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## **Dengue in Bangladesh 2019**

Dengue is the talk of the town at this moment in Bangladesh. A major outbreak in 2019, surpassing all records with a high mortality has terrorized the entire nation. Dengue is the most rapidly spreading mosquito-borne viral disease in the world. In the last 50 years, incidence has increased 30-fold.<sup>1</sup> An estimated 50–100 millions of dengue cases occur yearly resulting in 500,000 hospitalizations and 25,000 deaths.<sup>2</sup>

Dengue virus is an RNA virus from Flavivirus family, with four serotypes and transmitted by mosquito species *Aedes aegypti* and *Aedes albopictus*.<sup>3</sup>

The first record of a case of probable dengue fever is in a Chinese medical encyclopedia from the Jin dynasty (265–420 AD) which referred to a 'water poison' associated with flying insects.<sup>3</sup> In 1906, transmission by the *Aedes* mosquitoes was confirmed.<sup>4</sup> Ren Kimura and Susumu Hotta first isolated the dengue virus in 1943.<sup>4</sup>

The patterns of dengue viral diseases vary and include commonly mild undifferentiated fever, classical dengue fever (DF) and dengue haemorrhagic fever (DHF) often leading to dengue shock syndrome (DSS). Classical dengue fever is manifested as fever, pain symptoms (headache, muscle and joints pain, retro-orbital pain), rash and gastrointestinal symptoms (vomiting and diarrhoea), lasting for 3-4 days. DHF is characterized by widespread plasma leakage, as the fever subsides (Critical phase), that lasts 24-48 hours. Apart from capillary leakage and hypovolaemic shock; haemorrhage, hepatitis,

myocarditis, acute kidney injury and encephalitis are also reported in DHF.<sup>5</sup>

Dengue fever is classified into three groups for management purpose. Group A are dengue cases without any warning sign, can be managed at home. Group B comprises dengue patients with warning signs or co-morbid conditions like pregnancy and chronic organ failures need hospital admission. Group C, also called severe dengue, must be managed in hospital, and intravenous fluid is usually required.<sup>6</sup>

Dengue infection is diagnosed with NS1 antigen in the first 4 days or anti-Dengue IgM from day 7 onwards. None of these tests is positive on day 5-6 (window period of Dengue).<sup>6</sup> Complete blood count is of extreme importance as presence of leucopenia and thrombocytopenia indicate impending critical phase of DHF. Packed cell volume (PCV) is necessary to define DHF and also its value determines the treatment of DSS.<sup>6</sup>

DSS is defined as fall of SBP < 90 mm of Hg or DBP < 60 mm of Hg with other signs of shock [de-compensated shock] or a narrow pulse pressure of < 20 mm of Hg [compensated shock]. DSS is managed with judicious use of intravenous fluids and blood. Initial management includes rapid infusion of crystalloid solution, commonly Normal Saline. Refractory cases are treated with either rapid infusion of colloid solution, commonly Starch in Bangladesh (when PCV ≥ 45 percent) or blood (when PCV < 45 percent). Progressively slower infusion of normal saline is used



thereafter as the blood pressure improves and maintained for 24-48 hours.<sup>6</sup>

Southeast Asia is regarded as home of dengue viral diseases. In 1964, DENV-3 was responsible for classical dengue fever in Dhaka (Dhaka fever). In 1999, an outbreak of dengue fever with few cases of DHF was reported in Dhaka.<sup>7</sup> Most of the cases of Dengue occur in monsoon (May-August) and Post-monsoon (September-December) seasons, 50 & 49 percent, respectively, in Bangladesh.<sup>8</sup>

The escalating dengue situation in Bangladesh has been emerging as a serious public health problem. After a drop in the number of cases in 2017-18, sharp increase in cases is being observed in 2019. Number of cases reported till 18 August 2019 is 53182, which is almost seventeen-times that of the same period of 2018 (3175 cases).<sup>8</sup> Majority of the cases have been reported to be infected with DENV-3 serotype.<sup>8</sup> The most alarming part of this year's outbreak is the higher proportion of severe dengue and early severe complications, even in the febrile phase. Major haemorrhage is still extremely rare this year.<sup>8</sup> Careful monitoring of vital signs and fluid management are recommended as the cornerstone of treatment of severe dengue infection by Directorate General Health Services (DGHS). It is also advised to follow the National Guideline for Clinical Management of Dengue Syndrome (4<sup>th</sup> Edition, 2018) strictly. Use of Platelet concentrate, apheretic platelet, fresh frozen plasma, platelet rich plasma or intravenous immunoglobulin is strongly discouraged as these were found to be ineffective and often harmful in DHF and DSS in many studies.<sup>6</sup>

Use of full-sleeve dress, mosquito repellants and mosquito nets can prevent dengue infection. Vector control is crucial at this

moment. A prompt and effective measure by the concerned authorities is keenly expected to combat this deadly outbreak.

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## **Frequency of Head Neck Disease Surgery and its Outcome at District level Hospital of Bangladesh**

Moniruzzaman MM<sup>1</sup>, Nasser MJA<sup>2</sup>, Hanif A<sup>3</sup>, Islam T<sup>4</sup>, Pandit S<sup>5</sup>

### **ABSTRACT**

**BACKGROUND** : Neck diseases are common clinical problem throughout the world. These are also common clinical problem in Bangladesh.

**OBJECTIVE** : The purpose of the study was to know the frequency of head neck disease surgery in a district level hospital of Bangladesh and also to know the outcome of such surgery in the same setting.

**METHOD** : This prospective study was carried out during the period from August 2013 to June 2017, in the department of Otolaryngology, Head and neck surgery, Sheikh Hasina Medical College Hospital, Tangail. All patients admitted during the study period in the hospital, as a case of head-neck disease and needed surgery, were included in the study.

**RESULTS** : In this study majority of the patients were within 31- 60 years of age. Out of 110 patients, 81 patients (73.6%) were female and 29 patients (20.4%) were male. This shows female preponderance of neck disease. From the diagnosis report of neck specimen, over all incidence of multinodular goiter were 36.4%, solitary thyroid nodule were 13.6%, papillary carcinoma of thyroid 9.1%, adenocarcinoma minor salivary gland were 1.8%, tubercular lymphadenitis were 13.6 %, thyroglossal cyst, warthin tumour, pleomorphic adenoma, chronic sialadenitis, epidermal inclusion cyst each were 4.5% & chylocele, mucoepidermoid carcinoma of parotid, metastatic carcinoma of unknown origin each were 0.9%. Among these cases 102 (92.7%) had no malignant cell and 8 (7.3%) cases had malignant cell. Among 110 patients, 103 had no post-operative complications. Among the rest 7, 1 patient had left recurrent nerve injury, 1 had unilateral (right) recurrent nerve injury, 1 had zygomatic branch of facial nerve injury & 4 had parathyroid deficiency after surgery.

**CONCLUSION** : Surgery is the safer option in head neck diseases where surgery is indicated. With no or minimum complications, patient can lead a normal life after surgery.

**KEY WORDS** : Head Neck Disease, Surgery outcome , District level hospital

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## INTRODUCTION :

Neck diseases are common clinical problem throughout the world<sup>1</sup>. These are also common clinical problem in Bangladesh<sup>2</sup>. Most of the neck diseases are multinodular goiter, nodular goiter, papillary carcinoma of thyroid, thyroglossal cyst, warthin's tumour, pleomorphic adenoma, chronic sialadenitis, adenocarcinoma minor salivary gland, chylocele, epidermal inclusion cyst, tubercular lymphadenitis, metastatic carcinoma, mucoepidermoid carcinoma etc<sup>3</sup>. Most of these incidence occurred between 18-70 years of age. Majority of the people are affected by these diseases in the middle age 31-50 years of age. Diagnose report showed that females are more affected than male such as male female ratio 1:3<sup>1</sup>.

The patients who are affected by head-neck diseases, most of them has to undergo surgery. Most of the operations that are usually performed in neck disease are<sup>4</sup> :

1. Subtotal thyroidectomy
2. Hemi thyroidectomy
3. Total thyroidectomy
4. Superficial parotidectomy
5. Excision of the submandibular gland
6. Excision gland with neck dissection
7. M.N.D (Modified neck dissection)
8. Excision lymphnode
9. Radioiodine ablation
10. Neck dissection
11. Excision

With development of more effective chemo-radiation regimens, role of neck surgery have lessened in some cases where significant improvement in initial loco-regional control rates have been achieved.

Complications following neck surgery are a possible outcome like any other surgery. Globally speaking , among patients who had

undergone neck surgery, only 6.4% had some sort of complications post operatively<sup>5</sup>. Possible complications of head neck surgery are injury to the left and right Recurrent & Zygomatic branch of Facial nerve, Hypo-parathyroidism.

The purpose of this study was to know the frequency of head neck disease surgery in a district level hospital of Bangladesh and also to know the outcome of such surgery in the same setting.

## MATERIALS & METHODS :

This prospective study was carried out during the period from August 2013 to June 2017, in the department of Otolaryngology, Head and neck surgery, Sheikh Hasina Medical College Hospital, Tangail.

All patients admitted during the study period in the hospital, as a case of head-neck disease and needed surgery, were included in the study. Diagnosis of all the cases was done by detailed history, clinical examination & relevant investigations (Thyroid Hormone assay, Ultra sonogram, Thyroid scan, FNAC and Histopathological examination).

## RESULTS :

A total of 110 patients got admitted during the study period in the hospital, as a case of head-neck disease and needed surgery. Among them 81 (73.6%) were female & 29 (26.4%) were male (Table I) .

**Table I : Gender distribution of Patient (n=110)**

Gender	No. Of patient	Percentage (%)
Male	29	26.4
Female	81	73.6
	110	

**Table II : Frequency of Age distribution of the patients (n=110)**

Age of patient (years)	No. of patient	Percentage (%)
0-10	0	0
11-20	4	3.6
21-30	7	6.4
31-40	35	31.8
41-50	32	29.1
51-60	25	22.7
61-70	7	6.4
>70	0	0
110		

**Table III : Frequency of Disease diagnosis of the study subjects (n=110)**

Disease diagnosis	No. of patient	Percentage (%)
Multi-nodular goiter	40	36.4
Solitary Thyroid Nodule	15	13.6
Papillary carcinoma of thyroid	10	9.1
Thyroglossal cyst	5	4.5
Warthin's tumour	5	4.5
Pleomorphic adenoma	5	4.5
Chronic sialadenitis	5	4.5
Adenocarcinoma minor salivary gland	2	1.8
Chylocele	1	0.9
Tubercular lymphadenitis	15	13.6
Epidermal inclusion cyst	5	4.5
Mucoepidermoid carcinoma	1	0.9
Metastatic carcinoma of unknown origin	1	0.9
110		

Table II shows the frequency of age distribution of the patients. Out of 110 patients, no patients were found <10 years , 4 patients (3.6%) were between 11-20years , 7 patients (6.4%) were between 21-30 years, 35

patients (31.8%) were between 31-40 years, 32 patients (29.1%) were between 41-50 years, 25 patients (22.7%) were between 51-60 years, 7 patients (6.4%) were between 61-70 years of age group. No patients were found above 70 years of age.

Among 110 patients, 40 were diagnosed as having multi-nodular goiter, 15 as solitary Thyroid Nodule, 10 as papillary carcinoma of thyroid, 5 as thyroglossal cyst, 5 as warthin's tumour, 5 as pleomorphic adenoma, 5 as chronic sialadenitis, 2 as adenocarcinoma minor salivary gland, 1 as chylocele, 15 as tubercular lymphadenitis , 5 as epidermal inclusion cyst, , 1 as metastatic carcinoma & 1 as mucoepidermoid carcinoma (Table III).

**Table IV : Frequency distribution of different types of surgery done on study subjects (n=110)**

Types of surgery	No. of patients	Percentage (%)
Subtotal thyroidectomy	40	36.4
Hemi thyroidectomy	15	13.6
Total thyroidectomy	10	9.1
Superficial Parotidectomy	5	4.5
Excision in the sub-mandibular gland	5	4.5
Excision gland with neck dissection	2	1.8
M.N.D	1	0.9
Excision lymph node	15	13.6
Radioiodine ablation	10	9.1
Total parotidectomy	1	0.9
Neck dissection	1	0.9
Excision	5	4.5
110		

Table IV shows the different types of surgery done on the study subjects with their frequencies. Subtotal thyroidectomy were performed on 40(36.4%) patients ,Hemi thyroidectomy on 15(13.6%), Total thyroidectomy on 10(9.1%), Superficial

Parotidectomy on 5(4.5%) , Excision of the sub-mandibular gland on 5(4.5%), Excision gland with neck dissection on 2(1.8%), M.N.D on 1(0.9%), Excision lymph node on 15(13.6%), Radioiodine ablation on 10(9.1%),Total parotidectomy on 1(0.9%),Neck dissection on 1(0.9%)& Excision on 5(4.5%) patients.

**Table V : Frequency of malignancy of the study subjects (n=110)**

	No. of patient	Percentage (%)
No malignant cell	102	92.7
Malignant cell	8	7.3
	110	

**Table VI : Sex distribution of the study subjects in relation to malignancy**

Malignancy	Sex of the patient		Total
	Male (%)	Female (%)	
No malignant cell	27 (26.4%)	75 (73.6%)	102 (92.7%)
Malignant cell	2 (25%)	6 (75%)	8 (7.3%)

102 (92.7%) patients had no malignant cell , out of which 73.6% were female & 26.4% were male. 8 (7.3%) patients had malignant cell , out of which 75% were female & 25% were male. (Table V & VI). Table VII shows the frequency of malignancy in different disease diagnosed on study subjects.

103 (93.6%) patients had no post-operative complications. Besides that, 1(0.9%) patient had left recurrent nerve injury, 1(0.9%) had unilateral (right) recurrent nerve injury, 1(0.9%) had zygomatic branch of facial nerve injury & 4 (3.6%) had parathyroid deficiency after surgery. (Table VIII)

**Table VII : Frequency of malignancy in different disease diagnosed on study subjects**

Diseases	Malignancy	
	No malignant cell	Malignant cell
Multinodular goiter	40	0
Solitary Thyroid Nodule	15	0
Papillary carcinoma of thyroid	6	4
Thyroglossal cyst	5	0
Warthin's tumour	5	0
Pleomorphic adenoma	5	0
Chronic sialadenitis	5	0
Adenocarcinoma minor salivary gland	0	2
Chylocele	1	0
Tubercular lymphadenitis	15	0
Epidermal inclusion cyst	5	0
Mucoepidermoid carcinoma	0	1
Metastatic carcinoma	0	1
	102	8

**Table VIII : Frequency of Post-operative complications**

Post-operative complications	No. of patient	Percentage (%)
No complication	103	93.6
Left Recurrent nerve injury	1	0.9
Parathyroid deficiency	4	3.6
Unilateral (Right) recurrent nerve injury	1	0.9
Facial nerve injury (zygomatic branch)	1	0.9
	110	

**DISCUSSION :**

In this study, age of the 110 patients ranges from 18 to 70 years. But most (83.6%) of the patients were in the age range 31-60 years of age. Age distribution is more or less similar to other studies of different geographical location<sup>1</sup>.

In this study, out of 110 patients 73.6% were female and 26.4% were male, with male to female ratio 1:2.8. Female preponderance also found in other studies that was firmly consistent with this study<sup>1</sup>.

Among the head neck diseases that got admitted into the hospital during the study period, Multinodular goiter was the commonest (36.4%). Multinodular goiter is also the commonest endocrine problem worldwide<sup>5</sup>. Male female ratio of 1:5.6 shows female preponderance, which is consistent with the finding of other studies<sup>2-5</sup>.

The incidence of solitary nodular goiter globally is approximately 0.1% to 1.5% per year<sup>6</sup>. In our study, 13.6% were affected by nodular goiter with a male female ratio of 1: 6.5. This also correlates with other studies<sup>6,7</sup>.

Frequency of papillary carcinoma of thyroid in this study was 9.1%, with a male female ratio of 1:4. Average age of these patients was 35±11.2. That means the patients were below 50 years of age which corresponds with other studies as well<sup>8,9</sup>.

Male female ratio for thyroid gland swelling in this study was 1:4 and mean age 40±11.2, which corresponds with other findings<sup>10, 11</sup>. Frequency of Thyroglossal cyst, warthin's tumour, Pleomorphic adenoma, Chronic sialadenitis and Epidermal inclusion cyst was same (4.5%). This correlates with finding of other studies<sup>12-16</sup>.

Warthin's tumour is very rare in female. In our study, male female ratio of warthin's tumour was 4:1 and mean age 55. Male preponderance of this tumor occurring in middle age group also correlates with other studies<sup>12, 13</sup>.

Metastatic carcinoma of unknown origin is a very rare disease. We found only 1 male

patient & malignant cell was present. The age (70 yr) & gender correlates with finding of others<sup>17</sup>.

13.6% of our patients had tubercular lymphadenitis. Most of the patients were in the age range of 31-60 years with a male female ratio of 1:2. But another study done in Tanzania showed tubercular lymphadenitis occurring in younger patients of <30 years<sup>20</sup>.

Mucoepidermoid carcinoma is the most common type of salivary gland malignancy in adult. In our study we found only one 50 year old female, where malignant cell was present. We got one 35 year old female patient affected by chylocele & 2 patients affected by Adenocarcinoma minor salivary gland. In all cases malignant cell was present. Frequency, age distribution of such malignancies was similar in other parts of the world as well<sup>21-23</sup>.

Sheikh Hasina Medical College Hospital, Tangail is a district level hospital. All the above-mentioned head neck diseases were treated by surgical procedures. Appropriate surgical procedures were undertaken for specific type of neck diseases (Table IV). Though neck surgery is the safest treatment option for almost all above mentioned neck diseases, but complications of surgery is an unavoidable outcome. During our study period, out of 110 cases, only 7 patients experienced post-operative complications. The rest 103 patients experienced normal recovery following surgery.

The nature of complications in those 7 patients was varied according to the type of operation performed. The most common complication encountered was parathyroid deficiency (4 patients). Nerve injury also occurred in three separate occasions. The nerves injured were left recurrent nerve, unilateral (right) recurrent nerve & zygomatic

branch of facial nerve. Head neck disease surgery in different parts of the world produces similar kind of complications<sup>24-26</sup>.

### CONCLUSION :

With no pre or post-operative deaths, we can say that surgery is the safer option in above-mentioned head neck diseases. With no or minimum complications, patient can lead a normal life after surgery.

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## **Serum Electrolyte Level of Male Football Players in a Sports Academy of Bangladesh**

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### **ABSTRACT**

**BACKGROUND** : Football players have to go through regular intensive exercise and training. This exercise and training may results in functional changes in their electrolyte level. Among serum electrolytes sodium, potassium, chloride, bicarbonate levels are mostly affected. Each electrolyte has specific functions in the body. Slightest change in these electrolyte levels may have serious short term and long term effect on body functions.

**OBJECTIVE** : Football is a very popular game in Bangladesh and objective is to study the changes in electrolyte level of Bangladeshi football players & to provide baseline information to measure water and electrolyte requirement before going to training session and match play.

**METHOD** : It is a case control study done in the Department of Physiology, Dhaka Medical College from January 2013 to December 2013. 50 male football players of 20-30 years enrolled as a student of Bangladesh Krira Shikkha Protisthan (BKSP) were chosen as cases. 50 age-matched healthy non-athlete men were selected as controls. Anthropometric data was recorded using conventional techniques. Serum electrolytes level were measured in the Department of Biochemistry, BSMMU. Statistical analysis was performed using SPSS Version 12.

**RESULTS** : Mean age of cases were 22.76 years. Mean height of cases were 1.69 meter. Mean weight of cases were 61.14 kg. Mean BMI of cases were 25.76 Kg/m<sup>2</sup>. Significantly high BMI were found in cases. Mean ( $\pm$ SD) values of Serum Sodium, Potassium, Chloride & Bicarbonate in cases were  $138.60 \pm 5.04$ ,  $4.19 \pm 0.77$ ,  $101.54 \pm 2.34$  &  $26.98 \pm 4.57$  respectively. cases showed no significant changes of Sodium, Potassium & Chloride levels than controls whereas Bicarbonate levels were significantly ( $p < 0.001$ ) lowered than controls. Though mean values of electrolytes were within normal reference ranges, cases showed individual variability.

**CONCLUSION** : Players showed individual variability in their electrolyte levels though they are having similar training session or match play. So individual screening is necessary to know one's physiological adaptation to exercise & to determine water and electrolyte requirement of that individual. This will improve morbidity of football players in the long run.

**KEY WORDS** : Football players ,Serum Electrolytes, Bangladesh

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## INTRODUCTION :

Athletes have to go through regular intensive exercise and training. This exercise and training may result in functional changes in their electrolyte level. Though electrolytes are present in every body compartment (ECF & ICF), the electrolytes mostly affected in exercise are serum/plasma electrolytes<sup>1</sup>. The electrolytes that have a major role in body functions are sodium, potassium, chloride, bicarbonate etc. Slightest change in these electrolyte levels may have serious short term and long term effect on body functions. Electrolyte imbalance can affect heart, kidney and neural activity of such athletes.

Exercise causes heat production and it results in sweating to control body temperature. It can alter the body water and electrolyte balance. In a football match play, football players undergo exercise, which causes an increase in substantial body temperature and a significant electrolyte loss<sup>2</sup>.

In sweat, along with loss of water a variety of electrolytes and other solutes are also lost. Sweat is invariably hypotonic related to plasma, and contains sodium, the major cation of the extra cellular space<sup>3</sup>. Other important electrolytes are potassium, chloride and bicarbonate<sup>4</sup>.

The concentration of serum sodium is affected during exercise. Though, sodium and chloride ion move in the same direction, analysis of serum sodium ion concentration usually correlate with serum chloride ion concentration. On the other hand potassium also interrelates with both sodium and chloride to control fluid & electrolyte balances. As potassium is stored in muscle along with glycogen, breaking of glycogen to supply energy during exercise causes potassium depletion from muscle cells<sup>1</sup>.

Football is a team sports and football players undergo similar kind of exercise during their training session and match play. Some players lose a considerable amount of electrolytes and they need to replace these electrolytes during training or match play. Adequate pre-screening is necessary to find out water and electrolyte requirement of an athlete before their training session and match play. But players show individual variability in their electrolyte levels though they are having similar training session or match play. So individual screening is necessary to determine water and electrolyte need of individual athlete<sup>5</sup>.

There is lack of published data available regarding the electrolyte level of Bangladeshi football players. The present study has been designed to observe the serum electrolyte levels in male football players of Bangladesh. This will provide baseline information which will be helpful to measure water and electrolyte need before going to training session and match play.

## MATERIALS & METHODS :

This was a case control study done in the Department of Physiology, Dhaka Medical College from January 2013 to December 2013.

Fifty (50) male football athletes were chosen as case who were students of a renowned sport academy of Bangladesh named Bangladesh Krira Shiksha Protisthan (BKSP).

### **Inclusion criteria :**

1. Male, age between 20 - 30 years
2. Experience of playing football for > 3 years

**Exclusion criteria :**

1. Age <20 years or >30 years
2. History of Hypertension, Diabetes Mellitus, TB, Malignancy and associated pulmonary disease (e.g. asthma, pneumonia)
3. History of previous chest surgery
4. History of taking drugs such as steroid, aspirin, anti hypertensive, anti diabetic and lipid lowering agents.
5. History of regular alcohol consumption and smoking.

50 age-matched healthy non-athlete men were selected as controls.

**Data collection**

Anthropometric measurements of the subjects were done using conventional techniques.

Body mass index (BMI) of each subject was calculated using standard formula of BMI (BMI=Weight in kg/Height in m<sup>2</sup>)

Serum Sodium, Potassium & Chloride were measured by Ion Selective Electrode (ISE) method in Beckman Coulter AU auto-analyzer and Serum Bicarbonate was measured by Dimension in the Department of Biochemistry, BSMMU..

**Statistical analysis**

All the parameters were expressed as Mean ± SD (standard deviation). Comparison between the groups was done by unpaired Student's 't' test. P value of < 0.05 was accepted as level of significance. Statistical analysis was performed by using a computer based statistical program SPSS Version 12.

**RESULTS :**

Mean (±SD) age of the study population (cases) and control groups were 22.76 ± 1.91 and 21.64 ± 1.29 years respectively. Mean (±SD) height of the cases and control groups were 1.69 ± 0.05 and 1.68 ± 0.06 meter respectively. Mean (±SD) weight of the cases and control groups were 61.14 ± 8.81 and 54.80 ± 7.44 kg respectively (Table I).

**Table I: Anthropometric data of cases (Football Players) and controls (Healthy subjects)**

Parameters	Healthy subjects	Football Players
	Mean ± SD (n=50)	Mean ± SD (n=50)
Age (years)	21.64 ± 1.29	22.76 ± 1.91
Height (m)	1.68 ± 0.06	1.69 ± 0.05
Weight (kg)	54.80 ± 7.44	61.14 ± 8.81

Mean (±SD) BMI of the cases and control groups were 25.76 ± 3.29 and 23.31 ± 3.2 Kg/m<sup>2</sup> respectively. Unpaired Student's 't' test showed significant (p<0.001) differences of BMI between cases and controls (Table II).

**Table II: Comparison of BMI value between cases (Football Players) and controls (Healthy subjects)**

Groups	BMI (kg/m <sup>2</sup> )	p value
	Mean ± SD (n=50)	
Cases (Healthy subjects)	25.76 ± 3.29	<0.001
Controls (Football Players)	23.31 ± 3.2	

Mean ( $\pm$ SD) values of Serum Sodium, Potassium, Chloride & Bicarbonate in cases and controls are shown in Table III .

**Table III : Serum electrolytes level of cases and controls**

Parameters	Healthy subjects	Football Players
	Mean $\pm$ SD (Range)	Mean $\pm$ SD (Range)
Sodium	139.40 $\pm$ 2.47 (137-154)	138.60 $\pm$ 5.04 (121-146)
Potassium	4.26 $\pm$ 0.39 (3.60-5.30)	4.19 $\pm$ 0.77 (2.40-5.80)
Chloride	102.92 $\pm$ 5.64 (84.0- 115.0)	101.54 $\pm$ 2.34 (98.0-115.0)
Bicarbonate	30.48 $\pm$ 1.68 (27.0-34.0)	26.98 $\pm$ 4.57 (14.0-35.0)

Among total 50 cases, 37 (74%) had Sodium level <138 mmol/L, 22 (44%) had Potassium level <3.5 mmol/L, 22 (44%) had Chloride level <98 mmol/L & 30 (60%) had Bicarbonate level <23 mmol/L (Table IV).

**Table IV : Distribution of Serum electrolytes level in cases**

Parameters		Football Players (n=50)	
		Frequency	%
Sodium	<138 mmol/L	37	74
	>138 mmol/L	13	26
Potassium	<3.5 mmol/L	22	44
	>3.5 mmol/L	28	56
Chloride	<98 mmol/L	22	44
	>98 mmol/L	28	56
Bicarbonate	<23 mmol/L	30	60
	>23 mmol/L	20	40

Unpaired Student's 't' test was done to see any significant change of electrolyte levels occurred between cases and controls.

Sodium, Potassium & Chloride level shows no significant changes between groups with a 'p' value of 0.316, 0.579 & 0.113 respectively. Bicarbonate level varied significantly between cases and controls with a 'p' value of <0.001. (Table V)

**Table V : Comparison of Serum electrolytes level between cases and controls**

Groups	Parameters	p value
Healthy subjects (Cases) vs Football players (Group B)	Sodium	0.316
	Potassium	0.579
	Chloride	0.113
	Bicarbonate	<0.001

## DISCUSSION :

The present study has been designed to observe the serum electrolyte levels in male football players of Bangladesh. For this, a total number of 50 male football players of 20-30 years and with at least 3 years experience of playing football were selected as cases. 50 age-matched healthy male subjects were taken as controls.

In this study, anthropometric data (age, height, weight) of cases and controls were similar. But BMI was higher in cases (football players) than controls (healthy subjects). The difference of BMI was also statistically significant (p<0.001). Athletes having higher BMI is well justified because of their higher physical training.

In this study, serum electrolytes level of healthy subjects were within reference range and almost similar to the findings of various investigators from different countries<sup>6-9</sup>. Normal reference value for Sodium & Chloride considered in this study was 136-145 & 98-

107 mmol/L respectively. Mean serum sodium level in Football players were lower than that of healthy subjects. The difference was not statistically significant, though both values were within normal range. But among football players the lowest Sodium level recorded was 121 mmol/L, which is much less than the reference value. That indicates that some players developed subclinical hyponatremia. Mean serum chloride level in Football players were similar to that of healthy subjects & values was within normal range. None of the football players had chloride level below the normal range. These findings can be explained by the net loss of sodium and chloride through excessive sweating during vigorous training protocol. Sodium chloride loss associated with net dehydration may lead to observed hyponatraemia<sup>11</sup>.

Normal reference value for Potassium considered in this study was 3.5-5.1 mol/L. Mean serum Potassium level in Football players were lower than that of healthy subjects. The difference was not statistically significant, though both values were within normal range. But among the football players, the lowest Potassium level found was 2.4 mmol/L while the highest was 5.8 mmol/L. That indicates that some players developed subclinical hypokalemia and some hyperkalemia. Potassium is a major cation of ICF, stored in muscle fibers along with glycogen. In athletes, because of intense exercise, potassium shifts from ICF to ECF. As a result serum potassium level should increase. Lowered potassium in some athletes can be regarded as individual variation.

Normal reference value for Bicarbonate considered in this study was 21-32 mmol/L. Mean serum bicarbonate level was significantly ( $p < 0.001$ ) lower in football players than that of healthy subjects. Though mean serum bicarbonate levels in both groups

were within normal limits, football players had bicarbonate as low as 14 mmol/L. This finding can result from increased organic acid formed during vigorous exercise and also supported by observation found by other researcher as well<sup>12</sup>.

As Bangladesh is a temperate country, chances of loss of balance of electrolytes following sustained exercise is more. Imbalance in electrolyte level has many short terms and long term affects on a player. This study also portrays individual variability in their electrolyte levels though they are having similar training session or match play. In view of our results, and in agreement with earlier publications, we should consider screening athletes for preventing sudden electrolyte imbalance or loss during heavy training and match play. And take special attention in giving supplementation according to the need of an individual player.

#### CONCLUSION :

Players show individual variability in their electrolyte levels though they are having similar training session or match play. So individual screening is necessary to know one's physiological adaptation to exercise & to determine water and electrolyte requirement of that individual. This will improve morbidity of football players in the long run.

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## **Antibiotic Resistance and Usage : A Survey on the Knowledge, Attitude, Perceptions and Practices Among the Medical Students of a Tertiary Care Teaching Hospital**

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### **ABSTRACT**

**BACKGROUND** : Antibiotic resistance (ABR) is an important growing global health issue which needs to be addressed urgently. Judicious use of antibiotics is the only solution to curb this problem. Awareness of this fact among UG students, who are the future physicians, is extremely vital.

**OBJECTIVE** : To assess the knowledge, attitude and practices (KAP) related to antibiotic resistance and usage in undergraduate medical students.

**METHOD** : This cross sectional, questionnaire based survey was undertaken in a teaching hospital. The questionnaire was distributed to a batch of 97 medical students in their 4th year of MBBS, whereby their KAP regarding antibiotic use and resistance was assessed by a five point Likert scale, whose responses ranged from “strongly agree” to “strongly disagree” and “always” to “never”. Some questions were of true and false type. The data was analyzed by using simple descriptive statistics to generate frequencies, percentages and proportions.

**RESULT** : Indiscriminate antimicrobial use leads to the emergence of the growing problem of resistance was known to all 97(100%) of the participants. The number of respondents who agreed that ABR was an important and a serious global public health issue was 93(95.87%). 86(88.65%) of the respondents were aware that bacteria were not responsible for causing colds and flu.

**CONCLUSION** : Our study provides an important insight regarding the knowledge, attitudes and practices regarding antibiotic resistance and usage among the future doctors, which can be considered, in order to plan for an effective undergraduate curriculum.

**KEY WORDS** : Knowledge, Antibiotic resistance, Indiscriminate use

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## INTRODUCTION :

Antimicrobial agents are group of drugs which are basically used to kill or inhibit the growth of microorganism.<sup>1</sup>They are most commonly prescribed medicines and are often too misused.<sup>2</sup> As a result of injudicious use of antimicrobial agents can lead to the development of resistance which is an important growing global health issue which needs urgent reporting. The threat of antimicrobial resistance is rapidly progressing and intensifying. The awareness on its seriousness and significance is the first step towards curtailing its progress. Various approaches have been taken worldwide, to meet the challenges which are posed by its spread. One of the approaches which are commonly suggested is to undertake instructional and educational campaigns among the general population<sup>3</sup> and among the health care personnel<sup>4</sup> about antibiotic resistance and its dangerous consequences and regarding the steps which can limit its development and spread.<sup>5,6</sup>

Prescribers have an important role to play in the battle against antibiotic resistance, not only through their safe and rational prescribing, but also by promoting patient awareness and knowledge and imparting health education to the community regarding safe medication practices concerning antibiotics. Various studies have described the inability of the prescribing physicians in creating awareness & providing adequate education to the patients regarding antibiotic usage.<sup>3</sup>

The lack of adequate training during their undergraduate and postgraduate years may be responsible for their inability to undertake these tasks confidently. Hence, teaching about antimicrobial chemotherapy should form a vital part of both the undergraduate

and postgraduate medical curricula, considering the frequency with which these agents are prescribed and our continuing and increasing concern regarding antibiotic resistance<sup>7</sup>.It has been greatly emphasized that adequate training should be provided for the undergraduate medical, pharmacy and nursing students regarding the proper prescribing, dispensing and the usage of antibiotics respectively. It is an important measure which is widely proposed and documented, in order to promote the judicious use of antibiotics.<sup>8</sup>

Young doctors should be given more education during their undergraduate training regarding antibiotic resistance and appropriate prescribing. This is a crucial time period during which the importance of these issues should be emphasized, because once the doctors become qualified, it is difficult to change their deeply entrenched views and behavior.<sup>9</sup> The interventions which are undertaken to prevent and control antimicrobial resistance, usually aim to bring about behavioral changes in the target group, and the outcome of these interventions is affected by the previous beliefs and motivations which are held by this group<sup>10</sup>. Any educational intervention to be successful and for the changes to be sustained, it should change the knowledge, attitudes and practices (KAP) of the target group<sup>11</sup>. Therefore, before planning any training program or an educational activity, we have to be aware of the baseline KAP of the target population, which will assist us in devising a suitable approach and an effective curriculum. It is in this regards that this study was undertaken among 4th year undergraduate medical students, in order to assess their knowledge and attitude concerning antibiotic resistance, as well as their self reported practices which are related to antibiotic usage. A better understanding of what the

students know and believe about the issues of antimicrobial use and resistance can assist us in planning and devising an effective and a tailored educational intervention for them.

## **MATERIALS & METHODS :**

This study was a cross-sectional, questionnaire based survey which was undertaken in a tertiary care teaching hospital among a batch of 4th year MBBS undergraduate students.

The questionnaire which we used was developed by modifying the earlier ones which were used by Wester CW et al.<sup>12</sup>, Eng JV et al.,<sup>5</sup> and others<sup>13-15</sup>. The final questionnaire consisted of several parts. A 5-point Likert scale, whose responses ranged from 'very important' to 'unimportant' was used, both to assess the students' perceptions on the causes of ABR, as well as the factors which influenced their decision about the antibiotic selection and prescribing.

A series of questions which were intended to study the attitude of the participants regarding antibiotic resistance and usage, were analyzed by using a 5-point Likert scale, whose responses ranged from 'strongly agree' to 'strongly disagree'. Their self reported practices regarding antibiotic usage were also assessed by using a Likert scale which ranged from 'always' to 'never'.

The participants' knowledge was assessed by using a set of four questions. Three of these were of the True/False type and one was a Likert scale based question. Finally in the last part of the questionnaire, participants were asked an open ended question to give

solutions to curb this growing problem of antimicrobial resistance and their replies are tabulated in Tables.

The questionnaire was distributed to a batch of 97 medical students in their 4th year of MBBS, during one of their pharmacology classes. They were asked to complete the questionnaire anonymously informed consent was obtained from the participants, to utilize their data for research purposes. Simple descriptive statistics was used to generate frequencies, percentages and proportions. In order to simplify the analysis, we reduced the 5 point and 4 point response option of the Likert scale into 3 such as agree/disagree/undecided & yes/no/uncertain. The possible answers "strongly agree" and "somewhat agree" were considered as "agree" while "strongly disagree" and "somewhat disagree" were considered as "disagree" and remaining were undecided. Similarly, the possible answers "always" and "usually" were considered as "yes" while the answer "never" were considered as "no" and "sometimes considered as "uncertain".

## **RESULTS :**

The response rate was 100 per cent among the 97 students who were asked to participate in the survey. The results are tabulated as percentage in Table I, II, III, IV, V & VI.

Out of all the participants 91.7% (89) agreed that indiscriminate and injudicious use of antimicrobial agents leads to ineffective treatment. Around 86.59% (84) were aware that increase adverse effect of antimicrobials were also due to its indiscriminate uses, around 71.13% (69) agreed that it can cause prolongation of illness. Regarding emergence

of resistance total 100 % (97) believed that it is due to injudicious use of AMA. 92.78% (90) of the total participants agreed that it put some additional burden of medical cost to the patient. 94.84% (92) of total believed that if an AMA is taken too often it is less likely to work in future. 88.65% (86) of total responders were aware that common cold

and influenza were not caused by bacteria. Regarding antimicrobial resistance more than 95.87% of total participants agreed that it is an important and serious public health issue facing the world and our country whereas only 68.04% (66) agreed that it is a serious health issue in this hospital. (Table I & II)

**Table I : Participants knowledge regarding antimicrobial use (N=97)**

QUESTIONS	True	False
1. Indiscriminate and injudicious use of antimicrobials can lead to:		
A. Ineffective treatment	91.7%(89)	8.24%(8)
B. Increase adverse effect	86.59%(84)	13.4%(13)
C. prolongation of illness	71.13%(69)	28.86%(28)
D. Emergence of bacterial resistance	100%(97)	0%(0)
E. Additional burden of medical cost	92.78%(90)	7.21%(7)
2. If taken often, antimicrobials are less likely to work in the future	94.84%(92)	5.15%(5)
3. Bacteria cause common cold and influenza.	11.34%(11)	88.65%(86)

**Table II : Participants knowledge regarding antimicrobial resistance (N=97)**

QUESTIONS	AGREE	UNDECIDE	DISAGREED
Antibiotic resistance :			
a) An important and serious public health issue facing the world.	95.87%(93)	1.03%(1)	3.09%(3)
b) An important and serious public health issue in our country	95.87%(93)	1.03%(1)	3.09%(3)
c) An important and serious public health issue in our hospital	68.04%(66)	11.34%(11)	20.61%(20)

However, the attitude of the study populations regarding to antibiotics use and resistance was very casual and lax. Around 37.11% (36) of total participants still agreed that antimicrobials are safe drugs and hence can be commonly used medicine. While 54.63% (53) of total participant disagreed to

this statement. Likewise, 41.23% (40) of the total responders still agreed that skipping one or two doses of AMA are not associated with development of resistance. However, 92.78% (90) of total study population agreed that antimicrobial prescription should be based on culture and sensitivity report. Knowledge of

rationale use of AMA is essential for all doctors and medical students and 95.87% (93) of the total agreed to this statement. But only around 73.19% (71) of total study population agreed that there is abuse of AMA and only around 47.4% (46) agreed that abuse of AMA is the main cause of bacterial infection. 94.84% (92) of total population strongly agreed that antimicrobial resistance can affect health. (Table III)

In practice part around 55.6% (54) of total participants stated that when they are prescribed an AMA and if after taking 2-3 doses they feel better they never stop taking further treatment. 58.8% (57) said that they never save the remaining AMA. 74.2% (72) of

study population always completed the full course of treatment. 86.6% (84) of participants always checked the expiry date before buying an AMA and 19.6% (19) of total responders used AMA when they have cough and sore throat and 40.21% (39) uncertain about it. Majority; 90(92.8%) always consulted a doctor before stating an antibiotic. (Table IV)

The questionnaire consisted of a list of causes which could be responsible for the development of antibiotic resistance and the students were asked to rate them according to their importance. The corresponding ratings which were given by the students have been depicted in Table V.

**Table III : Participant attitude regarding antimicrobial use and resistance (N=97)**

QUESTIONS	AGREE	DISAGREE	UNDECIDED
1. Antimicrobials are safe drugs, hence they can be commonly used medication	37.11%(36)	54.63%(53)	8.24%(8)
2. Skipping one or two doses does not contribute to the development of antimicrobial resistance	41.23%(40)	46.39%(45)	12.37%(12)
3. Antimicrobial prescriptions should be based on culture and sensitivity report	92.73%(90)	2.06%(2)	5.15%(5)
4. Knowledge on rationale use of antimicrobial is essential for all doctors, nurses, & health care providers	95.87%(93)	1.03%(1)	16.49%(16)
5. Do you think there is abuse of antimicrobials	73.19%(71)	10.3%(10)	16.49%(16)
6. Is abuse of antimicrobials cause of bacterial infection	47.4%(46)	28.86%(28)	23.71%(23)
7. Can antimicrobial resistance affect health	94.84%(92)	2.06%(2)	3.09%(3)



**Table IV : Participants self reported practices regarding the antibiotic use**

QUESTIONS	ALWAYS	SOMETIMES	NEVER
1. The doctor prescribes a course of antimicrobial for you. After taking 2–3 doses you start feeling better			
– Do you stop taking further treatment?	21.64%(21)	22.7%(22)	55.6%(54)
– Do you save the remaining antibiotics for the next time you get sick?	16.49%(16)	24.7%(24)	58.8%(57)
– Do you discard remaining, left-over medication?	30.92%(30)	31.95%(31)	37.11%(36)
– Do you give the leftover antimicrobials to your friend they get sick?	21.6%(21)	31.95%(31)	46.3%(45)
– Do you complete the full course of treatment?	74.2%(72)	22.7%(22)	3.1%(3)
2. Do you consult a doctor before starting an antibiotic?	92.8%(90)	4.1%(4)	3%(3.1)
3. Do you check the expiry date of antimicrobials before using it?	86.6%(84)	8.2%(8)	5.2%(5)
4. Do you take an antimicrobial when you have cough and sore throat?	19.6%(19)	40.21%(39)	40.21%(39)

**Table V : Respondents' rating of the possible causes of antibiotic resistance according to their importance**

CAUSE OF ANTIBIOTIC RESISTANCE	IMPORTANT	UNSURE	UNIMPORTANT
Use of antibiotics for self-limited non bacterial infections	55.67%(54)	3.1%(3)	41.2%(40)
Use of antibiotics with a broader than necessary spectrum	69%(67)	9.3%(9)	21.6%(21)
Use of antibiotics for shorter than standard duration	58%(56)	13.4%(13)	29%(28)
Poor infection control measures	39%(38)	13.4%(13)	47.4%(46)
Use of antibiotics for self limited bacterial infections	56.7%(55)	7.21%(7)	36%(35)
Empirical antibiotic therapy (best guess therapy)	41.2%(40)	18.55%(18)	40%(39)
Lack of restrictions on antibiotic usage	78.3%(76)	4.1%(4)	17.5%(17)
Excessive antibiotic use in live stock (Animals reared for food)	54.6%(53)	20.6%(20)	24.7%(24)
Use of antibiotics for longer than standard duration	49.5%(48)	13.4%(13)	37.1%(36)

Lastly, the participants were asked an open ended question, to recommend a solution to curb this growing problem of antimicrobial resistance. Their replies are tabulated in Table VI.

**Table VI : Factors perceived as important to reduce antibiotic resistance by the participants**

WHAT ACCORDING TO YOU IS THE SOLUTION FOR THE GROWING PROBLEM OF ANTIMICROBIAL RESISTANCE ?	
Judicious, careful and rational use of medicines	36.08%(35)
Complete the full course of antimicrobials in the prescribed dose	26.64%(21)
Avoid self medication	12.37%(12)
Multidrug therapy	8.24%(8)
Symptomatic management in self limiting conditions	7.21%(7)
Awareness among patients by organizing public health campaigns	5.15%(5)
No response	5.15%(5)
Prescribe using culture sensitivity reports	3.09%(3)
New drug discovery	1.03%(1)

A list of factors which had to be considered before prescribing an antibiotic were provided and the students were asked to rate them according to the importance which they felt that these factors deserved. More than 80 percent of them gave importance to the adverse effect profile of the antibiotic and the risk of a super infection as well as the immune status of the patient. Nearly three quarters (75%) of the participants felt that the following factors were important to be considered—the ability of the antibiotic to

promote resistance, the in-vitro antibiotic sensitivity of the causative organism and the pharmacokinetic profile of the antibiotic. Only 55 (56.7%) participants felt that the cost was an important factor which deserved consideration before the prescription of an antibiotic.

## DISCUSSION :

Our study provides useful information about the knowledge, attitudes, perceptions and the practices of 4th year medical students with respect to antibiotic resistance and usage, which may be utilized to plan suitable educational interventions that aim at improving the antimicrobial prescribing and use. A majority of the students in our study were well aware of the global as well as the nationwide problem of antimicrobial resistance, but at the local hospital level, the antibiotic resistance was not considered to be a problem. A similar response was noted in previous studies <sup>16</sup>, where most of the respondents underestimated the prevalence of the antibiotic resistance at their own institution <sup>12,17</sup>. Case vignettes which illustrate the harmful effects of antibiotic resistance, may be utilized to improve the effectiveness of educational interventions or antibiograms that were previously used less successfully, to facilitate the correct estimation of the prevalence of the resistance at the institutional level <sup>12</sup>.

In this study all the participants (100%) were aware that indiscriminate antimicrobial use leads to emergence of bacterial resistance. this result is consistent with similar studies.<sup>18-21</sup>But in another study found that only85% of the total respondents believed that cause of bacterial resistance is due to its indiscriminate use.<sup>22</sup>91.7% of the total respondents in this study believe that ineffective treatment by

AMA is due to its indiscriminate use which is consistent with similar study conducted , but it is found to be only 85% in another study.<sup>19,22</sup>

The attitude of the study participants with regards to antibiotic use and resistance was found to be casual and lax. 21 (21.64%) participants believed that antibiotics were safe drugs; and that hence, they could be commonly used and 22.7 per cent (n = 22) were not knowledgeable of this and 54(55.6) participants disagree it.

But surprisingly, inspite of the casual attitude, the self reported practices of our study participants with regards to antibiotic use were found to be satisfactory. A majority 90 (92.8 per cent) always consulted a doctor before starting on an antibiotic and most of them 72 (74.2 per cent) always completed the full course of the prescribed treatment.

Previous studies have shown high rates of self medication (35 per cent) amongst medical students with respect to antibiotics <sup>24</sup>. However, this was not the case with our participants. Studies done previously showed that around 60% of the participants believed that antibiotics should be prescribed for viral diseases like sore throat and cough, and these type of belief can lead to usage of more and more antibiotics leading to bacterial resistance<sup>23</sup>, while in this study only 30% of the total respondents believe that antibiotics should not be taken in cough and sore throat and around 51% is uncertain which is very surprising but around 88.65% are well aware that bacteria does not cause common cold and influenza. So proper education regarding practice of antibiotics is necessary.<sup>23</sup>

Around 55.6% of total population of this study never stop taking antibiotics in spite of feeling better after taking 2-3 doses of antibiotics which is almost similar to the similar study.<sup>18</sup>

<sup>19</sup> When asked whether they check the expiry date of antibiotics before buying it around 86.6% of the study population respond positively with similar response rate found in other study .<sup>19</sup>

Since now a day there is no restriction on Over the Counter (OTC) dispensing of antibiotics without prescriptions so any antibiotics can be purchased OTC without prescriptions.<sup>18</sup> these kind of practices may cause abuse of antibiotics among the populations leading to development of resistance. In this study total 73.19% study population agree that there is abuse of antimicrobials with similar kind of results found in other study<sup>19</sup>

When they were asked to rate the important causes of antimicrobial resistance, most of the participants rated mutational and evolutionary changes in the microorganism and lack of restrictions on the antibiotic usage as very important causes. As in some previous studies, <sup>10</sup> .poor or lack of infection control measures were not considered to be an important cause for the resistance to develop, by most of the participants, which highlighted the lack of awareness regarding the significance of the infection control measures. The failure in implementing basic infection control practices has been one of the principle causes of the emergence and the dissemination of resistant organisms <sup>25</sup>.

Learning about the antimicrobial prescribing in pharmacology must be connected clearly with the infection control in microbiology <sup>26</sup>. The significance of simple measures like hand hygiene in the control of resistance should be endorsed <sup>12</sup> and its practice should be inculcated at an earlier stage of the medical education.

The virulence of the organism, the risk of adverse effects and super infection as well as

the immune status of the patient, were considered as the factors which deserved the most consideration before the prescription of an antibiotic. The ability of the antibiotic to promote resistance, the in-vitro antibiotic sensitivity of the causative organism and the pharmacokinetic profile of the antibiotic were given second priority. This demonstrates that the students were aware & concerned about the individual patient's benefit and harm, the dangerous consequences which result to the society due the indiscriminate antibiotic use may not be obvious to them.

Apart from teaching about antibiotic prescribing, the principles of the protocol development for antibiotic use in health care facilities, should form an integral part of the undergraduate teaching.<sup>24</sup> Measures like hand hygiene which are emphasized in the lectures, for the control of resistance should be inculcated in day to day life.<sup>12</sup> The medical education strategies should aim, to increase the knowledge and change the behaviour and practices among medical students. They have to be tailored as per the youngsters development, capabilities and experience.<sup>6</sup>

#### CONCLUSION :

Our study provides an important insight regarding the knowledge, attitudes, perceptions and practices regarding antibiotic resistance and usage among the future doctors, which can be considered, in order to plan for an effective undergraduate curriculum.

#### LIMITATIONS

The main limitation of this study is that the data provided is of local interest. It is based on a convenience sample which involved only one batch of 4th year medical students from one single teaching hospital.

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## **Prediction of Low Birth Weight Neonate by Measurement of Single Pre-Delivery Symphysis Fundal Height**

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### **ABSTRACT**

**BACKGROUND** : Prediction of low birth weight infant before birth is essential to prepare prompt care after delivery. Two common methods of estimation of birth weight are sonographic evaluation and clinical palpation. In developing countries, ultrasonography may be unavailable or not-affordable at times. Moreover lack of trained clinicians is also a major drawback. Measurement of Symphysis Fundal Height (SFH) using inexpensive and easily available non elastic tape has been recommended as a means of assessing birth weight in low resource countries.

**OBJECTIVE** : The aim of this study was to determine the value of single pre-delivery SFH as a predictor of birth weight and to find the cut off value of SFH as a predictor of low birth weight.

**METHODS** : This prospective study was conducted in the Dept of Obstetrics and Gynaecology in Dhaka Medical College and Hospital during the period of 1<sup>st</sup> January 2010 to 30 the June 2010. A total 520 admitted pregnant woman were studied. Pre-Delivery Weight (PDW), height, Symphysis Fundal Height (SFH) & Mid Upper Arm Circumference (MUAC) were measured. Pearson's correlation &  $\chi^2$  test was done as test of significance. Sensitivity, specificity, positive and negative predictive value of SFH at different cut-off level was calculated. ROC curve was constructed using Birth weight of neonate as gold standard.

**RESULTS** : This study found that mean age of pregnant mother was  $23.48 \pm 4.55$  years, gravida was  $2.02 \pm 1.57$ . About half (49.4%) of the women were nulliparous. Mean height was  $153.13 \pm 4.95$ cm, mean PDW was  $54.63 \pm 3.23$  kg , mean MUAC was  $23.21 \pm 2.45$  cm & mean SFH was  $31 \pm 3.23$  c. The birth weight of neonates significantly correlated with SFH, PDW, height & MUAC of mothers. Among them SFH showed highest significance. Mean SFH, PDW & MUAC explain 17%, 8% and 10% of the observed variation of birth weight respectively. Incidence of low birth weight infant was 13.5%. Cut-off point for SFH that has the best sensitivity and specificity in the prediction of low birth weight was 29 cm.

**CONCLUSION** : Symphysis Fundal Height measurement seems effective in predicting low birth weight neonate. It was a better predictor of birth weight than maternal height, pre-delivery weight or mid upper arm circumference. Prediction of low birth weight prior to delivery can improve delivery care and neonatal care including referral in well-equipped centre leading to improved peri-natal outcome.

**KEY WORDS** : Symphysis Fundal Height(SFH) , Low Birth Weight(LBW)

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## INTRODUCTION :

Birth weight is one of the most important indicators of safe pregnancy outcomes. One of the most expected pregnancy outcome is a normal delivery weight<sup>1</sup>. Identification of at-risk fetuses represents one of the challenging problems in modern Obstetrics, in spite of a wide range of clinical, biochemical and ultrasonography techniques available<sup>2</sup>. Ultrasonographic measurement include biparietal diameter, head circumference and femur length, which are reasonably sensitive for diagnosis of fetal growth, detecting about 85% of low birth weight babies<sup>3</sup>. But it is not readily available as a screening method in many hospitals, particularly in developing countries.

Low Birth Weight (LBW) is defined as a birth weight of <2500 gm<sup>4</sup>. It is resulted from either preterm birth or infant of restricted intrauterine growth<sup>5</sup>.

Hypoglycemia, asphyxia, Respiratory distress syndrome, intraventricular haemorrhage may affect the infant and these can lead to significant morbidity and mortality. Perinatal mortality has been found to be sharply increased in low birth weight infants<sup>6</sup>.

Perinatal mortality in Bangladesh is extremely high, which are 44 per 1000 live birth<sup>7</sup>. One of the major cause of perinatal mortality in Bangladesh is low birth weight<sup>8</sup>. In Bangladesh low birth rate is about 34%. Majority of population of Bangladesh are rural based. Most of the rural pregnant women do not avail the opportunity of regular antenatal checkup. Many women are unaware of their gestational age. They come to hospital during labour or just prior to labour .

Prediction of low birth weight infant before birth is essential to prepare prompt care after delivery. There are two common methods of estimation of birth weight: sonographic

evaluation and clinical palpation<sup>9</sup>. In developing countries like Bangladesh, ultrasonography may be unavailable or may not be affordable by patients .Moreover lack of trained personnel in ultrasonography is also a major factor. Physician estimates of birth weight by palpation are as reliable as, or superior to those made from ultrasonographic measurements of fetus<sup>10</sup>. However, their accuracy depends on experience, which may be lacking in many obstetric care personnel in developing countries<sup>9</sup>. That is why measurement of Symphysis Fundal Height (SFH) using inexpensive and easily available non elastic tape has been recommended as a means of assessing birth weight in low resource countries.

Tape measurement of symphysis fundal height has been suggested as a screening test for the detection of fetal growth retardation. It is regarded as a simple, inexpensive and non-invasive procedure and takes no cost to the patient. High applicability, accepted validity and no potential harm in SFH measurement favours this as a routine method to detect fetal growth disturbances<sup>11</sup>. Other measures for the prediction of birth weight include maternal height, pre-pregnancy weight, Mid upper arm circumference.

Usefulness of single, pre-delivery symphysis fundal height measurement for the prediction of low birth weight can be examined by comparing the value of different maternal anthropometric indices for predicting birth weight. With proven sensitivity, the test can be introduced as one of the screening procedure in intra-partum care. This will assist physicians in decision making regarding obstetric intervention, where USG is not available. Physicians in rural hospitals may also use this test as a guide to refer patients to tertiary centers for better neonatal services.



**Objectives of the study :**

The aim of this study was to determine the value of single pre-delivery SFH as a predictor of birth weight and to find the cut off value of SFH as a predictor of low birth weight.

**MATERIALS & METHODS :**

This prospective study was conducted in the Dept of Obstetrics and Gynaecology in Dhaka Medical College and Hospital. 520 pregnant women admitted for delivery between January 2010 and July 2010 at Dhaka Medical College Hospital was included in the study.

**Inclusion criteria :**

1. Singleton pregnancy
2. Admission for planned delivery or in early labour
3. A fetus in longitudinal lie
4. Intact membranes
5. Gestational age beyond 28 weeks.

**Exclusion criteria :**

1. Multiple pregnancy
2. Ruptured membranes
3. Transverse lie of fetus
4. Congenital abnormalities
5. Diagnosed polyhydramnios/oligohydramnios
6. Intrauterine death

All pregnant women fulfilling inclusion criteria during the study period were enrolled in the study. Informed written consent was taken from the participant and clearance from the ethical committee was also obtained.

**Variables recorded :**

- a. Maternal height
- b. Maternal Pre-Delivery Weight (PDW)
- c. Symphysis Fundal Height (SFH)
- d. Mid Upper Arm Circumference (MUAC)
- e. The Birth Weight of neonates

Data were collected by direct interview, physical examination, investigation and reviewing records of women using a structured data collection instrument.

Symphysis Fundal Height measurements were encountered at midline from the superior rim of pubic bone to the highest point of uterine fundus. The women were asked to empty their bladder beforehand. SFH measurements were taken in supine position with head slightly raised. While measuring the non-elastic tape was closely attached to the abdominal wall. Centimeter labeled side was hidden at the time of measurement.

Maternal height and weight were measured in cm & Kg respectively. Mid upper arm circumference was measured to nearest 0.1 cm with a measuring tape. The birth weight was recorded in Kg within 20 minutes of birth.

**Data analysis :**

The numerical data obtained from the study was compiled and analyzed in the computer based software, the Statistical Package for Social science (SPSS). Pearson's tests were done to assess correlations. Stepwise multiple regression analysis was done to examine the dependence of birth weight on other variables.  $\chi^2$  (chi-square) test was done for comparison of proportions. Level of significance was expressed as P value. P values <0.05 was considered as a level of significance.

Sensitivity, specificity, positive and negative predictive value was calculated using the following definitions.

**Sensitivity:** The percentage of persons with the disease of interest (LBW) who has positive test results.

**Specificity:** The percentage of persons without the disease of interest (LBW) who have negative test results.

**Positive Predictive Value :** The percentage of persons with positive test results who actually have the disease of interest (LBW).

**Negative Predictive Value :** The percentage of persons with negative test results who actually have not the disease of interest (LBW).

ROC (Receiver Operated Characteristic) curve was constructed using Birth weight of neonate as gold standard. Specificity was plotted on X-axis and sensitivity on Y axis.

**RESULTS :**

The mean age of the study population (pregnant mother) was 23.48 ±4.55 years with a minimum age of 15 years and maximum 40 years; mean height was 153.13 ± 4.95 cm; mean Symphysio Fundal Height was 31.79 ± 3.23 cm; mean Pre-Delivery Weight was 54.63 ± 3.23 kg & mean Mid Upper Arm Circumference was 23.21 ± 2.45 cm. The parity of the study population ranges from 0-12 in number & Gravida ranges from 0-16 in number (Table I).

**Table I : Characteristics of pregnant mothers (n=520)**

Characteristic	Mean ± SD (Range)
Age (in years)	23.48 ± 4.55 (15 – 40)
Para (in number)	0.87 ± 1.00 (0 – 12)
Gravida (in number)	2.02 ± 1.57 (0 – 16)
Height (in cm)	153.13 ± 4.95 (126 – 169)
Symphysio Fundal Height (SFH) (in cm)	31.79 ± 3.23 (21 – 45 )
Pre-Delivery Weight (PDW) (in kg)	54.63 ± 5.32 (40 – 80)
Mid Upper arm Circumference (MUAC) (in cm)	23.21 ± 2.45 (12 – 35)

42.8% of the pregnant mothers came from low economic class, whereas 47% came from lower middle, 10% from upper middle & 0.4% from high economic class. (Table II)

Table III shows that the mean Birth Weight of the newborn 2.76 ± 0.42 Kg. The minimum weight recorded was 1 kg & maximum 4.11 Kg.

**Table II : Socio economic status of pregnant mothers (n=520)**

Characteristics	Percentage (%)
Low	42.8
Low middle	47.0
Upper middle	10.0
High	0.4

**Table III : Birth weight of the newborn (n=520)**

Characteristics	Mean ± SD (Range)
Birth weight In Kg	2.76 ± 0.42 (1 – 4.11)

**Table IV : Correlation between Birth weight of the neonates with SPH, MUAC, PDW & Height of the mother (n=520)**

Dependant Variable	Independent variable	r value	P value
Birth Weight of the neonate	Symphysio Fundal Height (SFH)	0.42	<0.001
	Mid Upper Arm Circumference (MUAC)	0.32	<0.01
	Pre-Delivery Weight (PDW)	0.29	<0.01
	Maternal Height	0.12	<0.01

Table IV shows the correlation between Birth Weight of the neonate with different independent variables of the mother. Pearson’s correlation test revealed that the Birth weight of neonate significantly correlated with Symphysio Fundal Height ( $p<0.001$ ), MUAC ( $p<0.01$ ), Pre-Delivery Weight ( $p<0.01$ ) & Height ( $p<0.01$ ) of the mother.

Table V shows the stepwise regression analysis with birth weight as the dependant variable and characteristics of pregnant mother as independent variables.

**Table V : Stepwise regression analysis with birth weight as the dependant variable and characteristics of pregnant mother as independent.**

Model variables	r <sup>2</sup>
SFH	0.18
SFH + AG	0.28
SFH + AG +Height	0.23
SFH + AG +Height +PDW	0.23
SFH + AG +Height +PDW +Para	0.23
SFH + AG +Height +PDW +Para + Gravida	0.24
SFH+AG+Height+PDW+Para+Gravida+MUAC	0.24
SFH+AG+Height+PDW+Para+Gravida+MUAC +Age	0.24

Table VI shows that LBW babies were more when mother is para 0 (55.70%) & gravida 1 (50.70%). When SFH is <30 cm about 47.8% babies born were found to be LBW. Significant differences of LBW were found between changing SFH values. No significant relationships were found between LBW of newborn babies with MUAC & Height of mothers.

Table VII shows the performance of SFH as a predictor of LBW sensitivity, specificity, positive and negative predictive value of SFH at different cut-off level taking LBW as gold standard.

**Table VI : Comparison of effects of low birth weight of the neonates on different characteristics of the mothers (n=520)**

Characteristics	Birth weight (kg)		$\chi^2$ value	P value
	<2.5	≥ 2.5		
<b>Gravida</b>				
1	50.70%	45.60%	1.04	0.59
2	23.20%	29.90%		
≥3	26.10%	25.50%		
<b>Para</b>				
0	55.70%	48.50%	1.45	0.49
1	23.00%	29.90%		
≥2	21.30%	21.60%		
<b>SFH (cm)</b>				
<30	47.80%	23.90%	19.64	<0.001
30-32	31.90%	34.10%		
>32	20.30%	38.90%		
<b>MUAC (cm)</b>				
≤21	39.10%	17.30%	5.87	0.053
22-23	39.10%	53.00%		
≥24	21.70%	29.60%		
<b>Height (cm)</b>				
<150	30.00%	15.80%	9.98	0.07
150-152	21.40%	34.20%		
>152	48.60%	50.00%		

**Table VII : Sensitivity, specificity, positive and negative predictive value of SFH at different cut-off level**

SFH cut-off level	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
≤ 27 cm	12.9	98.4	56.3	87.6
≤ 28 cm	32.9	94.3	47.9	89.8
≤ 29 cm	47.1	71.2	24.8	73.1
≤ 30 cm	54.3	62.6	18.8	84.6
≤ 31 cm	62.9	87.4	19.0	90.6
≤ 32 cm	80.0	41.9	18.0	92.9

Fig. 1 shows the ROC curve for SFH. The maximum deviation of the curve from the diagonal line was observed at 29 cm level and it was taken as the cutoff point for SFH. At 29 cm, sensitivity of detecting LBW was 47.14% & specificity was 77.24%.

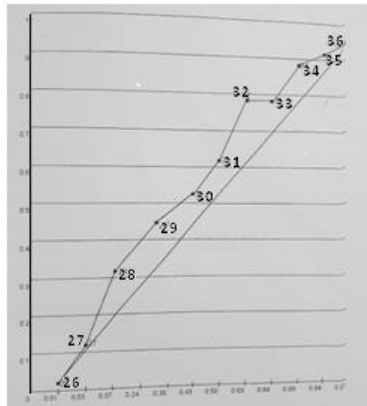


Fig. 1 : ROC curve for Symphysis Fundal Height

## DISCUSSION :

Low birth weight baby is associated with high perinatal mortality and morbidity. Accurate antenatal prediction of fetal weight is to be a good way to identify at risk pregnancy for low birth weight. Proper intranatal and post-natal care can reduce perinatal mortality and morbidity, which ultimately will improve the immediate and late outcome of the baby.

So, there should be a good reliable method for antenatal prediction of low birth weight. This study was designed to determine the cut of value of single predelivery symphysis fundal height as a predictor of low birth weight (PDW, Height, MUAC, age, parity, socioeconomic status remains constant).

In present study 13.5% babies were low birth weight with mean birth weight  $2.759 \pm .418$  Kg. This finding closely resembles with Challis et al<sup>12</sup>, where the investigators found the mean birth weight being 2.91 kg and low birth weight occurred in 16% of their study. Similarly, Rai et al<sup>13</sup> found the mean weight of the babies being 2.9 kg.

In present study 18.6% of teenage pregnancies (Age <18 years) resulted in low birth weight delivery. Incidence of low birth

weight babies decrease with increase in maternal weight and height showing significant correlation in this study.

In present study 49.8% of mothers height was  $\leq 1.52$  m. Walraven et al<sup>14</sup> & Rai et al<sup>13</sup> found similar findings.

The study showed a strong association between socio economic condition and fetal weight. The socio-economic condition strongly influences mother's nutritional status. Poor families cannot afford to supply the necessary protein and nutrients resulting in low birth weight. Also they don't go through any antenatal checkup at all.

Correlation between birth weight as dependent variable; whereas SFH, PDW, MUAC as independent variable showed that birth weight of new born babies significantly correlated with SFH, PDW and MUAC.

Multiple regression analysis with birth weight as the dependent variable; and SFH, PDW, MUAC, maternal height as independent variable showed that birth weight significantly correlated with SFH and MUAC. Stepwise multiple regression analysis with same dependent and independent variable showed that SFH alone explained about 18% of the observed variation in birth weight. Stepwise addition of other variables such as MUAC, PDW and maternal height increase the association but major contribution was by SFH. As have others, we found a good correlation between SFH measurement and birthweight<sup>15,16</sup>.

Begum F<sup>17</sup> found that SFH explained 31% of the observed variation of birth weight with correlation efficient of 0.56. In a study done in Tanzania, Walraven et al<sup>18</sup> showed SFH, PDW & MUAC respectively explain 41%,13%,4% of the observed variation in birth weight.

Performance of SFH measurement in prediction of low birth weight shows that sensitivity and negative predictive value increase gradually with increasing SFH but specificity and positive predictive value decreases. Similar type of findings was also found in study of Begum F<sup>17</sup>.

To determine the cut-off value for detecting low birth weight baby a ROC (Receiver operated characteristic) was constructed. The maximum deviation of the curve from diagonal line was observed at 29 cm and it was taken as the cut-off point. Begum F also found 29 cm as cut-off value for prediction of low birth weight.

Sensitivity of a test is the ability of the test to detect disease when it is present. At 29 cm cut-off level single pre-delivery SFH can detect 47.14% of LBW fetus.

Specificity of a test is ability of the test to identify patient without disease. 29 cm cut-off level single pre-delivery SFH can detect 77.22% of babies of normal birth weight.

Positive Predictive Value is the probability of patient having the disease. 29 cm cut-off level single pre-delivery SFH can predict that 24.81% of newborns of these mothers will be of LBW.

Negative Predictive Value is the probability of the patient without the disease. 29 cm cut-off level single pre-delivery SFH can predict that 73.08% of newborns will be of normal weight.

Our study corresponds with the findings of Hoelscher et al<sup>18</sup> & Begum F<sup>17</sup> that a SFH measurement of 29cm reasonably predicts low birth weight babies. Though, Walraven<sup>19</sup> study in Tanzania showed a value of 30 cm.

Cut-off level was chosen to include arbitrarily the lower 20% of the women. The detection

rate of SFH (66%) was 2-3 times greater than that of other three variables (PDW, MUAC and maternal height)<sup>19</sup>.

## CONCLUSION :

Symphysio Fundal Height measurement seems effective in predicting low birth weight neonate. It was a better predictor of birth weight than maternal height, pre-delivery weight or mid upper arm circumference.

To have a cut off level of SFH for prediction of low birth weight as a national standard we have to determine it with a large sample size covering different socio-economic groups and anthropometric variation. Intra observer and inter-observer variation also has to be considered.

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## **The Morphometry of the Vertebral Foramen of the Adult Dried Fifth Lumbar Vertebrae in Bangladeshi Population**

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### **ABSTRACT :**

**BACKGROUND :** Among the five lumbar vertebrae, the fifth lumbar vertebra is atypical, having larger body than the canal & is thus susceptible to narrowing of the vertebral canal (spinal canal stenosis), which ultimately results in compression of cauda equina & the emerging nerve roots. Lumbar spinal canal stenosis is considered to be a causative factor to low back pain. Accurate morphometric data will help in the diagnosis of such spinal diseases & play role in subsequent spinal surgery & instrumentation.

**OBJECTIVE :** The study aims to collect data from adult dry fifth lumbar vertebra in the Bangladeshi population to establish normative data & to find out whether they differ from those of other population.

**METHOD :** This cross-sectional study was carried out in the Department of Anatomy, Sir Salimullah Medical College, Dhaka from January 2012 to December 2012. A total of 153 fully ossified morphologically normal complete bones of dry human fifth lumbar vertebra of unknown sex were included in this study.

**RESULT :** This study observed that cephalic length of vertebral foramen (CeLVF), caudal length of vertebral foramen (CaLVF), vertebral foramen width (VFW) and transverse diameter of vertebral foramen (TDVF) were  $17.8 \pm 3.0$ ,  $20.5 \pm 2.0$ ,  $26.2 \pm 1.7$  and  $27.8 \pm 2.3$  mm respectively in male. The mean  $\pm$  SD of these same variables were  $17.9 \pm 2.6$ ,  $20.1 \pm 2.4$ ,  $25.0 \pm 2.0$  and  $26.1 \pm 2.6$  mm respectively in female. All values were significantly higher in male than that of female except cephalic length of vertebral foramen which are statistically non-significant between male and female (CeLVF  $p=0.761$ ).

**CONCLUSION :** To get normative data on Bangladeshi population, study with larger sample size of known age, sex, stature and ethnicity is needed. Comparative study between dry bones and the living bones by radiological methods are also recommended.

**KEY WORDS :** Cephalic length of vertebral foramen (CeLVF), Caudal length of vertebral foramen (CaLVF), Vertebral foramen width (VFW), Transverse diameter of vertebral foramen (TDVF)

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## INTRODUCTION :

The vertebral column is the central bony pillar of the body<sup>1</sup>. It has drawn much interest for the medical researchers because of the upright posture<sup>2</sup>. It acts as a firm support to the body, transfers the body weight to the legs, encloses & protects the spinal cord<sup>1</sup>. There are five lumbar vertebrae, of which the first four are typical & the fifth is atypical. The larger, triangular vertebral foramen of the fifth lumbar vertebra is for the lodgment & protection of cauda equina. Narrowing of the vertebral canal referred to as spinal canal stenosis which causes compression of cauda equina & the emerging nerve roots<sup>3</sup>.

At the level of the fifth lumbar vertebra, the vertebral bodies are larger than the canal & are thus susceptible to stenosis<sup>4</sup>. Spinal canal stenosis has primary, secondary & combined forms. Primary stenosis may be congenital or developmental, when it is due to defective postnatal development of the lumbar vertebrae. The latter includes achondroplastic stenosis & constitutional stenosis. In secondary stenosis, the spinal canal is developmentally normal & compression is due to an acquired condition such as degenerative changes from aging, injury, diseases, sequelae of spinal surgery or vertebral fracture<sup>5</sup>. The compression of neural structure in vertebral canal is associated with neurological complications such as pain in the back & lower limbs on walking, weakness & paraesthesiae along the distribution of the affected nerve roots<sup>6</sup>. Backache is an extremely common human phenomenon; a price mankind has to pay for their upright posture. It is a common cause of occupational & domestic disability in industrialized societies. Various causes have been attributed to low backache, but lumbar spinal canal stenosis as a causative factor is of great interest<sup>7</sup>.

Accurate anatomic descriptions of vertebral anatomy are necessary for the diagnosis of various spinal diseases, spinal surgery & instrumentation<sup>8</sup>. With the development of vertebral surgery & biomechanics as well as the improvement of recognition in vertebral column diseases, the overall anatomic data are needed to be provided. The data can be useful while carrying out surgical procedures with the help of model vertebral column in the operation theatre<sup>9</sup>. To diagnose spinal canal stenosis, it is important to know the normal value of spinal canal. For the radiologists, the normative values are helpful in radiological diagnosis of spinal canal stenosis for population concern. This study is conducted to determine the normal ranges of the spinal canal diameters in normal adult Bangladeshi. The findings of this study might be useful in providing morphometric data that can be used in anatomical, forensic, orthopaedic, neurosurgical & radiological practices.

## Objective

The aim of the present study is to collect data on the dimensions of the spinal canal from adult dry fifth lumbar vertebra in the Bangladeshi population to establish normative data & to find out whether they differ from those of other population.

## MATERIALS & METHODS :

This was a cross sectional analytic study, carried out in the Department of Anatomy, Sir Salimullah Medical College, Dhaka from January 2012 to December 2012. In this study, 153 fully-ossified dry human fifth lumbar vertebrae were collected from the Department of Anatomy and also from the students of Sir Salimullah Medical College and Medical College for women & Hospital, Uttara.

Sex of the collected bones were determined by using discriminant function analysis formula <sup>10</sup> & other sex differentiating features of the fifth lumbar vertebrae.

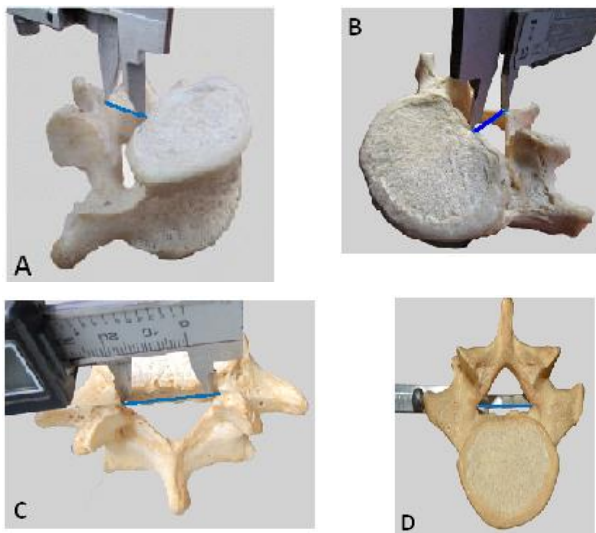
**Operational definitions for the variables used in the study** <sup>4,8,14</sup> :

**Vertebral Foramen Width (VFW)** : Maximum transverse distance between the upper border of the inner surfaces of left & right pedicles.

**Transverse Diameter of Vertebral Foramen (TDVF)**: Maximum transverse distance between the inner surfaces of two pedicles.

**Cephalic Length of Vertebral Foramen (CeLVF)** : Antero-posterior diameter at the cephalic border of the vertebral foramen.

**Caudal Length of Vertebral Foramen (CaLVF)** : Antero-posterior diameter at the caudal border of the vertebral foramen.



**Fig. 1** : Measurement of Caudal Length (A), Cephalic Length (B), Width (C) & Transverse Diameter(D) of Vertebral Foramen

All the measurements were recorded by Digital slide calipers in millimeter (mm). Each

variable was measured three times to exclude observer error and results were recorded as the mean of three values. Photographs were taken during measurements of the collected samples.

Data were analyzed by SPSS for Windows version 16.0. To evaluate the significance of the results between male & female, unpaired Student's 't' test were done. 'p' value <0.05 were considered as significant.

**RESULTS :**

Among 153 collected bones, 48.37% were of male bones & 51.63% female bones (Table I).

**Table I : Grouping of sample**

Sex	No. (%)
Male	74 (48.37%)
Female	79 (51.63%)

Mean  $\pm$  SD value of cephalic length of vertebral foramen were  $17.8 \pm 3$  mm in male and  $17.9 \pm 2.6$  mm in female. No significant difference were found between male and female bones ( $p=0.761$ ) (Table II). Mean  $\pm$  SD value of caudal length of vertebral foramen were  $20.5 \pm 2.0$  mm in male and  $20.1 \pm 2.4$  mm in female. No significant difference were found between male and female bones ( $p=0.271$ ) (Table II).

Mean  $\pm$  SD value of vertebral foramen width were  $26.2 \pm 1.7$  mm in male and  $25.0 \pm 2.0$  mm in female. Significant difference were found between male and female bones ( $p<0.001$ ) (Table III).

Mean  $\pm$  SD value of Transverse diameter of vertebral foramen were  $27.8 \pm 2.3$  mm in male and  $26.1 \pm 2.6$  mm in female. Significant difference were found between male and female bones ( $p<0.001$ ) (Table III).

**Table II :** Cephalic & Caudal length of vertebral foramen of fifth lumbar vertebrae of male & female, expressed in mm

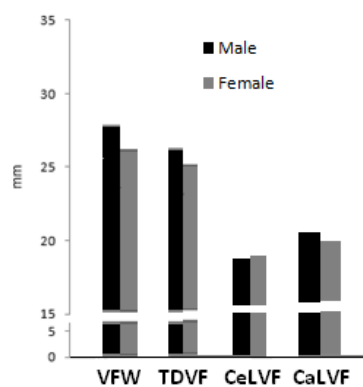
	Vertebral foramen	
	Cephalic length Mean ± SD (Range)	Caudal length Mean ± SD (Range)
Male (n=74)	17.8 ± 3 (13.04-24.91)	20.5 ± 2.0 (15.13-23.98)
Female (n=79)	17.9 ± 2.6 (13.01-24.7)	20.1 ± 2.4 (12.86-23.72)
p value	0.761*	0.271*

\* Unpaired Student's 't' test (Not-significant)

**Table III :** Vertebral foramen width & transverse diameter of vertebral foramen of fifth lumbar vertebrae of male & female , expressed in mm

	Vertebral foramen width Mean ± SD (Range)	Transverse diameter of Vertebral foramen Mean ± SD (Range)
Male (n=74)	26.2 ± 1.7 (21.48-28.95)	27.8 ± 2.3 (21.4-30.9)
Female (n=79)	25.0 ± 2.0 (20.33-29.76)	26.1 ± 2.6 (19.28-30.91)
p value	<0.001*	<0.001*

\* Unpaired Student's 't' test (Significant)



**Fig.1 :** Bar diagram showing vertebral foramen width (VFW), transverse diameter (TDVF), cephalic length (CeLVF) & caudal length (CaLVF) of vertebral foramen in male and female

## DISCUSSION :

The skeletal characteristics of different bones vary among populations and each population has specific standards to optimize the accuracy of identification. This cross-sectional study was carried out with an aim to establish the normal ranges of spinal canal diameters of adult dry human fifth lumbar vertebra. It is well established that the morphometrical data varies within different sex, race, ethnic & regional groups<sup>7</sup>. Population based normal variations of spinal diameters in Bangladeshi population is not well documented in literature. Hence there is a need for our own metrical data. The results of the current study were compared with the results of different researchers of abroad. Observed results of morphological parameters of the present study showed some similarities as well as dissimilarities with the available data present on different publications.

### Cephalic length of vertebral foramen

This study indicate that the mean ± SD of cephalic length of vertebral foramen were greater in female than that of male which was statistically non - significant (p = 0.761). The measured value of the present study was found dissimilar when it was compared with studies conducted by Allbright (2007)<sup>10</sup> on William M. Bass Skeletal Collection (male p=0.654, female p<0.001), Wescott (2005)<sup>11</sup> on Hamann-Todd Osteological Collection (male p=0.052, female p<0.001), Amonoo-Kuofi (1985)<sup>5</sup> on Nigerian (p <0.001), Eisenstein (1977)<sup>12</sup> on South African and Kang et al. (2012)<sup>13</sup> on Korean (male p <0.05, female p <0.05) population. Variation of skeletal morphology due to ethnic and racial difference might be the cause of this dissimilarity. The result of the present study was similar with Gupta and Singla (2011)<sup>14</sup> who worked on the population of North India (p=0.523) and Masharawi and Salame (2011)<sup>8</sup>

on Hamann-Todd Osteological Collection (male  $p=0.509$ , female  $p=0.083$ ).

### **Caudal length of vertebral foramen**

The calculated value of the present study showed that the mean  $\pm$  SD of caudal length of vertebral foramen was greater in male than that of female which was statistically non-significant ( $p=0.271$ ). There are differences between the mean values of the present study and the study conducted by Gupta & Singla (2011)<sup>14</sup> on North Indian ( $P<0.001$ ) and Postacchini et al. (1983)<sup>15</sup> on Italian and Indian skeleton in case of male. The reasons for these differences might be due to interplay of racial, ethnic and environmental factors. There was no available other study value to compare in case of female.

### **Vertebral foramen width**

The present study showed greater mean  $\pm$  SD of vertebral foramen width in male than that of female which is statistically significant ( $p < 0.001$ ). The measured value of the present study was not identical with Masharawi and Salame (2011)<sup>8</sup> who worked on the Hamann-Todd Osteological Collection (male  $p<0.001$ , female  $p<0.01$ ). The population studied belongs to the different geographical and environmental area which might be the reason for this dissimilarity. The observed value in this study was also dissimilar with Rakhawy (2010)<sup>4</sup>, Jadhav (2011)<sup>16</sup>, Tacar et al. (2003)<sup>17</sup>, Amonoo-Kuofi (1982)<sup>18</sup> and Anazi (2008)<sup>3</sup>. They all carried out radiological study on the population of Egypt, Maharashtra ( $p<0.001$ ), Turkey, Nigeria ( $p < 0.001$ ) and Saudi respectively. Two dimensional view of the three dimensional structures were used in the radiological study which might be the cause of this dissimilarity.

### **Transverse diameter of vertebral foramen**

In the present study, the mean  $\pm$  SD of transverse diameter of vertebral foramen is

greater in male than that of female which is statistically significant ( $p < 0.001$ ). The result observed in the present study was found dissimilar to the findings reported by Wescott (2005)<sup>11</sup> who worked on Hamann-Todd Osteological Collection ( $p<0.001$ ), Eisenstein (1977)<sup>12</sup> on South African and Attar et al. (2001)<sup>19</sup> on Turkish (male  $p=0.288$ , female  $p<0.05$ ) population. These dissimilarities might be due to variation in race and ethnicity. The values of the present study also showed dissimilarity with the studies conducted by Patel et al. (2012)<sup>20</sup> and Gupta and Singla (2011)<sup>14</sup> on Gujaratian (male  $p<0.001$ , female  $p=0.844$ ) and North Indian (male  $p<0.001$ ) respectively. Different food habit and culture could be the factors for this dissimilarity.

### **CONCLUSION :**

Comparison of the present study with the published data supports the view that there are probably subtle racial differences in size of the spinal canal. This strengthened the need for compiling tables for every population concern.

To get normative data on Bangladeshi population, study with larger sample size of known age, sex, stature and ethnicity is needed. Comparative study between dry bones and the living bones by radiological methods are also recommended.

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## **Thrombolytic Therapy in ST Elevation Myocardial Infarction : An Review**

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### **ABSTRACT**

*Achieving vascular reperfusion is the treatment goal of STEMI patients, which restores coronary flow, thus reduces infarct size and improves myocardial function and survival over the short-term and long-term. Though Primary percutaneous coronary intervention (PCI) is now the preferred mode of treatment, but thrombolytic therapy is the choice of treatment when primary PCI can not be done due to lack of facility and or time delay. Thrombolytic therapy should be given if primary PCI cannot be delivered within 120 minutes of FMC (First Medical Contact). This article reviews the currently available thrombolytics and their use in STEMI patients.*

*KEY WORDS : STEMI , PCI , Thrombolytics*

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### **INTRODUCTION :**

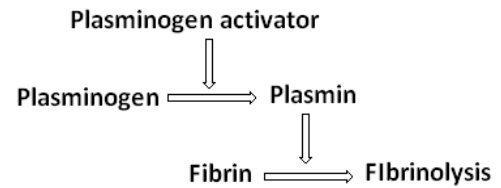
ST elevation myocardial infarction (STEMI), is one of the acute coronary syndromes but differs from the other presentations by being only diagnosed with clinical presentation and ECG changes alone, without awaiting for the results of biochemical markers of myocardial damage (eg, Troponin T). STEMI develops in the vast majority of cases when an atheromatous plaque undergoes disruption. Disruption of the plaque results in thrombus formation which can completely or partially occlude the affected coronary artery.

Coronary artery spasm may also contribute to a reduction in coronary blood flow at this time. Myocardial cell death begins after about 15 minutes of the onset of symptoms / ECG changes and progresses over a period of hours. The process is almost complete after twelve hours<sup>1</sup>.

Achieving vascular reperfusion is the treatment goal which restores coronary flow thus reduces infarct size and improves myocardial function and survival over the short-term and long-term. Primary percutaneous coronary intervention (PCI) is now the preferred mode of treatment, if can



be done within 2 hour from presentation to the emergency department<sup>2</sup>. But availability of a skilled intervention team and equipped catheterization laboratory is not always available. Thrombolytic therapy remains the only therapeutic option in that case as well as in time delay. NICE Clinical Guidelines (CG 167) state that thrombolysis should be given if primary PCI cannot be delivered within 120 minutes<sup>3</sup>. This article summarizes the history & evidence based and current use of thrombolytics in STEMI patients.

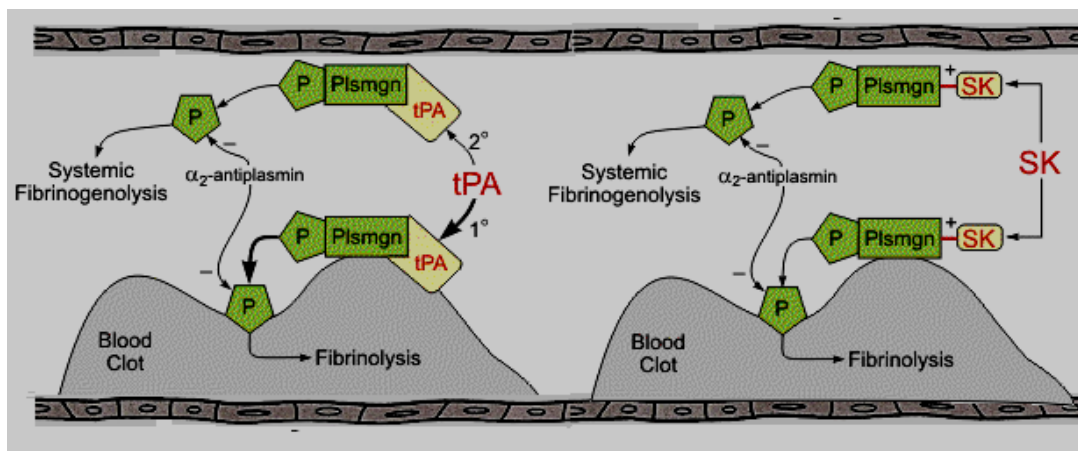


**Fig. 1 : Physiology of fibrinolysis**

The generational classification<sup>4</sup> of the thrombolytic agents is presented in Table I.

**Table I : Generational classification of the thrombolytic agents**

Generation of thrombolytic drug	Fibrin specific	Non-fibrin specific
First generation	-	1. Urokinase * 2. Streptokinase (SK)*
Second generation	1. Recombinant tissue plasminogen activator (t-PA)* 2. Alteplase	1. Pro-urokinase (scu-PA) 2. Anisoylated plasminogen streptokinase activator complex (APSAC) *
Third generation	1. Tenecteplase (TNK-tPA) * 2. Reteplase * 3. Monteplase 4. Lanoteplase 5. Pamiteplase	



P = Plasmin, Plsmgn = Plasminogen, tPA = tissue plasminogen activator, SK = Streptokinase, 1° = primary, 2° = secondary

**Fig. 2 : Comparison of mechanism of action of tPA & SK**



## **MECHANISM OF ACTION of THROMBOLYTIC AGENTS**

Plasmin (a serine protease enzyme) is activated from its inactive precursor plasminogen by various plasminogen activators. Plasmin then breaks down the fibrin clots, a process known as fibrinolysis.

Thrombolytic agents act as Plasminogen activators. Few Plasminogen activators are fibrin-specific, which preferentially activate fibrin-bound plasminogen. In contrast, non-specific plasminogen activators act on both fibrin-bound and circulating plasminogen<sup>5</sup>.

Tissue plasminogen activator (tPA) produces clot lysis through the following sequence: a) tPA binds to fibrin on the surface of the clot ; b) Activates fibrin-bound plasminogen; c) Plasmin is cleaved from the plasminogen associated with the fibrin; d) Fibrin molecules are broken apart by the plasmin and the clot dissolves.

It is important to note that plasmin also breaks down other circulating proteins, including fibrinogen. Although tPA is relatively selective for clot-bound plasminogen, it still activates circulating plasminogen thereby releasing plasmin, which can lead to the breakdown of circulating fibrinogen and cause an unwanted systemic fibrinolytic state<sup>6</sup>. Normally, circulating  $\alpha_2$ -antiplasmin inactivates plasmin, but therapeutic doses of thrombolytics lead to sufficient plasmin formation to overwhelm the limited circulating concentrations  $\alpha_2$ -antiplasmin.

Unlike tPA, SK is not fibrin specific and therefore binds equally with circulating and non-circulating plasminogen. Therefore, SK produces significant fibrinogenolysis along with clot fibrinolysis<sup>7</sup>. For this reason, tPA is generally preferred as a thrombolytic agent

over SK, especially when used for dissolving coronary and cerebral vascular thrombi.

Efficacy of thrombolytic drugs depends on the age of the clot. Older clots have more fibrin cross-linking and are more compacted; therefore, older clots are more difficult to dissolve. For treating acute myocardial infarction, the thrombolytic drugs should ideally be given within the first 2 hours. Beyond that time, the efficacy diminishes and higher doses are generally required to achieve desired lysis.

### ***Streptokinase (SK)***

Streptokinase is a protein, produced by various strains of  $\beta$ -hemolytic streptococci. It is not an enzyme, therefore does not proteolytically cleave plasminogen. Rather it binds to plasminogen and causes it to change conformation, thereby exposing its active site. The streptokinase-plasminogen complex then act as activator of additional plasminogen molecule<sup>8</sup>. Its activity is independent of its association with fibrin.

But because of its high antigenicity, repeat administration of streptokinase within six months of a previous dose is absolutely contraindicated due to risk of serious allergic reactions. It is no longer marketed in the United States but is used in other countries.

### ***Anistreplase (APSAC)***

Anistreplase (anisoylated plasminogen streptokinase activator complex; APSAC) is a derivative of streptokinase & has been mostly abandoned due to its high cost and considerable fibrinogenolysis<sup>6</sup>.

### ***Urokinase (u-PA)***

Urokinase is referred to as urinary-type plasminogen activator (u-PA) because it is formed by kidneys and is found in urine. As SK it also produces considerable

fibrinogenolysis<sup>9</sup>. One benefit over SK is that u-PA is non-antigenic; however, this is offset by a much greater cost. It has limited clinical use, preferably in pulmonary embolism.

**Tissue Plasminogen Activator (t-PA)**

Tissue plasminogen activator is a five-domain serine protease that has a very high affinity for fibrin<sup>7</sup>. It has not been shown to induce autoantibodies and rarely causes allergic reactions or hypotension.

- **Alteplase (rtPA)** is a recombinant form of human tPA. It has a short half-life (~5 min) and therefore is usually administered as an intravenous bolus followed by an infusion.
- **Retepase** is a genetically engineered, smaller derivative of recombinant tPA

that has increased potency and is faster acting than rtPA. Due to lack of fibrin binding domain and less fibrin specificity, reteplase is cheaper to produce than t-PA. Efficacy and safety of reteplase has been shown to be similar, but not superior, to streptokinase and t-PA. It is usually administered as IV bolus injections.

- **Tenecteplase (TNK-tPA)** is a t-PA derivative, genetically engineered with an extra glycosylation site in order to have a longer half-life . It has greater binding affinity for fibrin than rtPA[16].. Because of its longer half-life, it can be administered by IV bolus. It is only approved for use in acute myocardial infarction.

**Table 2 : Comparison of approved thrombolytic agents<sup>10</sup>**

Features	Thrombolytics			
	Streptokinase	Alteplase	Retepase	Tenecteplase
Dose	1.5 MU in 30 –60 min	Up to 100 mg in90 min (based on weight)	10 U X 2 (30 min apart) each over 2 min	30–50 mg (based on weight)
Bolus administration	No	No	Yes	Yes
Antigenic & Allergic reaction	Yes	No	No	No
Systemic fibrinogenolysis	Marked	Mild	Moderate	Minimal
90-min patency rates (%)	≈50	≈75	≈75	≈75
TIMI grade 3 flow (%)	32	54	60	63

**2013 Revised & 2004 ACC/AHA Guidelines for Fibrinolytic therapy in STEMI <sup>11</sup>**

Class I
<p>1. In the absence of contraindications, fibrinolytic therapy <b>should be administered</b> to STEMI patients with symptom onset within the prior 12 hours</p> <p>a) AND ST elevation of &gt; 0.1 mV in at least 2 contiguous precordial leads or 2 adjacent limb leads</p> <p>b) AND new or presumably new LBBB.</p> <p>c) AND at non-PCI-capable hospitals when the anticipated FMC-to-device time at a PCI-capable hospital exceeds 120 minutes because of unavoidable delays.<sup>12</sup></p> <p>d) AND when it is anticipated that primary PCI cannot be performed within 120 minutes of FMC. <sup>13</sup></p> <p>2. When fibrinolytic therapy is indicated or chosen as the primary reperfusion strategy, it should be administered within 30 minutes of hospital arrival.<sup>14</sup></p>

<b>Class III (Harm)</b>
<p>Fibrinolytic therapy <b><i>should not be administered</i></b> to</p> <ol style="list-style-type: none"> <li>a) asymptomatic patients whose initial symptoms of STEMI began more than 24 hours earlier.</li> <li>b) patients whose 12 lead ECG shows only ST segment depression except if a true posterior MI is suspected.</li> <li>c) patients with ST depression except when a true posterior (inferobasal) MI is suspected or when associated with ST elevation in lead aVR.<sup>15</sup></li> </ol>

<b>Class IIa</b>
<p>In the absence of contraindications, it is <b><i>reasonable to administer</i></b> fibrinolytic therapy to STEMI patients</p> <ol style="list-style-type: none"> <li>a) with symptom onset within the prior 12 hours and 12 lead ECG findings consistent with a true posterior MI</li> <li>b) with symptoms beginning within the prior 12 to 24 hours who have continuing ischaemic symptoms and ST elevation greater than 0.1 mV in at least 2 contiguous precordial leads or at least 2 adjacent limb leads.</li> <li>c) when PCI is not available, AND if there is clinical and/or electrocardiographic evidence of ongoing ischemia within 12 to 24 hours of symptom onset and a large area of myocardium at risk or hemodynamic instability.</li> </ol>

### ***Contraindications for Using Thrombolytics*** <sup>11</sup>

Absolute contraindications are:

1. Prior intracranial hemorrhage
2. Known cerebral vascular lesion
3. Brain malignancy
4. History of ischemic stroke within 3 months (except acute presentation of ischemic stroke)
5. Aortic dissection
6. Active bleeding / bleeding diathesis
7. History of head trauma within 3 months
8. Intracranial/spinal surgery within 2 months

9. Severe uncontrolled hypertension (unresponsive to emergency treatment)

Relative contraindications are :

1. History of ischemic stroke > 3 months old
2. Dementia
3. Other intracranial pathology
4. Major surgery in past 3 weeks
5. Internal bleeding within past 4 weeks
6. Non-compressible vascular punctures
7. Pregnancy
8. Active peptic ulcer
9. Oral anticoagulant therapy
10. Traumatic / prolonged CPR within 3 weeks

### ***Choice of thrombolytic agent*** <sup>16</sup>

The thrombolytic agent used in a particular individual is based on institution preference and the age of the patient.

In patients, presenting within 4 hours of symptom onset, the speed of reperfusion of the infarct vessel is of paramount importance and a high-intensity fibrinolytic regimen such as accelerated t-PA is the preferred treatment, except in those for whom the risk of death is low (e.g. a young patient with a small inferior MI) and the risk of ICH is increased (e.g. acute hypertension), in whom Streptokinase and accelerated t-PA are approximately equivalent choices.

For those, presenting between 4 hours and 12 hours after the onset of chest discomfort, the speed of reperfusion of the infarct vessel is of lesser importance, Streptokinase and accelerated t-PA are therefore generally equivalent options.

For those presenting between 4 and 12 hours from symptom onset with a low-mortality risk but an increased risk of ICH (e.g. older patients with inferior MI, systolic pressure > 100 mm Hg and heart rate < 100 beats/minutes), Streptokinase is probably preferable to t-PA because of cost considerations.

As an alternative to t-PA, a bolus fibrinolytic such as Tenecteplase OR reteplase is recently in practice for its ease of administration, a lower chance of medication errors and less non-cerebral bleeding.

### **Side Effects**

Intracranial bleeding (ICB) and subsequent cerebrovascular accident (CVA) is a serious side effect of thrombolytic use. The risk of ICB is dependent on a number of factors, including a previous episode of intracranial bleed, age of the individual, and the thrombolytic regimen that is being used. In general, the risk of ICB due to thrombolytic use for the treatment of an acute myocardial infarction is between 0.5 and 1 percent.<sup>17</sup>

Thrombolytic therapy to abort a myocardial infarction is not always effective. The degree of effectiveness of a thrombolytic agent is dependent on the time since the myocardial infarction began, with the best results occurring if the thrombolytic agent is used within two hours of the onset of symptoms.<sup>18</sup> If the individual presents more than 12 hours after symptoms commenced, the risk of intracranial bleed are considered higher than the benefits of the thrombolytic agent.<sup>19</sup> Failure rates of thrombolytics can be as high as 20% or higher.<sup>20</sup>

In cases of failure of the thrombolytic agent to open the infarct-related coronary artery, the patient is then either treated conservatively with anticoagulants or allowed to "complete the infarction" or PCI is then performed. PCI in this setting is known as "rescue PCI" or "salvage PCI". Complications, particularly bleeding, are significantly higher with rescue PCI than with primary PCI due to the action of the thrombolytic agent.

Depending on the thrombolytic agent being used, adjuvant anticoagulation with heparin or low molecular weight heparin may be of

benefit.<sup>21</sup> With tPA and related agents (reteplase and tenecteplase), heparin is needed to maintain coronary artery patency. Because of the anticoagulant effect of fibrinogen depletion with streptokinase and urokinase<sup>22</sup> treatment, it is less necessary there.<sup>21</sup>

### **CONCLUSION :**

In STEMI, thrombolytic therapy is the treatment of choice when primary PCI is not possible. The key to enhanced myocardial salvage and reduced long-term mortality is quick and complete administration of thrombolytic therapy. In a given clinical setting, the choice of thrombolytic agent should consider risk of mortality, ICH, age, timing of thrombolytic treatment and cost effectiveness in a given health care system. Maximal reperfusion and with minimal bleeding and reocclusion complications is the treatment goal for STEMI patients.

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## **Chronic Viral Hepatitis : Diagnosis & Treatment**

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### **ABSTRACT**

*Chronic viral hepatitis is caused by Hepatitis B, C, D and E viruses, leading to serious complications like cirrhosis of liver and hepatocellular carcinoma. Early diagnosis before the development of these complications and appropriate antiviral therapy can cure the disease in most of the cases.*

**KEY WORDS :** *Chronic Viral Hepatitis, Cirrhosis of Liver, Antiviral Therapy*

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### **INTRODUCTION :**

Viral hepatitis is the inflammation of liver induced by viral infection. 'Epidemic jaundice' has existed since early civilization. However, the viral aetiologies were discovered in the past few decades.<sup>1</sup> Five major viruses, namely Hepatitis A, B, C, D and E viruses (HAV, HBV, HCV, HDV and HEV) are responsible for almost all the viral hepatitis cases worldwide. All of these viruses are RNA viruses, except HBV. Chronic viral hepatitis, caused by all hepatitis viruses, except HAV, is defined as persistence of viral hepatitis for 6 months (3 months for HEV).<sup>2</sup>

### **EPIDEMIOLOGY**

2.3 billion people in the world are infected with hepatitis viruses. Approximate numbers of people infected with HBV, HCV, HDV and HEV worldwide are 2 billions, 185 million, 20 million and 20 million, respectively.<sup>3, 4</sup> WHO estimated that 1 in 3 people was infected with either HBV and HCV and 1.3 million died from this.<sup>5</sup>

### **PATHOGENESIS**

Viral hepatitis has diverse modes of transmission. HAV and HEV have faeco-oral transmission. HBV is transmitted through blood transfusion, surgical interventions,

needle sharing and injuries, sexual contact and perinatal. HCV is predominantly transmitted by transfusion. The virus localizes in the hepatocytes to induce both cellular and humoral immunities. The cytotoxic T lymphocytes destroy the virus-infected hepatocytes producing acute hepatitis. The pathogenic role of antibodies is yet to be established, but they are helpful in the diagnosis of the disease as sero-markers. Most of the acute viral hepatitis resolves spontaneously. A small proportion of HBV, HCV, HDV and also HEV (in immune-compromised host) infection can persist in the hepatocytes for longer period. When it extends beyond 6 months (3 months for HEV), the condition is defined as chronic hepatitis. In chronic hepatitis, apart from hepatocyte destruction, hepatic stellate cells, transform into fibroblast-like cells and produce reticular fibers leading to fibrosis. At the same time, hepatocyte regeneration continues. In a nutshell, hepatocyte destruction and regeneration along with fibrosis occur simultaneously in chronic hepatitis. The liver becomes an organ with nodules and intervening fibrous tissues - cirrhosis of liver.<sup>6</sup>

The course of disease varies according to the virus, mode of transmission and age of onset. Perinatally acquired HBV infection develops chronic hepatitis in 90 percent cases. The same virus produce chronic hepatitis in 10 percent cases in adult.<sup>7</sup> HCV leads to chronic hepatitis in 75 percent cases.<sup>8</sup> Only small proportion of HEV develop chronic hepatitis (0.1 percent).<sup>9</sup>

### **COURSE OF THE DISEASE**

Chronic viral hepatitis is diagnosed late in most cases because of absence of paucity of symptoms in early phase and slow progression. Early stage is often asymptomatic. Symptoms are non-specific like generalized weakness, anorexia, nausea and

upper abdominal discomfort. Another feature of this stage is lack of signs. Hepatomegaly is found in minority of patients.<sup>8</sup>

Progressive liver disease is characterized by development of cirrhosis and/ or flares of hepatitis. Hepatitis flares have clinical features similar to acute viral hepatitis including anorexia, nausea, vomiting, jaundice and tender hepatomegaly, but usually milder. SGPT and SGOT levels are raised.<sup>8</sup>

Cirrhosis is characterized by features of portal hypertension such as ascites, splenomegaly, distended abdominal veins and hematemesis and melaena from ruptured oesophageal varices. Ultrasonogram is characteristic showing a small liver with irregular echogenicity, splenomegaly and ascites. Serum albumin is low and prothrombin time is prolonged, indicating hepatic failure.<sup>8</sup>

Hepatic encephalopathy, characterized by altered sleep pattern, aggressive behavior, impaired level of consciousness and flapping tremor is not uncommon in cirrhosis. This condition is precipitated by excessive aspiration of ascitic fluid, constipation, ruptured oesophageal varices, high protein diet, infection and electrolyte imbalance. Hepato-renal syndrome, defined as pre-renal acute kidney injury in chronic liver disease, is a grave complication of cirrhosis. Spontaneous bacterial peritonitis, another common complication of cirrhosis is diagnosed when fever and abdominal pain develops in a cirrhosis case with diffuse abdominal tenderness and high neutrophil count and positive bacterial culture in ascitic fluid.<sup>10</sup>

Chronic hepatitis leads to hepatocellular carcinoma in minority of patients, more in chronic HCV hepatitis. It is usually a sequela of cirrhosis, but can develop without cirrhosis also. It is characterized by rapid worsening of symptoms, abdominal pain and tender hard hepatomegaly. Diagnosis is made with the aid



of focal lesion within the liver in ultrasonogram or CT scan and a raised serum alpha fetoprotein level.<sup>10</sup>

## DIAGNOSIS

Chronic viral hepatitis is diagnosed with the persistence of HBV, HCV or HDV for 6 months or HEV for 3 months. Chronic HBV hepatitis is diagnosed with a positive HBsAg by ELISA.<sup>11,12,13</sup> Chronic HCV hepatitis is diagnosed with a positive anti-HCV antibody and a positive HCV-RNA by PCR.<sup>14</sup> Chronic HDV hepatitis is diagnosed with a positive anti-HDV antibody by ELISA and a positive HDV-RNA by PCR.<sup>15</sup> Chronic HEV hepatitis is usually occurs in immune-compromised individuals. So Anti-HEV antibody is often absent. This condition is therefore diagnosed with a positive HEV-RNA by PCR.<sup>16</sup>

## TREATMENT

### CHRONIC HBV & HDV HEPATITIS

Antivirals are not required in all cases of chronic HBV hepatitis. Indications of antiviral therapy are:

1. Immune active stage defined as evidence of active hepatitis [SGPT increased more than twice of the upper limit or moderate/severe hepatitis on liver histopathology] and high viral load [HBV-DNA >20,000 IU/ml in HBeAg positive cases or >2,000 IU/ml in HBeAg negative cases].
2. Cirrhosis of liver
3. Chronic HBV hepatitis in pregnancy with HBV-DNA  $\geq 2,00,000$  IU/ml.<sup>11,12,13</sup>

Treatment regimen includes either oral antiviral or subcutaneous Pegylated Interferon Alpha (PEG-IFN $\alpha$ ). Oral agents are cheaper, but need to be used for a long

period, 12 months after SGPT is normal, HBV-DNA is undetectable and sero-conversion of HBeAg (Anti-HBe is positive). Current recommended antivirals are Entecavir 1 mg daily or Tenofovir 300 mg daily. PEG-IFN $\alpha$  has the advantage of shorter and definite duration of therapy (48 weeks) and weekly administration, but cannot be used in decompensated cirrhosis.<sup>11,12,13</sup> No additional treatment is required for chronic HDV hepatitis. Treatment of chronic HBV hepatitis clears HDV.<sup>15</sup>

### CHRONIC HCV HEPATITIS

Antivirals are indicated in all diagnosed cases of chronic HCV hepatitis. The regimen varies according to the genotype. The recommendations of European Association for Study of the Liver (EASL) is simple and followed in Bangladesh [Table I,II &III].<sup>14</sup>

**Table I : Antiviral regimen of chronic HCV hepatitis without cirrhosis<sup>14</sup>**

Genotype	Antiviral	Duration
1,4,5,6	LED+SOF	12 weeks
2	RBV+SOF	12 weeks
3	DAC+SOF	12 weeks

**Table II : Antiviral regimen of chronic HCV hepatitis with cirrhosis<sup>14</sup>**

Genotype	Antiviral	Duration
1,4,5,6	LED+SOF	24 weeks
2	RBV+SOF	16 weeks
3	DAC+RBV+SOF	24 weeks

**Table III : Daily dose of antivirals in chronic HCV hepatitis<sup>14</sup>**

Abbreviation	Antiviral	Daily dose
DAC	Daclatasvir	60 mg
LED	Ledipasvir	90 mg
RBV	Ribavirin	1000 mg
SOF	Sofosbuvir	400 mg

## CHRONIC HEV HEPATITIS

Chronic HEV hepatitis is a disease of immune-compromised individuals. Reduction in immune-suppression is the initial step in its management. If HEV is not cleared after 3 months, antiviral is indicated. Current recommendation is Ribavirin 600-1000 mg daily for 3 months. A further 3-month of Ribavirin can be given if HEV-RNA persists after 3 months.<sup>16</sup>

Refractory chronic HEV hepatitis can be treated with PEG-IFN $\alpha$  in patients with liver transplants.<sup>16</sup>

## CONCLUSION :

Chronic viral hepatitis is a potentially curable condition. Antiviral therapy started before the development of cirrhosis or hepatocellular carcinoma can give a complete cure. Early detection and treatment of chronic viral hepatitis is the key to reduction in morbidity and mortality in this condition.

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## Case Report

### Fish Bone Perforation of Terminal Ileum : A Rare Case Report

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#### ABSTRACT

Foreign Body ingestion is relatively not uncommon. However resultant perforation of the small bowel is fortunately rare. We report a case of a terminal ileum perforation due to a fish bone that presented with sign & symptoms of acute appendicitis. Establishing diagnosis can be difficult as foreign body bowel perforation can mimic other causes of acute abdomen. Diagnosis is made intra-operatively during exploration. Several loops of terminal ileum and omentum walling off an inter-loop inflammatory fluid collection and a fishbone were found that pierced the terminal ileum. This patient's gastrointestinal tract perforation was treated by laparotomy.

**KEY WORDS :** Foreign body, Fish bone, Acute Appendicitis, Terminal Ileum

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#### INTRODUCTION :

Sometimes foreign body can be ingested accidentally but majority of the cases it does not produce complication. However ingested sharp & pointed foreign body can pierce the intestine causing perforation and peritonitis<sup>1</sup>. Ingested foreign body can cause perforation of the bowel in a small proportion of patients. Fish bone ingestion is very common however resultant bowel perforation is rare. Terminal ileum perforations are not initially considered as part of differential diagnosis since they clinically mimic acute appendicitis and diverticulitis<sup>2, 3</sup>. Foreign body perforation of the bowel may present with symptoms of an

acute abdomen. Abdominal pain may begin centrally and then localize as peritonitis develops. We present our experience of the diagnosis and operative management of a case of fish bone perforation of the terminal ileum that presented as sign-symptoms of acute appendicitis. Patients may not recall the ingestion of a fishbone, particularly as passage to the distal gastrointestinal tract may be preceded by a significant lag time. Typically patients have a pre-operative working diagnosis of appendicitis or diverticulitis depending on the site of tenderness. The correct pre-operative diagnosis may be made in as little as 23% of cases<sup>4</sup>.

## CASE PRESENTATION :

A 70- years- old hypertensive, non diabetic and non asthmatic woman from Dinajpur, Bangladesh went to local clinic with upper abdominal pain which was moderately severe and localized to epigastrium. Later on that day pain had radiated to the whole abdomen with increasing severity. Senior consultant of that clinic investigated with blood count, USG whole abdomen, Troponin-I, ECG and Echocardiogram. Blood count showed neutrophilic leukocytosis (16,500/cmm) and mild hypertrophic change in ECG. Echocardiogram revealed a good ventricular function with 65% ejection fraction. A random blood sugar showed 5.8 mmol/L. The abdominal ultrasonography identified intense gas artifacts in the midline and minimal free fluid between intestinal loops and suggested acute appendicitis. Other investigation reports appeared normal. On that night she had been suffering from fever which was low grade but continuous. Next morning she felt nausea and vomited one time. She was treated conservatively. With no sign of improvement, on the next day she was referred to Dhaka for better management and was admitted on the same day in Shahabuddin Medical College Hospital. On admission, detailed history was taken. During thorough clinical examination we found her pulse rate was 101 beats per min and blood pressure recorded 140/90 mm of Hg as well as respiratory rate was 16 breaths per min, temperature recorded 101°F. Mc Burney's point tenderness to the right iliac fossa as well as rebound tenderness was elicited. Her abdomen was overall soft other than tender right iliac region which was mildly rigid. She has been taking Olmesartan 20 mg tablet at morning and Nebivolol 2.5 mg at bed time and her blood pressure was well controlled with drug. We decided for open appendicectomy after discussion with the patient party; Pre-anaesthetic checkup was performed and was operated on next day morning. A dose of broad spectrum antibiotics have been started after admission and was kept NPO as she had been treated earlier. Good nutritional support was given in intravenous root.

The patient's abdomen was accessed through right Grid-Iron incision under spinal anesthesia. Then gradual separation of subcutaneous tissue and splitting of muscle according to their direction were done. Peritoneum was then splitted open. Omentum was coiled up with loops of bowel formed early lump. Gentle finger dissection was done then caecum was visualized and appendix was identified and it was inflamed, swollen and friable. Appendicectomy was done after ligating base and mesoappendix. There was another soft lump was found near the ceacum consists of adherent loop of small intestine. Adhesiolysis was done bluntly by finger dissection. During adhesiolysis a sharp foreign body sensation was felt at the tip of the finger. After further exploration a sharp pointed foreign body was found piercing the terminal ileum which was taken out by long artery forceps. Then terminal ileum was mobilized to locate the site of perforation; approximately 10 cm proximal to ileocecal valve where the foreign body was imbedded to. That foreign body was a fish bone. Terminal ileum was perforated and was that much inflamed and swollen; before mobilization it formed the major portion of the early lump. The perforation was then repaired. There were a few collections of inflammatory exudates but fortunately no pus was found inside the loop. Peritoneal toileting was given by normal saline.

The resected appendix was sent for histopathological analysis. The recovered fish bone was approximately 4 cm long. A wide bored surgical drain was placed and the abdomen was closed.

When the patient's detailed history was obtained retrospectively during her follow-up in the post-operative period, it came to our knowledge that she had eaten a fish head and took few large mouthful bite 24 hours before the onset of her abdominal pain.

### Outcome and follow-up

The patient's recovery was good in spite of having fluctuating blood glucose level as she was preoperatively non diabetic. During post

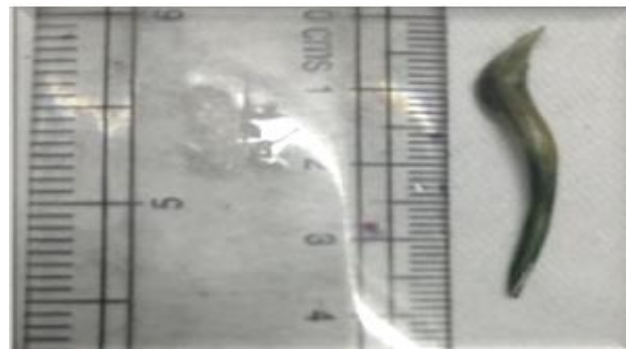
operative period short acting insulin was given to the drip to immediate control of blood glucose. On 3<sup>rd</sup> post operative day sips of water was started. On 5<sup>th</sup> postoperative day she has been discharged with advice.

## DISCUSSION :

Some patients of different age group admitted in hospital with foreign body ingestion. Foreign body ingestion is relatively common and usually a benign event. Most foreign bodies pass through the gastrointestinal tract within a week and only around 1% causes a perforation<sup>1</sup>. Any insoluble ingested foreign body may potentially cause bowel perforation, however the most commonly unintentionally ingested foreign bodies are fish bones, toothpicks, chicken bones and fragments of bone<sup>2</sup>. One of the most frequent reasons of emergency service admissions is foreign body ingestion. Patients at highest risk of ingestion include children, elderly, those with dentures, poor mental status and imprisoned people. Most foreign materials are passes via the faecal route after they pass the gastro-oesophageal junction. Nevertheless, 1% of ingested materials, especially those that are long and sharp-edged, result in GIS perforation. The materials that most often cause GIS perforation include sharp objects such as fish bones, chicken bones and toothpicks. However, pencils, nails, nail clippers; batteries may also result in GIS perforation, albeit rare. GIS perforation secondary to migration of biliary stents has previously been reported<sup>3</sup>.

Incidence of acute appendicitis is common in children. We found 70years old aged female admitted in this hospital with signs of acute appendicitis, though acute appendicitis is not common in this age. Even with a detailed clinical presentation, diagnosis may be difficult and delayed since the ingestion fish bones or other foreign bodies may not be mentioned in the history of the patient<sup>4,5</sup>. She was asked for her general illness but we missed a little detail about her meal; which was later on discovered by retrograde discussion with the patient. Fish bone is a

biological substance and supposed to be digested by gastric juice. In this case fish bone have passed through the gastro esophageal junction and perforated the terminal ileum. Fortunately this is not the first case. In December 2011 in Department of Surgery and Cancer, Imperial College London has reported a case<sup>2</sup>. We have experienced similar case in this hospital. Perforation in these areas can be complicated by abscess formation and peritonitis<sup>1</sup>. Our patient only presented to us with a low grade fever that is usually found in case of acute appendicitis.



**Fig. 1: Photograph of the fish bone discovered intra-operatively (scale is in centimeter)**

Several radiological investigations were performed including plain X-ray of chest, plain X-ray abdomen in erect posture and ultrasonography. Both of the X-rays appeared to be normal with no evidence of intestinal perforation or radio opaque foreign body. The use of ultrasonography as a diagnostic tool for the early detection of appendicitis is not new. Rather, ultrasonography is commonly used as the initial imaging technique in patients suspected of having appendicitis. Because aggressive treatment is indicated in most cases of foreign body-caused appendicitis, ultrasonography should be performed immediately after the appearance of signs and symptoms of acute appendicitis<sup>6</sup>. Ultrasonography was done accordingly. But we had no clue about the foreign body or any fish bone. Intestinal perforation secondary to ingestion of foreign materials may clinically mimic acute appendicitis or diverticulitis. Especially in cases with terminal ileum



involvement, which is the most frequent site for perforations, patients are operated on for acute appendicitis<sup>3, 5</sup>. The sensitivity of CT in detecting a fishbone was 7.4%; however, this rate increased to 100% in retrospective evaluation<sup>7</sup>. In our case we did not performed any CT scan but history of eating fish head 24 hours prior to onset of symptoms obtained retrospectively. Diagnosis of gastrointestinal perforation by plain X-Ray abdomen is not new. The erect chest x-ray (CXR) is the ideal first test for hollow organ perforation and as little as 10-20 mL of free air can be detected under the diaphragm. In our case we have not seen such findings to reach other differentials of acute abdomen. The fish bone was semi transparent in nature thus radiological investigation did not help. The diagnosis of abdominal complication due to fish bone ingestion is particularly difficult as the presentation may mimic common abdominal pathologies<sup>1</sup>.

The period of latency between ingestion of the FB and the onset of symptoms varies from hours to years. Complications usually depend on the size and shape of the FB<sup>8</sup>. Patient's symptoms started within 24 hours of taking a few big bites from fish head. The clinical presentation of bowel perforation secondary to fish bone ingestion can be hugely varied. The diagnosis is often difficult due to the large variety of sites of perforation, the frequent lack of awareness of having ingested a foreign body and the various clinical manifestations of perforation. Patients may present with fever and abdominal pain<sup>4</sup>. Initially pain was to the epigastric region, which later gives us the clue of movement of foreign body. Later the pain localized to the right iliac fossa and epigastric pain subsided. Clinical examination and laboratory investigation lead us to reach in favour of Acute Appendicitis.

#### CONCLUSION :

Perforation of small gut by fish bone is not usually common. But every time this event is being accidental and remain obscure by the patient and doctors. Patient will always come with the presentation of acute abdomen and

should be asked about the last 24 hours dietary component. Every case will not go in favour of a surgeon but careful steps can save both patient's time and life. Diagnostic tools may fail but a physician and surgeons can make the difference.

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