However, the interpretation of the test is complicated by cross-sensitivity induced by environmental mycobacteria and/or BCG-vaccination as explained earlier. Based on the above and the experience gained during various tuberculin surveys conducted by National Tuberculosis Institute and other organizations in various parts of developing countries, the following general interpretations can be made:[7]

1. Not all reactions to tuberculin are attributable to infection with tubercle bacilli.
2. Larger the size of induration at the test site, higher is the probability of presence of infection with tubercle bacilli. This is supported by the observation that tuberculosis morbidity increased with the size of induration.[7]
3. Almost all reactions with induration of 15 mm or more in size may be considered attributable to infection with tubercle bacilli, irrespective of the presence or absence of BCG-scar.
4. The formation of vesicles, bullae or necrosis at the test site indicates high degree of tuberculin sensitivity and thus presence of infection with tubercle bacilli.
5. The reactions with induration of less than 5 mm in size usually indicate lack of tuberculin sensitivity and thus absence of infection either with tubercle bacilli or with environmental mycobacteria. Simple trauma of the needle has been observed to give rise to induration usually in the range of 1-4 mm. However, some individuals infected with tubercle bacilli but suffering from severe degree of immune-suppression may show induration in this range.[8]
6. Among children without BCG-scar, the majority of reactions with indurations in the range of 5-9 mm. are attributable to cross-sensitivity to environmental Mycobacteria. Some of these children might actually have been vaccinated with BCG but do not show the BCG-scar. Thus, in a proportion of children without BCG-scar, the indurations in this range may be attributable to BCG-vaccination. Among children with BCG scar, the reactions with indurations, in this range may be attributable to BCG vaccination and/or infection with environmental *Mycobacteria*.
7. A reaction with induration between 10 to14 mm could be attributable to infection with tubercle bacilli or due to cross sensitivity to environmental mycobacteria and/or BCG-induced sensitivity. It is mainly the proportion of true infections in this range that varies from community to community and in different epidemiological groups. An induration in this size range is more likely to be attributable to infection with tubercle bacilli among high risk contacts e.g., infants of mothers suffering from tuberculosis, other children who have a history of contact with smear positive case of pulmonary tuberculosis or anti-TB treatment in the family, presence of symptoms or clinical findings suggestive of tuberculosis. The probability of a reaction in this range attributable to infection with tubercle bacilli is relatively higher among children without BCG-scar compared to those with scar. Population surveys have shown that there are two groups of individuals in any community, one consisting of those 'infected with tubercle bacilli' and the rest having no tuberculin sensitivity or sensitivity due to other causes[9, 10,11,12.]

   Repeat the test usually unnecessary unless the test injection or reading was performed unsatisfactorily. The repeat test should be given at a different site within 1 week of the first test[13].

   The majority of the reactions above a particular cut off point obtained from tuberculin surveys in respective areas signify infection with tubercle bacilli and majority of reactions below this cut off are due to other causes as explained above. However, there is always some degree of overlapping between the infected group and the rest even around these cut off points. Thus at any cut off point, some true infections will be missed and some others falsely included. These cut off points as obtained during epidemiological surveys have been found to vary between 10 to 15 mm in different parts of the country. However, it is impracticable to conduct tuberculin surveys all over the country to find suitable cut off points in respective areas. Therefore, the interpretation of reactions in 10-14 mm range requires more careful interpretation. In general, as the cut-off point moves to the left, there is increase in sensitivity of the test at the expense of specificity and vice versa. In clinical practice, it is best to consider other circumstances of the child as explained above to decide on the significance of the reactions with induration in this range[14,15].
8. The tuberculin reaction may be suppressed in the presence of immuno-suppressive states. The size of induration has been observed to be diminished among children who are suffering from tuberculosis disease specially those suffering from disseminated tuberculosis. This is because a few sensitized circulating T cells are available to participate in the reaction since most of these may be collected in the

tubercles lesions. The mean reaction size of tuberculin test has also been found to decrease with increasing grade of under nutrition[16].

Tuberculin induration size may similarly be diminished in presence of cancer, Hodgkin's disease, sarcoidosis and corticosteroid therapy. During HIV infection, though tuberculin sensitivity is not affected at the initial stages, a greater proportion of individuals show suppression of test reactions as the CD4+ T-lymphocytes counts decline[17].

The size of induration depends upon the degree of immune-suppression and the level of immune deficiency should be considered while interpreting tuberculin reactions[18].

9. The hypersensitivity takes about 4-8 weeks to develop after initial infection and thus infection with tubercle bacilli may be missed in the window period. Therefore, there should be a minimum period of 8 weeks between exposure and tuberculin test for detecting infection[18].

   For a decision on preventive chemotherapy, it is desirable to have a higher cut-off point of 15mm, to be more specific. Though chemoprophylaxis is not routinely recommended in our county, it may, be considered in particular situations e.g. HIV positive contact of a case of tuberculosis. Under the Revised National Tuberculosis Control Programme (RNTCP), every 0-6 year old asymptomatic child in contact with smear positive case is put on preventive chemotherapy. This is because the tuberculin test may not be available at every place and there is high risk of such children acquiring tuberculous infection[18].

   It does not need to be emphasized that the tuberculin test detects only the presence or absence of tuberculous infection. The presence of infection is not synonymous with disease and only about 10% of the infected children break down into disease over their lifetime. Half of this risk occurs within one to two years of getting infected[19]. Thus, tuberculin test should never be the sole criteria for diagnosing tuberculosis

   A tuberculin skin test should not be done for people: a) With a known tuberculosis infection. b) Who have had a previous severe reaction to the tuberculin antigens. c) With a skin rash that would make it hard to read the skin test[20].

False positive result:[21]

Due to the test's low specificity, most positive reactions in low-risk individuals are false-positives. A false positive result may be caused by nontuberculous mycobacteria or previous administration of BCG vaccine. Prior vaccination with BCG may result in a false-positive result for many years afterwards Some persons may react to the tuberculin skin test even though they are not infected with Mycobacterium tuberculosis. The causes of others false-positive reactions may include, but are not limited to, the following:

- Incorrect method of tuberculin test administration
- Incorrect interpretation of reaction
- Incorrect bottle of antigen used.

False negative result:

Those that are immunologically compromised, especially those with HIV and low CD4+ T cell counts, frequently show negative results from the PPD test. This is because the immune system needs to be functional to mount a response to the protein derivative injected under the skin. Some persons may not react to the TST even though they are infected with *Mycobacterium tuberculosis*. The reasons for other false-negative reactions may include the following:

- Cutaneous anergy (anergy is the inability to react to skin tests because of a weakened immune system)
- Recent tuberculosis infection (within 8-10 weeks of exposure)
- Very old tuberculosis infection (many years)
- Very young age (less than 6 months old)
- Recent live-virus vaccination (e.g., measles)
- Overwhelming disease
- Some viral illnesses (e.g., measles and chicken pox)
- Incorrect method of tuberculin test administration
- Incorrect interpretation of reaction

The tuberculin skin test is used to help diagnose latent infection or active disease. If doctor suspects that person have active tuberculosis, other tests, such as chest X-rays and AFB cultures in sputum, are used to confirm the diagnosis[22].

The US recommendation is that tuberculin skin testing is not contraindicated for BCG-vaccinated persons and that prior BCG vaccination should not influence the interpretation of the test. The UK recommendation is that interferon-γ testing should be used to help interpret positive Mantoux tests, and that serial tuberculin skin testing must not be done in people who have had prior BCG vaccination. In general, the US recommendation results in a much larger number of people being falsely diagnosed with latent tuberculosis, while the UK approach probably misses patients with latent

tuberculosis who should be treated[23].

Detection of the newly infected cases:

The tuberculin test does not distinguish between past and new infection. The incidence of disease among recently infected is much higher compared to the incidence among previously infected especially in the pediatric age group. Therefore, detection of newly infected may be important in some situations e.g. among children who showed a reaction of less than 10 min at an earlier test but have been exposed to a smear positive case thereafter. For detection of such new infection occurring in the intervening period between the two tests, there should be a significant increase in reaction size. Studies conducted in National Tuberculosis Institute have shown an increase of 14 mm and above among those infected during the intervening period when two tests were conducted 1½ to 3 years apart[24,25].

CONCLUSION

Tuberculin skin tests are ordered when the doctor wants to screen his patient for a exposure to tuberculosis. The tuberculin skin test may be done yearly in those that are part of a high-risk group - either because they have a disease that weakens their immune system or because they work or live around others in high-risk groups. Tuberculin skin tests are frequently done prior to a person joining an at-risk population, such as going to college or becoming a teacher or health care worker. Since tuberculosis is airborne and passed through respiratory secretions, tuberculin skin tests may be ordered when someone has been in close contact with a patient who has an active case of tuberculosis or when they have been in a foreign country where tuberculosis is more common. This would be done a few weeks after suspected exposure as it usually takes about 6 weeks after contact and initial infection before a positive result would emerge. In clinical practice, it would be more useful to consider an increase of 10 mm between the two tests as indicative of new infection. There should be a minimum period of 8 weeks between exposure and the second test. This applies to BCG-vaccinated as well as unvaccinated children. Tuberculin skin tests should not be done when a person has had a previous positive reaction as they are more likely to have a severe local reaction. The usefulness of the tuberculin test lies in performing a standard test and its careful interpretation. The significance of the test result cannot always be decided from the reaction size and depends upon other circumstances including the purpose of the test.

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JALALABAD MEDICAL JOURNAL

Case Report

Hutchinson-Gilford Progeria Syndrome- A Case Report

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ABSTRACT

Progeria is an extremely rare genetic disease of childhood, characterized by dramatic premature ageing. We present the case of a 14 years old boy who exhibited many signs and symptoms of progeria from his early childhood. The patient was diagnosed in the department of Paediatrics, Jalalabad Ragib-Rabeya Medical College Hospital, Sylhet and treated with supportive treatment and physiotherapy for 10 days and now the patient is in regular follow up. We conclude that progeria is by no means a rare but interesting case, this lead us to report this case in the journal.

Key words: *Progeria, Hutchinson-Gilford Progeria Syndrome, LMNA gene*

[Jalalabad Med J 2011; 8(2): 82-4]

INTRODUCTION

Progeria is a condition, which derives its name from 'geras' the Greek word for old age, estimated to affect one in eight million newborn worldwide and its most striking feature resemble accelerated ageing. Dr Jonathan Hutchison and Dr Hasting Gilford described the disease in 1886 and 1904[1]. This extremely rare childhood disorder is caused by a point mutation in position 1824 of the LMNA gene. This mutation causes replacement of cytosine with thymine, creating unstable form of the lamin A protein. Lamin A is a part of the building blocks of the nuclear envelope, the absence of which causes accelerated aging[2]. Newborn children with progeria usually appear normal. However, within a year, their growth rate slows and they become much shorter and weight much less than others of their age. Within 10 years of life, they develop classical signs of progeria like characteristic facies, beaked nose and alopecia, loss of subcutaneous fat, scleroderma and loose aged-looking skin, head appears too large for face, prominent scalp veins, prominent eyes, micrognathia, high pitched voice, delayed and abnormal tooth formation with overcrowding of teeth, stiff joints, hip dislocation, but motor and mental development is always normal[3,4]. Patients do not develop physically mediated "wear and tear" conditions commonly associated with ageing, like cataracts and osteoarthritis[5]. Diagnosis is suspected according to signs and symptoms and it can be confirmed through a genetic test[5]. In case of treatment, no treatment has been proven effective. Most treatment focuses on reducing complication. Although there may not be any successful treatment for progeria itself but there are treatments for the problems it causes, such as arthritis, respiratory and cardiovascular problems[6].

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CASE REPOERT

A 14 years old boy of consanguineous parents got admitted in Paediatric ward of Jalalabad Ragib-Rabeya Medical College Hospital with the complaints of not growing well since his 2nd year of life. He also complained stiffness and deformity in spine and ankle joints which made his daily activities difficult. He was exclusively breast fed for 6 months then had balanced family diet. His development was age appropriate but he was not growing well as a child of his same age. He was otherwise a healthy boy up to 2 years of age. At his 2nd year of life, his mother noticed his face was

disproportionately small in comparison to his head. His eyes became abnormally prominent and nose became small and jaw was also underdeveloped. He also got overcrowding of teeth at 5 years of age. By the 10th year of life, he was gradually losing his scalp hair and eye brow and his skin was unusually taut, wrinkled over buttocks, legs and abdomen. He was progressively developing deformity in ankle joints. On examination, he was severely wasted and stunted (Weight for age Z score= -7.25; height for age Z score= -6.71; weight= 9 kg; height=108 cm). He was mildly anaemic, normotensive, bluish colorization around the mouth was present, mild clubbing present. Visible apex beat was seen at left 5th intercostal space, 2 cm lateral to left mid clavicular line. All his joints were stiff, deformed but there was no pain or swelling, muscle tone and deep reflexes were normal but muscle power was diminished. On eye examination no cataract or arcus senillis was seen. On laboratory investigation, WBC total count and differential count were within normal limit, ESR was 20 mm in 1st hour, haemoglobin level was 9 gm/dl, blood glucose 2 hours after breakfast was 78 mg/dl. X-Ray of chest revealed mild cardiomegaly and lumbosacral spine revealed degenerative changes. Fasting serum cholesterol was 370 mg/dl. Serum electrolyte analysis revealed hyponatraemia. ECG changes were within normal limit. After considering all the clinical features and laboratory reports, we diagnosed him as a case of progeria. We treated him with balanced diet, physiotherapy, vitamin supplements, oral calcium, zinc and potassium for 10 days. He physically improved following supportive treatment and could perform his daily works alone without the help of others. He was discharged with advice for regular follow up.

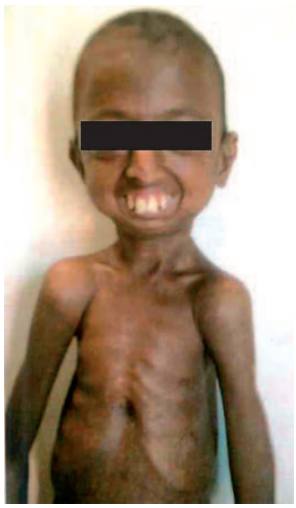

Figure 1: *showing alopecia, characteristic facies, beaked nose, prominent eyes, under developed jaw.*

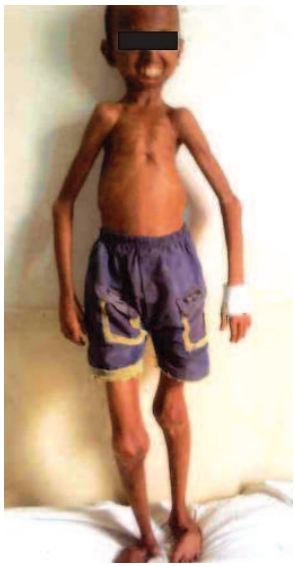

Figure 2: *showing deformity of spine, ankle joints and loss of subcutaneous fat.*

DISCUSSION

Progeria, one of the rarest fatal genetic condition of childhood, have been only 100 reported cases since first diagnosis[7]. In 2003, NHGRI (National Human Genome Research Institute) researchers, together with the Progeria Research Foundation, New York State Institute for Basic Research in Developmental Disabilities and the University of Michigan, discovered that the nuclear lamina, a protein containing layer attached to the inner nuclear membrane, is composed of a family of polypeptides with the major components being the lamin A, B_1, B_2 and C. Lamin A and C are formed by alternative splicing of the LMNA gene transcript[3,8]. Progeria is caused by a tiny, point mutation in LMNA gene through farnesylation and methylation. Researchers found that the mutation responsible for Hutchinson-Gilford Progeria Syndrome (HGPS) causes the LMNA gene to produce an abnormal form of the lamin A protein, that de-stabilize the cell's nuclear membrane in a way that may be particularly harmful to tissues routinely subjected to intense physical force, such as the cardiovascular and musculoskeletal systems and the most common HGPS mutation is a G608G (GGC>GGT) mutation in exon 11 that acts as a dominant negative mutation[3]. Experts believe that progeria is not a hereditary disease and it is due to a rare gene change which happens purely by chance. A non-twin sibling runs the same risk of having progeria as any other child from another family. In about 1 in every 100 cases of HGPS the syndrome is passed down to next generation within the same family[8]. There are, however, other Progeria syndrome

that run in families, they include Wiedemann-Rautenstrauch syndrome and Werner syndrome. In Wiedemann-Rautenstrauch syndrome, also known as Neonatal Progeria Syndrome, onset of aging begins in the womb and signs and symptoms are apparent at birth. Werner syndrome begins in adolescence or early adulthood. These inherited progeroid syndromes also cause rapid ageing and shortened life span[3]. In case of prognosis, patients usually have severe atherosclerosis and death occurs as a result of complication of cardiac or cardiovascular diseases, generally between age 5 and 20 years with a median life span of 13 years, cataracts and tumors have infrequently been noted but many changes associated with normal ageing in adults, such as presbycusis presbyopia, arcus senillis, osteoarthritis, senile personality changes or Alzheimer disease, are not found[3]. There is no cure of progeria but we can treat some of the symptoms by hydrotherapy, maintenance of proper nutrition, calcium supplementation, vitamin-E, aspirin and fluoride as supportive treatment of progeria[9]. Now a day, farnesyltransferase inhibitors (FTIs) is used for treating cancer. FTIs might reverse the nuclear structure abnormalities that are believed to cause progeria but still under trial. Growth hormone treatment has also been attempted[9,10]. Genetic analysis was not done in this case because of limited opportunity of such test in our country.

CONCLUSION

Progeria is a very rare disease having no specific or curative treatment but early diagnosis and intervention may lengthen and improve the quality of life. Further research on progeria is required as it may reveal the secret of ageing and ultimately open the door for treatment of many other age-related disorders.

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JALALABAD MEDICAL JOURNAL

Case Report

Sebaceous Adenoma- A Case Report

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ABSTRACT

Sebaceous adenoma is an uncommon disease. Sometimes it is associated with internal malignancy with serious consequences and on the other end a solitary sebaceous adenoma is a curable disease. This case is of a 75 years old diabetic male presented with a recurrent solitary sebaceous adenoma scalp, who underwent excision 3 years back. Wide excision was performed and no recurrence was seen on follow up after about 2 years. The aim of reporting this case was to show that this condition though occurs rarely in our community and without wide excision it may recur and also to emphasize that it may be a manifestation of an internal malignancy.

Key word: *Sebaceous adenoma, Muir-Torre syndrome, Internal malignancy.*

[Jalalabad Med J 2011; 8(2): 85-7]

INTRODUCTION

Sebaceous glands are oil producing glands present in dermis and usually attached to hair follicles. Sebaceous glands present over the entire body (except palm of hand and soles of the foot), most abundant on scalp and central face[1,2,3]. Sebaceous adenoma is defined as a benign epithelial neoplasm composed of sebaceous gland like structures or tumors with well recognized sebaceous differentiation by microscopic examination. Skin adnexal tumors with sebaceous differentiation are uncommon, difficult to classify and may be controversial. The main controversy concerns the microscopic features which may vary from well to poorly differentiated and sometimes undifferentiated varieties[4,5,6]. Large series of cases for comparison and follow up have not been published also there were few reported cases of solitary sebaceous adenoma. Patient with numerous sebaceous adenomas and or other neoplasm with sebaceous differentiation associated with internal malignancy, the clinical condition known as Muir-Torre Syndrome[7,8,9]. The exact incidence of sebaceous adenoma is not known[3,6]. No reported predisposition for any particular race has been identified. Sebaceous adenoma affects men and women equally. Common in middle aged and elderly individual after the age of 50 year. Mean age of onset is 60 year. Frequently appear on the face and scalp.

Sebaceous adenomas do not have a potential for aggressive growth or metastasis that cause death[6,9,10]. Local recurrences are occasionally encountered following incomplete removal of the tumor. The reported case developed local recurrence probably for inadequate clearance.

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CASE REPORT

A 75 year diabetic male patient admitted in the department of Surgery in Jalalabad Ragib-Rabeya Medical College Hospital with the complaints of painless swelling over the scalp for six months with occasional bleeding from the surface of the swelling and it was slowly increasing in size. He had history of swelling at the same site 3 years back for which he underwent excision under local anaesthesia. On examination, his pulse was 82 beats/min, blood pressure was 150/90 mm of Hg, temperature was 98^0F. A firm reddish swelling of 1x1cm was present on right

occipitoparietal region, surface of which was irregular with a central ulceration (Figure-1). Induration around the swelling was present. It was not fixed with underlying structures. Scar mark of previous surgery was present. Neck glands were not palpable. X-ray skull revealed no bony involvement and FNAC of the swelling revealed benign adnexal tumour of skin. Wide local excision of the swelling was done under local anaesthesia. Incision was made 1cm away from the indurated area, keeping the swelling in center. After proper haemostasis wound was closed with atraumatic prolene no.1/0. Excised tissue was sent for histopathological examination. All stitches were removed on 5th post-operative day and the wound was healthy at that time. Histopathological examination revealed sebaceous adenoma (Figure-2). Patient was discharged after removal of stitches with necessary advice.

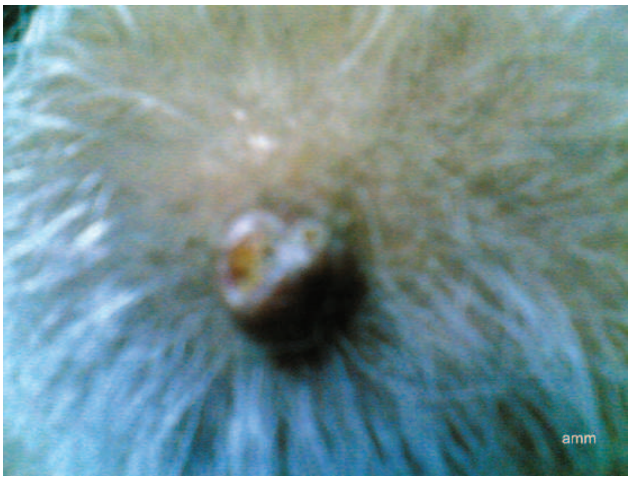

Figure-1: *Sebaceous adenoma over scalp.*

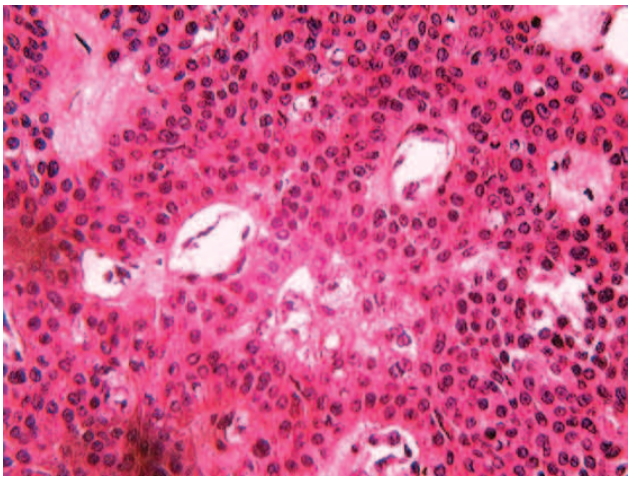

Figure-2: *Photomicrograph of sebaceous adenoma (H&E stain, X400).*

DISCUSSION

Cutaneous sebaceous adenoma presents as a slow growing painless firm masses. They predominantly appear during the sixth or seventh decades of life[11] as solitary lesion on the face and scalp[12], which was matched with the age and clinical features of present case who presented with a recurrent slow growing tumor on scalp, for which he was treated by excision under local anaesthesia 3 years back. Rulon and Helwig[4] in a large series study of cutaneous sebaceous neoplasms, reported their occurrence mainly on the nose, cheek or scalp with a slow rate of tumor growth in 80% of cases. Histologically, sebaceous adenomas are benign neoplasms basically consisting of sebaceous cells arranged in nests with minimal atypia or pleomorphism and no tendency to invade local structures[10]. They are typically circumscribed, and may be solid or cystic[13]. Size ranges from less than 1cm to more than 5 cm in diameter and clinical appearance often mimic with basal cell carcinoma. Sebaceous differentiation may result from a metaplastic process as a result of ductal obstruction from a tumor or inflammatory process. It may be congenital in origin or it may naturally develop later in life[14]. Laboratory investigations required to exclude possible occult internal malignancies e.g. GIT, hematological or laryngeal carcinoma in patient with cutaneous sign of Muir-Torre syndrome is of diagnostic value. Tests include complete blood count, peripheral blood film studies, bone marrow examination. Immunocytochemistry (Cytokine 19) is useful for separating sebaceous adenoma from basal cell carcinoma. Epithelial membrane antigen (EMA) stain positive in sebaceous adenoma. S-100 protein, CEA-stain positive in sweat gland neoplasm[3,14,15,16]. MCH-1, MCH-2 immunostains to paraffin embedded sections show loss of expression suggest Muir-Torre syndrome[15,16,17]. Abdominal CT scan and MRI to detect occult internal malignancies in patient with Muir-Torre syndrome is essential. Upper GI endoscopy (to check for an occult gastric carcinoma), sigmoidoscopy (to screen for colonic carcinoma) and laryngoscopy (to rule out occult laryngeal carcinoma) are also required. A biopsy of skin tumor required for histopathological examination and accurate diagnosis of sebaceous adenoma. In our case, we have done FNAC from tumor and skull X-ray preoperatively to exclude bony involvement. Surgical treatment aimed at completely removing the tumor and preventing regrowth[3,5,18]. Solitary tumor treated with complete surgical excision has 100% cure rate. Incomplete removal has occasionally resulted in local

recurrence[1,2,5,9,18] that has occurred probably in our case.

CONCLUSION

Solitary sebaceous adenoma is a benign condition. It is completely curable with surgical excision but the excision should be wide to avoid local recurrence. Patient with multiple sebaceous adenomas may have Muir-Torre syndrome therefore the possibility of internal malignancy should be considered.

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Miscellaneous

News

Postgraduate Training Recognized by BCPS

A high powered inspection team consisted of eight members from Bangladesh College of Physicians and Surgeons (BCPS) Dhaka, headed by Professor Syed Mokarrom Ali, visited the Jalalabad Ragib-Rabeya Medical College and Hospital on 27-12-2010. On the recommendations of the inspection team, the Council of Bangladesh College of Physicians and Surgeons (BCPS) has renewed recognition to the departments of Paediatrics, Ophthalmology, Otolaryngology, Psychiatry, Pathology (Histopathology) and Orthopaedic Surgery for imparting training to the resident doctors provisionally for a period of five years with effect from 21-09-2009. The Council has granted recognition to the department of Paediatric Surgery for imparting training to the resident doctors provisionally for a period of five years with effect from 13-02-2010. The training will be accepted for appearing in the FCPS Part-II examination in these specialties. The postgraduate training imparted from the departments of Surgery, Medicine and Obstetrics & Gynaecology were recognized by Bangladesh College of Physicians and Surgeons (BCPS) earlier in 2003.

Seminars

The following seminars held in Jalalabad Ragib-Rabeya Medical College (JRRMC) during the January 2011 to June 2011:

1. A seminar on "Polycystic Ovary Syndrome (PCOS)" held on 31st March 2011 organized by Department of Obstetrics and Gynaecology, JRRMC.
2. A seminar on "Infective Endocarditis" held on 28th April 2011 organized by Department of Cardiology, JRRMC.
3. A seminar on "Enteric Fever" held on 19th May 2011 organized by Department of Paediatrics, JRRMC.
4. A seminar on "Skin Manifestation of Diabetes Mellitus" held on 9th June 2011 organized by Department of

Corrigendum

In the Jalalabad Medical Journal Vol-08, No-01 January 2011, the word "Stage-III" was mistakenly written as "Stage" in page 41.

Instructions for Author(s)

Manuscripts on clinical, review, experimental and historical topics pertinent to medical sciences are accepted for the publication in this journal. The papers are accepted for the publication with an understanding that they are solely submitted for this journal. The statements, comments or opinions expressed in the papers are exclusively of author(s), not of editor(s) or publisher. The manuscripts are to be prepared as described in following instructions. 3 (three) hard copies are to be submitted. Letters about potentially acceptable manuscripts will be sent after review process is complete. No manuscripts will be returned if not accepted for publication. In addition an electronic/digital version of the manuscript composed in MS word 98/2000 should be submitted in a diskette.

Preparation of manuscripts

Manuscripts should be typewritten, double-spaced throughout (including references and tables) on one side of good quality A4 sized paper, with margins of at least 25 mm. Each component of the manuscript should begin on a new page in the sequence of title or cover page, abstract with key words, text, acknowledgement, references, tables and legends for illustrations.

Title page will contain

a). Concise and informative title of the article
b). Author(s) name, highest academic degree(s).
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Abstract and key words

An informative abstract not more than 250 words should briefly describe the objectives, materials and methods, results and conclusion. Number of key words should not more than ten and none that are in the title.

Text should contain Introduction, Materials and Methods, Results and Discussion in sequence.

Introduction

It should briefly disclose the purpose of study. It will help the readers with the problem finding. It should be clear in nature and purpose.

Materials and Methods

Clearly it should include materials, experimental procedures, methods etc. Mention the nomenclature, source of material, equipment with manufacturer's details in parentheses. Describe new methods in sufficient detail indicating their limitation. Established methods should be cited with authentic references. Ethical standards should be followed in reporting experiments done in human subjects. Precisely identify the dosage and route of administration, when drugs or chemicals are used. Measurements and data should be stated in SI unit, or if SI unit does not exist, use an internationally accepted unit. Abbreviations and acronyms should be used for widely used terms and names, which occurs consistently and frequently in the manuscript.

Results

It should be presented in logical sequence in text, tables or illustrations. Duplications of data in the tables or illustrations should be avoided. Emphasize or summarize only important observations.

Discussion

Emphasize the new and important aspects of the study and conclusion derived from them. Detail data written in introduction and other portions of text should not be repeated. The implication of results and their limitations including suggestion for future research should be included in the discussion.

References

Number the references consecutively in order mentioned in the text. Full list of reference should include all authors. Avoid using abstracts as references. References to paper accepted but not yet published should be designated as 'in press' or 'forthcoming'. Authors should obtain written permission to cite such papers as well as verification that they have been accepted for publication. Information from manuscripts submitted but not accepted should be cited as 'unpublished observations' with written permission from the source. Use the styles of example below, which are based on the formats used by US National Library of Medicine (NLM) in the Index Medicus. The title of journals should be abbreviated according to the style used in Index Medicus.

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associated with an increased risk for pancreatobiliary disease. Ann Intern Med 1996; 124 (11): 980-3.
As an option, if a journal carries continuous pagination throughout a volume (as many journals do) the month and issue number may be omitted.
b) More than six authors
Parkin DM, Clayton D, Black RJ, Masuyer E, Friedl HP, Ivanov E, et al. Childhood leukaemia in Europe after chernobyl: 5 year follow-up. Br J Cancer 1996; 73:1006-12.
c) No author given
Cancer in South Africa (editorial). S Afr Med J 1948; 84:15
d) Organization as author
The cardiac society of Australia and New Zealand. Clinical exercise stress testing. Safely and performance guidelines. Med J Aust 1990; 146: 267-9.

Books and monographs
a) Personal author(s)
Laurence DR, Bennett PN, Brown MJ. Clinical Pharmacology. 8th ed. New York: Churchill Livingstone; 1997.
b) Editor(s),compiler(s) as author
Norman IJ, Redfern SJ, editors. Mental health care for elderly people. 5th ed. New York: Churchill Livingstone; 1999.
c) Organization as author and publisher
World Health Organization. Ethical criteria for medical drug promotion. Geneva: World Health Organization; 1988.
d) Chapter in a book
Phillips SJ, Whisnant JP. Hypertension and stroke. In: Laragh JH, Brenner BM, editors. Hypertension: pathophysiology, diagnosis and management. 2nd ed. New York: Raven Press; 1995. p 465-9.
e) Dissertation or thesis
Kaplan SJ. Post hospital home health care: the elderly access and utilization (dissertation). St. Louis (MO): Washington Uni; 1995.

Other published material
a) Newspaper article
Lee G. Hospitalization tied to ozone pollution: study estimates 50,000 admissions annually. The Washington post 1996; June 21; sect. A: 3 (col. 5).
b) Dictionary and similar references
Student's medical dictionary. 26th edi. Baltimore: Williams and Wilkins; 1995. Apraxia; p.119-20.

Unpublished material
a) In press
Leshner AI. Molecular mechanisms of cocaine addiction. N Eng J Med (in press) 1997.

Electronic material
a) Journal articles in electronic format
Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis [serial online] 1995 Jan-Mar [cited 1996 June 5]; 1(1): [24 screens]. Available from: URL: http://www.cdc.gov/ncidod/EID/eid.htm
b) Monograph in electronic format
CDI, clinical dermatology illustrated [monograph on CD-ROM]. Reeves JRT, Maibach H. CMEA Multimedia group, producers. 2nd ed. Version 2.0. San Diego: CAEA; 1995.
c) Computer files
Haemodynamics III: The ups and downs of haemodynamics [computer program]. Version 2.2. Orlando (FL): Computerized Educational Systems; 1993.

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Acknowledgement should appear at the end of the manuscripts before references.

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Manuscripts are usually examined by the editorial staff and are sent to outside reviewers. Author's suggestion regarding the names of possible reviewers is encouraged, but editorial board reserves the right of final selection.

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