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## Gastrocnemius muscle flap coverage for exposed upper tibia and knee – a prospective study

Md Abdul Gani Ahsan<sup>1</sup>, Kazi Md Salim<sup>2</sup>, Ishtiaque-Ul-Fattah<sup>3</sup>, Hamudur Rahman<sup>4</sup>

### Abstract

Management of exposed tibia and knee as a result of any injury is challenging condition. The poor vascularity of this area causes high incidence of infection rate in open fracture; especially in delayed management waiting for granulation tissue. However the versatility of the gastrocnemius muscle flap for soft tissue reconstruction around the knee, upper third of the leg & lower third of the thigh is well known. The objective of the study is to evaluate the results of the gastrocnemius muscle flap with its complications. Ten patients in between 2008-2014 with soft tissue defect over proximal third tibia and knee were included in this study. All the patients were provided soft tissue coverage with medial head of gastrocnemius muscle flap with split thickness skin graft on it. All the flaps survived with primary healing of the wound except one patient who developed wound infection, managed by wound drainage, irrigation and antibiotic. Gastrocnemius muscle flap is an excellent local option to cover exposed upper one third of tibia and knee. It does not sacrifice the whole function of the muscle. Due to its well known vascular pattern, longer arc of rotation, this flap can cover the defects of different size and shape around the knee.

[OMTAJ 2014; 13(1)]

### Introduction

Soft-tissue reconstruction of the lower limb presents with a difficult problem to orthopaedic and plastic surgeon yet a common problem.<sup>1,2</sup> There are standard

operative procedures for the management of open fractures of lower extremity to reduce the risk of non-union and osteomyelitis. Early vascularized soft tissue coverage is mandatory to avoid these complications.<sup>3,4</sup> There are a number of flap procedures to cover the exposed bones or joints, obliterate the dead space; which helps to eradicate infection by increased vascularity of this area.

In 1971 Ger<sup>5</sup> first introduce muscle flap in this context and gained wide popularity<sup>6</sup>. Muscle flaps are also suitable for coverage of open joint and exposed orthopedic implants.<sup>7</sup> Gastrocnemius muscle is frequently employed as a local flap for coverage of soft tissue defects in the upper two thirds of the leg<sup>8</sup> and around the knee.<sup>9</sup> The site and size of the gastrocnemius muscle belly and its transfer does not adversely impair function of the limb. For this reason it an ideal flap to cover wound in the region of proximal tibia and knee.<sup>10</sup>

The bony union is affected by many factors like age, nutritional status of the patient, quality of fixation and presence of infection etc.<sup>11</sup> Present study was not designed to cover all these variables. The role of muscle flap in improving the bony union and control of osteomyelitis is already proven.<sup>12</sup> The purpose of this study was to assess the reliability of this flap in terms of its survival only.

### Materials and Methods

These six years (2008 –2013) descriptive study was conducted at department of orthopaedic surgery, Sylhet MAG Osmani Medical College Hospital; Sylhet Women's Medical College Hospital and other private hospital in Sylhet; including 10 patients (9 males and 1 female with the age ranging 11 to 47 years). These patients had small to medium sized defects involving proximal third of the tibia and knee. Defect size ranged from  $4 \times 4$  cm<sup>2</sup> to  $6 \times 5$  cm<sup>2</sup> (Table-1). In all cases of trauma emergency operative procedure includes wound debridement and bony stabilization done by external fixator those were associated with

1. Associate Professor, Department of Orthopaedics, Sylhet Women's Medical College
2. Professor, Department of Orthopaedics, Sylhet Women's Medical College
3. Associate Professor, Department of Orthopaedics, Sylhet MAG Osmani Medical College
4. Medical Officer, 250 Beded TB Hospital, Shyamoli, Dhaka

Gustillo-Anderson type IIIB fracture tibia (Fig 1A). In osteomyelitis cases the wound thoroughly debrided was done to ensure complete removal of necrotic tissues and infected bone (Fig 1A, 1B). Soft tissue coverage was provided with medial head of Gastrocnemius muscle flap after 1-4 weeks of trauma (Fig 1C- 1E).

**Surgical anatomy-** The type-I Gastrocnemius muscle flaps with their only one neurovascular pedicle (unique and independent) for each muscle belly. The neurovascular pedicle enters the upper pole of the lateral belly from its medial side and the medial belly from its lateral side at the level of the fibular head, situated close to origin the heads of gastrocnemius muscle. One pedicle (sural artery) at the level of the knee joint arises from the popliteal artery and another pedicle above the level of the knee joint. Each course a few centimeters with its venae comitantes before entering the anterior aspect of the proximal muscle belly with the innervating branches of the tibial nerve.<sup>13,14</sup> There is an anastomosing network of arteries and veins (without nerves) between the two bellies of the gastrocnemius muscle. The entrance of the neurovascular pedicle divides each muscle belly into superficial and deep portions. The main neurovascular pedicle gives independent branches (artery, vein and nerve) to both the superficial and the deep compartments of each muscle belly. The direction of the main pedicle was always from the upper pole towards the lower pole. So, each head of the gastrocnemius muscle was easily split in the coronal plane (like opening a book with the binding situated in the midline of the leg).<sup>15</sup>

**Surgical procedure -** All the patients were operated in semi-lateral position with external rotation and abduction at hip joint at affected side. Tourniquet was applied in all the patients. Skin incision was made 2-3 cm posterior and parallel to the medial border of the tibia from the popliteal fossa to below mid-calf level or existing open wound was extended both proximally and distally. Incision was deepened to deep fascia and medial head of gastrocnemius was identified and separated from deep soleus muscle. Distal end of muscle was sharply divided from the Achilles tendon include some portion of tendinous material with the muscle belly as this improved suture holding(Fig 1C,1D). It was then divided and separated from lateral gastrocnemius at the mid line raphe and transfer anteriorly to cover the defect and flap fixed by 4/0 vicryl suture (Fig 1D, 2B). The muscle was covered by partial thickness skin graft (Fig 1E, 2C). Care should

be taken to avoid injury to sural nerve and short saphenous vein. The arc of rotation will increase by detaching gastrocnemius origin (Fig 1C). Head of gastrocnemius origin was detached if flap was failed to cover the wound area or create over traction to the flap. Donor site was closed over a vacum drain. Above knee posterior plaster splint was applied for two week in every patient to avoid skin graft loss because of underlying muscle movements. Post operatively patients were kept in the bed with elevation of the operated limb for 3 weeks to reduce pain and swelling. First dressing change was done on 6th postoperative day. Patients were discharged on 10<sup>th</sup> post operative day. First follow up visit was one week after the discharge and then 2-3 weekly. Patients were evaluated for flap outcome in terms of flap survival.

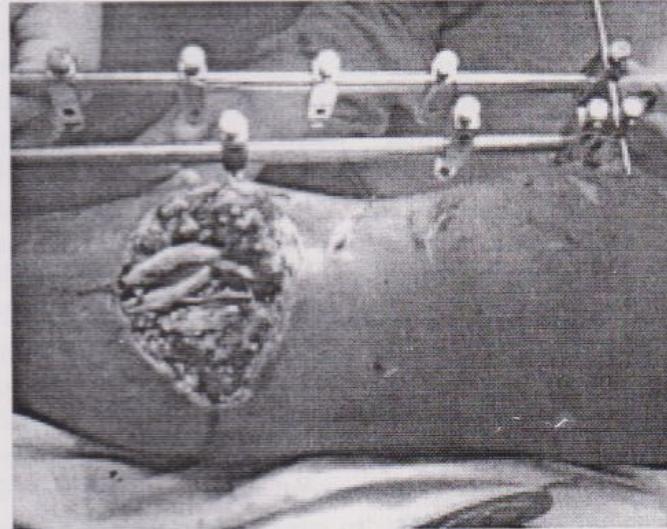


Fig 1A. A 15 days old wound with exposed infected bone just below the knee with purulent discharge.

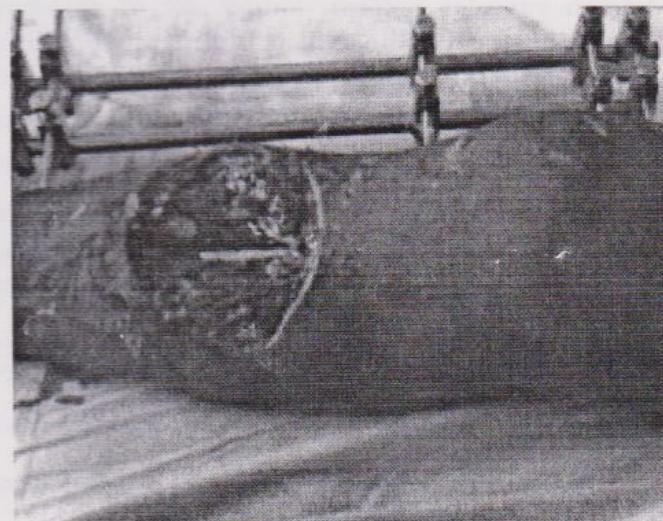


Fig 1B. After debridement of the wound

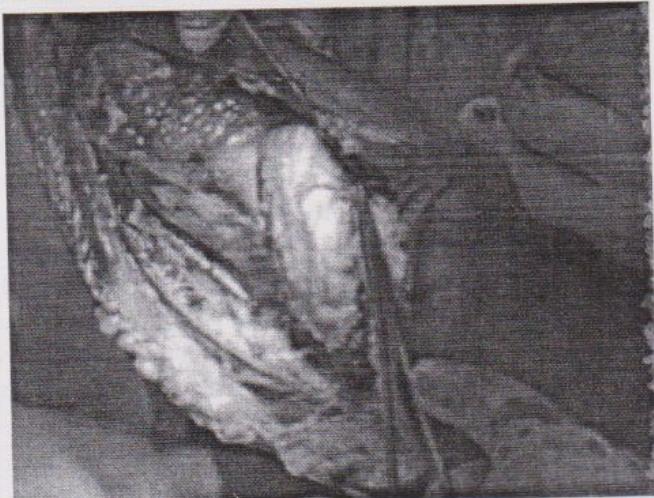


Fig 1C. Transposition of gastrocnemius muscle through a subcutaneous tunnel.

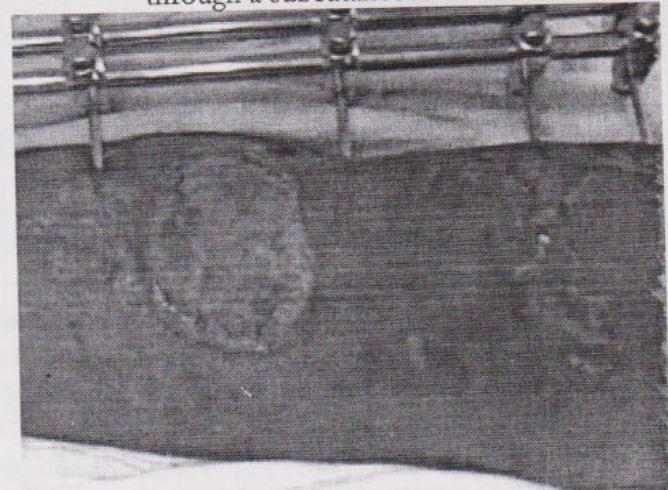


Fig 1D. Wound coverage with flap.

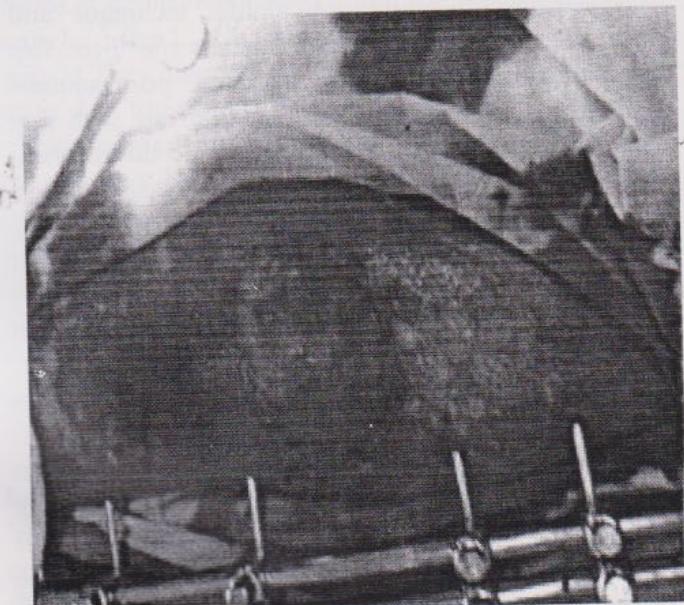


Fig 1E. Flap covers with partial thickness skin graft.



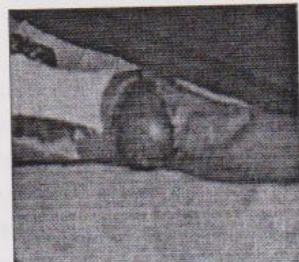
Fig 1F. Satisfactory healing of the flap covers area; 1 year later.



2A



2B



2C



2D

Fig 2A. Two weeks old wound with exposed knee;  
Fig 2B. Medial head of gastrocnemius muscle detached from insertion into Achilles tendon and muscle anchored into defect; Fig 2C. Skin-grafted muscle flap after 2 weeks; Fig 2D. Satisfactory healing of the flap covers area after 1 month.

## Result

In this study ten patients (9 male and 1 female) with open tibial fractures (GA Type-IIIB) in the proximal third of leg (seven cases) or traumatic soft tissue loss over knee (three cases). All soft tissue defects were reconstructed by medial head of gastrocnemius muscle flap and split thickness skin graft on it. Follow up

period ranged from 3 months to 2 years. Nine patients (90%) achieved primary healing and only one (10%) patient developed wound infection. This patient with wound infection was treated with wound drainage and intravenous antibiotics which recovered within 1 week.

As regard donor site morbidity, no functional disturbance but mild depression present at donor site in 2 cases. Ultimately all the patients achieved wound healing with good cosmetic outcome without functional disturbance for this muscle transfer.

Table: Clinical characteristics of the patients

Patient No.	Age/ Sex (Years)	Etiology	Associated fracture	Flap size (cm <sup>2</sup> )	F/U (Months)	Complications	Risk factor
1	30/M	RTA	Tibia-Fibula	4x4	12	No	Smoking
2	46/M	RTA	Tibia-Fibula, Femur	5x5	24	No	No
3	11/F	RTA	-	6x5	6	DDS	No
4	27/M	RTA	Tibia-Fibula	4x3	15	No	Smoking
5	47/M	RTA	Tibia, Fibula	3.5x3	6	Infection	Smoking
6	23/M	RTA	-	4x4	7	No	Smoking
7	35/M	RTA	Tibia, Fibula	4x4	10	No	Smoking
8	26/M	RTA	-	5x3	6	DDS	No
9	40/M	RTA	Tibia-Fibula	6x4	6	No	Smoking
10	28/M	RTA	Tibia-Fibula	5.5x4	3	No	Smoking

RTA- Road Traffic Accident, F/U- Follow-up, DDS-Depression donor site

## Discussion

Finding an appropriate soft-tissue resurfacing material without functional impairment and donor site morbidity to reconstruct lower extremity defects can be a difficult task. There are lack of intervening muscle between the skeletal elements and the skin, limited mobility of the overlying skin.<sup>17</sup> Due to better understanding of anatomy and vascular patterns of the areas; there are available choices to cover a wider range of soft tissue defects around knee. Local options for soft tissue coverage of these areas are includes muscle, myocutaneous, fasciocutaneous and adipofascial flaps. Muscle flaps have been one of the most important flaps for the management of a compound fracture;<sup>5</sup> especially in open tibial fractures due to poor vascularity of this region.<sup>18</sup> Displaced open tibial fractures (Type-IIIB) deprive its endosteal and periosteal blood supply. This is the most important cause of delayed union and non union of fractures as well as chronic osteomyelites of tibia.<sup>19</sup> Muscle flaps with their excellent intrinsic blood supply and mouldable nature that can fill these irregular

cavities of the bone (Fig 1B-1D), are the best solution for such defects.<sup>20</sup>

Free tissue transfer has become a gold standard option for the large complex defects of the lower limb.<sup>31</sup> This is a one-stage procedure but it requires a long operative time, experienced, skillful technique and patent vascular status of the recipient site. Free flap transfer to the lower limb in chronic posttraumatic conditions have a higher complication rate with flap loss in up to 10% of cases, mainly due to the recipient vessel<sup>22</sup> and refractory spasm of these vessels, due to post-traumatic vessel disease (PTVD).<sup>23</sup>

A local random-pattern skin flap has an indistinct perfusion pattern and is limited in size. These flaps were limited by a length-to-width ratio ranging from 5:1 for the face to 1:1 for the lower extremities.<sup>24</sup>

Fascial and fasciocutaneous flaps can provide an excellent alternative for coverage of defects, even when bone has to be covered.<sup>25</sup> The medial adipofascial flap based on the vascular network supplied by the saphenous artery and the posterior tibial artery perforators can be harvested on the anteromedial aspect of the leg and can be mobilized to cover defects located between the patella and the

heel.<sup>26</sup> But it causes a relative hypoesthesia at the donor site.

The cross-leg flap has the disadvantage of long-term immobilization and several operative stages.<sup>27</sup> Turning-over of tissues as adipofascial or as a cutaneous (skin) flap is well established.<sup>28,29</sup> However, these are random pattern flaps.<sup>30</sup>

Myocutaneous flaps have proven to be very reliable in treating these difficult wounds.<sup>16</sup> Simple muscle flaps covered with split skin grafts are equally effective but are less bulky. They therefore produce less of a bulging contour deformity of the lower leg and also have less donor site morbidity.<sup>21</sup>

The surgical options in the repair of lower extremity soft tissue defects with ipsilateral gastrocnemius muscle transfer and cross leg medial head gastrocnemius muscle flap transfer from the opposite leg. We have not used the cross leg gastrocnemius muscle flap because of difficulties in postoperative immobilization and its attendant morbidity.<sup>31</sup> If ipsilateral gastrocnemius muscle is not suitable for transfer, then the free flap coverage of the defect is the next best option. Bashir<sup>32</sup> described the gastrocnemius tenocutaneous island flap that is based on the medial head of gastrocnemius muscle but the skin island is sited over the tendinous portion at the lower end of the muscle. The gastrocnemius muscle flap has been studied in detail and seven maneuvers that will allow the surgeon to gain more versatility with the medial and lateral gastrocnemius muscle have been emphasized.<sup>33</sup>

Neale et al<sup>34</sup> have reviewed about the complications of muscle flap transposition for traumatic leg defects. They mention that the causes of complications were due to technical error, inadequate debridement, use of diseased and traumatized muscle and unrealistic objectives. We feel that careful preoperative evaluation, surgical planning, adequate debridement of bone and soft tissues with the transfer of healthy and non-traumatized muscle are essential to avoid these complications. When these basic surgical tenets are not violated, gastrocnemius muscle provides the best form of coverage for the defects located over upper 1/3 of tibia and knee.

Muscle flap with axial pattern of blood supply have had significant impact on reconstructive surgery and have revolutionized the management of large composite tissue defects. The gastrocnemius muscle flap provides enough volume and length to repair large defects of the upper third of the leg and knee joint with minimum donor and recipient site morbidity.

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# BRONCHIAL BRUSH CYTOLOGY: AN USEFUL METHOD IN THE DIAGNOSIS OF BRONCHOSCOPICALLY VISIBLE BRONCHIAL CARCINOMA

Shamim Akhter Mimi<sup>1</sup>, Sheikh AHM Mesbahul Islam<sup>2</sup>, Md. Delwar Hossain<sup>3</sup>, Md. Tabibul Islam<sup>4</sup>

## Abstract

Lung cancer is the leading cause of cancer deaths in developed countries and is rising at alarming rates in developing countries. Recently bronchial brush cytology seems to be the most rewarding in the diagnosis of bronchial carcinoma because of its high sensitivity. To see the usefulness of bronchial brush cytology in the diagnosis of bronchoscopically visible bronchial carcinoma. This cross-sectional observational study was conducted in the Department of Pathology, Sylhet MAG Osmani Medical College & Hospital, Sylhet, Bangladesh during the period of November 2012 to November 2014. A total 174 patients with bronchoscopically visible suspected bronchial carcinoma were included. Bronchial brushing was done by competent pulmonologist. Bronchial brushings were smeared directly on to glass slides and were immediately immersed in a koplin's jar filled with 95% alcohol. Staining and cytological examination was done in the pathology laboratory. The age range was 20-95 years with the mean age of  $59.19 \pm 12.33$  years. Most of the patients (74.7%) were in the age above 50 years. There were 160 (92.0%) male and 14 (8.0%) female with a ratio of 11.4:1. Brush cytology showed 126 (72.4%) malignant, 3 (1.7%) suspicious and 45 (25.9%) non-representative smears. Malignant lesions were squamous cell carcinoma (53.5%), small cell carcinoma (12.6%), adenocarcinoma (4.6%) and

undifferentiated carcinoma (1.7%). The results of the brush cytology showed a sensitivity of 72.4%. Bronchial brush cytology is a useful diagnostic procedure to reach an accurate diagnosis in bronchoscopically visible bronchial carcinoma.

[OMTAJ 2014; 13(1)]

## Introduction

Lung cancer is the most common cause of death from cancer worldwide, causing 1.4 million deaths per year.<sup>1</sup> It is the leading cause of cancer deaths in developed countries and is also rising at alarming rates in developing countries. Deaths due to lung cancer are more than those due to colorectal, breast and prostate cancers put together.<sup>2</sup> The occurrence of lung cancer in Bangladesh is 16.7% of all cancers and is the most common cancer (25%) among the male cancer patients with 6.1:1 male female ratio.<sup>3</sup>

Bronchial carcinoma has one of the lowest survival outcomes.<sup>3</sup> Before starting treatment a clear distinction between small cell and non-small cell carcinoma must be made, for that histopathology remains the mainstay of confirmation of diagnosis.<sup>4</sup> For early diagnosis different diagnostic modalities are available which include; radiology, bronchoscopy, bronchial biopsy, exfoliative cytology, brushing, washing and fine needle aspiration cytology.<sup>5</sup>

Flexible bronchoscopy plays a central role in the diagnosis of lung malignancy especially in endobronchial (endoscopically visible) tumours.<sup>6,7</sup> Bronchoscopy allows the sampling of cytological specimens as well as biopsies for histological diagnosis. Bronchoscopic cytological methods include bronchial washings, bronchial brushings, bronchoalveolar lavage, and transbronchial and endobronchial needle aspirations;<sup>8</sup> different methods have potentially important differences in the diagnostic sensitivity;<sup>9,10</sup> and each of these modalities has an average yield of 50 to 85%.<sup>11</sup> When an endobronchial tumour is visible at bronchoscopy, forceps biopsies are the most common specimen collected and usually have

1. Senior consultant, Pathology, Sylhet MAG Osmani Medical College Hospital.
2. Assistant Professor, Respiratory Medicine, Sylhet MAG Osmani Medical college.
3. Assistant Professor, Respiratory Medicine, Sylhet MAG Osmani Medical college.
4. Junior Consultant, Leprosy Hospital, Sylhet.

the highest diagnostic yield.<sup>8</sup> However bronchial brushing is easily performed and well tolerated procedure than endobronchial biopsy without hazard of bleeding and pneumothorax associated with of endobronchial biopsies.<sup>11</sup> In detecting lung malignancy sensitivity of bronchial brushing varies between 48-85.1% in different studies.<sup>8,9,12-16</sup>

This study was designed to evaluate the diagnostic yield of bronchial brush cytology in bronchoscopically visible bronchial cancer.

### Materials and Methods

This cross-sectional observational study was conducted in the Department of Pathology, Sylhet MAG Osmani Medical College Hospital, Sylhet, Bangladesh during the period of November 2012 to November 2013. A total 174 patients with bronchoscopically visible suspected bronchial carcinoma were included. Inclusion criteria were radiological lesion suggestive of centrally placed malignancy lung cancer and visible by fibreoptic bronchoscopy. Bronchial carcinoma approaching carina, haemorrhagic diathesis, anti-coagulant therapy, refusal of fibreoptic bronchoscopy or to enroll in this study was excluded.

Informed written consent was obtained from the patients or attendants after full explanation of the details of the disease process.

A rapid diagnostic work up was made by clinical history, through physical examinations and necessary investigations such as X-ray chest P/A and Lateral view, Blood for CBC and ESR, Sputum for AFB, Bleeding time and Clotting time, ECG.

Fibreoptic bronchoscopy was performed transnasally with the Olympus BF 1T-30 flexible bronchoscope (Olympus, Tokyo, Japan) in the Department of Medicine, Sylhet M.A.G. Osmani Medical College Hospital, Sylhet by competent pulmonologist.

Flexible bronchoscope was introduced and the tracheobronchial tree was systematically examined. An obvious endobronchial lesion was ulcerating, fungating, infiltrating, nodular, necrotic or polypoid, with colours ranging from light to dark red or form dirty yellow to cream or white. To rule out the underlying pathology, any mucus or purulent material covering the mucosa or occluding a bronchial segment was removed.

When an endobronchial lesion was visualized, the brush was inserted through fibreoptic bronchoscope channel and was moved to and fro over the endobronchial lesion, entrapping the bits of tissues and cells between the bristles. After the removal from the bronchoscope,

the brush was advanced to make smear directly on the clean glass slides, which were immediately immersed in a Koplin's jar filled with 95% alcohol. The jar was sent to the laboratory for expert opinion from pathologist.

Staining and cytological examination was done in the pathology laboratory using Papanicolaou stain.

Cytological specimens that showed atypical or suspicious cells were regarded as non-diagnostic. Cytological analysis was considered positive only when large numbers of definitely malignant cells were present.

The patient's vital signs were observed for symptoms of chest pain, dyspnoea, haemoptysis and cardiovascular instability. The patient was examined in observation room for an hour to see any immediate complication and if necessary immediate X-ray chest was done and managed accordingly. In remainder patients X-ray chest was done in the next morning for detection of pneumothorax.

### Results

The age of the patients ranged from 20-95 years with the mean  $59.19 \pm 12.33$  years and 74.7% of patients were aged above 50 years (Figure-1).

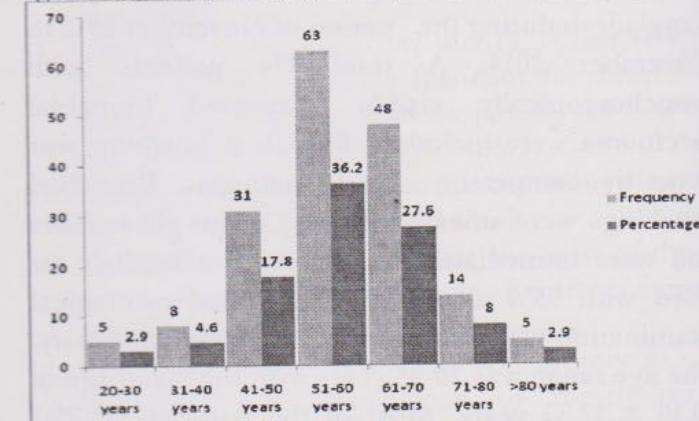


Figure 1: Distribution of age of the patients (n=174)

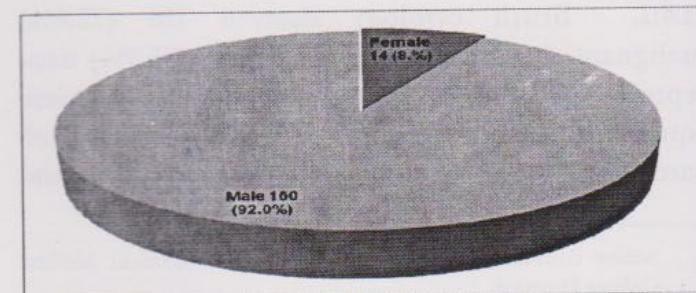


Figure 2: Sex distribution of the patients (n=174)

There were 160 (92.0%) male and 14 (8.0%) female with a ratio of 11.4:1 (Figure-2). Brush cytology showed 126 (72.4%) malignant, 3 (1.7%) suspicious and 45 (25.9%) non-representative smears (Figure-3).

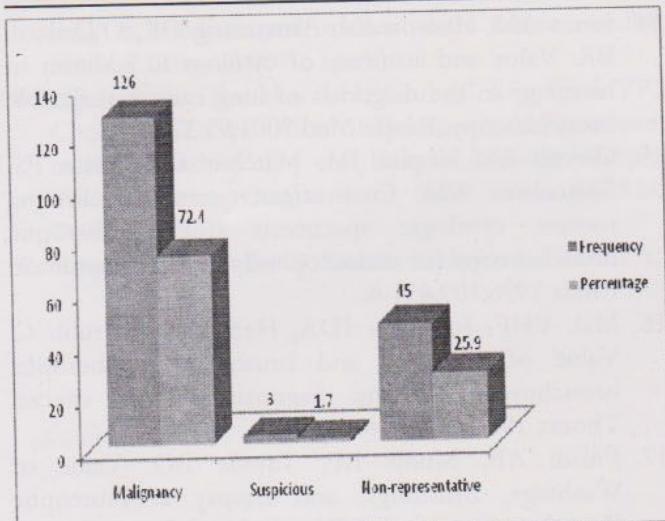


Figure 3: Distribution of patients with cytological diagnosis (n=174)

Table I: Spectrum of bronchial brush cytodiagnosis (n=174)

Cytological diagnosis	Frequency	Percentage
Adenocarcinoma	8	4.6
Squamous cell carcinoma	93	53.5
Well differentiated	80	46.0
Poorly differentiated	13	7.5
Small cell carcinoma	22	12.6
Undifferentiated	3	
Suspicious	3	1.7
Non representative	45	25.9

Malignant lesions were squamous cell carcinoma (53.5%), small cell carcinoma (12.6%), adenocarcinoma (4.6%) and undifferentiated carcinoma (1.7%) (Table-I). The results of the brush cytology showed a sensitivity of 72.4%.

Respiratory distress (8.6%) and minor bleeding (5.2%) occurred as a minor complication of bronchoscopy procedure. No major complication occurred in any patients

## Discussion

Flexible bronchoscopy and different sampling of cytological specimens plays a central role in the diagnosis of lung malignancy especially in endobronchial (endoscopically visible) tumours.<sup>6,7</sup> In the present series of 174 patients of endobronchial lung lesion suggestive of malignancy were subjected to bronchial brushing cytology, conclusive cytodiagnosis were made in 126 cases resulting in diagnostic accuracy of 72.4%. The diagnostic yield of brushings in patients with

endoscopically visible (central) tumors varies from 52 to 85.1% in some other studies.<sup>8,9,12-18</sup>

Out of 174 patients male were predominate with a ratio of male to female of 11.4:1. Similar male preponderance of bronchial carcinoma were reported in several other studies.<sup>3,17,19-21</sup> Male-female ratio in this study is markedly increased which can be explained by some reasons like small sample size, less reporting of female patients in a tertiary care hospital and less common smoking habit in female in our country.

The age of the patients ranged from 20-95 years with the mean  $59.19 \pm 12.33$  years. This result was correlated with the study of Hassan et al.<sup>19</sup> that age of the patients ranged from 35 to 85 years with the mean age of 60.14 years. This result was also in agreement with other studies.<sup>22-24</sup> While Shah et al.<sup>25</sup> reported the mean age of their patients with bronchial carcinoma was 45.6 years which was lower than the present study and Santos-Martinez et al.<sup>20</sup> reported that the mean age was  $67.1 \pm 11.1$  years, which was higher than the present study. This study also showed that 74.7% of patients were aged above 50 years. This result was almost similar to the study of Hassan et al.<sup>19</sup> that 77.8% of patients were in the age group of above 50 years.

Malignant lesions were squamous cell carcinoma (53.5%), small cell carcinoma (12.6%), adenocarcinoma (4.6%) and undifferentiated carcinoma (1.7%). In this regards Agarwal et al.<sup>26</sup> reported that bronchial brush cytology showed squamous cell carcinoma in 50.0%, adenocarcinoma in 10.0% and large cell carcinoma in 40.0% of cases. Rawat J et al.<sup>27</sup> found squamous cell carcinoma in 51.4%, adenocarcinoma in 11.21%, large cell carcinoma in 3.73%, unclassified in 15.88% and small cell carcinoma in 17.75% cases.

Complications of bronchial brushing were respiratory distress and minor bleeding, both of which were easily manageable. Thereby the hazard of bleeding and pneumothorax associated with of endobronchial biopsies may be avoided.<sup>11</sup>

The most important is that the brush is stroked back and forth over a considerable (1 to 2 cm) surface of the tumour, increasing the likelihood of obtaining some cells with malignant characteristics on the bristles of the brush. On the other hand the biopsy forceps has a cup diameter only slightly greater than 1 mm; the specimens obtained with the biopsy forceps are small and come from only one area of what appears to be tumour.<sup>28</sup>

In conclusion bronchial brush cytology is a useful diagnostic procedure to reach an accurate diagnosis in endoscopically visible suspected lung cancer and further study in this regards is warranted.

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## A comparative study of Coronary Angiographic (CAG) findings between diabetic and nondiabetic Patients

Mohammad Nurul Afsar<sup>1</sup>, Kamal Ahmed<sup>2</sup>, Sufia Rahman<sup>3</sup>

### Abstract

Patients with diabetes mellitus have a higher prevalence of atherosclerotic heart disease and a higher incidence of myocardial infarction than the general population. Diabetic patients also have several hematologic, metabolic abnormalities not present in their nondiabetic counterparts that may predispose them to formation of morphologically complex plaques.

Percutaneous coronary angiography (CAG) was performed in 120 consecutive patients with suggestive of ischaemic chest pain. The population consisted of 45 (37.50%) diabetic and 75 (62.50%) nondiabetic patients. We observed positive angiographic lesion among both groups comparing site & number of vessel(s) involvement also average percentage of stenosis. The presence of coronary risk factors was not significantly different between the two populations. Total positive angiographic lesion was 79 (65.83%) in both groups. Among the Diabetes mellitus patients positive CAG finding 37 (82.22%). The recognized lesions were single vessel disease (SVD) 10 (27.02), double vessel disease (DVD) 15 (40.54%), triple vessel disease (TVD) 12 (32.43%), diffuse lesions 4 (10.80%) and average vessel stenosis 83.63%. On the other hand, total positive angiographic lesion was 42 (56%) in nondiabetic group; among them single vessel disease (SVD) 14 (33.33%), double vessel disease (DVD) 17 (40.47%), triple vessel disease (TVD) 11 (26.19%), no diffuse lesions was found and average vessel stenosis was 78.03%.

The results of the angiographic finding suggest that diabetic patients have a higher incidence of coronary heart disease (CHD), DVD, TVD, diffuse lesion & marked stenosis of coronary vessel than

nondiabetic patient. This increased frequency of complex lesion morphology is more difficult to treat by definitive intervention like percutaneous transluminal coronary angioplasty (PCI) & coronary artery bypass graft (CABG).

[OMTAJ 2014; 13(1)]

### Introduction

Diabetes mellitus (DM) is a well-established risk factor for development of coronary artery disease (CAD).<sup>1,2</sup> Coronary atherosclerosis is not only more prevalent in diabetic patients but also more severe. The reported prevalence of coronary artery disease in diabetic patients ranges from 9.5% to 55%.<sup>3,4</sup> whereas prevalence of 1.6% to 4.1% have been observed in the general population.<sup>5,6</sup> Incidence of heart diseases & ischaemic heart mortality was shown to be 4 times higher in people with Type-2 DM.<sup>7</sup> Type -1 DM was seen to be associated with at least a 10 fold increase as compared with people without diabetes.<sup>8</sup> In people with DM 40%, 15%, 10% death occur due to ischaemic heart disease (IHD), other heart diseases & cerebrovascular disease (CVD) respectively.<sup>9</sup> Several in vivo and postmortem studies have shown that diabetic patients have more diffuse and severe coronary artery disease than the general population.<sup>1,10,11</sup> In addition, the relative risk of myocardial infarction (MI) is greater in diabetic patients than in the normal population.<sup>12</sup> The cause of this difference in the diabetic population is not well understood. But it is suggested that diabetic patients have several hematologic, and metabolic abnormalities not present in their nondiabetic counterparts<sup>13, 14, 15</sup> that may predispose them to formation of more complex plaque. To date, very few studies, have attempted to explain these differences between diabetic and nondiabetic patients in our country. Thus this prospective cross sectional study was designed to find out the morphological pattern of coronary lesion in patient with diabetes mellitus and to compare with nondiabetic patients in a peripheral teaching Institute of Bangladesh.

1. Assistant Professor of Cardiology  
North East medical College, Sylhet.
2. Assistant Professor of Medicine  
North East medical College, Sylhet
3. Professor (Emeritus), Department of Cardiology  
North East medical College, Sylhet

## Materials and Methods

120 cases of males and females, who presented in the department of Cardiology, North east Medical college Hospital (NEMCH), Sylhet, from August 2008 to September 2009, were included in this study. Involved patients were selected on the basis of inclusion and exclusion criteria as mentioned below. The study was approved by the review committee of the Medical College.

### 1. Study population

#### 1.a. Inclusion criteria

All patients clinically diagnosed or documented to have CAD, who required coronary angiography (CAG) was taken as study population. Informed consent was taken from all patients.

#### 1. b. The grouping of study population

The study population was divided into two groups as follows

##### • The study group I

Patients presented with features of ischaemic heart disease (IHD) & having DM (DM group)

##### • The study group II

Patients presented with features of ischaemic heart disease (IHD) but without DM (non DM group)

#### 1.c. Criteria's for diagnosis of DM

Patient who fulfilled the diagnostic criteria for DM recommended by The World health organization (WHO) in 2000 AD<sup>16</sup> as below, with or without other cardiovascular risk factors (e.g. smoking, hyperlipidaemia etc)

- Patient complaints of symptoms suggestive of DM (polyuria, polydipsia, wt loss) with one of the following...

1. Fasting plasma glucose  $\geq 7.0$  mmol/L ( $\geq 126$  mg/dl)

2. Random plasma glucose (or 2 hrs after an ideal OGTT)  $\geq 11.1$  mmol/L ( $\geq 200$  mg/dl)

(In asymptomatic patient two samples are required to confirm the diagnosis)

#### 1.d. Criteria's for diagnosis of non DM cases

Patient do not meet the above WHO criteria's for confirm the diagnosis of DM, with or without other cardiovascular risk factor (e.g. smoking, hyperlipidaemia etc).

#### 1.e. criteria's for coronary artery disease (CAD) & Coronary Angiography (CAG)

1. Chronic stable angina pectoris with positive E.T.T (with or without previous MI)

2. Unstable angina pectoris
3. Atypical chest pain with positive E.T.T
4. After acute MI (with or without persistent angina)
5. Asymptomatic patient with noninvasive evidence of myocardial ischaemia (ECG, ECHO)

#### 1.f. Exclusion criteria's

1. Patient with hypertrophic or dilated cardiomyopathy
2. Patient with valvular heart disease
3. Patient with congenital heart disease

## 2. Coronary Angiographic (CAG) Procedure

CAG & where needed left ventriculography were done in all patients by standard Jud kin's technique through femoral approach by modified Seldinger technique using non ionic dye. Multi angled standard views were recorded for analysis. A comprehensive analysis of Coronary Angiogram (CAG) was done, severity & extent of arterial disease were measured by eye estimation. The pre requisites for CAG were followed according to the hospital protocol, then morphological characteristics of lesion was analyzed

- a) Positive CAG -taken when coronary artery stenosis  $\geq 50\%$
- b) Negative CAG - taken when coronary artery stenosis  $< 50\%$
- c) According to branches of coronary artery involvement -

1. single vessel disease (SVD) -one coronary artery involve
2. double vessel disease (DVD)- two coronary artery involve
3. triple vessel disease (TVD) -three coronary artery involve
4. Diffuse lesion -diffusely involved one or more coronary artery

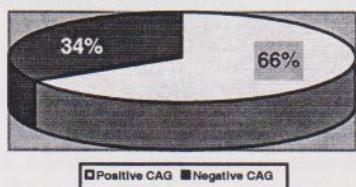
## 3. Statistical analysis

After processing of all available information, statistical analysis of their significance was done. The patients were grouped into those with & without DM having CAG. All parametric values were expressed as mean & nonparametric values were expressed in percentage (%). The significance of difference between two groups were determined by using unpaired student's 't' test, Pearson's chi-square test & 'z' test where applicable. 'P' value of less than 0.05 was considered to be significant.

## Results

Total Number of patients studied -120

### Diagnostic Yield (Sensitivity) of CAG



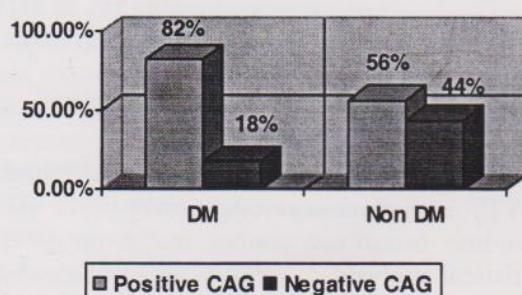
**Fig- 1:** Pie chart showing diagnostic yield of CAG among pts with IHD

### Distribution of patient



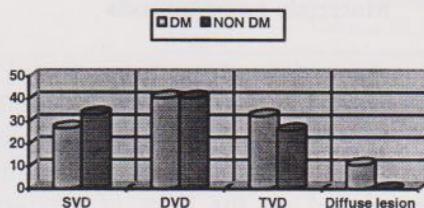
**Fig- 2:** Pie chart showing distribution of patient undergone CAG

### Positive angiographic lesion among DM & Non DM group



**Fig- 3:** Bar diagram showing positive angiographic lesion

### Pattern of Vessels involvement in DM and Non DM patients. (N = 120 = 100%)

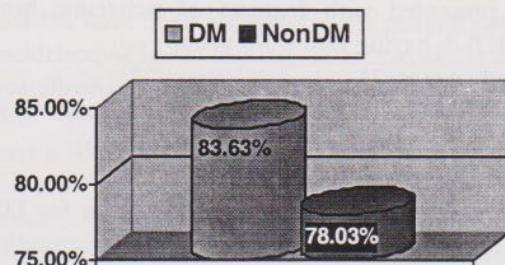


**Fig-4:** Bar diagram showing pattern of vessels involvement

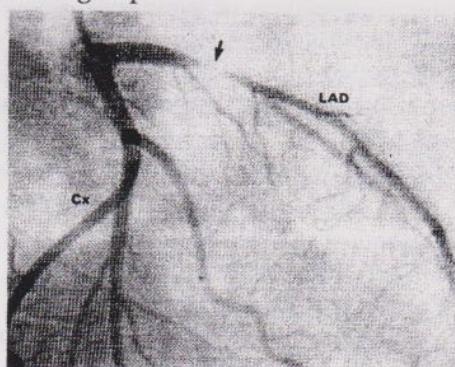
### Percentage of Vessel stenosis in DM and Non DM group

	DM	Non DM
LMCA	81%	70%
LAD	81.48%	79.41%
LCX	87.4%	79.55%
RCA	84.65%	83.15%
Average	83.63%	78.03%

**Table-1:** shows percentage of vessel stenosis in DM and Non DM group



**- 5:** Bar diagram shows average vessel stenosis in DM and Non DM group



**Figure - 6:** SVD (left anterior descending artery – LAD)

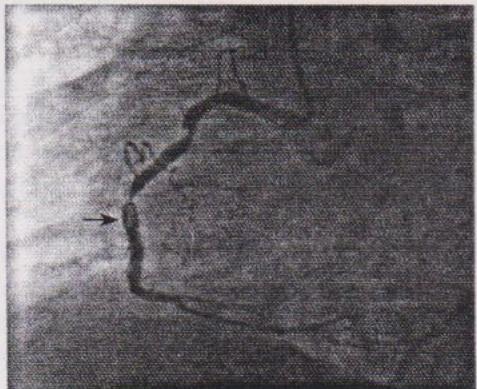


Figure 7: SVD (right coronary artery – RCA)

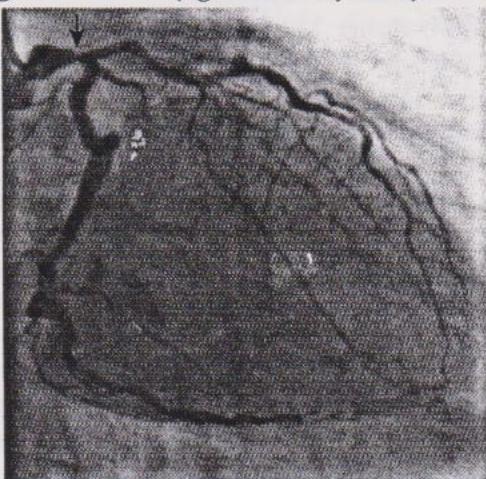


Figure 8: SVD (left main stream – LCA)

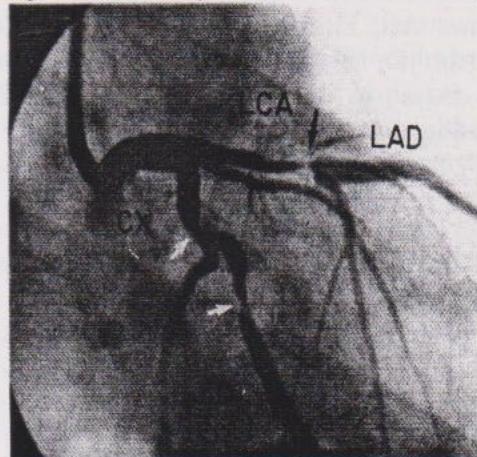


Figure 9: DVD (left anterior descending & circumflex)

### Discussion

Although many of the well established risk factors are described for formation of atherosomatous plaque, glucose intolerance (DM) accounts for a major part of the high incidence of IHD in certain ethnic groups in South Asia.<sup>16</sup> This study demonstrates incidence &

difference of coronary heart disease (CHD), DVD, TVD, diffuse lesion among symptomatic diabetic and nondiabetic patient. The prevalence of coronary artery disease (more than 50% diameter stenosis) is more in DM patients (82.22%) compared to their non DM counterparts (56%). Moreno et al<sup>17</sup> found the incidence of thrombus was higher in patients with diabetes than in patients without diabetes (62% versus 40%). Our study also demonstrates that diabetic patients had a higher prevalence of three-vessel disease (TVD) (32.43% versus 26.19%) and lower prevalence of single-vessel disease (SVD) (27.02% versus 33.33%). Jose A, Silva et al<sup>18</sup> found diabetic patients had a higher prevalence of three-vessel disease (47% versus 31%) and lower prevalence of single-vessel disease (18% versus 32%) than nondiabetic patients, although these differences were not statistically significant. In one large autopsy study, Waller et al<sup>11</sup> reported that 91% of patients with adult-onset diabetes (type II) had severe (>75%) narrowing of at least one major coronary artery and 81% had severe two- or three-vessel involvement. Our study demonstrates average vessel stenosis 83.63% in DM group as against 78.03% in the non diabetic individuals. Whether or not coronary atherosclerosis is more diffuse in diabetic patients is controversial.<sup>11,19</sup> In the autopsy study of Waller and coworkers<sup>11</sup> the diabetic patients had more severe stenosis. However, in another autopsy study by Crall and Roberts,<sup>20</sup> more extensive and diffuse coronary artery disease was found in diabetic patients. In our study 10.80% DM patients showed diffuse stenosis which was absent in the non DM group.

### Limitation of the study

This was a small scale study & does not represent the whole CAD population of the region. So, a large scale study is warranted.

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## Selective immune markers in pulmonary tuberculosis

Premananda Das<sup>1</sup>, Osul Ahmed Chowdhury<sup>2</sup>, Taskina Ahmed Chowdhury<sup>3</sup>

### Abstract

This cross-sectional study was carried out in the Department of Microbiology, MAG Osmani Medical College, Sylhet, from January 2012 to December 2012 to find out the change of selected immune parameters in newly diagnosed smear positive pulmonary tuberculosis patients after treatment. Fifty three patients were enrolled fulfilling the exclusion and inclusion criteria. Complete blood counts, ESR, CD4/ CD8 cell counts and CD4/CD8 ratio, total serum protein, albumin, globulin and A/G ratio were assessed before initiation and after two months of anti-TB treatment. The clinical presentations were also noted.

The age range of the patients were 15-64 years. Fifty three patients were enrolled for study. All presented with cough and fever, 90.6% presented with night sweats, 56.6% with chest pain, 28.3% with haemoptysis and 56.6% with history of weight loss. After two months of treatment with conventional anti-tubercular chemotherapy, there were marked improvement of symptoms (92.5% for cough, 92.5% for fever, 91.6% for night sweats, 93.3% for chest pain, 100% for haemoptysis and 86.7% gained weight). All of the patients presented with sputum smear positive for AFB and unilateral or bilateral pulmonary involvement shown by chest radiograph. After two months of treatment overall improvement of sputum smear positive for AFB were 92.5% and for X-ray chest 92.5%. Total counts of RBC, HCT, Hb, & MCHC were lower at diagnosis which significantly increased after two months of treatment. Increased ESR revealed at the time of diagnosis, significantly decreased after two months of treatment. Differential counts of lymphocyte were

decreased at diagnosis which significantly increased after two months of treatment. The total counts of Platelets also increased after treatment.

In our study CD4 & CD8 cell counts were normal at diagnosis and increased significantly after treatment but the increment was more in CD4. Therefore, the CD4/CD8 ratio was increased significantly after two months of treatment ( $P$  value- 0.015). Total serum protein and albumin was near lower limit of normal range at diagnosis and increased significantly after treatment ( $P$  value <0.001). Globulin at diagnosis was near upper limit of normal range and decreased after treatment but changes were insignificant ( $P$  value <0.122). As a consequence, the Albumin/Globulin ratio increased significantly after treatment ( $P$  value <0.001).

It may be concluded that selective immune parameters (CD4 & CD8) can be used in assessment of therapeutic efficacy of pulmonary tuberculosis patients.

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### Introduction

Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis*. Characteristic features include patient-to-patient airborne transmission, a prolonged latency period between the initial infection and overt disease, a granulomatous response associated with intense tissue inflammation and damage, and prominent pulmonary disease, although many other organs can be involved as well<sup>1</sup>.

Tuberculosis (TB) caused by *Mycobacterium tuberculosis* (MTB), a small, rod-shaped, aerobic, non-spore-forming bacilli. In 2006, there were an estimated 9.2 million new cases, 14.4 million prevalent cases and 1.5 million deaths attributable to TB. It is estimated that around one-third of the world's population has latent TB. The majority of cases occur in the world's poorest nations<sup>2</sup>.

1. Lecturer, Department of Microbiology  
Sylhet MAG Osmani Medical College
2. Professor, Department of Microbiology  
Sylhet MAG Osmani Medical College
3. Medical Officer, Iswardi Thana Health complex, Pabna

Tuberculosis (TB) is a major public health problem in Bangladesh. Pulmonary tuberculosis (PTB) is the most common form of TB and occurs in about 80% of cases<sup>3</sup>.

According to WHO (2009)<sup>3</sup> smear-positive pulmonary TB (PTB+) is defined as a patient with: at least two sputum specimens positive for Acid Fast Bacillus (AFB) or a patient with only one sputum specimen positive for AFB and chest radiological X-ray abnormalities consistent with active TB and diagnosis made by a graduate physician; or a patient with only one sputum specimen positive for AFB and a culture positive for *M. tuberculosis*.

Tuberculosis (TB) is a chronic infectious disease in which the cellular immunity (specifically CD4 and CD8 lymphocytes) provides the most important defense in controlling infection. CD4 lymphopenia is a well-defined risk factor for the development of active tuberculosis in patients infected with Human Immunodeficiency Virus. In HIV - negative patients, CD4 and CD8 cell count suppression has been associated with TB infection.<sup>4</sup>

The capability of responding to immunologic stimuli rests mainly with lymphoid cells which evolve into two main lymphocyte populations: T cells and B cells. T-cell precursors differentiate into immuno-competent T cells within the thymus and can express both antigen receptors and the various CD ('cluster of differentiation' or 'clustered determinants') proteins like CD3, CD4, CD8, etc. on their surface. T cells are subdivided into two major categories on the basis of whether they have CD4 or CD8 proteins on their surface; CD4 positive T cells are helper T cells and CD8 positive T cells are cytotoxic T cells<sup>5</sup>.

A low CD4 T- lymphocyte count at the time of diagnosis of tuberculosis does not clarify whether the low count is a predisposing factor for or a consequence of the disease. Patient without HIV infection but with tuberculosis and CD4 T-lymphocyte depletion at presentation normalize their CD4 cell count with anti- tuberculosis treatment. This normalization strongly suggests that tuberculosis is a reversible cause of CD4 lymphocytopenia.<sup>6</sup>

Severity of pulmonary tuberculosis is expected to be more with lower CD4 counts. It is not certain how CD4 counts are diminished in pulmonary tuberculosis. Some probable mechanism may be, lymphocyte homing in affected tissue, increase apoptosis induced by tubercle bacilli or impaired thymus function. It has been shown that CD4 reduction in tuberculosis is a

reversible phenomenon which returns to normal with successful anti-tuberculosis treatment.<sup>7</sup>

CD4 and CD8 T-cells percentages may help to find out the immune status of TB patients before and after the completion of anti-tuberculosis therapy (ATT).<sup>8</sup> There is also a close relationship between the acid-fast bacilli in sputum and abnormal indices, particularly those of body weight, Hb, WBC, ESR and level of different serum proteins. Failure of these indices to return to normal was invariably associated with persistent excretion of acid-fast bacilli<sup>9</sup>. Patients with PTB have lower serum total proteins and serum albumin but higher plasma gamma globulin levels than controls.<sup>10</sup>

The possible causes for the low albumin and total proteins in pulmonary tuberculosis patients were considered to be nutritional, enteropathy and acute phase reactant proteins. The hepatic synthesis of acute phase reactant proteins is induced by cytokines such as interleukin-6 and tumor necrosis factor- $\alpha$ .<sup>11</sup>

There are many immune parameters related to pulmonary tuberculosis e.g. CD4/CD8 T cell & other blood cell counts, Interleukins, ESAT-6, CFP-10,  $\gamma$ -interferon, different serum proteins including immuno-globulin, and CRP. But according to available investigation facilities and importance, we decided to estimate CD4 & CD8 T cell count, CBC, total serum protein, albumin and globulin.

## Materials and Methods

This was a cross sectional study, carried out in the Department of Microbiology, Sylhet M. A. G. Osmani Medical College, Sylhet, from 1st January 2012 to 31st December 2012.

Patients were newly diagnosed cases of smear positive pulmonary tuberculosis attended in Chest Disease clinic, Shahi-Eidgah, Sylhet and DOT centre, Sylhet M. A. G. Osmani Medical College Hospital, selected according to inclusion & exclusion criteria. Newly diagnosed cases of smear positive pulmonary tuberculosis, willing to participate in this study, of age between 15 & 64 years were included. Exclusion criteria were- Patients unwilling to participate in this study, smear negative pulmonary tuberculosis patients, treatment failure/ relapse cases, patients of pulmonary tuberculosis on anti-TB drugs, HIV infection or any other immunodeficiency disorder, Renal failure, Diabetes mellitus, Patients those receiving corticosteroid or any other immunosuppressive drugs. Data were collected by semi-structured and pre-

designed questionnaire prepared by the investigator. Total 53 cases of new smear-positive Pulmonary Tuberculosis patients participated in this study. Informed written consent was taken from the patients. Permission of ethical committee of Sylhet MAG Osmani Medical College was obtained. The clinical histories of the patients were noted. With all aseptic precaution blood samples were collected and following investigations were done at diagnosis and after two months of anti-TB treatment with conventional combined chemotherapy that included rifampicin, isoniazid, pyrazinamide and ethambutol. Investigations were: Complete blood counts, ESR, CD4 / CD8 cell counts and CD4/CD8 ratio. Estimation of total serum protein, albumin, globulin.

Data were presented as mean  $\pm$  SD. *P*-value  $<0.05$  was taken as statistically significant. All data were checked and analyzed with the help of SPSS, version 17. Student's 't'-test was done as a test of significance.

## Results

Age ranges of the patients were 15-64 years. Most of the patients were in the age group of 55-64 years of age 17(32.1%). Most of the patients were male 46(86.8%) and smoker 42(79.2%). The patients suffering from smear positive pulmonary tuberculosis were mostly low income group 31(58.5%) and had primary level of educational status 31(58.5%). Presenting clinical features of the study subjects were presented in Table -I & II

**Table - I : Clinical characteristics of study subjects**

Clinical characteristics	At diagnosis		After two months of treatment	
	Frequency (n=53)	Percentage	Frequency(n=53)	Percentage
Cough	53	100	4	7.5
Fever	53	100	4	7.5
Night Sweat	48	90.6	4	7.5
Chest Pain	30	56.6	2	3.8
Heamoptysis	15	28.3	0	0
H/O weight loss	30	56.6	4	7.5

**Table - II : Symptomatic change of study subjects after treatment (n = 53)**

Symptoms	At diagnosis		After two months of treatment	
	Frequency (%)	Frequency (%)	No. of pts improved	Percentage of improvement
Cough	53(100)	4(7.5)	49	92.5
Fever	53(100)	4(7.5)	49	92.5
Night Sweat	48(90.6)	4(7.5)	44	91.6
Chest Pain	30(56.6)	2(3.8)	28	93.3
Heamoptysis	15(28.3)	0(0)	15	100
H/O weight loss	30(56.6)	4(7.5)	26	86.7

Improvement of smear positive pulmonary tuberculosis patients based on diagnostic sign (sputum smear for AFB and chest X-ray) were presented in Table - III.

**Table - III: Diagnostic signs of smear positive pulmonary tuberculosis study subjects**

Diagnostic signs	At diagnosis		After two months of treatment	
	Frequency	Frequency N (%)	Improvement N (%)	Total improvement N (%)
Sputum smear for AFB	Scanty	5(9.4)	1(1.9)	4(80)
	(+)	10(18.9)	2(3.8)	8(80)
	(++)	19(35.8)	1(1.9)	18(94.7)
	(+++)	19(35.8)	0(0)	19(100)
CXR	Unilateral	50(94.3)	4(7.5)	46(92)
	Bilateral	3(5.7)	0(0)	3(100)
				49(92.5)

Weight and BMI change of study subjects were presented in Table – IV.

**Table – IV:** Changes of weight and BMI of study subjects

Variables	At diagnosis (Mean $\pm$ SD)	After two months of treatment (Mean $\pm$ SD)	t-value	P-value
Weight(kg)	44.68 $\pm$ 6.145	46.66 $\pm$ 5.893	10.6	<0.001
BMI (kg/m <sup>2</sup> )	17.13 $\pm$ 1.93	17.95 $\pm$ 1.86	10.3	<0.001

Paired 't'-test was done and P-value <0.05 was taken as significant.

Haematological status of study subjects was presented in table V & VI.

**Table – V:** Haematological status of study subjects (RBC, Platelets & ESR)

Hematological status	At diagnosis (Mean $\pm$ SD)	After two months of treatment (Mean $\pm$ SD)	t-value	P-value
RBC (10 <sup>6</sup> /μl)	3.92 $\pm$ 1.02	4.59 $\pm$ 0.66	3.84	<0.001
Hb (gm/dl)	9.5 $\pm$ 2.22	11.1 $\pm$ 1.67	4.20	<0.001
HCT (%)	26.49 $\pm$ 6.54	30.08 $\pm$ 4.61	3.29	0.002
MCV(fL)	68.13 $\pm$ 8.79	65.69 $\pm$ 6.27	1.79	0.079
MCH(pg)	24.75 $\pm$ 3.31	24.43 $\pm$ 2.38	0.69	0.493
MCHC(gm/dl)	36.19 $\pm$ 2.78	37.21 $\pm$ 1.70	2.75	0.008
Platelet (10 <sup>3</sup> /μl)	269.15 $\pm$ 129.563	289.43 $\pm$ 111.872	0.893	0.376
ESR (mm in 1st hour)	86.98 $\pm$ 15.51	13.92 $\pm$ 18.69	25.88	<0.001

Paired 't' test was done and P-value <0.05 was taken as significant.

**Table – VI:** Hematological status of study subjects (WBC- total counts and differential counts)

Hematological status	At diagnosis (Mean $\pm$ SD)	After two months of treatment (Mean $\pm$ SD)	t-value	P-value	
TC of WBC (10 <sup>3</sup> /μl)	8.77 $\pm$ 4.4	9.43 $\pm$ 3.33	1.022	0.311	
DC of WBC (10 <sup>3</sup> /μl)	Neutrophil Lymphocyte Eosinophil Basophil Monocyte	4.84 $\pm$ 3.64 2.75 $\pm$ 1.99 0.542 $\pm$ 0.746 0.68 $\pm$ 0.07 0.057 $\pm$ 0.389	4.61 $\pm$ 2.43 3.69 $\pm$ 1.39 0.408 $\pm$ 0.28 0.057 $\pm$ 0.069 0.551 $\pm$ 0.24	0.385 5.874 1.273 2.237 0.281	0.722 <0.001 0.209 0.261 0.780

Paired t test was done and P-value <0.05 was taken as significant.

Immunological markers (CD3, CD4, and CD8 subsets of lymphocytes) were shown in Table – VII

**Table – VII:** Change of immunological markers of study subjects (n = 53)

Immunological Markers	At diagnosis (Mean $\pm$ SD)	After two months of treatment (Mean $\pm$ SD)	t-value	P-value
CD3 (cells/μl)	1111.09 $\pm$ 564.53	1459.57 $\pm$ 503.35	9.235	0.000
CD4 (cells/μl)	529.23 $\pm$ 204.95	887.28 $\pm$ 247.90	11.950	0.000
CD8 (cells/μl)	504.92 $\pm$ 341.48	589.51 $\pm$ 284.76	2.330	0.024
CD4/CD8 ratio	1.313 $\pm$ 0.727	1.66 $\pm$ 0.629	2.505	0.015

Paired 't' test was done and P-value <0.05 was taken as significant.

Level of total serum protein (gm/dl), Albumin, Globulin and Albumin/Globulin (A/G) ratio were presented in Table – VIII.

**Table –VIII:** Change of Biochemical markers of study subjects (n = 53)

Biochemical markers	At diagnosis (Mean $\pm$ SD)	After two months of treatment (Mean $\pm$ SD)	t-value	P-value
Total Serum Proteins (gm/dl)	6.732 $\pm$ 0.497	7.360 $\pm$ 0.453	17.764	0.000
Albumin (gm/dl)	3.366 $\pm$ 0.065	4.083 $\pm$ 0.355	11.488	0.000
Globulin (gm/dl)	3.166 $\pm$ 0.4780	3.074 $\pm$ 0.3193	1.570	0.122
A/G ratio	1.0989 $\pm$ 0.2928	1.3432 $\pm$ 0.1766	6.089	0.000

Paired 't' test was done and P-value  $<0.05$  was taken as significant.

## Discussion

This cross-sectional study was carried out in the Department of Microbiology, MAG Osmani Medical College, Sylhet, from January 2012 to December 2012. There are many immunological and hematological parameters changed in pulmonary tuberculosis, by disease process and in response to treatment. ESR and CRP though non-specific inflammatory parameters, are traditionally used in relation to diagnosis and monitoring treatment response. The aim of this study was to evaluate the change of some selective immune parameters in smear positive pulmonary tuberculosis patients after anti-tuberculosis treatment.

Tuberculosis is a chronic infectious disease in which cellular immunity (reflected by change of CD4 and CD8 lymphocytes) provides the most important defense in controlling infection. It is expected that there might be some suppression of immune system prior to diagnosis and treatment of tuberculosis. During treatment there might be an improvement of immune status as well as hematological and biochemical parameters depending on treatment efficacy. CD4 and CD8 counts, being more specific immune markers may be useful along with traditional markers (microscopic examination and culture of sputum, chest X-ray, counts of WBC) for diagnosing and monitoring of smear positive pulmonary tuberculosis patients.

In this study, age range of the patients was 15-64 years, mostly in 55-64 years age group. The most of the patients were male (86.6%) and smoker (79.2%), mostly of low income group (58.5%) and had primary level of education (58.5%).

According to Zaman et al (2012)<sup>12</sup> Tuberculosis prevalence was higher in males in Bangladesh, highest in 55-64 years age group and also was highest in

persons with no education. In a study by Berhe, Enquselassie and Aseffa, (2012),<sup>13</sup> most of the patients were male (54.3%), low income (62.4%), and low educational level (80.6%). According to Matsumoto et al, (2012)<sup>14</sup> prevalence of smoking among male patients with smear positive pulmonary tuberculosis patients in Osaka was 71.4% between ages 20-60 years.

Male have a more chance of exposure to bacilli in crowded areas. Smokers were vulnerable to airborne infection due to respiratory epithelial disruption by chronic irritation with smoke. Low income, nutritional deficiencies and infection works as a vicious cycle. Sometimes it is enhanced by ignorance and educational lacking.

In this study, out of 53 patients, all presented with cough and fever, 90.6% presented with night sweats, 56.6% with chest pain, 28.3% with haemoptysis and 56.6% with history of weight loss. After two months of treatment with conventional anti-tubercular chemotherapy there was marked improvement of symptoms (92.5% for cough, 92.5% for fever, 91.6% for night sweats, 93.3% for chest pain, 100% for haemoptysis and 86.7% gained weight). All of the patients in our study presented with sputum smear positive for AFB and unilateral or bilateral pulmonary involvement shown by chest radiograph. After two months of treatment overall improvement of sputum smear positive for AFB was 92.5% and for X-ray chest was 92.5%.

In a comparative study of clinico-radiological profile of new smear positive pulmonary tuberculosis cases among young adult (18-59 years) and elderly ( $\geq 60$  years) people in a tertiary care hospital at Dehradun<sup>15</sup> shown that there were hemoptysis (29.5% vs 6%), fever (95.4% vs 76%) and night sweats (54.5% vs 18%). According to Ferdous et al, (2008)<sup>16</sup> about 78%

of the patients with pulmonary tuberculosis patients had BMI < 18.5. Aziz et al, (2002)<sup>17</sup> found that there was a history of weight loss in 78.3% of the patients and fever, productive cough, night sweats, and raised ESR were the most common findings in pulmonary tuberculosis patients. In our study mean weight of the patients was 44.68 kg and mean BMI was 17.13.

The clinical presentation and diagnostic signs of pulmonary tuberculosis patients in our study is consistent with the related other studies. The weight loss is a consequence of reduce

intake of food due to nausea induced by *Mycobacterium Tuberculosis* stimulated TNF- $\alpha$  production.

In this study, total counts of RBC ( $N \times 10^6/\mu\text{L}$ ) was at diagnosis  $3.92 \pm 1.02$  and after two months of treatment  $4.59 \pm 0.66$ , Hb (gm/dl), HCT (%), MCV (fl), MCH (pcg), MCHC (gm/dl) was  $9.5 \pm 2.22$ ,  $26.49 \pm 6.54$ ,  $68.13 \pm 8.79$ ,  $24.75 \pm 3.31$ ,  $36.19 \pm 2.78$  at diagnosis and  $11.1 \pm 1.67$ ,  $30.08 \pm 4.61$ ,  $65.69 \pm 6.27$ ,  $24.43 \pm 2.38$ ,  $37.21 \pm 1.70$  after two months of treatment, respectively. Total counts of platelets ( $10^3/\mu\text{L}$ ) and ESR (mm in 1<sup>st</sup> hour) was  $269.15 \pm 129.563$  &  $86.98 \pm 15.51$  at diagnosis and  $289.43 \pm 111.872$  &  $13.92 \pm 18.69$  after treatment, respectively. Total counts of WBC ( $10^3/\mu\text{L}$ ) were  $8.77 \pm 4.4$  at diagnosis and  $9.43 \pm 3.33$  after treatment. Differential counts ( $10^3/\mu\text{L}$ ) of Neutrophil, Lymphocyte, Eosinophil, Basophil, & Monocyte was  $4.84 \pm 3.64$ ,  $2.75 \pm 1.99$ ,  $0.542 \pm 0.746$ ,  $0.68 \pm 0.07$ , &  $0.057 \pm 0.389$  at diagnosis and  $4.61 \pm 2.43$ ,  $3.69 \pm 1.39$ ,  $0.408 \pm 0.28$ ,  $0.057 \pm 0.069$ , &  $0.551 \pm 0.24$  after two months of treatment, respectively.

A study conducted by Akpan, Josephine, Ephoria, (2012)<sup>18</sup>, on hematological changes in pulmonary tuberculosis infection in Calabar, Nigeria, showed significantly lower values of PCV, Hb, MCH, MCHC ( $P < 0.05$ ) in pulmonary tuberculosis patients. ESR showed significantly higher values which decreased significantly ( $P < 0.05$ ) as anti- tuberculosis therapy progressed. Another study done by Dosumu, 2001<sup>19</sup>, in Nigeria on newly diagnosed pulmonary tuberculosis cases observed that the mean WBC increased from  $3.5 \times 10^9/\text{L}$  to  $5.5 \times 10^9/\text{L}$  after eight months of treatment, at the same time the mean Platelet counts did not change significantly from the initial value of  $245 \times 10^3/\text{cm}^3$ . Study by Afzal et al (2010)<sup>8</sup> revealed that differential leukocyte counts in tuberculosis patients had significantly increased percentage of neutrophils, lymphocyte percentage were significantly decreased

and there was no significant difference in monocytes percentage compared to controls.

In our study, RBC, HCT, Hb, & MCHC were lower at diagnosis which significantly increased after two months of treatment. ESR was increased at diagnosis and significantly decreased after two months of treatment. Differential counts of lymphocyte were decreased at diagnosis which significantly increased after two months of treatment.

Change of other WBC parameters after treatment was not statistically significant.

Findings of red cell indices in this study were consistent with normocytic anaemia in pulmonary tuberculosis. Increased ESR is an established marker of tuberculosis.

There was decreased ESR after treatment which was indicative of anti- tubercular treatment response.

In the present study, mean value (cells/ $\mu\text{L}$ ) of CD3 & CD4 were  $1111.09 \pm 564.53$  &  $529.23 \pm 204.95$  at diagnosis and  $1459.57 \pm 503.35$  &  $887.28 \pm 247.90$  after two months of treatment, respectively. Both were near lower limit of normal at diagnosis and increased significantly ( $P$  value  $< 0.001$ ) in response to treatment. Normal values of CD3 and CD4 are (688-1955) and (335-1298), respectively. CD8 cell counts were  $504.92 \pm 341.48$  and  $589.284.76$ , at diagnosis and after treatment, respectively. Normal CD8 cell counts are (144-796). In our study CD8 cell counts were normal at diagnosis and increased significantly ( $P$  value 0.024) after treatment but the increment is relatively less than CD4. Therefore, the CD4/CD8 ratio was increased significantly from  $1.313 \pm 0.727$  to  $1.66 \pm 0.629$  after two months of treatment ( $P$  value- 0.015).

Studies in relation to immune status of pulmonary tuberculosis patients showed variable results.

Devoudi et al (2008)<sup>7</sup> stated that severity of pulmonary tuberculosis is expected to be more with lower CD4 counts and was observed that CD4 cell counts returned to normal with successful anti- tuberculosis treatment with conventional chemotherapy.

There are studies partially consistent with our study. Uppal et al (2004)<sup>20</sup> showed that CD4 counts in tuberculosis patients were significantly lower than normal at diagnosis but returns

near normal on completion of two months of treatment. CD8 values were normal at diagnosis and increased significantly with treatment, consistent with lower CD4 and higher CD8 values, the CD4/CD8 ratio was significantly lower at diagnosis which increased accordingly after treatment. Another study at King Khalid University Hospital, Riyadh, Saudi

Arabia, by Abdullah et al (2008)<sup>21</sup> found lowered CD3 and CD4 cell counts at diagnosis, CD8 cells were not significantly changed with disease.

Gouda et al (2008)<sup>22</sup> showed that CD4 and CD8 cell counts were increased rather than decreased at diagnosis of pulmonary tuberculosis. The frequency of CD4 cells was higher than CD8 cells in peripheral blood of pulmonary tuberculosis patients. The finding of this study was not consistent with our study. We found normal CD4 and CD8 values (CD4 values near lower limit of normal) at diagnosis and after treatment both were increased but the increment were more in CD4 cell counts. Prior to the treatment, frequency of CD4 cells were near lower limit of normal. It may be explained by down regulation of proliferation of CD4 cells by CD8 suppressive lymphocytes that also suppress anti-mycobacterial action of macrophages, in an attempt to cause less tissue damage. Lymphocyte homing in affected tissue rather than circulation and increased apoptosis induced by tubercle bacilli also play role in reduction of CD4 cells. (Davoudi et al, 2008)<sup>7</sup>

After treatment CD4 cells were expected to rise due to lowered load of bacilli. CD8 cells were expected to decrease to maintain a fine balance between CD4/CD8 cells in peripheral circulation. Increased CD8 cells in our study, could be explained by probable help of CD4 cells for the development of CD8 cells, yet the rise of CD8 cells was relatively less than the rise of CD4 cells reflected by increased CD4/CD8 ratio.

In this study total serum protein (gm/dl) and albumin was near lower limit of normal range,  $6.732 \pm 0.497$  &  $3.366 \pm 0.065$  at diagnosis and increased significantly to  $7.360 \pm 0.453$  &  $4.083 \pm 0.355$  after treatment, respectively (*P* value  $<0.001$ ). Globulin at diagnosis was near upper limit of normal range,  $3.166 \pm 0.478$  and decreased to  $3.074 \pm 0.319$  (*P* value  $<0.122$ ). The Albumin/Globulin ratio increased significantly from  $1.098 \pm 0.292$  to  $1.343 \pm 0.176$  after treatment (*P* value  $<0.001$ ). The findings were similar to the study by Damburam et al (2012) in which patients with PTB had lower serum total proteins and serum albumin but higher plasma gamma globulin levels than controls.

The hypergammaglobulinemia, is most probably due to immunologic response to the tubercle bacilli. The cause of hypo-albuminaemia may be due to poor nutritional status and reduced synthesis induced by cytokines such as IL-6 and TNF- $\alpha$ .

It may be concluded that, CD4 and CD8 counts may be considered in assessment of tuberculosis at diagnosis as well as monitoring treatment response.

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## Correlation of Peripheral and Central Pulse Pressure with the Extent of Coronary Artery Disease

Golam Mohammad Mohiuddin<sup>1</sup>, Muhammad Shahabuddin<sup>2</sup>, S M Habibullah<sup>3</sup>, Anamur Rahman<sup>4</sup>,  
Fakhrul Islam<sup>5</sup>, Mohammad Sirajur Rahman<sup>6</sup>

### Abstract

The relative importance of the different components of the arterial pressure wave in determining cardiovascular risk is a continuing debate. The objective of the study was to correlate central and peripheral pulse pressures with the extent of coronary artery disease. A total of 85 consecutive cases of IHD (CSA, UA, NSTEMI, STEMI) who underwent diagnostic coronary angiography were selected. Patients with previous PCI or CABG, peripheral vascular disease, congenital heart disease, valvular heart disease and cardiomyopathy were excluded. Brachial BP measurements performed just before coronary angiography with valid aneroid sphygmomanometer. Intra-aortic pressures were recorded during angiography using a fluid filled Judkins catheter at ascending aortic lumen before giving contrast media at a paper speed of 100 mm/sec. Angiogram was done and extent of coronary artery disease were done. No coronary artery disease was found in 16(18.8%) patients, single vessel disease in 27(31.8%) double vessel disease in 24(28.2%) and triple vessel disease in 18(21.2%) patients. Statistically significant positive correlation between brachial systolic( $r=0.457; p<0.001$ ) and pulse pressure( $r=0.584; p<0.001$ ) with number of diseased vessel was found but with brachial diastolic pressure, there was a negative correlation( $r=-0.183; p=0.093$ ). Again aortic systolic BP and pulse pressure had positive correlation( $r=0.227; p=0.036$  and  $r=0.334; p=0.002$ ) and aortic diastolic BP had negative

correlation( $r=-0.145; p=0.184$ ). From this study it was concluded that central pulse pressure and systolic pressure correlated with the number of diseased vessels, but diastolic pressure did not correlate. Brachial pulse pressure and systolic pressure also correlated with the number of disease vessels, but diastolic pressure did not correlate. Peripheral pulse pressure and systolic pressure correlates with number of diseased vessels as good as that of central pulse pressure and systolic pressure.

[OMTAJ 2014; 13(1)]

### Introduction

Coronary heart disease (CHD) is a worldwide health epidemic. In the United States, for example, it is estimated that 13.7 million Americans have CHD, including more than 7.2 million individuals who already have had a myocardial infarction.

The South Asian countries of India, Bangladesh, Pakistan, Srilanka and Nepal contribute the highest proportion of the burden of cardiovascular diseases (CVDs) compared to any other region globally.<sup>1</sup> Bangladesh with 150 million people has got many health problems among which cardiovascular diseases are very important. In a survey conducted in the country, it was found that hypertension is the commonest cardiovascular disease being present in 7 percent population, followed by rheumatic heart disease (RHD), which was detected in 12.87 per thousand populations. It is followed by CAD (6.6/1000 population) and congenital heart disease (CHD) (7.1/1000 population).<sup>2</sup>

In 1975, the incidence of ischemic heart disease (IHD) in Bangladesh was reported to be 3 per thousand.<sup>3</sup> Then subsequently in 1985, the same authors reported the increased incidence of 14 per thousand.

Myocardial infarction is one of the leading cause of death in Bangladesh mostly in the 4<sup>th</sup> decade of life. It is observed that unheralded myocardial infarction was

1. Assistant Registrar, Cardiology
2. Associate Professor, Cardiology
3. Assistant Professor, Cardiology
4. Assistant Registrar, Cardiology
5. Assistant Registrar, Cardiology
6. Medical Officer, Cardiology

Sylhet M.A.G Osmani Medical College and Hospital

common (32%) among younger age group that was comparable with a previous retrospective study of premature coronary artery disease.

Atherothrombosis, is the main cause of myocardial infarction, coronary death, heart failure, and large artery stroke<sup>4</sup>. This development of life threatening vulnerable atherosclerotic plaques, in the coronary and carotid arteries is the leading cause of death and severe disability, not only in affluent countries, but also worldwide<sup>5</sup>. Most heart attacks occur among people with average or slightly elevated risk factor levels and recurrent events still occur despite lowering of these levels), indicating we need better detection treatment of those who are destined for a heart attack.<sup>6</sup>

Better detection of at-risk individuals may be achieved by visualizing the diseased arterial wall rather than just assessing risk factors for getting the disease<sup>7</sup>. For every 20 mm Hg systolic or 10 mmHg diastolic increase in blood pressure there is a doubling of mortality from both ischemic heart disease and stroke in all age groups from 40 to 89 years. In younger people, blood pressure is determined largely by peripheral vascular resistance, whereas in older people blood pressure is determined mainly by the stiffness of central conduit vessels.<sup>8</sup> The importance of systolic pressure was never in doubt, a series of studies showing that a high systolic pressure was the best predictor of risk in the elderly, but also a low diastolic pressure was associated with increased risk<sup>9</sup>. Subjects younger than age 50 years the best predictor of risk was a high diastolic pressure, but in those older than age 60 years systolic pressure was the best predictor. An analysis of the MRFIT data, which found that the highest-risk group was patients who had a systolic pressure above 160 mm Hg and a diastolic pressure below 80 mm Hg<sup>10</sup>. The arterial pressure wave in the brachial artery looks very different from the waves recorded at more proximal sites, where the damage to target organs, such as the heart and brain, occurs. Recent studies have shown that central blood pressures are independent predictors of outcomes and may even be better predictors of cardiovascular mortality than peripheral blood pressures. Usefulness and feasibility of integrating measurements of central arterial blood pressures into routine medical practice are areas of intense ongoing research<sup>11</sup>.

### Methodology

This was a Cross-sectional comparative study done in Department of cardiology, Sylhet MAG Osmani

Medical College Hospital during the Period July 2010 to June 2012. All patients with Ischemic Heart Disease (IHD) admitted in the department of cardiology, SOMCH was taken as a study population. Patients admitted in cardiology ward of SOMCH with IHD who underwent for CAG and those who fulfilled the inclusion and exclusion criteria Study Sample.

### Variables

1. Peripheral (Brachial) blood pressure- systolic, diastolic and pulse pressure.
2. Central aortic pressure (systolic and diastolic).
3. Central pulse pressure.
4. Number of involved vessels (SVD,DV,TVD)

### Procedure

Considering the enrolment criteria, 85 consecutive patients with IHD were selected. After explaining the study procedure in details, written consent was taken for each subject. Meticulous history and detailed clinical examination were carried out and recorded in pre designed structured pro-forma. Present and recent use of drugs was recorded. Brachial BP measurements were performed just before CAG by aneroid sphygmomanometer in the sitting position after a 5 min rest in the laboratory, using the first and the fifth Korotkoff sounds for SBP and DBP, respectively.

The higher of the two consecutive BP (both arms) measurements were recorded. Intra-aortic pressure was recorded before coronary angiography using a fluid-filled Judkins catheter (Cordis), the tip of which placing at the centre of the ascending aortic lumen, at a paper speed of 100mm/sec.

Aortic PP was calculated as the difference between aortic SBP and aortic DBP. Coronary artery stenosis was assessed by quantitative coronary angiography and stratified into significant and non-significant stenosis. The disease severity was evaluated by counting the number of major epicardial coronary arteries (left main, left anterior descending, circumflex and right) affected with  $\geq 1$  significant stenosis.

CAD severity was scored as 0 (normal or non-significant angiographic vessels), 1 (1-vessel disease, SVD), 2 (2-vessel disease, DVD), or 3 (3-vessel disease, TVD).

### Statistical methods

Data were collected by investigator and then recorded in a structured preformed questionnaire. The quantitative data was expressed as mean and standard deviation and qualitative data as frequency distribution

and percentage. Data were processed and analyzed using computer based SPSS (statistical package for social science) soft-ware for windows, version 16. Data presented on categorical scale was compared between groups with the help of Chi-square ( $\chi^2$ ) or Fisher's Exact Probability Test. Quantitative data was compared between groups using Student's t-Test, multivariate logistic regression analysis and fisher's exact test, as applicable.  $P$  value of less than 0.05 was considered as significant.

## Results

The findings of the study were presented below

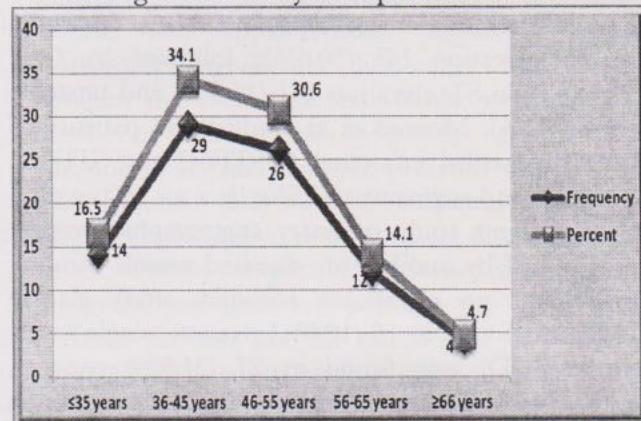


Figure- 1: Distribution of patients by age

Age of the patients ranged from 20 to 70 years with the mean age of  $46.9 \pm 9.8$  years. Figure-1 demonstrates that 29 (34.1%) patients were in the age group of 36 to 45 years, 26 (30.6%) patients were in the age group of 46 to 55 years, 14 (16.5%) patients were in the age group up to 35 years, 12 (14.1%) patients were in the age group of 56 to 65 years and 4 (4.7%) patients were in the age group of 66 or above years.

Table-I: Comparison of different parameter of blood pressure and coronary artery disease

Blood pressure (mmHg)	No CAD	SVD	DVD	TVD	P value
<b>Aortic</b>					
Systolic (mmHg)	Range	125.0 (14.0)	110-170	123.3 (18.1)	100-165
Diastolic (mmHg)	Range	80.3 (9.2)	65-100	74.3 (9.3)	60-95
Pulse pressure (mmHg)	Range	44.7 (13.0)	20-70	49.1 (16.5)	24-85
<b>Brachial</b>					
Systolic (mmHg)	Range	122.5 (14.4)	110-170	135.7 (11.0)	110-170
Diastolic (mmHg)	Range	78.1 (7.5)	70-100	72.8 (5.9)	60-80
Pulse pressure (mmHg)	Range	44.4 (10.9)	30-70	63.0 (9.9)	40-80

ANOVA test was applied to find out the level of significance. Data were presented as mean (SD).

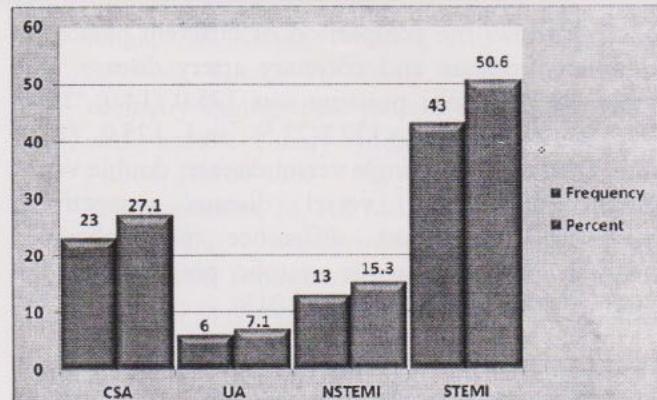


Figure-2: Distribution of patients by clinical types of CAD

Figure-2 shows the most common clinical types of CAD in this study was ST elevation MI (50.6%), followed by CSA (27.1%), Non-ST elevation MI (15.3%) and unstable angina (7.1%).

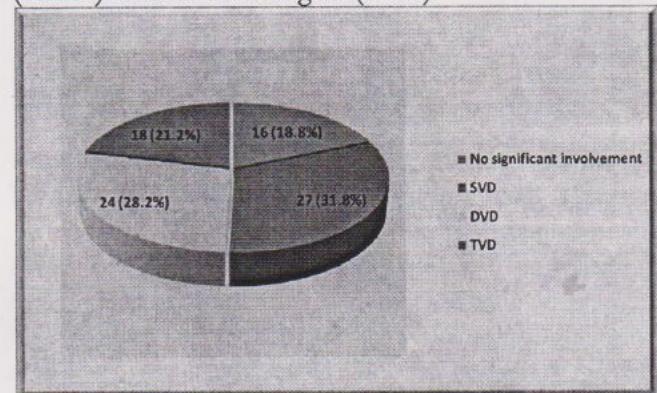
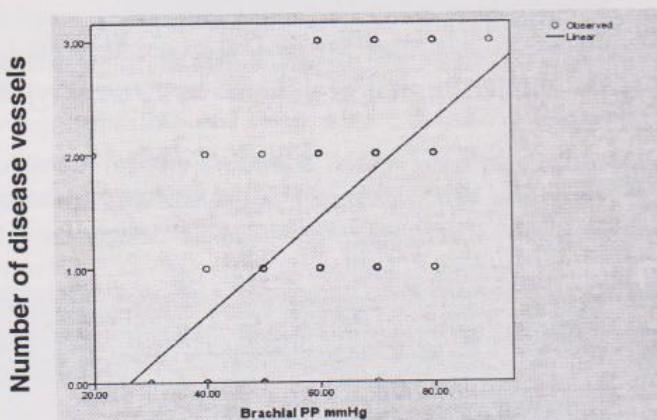


Figure-3: Distribution of patients by coronary artery involvement

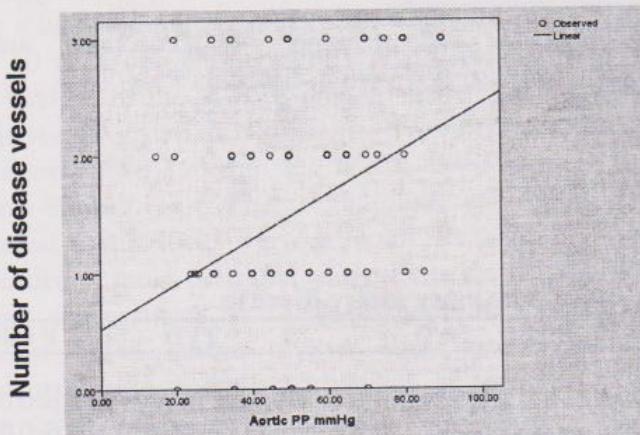
Distribution of patients by coronary artery involvement was shown in figure-3.

Table-I: shows the comparison of different parameter of blood pressure and coronary artery disease. The mean aortic systolic pressure was 125.0 (14.0), 123.3 (18.1), 122.3 (18.8), 139.7(22.5) and 125.0 (14.0) mmHg in no CAD, single vessel disease, double vessel disease and triple vessel disease respectively. Statistically significant difference was observed between the mean aortic systolic pressure ant the number of disease vessels ( $p=0.015$ ).



**Figure-4:** Scatter diagram showing correlation between brachial PP (mmHg) with number of disease vessel (n=85)

Correlation between brachial PP (mmHg) with number of disease vessel was shown in figure-4. There was a significant positive correlation between brachial PP (mmHg) and number of disease vessel ( $r=0.584$ ;  $p<0.001$ ).



**Figure-5:** Scatter diagram showing correlation between aortic PP (mmHg) with number of disease vessel (n=85)

Correlation between aortic PP (mmHg) with number of disease vessel was shown in figure 5. There was a significant positive correlation between Aortic PP (mmHg) and number of disease vessel ( $r=0.334$ ;  $p=0.002$ ).

## Discussion

The present study findings were discussed and compared with previously published relevant studies. The mean age of the patients ranged from 20 to 70 years with the mean age of  $46.9 \pm 9.8$  years. Another study shows 29.7% were 18 to 39 years, 48.5% were 40-59 years, 21.8% were 60 to 74 years. The age range was almost similar in this study. <sup>12</sup> Male was predominant in this study (95.3%) than female (4.7%). Male female ratio was 20.3:1 in this study which differ from Lee et al (1997) and HOPE studies where they found male female ratio was 2.4:1 and 1.5:1 respectively.

The most common clinical types of CAD in this study was ST elevation MI (50.6%), followed by CSA (27.1%), Non-ST elevation MI (15.3%) and unstable angina (7.1%). Mourad et al studied 1337 patients of whom myocardial infarction (NSTEMI and STEMI) was 13.2% and angina was 43.5%. <sup>13</sup>

In this current study coronary angiographic severity was assessed by number of diseased vessels. Among the patients no significant coronary artery disease (CAD) was found in 16 (18.8%) patients, single vessel disease (SVD) was found in 27 (31.8%) patients; double vessel disease was found in 24 (28.2%) patients; TVD: Triple vessel disease was found in 18 (21.2%) patients. In this study, the central blood pressure of the subjects were categorized into four groups according to number of diseased vessels. The mean aortic systolic pressure was 125.0 (14.0), 123.3 (18.1), 122.3 (18.8), 139.7(22.5) and 125.0 (14.0) mmHg in no CAD, single vessel disease, double vessel disease and triple vessel disease respectively. Statistically significant difference was observed between the mean aortic systolic pressure and the number of diseased vessels ( $p=0.015$ ).

Roman et al showed the mean central systolic blood pressure was  $121 \pm 17$  mm of Hg in no CAD patients and  $127 \pm 22$  mm of Hg in patients having CAD, thus support the present study. <sup>14</sup> The mean aortic diastolic pressure was 80.3 (9.2), 74.3 (9.3), 70.9 (10.5) and 76.1 (13.2) mmHg in no CAD, single vessel disease, double vessel disease and triple vessel disease respectively. Statistically no significant difference was observed between the mean aortic diastolic pressure and the number of disease vessels ( $p=0.015$ ).

Jankowski et al also showed same result, thus support the present study. <sup>15</sup> The mean aortic pulse pressure was 44.7 (13.0), 49.1 (16.5), 51.4 (16.1) and 63.6 (21.9) mmHg in no CAD, single vessel disease, double vessel

disease and triple vessel disease respectively. Statistically significant difference was observed between the mean aortic pulse pressure and the number of disease vessels ( $p=0.010$ ).

Benetos et al in a study showed pulse pressure was an independent predictor of cardiovascular mortality.<sup>16</sup> The central systolic blood pressure and pulse pressure increased significantly ( $p<0.05$ ) with number of diseased vessels but central diastolic pressure not significantly increased in all studied patients.

On the other hand it was observed in this current study that the mean brachial systolic pressure was 122.5 (14.4), 135.7 (11.0), 132.9 (14.6) and 147.2 (12.3) mmHg in no CAD, single vessel disease, double vessel disease and triple vessel disease respectively. Statistically significant difference was observed between the mean brachial systolic pressure and the number of disease vessels ( $p<0.001$ ).

The mean brachial diastolic pressure was 78.1 (7.5), 72.8 (5.9), 68.3 (8.2) and 75.0 (6.2) mmHg in no CAD, single vessel disease, double vessel disease and triple vessel disease respectively. Statistically significant difference was observed between the mean brachial diastolic pressure and the number of disease vessels ( $p<0.001$ ). The mean brachial pulse pressure was 44.4 (10.9), 63.0 (9.9), 64.6 (13.5) and 72 (8.8) mmHg in no CAD, single vessel disease, double vessel disease and triple vessel disease respectively. Statistically significant difference was observed between the mean brachial diastolic pressure and the number of disease vessels ( $p<0.001$ ).

From this study it may be concluded that central pulse pressure and systolic pressure correlated with the number of diseased vessels, but diastolic pressure did not correlate. Brachial pulse pressure and systolic pressure also correlated with the number of diseased vessels, but diastolic pressure did not correlate. Peripheral pulse pressure and systolic pressure correlates with number of diseased vessels as good as that of central aortic pulse pressure and systolic pressure.

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## SINGLE STAGE ORAL MUCOUS MEMBRANE GRAFT URETHROPLASTY FOR LONG SEGMENT ANTERIOR URETHRAL STRICTURE

Md. Shafiqul Islam<sup>1</sup>, Md. Abdul Alim<sup>1</sup>, Kaiser Ahmed<sup>2</sup>, Promode Ranjan Singh<sup>3</sup>  
Nitai Pada Biswas<sup>4</sup>, Md. Abdur Rahim<sup>5</sup>

### Abstract

Stricture urethra is a common and chronic urological problem. Many options are there for their management, but all of these techniques are associated with high recurrence rate except oral mucous membrane graft urethroplasty. We used this technique for the management of patients with stricture urethra. To evaluate the result of single stage oral mucous membrane graft urethroplasty for the treatment of long segment anterior urethral stricture. Between June, 2011 to July, 2013, thirty patients underwent oral mucous membrane graft urethroplasty at urology department of Sylhet MAG Osmani Medical College Hospital (SOMCH) and some other hospitals in Sylhet city. Age range was 25-45 years. All patients had stricture urethra greater than 5cm. Follow up period was 3 months to 3 years.

The procedure was done through a 6cm long midline perineal incision. Bulbar urethra was mobilized first. The urethra was dissected off the corpora upto the coronal sulcus by invaginating the penis. The urethra was opened vertically and dorsally upto corona. Meatotomy was then performed dorsally and the incision extended proximally throughout the glans. Oral mucous membrane was harvested from the cheek or from the inner side of lower lip.

The oral mucous membrane grafts (OMG) were applied throughout the whole length of the corpora and sutured with the edges of the incised urethra mucosa over a 14fr Foley's catheter. The distal end of the graft was brought out through the meatus and attached to the meatal margin and glans. Catheter removed after 3 weeks. 27 patients are voiding well without any further intervention. Two required OIU and one required meatoplasty.

Single stage oral mucous membrane graft urethroplasty for long segment urethral stricture is a difficult procedure but the results are encouraging. This technique maintains natural shape of the penis and glans in functional and cosmetic points of views.

[OMTAJ 2014; 13(1)]

### Introduction

Stricture urethra is a common and chronic urological problem. Many options are there for their management. Visual internal urethrotomy (VIU) may be useful for short annular strictures, but this procedure is associated to a very high recurrence rate.<sup>1</sup> Urethral reconstruction with excision of the strictured segment and end to end anastomosis is successful in more than 95% of the patients with a stricture of upto 2cm in length.<sup>2</sup> Patient with long strictures (>2cm) are not suitable for end to end urethroplasty due to risk of postoperative chordee formation.<sup>3</sup> Substitution urethroplasty is ideal for the management of long anterior urethral strictures. The material for substitution urethroplasty remains controversial.<sup>4</sup> Urethra is best substitute for urethra - Turner Warwicks opinion is still true.<sup>3</sup> However in recent times there has been a wider use of buccal mucosal graft versus other substitutes such as genital or extragenital skin. Buccal mucosa offers the advantages of being accustomed to a wet environment, having good vascularity, hairless, easy to harvest, thick epithelium

1. Assistant Professor, Department of Urology, Sylhet MAG Osmani Medical College, Sylhet.
2. Assistant Registrar, Department of Urology, Sylhet MAG Osmani Medical College, Sylhet.
3. Associate Professor, Department of Urology, Sylhet MAG Osmani Medical College, Sylhet.
4. Assistant Professor, Department of Urology Sir Salimullah Medical College, Dhaka.
5. Indoor Medical Officer, Department of Urology Sylhet MAG Osmani Medical College Hospital, Sylhet.

making it easy to handle, less chance of graft contraction, having a thin lamina propria allowing easy inosculation, reduce rate of pseudodiverticulum formation.<sup>4</sup> Humby was the first person to describe buccal mucosa grafting in 1941, but the procedure became widely used in the 1990s and onwards<sup>6</sup>. We present our initial experience with dorsal buccal mucosa graft (BMG) urethroplasty through a dorsal sagittal urethroplasty technique for repairing long anterior urethral strictures.

### Material and Methods

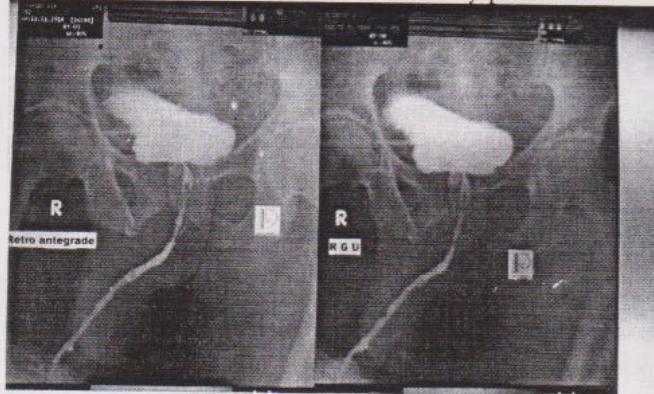
Between June, 2011 to July, 2013, thirty patients with long anterior urethral stricture were managed by single stage urethroplasty with a dorsal onlay BMG. Preoperative evaluation included history, physical examination and appropriate investigations, AUA symptom scores assessment, USG of KUB with MCC with PVR, Uroflowmetry, RGU and MCU to see the severity, location and length of stricture segment (Pic1 and Fig1). Other investigations were done for anaesthetic fitness. Of the strictures 8 were inflammatory, 15 associated to lichen sclerosis (Bxo), 5 were idiopathic in origin, 2 due to trauma. Mean stricture length as measured by preoperative RGU was 9cm (5-13), sites of strictures were panurethral in 12 and penile urethral in 18.

The procedure was done through a 6cm long midline perineal incision. Bulbar urethra was mobilized first. The urethra was dissected off the corpora upto the coronal sulcus by invaginating the penis. The urethra was opened vertically and dorsally upto corona. Meatotomy was then performed dorsally and the incision extended proximally throughout the glans.

Oral mucous membrane was harvested from the cheek or from the inner side of lower lip. Harvesting technique includes infiltration of lignocaine with adrenaline in the mucous membrane to facilitate harvesting with sharp and blunt dissection. Stensen's duct and its opening were protected all the way.

The oral mucous membrane graft (OMG) was sutured, splayed and quilted over the corpora cavernosa using 5/0 vicryl quilting sutures for reinforcement with good support and minimizing the dead space. Then graft was sutured with the edges of the incised urethral mucosa over a 14fr foley's catheter using 4/0 vicryl. Generally 2-3 grafts were needed. The distal end of the most distal graft was brought out through the meatus and attached to the meatal margin and glans. Catheter removed after 3 wks.

A pericatheter urethrogram was done 3 weeks after operation and voiding trail given (Fig2). At 3 months after catheter removal, AUA symptom scores assessment, RGU & MCU, Uroflowmetry were performed. A successful outcome is defined as normal voiding with no indication for secondary procedure.



Pic1: Pre-operative RGU.

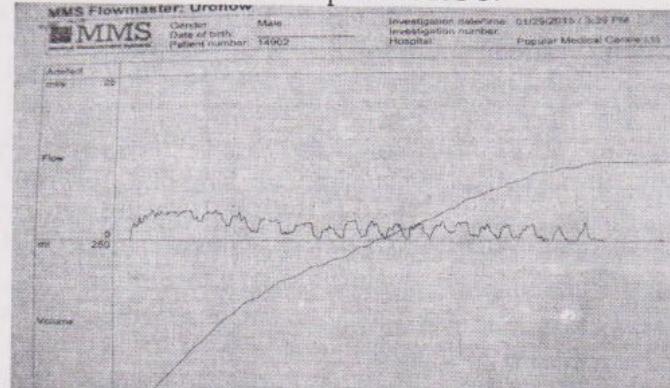


Fig1: Pre-operative uroflowmetry.

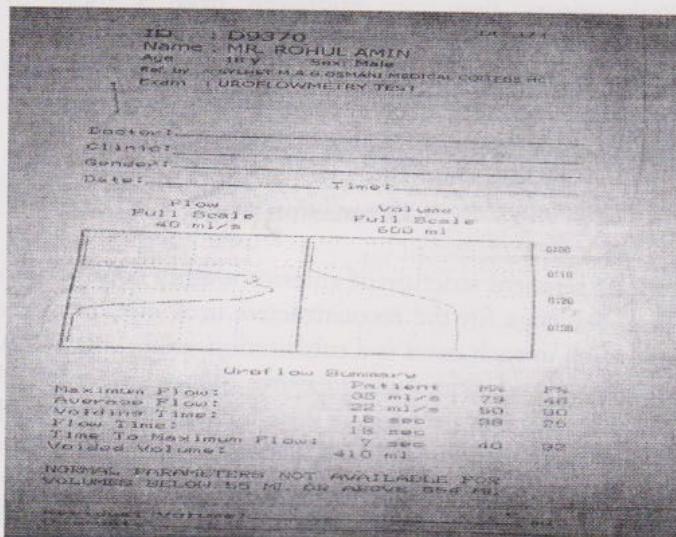


Fig2: Post-operative Uroflowmetry.

Table I- Etiology of strictures.

Causes of strictures	No. of Patients
Idiopathic	05
Traumatic	02
Lichen sclerosis(BXO)	15
Inflammatory	08
Total	30

Table II- Sites of strictures.

Sites	No. of Patients
Panurethral	12
Penile	18
Total	30

## Results

A total of 30 patients included in this study. The mean age of these men was 35(25-45) years, Mean follow up period was (3-36) months. Three patients showed extravasation of contrast medium on pericatheter urethrogram after 3 weeks of operation at anastomotic site and managed successfully by extended catheterization for another 2 weeks. When repeat contrast study showed no leak, voiding trial was given. Two patients developed stricture at proximal anastomotic site. They voided normally after single attempt of VIU. One patient developed meatal stenosis and was treated by meatoplasty. These three patients considered to be failed case. Three patients developed wound infection, managed successfully with the change in antibiotics as per wound swab culture sensitivity test.

No patient developed diverticulum, fistula, sacculation formation, protrusion of the graft at external meatus. Peak urinary flow rate improved from a mean of 6ml/sec to 20ml/sec after 6wks postoperatively. AUA symptom scores decreased from a mean of 21.2 (14-33) preoperatively to 5.2 (4-7) after 6wks postoperatively. No major donor site complications were noted.

## Discussion

A long segment stricture of anterior urethra continues to be a challenge for the reconstructive urologist. The best approach in such cases is a substitution urethroplasty.<sup>7</sup> A number of techniques using various tissues have evolved to deal with this problem. These include split skin and full thickness grafts, bladder mucosa, buccal mucosa and new tissue engineered substitutes available over the shelf. Scrotal skin was used but felt into disfavour because of high rate of complications. Similarly, after the initial enthusiasm with the bladder mucosa as a urethral substitute there was problems with harvesting tissue for substitution and of meatal exuberance.<sup>8</sup>

Humby was the first to use buccal mucosa for urethral reconstruction in a series of single stage hypospadias repair. But BMG urethroplasty has emerged as a popular technique in 1990s. Whether to place the graft dorsally, ventrally or laterally is still controversial now. Ventral onlay graft is more prone to fistula formation, sacculation, diverticula formation leading to urinary stasis and ejaculatory dysfunction<sup>4</sup>. On the other hand dorsal onlay graft procedure for the anterior urethral stricture provides the advantages of better mechanical support by the corporal bodies for the grafts better take up, with less incidence of sacculation and fistula formation<sup>9,10</sup>. It has been reported that dorsally placed graft can do better because of better mechanical support for the graft and a richer vascular bed over the underlying corporal bodies<sup>11</sup>. In different series, dorsal onlay BMG urethroplasty has shown a success rate from 87.5% to 100% with a follow up ranging from 22 to 41months.<sup>12,13</sup>

Results of our series are almost 90% at follow up of 3-36 months. Two patients developed stricture at anastomotic site and managed by OIU and CISC. One patient developed meatal stenosis and managed by meatoplasty. Our success rate for dorsal onlay buccal mucosa graft is comparable with other studies.<sup>12,13,14,15</sup> None of our patients developed significant complications or morbidity at donor site. Use of the AUA symptom scores to assess outcomes of urethroplasty was previously used in different series with BMG urethroplasty for bulbar urethral reconstruction.<sup>5,16</sup> In those series, it has already been reported that there is an inverse relationship between the peak urinary flow rate and AUA symptom scores.<sup>5</sup> Our study similarly comparable in preoperative and postoperative AUA symptom scores in successful cases. The result of the study is also compatible with above studies.

In conclusion, single stage oral mucous membrane graft urethroplasty for long segment anterior urethral stricture is a difficult procedure but the results are encouraging. This technique maintains natural shape of the penis and glans in functional and cosmetic points of views. Further long term follow up should be continued to confirm durability of the results.

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## Mastalgia of Women of Reproductive Age Group: Evaluation by High Resolution Breast Ultrasound & Serum Prolactin Hormonal Assay

Kamrun Nahar<sup>1</sup>

### Abstract

Mastalgia is a major complaints of the young women of the reproductive age group; hence a frequently used indication of the physicians to do high resolution breast ultrasound & serum prolactin hormonal assay. Ultrasound is the cost effective, non-invasive & sensitive diagnostic modality to establish a diagnosis or guide to other investigations to find out or to exclude the pathologies. Hyperprolactinaemia is also associated with mastalgia. The aim of the study was to evaluate the women of the reproductive age group with mastalgia by high resolution ultrasound & serum prolactin hormonal assay. This cross sectional study included 85 women of reproductive age group who were referred to CNMU, Sylhet in the period from April 2010 to May 2011 for high resolution breast USG & serum prolactin hormonal assay with the indication of mastalgia with or without galactorrhoea & lumpiness of breast. A detailed history was taken including menstrual history, history of mastalgia; either cyclical or a-cyclical; lactational history, past and family history of any breast disease, any trauma to the breast etc. The age ranges from 15 years to 45 years of women. Pregnant women, lactating mother & patients with recent trauma to the breast were excluded from the study. Drugs associated with hyperprolactinaemia were also excluded. Breast ultrasound was performed by Volusion 730 ProV using 7.5 to 12 MHz linear transducer, SIEMENS Model : 10033322 using 5 to 10 MHz linear transducer. For prolactin hormonal assay serum samples were taken from venous blood after centrifugation. The assay was done by RIA method which is a competitive binding method. Inter-assay & intra-assay quality control tests were also done for accuracy. The normal reference value of prolactin is < 460 mIU/L in case of women. Out of 85 patients, 62 patients (72.94%) were present with only mastalgia, 32 patients (37.65%) were present with mastalgia & lumpiness & 14 patients (16.47%) were present with mastalgia & galactorrhoea. Patient's complaints were categorized in relation of their

menstrual cycle. 52 patients (61.18 %) had cyclical mastalgia & 33 patients (38.82%) had non-cyclical mastalgia. The median duration of cyclical mastalgia was three years (mean 3.5 years) and that of non-cyclical mastalgia was one year (mean 2.1 years). The median age of cyclical mastalgia patients was 34.5 years (mean 34.63 years) and that of non-cyclical mastalgia patients was 38 years (mean 36.91 years). In USG findings 45 patients (52.94%) showed normal sonographic study, 26 (30.59%) patients detected fibro-cystic change, 06 patients (7.06%) showed dilated ectatic ducts, 04 patients (4.70%) detected fibro-adenoma, 02 patients (2.35%) showed solid irregular (malignant) masses & 02 patient (2.35%) showed abscess. All the positive USG findings were correlated with FNAC reports. Sonography & serum prolactin hormonal assay provided useful information for cause evaluation of mastalgia in reproductive age group & thus helps a lot in the management of the patients.

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### Introduction

Mastalgia means breast pain. Many of the young patients present with mastalgia, nodularity or asymmetry<sup>1</sup> but a small proportion may indeed present with a lump. Mastalgia usually indicates the presence of some underlying process or disease within the breast, which in most cases is benign. In general terms, mastalgia can be one of the two types-cyclical and non-cyclical; depending on the relationship to the menstrual cycle. Cyclical mastalgia is the most common type. Virtually almost all women experience a degree of pain or discomfort in their breasts at some time of their lives; this is normal and most often occurs in the week prior to menstruation. Cyclical mastalgia normally affects both breasts, but can be unilateral. Many women also feel "nodules" or "lumpiness" in the breast when the pain is present. Non-cyclical mastalgia, as its name suggests, is pain in the breast that is not related to the menstrual cycle. A number of conditions can give rise to non-cyclical mastalgia, each with certain additional symptoms

1. Senior Medical Officer  
Institute of Nuclear Medicine & Allied Sciences, Sylhet.

or clinical signs that aid diagnosis. Prolactin is a peptide hormone produced by the anterior pituitary gland primarily associated with lactation and plays a vital role in breast development during pregnancy. Hyperprolactinemia is the presence of abnormally-high levels of prolactin in the blood. Several physiologic and pathologic conditions can result in increased plasma prolactin levels. The aim of the study was to evaluate the women of the reproductive age group with mastalgia by high resolution USG & serum prolactin hormonal assay.

### Material and Methods

This cross sectional study included 85 women of reproductive age group who were referred to CMNU Sylhet for serum prolactin hormonal assay with the indication of mastalgia with or without galactorrhoea. Along with prolactin hormonal assay the patients were also referred for high resolution breast USG at CNMU, Sylhet. The study period was from April 2010 to May 2011. The age ranges from 15 years to 45 years of women. Pregnant women & lactating mother were excluded from the study. Breast ultrasound was performed by Volusion 730 ProV using 7.5 to 12 MHz linear transducer, SIEMENS Model : 10033322 using 5 to 10 MHz linear transducer.

Patients position was supine with ipsilateral arm comfortably elevated over the patient's head provides a more stable scanning surface. For the lateral margin of the breast -- patient can be rolled slightly toward the opposite side. The both axilla were also scanned to look for enlarged lymph node. For prolactin hormonal assay serum samples were taken from venous blood after centrifugation. All the assay were done by RIA method which is a competitive binding method. Inter-assay & intra-assay quality control tests were also done for accuracy. The normal reference value for prolactin is < 460 mIU/L in case of female. Pregnant women, lactating mother & patients already diagnosed and treated for breast lump, post-traumatic or post-infective breast swelling were excluded from the study. Drugs associated with hyperprolactinaemia were also excluded. A detailed history was taken including menstrual history, history of mastalgia, lactational history, past and family history of any breast problem.

### Results

Total 85 patients were evaluated by high resolution breast ultrasound & serum prolactin hormonal assay. Among them 62 patients (72.94%) were present with only mastalgia, 32 patients (37.47 %) were present with mastalgia & lumpiness of one or both breasts & 14

patients ( 16.47%) were present with mastalgia & galactorrhea, (Table 1).

Patient's complaints were categorized in relation of their menstrual cycle. 52 patients (61.18%) had cyclical mastalgia and 33 patients (38.82%) had non-cyclical mastalgia. The median duration of cyclical mastalgia was three years (mean 3.5 years) and that of non-cyclical mastalgia was one year (mean 2.1 years). The median age of cyclical mastalgia patients was 34.5 years (mean 34.63 years) and that of non-cyclical mastalgia patients was 38 years (mean 36.91 years) (Table II).

In USG findings, 45 patients ( 52.94%) showed normal sonographic study, 26 patients (30.59%) detected fibro-cystic change, 06 patients (7.06%) showed dilated ectatic lactiferous ducts, 04 patients (4.70%) detected fibro-adenoma, 02 patients (2.35%) showed solid irregular (malignant) masses & 02 patient ( 2.35%) showed abscess (Table III). In serum prolactin hormonal assay 35 patients (41.18 %) showed increased prolactin level & 50 patients (58.82%) showed normal prolactin level (Table IV).

### Discussion

Evaluation of breast pain is important to determine whether the pain is due to normal physiological changes related to hormonal fluctuation or to a pathological process such as breast cancer. One major benefit of ultrasound is to directly relate the physical examination findings with real time imaging results. Breast pain is usually mild, although approximately 11 percent of affected women will describe their pain as moderate to severe.<sup>2</sup>

In a large cohort of women 40 to 69 years of age enrolled in a health maintenance organization, breast pain was the most common breast related symptom prompting evaluation and accounted for almost one-half of breast related office visits.<sup>3</sup>

Breast pain may occur in one or both breasts or in the under arm (axilla) region of the body. Two thirds of screened patients in most series complain of breast pain, of which more than 50% is cyclical in nature.<sup>4-5</sup> It most often occurs during the luteal phase as a result of increased water content in breast stroma caused by increasing hormone levels.<sup>6</sup> While most patients only require reassurance of the benign nature of their complaint, up to 15% will require further therapy.<sup>7</sup> Studies have shown that in a standard breast clinic or general surgery practice setting, 15% of premenopausal women will have clinically significant cyclical mastalgia.<sup>8</sup>

The cause of cyclic breast pain is unclear. One theory, popular in Europe, suggests that higher than normal levels of the hormone prolactin may be involved.<sup>9</sup> Another theory attributes the condition to an imbalance of essential fatty acids.<sup>10</sup> Non cyclical mastalgia is more difficult to diagnose and treat, not only because it is difficult to pinpoint the cause but also because the pain is not hormonal.

Mastalgia is more common in pre-menopausal women than in postmenopausal women, and it is rarely a presenting symptom of breast cancer. Although one study found that 36 (15 percent) of 240 women with operable breast cancer reported having breast pain, only 16 (7 percent) presented with mastalgia alone.<sup>11</sup> The frequency of breast cancer reported for women presenting with breast pain ranges from 1.2 to 6.7 percent.<sup>12</sup>

Menstrual irregularity, emotional stress and medication changes have been shown to exacerbate mastalgia. Fibrocystic breast changes or fibrocystic breast disease is a condition of breast tissue affecting an estimated 30-60% of women and at least 50% of women of childbearing age.<sup>13</sup> It is characterized by multiple non-malignant lumps, which vary in size throughout the month and are frequently accompanied by premenstrual breast pain and tenderness. A benign component of premenstrual syndrome, FBD is considered a risk factor for breast cancer, but is not as significant a risk factor as family history, early onset of menstruation, and late or no first pregnancy. Because the condition is typically related to the normal hormonal fluctuations in a woman's body, tends to wane after menopause.

The fibrocystic condition refers to the tenderness, enlargement, and/or changing "lumpiness" that many women encounter just before or during their menstrual periods. It is primarily diagnosed based on the symptoms, clinical breast exam. The USG appearance of the breast in this condition is extremely variable since it depends on the stage and extent of morphological changes. In the early stages, the USG appearance may be normal, even though lumps may be palpable on clinical examination. There may be focal areas of thickening of the parenchyma, with or without patchy increase in echogenicity. Discrete single cysts or clusters of small cysts may be seen in some. Focal fibrocystic changes may appear as solid masses or thin-walled cysts. About half of these solid masses are usually classified as indeterminate and will eventually require a biopsy.<sup>14</sup>

An ultrasound shows whether the lump is a fluid-filled cyst or a solid lump. It also shows whether a cyst is a "simple cyst" or "complex cyst." It has excellent

contrast resolution. Simple cysts are typically round or oval and have smooth edges. Complex cysts can be filled with debris and may sometimes require aspiration to confirm that they are indeed benign cysts. Breast ultrasound is the best way to identify and diagnose breast cysts because it is accurate 95 to 100% of the time.

Cysts are a common cause of dominant breast masses in pre-menopausal women more than 40 years of age but an infrequent cause of such masses in younger women. In one study,<sup>15</sup> cysts accounted for only 10 percent of breast masses in women less than 40 years of age. Approximately 7% of all women will encounter a palpable cyst in their lifetime.<sup>16</sup> Although cysts may occur at any age, they are relatively uncommon in postmenopausal women who are not taking hormones. Ultrasound is commonly performed as they produce clear images of the breast and clearly distinguish between fluid-filled breast cysts and solid masses. The ultrasound exam can better evaluate dense tissue of the breast; hence it is often undergone by young patients, under 30 years old.

The most common cause of pathologic nipple discharge is intraductal papilloma, followed by duct ectasia.<sup>17</sup> If a palpable mass is present in association with a discharge, the likelihood of cancer is greatly increased.

Typically, duct ectasia may appear as a single tubular structure filled with fluid or sometimes may show multiple such structures as well. Old cellular debris may appear as echogenic content. (Figure 1) If the debris fills the lumen, it can be sometimes mistaken for a solid mass, unless the tubular shape is picked up. Correlation of duct widening with the "classical" symptoms of duct ectasia syndrome is unclear. However, duct widening was recently very strongly correlated with noncyclic breast pain.<sup>18</sup>

Elevated levels of other hormones (e.g., prolactin, estrogens) both internally produced and ingested as birth control pills, are known to increase prolactin secretion by the pituitary gland. In women with FBD, levels of prolactin are typically found to be elevated. Hyperprolactinemia causes typical symptoms in premenopausal women causes hypogonadism, manifested by infertility, oligomenorrhea, or amenorrhea<sup>19</sup> and less often by galactorrhea.

In conclusion, mastalgia is a frequent complaint of women of reproductive age group and it may represent various pathological conditions. The uncertainty over the presence of a lump or induration (nodularity) of the breast can be frightening to a woman and needs proper clinical assessment & diagnostic evaluation like high resolution breast USG & serum prolactin hormonal assay.

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## Mycetoma of Hand: a case report with unusual presentation

Swajal Chandra Das<sup>1</sup>, N.K.Paul<sup>2</sup>, Mostaque Ahmed Bhuiyan<sup>1</sup>,  
 Md. Ashikur Rahman<sup>2</sup>, Nibedita Das Pew<sup>3</sup>

### Abstract

Mycetoma is a chronic granulomatous disease characterised by localised infection of subcutaneous tissues by actinomycetes or fungi. The inflammatory response can extend to the underlying bone. Mycetoma implantation occurs mainly in the bare foot in semi desert regions throughout the tropics. The skull and knees may also be implanted, usually by thorns. Mycetoma was described first in the mid-1800s and was initially called Madura foot, as mainly affecting the foot. The affection of hand is uncommon. We present here a case of middle age women who presented with swelling, multiple nodular lesions, burning sensation, discharge and gradual restriction of movement for long times. Radiograph showed extension in bone and soft tissue with patchy areas of bone destruction, reactive sclerosis and a shaggy periostitis with bone resorption involving 3<sup>rd</sup>, 4<sup>th</sup>, 5<sup>th</sup> metacarpal bones. She was treated conservatively.

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### Case report:

A 40 years old female, housewife, from a village of Jogonnathpur, Sunampong presented with complaint of gradually increasing painless nodular swelling of the right hand associated with progressive development of discharging sinuses, of about 8-10 years duration. She did not give any positive history of direct prick or any significant trauma & noticed gradual nodular swelling (Figure1) over right hand for last few years. She also complains of burning sensations over the lesions. She took symptomatic treatment from local practitioners. About 07 months back she was admitted in Sylhet

MAG Osmani Medical College Hospital for better treatment.

Local examination revealed a diffuse swelling with multiple nodules & tumors varying in sizes from 1x3 cm in diameter present over right hand predominantly at dorsum, sparing the fingers and thumb.

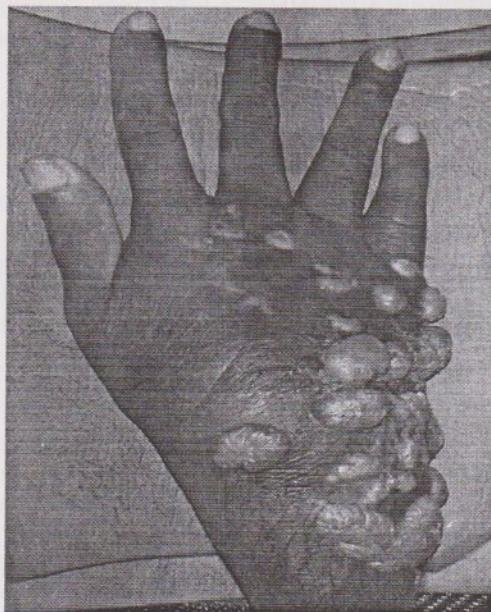


Figure 1: Dorsal and ventral aspect of hand showing nodular swelling and discharging sinuses.



Figure 2: Radiograph shows patchy areas of bone destruction, irregular sclerosis involving 3<sup>rd</sup>, 4<sup>th</sup>, 5<sup>th</sup> metacarpal bones with periosteal reaction.

2. Assistant Professor of Radiology & Imaging, Sylhet MAG Osmani Medical College
3. Associate Professor of radiology & Imaging, Sylhet MAG Osmani Medical College
4. Assistant Professor of Pathology, Sylhet MAG Osmani Medical College.

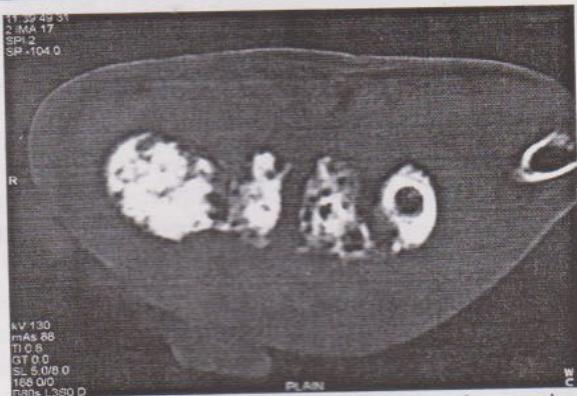


Figure 3: CT scan shows irregular bone destruction & sclerosis involving 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup>, 5<sup>th</sup> metacarpal bones. She was diagnosed as a case of mycetoma of hand & is treating currently with conservatives .Histological examination of skin from hand confirmed the diagnosis. She continued the treatment for 07 months and the sinus got healed.

### Discussion

Mycetoma is a chronic infection caused by actinomycetes or fungi, or both. This infection results in a granulomatous inflammatory response in the deep dermis and subcutaneous tissue, which can extend to the underlying bone. Mycetoma is characterized by formation of grains containing aggregates of organisms that may discharge through the skin surface via multiple sinuses. This disease was described first in 1842 and initially names Madura Foot, after the region of Madura in India, where it was first identified.<sup>1</sup>

More than 20 species of fungi and bacteria can cause mycetoma. About 60% of mycetoma is caused by bacteria (actinomycetomas), and 40% is caused by true fungi (eumycetoma). This condition is endemic to Africa, Mexico and India. The disease also can be found in areas of Central and South America as well as in the Middle East or Far East between latitude 15°S and latitude 30°N. No particular risk based on race has been described. The male-to-female ratio is 5:1. It most frequently is found in patients aged 20–40 years.<sup>1</sup> Infection of the foot (and less commonly the hand, arm, leg or scalp) results from posttraumatic soft tissue invasion by organisms that live in the soil.<sup>1</sup> We report a case of mycetoma hand though patient unable to noticed any significant trauma.

It commonly occurs on foot followed by hand, knee, arm, leg, head and neck, thigh and the perineum. Other rare sites include eyelids, testes, lymph node and middle ear cleft<sup>2</sup>.

Different organisms are found in different regions—*M.mycetoma* in the middle East, Africa and India, and *S.somaliensis* and *pelletieri* in the Sudan<sup>3</sup>. In our patient, causative organism was actinomycosis.

Lesions due to *M. mycetoma* are usually localised as large well defined black fungus balls which can be seen on soft tissue radiographs. These erodes the cortices and cause cystic defects in the medulla. With superadded infection via the implantation track, gross bone destruction results. Reactive sclerosis and a shaggy periostitis with bone resorption give an appearance likened to 'melting snow'<sup>3</sup>. In our patient, soft tissue swelling with nodules ,irregular bone destruction, sclerosis, shaggy periostitis was found on radiograph & CT scan.

Plain radiographic classification of the pattern, extent and severity of bone involvement in mycetoma of the foot can be used in planning and monitoring treatment response.<sup>4</sup> In this classification, stage 0 indicates the presence of only soft tissue swelling without bone involvement. Stage 1 refers to the extrinsic pressure effects on the intact bones in the vicinity of an expanding granuloma. Stage 2 reflects periosteal reaction of the bone without actual intraosseous invasion. Cortical erosion and medullary invasion occurs in stage 3. If the disease spreads longitudinally along a single ray, this is defined as stage 4. Horizontal transverse spread along a single row represents stage 5. Multidirectional spread due to uncontrolled infection is classified as stage 6.<sup>4</sup> Our patient shows multidirectional spread. Plain x-rays are used to assess evidence of bone involvement. CT scan or MRI may be more sensitive in the early stages.

The organism is inoculated traumatically through soil in the form of thorn prick, trauma leading to ulceration, blunt trauma and wicks. Clinically they present as progressive granulomatous lesion, sinus tract formation and discharge of grains, tumefaction and spreading into adjacent tissue, bone fascia and ligaments<sup>4</sup>. The clinical findings of our patient nearly the same as other authors.

The grains discharged from sinus tracts may be white, yellow, brown, red or black depending upon the causative agent<sup>4</sup>. Discovery of these typical grains which are compact colonies of the causative organism and their direct microscopically and cultural examination clinches the diagnosis and differentiates this condition from superficially similar disease like tuberculosis, leprosy, syphilis, elephantiasis, blastomycosis, neoplasm and others. Microscopic

examination of the granules shows branching hyphae and spores.

The treatment is by specific chemotherapeutic agents against the causative organism with or without surgery. Several clinical strategies are available for the treatment which includes surgery, ketoconazole, voriconazole, itraconazole and amputation<sup>5</sup>. Amputation may be required for some resistant cases. Ketoconazole or Itraconazole in combination with surgical intervention is recommended for eumycetoma. But, in all cases medical supervision is required as this condition is prone to recurrences.<sup>6</sup>

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## Gastric Teratoma in a 3<sup>1</sup>/<sub>2</sub> months old male baby: A rare case report and literature review

Md. Shamsur Rahman<sup>1</sup>, Foysol Ahmed<sup>2</sup>, Md. Sirazul Islam<sup>3</sup>

Md. Ibrahim Khalil<sup>3</sup>, Abdus Salam Howlader<sup>4</sup>, Md. Abed Hossain<sup>5</sup>

### Abstract

Gastric teratomas are very rare tumours and accounts for less than 1% of all teratomas occurring in infants and children. It is usually seen in male infants who present with upper abdominal mass and commonly it is benign. This report describes a large immature gastric teratoma in a 3<sup>1</sup>/<sub>2</sub> months old male infant who presented with a palpable mass in abdomen, occupying upper half of abdomen. The mass was excised completely with portion of the stomach wall. The rarity of the origin of teratoma in addition to its immature variety prompted us to report this case.

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### INTRODUCTION

Teratomas are relatively common embryonal tumors that arise from totipotent cells and usually contain elements from all the three germ layers, ectoderm, endoderm and mesoderm<sup>1</sup>. Commonly, they are seen in the ovary, testes, sacrococcygeal area and retroperitoneal space. They can be benign or malignant<sup>2</sup>. Gastric teratomas on the other hand are very rare, usually seen in male infants and who present with a palpable upper abdominal mass that can attain a large size.

The histopathology confirms the diagnosis. The recommended therapy for gastric teratomas is total surgical excision. This report describes a large immature gastric teratoma in a male infant.

1. Associate Professor, Department of Paediatric Surgery, Sylhet MAG Osmani Medical College, Sylhet.
2. MS, Paediatric Surgery, Thesis Part Student, Sylhet MAG Osmani Medical College, Sylhet.
3. Assistant Registrar, Department of Paediatric Surgery, Sylhet MAG Osmani Medical College, Sylhet.
4. Anaesthesiologist, Department of Anaesthesiology, Sylhet MAG Osmani Medical College Hospital, Sylhet.
5. Professor of Pathology, Jalalabad Ragib-Rabeya Medical College, Sylhet.

### Case report:

A three and half month old male infant presented with a mass in abdomen, noted by parents at the age of one and half months that has progressed rapidly. Last 15 days patient developed respiratory distress specially on lying posture. Physical examination showed a pale, lethargic and irritable infant with stable vital signs. Abdomen was distended with a palpable intra-abdominal, slightly tender mass that occupies the epigastrium, both hypochondrium, most of umbilical and left lumbar regions. The mass is about 15x13 cm size, firm to hard in consistency with uneven surface and ill defined margins ( Picture-1 ).

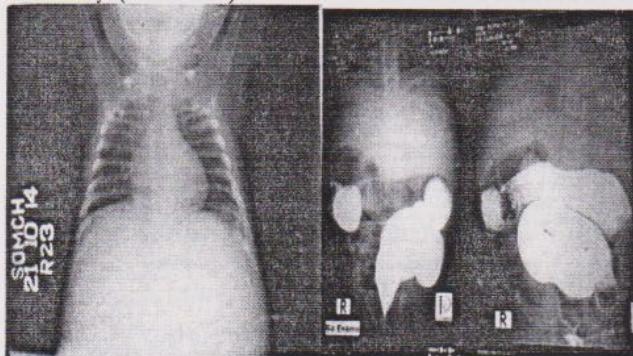


Pic 1: pre -operative view

Systemic examination revealed no abnormalities. Laboratory examination showed hemoglobin-6.6 gm/dl, ESR-120 mm in first hour. The alpha fetoprotein was more than 450ng/dl. Others laboratory parameters were within normal limits.

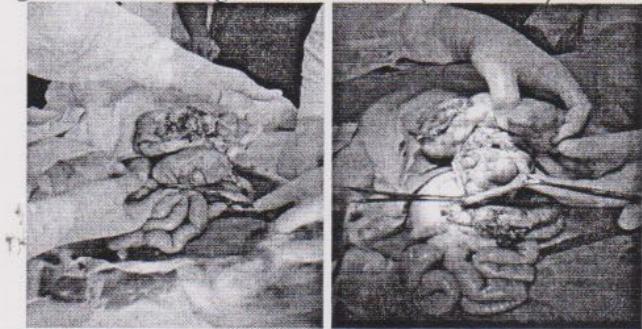
Abdominal ultrasound showed a large mixed echoic lesion (12.6 cmx9.4 cm) noted in the left upper and mid abdomen which is closely related to left lobe of liver and separated from left kidney and spleen. Abdominal radiograph depicted a homogenous

opacity with no calcification occupying most of the abdominal cavity and displacing the bowel inferiorly (Picture-2). Barium enema X-ray indicated the transverse and descending colon to be displaced inferiorly (Picture-3).



Pic 2; plain X-ray abdomen. Pic 3; Barium enema. Upper gastro-intestinal contrast X-ray study and CT scan were not performed.

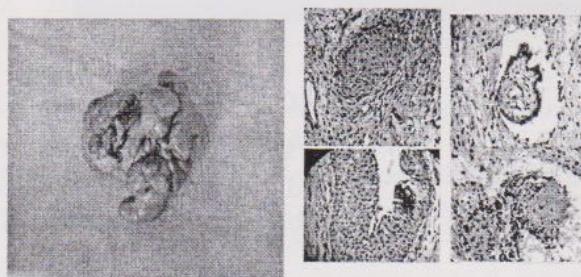
Preoperative differential diagnoses were neuroblastoma, retroperitoneal teratoma and abdominal lymphoma. Patient was explored through a supra-umbilical transverse incision and was found to have a large abdominal tumor occupying most of the abdominal cavity. The tumor arising from the anterior wall of the stomach near the lesser curvature, away from esophago-gastric junction (Picture-4). There was no sign of metastasis. The tumor had exogastric and endo-gastric extension (Picture-5)



Pic 4: Tumor arising from Stomach, Pic 5 : tumor with exo-gastric and endo-gastric extension

Excision in-toto including the involved stomach wall was performed. The defect created was closed in two layers.

The excised tumor was 13x11.5x10 cm in size and weight 800 grams, consisted of multinodular bluish-white soft tissue that appeared encapsulated with a filamentous membrane (Picture-6). Specimen was sent for histopathology. Features were consistent with immature teratoma (Picture7).



Pic 6; excised tumor

Postoperative course was uneventful. On 10<sup>th</sup> POD, the alpha fetoprotein level decreased to 218 ng/dl.

## Discussion

The frequently occurring teratomas in pediatric patients comprise of sacrococcygeal teratoma followed by those originating from mediastinum, gonads, retroperitoneal region and so on. Gastric teratomas are extremely rare tumours and cases are frequently reported in infancy and neonatal period (> 90%), however, there have been reports of this tumour in older children as well<sup>9</sup>. For unknown reasons, there is a male preponderance with 90% of cases reported in boys and mostly seen in infants<sup>3,4,12, 14,15</sup>.

First case of gastric teratoma was reported in 1922 by Eustermann et al.<sup>11</sup> Over a period of 54 years, Curtis et al.<sup>7</sup> reported 21 infants and children with primary gastric tumors, 4 of them only had immature gastric teratoma<sup>1</sup>. The site of origin of gastric teratoma is variable though most of the cases have been reported to arise from the greater curvature and posterior wall of the stomach, however, other sites such as lesser curvature have also been documented<sup>16</sup>. In our case tumor originated from the anterior surface of stomach, near the lesser curvature away from the esophago-gastric junction.

The clinical features depend upon the site of origin, size, and endo-gastric component. Exogastric growths are common (58-70%) in contrast to endogastric growths (30%). The usual features are abdominal distension and mass followed by vomiting, constipation, and respiratory distress. In case of intramural extension the patients may present with hematemesis, abdominal pain, melena, vomiting, and rarely with gastric perforation<sup>16,17</sup>. Our patient belonged to both exo-gastric and endo-gastric variety that presented as abdominal mass with respiratory distress. Abdominal radiograph usually delineates a mass effect that displaces the bowel gas shadows to a side. In about 50% cases, abdominal radiographs

shows calcifications and bone densities which are hall marks of intra-abdominal teratomas. CT scan is the modality of choice. When combined with intravenous and oral contrasts, they can detect the origin of the tumour, its relation with gastrointestinal tract and major blood vessels, presence of bones and calcifications, tumour extent and presence of metastasis. Other modalities like barium meal and gastroscopy has a limited role in the diagnosis of gastric teratoma<sup>16,17,18</sup>. In this case abdominal radiographs showed mass effect without calcification and displacement of bowel loops inferiorly. The monitoring of AFP and beta-HCG reflect the treatment response after excision and may be of significant value where chemotherapy is recommended (immature variety)<sup>16</sup>. In our case the preoperative AFP level was reduced significantly after 10 days of excision. The histopathology confirms the diagnosis and specifies the maturity of the teratoma. A grading system, based on histopathological findings, divides the gastric teratoma in two main types, mature teratoma (grade 0) and immature teratoma (grades 1, 2, 3). Mature teratoma is characterized by well differentiated tissues from all the three germinal layers. Immature teratoma on the other hand is characterized by the presence of immature neuroectodermal tissue along with other germinal layers structures. Immature teratomas are divided into three grades. In grade 1, the immature neuroectodermal tissue is confined to one site in a slide, whereas in grades 2 and 3, the immature tissue is found in less than 4 and more than 4 fields per slide, respectively. Till date only about 100 cases of gastric teratomas are recorded, of which less than 15 cases of immature variant have been described.

Malignant potential increases with higher histopathological grades<sup>3,4,5,6,7,8,13,15</sup>. Our case falls in grade 3 immature teratoma on the basis of presence of immature neuroglial element at multiple sites. The management of gastric teratoma is surgical excision of the tumor and part of its attachment to the stomach. This is usually curative and rarely partial or total gastrectomy is necessary<sup>19</sup>. The majority of gastric teratomas however are benign and in the presence of immature neuroepithelium tissue, these tumors are considered malignant, but even then, the prognosis is excellent after total excision. Many authors depicted no recurrence after complete excision of the immature gastric teratoma even in grade 2 and 3; and there had not been any use of postoperative chemotherapy or radiotherapy, however in a case where the AFP start rising after few months of complete excision of

teratoma, chemotherapy is added<sup>16,17,18</sup>. Gupta et al.<sup>3</sup> in a review of 10 cases of gastric teratomas reported 2 patients with immature grade 3 gastric teratoma, one of them infiltrated the left lobe of the liver and the transverse colon, while the other had metastasized to the regional lymph nodes and omentum but in spite of this and following complete excision, there was no recurrence after a mean follow-up of 4.2 years without chemo or radio therapy. Bourke et al.<sup>5</sup> reported a malignant gastric teratoma in a 4-month-old male child that was totally excised and was well after 12 month follow-up. Balik et al.<sup>6</sup> reported the second case of malignant gastric teratoma in an infant that was also treated by total excision. Ukiyama et al.<sup>10</sup> on the other hand reported a recurrent yolk sac tumor following resection of a neonatal immature gastric teratoma. This calls for a close follow-up of all patients with immature gastric teratoma. Serum alpha fetoprotein is a useful marker in these patients for evidence of recurrence or the presence of residual tumor.

In conclusion, Gastric teratomas are extremely rare tumours and must be considered in the differential diagnosis of childhood abdominal tumors. The majority of gastric teratomas are benign, and total surgical excision is curative even in malignant cases. A close follow-up is however mandatory for those with immature gastric teratoma.

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