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Contents

Editorial

Depression: An Emerging Global Health Issue to Intervene

Chaklader M A[a], Yasmeen S[b]

It's very rare to find anyone who never feels hopeless or sad or depressed in their entire lifetime. But when we call it depression? Depression is a common mental disorder that presents with depressed mood, loss of interest or pleasure, decreased energy, feelings of guilt or low self-worth, disturbed sleep or appetite, and poor concentration. Moreover, depression often comes with symptoms of anxiety. These problems can become chronic or recurrent and lead to substantial impairments in an individual's ability to take care of everyday responsibilities and quality of life as well.

Depression is a significant contributor to the global burden of disease and affects people in all communities across the world. Today, depression is estimated to affect 350 million people. The World Mental Health Survey conducted in 17 countries found that on average about 1 in 20 people reported for having an episode of depression in the previous year. At its worst, depression can lead to suicide. Almost 1 million lives are lost yearly due to suicide, which translates to 3000 suicide deaths every day. It is the leading cause of disability worldwide for both males and females in terms of total years lost due to disability. The burden of depression is 50% higher in females than males (WHO, 2008).

Depressive disorders often start at a young age, reduce people's functioning and are often recurring. In fact, researches in developing countries found that maternal depression may be a risk factor for poor growth in young children (Rahman et al, 2008). This status of maternal mental health in low-income countries may have a substantial influence on growth during childhood including depression affecting not only this generation but also the next.

The demand for curbing depression and other mental health conditions is on the rise globally. Amongst the multifactorial causes genetic, intrinsic biochemical components, psychological factors, trauma etc. are remarkably important. Recognizable risk factors are academic stress, poor achievement, unrealistic expectation, relation problem, loneliness and drug addiction.

For managing depression talking to a trusted person is the first step to treatment and recovery of depression. Many experts suggest using both psychotherapy and medications to treat depression. Other measures are psychosocial treatments, electroconvulsive therapy (ECT) and self-care.

Despite the known effectiveness of treatment for depression, the majority of people in need do not receive it. Where data are available, this is globally fewer than 50%, but fewer than 30% for most regions and even less than 10% in some countries. Barriers to effective care include lack of resources, lack of trained service providers at all levels, and the social stigma associated with mental disorders.

The global burden of depression poses a substantial threat and challenge at socioeconomic level and clinical level as well. Despite having resource limitations there are a number of well-defined and evidence based strategies that can effectively address or combat this problem. For common mental disorders like depression is being managed in primary care settings where the key interventions are treatment with generic antidepressant drugs and brief psychotherapy. Again economic analysis has indicated that treating depression in primary care is feasible, affordable and cost-effective. Many prevention programs implemented across the lifespan have provided evidence on the reduction of elevated levels of depressive symptoms. Effective community approaches to prevent depression focus on - strengthening of protective factors and the reduction of risk factors. Examples of strengthening protective factors include school-based programs targeting cognitive, problem-solving and social skills of children and adolescents as well as cultural & physical exercise programs (sports & games) for them. Interventions for parents of children with conduct problems aimed at improving parental psychosocial well-being by information provision and training in behavioral childrearing strategies may reduce parental depressive symptoms, with improvements in children's outcomes.

Depression is expected to be one of the leading causes of morbidity by 2020. Currently, pharmacotherapy represents the first line treatment for depressive disorders but in order to reduce the burden of depression, other methods of treatment such as counseling and psychotherapy should also be considered. This combinations of treatments reduce the relapse of depression in the long run. Most importantly, depression prevention strategies should be adopted nationwide and worldwide focusing best at primordial and primarily levels. In order to implement these strategies, however, more evidence-based research on the prevention of depressive disorders is required.

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Original Article

Weight Gain in Tuberculosis Patients after Six Months of DOTS Treatment in a Selected Tertiary Hospital

Alam M T[a], Fardeen K M[b], Monoshij A[c], Rahman AFM S[d], Bhuiyan M E[e], Alam R F[f]

Abstract

Background: Tuberculosis is a major public health problem in Bangladesh. Alternatives to radiographs and culture are needed in high burden countries to assess whether response to treatment of TB is satisfactory.

Objective: To assess the weight gain in patients at the end of 6 months of anti-TB treatment as an evaluation tool of treatment response.

Methods: This prospective cross-sectional study was conducted in Bangladesh Medical College Hospital out-patient DOTs centre and included 96 patients with active TB, who were followed over a period of 6 months. Body weights were recorded twice- at diagnosis PTB-0 and at the end of six months of treatment PTB-6. Difference of body weight within six months were measured for assessing the treatment response. Data were analyzed by SPSS software version 23.0. Significant difference of weight gain was tested by paired t test.

Results: Among 96 patients of Tuberculosis 41 were males and 55 were females. The age range of the patients was between 4 - 71 years. Our results showed the mean body weights at PTB-0 and PTB-6 were respectively 46.5±13.4 and 48.8±13.7 Kg. Paired t-test of body weight at PTB-6 and PTB-0 showed significantly higher mean body weight for PTB-6 group ($p < 0.0005$) thus suggesting 6 months of treatment helped significant body weight gain in patients. Among 96 patients, 3 patients showed weight loss between 2-5kgs, 6 patients showed no change in weight and 87 patients showed weight gain. The weight measured at 0 months and 6 months showed a positive correlation value of 0.990.

Conclusion: Monitoring the baseline weight and serial weight gain to see the response to anti-TB treatment in developing countries with limited resources may be considered as an important tool in evaluating the treatment response.

Keywords: Tuberculosis, Weight Gain, DOTS

Introduction:

Tuberculosis (TB) remains a major global public health problem.[1] One-third of the world's population and 50% of adults in Sub-Saharan Africa, South Asia and South-East Asia are infected, representing an enormous pool of individuals at risk for developing tuberculosis.[2] People with low socioeconomic status tend to live in crowded conditions that are conducive for increasing transmission of the tubercle bacilli. Thus it brings a result of a higher incidence of TB among such people.[3] Prevalence of underweight is more common with TB than non-TB patients.[4] Tuberculosis patients often suffer from severe weight loss, which is considered to be immunosuppressive and a major determinant of severity in outcome of disease.[5] Among persons, underweight at the time of diagnosis, weight gain of 5% or less during the first 2 months of treatment is associated with an increased relapse risk.[6] Over the years different studies have shown that following the initiation of ATT (anti-tubercular treatment) there has been weight gain in patients.[7,8] In groups of patients with pulmonary tuberculosis treated with Isoniazid, a remarkable gain in weight has been one of the principle effects reported. Compared with other treatments, weight gain has been so marked as to lead to the suspicion that a non-specific effect on metabolism was involved as well as a direct effect on the disease.[9]

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Materials and Methods:

A prospective cross-sectional study was carried out in the outpatient centre for DOTS (Directly Observed Treatment Short Course) of Bangladesh Medical College Hospital

from January 2014 to June 2015. There were a total of 96 patients who were selected by purposive sampling. Their body weight at the beginning of treatment and at 6 months of treatment were measured. Inclusion criteria was patients of all ages presenting with any form of active TB. Exclusion criteria were patients with other co morbid status, patients having adverse drug reactions to anti-TB drugs and drug resistant tuberculosis. Data were analyzed with software SPSS version 23.0. Statistical analysis for significant weight gain was done by paired t test and correlation analysis.

Results:

Among 96 tuberculosis patients 41 and 55 were male and female respectively. Age range was from 4-71 years.

Table 1: Mean weight of TB patients at starting and after 6 months of treatment (N=96)

Paired Samples	Mean weight	Std. Deviation	Std. Error Mean
Starting weight (Kg)	46.521	13.4109	1.3687
Weight after 6 months (Kg)	48.760	13.7011	1.3984

The mean body weights at PTB-0 and PTB-6 were respectively 46.5±13.4 and 48.8±13.7 kg.

Table 2: Paired sample correlation between starting weight & weight after 6 month (Kg)

Starting weight & weight after 6 months	N	Correlation	Sig.
	96	0.990	0.000

Starting weight and weight after 6 months in Kg are strongly and positively correlated ($r = 0.990$; $p<0.0005$).

Table 3: Mean weight gain from starting weight to weight at 6 month of treatment

	Paired Differences					t	df	Sig. (2-tailed)
	Mean Wt gain	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
Pair 1 Starting Weight (kg) - Weight after 6 months (kg)	-2.2396	1.9721	.2013	-2.6392	-1.8400	-11.127	95	0.000

Among 96 patients 87 showed weight gain, 3 patients had weight loss 2-5 kgs and 6 had no change in weight. The mean weight gain was 2.302 kg.

There was a statistically significant average/mean difference between Starting weight in kg and Weight after 6 months in kg (t_{95} =-11.127, $p < 0.0005$) as shown in Table-3.

Discussion:

Current advances in tuberculosis research has drawn the attention of clinicians to focus on body weight gain during treatment to ensure good prognosis, since wasting is recognized not only as a prominent feature of tuberculosis but also as one of the determinants of the disease severity and outcomes.[10] Wasting in TB patients may partly be mediated by upregulation of plasma peptide YY and downregulation of leptin levels with resulting appetite suppression. It is well known that bacterial endotoxins in tuberculosis cause a profound, although transient loss of body weight.[11] The reasons given for this include dehydration caused due to reduced water intake and wasting due to "anabolic block" or impaired anabolic response to feeding.[12] Weight gain during the first 3 months of treatment is an important predictor of long-term treatment success in underweight patients. More than 5% weight gain during the first 3 months of treatment was associated with good outcome.[13]

Nutrition plays a vital role at every stage of TB. Our patients were from different socioeconomic backgrounds and their nutritional status, any micro or macro-nutrient deficiencies were not excluded. TB is more common among malnourished individuals and follows a more severe course, with more adverse outcomes.[14] People with low BMI are more prone to TB and TB itself cause weight loss in patients. It is thought that in patients with active TB the appetite regulatory hormones like leptin level is reduced.[15,16]

It is to be remembered that a weight gain of 5% or less during the first 2 months of therapy is associated with an increase risk of relapse even after controlling other risk factors for relapse. Khan and his team also mentioned in the same study that it is unclear whether persons are at increased relapse risk if they do not gain weight during two months of intensive therapy, or whether they are at increased relapse risk because they do not gain weight.[17] They suggest that every effort to be made to have

underweight patients undergo more than 5% weight gain during the first 2 months if therapy, and/or additional interventions (e.g., extend duration of anti-TB treatment).

A large number of patients do not complete treatment course as a result of inadequate knowledge about TB, HIV co-infection, opting for herbal medication, previous default and low socioeconomic status.[18] Studies have shown that the introduction of DOTS has significantly improved treatment outcomes in TB patients.[19]

We measured weight at 0 months and at 6 months. Monthly measurement of weight would help identify poor prognosis, or failed treatment response. Our study group had age range between 4-71 years. Younger patients are likely to gain more body weight during treatment compared to older patients.[20]

The study showed that after the initiation of treatment, most patients have gained weight. The study, however, did not take into account other factors that affect the course of the disease and its treatment response. Loss of weight following treatment may be a result of poor compliance and socioeconomic status etc. These independent variables were not included in our study.

Our study has several limitations. First, body weight was abstracted from patient's treatment cards and serial weights at some follow-ups were not available for all patients. Most of the patients were poor and baseline malnutrition may have been caused by limited access to food, anorexia and increased catabolism of energy and nutrients because of TB. Similarly, weight gain during treatment might have been due, in part, to response to anti TB drugs. Patients were not checked for HIV co-infection, weight machine was not calibrated regularly.

The strength of our study was, more than half of our patients were underweight before treatment, therefore, we had reasonable statistical power to detect an association between weight gains during treatment. Patients were diagnosed based on results of Gene Xpert, smears and cultures.

Conclusion:

In conclusion, our study shows that anti-TB treatment causes weight gain. Thus, weight loss during therapy should be used as part of routine clinical evaluation to take appropriate decision, particularly in developing world, where resources are limited and chest radiographs and sputum cultures cannot always be obtained. TB patients should be educated on optimizing nutritional intake as part of the routine management of TB control programs.

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Original Article

The Optimal Site of Mesh Repair in Ventral Hernia: Sublay Vs Onlay Mesh Repair

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Abstract

Background: Ventral hernia results from biological problem of stable scar tissue formation and mesh repair is the surgical method of choice. However, the site of mesh placement is still a subject of much debate among surgeons.

Objective: To compare sublay and onlay techniques for operative management of ventral hernia regarding duration of operation, wound complications, hospital stay and late complication, chronic pain, recurrence etc.

Method: This Prospective cross-sectional comparative study was done in Bangladesh Medical College Hospital from January 2010 to January 2013. Total 80 cases of ventral hernias with defect size = 5 inch were included in this study. Mesh was placed alternatively in Sublay (Group A) and Onlay (Group B) position. Observations were made regarding operating time and ease of operation, drain period, incidence of early post operative complications, hospital stay and rest from work. Total 24 months follow up was carried out in OPD and over telephone to detect late post operative complications such as discharging sinus formation, neuralgia and recurrence. Conclusions were made using unpaired student t- test.

Results: Mean total time of operation in Sublay group (Group A) was 64.58±14.51 minutes and in Onlay group (Group B) was 56.07±16.97 minutes (p value = 0.018). Duration of hospital stay in Sublay group 4.88±0.88 days and in Onlay group 6.35+-1.58 days. The p-value was found significant in cases of other parameters such as drain time, hospital stay and rest of work in between the two groups. Postoperative complications were also found as more in Onlay group.

Conclusion: Onlay meshplasty is a quick and technically easy procedure, but associated with higher post-operative complications. On the contrary, Sublay repair seems to be associated with less post-operative complications than its onlay counterpart.

Keywords: Sublay mesh repair, Onlay mesh repair, Ventral hernia

Introduction:

Ventral hernias are commonly encountered in surgical practice. This includes both spontaneous and most commonly, incisional hernia after an abdominal operation. The estimated incidence of ventral hernia is about (15-25) %.[1] There is now ample evidence that suture repair has a recurrence rate as high as 50% even those for smaller defects.[1] Recurrence, the ultimate nightmare of a surgeon adds significantly to healthcare costs and poses further economic burden. Confronting the fact that ventral hernia results from biological defect of mature scar tissue formation, mesh technique today is the method of choice for hernia repair. However, the best position for inserting the mesh has not been conclusively established as per literature as each of the procedure carries its own sets of complications.

The aim of the study was to compare sublay and onlay mesh techniques influencing the outcome with regards to duration of operation, hospital stay, early and late post-operative complications and recurrence.[9]

Materials and Methods:

This prospective cross sectional comparative study was done between January 2010 to January 2013. A total of 80 patients underwent Open Mesh repair of ventral hernia in Bangladesh Medical College Hospital. Among them 62 were female and 18 were male. The defect was less than 5 inches in size in all patients.

Among them 40 underwent Sublay repair (Group-A) and 40 underwent Onlay repair (Group-B). All the patients were given single dose of 1.00 gm of Ceftraixone at induction and thereafter Cefuroxim (500 mg) was given orally for 7 days.

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In all cases, Polypropylene mesh were used and the post operative outcome was monitored especially with parameters such as Operative time, Drain period, Hospital stay, Required rest from work, Post–operative complications.

Operative Technique:
Transverse incision was made in the centre of the hernia defect. The dissection continued through the subcutaneous tissue and the sac was mobilized. The neck of the sack was then dissected from the adjacent tissue by a combination of sharp and blunt dissection, which was then carried down to the masculo-aponeurotic layer of anterior abdominal wall. Sac was then opened and the content of the sac was then reduced. The redundant sac was then excised up to level of the neck of the sac.

Onlay Mesh Placement:
The defect at the neck was closed by direct closure of the masculo-aponeurotic layer by 1/0 Prolene and the mesh was placed directly above the repaired defect and drain was kept in situ.

Sublay Mesh Placement:
A zone was developed between the peritoneum and the posterior rectus sheath by careful blunt dissection all round up to 3-5 cm beyond the edge of the defect. Peritoneal edge is approximated with a continuous 2/0 Prolene. A polypropylene mesh is placed and anchored in the developed plane between the peritoneum and the muscle layer. Finally the musculo-aponeurotic defect is closed using a 1/0 Prolene; keeping a drain in retromascular space (Fig-1, Fig-2 & Fig-3)

Statistical Analysis:
All data entered by using Microsoft Excel and analyzed in Statistical Package for Social Sciences (SPSS 16.0 version). Student's t-test was done to compare Sublay mesh repair (Group-A) and Onlay mesh repair (Group-B). The test of significance was calculated and p values < 0.05 was accepted as level of significance.

Results:
Table 1: Comparison of different parameters in Sublay and Onlay groups

Parameters	Sub-lay (Group-A) (n=40) Mean±SD	Onlay (Group-B) (n=40) Mean±SD	p value
Operation time (minutes)	64.58±14.51	56.07±16.97	0.018**
Drains period (days)	4.08±0.92	5.35±1.27	<0.001**
Discharge (days)	4.88±0.88	6.35±1.58	<0.001**
Rest of work (days)	20.0±4.93	25.40±7.71	<0.001**

n = Number of subjects ** = Significant

Operative Time: The mean operating time in Group-A (Sublay mesh repair) was 64.58±14.51 minutes and Group-B (Onlay mesh repair) 56.07±16.97 minutes. The p value was found significant (p=0.018).

Outcome: Drains were given in both groups. The drain kept for longer time in Onlay group 5.35±1.27 days than the Sublay group 4.08±0.92 days and it was found statistically significant (p=0.001). The Onlay group also had a longer hospital stay 6.35±1.58 days in comparison to the Sublay group 4.88±0.88 days.

The Onlay group required longer recuperation time 25.40±7.71 days than the Sublay group 20.0±4.93 days. The p value was <0.001 and found as significant in both these parameters as shown in Table 1.

Table 2: Postoperative (Immediate) complications in Sublay and Onlay groups

Post-Operative Complication	Sublay (Group-A) (n=40) No. (%)	Onlay (Group-B) (n=40) No. (%)
Superficial wound infection/Erythema/ cellulites	2 (5.0%)	3 (7.5%)
Seroma/Haemotom formation	2 (5%)	4 (10.0%)
Flap Necrosis	0 (0%)	2 (5.0%)
Sinus formation	0 (0%)	2 (5.0%)

Postoperative complications:
Immediate: 3 patients (7.5%) of the Onlay group (Group B) had superficial surgical site infection and 4 patients (10%) had seroma/ hematoma (Table-2). The same complications were seen in Group A (Sublay) in a slightly less frequency; superficial wound infection was seen in 2 patients (5%) and seroma /heamtoma was seen in 2 patients (5%).

Flap necrosis and sinus formation were not seen in any of the patients undergoing Sublay mesh-plasty but seen in 2 patients (5%) in Onlay meshplasty.

Table 3: Post-Operative (Delayed) Complications in Sub-lay and Onlay Groups

Post-Operative Complication	Sublay (Group-A) (n=40) No. (%)	Onlay (Group-B) (n=40) No. (%)
Recurrence	0 (0%)	0 (0%)
Neuralgia Mild pain Annoying/bothersome pain	12 (30.0%) 2 (5.0%)	14 (35.0%) 5 (12.5%)

Delayed: Pain was noted in 14 of the patient of Sublay group (Group A); 2 of them described it as annoying/ bothersome the rest described it as mild pain, occasionally occurring.

In Onlay group (Group B), 19 (47.5%) of the patients, complained of chronic pain characterized as mild by 14 (35%) patients and annoyingly bothersome by 5 (12.5%) of the patients. In the two year follow-up no recurrence was of the hernia was recorded in either of the group (Table 3).

Discussion:

Mesh placement in ventral hernia is the gold standard as it can restore the myo-fascial integrity of the abdominal wall in a tension free manner. Rightly so, successful mesh repair has brought down the recurrence to a negligible rate.[1]

Onlay repair is popular worldwide as it is technically less challenging and time consuming, avoids direct contact with the abdominal viscera and imparts tension free repair. The finding of this study also supports that, showing average operative time is more in the sublay mesh plasty (64.58±14.51 minutes) compared to onlay meshplasty (56.07±16.97 minutes).

The Sublay technique poses more challenge and requires expertise, as a complex sub-muscular, pre-peritoneal space needs to be created for the successful mesh placement. While in the onlay technique where the mesh is placed superficial to fascial defect, in the Sublay technique however, the mesh is placed deep to the fascial defect (Pre-peritoneal/ retro-muscular/ retro-rectus).

One of the main problems in the use of prosthetic materials is a potential infective complication, which might develop in up to 13.6% after hernia repair.[2] Although Onlay repair is thought to be easier and quicker to perform, it has been suggested that the dissection of the suprafascial space would promote seroma formation and surgical site infection (SSI).[3,4] It was seen in this study, that SSI and seroma formation was seen in slightly higher numbers of patients undergoing onlay mesh repair.

SSI could be explained by the more superficial position of onlay mesh placement makes it easier for bacterial colonization. Additionally, mesh positioning on the posterior rectus fascia would benefit from a more vascularized area compared with the onlay position. [2, 5] Other complications, such flap necrosis, sinus formation was absent in the sublay meshplasty group. This is reflected in the post-operative convalescence as the onlay group had longer hospital stay than sublay group.

Post operative chronic pain is another debilitating complication ranging from mild to significantly severe enough to hamper the daily life. In our study, the onlay group had more patients with chronic pain (47.5%), in comparison to the sublay group, where 35% of the patients complained discomfort or pain. Although, it seems plausible that the dissection of the space between the posterior rectus fascia and the rectus muscle is a more elaborate procedure and with more possibilities to damage, ligate, or cut nerves and thus induce (chronic) pain.[6]
The main point of debate is the incidence of recurrence. Sublay repair is assumed by many to reduce hernia recurrence. As ventral hernias especially incisional hernias associated with mesh reinforcement tend to recur within 2 years after repair, so our follow-up was extended for 2 years.[7-10] A nationwide survey of surgical practice and results in Sweden revealed a recurrence rate of 29% with sutured repair, 19% with onlay repair, and 7% after sublay repair at a follow-up of less than 2 years.[1, 10] This reduction of recurrence might be caused by a higher tensile strength of the abdominal wall after sublay meshplasty and the intra-abdominal pressure would fix the mesh between the posterior fascia and the abdominal muscle. But experimental studies on this matter have not been conclusive yet.[4, 6] In this study, neither group reported recurrence of the hernia within the two year follow-up.

Limitation:

The weakness of our straightforward study is the small group of patients. The strength of the study is the high percentage of follow-up examinations, which suggests that our results are valid, with regards to the overall significance. The confounding variables such as obesity, smoking, diabetes were not factored in.

Conclusion:

Open sublay repair of hernias, placing mesh in the sub-muscular or preperitoneal plane, is highly effective with a low recurrence and acceptable complication rates. New developments in hernia surgery will continue to provide patients and surgeons a range of diverse options to manage and prevent hernias.

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Original Article

Dyslipidemia in Patients with Acute Myocardial Infarction in a Tertiary Level Hospital in Bangladesh

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Abstract

Background: Acute myocardial infarction (AMI) is one of the important reasons of death in the world as well as a leading cause of mortality in Bangladesh, like other South Asians.

Objectives: To assess dyslipidemia in patients with acute myocardial infarction in a tertiary level hospital in Bangladesh.

Methods: This cross sectional study was carried out in the Department of Cardiology & Biochemistry in Dhaka Medical College Hospital, Dhaka, Bangladesh from July 2012 to June 2013. Study group included 125 patients with acute myocardial infarction selected by using non-random sampling technique. After taking informed consent data were collected by structured questionnaire. Fasting levels of serum total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol and triglycerides were measured by enzymatic methods. The descriptive analysis was carried out by using the SPSS (Statistical Package for Social Sciences) software.

Results: Serum lipids and lipoproteins were estimated in 125 patients with AMI within 24 hours of acute episode. Among 125 patients 74.05% ST-elevated myocardial infarction (STEMI) and 25.95% non-ST-elevated myocardial infarction (NSTEMI). Among the AMI patients, 95.2% (n=119) were suffering from dyslipidemia. Increase level of TC (>200mg/dl), TG (>150mg/dl) and LDL-C (>100mg/dl) were found in 41.5% (n=39), 77.7% (n=73), 52.1% (n=49) respectively and decreased level of HDL-C (male<40mg/dl & female <50mg/dl) was found in 47% (n=50) of STEMI patients. In case of NSTEMI increased TC, TG and LDL-C found in 36.5% (n=11) 74.2% (n=23), 61.3% (n=19) respectively and decreased HDL-C in 48.4% (n=15). Women had higher level of TC, TG and LDL-C in comparison to men 208.56±42.39 mg/dl Vs183.2±47.04 mg/dl, 206.29±93.17 mg/dl Vs 194.54±64.85 mg/dl, 111.61±35.88 mg/dl Vs 105.10±35.31mg/dl respectively. But TC is significantly higher in female than male (p= 0.004). No significant difference was found in component of lipid profile in STEMI & NSTEMI.

Conclusions: Dyslipidemia which is a risk factor for MI needs to be controlled among cardiac patients. Changing of dietary and daily activities of people can help to prevent future atherogenic damage in AMI patients.

Introduction:

Acute myocardial infarction (AMI) is the leading cause of mortality in Bangladesh. Hyperlipidemia is an elevated concentration of lipids in the blood. The major plasma lipids of interest are total cholesterol and the triglycerides. It is closely related to the terms hyperlipoproteinemia (elevated levels of lipoproteins). It is not a disease but a metabolic derangement that can be secondary to many diseases and can contribute too many forms of disease, most notably cardiovascular disease including myocardial infarctions (known as a heart attack, which is a disease state that occurs when the blood supply to a part of the heart is interrupted. The resulting ischemia or oxygen shortage causes damage and potential death of heart tissue). When cholesterol levels combined with triglycerides, a type of fat in the blood, high levels of LDL cholesterol can build up in the arteries and form plaques. Plaques can cause atherosclerosis, or the narrowing and hardening of the arteries. While atherosclerosis often shows no early symptoms, it can lead to heart attack or stroke. Treatments for high cholesterol and high triglyceride levels range from diet and exercise to medication and other medical procedures.

The mortality rate of MI is approximately 30% and for every 1 in 25 patients who survive the initial hospitalization, dies in the first year after AMI. In 1990 around 25% of deaths in India were attributed to cardiovascular disease (CVD). Also it is predicted that the cases of CVD may increase from 2.9 crores in 2000 to as many as 6.4 crores in 2015.[1]

Few primary risk factors have been identified with the development of atherosclerotic coronary artery disease and

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MI such as dyslipidemia, diabetes mellitus, hypertension, male gender and family history of atherosclerotic arterial disease. The presence of any risk factor is associated with doubling the relative risk of developing atherosclerotic coronary artery disease.[2,3]

The diagnosis of AMI is usually based on clinical symptoms and on electrocardiographic (ECG) findings of the patient and an increase of serum biochemical (Troponin I) markers as per WHO recommendations.[4] The treatment of dyslipidemia after myocardial infarction is essential and beneficial because these patients are at the highest risk for future cardiac events.[5]

Indians are four time more prone to AMI as compared to the people of other Asian countries due to a combination of the genetic and lifestyle factors that promote metabolic dysfunction. The risk of cardiovascular disease is predicted by various factors such as age, sex, smoking, hypertension and dyslipidemia.[6]

Elevated serum TC, TG and LDL-C are well established risk factor for cardiovascular disease.[7-11] A low serum HDL-C level is therefore, thought to be an independent cardiovascular risk factor that leads to the development of atherosclerosis and related cardiovascular events.[12] Many large scale studies have shown a high correlation between total plasma cholesterol and LDL levels and the severity of atherosclerosis as judged by the mortality rate from ischemic heart disease.[13]

The pathogenesis of acute myocardial infarction (AMI) is multifactorial; however, several studies have implicated impaired lipid metabolism as one of the crucial factors in the development of this disease. Kumar et al.[14] observed significantly higher TC and TG levels and lower HDL-C levels in AMI patients. Li et al.[15] have shown that the cases with low HDL-C level had rates of AMI events and CVD mortality similar to those of the entire group, including hyperlipidemia. However, AMI attacks and deaths decreased significantly at the normal and high HDL-C levels, indicating that protective effect of HDL-C against coronary artery disease is more prominent in people with low lipid level.

The above literature clearly indicates an important role of lipids metabolism in AMI. However, the biomarker value of various components of lipids profile is not clear due to conflicting findings in various studies. Bangladesh is double-burdened with communicable and non-communicable diseases. In the context of socioeconomic transition, the communicable diseases are coming under control, whereas the non-communicable diseases (NCDs) and their risk factors are rising. The Health, Nutrition and Population Sector Programme (HNPSP) is now in operation that responds to the increasing need for prevention and management of NCDs. Government has formulated National Non-communicable Disease Strategy and plan of action.

Materials and Methods:

This cross sectional study was carried out in the Department of Cardiology & Biochemistry in Dhaka Medical College Hospital, Dhaka, Bangladesh from July 2012 to June 2013. The Institutional Ethical Committee clearance was obtained. The patients presenting within 24 hrs of chest pain suggestive of MI, whose diagnosis of acute MI was made on patient history, symptoms, abnormalities with ECG findings as assessed by attending physician and biochemical marker (Troponin I) were selected for the study. Study group included 125 subjects with acute myocardial infarction selected by using non-random sampling technique. After taking informed consent data were collected by structured questionnaire. Fasting blood samples were taken as soon as possible after admission. A venous blood sample was collected from all the subjects after 12-hours overnight fast. The samples were centrifuged for 10 minutes at 3000 rpm. Fasting levels of serum total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol and triglycerides were measured by enzymatic methods. The descriptive analysis was carried out by using the SPSS (Statistical Package for Social Sciences) software.

Exclusion:

Patients with sepsis, congenital heart disease, pericarditis, pulmonary embolism, thyroid dysfunctions, end stage renal and liver disease were excluded from the study.

Laboratory Measurements:

Total Cholesterol was estimated by enzymatic end point (CHOD-PAP) method (Allian et al. 1974).[16]

Triglyceride was estimated by enzymatic (GPO-PAP) method (Bucolo and David 1973).[17]

HDL Cholesterol was estimated by enzymatic end point (CHOD-PAP) method (Lopes-Virella et al. 1977).[18]

LDL- Cholesterol was estimated by using Friedewald's formula (Friedewald, Levy and Fredrickson 1972).[19]

Normal lipid profile values:

Ideal values on a lipid profile include total cholesterol levels below 200mg/dl, low-density lipoprotein cholesterol should remain under 100mg/dl, with high-density lipoprotein cholesterol levels higher than 60 mg/dl and triglyceride levels under 150mg/dl.

Dyslipidemia:

A disorder of lipoprotein metabolism and transport in which hyper or hypo lipoproteinaemia occur. Usually excessive increase of TG and total cholesterol but other lipoprotein are increased (e.g. LDL-C, VLDL-C) and HDL-C decreased. Dyslipidemia may be manifested by elevation of any of the total cholesterol (>200mg/dl), triglyceride (>150mg/dl), bad LDL-C (>100mg/dl) and a decrease in good HDL-C (male<40mg/dl & female <50mg/dl).

Results:

Table 1: Distribution of lipid profile of the study subjects based on sex (n=125)

Parameter (mg/dl)	Mean ± SD (n=125)	Male (n=84) Mean ± SD	Female (n=41) Mean ± SD	P value
Serum TC	191.5±46.9	183.2±47.04	208.56±42.39	0.004
Serum TG	198.3±75.1	194.54±64.85	206.29±93.17	0.414
Serum LDL-C	107.2±35.4	105.10±35.31	111.61±35.88	0.337
Serum HDL-C	43.5±14.9	42.95±14.21	44.65±16.59	0.552

p- Value <0.05, considered as significant.

Among the 125 study subjects the Mean±SD serum TC, TG, LDL-C and HDL-C were 191.5±46.9 mg/dl, 198.3±75.1mg/dl, 107.2±35.4 mg/dl, 43.5±14.9 mg/dl respectively. But females had increased level of TC, TG, LDL-C and decreased HDL-C. But TC is significantly higher in female than male (Table 1). P value reached from independent T test.

Table 2: Distribution of the study subjects according to lipid profile (n=125)

Lipid status	Frequency (No.)	Percentage
Normal lipid profile	6	4.8%
Dyslipidemic	119	95.2%
Total	125	100%

Most of the AMI patients 95.2% (n=119) were suffering from dyslipidemia and only 4.8% (n=6) have normal lipid profile (Table 2).

Table 3: Distribution of AMI patients according to lipid profile (n=125)

Lipid profile	Study subjects		Total	P value
	STEMI (n=94)	NSTEMI (n=31)		
TC				
Normal (<200 mg/dl)	55 (58.5%)	20 (64.5%)	75 (100%)	0.554
Raised (=200 mg/dl)	39 (41.5%)	11(35.5%)	50 (100%)	
TG				
Normal (<150 mg/dl)	21 (22.3%)	8 (25.8%)	29 (100%)	0.692
Raised (=150 mg/dl)	73 (77.7%)	23 (74.2%)	96 (100%)	
LDL-C				
Normal (<100 mg/dl)	45 (47.9%)	12 (38.7%)	57 (100%)	0.374
Raised (=100 mg/dl)	49 (52.1%)	19 (61.3%)	68 (100%)	
HDL-C				
Normal (male=40mg/dl & female=50mg/dl)	47 (50%)	16 (51.6%)	63 (100%)	0.876
Decreased (male<40mg/dl& female<50mg/dl)	47 (50%)	15 (48.4%)	62 (100%)	

On the basis of ECG findings, among 84 male, 22.6 % (n=19) were suffering from NSTEMI and 77.4 % (n=65) from STEMI. Among 41female 29.3 %(n=12) and 70.7 %(n=29) were suffering from NSTEMI and STEMI respectively.

Among the STEMI increased TC, TG and LDL-C found in 41.5% (n=39), 77.7% (n=73), 52.1% (n=49) respectively and decreased HDL-C in 50% (n=47). In case of NSTEMI increased TC, TG and LDL-C found in 35.5% (n=11) 74.2% (n=23), 61.3% (n=19) respectively and decreased HDL-C in 48.4% (n=15) as shown in Table 3. No significant difference was found in component of lipid profile in STEMI & NSTEMI. P value reached from Chi-square test.

Discussion:

Cardiovascular disease (CVD) is a major cause of premature death throughout the world as well as developing country like Bangladesh. The underlying pathology is atherosclerosis, which develops over many years and is usually advanced by the time symptoms occur, generally in middle age. Acute coronary events (heart attacks) and cerebro vascular events (strokes) frequently occur suddenly, and are often fatal before medical care can be given. Risk factor modification can reduce clinical events and premature death in people with established cardiovascular disease as well as in those who are at high cardiovascular risk due to one or more risk factors. The treatment of dyslipidemia after myocardial infarction is an important task as far as post MI is considered.

In present study TC and TG levels increased 41.5% & 77.7% in STEMI and 35.5% & 74.2% in NSTEMI patients. It is reported that elevated TG levels may depends on genetic and nutritional basis. TG change level may because inherited abnormality of very low density lipoprotein. It may happen because of increased flowing of fatty acids and impaired elimination of VLDL from the plasma. Our results are supported by other researchers.[13]

LDL cholesterol has found to be elevated 52.1% in STEMI and 61.3% in NSTEMI. LDL carries the most of the cholesterol in the plasma and increasing of LDL depends on increasing of total cholesterol.[13,20] Decreased level of HDL-C found in 50% in STEMI and 48.4% in NSTEMI. Low HDL-C is shown to be associated with higher prevalence and incidence of coronary artery diseases.[13,20]

An analysis from the INTERHEART Study[21] showed about 10 mg/dl lower mean LDL-C levels in Asians compared with non-Asians, a greater proportion of Asian had LDL-C = 100 mg/dl, HDL-C levels were slightly lower among Asians compared with non-Asians. Liberal use of saturated fats and transfats, deep frying, reuse of cooking oil, and overcooking leading to destruction of folates may all contribute to dyslipidemia in this population.[22]

Studies exclusively related to dyslipidemia are sparse in Bangladesh. In a study involving secretariat employees in Dhaka, abnormal fasting TC, LDL-C, HDL-C and TG were found to be 17.3%, 48.5%, 75.6% and 48.5%, respectively.[23] In our study, increased TC, TG and LDL-C found in 41.5% (n=39) 77.7% (n=73), 52.1% (n=49) respectively and decreased HDL-C in 47% (n=50) in STEMI. In case of NSTEMI increased TC, TG and LDL-C

found in 36.5% (n=11) 74.2% (n=23), 61.3% (n=19) respectively and decreased HDL-C in 48.4% (n=15). No significant difference was found in component of lipid profile in STEMI & NSTEMI. Present study showed women had higher level of TC, TG and LDL-C in comparison to men 208.56±42.39 mg/dl Vs183.2±47.04 mg/dl, 206.29±93.17 mg/dl Vs 194.54±64.85 mg/dl, 111.61±35.88 mg/dl Vs 105.10±35.31mg/dl respectively after the age of 50 years. But TC is significantly higher in female than male.

Conclusion:

The study concludes the importance of assessing the lipid profile even in normal subjects as it is one of the atherogenic factor for the development of MI and other coronary complications. In our study mean serum levels of TC, TG, LDL-C have been increased and more than 95.2% AMI patient suffered from dyslipidemia. All the people should undergo lipid profile evaluation regularly to decrease the incidence, morbidity and mortality from this disease. Coronary artery disease is highly prevalent in Bangladesh. At the advent of the new millennium, we are really unclear about the real situation. Along with the classical risk factors, genetic make-up and environmental factors unique to our population may exist. We have no more time to lose. Large-scale, preferably, nation-wide survey and clinical research should be conducted to determine the different aspects of CAD in Bangladesh. The information available thereby, would help to formulate national policy to combat the deadly epidemic more efficiently in future.

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Original Article

Frequency, Distribution, Size and Clinical Significance of the Carabelli Trait among Bangladeshi People

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Abstract

Background: The Carabelli trait is an extra cusp or tubercle or a groove seen on the mesial aspect of the mesiopalatal cusp of maxillary permanent molars and maxillary second deciduous molars. Its prevalence varies among the people of different countries.

Objective: To find out the number, frequency, distribution, size, sex dimorphism & clinical significance of Carabelli trait in Bangladeshi people.

Methods: A cross sectional study was performed in Bangladesh Dental College, different dental chambers and dental camps during the period of June 2013 to May 2016. A total no of 434 subjects ranging from 6 years to 65 years were investigated. All the maxillary molars were carefully examined for the occurrence of Carabelli trait and presence of caries.

Results: Out of 434 subjects Carabelli trait was found in 228 subjects (52.53%) with presence of bilateralism in 71.93%. Subject's prevalence in males was greater (59.66%) than females (47.67%). Carabelli trait was found in maxillary first permanent molars in 29.49% cases as cusp expression & 16.59% cases as groove expression. In maxillary second permanent molars it was found in 3.44% cases as cusp expression & 1.06% cases as groove expression. In maxillary third permanent molars Carabelli trait was found in 3.17% cases as cusp expression & 0.53% cases as groove expression. Trait was found in maxillary second deciduous molars in 46.43% cases as cusp expression and 21.43% cases as groove expression. This structure was not found in maxillary first deciduous molars. Caries related to Carabelli trait was found only in two subjects (0.46%).

Conclusion: Frequency of occurrence of Carabelli trait is moderate among Bangladeshi people, with minimum presence of carious lesions. Further study in different institutional capacity is recommended.

Keywords: Cusp of Carabelli, Carabelli trait, carious lesions, caries, grooves, bilateralism, male bilateralism, Bangladesh.

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Introduction:

Cusp of Carabelli or tubercle of Carabelli is a fifth cusp or at least a small elevation, is commonly found on the lingual side of the mesio-lingual cusp about half-way between its apex and the cervical margin of maxillary first permanent molar tooth.[1] It may also found in maxillary second and third permanent molars and in maxillary second deciduous molar teeth. It is also known as tubercle of Carabelli, Carabelli tubercle, trait of Carabelli, molar tubercle, fifth cusp, accessory cusp or tuberculum anomale of George Carabelli. This additional cusp was first described in 1842 by the Hungarian George Carabelli.[2] The fifth cusp in the upper molars or Carabelli trait is the most commonly occurring dental morphological characteristic that is useful in forensic, anthropological and ethnic studies.[3] It has no established etiology, nor known function. It may entirely absent in some individuals and present in others in a variety of forms. The level of expression of Carabelli trait varies from a small pit or groove to a well-developed cusps. It may be a result of interaction between genetic and environmental factors.[4] Its ethnic variation probably the most significant aspect of Carabelli trait. Studies done in other countries reported of prevalence, expression, size, shape, symmetry, dentition predilection, inheritability and morphogenesis of Cusp of Carabelli on different populations.[5] However, studies demonstrating the

prevalence of Cusp of Carabelli in Bangladeshi population have not been reported so far. The aim of this study was to determine the frequency, distribution, size, sex dimorphism and clinical significance of Carabelli trait in Bangladeshi population. Findings from the study would be helpful in reflecting the Carabelli trait in Bangladeshi population and could be implied in dental identification process.

Materials and Methods:

A cross sectional study was carried out in Bangladesh Dental College, different dental chambers, and dental camps during the period of June 2013 to May 2016. The study included 434 subjects. Among the subjects 176 were males and 258 were females. In case of adult subjects (378 subjects), the criteria for inclusion was the presence of maxillary permanent molar teeth. In case of children (56 subjects), the criteria for inclusion was the presence of maxillary deciduous molars and maxillary first permanent molars. Subjects with severely carious, restored or missing molars on any side were excluded. The required consent from the subjects and parents (in case of children) were obtained after explaining them about the examination method and those willing to participate were included in the study. A special proforma was designed to collect the data. To avoid intra observer variance in 434 subjects this study excluded the assessment of level of expression of the Carabelli trait. During examination subjects were seated comfortably in a dental chair and examined under sufficient lighting condition with examination gloves, mouth mask, dental mirror and dental probe. All the maxillary molars were carefully examined for the presence or absence of the cusp of Carabelli and groove (unilateral or bilateral). Smooth palatal aspect of the mesio-palatal cusp of the maxillary molars, was recorded as trait absent. The presence of elevation in the form of a cusp or tubercle or a groove was recorded as trait present (Figure 1 & 2). Frequency, size, distribution, sexual dimorphism, caries incidence, plaque accumulation, attrition, fracture were also examined and recorded carefully. The data were presented by using tables and diagrams. Data analysis was done by using software SPSS.

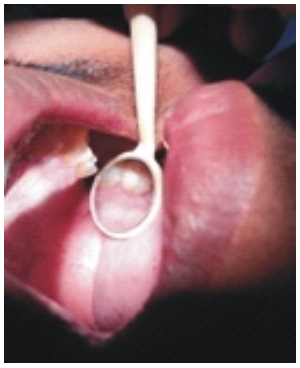

Figure 1: Cusp of Carabelli present in maxillary first and second permanent molars in a male subject

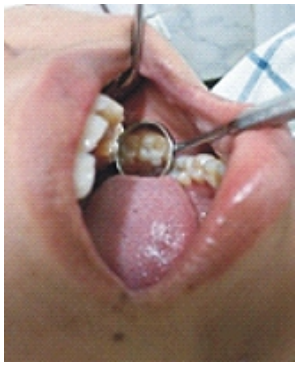

Figure 2: Cusp of Carabelli present in maxillary first and second permanent molars in a female subject

Results:

Table 1: Showing distribution of cusp of Carabelli, groove expression & Carabelli trait in male and female subjects

Cusp of Carabelli, Groove expression Carabelli trait	Cusp of Carabelli				Groove expression				Carabelli trait			
	Numbe (%)	Present	Bilateral No.(%)	Unilateral No.(%)	No.	Present No. (%)	Bilateral	Unilateral	No.	Present	Bilateral	Unilateral
Male	176 (100)	72 (40.91)	57 (79.17)	15 (20.83)	176 (100%)	33 (18.75)	22 (66.67)	11 (33.33)	176 (100%)	105 (59.66)	79 (75.24%)	26 (24.76%)
Female	258 (100)	66 (25.58)	54 (81.82)	12 (18.18)	258 (100%)	57 (22.09)	31 (54.39)	26 (45.61)	258 (100%)	123 (47.67)	85 (69.11%)	38 (30.89%)
Total	434 (100)	138 (31.80)	111 (80.43)	27 (19.57)	434 (100%)	90 (20.74)	53 (58.89)	37 (41.11)	434 (100%)	228 (52.53)	164 (71.93%)	64 (28.07%)

Table 1 shows the distribution of cusp of Carabelli, groove expression & Carabelli trait in different maxillary molar teeth. Among 434 subjects, cusp of Carabelli was present in138 cases (31.80%) with bilateralism of 80.43%, while groove expression was present in 90 cases (20.74%) with bilateralism of 58.89% and Carabelli trait was present in 228 cases (52.53%) with bilateralism of 71.93%. Male predominance was seen in case of cusp of Carabelli & Carabelli trait but female predominance was seen in groove expression.

Table 2: Showing prevalence and bilateralism of Carabelli trait in different teeth

Tooth	Carabelli Trait	Number	Present	Bilateral	Unilateral
Maxillary 1st permanent molar	Male	176 (100%)	96 (54.55%)	72 (75%)	24 (25%)
	Female	258(100%)	104 (40.31%)	74 (71.15%)	30 (28.85%)
	Total	434 (100%)	200 (46.08%)	146 (73%)	54 (27%)
Maxillary 2nd permanent molar	Male	148 (100%)	09 (6.08%)	06 (66.67%)	03 (33.33%)
	Female	230 (100%)	08 (3.48%)	07 (87.50%)	01 (12.50%)
	Total	378 (100%)	17 (4.50%)	13 (76.47%)	04 (23.53%)
Maxillary 3rd permanent molar	Male	148 (100%)	07 (4.73%)	05 (71.43%)	02 (28.57%)
	Female	230 (100%)	07 (3.04%)	06 (85.71%)	01 (14.29%)
	Total	378 (100%)	14 (3.70%)	11 (78.57%)	03 (21.43%)
Maxillary 2nd deciduous molar	Male	28 (100%)	18 (64.29%)	16 (88.89%)	02 (11.11%)
	Female	28 (100%)	20 (71.43%)	14 (70%)	06 (30%)
	Total	56 (100%)	38 (67.86%)	30 (78.95%)	08 (21.05%)

Table 2 Shows the prevalence and bilateralism of Carabelli trait in different maxillary molar teeth. Among 434 subjects, 200 (46.08%) subjects had Carabelli trait in maxillary 1st permanent molar with a bilateralism of 73%, in maxillary 2nd & 3rd permanent molars out of 378 subjects Carabelli trait was found in 17 (4.50%) & 14 (3.70%) subjects respectively with a bilateralism of 76.47% & 78.57% and in maxillary 2nd deciduous molar among 56 subjects Carabelli trait was found in 38 (67.86%) subjects with a bilateralism of 78.95%. Male predominance was seen in all the maxillary permanent molar teeth but female predominance was seen in Maxillary 2nd deciduous molar.

Table 3: Showing prevalence and bilateralism of cusp of Carabelli in different teeth

Tooth	Carabelli Trait	Number	Present	Bilateral	Unilateral
Maxillary 1st permanent molar	Male	176 (100%)	68 (38.64%)	54 (79.41%)	14 (20.59%)
	Female	258(100%)	60 (23.26%)	48 (80%)	12 (20%)
	Total	434 (100%)	128 (29.49%)	102 (79.69%)	26 (20.31%)
Maxillary 2nd permanent molar	Male	148 (100%)	07 (4.73%)	05 (71.43%)	02 (28.57%)
	Female	230 (100%)	06 (2.61%)	06 (100%)	00 (0%)
	Total	378 (100%)	13 (3.44%)	11 (84.62%)	02 (15.38%)
Maxillary 3rd permanent molar	Male	148 (100%)	06 (4.05%)	04 (66.67%)	02 (33.33%)
	Female	230 (100%)	06 (2.61%)	06 (100%)	00 (0%)
	Total	378 (100%)	12 (3.17%)	10 (83.33%)	02 (16.67%)
Maxillary 2nd deciduous molar	Male	28 (100%)	16 (57.14%)	14 (87.50%)	02 (12.50%)
	Female	28 (100%)	10 (35.71%)	10 (100%)	00 (0%)
	Total	56 (100%)	26 (46.43%)	24 (92.31%)	02 (7.69%)

Table 3 shows the prevalence and bilateralism of cusp of Carabelli in different maxillary molar teeth. Among 434 subjects 128 (29.49%) subjects had cusp of Carabelli in maxillary 1st permanent molar with a bilateralism of 79.69%, in maxillary 2nd & 3rd permanent molars out of 378 subjects Carabelli cusp was found in 13 (3.44%) & 12 (3.17%) subjects respectively with a bilateralism of 84.62% & 83.33% and in maxillary 2nd deciduous molar among 56 subjects Carabelli cusp was found in 26 (46.43%) subjects with a bilateralism of 92.31%. Male predominance was seen in all the above mentioned teeth.

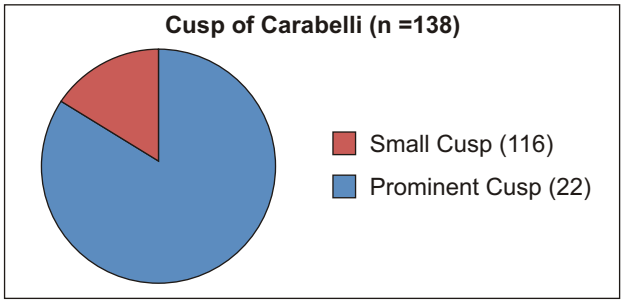

Figure 3: Showing variation of size of Carabelli cusp

Figure: 3 Shows that out of 138 subjects of which cusp of Carabelli was found, 116 (84.06%) of them had small cusp and 22 (15.94%) of them had very prominent cusp.

Table 4: Showing prevalence and bilateralism of groove expression of Carabelli trait in different teeth

Tooth	Carabelli Trait	Number	Present	Bilateral	Unilateral
Maxillary 1st permanent molar	Male	176 (100%)	28 (15.91%)	18 (64.29%)	10 (35.71%)
	Female	258(100%)	44 (17.05%)	26 (59.09%)	18 (40.91%)
	Total	434 (100%)	72 (16.59%)	44 (61.11%)	28 (38.89%)
Maxillary 2nd permanent molar	Male	148 (100%)	02 (1.35%)	01 (50%)	01 (50%)
	Female	230 (100%)	02 (0.87%)	01 (50%)	01 (50%)
	Total	378 (100%)	04 (1.06%)	02 (50%)	02 (50%)
Maxillary 3rd permanent molar	Male	148 (100%)	01 (0.68%)	01 (100%)	00 (0%)
	Female	230 (100%)	01 (0.43%)	00 (0%)	01 (100%)
	Total	378 (100%)	02 (0.53%)	01 (50%)	01 (50%)
Maxillary 2nd deciduous molar	Male	28 (100%)	02 (7.14%)	02 (100%)	00 (0%)
	Female	28 (100%)	10 (35.71%)	04 (40%)	06 (60%)
	Total	56 (100%)	12 (21.43%)	06 (50%)	06 (50%)

Table-4 shows the prevalence and bilateralism of groove expression of Carabelli trait in different maxillary molar teeth. Among 434 subjects 72 (16.59%) subjects had groove expression in maxillary 1st permanent molar with a bilateralism of 61.11%, in maxillary 2nd & 3rd permanent molars out of 378 subjects groove expression was found in 04 (1.06%) & 02 (0.53%) subjects respectively with a bilateralism of 50% in both cases and in maxillary 2nd deciduous molar among 56 subjects groove expression was found in 12 (21.43%) subjects with a bilateralism of 50%. Female predominance was seen in maxillary 1st permanent molar & maxillary 2nd deciduous molar teeth but in maxillary 2nd & 3rd permanent molars male predominance was seen.

Discussion:

Carabelli trait or Carabelli structure is important for determination of ethnicity and for forensic dentistry. It is also important in many science fields like anthropology, genetics, evolution science etc. Its prevalence varies in different regions and among different races. This study is completely new in Bangladesh though there are many studies about this morphological variation of teeth in different countries of the world. In this study an attempt was made to determine the frequency, distribution, size, sexual dimorphism and caries prevalence of Carabelli trait among Bangladeshi population. In our study the prevalence of Carabelli structure was found in 228 subjects (52.53%) out of 434 subjects, of this 31.80% found as cusp expression and 20.74% found as a groove expression as shown in Table-1. So it can be said that in Bangladeshi population Carabelli trait found as a moderate prevalence. Frequency of Carabelli trait varies among different races for example a higher frequency was seen in North West European origin Americans-83.5%[6], Aboriginal Australians-80%[7], Finish population-79%[8], South Africans-79.2%[9], Nepalese-68.3%[10]. A moderate prevalence was seen in Saudi Arabians-58.7%[11] and 57.6%[12]; Indians-52.7%[13]; Brazilians-51.6%[14]; Malaysians-52.2%[15]; Russians-50%[16]; Mixed Europeans-50%[17]. Low prevalence was seen in Eastern Greenland Eskimos-0%[18], Japanese-10.7%[17], Nigerians-17.43%[19], and Modern Chinese-21%[20].

In this study, cusp of Carabelli was found in 31.80% cases as shown in Table-1 which is in agreement with the study in Pakistan by Khan DB et al.[21] who reported the prevalence of this cusp to be 29.7%, in Iraq by Talabani et al.[22] reporting the prevalence as 30% and Hassanali[23] reported the prevalence as 26-27% but different from the result of the studies by Falomo OO[19], Rusmah M.[15], where the prevalence of cusp of Carabelli was reported as 17.43% and 52.2% respectively.

In Saudi population the occurrence of Carabelli trait was 41.7% shown by Syed Sadatullah et al.[5] and 57.6% by Salah Al Shethri[12], 65.34% in the contemporary study population in Hungary[24], 61% in a study from Tehran[25], in India 63.7% in maxillary first permanent molar and 8% in maxillary second permanent molar in the target population shown by Kamatham et al.[26], Kannapan JG et al.[13] shows 52.77% of maxillary first permanent molars displayed the trait. A study by Khraisat A et al.[27] among Jordanian population showed that the prevalence of Carabelli trait in maxillary first permanent molar was 65% and second permanent molar was 3.8%. It was 65.34% in a Hungarian study[28].

Our finding about Carabelli trait was 52.53% as shown in Table-1 present among all teeth and in case of maxillary first permanent molars it was found in 46.08% subjects, in maxillary second permanent molars it was found in 4.50% subjects, in maxillary third permanent molars it was found in 3.70% subjects, in maxillary deciduous second molars it was found in 67.86% subjects as shown in Table-2. So our study clearly matches with some study and in contrast with some other study. Though the frequency of the trait was a moderate prevalence (52.53%) but the cusp as a separate entity was found only in 31.80% subjects as shown in Table-1, of which in maxillary first permanent molars it was found in 29.49% subjects, in maxillary second permanent molars it was found in 3.44% subjects, in maxillary third permanent molars it was found in 3.17% subjects and in maxillary second deciduous molars it was found in 46.43% subjects as shown in Table-3. This study differ in a study by Khan DB et al.[21] and Talabani RM et al.[22] who showed a total absence of cusp of Carabelli in maxillary second permanent molars, but matches with the study by Subedi N et al.[10], Syed Sadatullah et al.[5], Falomo OO[19], Shethri SA[12]; all of them showed the presence of Carabelli cusp in maxillary second permanent molars.

Not many study about the prevalence of Carabelli trait in maxillary third permanent molar was found to be done, Falomo OO[19] reported only one subject who had Carabelli cusp on maxillary third permanent molar, so our study will also help to find the frequency and distribution of Carabelli trait in maxillary third permanent molar. Our study on maxillary second deciduous molar which had the highest percentage of trait presence may also help to find Carabelli trait's prevalence in this tooth.

None of the subjects had the trait only in second molars which matches with the study by Subedi N et al.[10]. But in maxillary third molars and second deciduous molars 2 subjects found on each, of which trait was found without association with first or second molars.

Groove expression was found in 16.59% in maxillary 1st permanent molars, 1.06% in maxillary 2nd permanent molars, 0.53% in maxillary 3rd permanent molars, 21.43% in maxillary 2nd deciduous molars as shown in Table-4 which defers from the study by Kamatham et al.[26] who showed that pit or groove was found in 62.2% of primary second molars, 33.1% of permanent first molars and 6.9% of permanent second molars. Díaz E et al.[29] also showed that the fossa forms of the Carabelli trait were one of the most frequent dental crown features.

The most common form of the trait observed in our study was the presence of small cusp or tubercle which was found in 116 subjects (84.06%) which matches with the study by Khan DB et al.[21] Out of 138 subjects of which Carabelli cusp was found, 22 (15.94%) of them had a very prominent cusp as shown in Figure-3 which differ from the study by Subedi N et al. [10] who found the presence of prominent cusp in 15 cases (7.31%) out of 205.

There was a significant variation among male & female subjects found in our study; the trait was seen in 59.66% cases in male and 47.67% cases in female and the Carabelli cusp was seen in 40.91% cases in male and 25.58% cases in female but groove expression was seen in 18.75% cases in male and 22.09% cases in female as shown in Table-1. This study of male predominance of Carabelli cusp and trait matches with the study by Bermudez De Castro JM[30], Khraisat A et al.[27] and Khan DB et al.[21]. But Hsu JW et al.[31] in a Chinese study and Tsai PL et al.[32] in a study from Taiwan had shown that the trait was more common in females. No significant sex dimorphism of the trait was shown by Falomo OO[19], Rusmah M.[15], Kieser JA[33], Talabani et al. [22], Harris EF [34]and Sudebi et al.[10].

Bilateralism of the Carabelli trait was observed in 75.24% cases in male & 69.11% cases in female as shown in Table-1. In maxillary first permanent molars bilateralism was seen in 73% cases, in maxillary second permanent molars bilateralism was present in 76.47% cases, in maxillary third permanent molars bilateralism was found in 78.57% cases and in maxillary second deciduous molars bilateralism was present in 78.95% cases as shown in Table-2. Bilateralism was seen in maxillary first permanent molars in 70.71% in a study by Falomo OO in Nigeria[19], 82.2% in a study from Saudi Arabia by Shethri SA[12], 75.6% in a study from Pakistan by Khan DB et al. [21] which matches our study but in a study from Iraq by Talabani et al.[22] showed only 56% cases as bilateral and a study by Iwai-Liao Y et al.[35] showed that Carabelli tubercle on maxillary first molars were always bilateral. So bilateralism is a common feature of Carabelli trait though the percentage may vary among different races.

There was no statistically significant variation found in right and left side of the dentition. Some previous studies by Ferreira, M. A. et al.[14], Rusmah M.[15] have proved similar correspondence between right and left sides whereas another study by Meredith, H. V. & Hixon, E. H.[6] reported discordance.

In our study caries related to Carabelli trait was found only in two subjects out of 434 (0.46%). So caries incidence related to Carabelli trait was quite insignificant. But prominent pits-grooves of cusps & grooves produce a stagnation area and can be foci for plaque retention and caries development. A study from Nigeria[19] also showed that caries incidence related to Carabelli structure was insignificant.

Conclusion:

Frequency of occurrence of Carabelli trait is moderate among Bangladeshi people. Its frequency and distribution varies among male, female and children. It is more common in maxillary second deciduous molars and maxillary first permanent molars and rare in maxillary

second and third permanent molars. The bilateral presence of the trait was common. Presence of carious lesions was minimum. Findings of the study may provide a useful aid to forensic odontology for identification of person. Further study in different institutional capacity is recommended.

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Original Article

Protective Role of Ethanolic Extract of *Nigella Sativa* Seeds in the Development of Gastric Ulcer in Experimental Rats

Sultana N[a], Akhter MS[b], Ahmed N[c], Momtaz A[d], Afrin S[e]

Abstract

Objective: To evaluate the gastro protective effect of *Nigella sativa*.

Methods: Alcoholic extract of *Nigella sativa* was prepared with the help of soxhlet's apparatus. Thirty (30) albino rats of 150-175gm of either sex were divided into five groups with 6 rats in each group. Rats of group A & B were administered normal saline (2 ml/kg) and aqueous suspension of aspirin (200mg/kg) po respectively. Group C, group D & group E were administered normal saline (2 ml/kg), alcoholic extract of *Nigella sativa* (150 mg/kg) & omeprazole suspension (20 mg/kg) po respectively for 8 days. After 8 days of treatment, animals were fasted for 24 hours. Then administration of aqueous suspension of aspirin (200 mg/kg)was done and after 4 hours all rats were sacrificed and prepared for dissection.

Results: Aspirin administration caused marked gastric damage in control group which was prevented in Omeprazole and *Nigella sativa* extracts treated groups significantly but the protective role of alcoholic extract of *Nigella sativa* was less than that of Omeprazole.

Conclusion: Alcoholic extract of *Nigella sativa* showed significant protection against aspirin induced gastric ulcer in experimental rats.

Keywords: *Nigella sativa*, Aspirin, Omeprazole, Gastro protection.

Introduction:

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most widely used drugs worldwide. NSAIDs are used very commonly in long term basis like in rheumatoid arthritis, post myocardial infarction etc. in spite of this they have significant adverse effects related burden to the community. Among the NSAIDs the prototype drug aspirin has still significant role as an antiplatelet, anti-inflammatory, analgesic and antipyretic agent. Both higher and lower doses of aspirin have significant risk to develop gastric damages which may be in the form of dyspepsia, gastritis, haemorrhage, ulceration or even sometimes perforation.

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Nigella sativa is commonly known as "kalojira/black cumin" belongs to family *Ranunculacea*, an annual herb. Seeds are small, trigonus, angular and black externally with white inside. Odour of seed is aromatic with bitter taste[1]. It is reported to have various pharmacological activities like antidiabetic, analgesic, anti-inflammatory, antioxidant, antitumour, wound healing and very few reports on gastroprotective role against aspirin induced gastric ulcer in rats[2-7].

Although, to prevent gastric ulcer many of the drugs are available like PPI, H2 blockers but they also have some adverse effects. Newer drugs which have minimal adverse effects with maximum benefits are continuously searched worldwide to prevent gastric ulcer induced by NSAIDs. So, in this regard study was planned to evaluate the protective role *of Nigella sativa* against aspirin induced gastric ulcer in experimental rats.

Materials and Methods:

The study was conducted in the Department of Pharmacology & Therapeutics, Dhaka Medical College in collaboration with Department of Pathology, Delta Medical College, Dhaka, from January 2010 to December 2010.

Experimental animals:

The experiment was carried out on a total number of 30 healthy albino rats. The rats were aged between 8-10 weeks of both sexes & weighing between 150-175 gm. They were kept in medium sized metallic cages in animal house of Pharmacology Department at Dhaka Medical College, Dhaka. They were allowed to live at room temperature, fed on standard pellets of rat food & allowed to drink tap water.

Plant material:
Alcoholic extract of *Nigella sativa* was made from kalojira which was bought from local market of Dhaka, Bangladesh.

Drugs & chemicals:
i) Aspirin was bought from local medicine shop, Dhaka, Bangladesh.

ii) Omeprazole sachet was bought from local medicine shop, Dhaka, Bangladesh and diluted with water to make suspension.

iii) 0.9% Sodium Chloride (normal saline) & distilled water were supplied by the Department of Pharmacology of Dhaka Medical College, Dhaka, Bangladesh.

Preparation of plant extract:
1000 gm of *Nigella sativa* (kalojira) was purchased from the local market. The seeds were dried & crushed into coarse powder which was macerated with alcohol (99%v/v) using soxhlet apparatus. The extract was evaporated by rotator evaporator at an optimum temperature of 40-50° c under vacuum. The extractive value (v/v) of alcoholic dry extract was 4.25%.

Experiment design:
The experiment was divided into 2 parts: Experiment-1 & 2

Experiment-1:
It was comprised of 12 rats which were divided into 2 groups each having 6 rats. Groups were labelled as Group-A & Group-B.

Group-A: This group was served as control group & they were provided with normal saline (2 ml/kg body wt) orally by gastric tube.

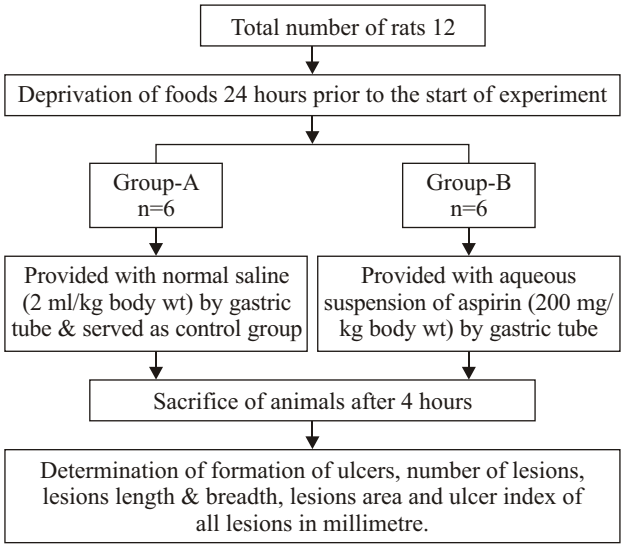

Fig 1: Flow chart of Experiment-1

Group-B: This group was provided with aqueous suspension of aspirin (200 mg/kg body wt) orally by gastric tube. After 4 hrs all rats were sacrificed by an overdose of diethyl ether & stomach was collected for gross & histological study. Experiment on these groups was carried out to evaluate the effect of aqueous suspension of aspirin in rats.

Experiment-2:
It was comprised of 18 rats. They were divided into 3 groups each containing 6 rats labelled as Group-C, Group-D & Group-E.

Group-C: This group was served as disease control group & were provided with normal saline (2 ml/kg body wt) orally by gastric tube for 8 days.

Group-D: They were provided with alcoholic extract of *Nigella sativa* (150 mg/kg body wt) orally by gastric tube for 8 days.

Group-E: They were provided with omeprazole suspension (20 mg/kg body wt) orally by gastric tube for 8 days.

After 8 days of treatment, animals of all groups were fasted for 24 hrs. Then administration of aqueous suspension of aspirin (200 mg/kg body wt) by gastric tube & after 4 hrs, all rats were sacrificed by an overdose of diethyl ether & stomach was collected for gross & histological study. Experiment in these groups was carried out to evaluate the protective role of alcoholic extract of *Nigella sativa* on aspirin induced gastric ulcer in rats as compared to omeprazole.

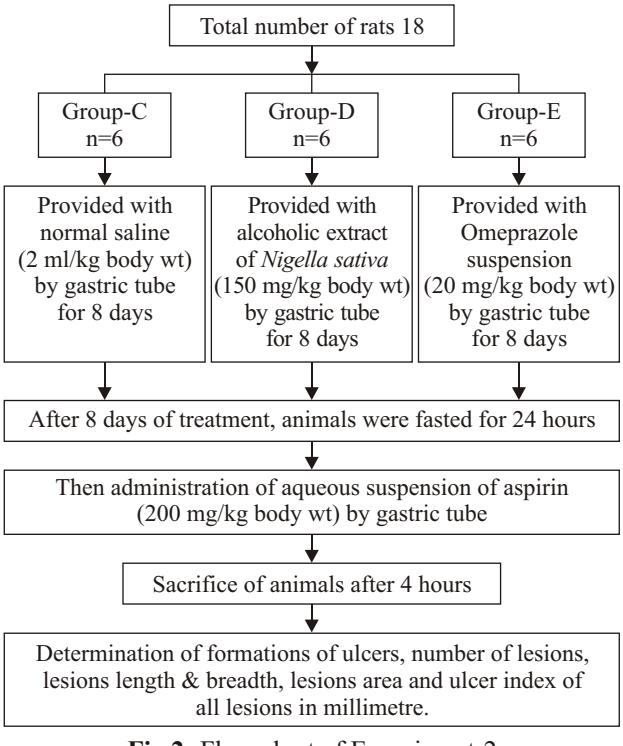

Fig 2: Flow chart of Experiment-2

Morphological parameter studied:
i) Number of lesion (Mean ± SD) per rat in each group

ii) Individual lesion length & breadth in millimetre (Mean ± SD) for each group

iii) Individual lesion area (length × breadth) in square millimetre (Mean ± SD) for each group

iv) Mean ulcer index (sum of length of all lesions in each stomach) in millimetre for each group.

Statistical analysis:
All relevant information for each rat was recorded in a redesigned data collection sheet. Collected data were screened & compiled. All data were recorded in tabulated form & the results were expressed as Mean ± SD. The significance of the differences in the values was performed by paired t-test.

Results:

Table 1: The effect of Aspirin on mean number of lesion, lesion length, lesion breadth, lesion area and lesion index in each group

Parameters	**Group-A** (Mean ±SD)	**Group-B** (Mean ± SD)	p value
Mean number of lesion	0	4.83 ± 0.75	<0.001**
Mean lesion length	0	6.52 ± 3.80	
Mean lesion breadth	0	1.63 ± 1.35	
Mean lesion area	0	13.58 ± 15.91	
Mean lesion index	0	31.50 ± 9.61	

P = < 0.001** = highly significant

Group-A was served as control group and was provided with normal saline (2 ml/kg body wt) by gastric tube.

Group-B was provided with aqueous suspension of aspirin (200 mg/kg body wt) by gastric tube.

Table 1 shows the effect of aqueous suspension of aspirin in rats. Group-A had no lesion in the stomach but in Group-B the Mean number of lesion, lesion length, lesion breadth, lesion area & lesion index were 4.83 ± 0.75, 6.52 ± 3.80, 1.63 ± 1.35, 13.58 ± 15.91 and 31.50 ± 9.61 respectively. Result showed p value < 0.001, which was highly significant. Thus, aqueous suspension of aspirin was shown to have strong ulcer producing effect in rats.

Table 2: The effects of alcoholic extract of *Nigella sativa* on mean number of lesion, lesion length, lesion breadth, lesion area & lesion index

Parameters	**Group-C** (Mean ±SD)	**Group-D** (Mean ± SD)	p value
Mean number of lesion	5.33 ± 0.82	4.17 ± 0.75	<0.001**
Mean lesion length	6.75 ± 3.71	3.48 ± 2.25	
Mean lesion breadth	1.63 ± 1.29	0.77 ± 0.48	
Mean lesion area	13.66 ± 15.14	1.30 ± 3.55	
Mean lesion	36.00 ± 11.08	14.51 ± 2.47	

P = < 0.001** = highly significant

Group-C was ulcer control group and they were provided with normal saline (2 ml/kg body wt) for 8 days.

Group-D was provided with alcoholic extract of *Nigella sativa* (150 mg/kg body wt) for 8 days.

Table 2 Shows a significant reduction in ulcer number, ulcer length, ulcer breadth, ulcer area & ulcer index seen in Group-D which was pre-treated with alcoholic extract of *Nigella sativa*. Result showed p value < 0.001, which was highly significant. Thus, alcoholic extract of *Nigella sativa* showed to have a significant gastro-protective effect in rats.

Table 3: The comparative gastro-protective effects of *Nigella sativa* & Omeprazole in rats

Parameters	**Group-C** (Mean ±SD)	**Group-D** (Mean ± SD)	p value
Mean number of lesion	4.17 ± 0.75	4.33 ±1.03	>0.05**
Mean lesion length	3.48 ± 2.25	2.38 ± 1.84	
Mean lesion breadth	0.77 ± 0.48	0.64 ± 0.66	
Mean lesion area	1.30 ± 3.55	2.58 ± 5.26	
Mean lesion	14.51 ± 2.47	9.91 ± 2.82	

P = > 0.05 = not significant

Group-D was provided with alcoholic extract of *Nigella sativa* (150 mg/kg body wt) for 8 days.

Group-E was provided with Omeprazole suspension (20 mg/kg body wt) for 8 days.

Table 3 Shows there was less significant reduction of ulcer number, ulcer length, ulcer breadth, ulcer area & ulcer index observed in group-D in comparison with group-E (p value > 0.05). Thus, *Nigella sativa* showed to have fewer efficacies as Omeprazole in gastro-protection in experimental rats.

Discussion:

The gastric epithelium is under constant assault by a series of endogenous noxious factors, including HCl, pepsin and bile salts as well as exogenous substances such as medications, alcohol and microorganisms. The present study showed that aspirin at a single dose of 200 mg/kg per oral in 24 hours fasted rats caused significant damage to the gastric mucosa. Histological findings also supported the gastric mucosal damage.

In an effort to further search, the present study is undertaken to find out safe agents for the prevention of peptic ulcer from our indigenous medicinal plants. The gastro protective efficacy of *Nigella sativa* extract is determined in albino rats having aspirin induced ulcers. The aspirin model has already been utilized for screening the new compounds for their anti-ulcer effects. Use of this model for the same purpose has been employed for several workers including Akhtar and Munir (1989), Eddleston et al (1994) & Shah and Khan (1997).[8,9]

When we observed the experimental Group-D in which *Nigella sativa* was given for 8 days for the prevention of gastric ulcer, the results were favourable. Four animals showed normal & intact mucosa with reparative changes in mucosal surface and two animals showed mild acute & chronic inflammation with infiltration of neutrophils, lymphocytes & macrophages. In experimental Group-E, Omeprazole was used as a reference drug to compare the effect of *Nigella sativa* on gastric mucosa. After 8 days of pretreatment with omeprazole, one animal showed mild chronic inflammation with healing ulcer, one animal had mild degree of ulceration with signs of chronic inflammation & rest of the animals were found normal with no signs of inflammation. When comparing all the twelve rats of these two groups, the difference in protecting ulcer in rats was statistically not significant ($p > 0.05$). The healing results of *Nigella sativa* and Omeprazole are consistent with that of Shoiab and Munir (1989) and Akhter et al (1998); in which the drug was used as a reference for the treatment of gastric ulcer.[8,9,10]

Conclusion:

Nigella sativa has a very effective role in prevention of gastric ulcer but its efficacy in ulcer prevention is less in comperison with Omeprazole. In Bangladesh, *Nigella sativa* is not used in the gastric ulcer therapy in routine practice. On the basis of present study, it is suggested that further broad spectrum studies as well as clinical trials should be conducted before the use of this product as routine medicine.

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Review Article

Electrolyte Imbalance in Dengue Infected Patients

Khanduker S[a], Ahmed R[b]

Abstract

Dengue viral infections are one of the most important mosquito borne diseases in the world. They may be asymptomatic or may give rise to undifferentiated fever, dengue fever, dengue haemorrhagic fever (DHF), or dengue shock syndrome (DSS). According to the course of the disease so many complications may occur. The most severe complication occurs in dengue shock syndrome. Sudden hypotension occurs in the onset of shock which is often accompanied by metabolic acidosis or electrolyte disturbances. This review considers the recent evidence in this field and concludes that along with metabolic acidosis mild hyponatremia is the most common electrolyte disorder. Others are hypokalemia, hypocalcemia, increased chloride levels and decreased zinc level. Careful monitoring of electrolytes, acid base status and renal function are necessary for the early diagnosis of dengue infection. Knowledge of electrolyte imbalance is very necessary for preventing further complication or treatment of the disease.

Keywords: DF, DHF, DSS, Electrolyte imbalance, Hyponatremia, Hypokalemia.

Introduction:

Dengue is a transmittable disease caused by the DEN virus (DENV), which is the member of the genus Flavivirus, in the family Flaviviridae. The virus is 40-50mm single stranded about 11Kb in length. Dengue virus has four distinct but closely linked serotypes (DEN-1, DEN-2, DEN-3 and DEN-4) all of them can cause dengue fever (DF) and dengue hemorrhagic fever (DHF)[1]. DEN-2 was the predominant serotype in the 1980s and in the early 1990s, but in recent years, DEN-3 has been more predominant.[2]

Transmission:

Dengue is transmitted by the bite of an infected Aedes mosquito. The female Aedes mosquito gets infected with the dengue virus after sucking blood from an infected person during acute febrile illness. *Aedes aegypti* is the most important epidemic vector. *A. albopictus* and *A. polynesiensis* may act as vectors in some geographic locations. *Aedes aegypti* is seen in abundance in at-risk areas. The Aedes mosquito rests indoors, mainly in living rooms and bedrooms, and in small collections of water, such as flowerpots or coconut shells. Eggs can survive for long periods. Improper disposal of garbage or inadequate wastewater drainage may be responsible for high mosquito densities in endemic areas. Significant increases in the mosquito larval populations are seen during the rainy season. This may be a reason why the epidemics of dengue tend to coincide with the rainy season. Uncontrolled population growth, unplanned and uncontrolled urbanization, inadequate waste water management and lack of effective mosquito control have been implicated in the increased distribution and density of the vector and also the increased spread of the virus.[3,4]

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Incidence:

Dengue infection was initially described only in tropical areas, however over the past few decades has been found in many parts of the world. World health organization has reported 2.5 billion people live in areas where dengue viruses can be transmitted (WHO 2009).[5] The highest incidence of Dengue is seen in Southeast Asia, India and the American tropics.[6] In South East Asia, the average annual figure of DHF cases has increased from10,000 in the 1950s to more than 200,000 in the 1990s.[7,8]

Clinical classification:

Dengue virus infections may be asymptomatic or may have three main clinical manifestations.[9,10]

1) Undifferentiated febrile illness (UF) or viral syndrome
2) Dengue fever (DF)
3) Dengue hemorrhagic fever (DHF)
   - DHF without shock;
   - Dengue shock syndrome (DSS).

Symptoms:

Dengue infection may be asymptomatic or may present as an undifferentiated febrile illness or as dengue hemorrhagic fever including dengue shock syndrome. DHF and DSS are classified into into 3 phases febrile, critical, and convalescent.[11,12] The onset of fever is very high with severe headache(especially in the retro-orbital area), arthralgia, myalgia, anorexia, abdominal discomfort and sometimes a maculopapular rash. The fever may be biphasic and tends to last for 2-7 days. Although haemorrhagic manifestations are uncommon in dengue

fever petechiae/purpura, gastrointestinal bleeding, epistaxis and gingival bleeding have been observed in some individuals. A positive tourniquet test has been reported in many individuals with dengue fever possibly due to reduced capillary fragility.[13,14]

Complications of Dengue:

Severe dengue infections may give rise to many complications as Dengue haemorrhagic fever and disseminated intravascular coagulation (DIC) dengue shock syndrome (DSS), liver failure, cerebral haemorrhage or oedema, encephalopathy ,cranial nerve palsies, myocarditis, rhabdomyolysis and haemolytic uremic syndrome, Acute respiratory distress syndrome and renal failure.[11,15,16.] Although these complications are rare but in recent years they have been reported with increased frequency.[17] As a consequence of complications of DHF bleeding manifestations occur from various organs having platelet count $<100\times10^{9}$/L with positive tourniquet test. Severe plasma leakage leads to Dengue shock syndrome. Sudden hypotension occurs during shock which may accompanied by metabolic acidosis. This may lead to disseminated intravascular coagulation with massive haemorrhage.DSS may be accompanied by encephalopathy due to metabolic acidosis and electrolyte disturbance.[18,19]

Pathophysiology of electrolyte imbalance in dengue:

Sodium is an essential nutrient in human body which regulate blood volume, blood pressure, osmotic equilibrium and P^{H}. Mild hyponatremia with a serum sodium 130-134mEq/Lwas the common electrolyte disturbance seen in both patients with DF and DHF, especially in shock patients.[20] Sodium is the important mineral in neuron function and osmoregulation between cells and the extracellular fluid. The distribution of sodium ions are mediated in all animals by Na/K ATPase. The reason for hyponatremia in classic dengue fever patients is uncertain. It is thought to be caused by peripheral fluid extravasation and resulting intravascular hypovolemia. It might be the consequence of salt depletion, excess water from increased metabolism, decreased renal excretion, transient inappropriate antidiuretic hormone or the influx of sodium in cells as a result of dysfunction of sodium potassium pump. [21,22]

Previous studies have identified that dengue patients are 9.5 times more likely to have clinically significant hyponatremia (Na<130mmol/L) than patients with similar febrile illnesses. Hypovolemia, confirmed by a urine sodium of <20mmol/L was also found to be 8.1 times more common in dengue patients. [23,24] Patients who present with dengue associated hyponatremia with a normal or elevated urine sodium have been hypothesized to have transient syndrome of inappropriate secretion of antidiuretic hormone (SIADH). Antidiuretic hormone (ADH) release is controlled by hypothalamic osmoreceptors. These osmoreceptors are extremely sensitive and respond to as little as 1% variation in tonicity. In patient with shock a hypovolumic stimulus will override a hypotonic inhibition and volume will be conserved at the expense of tonicity. This mechanism may account for the rapid fall in sodium levels in dengue shock syndrome. [25]

Mild hypokalemia with a serum potassium between 3.0-3.5 mEq/L is a well-documented electrolyte imbalance in patients of dengue fever, its prevalence has been found to vary from 14% to 28% in dengue patients. In dengue fever along with other infectious disorders, cause of hypokalemia is inadequate dietary intake and breakdown of tissues releases potassium into the extracellular compartment.[26] There is loss of potassium due to vomiting and diarrhea in febrile phase of dengue fever. The virus infection led to acute neuromuscular weakness due to hypokalemia.[20] The cause of hypokalemia may be due to poor intake and an increase renal excretion due to activation of renin-angiotensin and aldosterone system secondary to volume depletion.[27]

Conversely, in dengue hypokalemic paralysis was found in 13% of the patients in another study.[28] The exact mechanism for hypokalemic paralysis in dengue infection is not known. The possible mechanisms postulated are redistribution of potassium into the cells or transient renal tubular abnormalities leading to increased urinary potassium wasting. Endogenous granulocyte macrophage-(GM-CSF) and related cytokines in response to neutropenia may be another putative factor leading to intracellular shift of potassium. Increased catecholamine levels in response to stress of the infection and secondary insulin release can result in intracellular shift of potassium and hypokalemia. [29,30,31,32]

In persons infected with dengue virus, extracellular calcium plays an important role in platelet aggregation and for the regulation of the immune response.[33] Several causes for low blood calcium levels have been suggested, including reduced Na+-K+ adenosine triphosphatase (ATPase) activity, reduced Ca^{2+}-ATPase activity, acquired parathyroid hormone deficiency, renal one-alpha hydroxylase insufficiency, reduced dietary vitamin D intake, and reduced dietary calcium intake.[34]

Discussion:

The minerals those are significant assist and maintain the normal physiological mechanisms in the body are divided into two groups: as a) macrominerals (eg. Sodium, potassium, calcium, magnesium, chlorine, sulpher etc) and b) microminerals or trace elements (eg. zinc, lead, copper, cobalt, manganese, molybdenum, chromium, nickel and iron) which consist of metals present in biological fluids at concentrations less than 1mg/g weight.[35] In dengue patients the critical phase of DHF is the period of plasma leakage, begins during the transition from febrile to the afebrile phase. The plasma leakage may lead

to hypovolumic shock (DSS). Patient with prolonged or uncorrected shock may develop more complicated course with metabolic acidosis and electrolyte imbalance, multiple organ failure severe bleeding from various organs.[12] Electrolyte disturbances take place in dengue infection and renal dysfunction also have been reported in these patients from various studies. They are individually discussed.

Sodium:
The most common electrolyte imbalance found in dengue patients are hyponatremia Long years ago in 1973 Varavithya found hyponatremia among the dengue patients of Thailand.[36] Then Mekmulica et al in 2005 found sodium level 132meq/L. They also found that dengue patients are 9.7 times more likely to have clinically significant hyponatremia(<130mmol/L) than patients with similar febrile illnesses.[23] Again in 2010 Lumpaopong et al found serum sodium level was 133meq/L.[27] Among the Indian studies in 2008 Dhooria found hyponatremia (<125 meq/L),[15] in 2014 Caroline Rose found mean sodium level 129.38meq/L[22] and similarly in 2015 Bhagyamma found mean level of sodium 130.6meq/L.[37] Again in 2015 Unnikrishnan found sodium level <135meq/L among the elderly dengue patients.[38] Varavithya demonstrated low 24-hour urine sodium levels in dengue patients with shock.[36] Mekmullica confirmed hypovolemia with urine sodium of <20mmol/L among dengue fever patients. This finding may be explained by the decreased renal blood flow, which is a consequence of the depletion of the ECV.[23]

Potassium:
Lumpaopong et al in 2010 reported mild hypokalemia common in dengue patients.[27] Caroline rose in 2014 found hyperkalemia where mean value of potassium in dengue confirmed patients were 5.4 meq/L.[22] Bhagyamma found value of Potassium in dengue patients were 3.07 meq/L in 2015.[37] Kumar found potassium level 2.50mmol/L in 2014. Misra 2006, Garg 2013, Malhotra 2014 and Kumar 2014 also found hypokalemic paralysis in dengue patients.[29,30,31,32]

Chloride:
Syed et al in pakistan found serum chloride level is increased significantly in dengue patients than healthy individuals 107.07 meq/L in 2014.[39] Caroline rose in India also found significant increase of chloride level 115 meq/L.[22] Bhagyamma demonstrated that the levels of chloride in serum of dengue patients increased significantly than the healthy individuals in 2015.[37]

Biocarbonate:
Decreased biocarbonate is the primary defect of metabolic acidosis. Metabolic acidosis were present in some patients with DF and DHF. Lumpaopong et al in 2010 found serum bicarbonate less than 18 mEq/L.[14] The etiology of metabolic acidosis may be starvation, ketoacidosis, lactic acidosis or compensation for respiratory alkalosis.[27] Varavithya et al in 1973 showed metabolic acidosis and respiratory alkalosis were common in patients with DHF, especially in severe cases.[36]

Calcium:
Castila-Guerra et al in 2006 found acute hypocalcemia. They also stated hypocalcemia associated with increased neuromuscular excitability and tetany among the dengue patients.[40] Syed et al in 2014 found decrease calcium level of dengue patients than healthy individuals (8.09 Vs 9.22 meq/L) in pakistan.[39] Low blood calcium levels have been demonstrated in dengue infection by Bunang2011, Udiino 2008, Kapoor 2012 and Wiwanitkit 2012.[41,42,43,44]

Other Heavy metals:
The majority of the trace elements include selenium, zinc, copper, cobalt, manganese, chromium, nickel and iron are essential nutrients for humans and animals. Trace elements deficiencies and infectious diseases are correlated with each other as they frequently co exist and reveal complex interactions. Various trace elements perform antiviral activity by inhibiting virus replication in the host cells.[35] Among the heavy metals zinc, lead and chromium of dengue patients were compared with healthy individuals. There are not so many researches regarding this. In dengue patients low serum level of zinc are found. Zinc deficiency is known to happen along with an imbalance of Th-1 cell and Th-2 cell resulting in deregulated resistance to infection so can increase the hazard of morbidity and mortality of infection.[45] Sara Sayed et al in 2014 found increased serum lead level, decreased chromium level and decreased serum Zinc level in serum of dengue patients .[39]

Conclusion:

Like other complications of dengue infection electrolyte imbalance is one of the most severe form. Life threatening situations may occur from electrolyte imbalances in dengue. So to prevent further complication prevention of electrolyte imbalance is necessary. According to several studies mild hyponatremia and hypokalemia is the common electrolyte disturbance in dengue patients. Renal involvement is mild. Careful monitoring of electrolytes and acid base status should include more severe cases, to assess renal tubular function and evaluate the etiology of the electrolyte disturbances.

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Case Report

Drug-Resistant Tubercular Meningitis: a Challenging Disease to Diagnose and Treat

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Abstract

Among extra-pulmonary tuberculosis (TB), meningeal tuberculosis (MTB) is a severe disease, not only because of its bizarre presentation making it difficult to diagnose but also for its high mortality despite the availability of effective and specific treatment. The more alarming picture is that for the last few years there is an increase in the prevalence of drug-resistant TB (both pulmonary and extra-pulmonary) in the developing world. We got a male patient of 48 years old, who was on category I anti-tubercular chemotherapy for tubercular pleural effusion. After 2 months, during his continuation phase of treatment, he again became febrile with headache, vomiting, and altered sensorium. There were signs of meningeal irritation and cerebrospinal fluid (CSF) study confirmed the presence of rifampicin-resistant tuberculosis (RR-TB). 2nd line antibiotics were started promptly as per WHO treatment guideline for drug-resistant TB, but unfortunately, the patient died on 12th day of hospital admission.

Keywords: Tubercular meningitis, Drug-resistant TB, Rifampicin-resistant TB (RR-TB), Multidrug-resistant TB (MDR-TB)

Introduction:

Worldwide, tuberculosis is one of the leading causes of death due to infectious disease and among countries, Bangladesh ranks fourth for the prevalence of both TB and TB mortalities.[1] In the combat of reducing this large burden, the emergence of drug-resistant tuberculosis has been complicating the scenario.

Infection with *Mycobacterium tuberculosis* strain, which is resistant to at least two of the most effective anti-tuberculosis medications, isoniazid (INH) and rifampicin (RFP) is called multidrug resistance TB (MDR-TB). In addition to this, when the strain is resistant to any fluoroquinolone, and at least one of three second-line injectable drugs (capreomycin, kanamycin, and amikacin), it is called extensive drug resistance (XDR) TB. Rifampicin resistant TB (RR-TB) includes resistance to rifampicin with or without resistance to any other drugs and is treated as a case of MDR-TB.[2,3] According to WHO, in the year of 2014, in our country, MDR-TB rate among all newly diagnosed and previously treated cases is estimated at 1.4% and 29% respectively.[1]

Multidrug-resistant (MDR) pulmonary TB is relatively well studied , whereas, publication of MDR-TB meningitis (MDR-TBM) are mostly limited to case reports and a single case series and to-date there is no standard evidence-based guidance, specifically devoted for the treatment of the MDR-TBM cases. To make the picture more complicated, most of the available second-line anti-TB drugs have inadequate blood-brain-barrier (BBB) penetration leading to the fatal outcome.

Here, we present a case report of a patient with tuberculous pleural effusion, who during the continuation phase of standard anti-TB chemotherapy category- I, presented with drug-resistant TB meningitis.

Case Presentation:

A 48 years old HIV-negative man presented on May 2016, with the complaints of, low-grade evening rise of temperature for 2 months and significant weight loss (7kg) within that period. For last 4-5 days, he had left lower chest pain with respiratory distress. There was no productive cough, headache, altered bowel habit, joint pain or abdominal pain. On examination he was cachectic (BMI-16 kg/m^2), body temp 101ºF and pulse 114/min. Breath sound was diminished on left 3rd intercostal space to downwards; vocal fremitus and vocal resonance were also found decreased. All other systemic examinations revealed no abnormality. On investigation, haemoglobin was 11.9 gm/dl, WBC count 7400/mm^3, ESR 55 mm in 1st hour. Chest X-ray postero-anterior view showed left-sided large pleural effusion. Pleural fluid cytology revealed total count of WBC 1250/mm^3, where neutrophil 10%, lymphocyte 90%; biochemistry showed glucose 76 mg/dL, protein 6.3 gm/dL and adenosine deaminase (ADA) 53 U/L. Gram staining showed no organism and no acid-fast bacilli (AFB) was seen in Ziehl-Neelsen (ZN) stain. Tuberculin skin test was positive (29 mm at 72 hours). Examination of 3 samples of induced sputum (including 2 early morning samples) showed no AFB. Although there was no confirm

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microbiologic evidence of tuberculosis infection, relying on the suggestive clinical scenario and cytological and biochemical findings of pleural fluid, treatment with fixed dose combination anti-TB chemotherapy category I was commenced. To prevent pleural adhesion oral prednisolone was also added for 21 days. After 6 days of starting treatment, he became afebrile and was discharged from the hospital with advice.

The patient had successfully completed his intensive phase of treatment for 2 months without any complications. But, on the 9th day of continuation phase, he developed fever, which was initially low grade, then became high grade, continued in nature. Fever was associated with severe headache and vomiting. Prior to hospitalization, he was drowsy, disoriented with altered level of consciousness. On admission, his GCS was 10/15; temperature 102ºF. Systemic examination revealed he had neck rigidity along with bilateral positive Kerning's sign. Lab reports showed high ESR (96 mm) with normal WBC count and moderate hyponatraemia (122mmol/L). Findings of his CT scan of the brain were unremarkable. Lumbar puncture was performed and CSF study revealed lymphocytic pleocytosis (250/mm^3, lymphocyte 70%), high protein level (360 mg/dL) and low glucose concentration (15 mg/dL). CSF ADA was 21 U/L; smear microscopy showed no organism. Xpert MTB/RIF test of CSF sample detected Mycobacterium tuberculosis which was resistant to rifampicin. Along with supportive care, treatment was started with injectable levofloxacin, amikacin, linezolid, meropenem, pyrazinamide and high dose isoniazid. As an adjunctive therapy dexamethasone and mannitol 20% were also used. Despite all efforts, patient's condition was deteriorating and he was shifted to ICU for better management. Repeat CSF sample was sent to exclude XDR-TB. While waiting for drug sensitivity report, 2nd line antibiotics were going on in full dose with simultaneous monitoring for adverse drug effects. Unfortunately, the patient died on 12th day of hospital admission.

Discussion:

Central nervous system (CNS) tuberculosis constitutes 5% of extra-pulmonary TB cases.[1,4] Though it can manifest in several forms such as tuberculoma, brain abscess; the commonest is meningeal tuberculosis. Almost all cases are due to secondary infection by *Mycobacterium tuberculosis* disseminated from a primary pulmonary focus. The development of the disease is insidious and in the course, 3 clinical stages (prodromal phase, phase of neurological symptoms and phase of paresis) may be differentiated; but unfortunately, not all patients exhibit all three stages conspicuously which contributes to late diagnosis, and delayed implementation of a specific treatment resulting in worse prognosis. The common manifestations are fever, anorexia, weight loss, vomiting, headache, photophobia, signs of meningismus, cranial nerve paralysis (specially oculomotor, abducens and facial nerve), seizure, altered sensorium and coma.[5,6] Some may present with classical features of acute stroke due to vasculitis resulted from meningeal inflammation.[7,8] So, in a country of the high prevalence of tuberculosis, TBM should be kept in mind as a differential diagnosis in any atypical neurologic presentation.

The confirmed diagnosis of TBM can be challenging and may be based only on presenting clinical features and presumptive CSF findings without definitive bacteriologic identification. In CSF, presence of lymphocyte-predominant pleocytosis (100-500 cells/μL), elevated protein (100-500 mg/dL) along with reduced glucose level (<45 mg/dL) increase the probability of TBM.[9]

An acid-fast smear of CSF specimen has a relatively low sensitivity (20%40%) and results are highly dependent on sample volume, accurate method of collection, prompt transport to the lab and analysis, and the technical expertise of lab personnel.[2,10] Culture of tubercle bacilli in a solid or liquid medium is the gold standard methods for microbiological confirmation of TB, but the process is time-consuming taking several weeks and also has very low yielding.[2] Despite, it should be performed because determination of drug susceptibility has important impact on identification of drug-resistant cases and initiation of appropriate antibiotics for favorable outcome.

Neuro-imaging can be a helpful aid for presumptive diagnosis of TBM, and magnetic resonance imaging (MRI) is the radiologic technique of choice. Basal meningeal enhancement, hydrocephalus, and cerebral edema are common radiographic features of tubercular meningitis but none are pathognomonic.[11]

For rapid and more accurate diagnosis, molecular diagnostic methods have been developed recently with higher sensitivity and specificity. Nucleic acid amplification (NAA) techniques, especially polymerase chain reaction (PCR) are most widely accepted. Since 2010, Xpert MTB/RIF has been used as an initial diagnostic test for rapid detection of rifampicin-resistant TB. Line probe assay (LPA) can reliably identify resistance to fluoroquinolones or injectable second-line medications.[12] So, it is recommended by WHO, for patients with confirmed rifampicin-resistant TB or MDR-TB, this genotypic drug sensitivity test (second line LPA) may be used initially instead of phenotypic culture-based methods for early detection of XDR-TB. It is important to note that commercial NAA can confirm TBM but a negative result cannot exclude the diagnosis. So, clinical judgment is essential before refuting a suspected TBM.

Active drug-resistant TB develops principally in two ways: i) primary resistance and ii) acquired or secondary resistance. Direct transmission of the drug-resistant tubercle bacilli from an infected host leads to the development of primary resistance, whereas acquired resistance occurs in previously treated drug-susceptible

TB patients, mostly due to non- compliance, inadequate dosing or combination, poor regulation of medicines, lack of adherence to treatment etc. resulting in a natural mutation of drug-resistant strains. The presence of concomitant HIV infection, diabetes mellitus, under-nutrition, malabsorption, alcoholism, substance abuse or other immune-compromised conditions increase the susceptibility of developing drug-resistant TB.[3,13,14]

In 2016 WHO published an updated treatment guideline for drug resistance TB where all available second-line anti-TB medicines are reorganized into different groups depending on current research evidence of their safety and efficacy. Group A is comprised of fluoroquinolones, namely levofloxacin, moxifloxacin and gatifloxacin; group B has amikacin, capreomycin, kanamycin, (streptomycin); and group C constitutes of ethionamide (or prothionamide), cycloserine (or terizidone), linezolid, clofazimine. In new classification, p-aminosalicylic acid, imipenem-cilastatin, meropenem, amoxicillin-clavulanate, thioacetazone are not part of the core MDR-TB regimen, rather they are grouped in D3 as 'add-on agent' [Table-1]. It is recommended that during the intensive phase of treatment, an RR-TB or MDR-TB patient should receive at least five effective TB antibiotics and the standard regimen should consist of pyrazinamide plus four core second-line medicines - one chosen from group A, another from group B, and at least two from group C. Because of an absolute contraindication or significant toxicity, if the agents cannot be chosen as above, to make it a regimen of total five effective drugs, antibiotics from group D (preferably D2, or if not possible, from D3) may be added. It is advised to administer high-dose isoniazid and/or ethambutol to strengthen the regimen further until susceptibility results are confirmed.[2]

Table 1: Medicines recommended for the treatment of rifampicin-resistant and multidrug-resistant TB[2]

A. Fluoroquinolones		Levofloxacin Moxifloxacin Gatifloxacin
B. Second-line injectable agents		Amikacin Capreomycin Kanamycin (Streptomycin)
C. Other core second-line agents		Ethionamide / Prothionamide Cycloserine / Terizidone Linezolid Clofazimine
Add-on agents (not part of the core MDR-TB regimen)	D1	Pyrazinamide Ethambutol High-dose isoniazid
	D2	Bedaquiline Delamanid
	D3	p-aminosalicylic acid Imipenem-cilastatin Meropenem Amoxicillin-clavulanate (Thioacetazone

Since there is no randomized control trial determining optimal treatment regimen for MDR-TB meningitis; the design, dose and the duration of therapy are extrapolated from the studies available for MDR-pulmonary TB. So, individual drug susceptibility result is the best guide to treating an RR/MDR TBM patient successfully. The major concern is that, due to variable penetration of blood-brain-barrier, most of them fail to reach CSF in the desired therapeutic concentration. Again, lower efficacy and higher toxicity often preclude their successful use in TBM. Currently, available data suggests that the fluoroquinolones, ethionamide (or prothionamide), cycloserine (or terizidone) and linezolid have good CNS penetration, as do Pyrazinamide and high dose isoniazid.[15-18] Kanamycin, amikacin, and streptomycin reach CSF only in presence of meningeal inflammation. Two promising new anti-TB drugs of D2 group (bedaquiline and delamanid) are on phase- III clinical trials, but their capacity to penetrate the BBB has yet to be explored extensively.

An MDR-TB meningitis patient should receive 8 months of therapy in the intensive phase and total 20 months of treatment is recommended for a new case, but the duration must be individualized and may be lengthened according to the clinical response. Now-a-days, intra-thecal delivery of antibiotics is being tried in some centres with a higher cure rate but it is not still widely used and has its own demerits.[19] Several novel anti-TB antibiotics are being tested as an effort to expand treatment options for MDR-TB; sudoterb (a pyrrole derivative), PA-824 (a nitroimidazo-oxazine), and SQ109 (an analogue of EMB) are currently in phase II trials.[20,21]

Most of the neurologic complications of TBM are thought to be due to an exaggerated inflammatory response of the host to bacteria, resulting in tissue injury and raised intracranial pressure (ICP). So, concomitant use of steroids for 1-2 months has been shown improved clinical outcome.[22] In patients with hydrocephalus, surgical interventions such as ventriculo-peritoneal shunt and endoscopic third ventriculostomy may be needed to relieve elevated ICP.[23,24]

According to several case series, in-hospital case-fatality of drug-resistant TBM is about 57- 79%, with significant functional impairment in up to 50% of survivors.[25,26] The neurological sequelae includes cranial nerve palsies, seizures, ataxia, spastic hemiparesis, blindness, deafness, ophthalmoplegia and mental retardation and psychiatric disorders.[14,26] Poor prognostic factors are severe neurologic involvement at presentation, extreme of age, co-morbidities, late diagnosis, and rapid progression of the disease.

Conclusion:

Even in this 21st century, drug-resistant tubercular meningitis is a challenging disease to diagnose and treat successfully. But, early diagnosis and prompt initiation of appropriate treatment are crucial to reducing the high

mortality and morbidity associated with this disease. So, newer diagnostic techniques with improved performance are desperately needed for rapid and accurate identification of drug- resistant cases, especially in resource poor, high endemic countries. The development of well-tolerated and cost-effective antibiotics with adequate CSF penetration remains a continued need. Additionally, to optimize treatment regimen for MDR-TBM, conduction of randomized controlled trials are important to find the best possible combination of available second-line drugs. And last but not the least, it is our responsibility to come forward, create awareness and do necessitate for preventing the emergence of drug-resistant tuberculosis in the country.

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Case Report

Placenta Percreta: A Nightmare for Obstetrician

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Abstract

Morbidly adherent placenta is a life threatening complication of pregnancy. A woman of 32 weeks pregnancy, aged 24 years, 2nd gravida, with previous history of caesarian section, was admitted in Enam Medical College Hospital with antepartum hemorrhage. Ultrasonography revealed it as a case of Placenta Percreta. After receiving conservative treatment, she gradually improved. However, after 36 hours of admission the patient became unstable due to severe per vaginal bleeding. So, emergency caesarean section was done with transfusion of 2 units of blood. After opening the abdomen, engorged vessels were all over the uterus penetrating the visceral peritoneum thus the base of the bladder wall. There was no such vessel-free part of the wall where incision could be given safely. Moreover there was also adhesion between the bladder wall and lower segment of uterus. After ligating some vessels an incision was given in uterine wall and a 1.2 kg asphyxiated baby was delivered with difficulties. Placenta could not be removed as it was tightly adhered to all over its attachment as morbid adhesion. There was huge hemorrhage from the cut edges because of large sinuses. So, caesarean hysterectomy was done only to save the life of the mother. During the hysterectomy bladder could not be separated from the uterus as it was invaded by the uterine vessels. As a result, repairing of the bladder injury was done by urologist. Unfortunately, patient developed severe shock, even after transfusion of six units of blood per operatively. She was transferred to Intensive Care Unit for further monitoring and critical care management. Gradually her condition improved and shifted from HDU to general ward. On ninth post-operative day she was discharged from hospital with good health status.

Conclusion: Key to successful management of such case is antenatal diagnosis by expert radiologist and anticipation of hemorrhage. Planned management by multidisciplinary team of experienced obstetrician, urologist and anesthesiologist yields better outcome for these patients. Antenatal diagnosis of morbidly adherent placenta is very important to prevent such kind of maternal morbidity.

Keywords: Morbid Adherent Placenta (MAP), Caesarean Hysterectomy.

Introduction:

Morbidly adherent placenta is (MAP) a life threatening complication of pregnancy. According to the American College of Obstetrics and Gynecology its incidence is 1:2500 per delivery.[1] Morbidly adherent placenta in association with placenta praevia and previous caesarean section delivery has a high statistical significance as the rate of caesarian section is increasing day by day globally.[2] Recent reports suggest frequency per normal delivery between 1:2500 and 1:110.[3] It has risen to 10 fold in the past 50 years.[4] During pregnancy MAP may be either asymptomatic or may present with antepartum hemorrhage, abdominal pain and acute abdomen, while intra-partum it may present as retained placenta, postpartum hemorrhage (PPH) or uterine rupture.

MAP remains the greatest challenge in modern obstetrics.[5] It is defined as the abnormal adherence either in whole or in part of the placenta to the underlying uterine wall. It is classified into 3 types according to the degree of adherence as, a) Placenta Accreta - chorionic villi adherent to superficial myometrium, b) Placenta Increta - chorionic villi involving myometrium and c) Placenta Percreta - chorionic villi penetrating full thickness myometrium and involving serosa.[6] By the amount of placental involvement 3 types of MAP are namely- a) Focal Adherence - when part of the cotyledon is involved, b) Partial Adherence - when more than one cotyledon is involved and c)Total Adherence - when whole placenta is involved, are described.

The maternal risk appears to occur at the time of placental separation resulting in severe hemorrhage, disseminated intravascular coagulation (DIC), requirement of massive blood transfusion, need for intensive care, hysterectomy and occasionally maternal death.[7] It is essential that MAP should be diagnosed earlier and adequate preoperative measures should be taken to reduce its high morbidity and mortality. With the advent of radiological facilities of Doppler Ultrasound and MRI, antenatal diagnosis has brought revolution in the management of these cases. The colour Doppler Ultrasound criteria used for the diagnosis of MAP includes:[8]

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- Thinning of anterior lower uterine segment of less than 1mm.
- Lacunae vascular spaces (Swiss cheese appearance) and inter-parenchymal placental lacunar flow.
- Extension of placental tissue beyond uterine serosa and bladder uterine serosa
- Hypervascularity.
- Prominence of subplacental venous complexes.

Successful management of MAP includes antenatal diagnosis and pre-operative preparation by a multidisciplinary team. Advances in antenatal diagnosis have led to significant improvement in maternal outcome with MAP.[9] Early diagnosis is important as morbid adherent of placenta is associated with life threatening condition like uterine rupture, massive hemorrhage and need for hysterectomy with subsequent loss of fertility. Here a case of 32 weeks pregnancy with placenta percreta is presented where a timely & multidisciplinary team approach could manage the life of the mother.

Case Presentation:

A young lady, aged 24 years, mother of one child with history of caesarean section presented at her 32 weeks pregnancy with severe per vaginal bleeding for 3 days. She was diagnosed initially as a case of antepartum hemorrhage and managed conservatively. She was given complete bed rest and some antispasmodic and oral tocolytics. Gradually her bleeding stopped. However after 36 hours of admission, she developed abdominal pain and bleeding which was huge in amount. So, emergency caesarean section was done with two units of fresh blood transfusion at 1.00 am of night. After opening the abdominal cavity there was huge engorged vessels all over the uterus which also penetrated the visceral peritoneum thus the base of the bladder wall. There was no such vessel free part of the wall where incision can be given safely. Moreover as she had previous history of caesarean section there was also adhesion between the bladder wall and lower segment of uterus (Fig-1). After ligating some vessels an incision was given in the lower part of upper segment of uterus and a 1.2 kg asphyxiated baby was delivered with difficulties. Placenta could not be removed as it was tightly adhered to all over its attachment as morbid adhesion. There was huge hemorrhage from the cut edges because of large sinuses. So after proper examination immediate decision for hysterectomy was taken only to save the life of the mother. Anesthesiologist switched to general anesthesia from regional as patient developed severe hypotension with respiratory distress while operating. Junior doctors were trying to arrange more blood from donors. During the hysterectomy, bladder could not be separated from the uterus as it was invaded by the uterine vessels. So, expert urologist did repairing of bladder injury as it was adhered to the placenta and become open while trying to separating the placenta. After the procedure, a careful toileting and checking was done for any iatrogenic injury to bladder, ureters or gut. Abdomen was closed in layers after proper haemostasis and a drain tube was kept in situ. Unfortunately, later on, patient developed severe shock even after getting six units of blood transfusion. She developed tachycardia, hypotension and skin became cold and calm. So, she was transferred to ICU for further support. In ICU, she was given two vasoactive infusion (Noradrenalin and Dopamine) and high flow supplementary oxygen (8litre/min). However, her respiratory rate was going up and she developed breathlessness. So, she was kept into artificial ventilation. Her ECHO shows severe antero-lateral ischaemia with Ejection Fraction only 45% and bilateral congested lung field. Blood picture showed haemo-concentration and leucocytosis with increased level of FDP (Fibrin Degradation Products). Gradually after three days, patient became stable, ventilation was with drawled and started to taper all the vasoactive drugs. On fourth postoperative day she was transferred into HDU (High Dependency Unit) and kept under close monitoring and shifted to general ward in next day. She was discharged on her ninth postoperative day in a good health status.

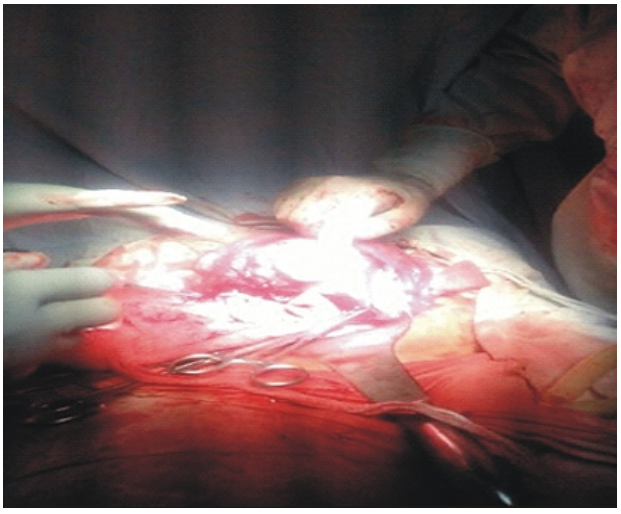

Fig 1: Per-operative findings of morbid adhesion of placenta

Discussion:

The epidemic of placental invasion is escalating due to rising rate of caesarean sections. It has raised to 10 fold in past 50 years.[10] Clark et al observed an increased incidence of placenta praevia after caesarean section from 0.26% in women with a normal uterus to 0.65% after one and up to 10% after 4 or more caesarean sections.[11] Some studies reported that risk of placenta accreta increased to 39% for those who had previous 2 caesarean sections.[12] About 75% cases of morbidly adherent placenta are associated with placenta praevia. In the presence of the risk factors, previous caesarean section and placenta praevia, obstetricians must have a high index of suspicion for placenta accrete.[13]

Morbidly adherent placenta is associated with significant maternal morbidity, including massive hemorrhage, DIC, hysterectomy, bladder and ureteric trauma, ARDS and acute tubular necrosis.[14] Recognition of the high morbidity and mortality associated with morbidly adherent placenta and a multidisciplinary approach is recommended. Interventional radiologist, anaesthetist, haematologist, neonatologist and an experienced obstetrician play crucial role.[15] Particular considerations should be given to the anticipation and management of massive hemorrhage, including availability of pack cells, platelets, fresh frozen plasma, and cryoprecipitate. All efforts should be made to control hemorrhage after delivery. Internal iliac artery, uterine artery ligation are performed in some cases to control hemorrhage. Strategies include leaving the placenta in situ after delivery with surgical uterine devascularisation, embolisation of the uterine vessels, uterine compression sutures and/or over sewing of the placental vascular bed.[16] A conservative approach was first described by Arulkumarran and colleagues in 1986 by using systemic methotrexate.[17] Severe intrauterine infection and life threatening hemorrhage can occur which may require emergency hysterectomy; thus such patients should be carefully monitored and extensively counseled regarding risks.[18] Methotrexate has an important role in conservative management of placenta percreta with bladder invasion and it has been used in many patients.[19]

Conclusion:

Antenatal diagnosis of morbidly adherent placenta is very important even in early weeks of gestation to prevent such kind of maternal morbidity from pregnancy and delivery. A national guideline should be developed regarding organization of obstetric care and timing of ultrasound, Doppler examination and management interventions in such cases.

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Case Report

Heterotopic Pregnancy: A Case Report

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Abstract

Heterotopic pregnancy is a rare complication of pregnancy and its every bit can be as dangerous as an ectopic pregnancy. A high index of suspicion can help in timely diagnosis and appropriate intervention. Here we reported a case of heterotopic pregnancy in a 27-years aged woman presented with haemo-peritoneum from ruptured tubal pregnancy with live intrauterine gestation at 6 weeks of amenorrhea, diagnosed on ultrasound examination. Emergency open laparotomy followed by right salpingectomy was performed. Postoperative trans-vaginal ultrasonogram showed a persistent viable IUP (Intrauterine pregnancy) which was allowed to continue. Pregnancy was uneventful and patient delivered a healthy baby at term.

Keywords: Assisted reproduction, Ovulation induction, Heterotopic pregnancy, Salpingectomy.

Introduction:

A heterotopic pregnancy (HP) is multiple gestation in which there is a nonviable extrauterine (ectopic) and a potentially viable intrauterine pregnancy occur simultaneously.[1,2,3] The incidence of heterotopic pregnancy is very low.[4] In natural conceptions, the incidence of HP has been estimated to be 1 in 10000 to 1 in 30000 pregnancies.[1,2] The incidence of HP appears to be higher in women who have been treated for infertility with some form of artificial reproductive technology (ART), 3 with an estimated incidence at between 1 and 3 in 100 pregnancies[3] and as high as 1 in 900 with ovulation induction.[4]

We present a rare case of heterotopic pregnancy with live intrauterine gestation and ruptured adnexal gestation in an ovulation induced conception.

Case Presentation:

A 27 years old lady, gravida 3, para 2 (both baby born at term by LUCS but died within 24hrs of birth due to congenital heart disease) presented to the infertility OPD at about 6 weeks of gestation with abdominal pain. She described the pain as sporadic, mostly on the right side, exacerbated by movement and resolving with rest. Vital parameters and abdominal findings were normal, same-day Ultra sonogram showed a single intrauterine gestational sac but no visualized embryo, the adnexa were unremarkable. Patient was admitted for observation.

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Her 1st conception was with ovulation induced drug about 8 years after of her marriage, 2nd conception was also with ovulation induction. This time she also conceived after taking Letrozol for 2 cycles.

She had no H/O rheumatic/congenital heart disease. Her Echo-cardiography was normal. After admission pain subsided with conservative treatment. After 2 days, she awoke at midnight with nausea and severe abdominal pain. She denied fever, chills and dysuria. On examination, she was in distress and appeared moderately ill. Body temperature was 97^0 F, BP-120/70 mm of Hg, abdominal palpation elicited right lower quadrant tenderness, ultrasonographic imaging revealed a viable intrauterine pregnancy (IUP) and intra abdominal collection of blood including pouch of Doglus. Impression was ruptured ectopic pregnancy along with viable IUP.

With all asepsis patient underwent emergent open laparotomy under spinal anaesthesia. This revealed a rupture in the middle third of the right fallopian tube, the entire tube was oedematous. A right salpingectomy was performed. Patient remained stable after surgery.

Postoperative obstetrical Ultrasonogram showed a persistent viable IUP. The intrauterine alive gestation was allowed to continue. Pregnancy was given progesterone support up to 20 weeks of pregnancy. There after patient was under regular antenatal checkup and delivered at healthy baby at term.

Discussion:

A woman who is experiencing a heterotopic pregnancy may or may not have symptoms. What's scary is that about 50% of HP are diagnosed only when the fallopian tube ruptures, at which point emergency surgery is needed.[1]

If symptoms are present prior to a ruptured fallopian tube, the symptoms are the same as those of ectopic pregnancy.[1] In review of 66 cases of HP abdominal pain alone was found to be the most common presenting symptom of HP.[5] Vaginal bleeding was present in 21 cases.

It is very difficult to diagnose HP early. Several experts have recommended that all high-risk women who continue to have ectopic pregnancy (EP) symptoms despite a confined pregnancy in the uterus should be screened for heterotopic pregnacy.[1]

Ultrasonagraphic findings: Given the overlap in clinical presentation imaging is critical for diagnosis. However, clear and simultaneous visualization of both intrauterine and extrauterine pregnancies are not always possible, especially early in gestation. In patients treated with ART, ovarian hyperstimulation syndrome is a frequent occurrence that can mask the presence of an EP.[6]

However, in a review of 80 Patients with HP, Ultrasonographic findings were definitively diagnostic in only 25% of patients; Laparoscopy or Laparotomy was diagnostic in the remaining 75% of patients.[6]

The reported gestational age at diagnosis of HP ranges from 5 to 20 weeks, with a mean of 8 ±3 weeks[6]

HP may have similar signs and symptoms as a normal intrauterine pregnancy, a normal intrauterine pregnancy and a ruptured ovarian cyst, a corpus luteum or any surgical condition of acute abdomen.

Bicornuate uterus gestation in both cavities may also simulate a HP.[4]

Blood tests and USG can be used to differentiate these conditions.[7]

Majority of the reported heterotopic pregnancies are of singleton intrauterine pregnancies. Triplet and quadriplet heterotopic pregnancies have also been reported, though extremely rare.[8,9] It can be multiple as well.[10]

In a general population, the major risk factors for HP are the same as those for ectopic pregnancy. For women in an assisted reproductive program, there are additional factors.[7]

Similar to EP, most cases of HP occur in the fallopian tube, other commonly affected sites include the cervix and a cesarean delivery scar.[6] HP occurring in the tube stump and cornual region has also been reported.[3]

EP remains the leading cause of maternal death in the 1st trimester [2] & accounts for 10% to 15% of all maternal death.[10] However the risk of later presentation and life threatening hemorrhage and hemorrhagic shock is high in HP because of its diagnostic challenge.[3]

HP usually need treatment upon detection and carries the same risks that any other ectopic pregnancy would carry. It is usually possible to treat HP without terminating the IUP. This typically means surgical treatment.

Laparoscopy is preferred over laparotomy for the treatment of HP because of its favourable profile for less bleeding, pain, hospitalization, recovery time less and cost.[2] For an extrauterine gestation in a tubal location, salpingectomy is indicated over salpingostomy.[2] The later may result in incomplete removal and persistent EP, which would be impossible to identity with serial HCG levels given the existing lUP.

Some studies have found that HP also carry an increased risk of miscarriage of lUP (especially if the HP was diagnosed after rupture) but about 67% of women are able to carry the intrauterine baby to term following treatment, so chances are good that the remainder of the pregnancy will be fine.[11]

Conclusion:

Although the likelihood of a coexisting extrauterine gestation is extremely small after ultrasonographic confirmation of a lUP, this case highlights the need for a high index of suspicion for HP in patients, who present with signs and symptoms potentially consistent with an ectopic pregnancy. A timely interval can result in a successful outcome of the intrauterine fetus.

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College News

College Events:

- The commencement ceremony 1st year of MBBS students, BM-31, Session: 2016-2017 was held on 11th January 2017 in the campus of Bangladesh Medical College.
- Annual Sports and Cultural competition 2016 of BMC and BDC was held from 22.10.2016 to 27.10.2016 at College Campus.
- The Victory Day 16th December 2016 was celebrated at Bangladesh Medical College and Hospital premises.

Seminar in BMC:

- A Seminar on "Type II Diabetes and its Management" was held on 19th January, 2017 in BMC. The Speaker was Dr. Yasmin Aktar, MD (EM), Consultant Endocrinologist of BMCH.
- A Seminar on "Current Strategy for TB Control Programme in Private Sector in Bangladesh and Advanced TB Investigations at Low Cost" was held on 20th October, 2016. The Speakers were the experts and researchers from icddr,b.

Participation in the International Conferences/Seminars/Workshop/ Congress/Meetings:

- Dr. Akhil Chandra Biswas, Associate Professor, Dept. of ENT, Bangladesh Medical College attended the 18th Annual Conference of Skull Base Surgery Society of India held from 8-11 September, 2016 in India.
- Dr. Syed Khalid Hasan, Associate Professor, Dept. of Surgery, Bangladesh Medical College attended the International Society of University Colon and Colorectal surgeons held in Mumbai, India from 23-25 September, 2016.
- Prof. Dr. M. Touhidul Haque, Professor and Head of the Dept. of Cardiology, Bangladesh Medical College attended the International Training Program held from 26th September to 1st October, 2016 in Verona, Italy.
- Dr. Md. Tarek Alam, Associate Professor, Dept. of Medicine, Bangladesh Medical College attended the 21st Congress of Asian Pacific Society of Respirology held in Bangkok, Thailand from 12-15 November, 2016.
- Prof. Zafor Md. Masud, Professor and Head of the Dept. of Oncology, Bangladesh Medical College attended Inter-Disciplinary Workshop to Enhance Assessment and Management of Lung Cancer (IDEAL) in Singapore from 9-11 November, 2016.

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