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ORIGINAL ARTICLES

Therapeutic Response Patterns of High and Repetitive Doses of Salbutamol in Patients with Severe Acute Asthma

Adnan Yusuf Choudhury[1], Saifuddin Choudhury[1], Md. Abdur Rouf[2], Rajashish Chakarborty[3], Shamim Ahmed[3], AKM Mostafa Hossain[4], Asif Mujtaba Mahmud[4], Md. Ali Hossain[5], Mirza Mohammed Hiron[5], Md. Mostafizur Rahman[6].

Abstract

Severe acute asthma continues to be a major cause of hospital admission for patients suffering with bronchial asthma Nebulized (alternatively through MDI with spacer device) B2-adrenergic agonists are still the first line drugs for a rapid bronchodilation and an easily administered drug during acute asthma attack.

Purpose of this study was to assess therapeutic response patterns of severe acute asthma patients to high and repetitive doses of salbutamol.

A total number of 79 patients were taken initially for the study. Out of them, 4 patients could not complete the procedure due to intolerable side effects (i.e. palpitations) and 5 patients were excluded early in the treatment course due to lack of remarkable improvement on earlier follow ups as evidenced by not improving or deteriorating SaO2 and PEER. 8 patients complained of tremor during the procedure but were not severe enough for withdrawal from the protocol. Data of 70 patients were available for final analysis.

The patients were treated with 4 puffs of salbutamol (100μg in each puff) delivered by metered dose inhaler through a spacer device at 10 minutes interval for 2 hours (total 48 puffs in 12 times). 53 patients (75.7%) achieved the discharge threshold at the end of 2 hours of treatment. 17 patients (24.3%) failed to reach the discharge threshold. Out of them, 12 ultimately got admitted into hospital. 5 of them improved in ED after another hour of intensive therapy with all conventional medication.

Analysis of variables reveals statistically significant decrease in respiratory rate, use of accessory muscles, wheezing and dyspnoea. Heart rate increased significantly but there were very little change in systolic and diastolic blood pressures.

Arterial oxygen saturation (SaO_2) increased significantly but the most significant improvement was noted in peak expiatory flow rate (PEER) both in litre/min and percent predicted.

Ultimately the study substantiates that high and repetitive doses of salbutamol (the dose of which in this study was 400μg every 10 minutes interval for a period of 2 hours) delivered by metered dose inhaler through a spacer device is an effective, well tolerated, user friendly emergency therapeutic procedure for patients with severe acute asthma.

[Chest & Heart Journal 2004; 28(2) : 37-45]

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Introduction

Asthma is an important disorder of the airways with significant mortality and morbidity. Globally it affects about 100 million people. According to the first national asthma prevalence study (NAPS) in Bangladesh in 1999, about 7 million people (5.2% of the population) are suffering from current asthma, i.e. atleast three episodes of asthma attack in last 12 months, more than 90% of whom do not take modern treatment. Unfortunately more than half of these patients are innocent children, i.e. 7.4% of the total paediatric population (1-15 years of age). The disease causes physical, emotional and financial suffering for patients leading to a deleterious effect on overall socio economic structure of the country.

Patients suffering from asthma presents with variety of symptoms ranging from chronic respiratory difficulty to episodes of acute exacerbation.

Severe acute asthma is one of the common causes of hospital admission, which is a major financial and social problem for asthma patients.

There are certain standardized treatment plan for management of severe acute asthma but most of them are feasible in well equipped hospital environment. But plenty of work to be done for formulating a management plan feasible for patient locating outside the hospital facilities eg. in a very remote rural areas or during patient transport to hospitals where a good length of time is required usually.

Inhaled ß-adrenergic agonists as salbutamol is the conventional treatment for acute asthma.

The dose of ß-agonists is emperic at best and it should be based on response and side effects.[7] There is evidence that patients with acute asthma respond to increasing doses of ß-agonists[8,9,19].

Cumulative or repetitive dose technique produces greater bronchodilation then an equivalent single dose of aerosolized bronchodilator.[1]

Metered dose inhaler plus holding chamber is equivalent in effectiveness to nebulizer in emergency department treatment of severe acute asthma and decrease amount of dose needed for MDI group (1/6th of nebulizer group).[3]

Intensive sympathomimetic stimulation even in combination with methylxanthene remarkably well tolerated by cardiovascular system of severe acute asthma patients. [4]

Australian National Asthma Council recommendation for aborting an acute asthma attack or to treat patient until rescue ambulance appears is to give 4 puffs of reliever medication every 4 minutes .[5] British Thoracic Society recommendation in this regard is at least 20-50 puffs of salbutamol inhaler 5 at a time may be required for maximum bronchodilation in patients with acute asthma.[3]

If a single drug like salbutamol delivered through MDI with spacer devices in high & repetitive doses can control severe acute asthma effectively atleast in a good proportion of patients and if patient tolerability of this treatment protocol remains satisfactory then it can be included in the asthma management guideline for its use in domestic situation, in rural areas; in any outdoor setting or during patient transport from rural areas which can ultimately reduce hospital admission and benefits all socio-economic groups of patients.

Materials & Methods

This prospective sequential study was carried out in Asthma Outpatient Department, Asthma Centre, National Institute of Diseases of the Chest & Hospital (NIDCH), Mohakhali, Dhaka during the period of July 2002 to June 2004.

A total numbers of 79 consecutive patients who were previously diagnosed and registered as suffering from Bronchial asthma in the Asthma Centre, NIDCH, Dhaka and who came with the sign symptom of severe acute asthma, met the selection criteria and gave written consent were taken initially for the study. Out of these 79 patients, 4 patients could not complete the procedure due to intolerable side effects (eg. Palpitations) and 5 patients were excluded early in the treatment course due to lack of remarkable improvement on earlier follow ups as evidenced by not improving or deteriorating arterial oxygen saturation and PEER. 8 patients complained of tremor but were not severe enough for withdrawal from the protocol. Data of 70 patients (n=70) were available for final analysis.

To be included in this study following criteria were considered essential:

- Patient previously diagnosed and registered as suffering from Bronchial asthma in Asthma Centre, NIDCH, Dhaka and who came with the sign symptoms of severe acute asthma.
- Age - 18 to 50 years
- PEER - <50% but >30% of the predicted value.
- No H/o smoking, chronic cough, cardiac, hepatic, renal or other medical diseases or patient having pregnancy.

Exclusion criteria for this study were:

- Patient <18 years or >50 years of age
- Patient with history of smoking, chronic cough, cardiac, hepatic, renal or other medical diseases or patient having pregnancy.
- Chest X-ray with pleural effusion, pneumonia.

The patients were treated with 4 puffs of salbutamol (100μg in each puff) delivered by metered dose inhaler through a spacer device at 10 minutes interval for 2 hours (total 48 puffs in 12 times).

As $ß_2$-agonist as salbutamol is the main tool for treatment of severe acute asthma and as it is an acute life threatening emergency situation, no group of patient could be given placebo or any treatment plan, which was devoid of any bronchodilator drug. So, creation of usual control group was not possible here and hence the patients pretreatment variables were taken as control and compared with the post treatment variables to find out any statistically significant changes and post treatment variables at 30, 60, 90 and 120 minutes were compared to each other for the same purpose.

The following study procedure was followed for each patient:

As the patient presented to the emergency department of asthma centre with acute respiratory distress they were clinically assessed with brief history of attack, duration, medication used, etc.

Physical examination of the patients were done with record of vital signs of acute attack as well as chest findings.

The exclusion criteria was carefully ruled out.

Objective measurement of airway obstruction were recorded with the peak flow meter.

Treatment of the study group : The patients were treated with salbutamol metered dose inhaler attached to a volumetric plastic spacer pretreated with detergent. Each puff delivered 100 μg of salbutamol from the canister.

After the inhalation, the patients were asked to hold breath as far as possible to a maximum of upto count 10 and then exhale out into the spacer again. The lips closed around the mouthpiece during the total procedure. The procedure was repeated two times for each puff and a total of 4 puffs were pressed into the spacer in every 10 minutes until the end of the protocol at 120 minutes.

During the first two inhalation the procedure were carried out by the principal investigator. Subsequently the attendant of the patient were instructed to perform the procedure under direct supervision of the investigator. On abatement of the severe distress (PEFR>55%) the patient himself/herself were instructed to try to perform the procedure.

The whole procedure was supervised and if the patient coughs the procedure was interrupted and started again.

Arterial oxygen saturation (SaO_2) was measured with an pulse oxymeter attached to patients fingertip and the reading was taken at the beginning of protocol treatment and at 30, 60, 90 and 120 minutes.

Pulse oximetry was performed with the patient breathing room air and oxygen was given as required.

The following discharge or admission criteria were followed for each patient included in the study.

a) Discharge criteria: During or at the end of the protocol patient will be considered ready to be sent home if they became -

- asymptotic
- free of accessory muscle use
- PEER >70% of the predicted value

b) Admission criteria: Patient with a poor response after 2 hours of treatment -

- persistent wheezing or dysponce
- accessory muscle use
- PEER <55%

were admitted to hospital.

After 2 hours of intensive bronchodilator therapy the patients whose PEER was <70%, but >55% were given another hour of intensive bronchodilator therapy through nebulization along with systemic corticosteroid and oxygen inhalation.

If any patient continued to deteriorate following salbutamol therapy as evidenced by not improving or deteriorating SaO_2 & PEER then they were put immediately on conventional therapeutic procedure and considered for admission.

Data collection and processing: all data were collected in specific proforam and statistical analysis done.

Unpaired t-test was applied to determine any statistical significance in sex distribution and age. Chi square test was applied to determine any statistically significant difference in medication use among the two sexes studied.

The mean distribution of respiration, heart rate, systolic and diastolic blood pressure, arterial oxygen saturation (SaO2), PEER in L/min, PEER in percent predicted, accessory muscles use, presence of wheezing, presence of dyspnoca before and after treatment at 0, 30, 60, 90 and 120 minutes were measured and paired t-test was applied to find out any statistical significance of their differences.

To eliminate the bias of gender, age and height the values of observed PEER were expressed as percentage of normal PEER value. Published normogram for men and women were used to calculate the normal values for PEER (National asthma guidelines, 2001).

Results

Table I

Age and sex distribution of the study population

Age in years	Sex		Total	p value
	Male	Female		
<25	9(39.1)	13(27.7)	22(31.4)	
25-34	9(39.1)	25(53.2)	34(48.6)	0.817(NS)
35-44	3(13.0)	6(12.8)	9(12.9)	
≥45	2(8.7)	3(6.4)	5(7.1)	
Total	23(32.9)	47(67.1)	70(100.0)	
Mean ± SD	27.9±8.1	28.3±7.3	28.2±7.6	
(Range)	(19-50)	(18-46)	(18-50)	

Figure in parenthesis indicate percentage
p>0.05 in unpaired 't' test
NS = not significant

Table II

Medication used before salbutamol treatment

Medication	Sex		Total	p value
	Male (n=23)	Female (n=47)	(N=70)	
ß agonise used in past 24 hours.				
Yes	22(95.7)	46(97.9)	68(97.1)	1.000
No	1(4.3)	1(2.1)	2(2.9)	
Theophylline used in 24 hours				
Yes	7(30.4)	19(40.4)	26(37.1)	0.416
No	16(69.6)	28(59.6)	44(62.9)	
Steroid used in past 7 days				
Yes	9(39.1)	25(53.2)	34(48.6)	0.269
No	14(60.9)	22(46.8)	36(51.4)	

N.B.
Figure in parenthesis indicate percentage
p>0.05 in chi-square test

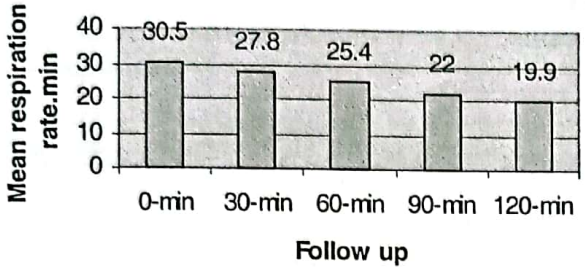

Fig.- 1: *Mean rate of respiration per minute following treatment with salbutamol*

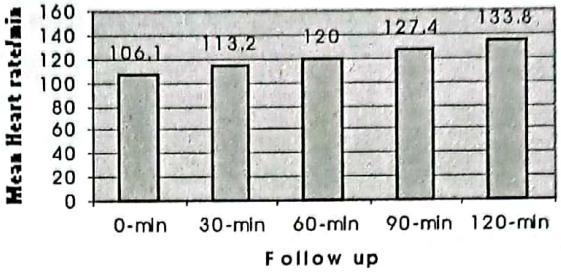

Fig.- 2: *Mean heart rate per minute following treatment with salbutamol*

Table III

Mean distribution of systolic blood pressure before and after treatment

Time of measurement	Systolic BP at specific time (min)	N	Mean±SD	Mean difference	p value
0 to 30 minute	0	70	116.5±20.7	0.21	0.495
	30	70	116.7±20.5		
30 to 60 minute	30	70	116.7±20.5	0.43	0.083
	60	70	116.3±20.6		
60 to 90 minute	60	70	116.3±20.6	0.21	0.321
	90	70	116.1±20.7		
90 to 120 minute	90	70	116.1±20.7	0.21	0.321
	120	70	116.3±20.9		

N.B: p>0.05 in paired 't' test

Table IV

Mean distribution of Diastolic blood pressure before and after treatment

Time of measurement	Diastolic BP at specific time (min)	N	Mean±SD	Mean difference	p value
0 to 30 minute	0	70	73.7±8.5	0.79	0.047*
	30	70	72.9±8,1		
30 to 60 minute	30	70	72.9±8.1	0.86	0.033*
	60	70	72.1±8.1		
60 to 90 minute	60	70	72.1±8.1	0.64	0.129^{NS}
	90	70	72.7±8.0		
90 to 120 minute	90	70	72.7±8.0	0.21	0.409^{NS}
	120	70	72.5±7.9		

N.B:
*p<0.05 in paired 't' test
NS= not significant

Table V

Mean distribution of Arterial Oxygen Saturation (SaO_2) before and after treatment

Time of measurement	SaO_2 at specific time (min)	N	Mean±SD	Mean difference	p value
0 to 30 minute	0	70	94.00±1.3	0.29	0.001***
	30	70	94.29±1.6		
30 to 60 minute	30	70	94.29±1.6	1.31	0.001***
	60	70	95.60±1.3		
60 to 90 minute	60	70	95.60±1.3	0.77	0.001 ***
	90	70	96.37±1.6		
90 to 120 minute	90	70	96.37±1.6	0.64	0.001***
	120	70	97.0±1.4		

N.B.: ***p<0.001 in paired 't' test

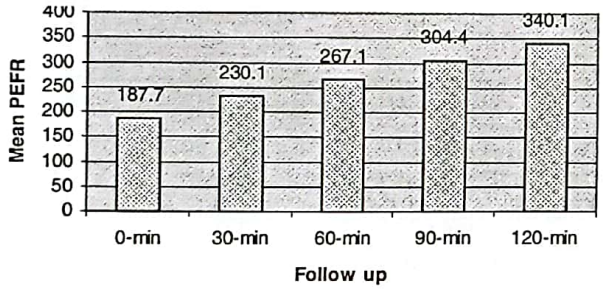

Fig. – 3: *Mean distribution of PEFR in litre per minute following treatment with salbutamol*

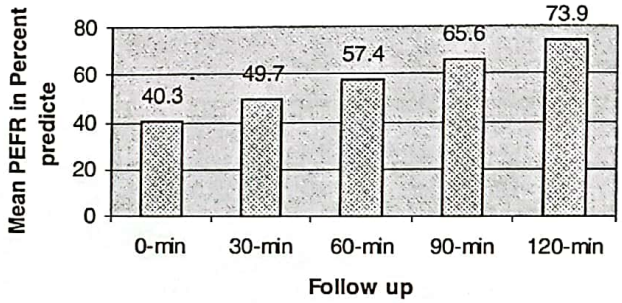

Fig. – 4: *Mean distribution of PEFR in percent predicted following treatment with salbutamol*

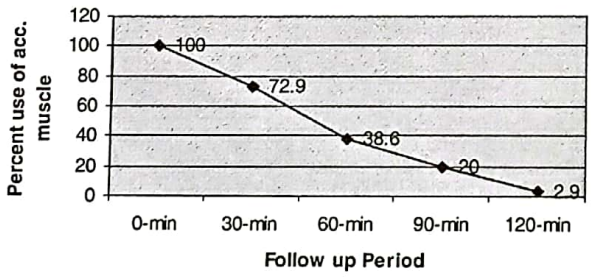

Fig- 5: *Percent use of accessory muscle during different period of follow up*

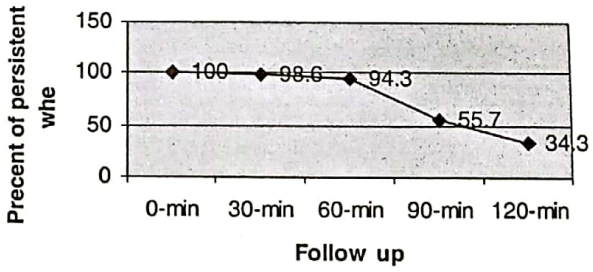

Fig. – 6: *Percent of persistence of wheezing at different time of follow up*

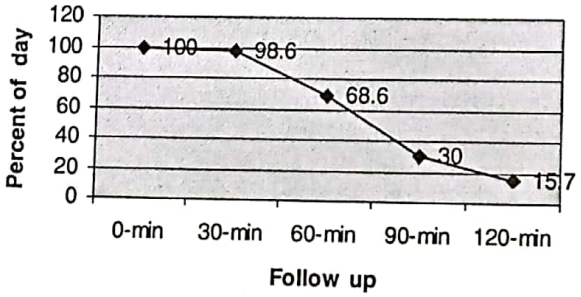

Fig. – 7: *Percent of persistence of dyspnoea at different time of follow up*

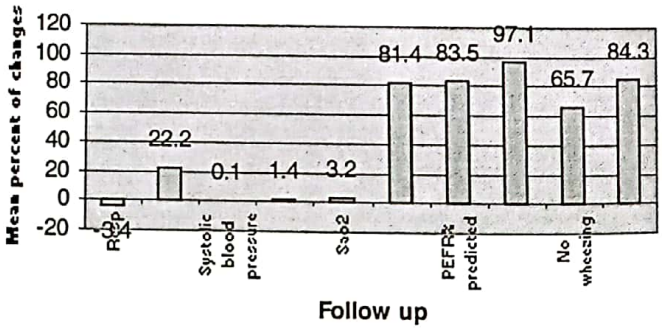

Fig. – 8: *Mean percent of changes of studied parameters following treatment with salbutamol*

Discussion

The mean age of patients were 28.2±7.6 years ranging from 18-50 years.

Among the studied patients 23 (32.9%) were male & the rest 47 (67.1%) were female. Male female ratio was approximately 33:67. The number of females were more because a good number of male patients were excluded due to presence of smoking history. There was no statistically significant mean age difference exists between male and female patients although the mean age was higher among females (28.3±7.3 years) compared to male patients (27.9±8.1 years).

Regarding use of medications prior to ß-agonist therapy it shows that 97.1 % and 37.1 % patient used $ß_2$-agonist and theophylline within 24 hours preceding the therapy and 48.6% used steroid with 7 days preceding the protocol therapy. It shows that most of the patient used B_2 agonist in my study contrary to only 68.9% in study done by Rodrigo et al. (1998).[6] The reason for this difference may be following - all the study population of this study was previously diagnosed and registered as suffering from Bronchial asthma in Asthma Centre, NIDCH and hence they got a good education regarding asthma medication specially about the reliever drugs and they used it in the face of dyspnocis exacerbation though inadequately perhaps.

The baseline respiratory rate was 30.5±3.2 per minute and it was decreased to 19.9±2.9 per minute at the end of the protocol therapy. Analysis showed that in each follow up respiratory rate decreased significantly compared to previous one ($p<0.001$). The baseline respiratory rate in article of Rodrigo's[6] was 22.1±5.01 which was a bit lower then this study but the cause of it was not clear. They have not reported about serial correlation of respiratory rate after salbutamol therapy. A decrease of respiratory rate in subsequent follow up in this study probably reflects reduction of dyspnoca by adequate bronchodilatation.

Regarding heart rate, the baseline value in two studies were 106.1±8.7 per minute and 102.7±19.3 per minute respectively. It showed that mean values are similar in two studies although the range is wider in study done by Rodrigo's. Data showed that heart rate increased significantly following administration of salbutamol and at the end of 120 minutes of intense therapy mean heart rate reached to 133.8±7.6 per minute.

Fanta et al. (1982)[4] in their paper showed that intensive sympathomimetic stimulation even in combination with methylxanthene remarkably well tolerated by cardiovascular system, although small but significant mean increase in heart rate may occur. They emphasized with support of their findings that sympathomimetic agent do not have the same haemodynamic consequences as they do during treatment of mild chronic asthma or as found in normal subjects.

In this study though heart rate increased significantly but was well tolerated by most of the subjects although in a small number of patients (4 out of 79), protocol therapy could not be completed due to palpitation intolerable to the patients.

Regarding changes of blood pressure following protocol therapy, data showed that changes of systolic blood pressure was not significant and although in first 2 follow ups (in 30 & 60 minutes) diastolic blood pressure reduced significantly, in subsequent follow up the decreasing trend was not significant statistically.

The baseline arterial oxygen saturation SaO_2% was 94.0±1.3. Following administration of protocol therapy SaO_2 increased significantly in each follow up and at the end it reached to 97.0±1.4.

Rodrigo et al (1998) stated that the most important and significant changes following administration of repetitive doses of ß-agonise occurs in case of PEER. They found dose related increases in PEER was observed when data from all patients were analyzed. With each increment in salbutamol dose, PEER rose significantly over the baseline value ($p=0.0001$ for all comparisons). The baseline PEER was 160.8±48.3 L/min or 31.3±7.91 percent of predicted and at the end of 3 hours of protocol it reached 295.6±96.7 L/min or 58.1±12.6% of predicted. In their study inclusion criteria was open for all patients suffering from severe acute asthma but in this study the inclusion criteria was restricted to PEER value in a range of 30-50%. That indicates that this study population was less seriously affected then their study and that is why in this study baseline PEER was 187.7±37.2 L/min or 40.3±5.0 percent of predicted, which was higher

then their value and by the end of 2 hours of protocol therapy it reached 340.1±69.9 L/min or 73.7±9.8 percent of predicted.

The relatively lower response in study of Rodrigo's validates the fact that patient with more severe disease responds poorly to protocol therapy.

And this fact was also supported by Idris et al. (1993)[2]. In their paper, they observed that pretreatment FEV_1 was significantly inversely related to the number of treatment required. Thus, patient with the most severe asthma required a longer stay in ED and more treatment before becoming asymptotic.

Data also showed that at the beginning of protocol therapy all of the patient uses their accessory muscle to assist their respiratory effort, has dysponea and wheezing but at the end of 2 hours of protocol therapy accessory muscle used by only 2.9% of the patient, dysponea was complained by 15.7% of the patient and wheezing was found in only 34.3% of the patient.

Rossing et al. (1983)[14] in their paper showed that no significant differences exist in either the amount of bronchodilatation or the incidence adverse effects in those who had or had not taken sympathomimetics as outpatients before presenting to ED with severe acute attack.

These findings were supported by our findings of effect of previous medication history on outcome of ß-agonist therapy. Data showed that no significant differences observed in outcome parameter whether the patient had taken ß-agonist, Xanthene derivatives or steroid previously or not.

Ultimately the study substantiates that high and repetitive doses of salbutamol (the dose of which in this study was 400µg every 10 minutes interval for a period of 2 hours) delivered by metered dose inhaler through a spacer device is an effective, well tolerated emergency therapeutic procedure for patient with severe acute asthma.

The observation also shows that under supervision of the investigator patients attendant as well as the patient him/herself were able to carry out the procedure. This demonstrates that this procedure is convenient and user friendly. Furthermore this procedure dose not involve expensive apparatus like nebulizer which requires external source of energy (eg. electricity).

Conclusion

Repetitive doses of salbutamol delivered by MDI through spacer device is an effective modality for management of patient with severe acute asthma.

The procedure is effective at a dose of 400µg salbutamol (4 puffs of MDI) at 10 minutes interval for 2 hours (total 48 puffs in 12 times).

It is well tolerated by most of the patients as shown by absence of major side effects.

It is convenient and user-friendly procedure easily understood by patients and their attendants.

It is a cheap method which dose not involve technical equipment like nebulizer and is not dependant on external source of energy.

The procedure is easily applicable in domestic environment and low facility emergency or outpatient department particularly in rural settings. In addition, it can play a crucial role till arrival of rescue services like ambulance as well as during transport of the patient to hospital.

The outcome of the study is not influenced by the patients previous intake of medicine.

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Transcatheter Closure of Atrial Septal Defect with Amplatzer Septal Occluder : Early Clinical Experience in Children of Bangladesh

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Abstract

The Amplatzer Septal Occluder (ASO) is a self expanding, double disk linked together by a short connecting waist corresponding to the size of the Atrial Septal Defect (ASD). The device is delivered trans-catheter to the left atrium and than pulled back to right atrium and is released by unscrewing it from its delivery system. Twenty children with ASD secundum were selected for device closure with ASO from June 2001 to June 2003. Ten cases were taken into the cardiac catheterization laboratory and two were postponed after balloon sizing of the ASD. Eight cases had successful implantation of the ASO without any complications. Rest ten cases are in the waiting list for device closure. All 8 cases were discharged from hospital after 24 hours observation period. Tablet Aspirin 5mg per kg body weight once daily was advised for 6 months. Follow up was done at 1,3,6,9,12,18 and 24 months and yearly thereafter. First case is under follow up for last 3 years and last case is under follow up for last one year and no complications observed in this period.

[Chest & Heart Journal 2004; 28(2) : 46-49]

Introduction

Trans-catheter technique for closure of Secundum Atrial Septal Defect (ASD) have been in evolution since the original report by King and Mills in 1976.[1, 2] Intracardiac defects can be closed with septal occulder, umbrella or buttoned device. Recent procedural modifications have been introduced in an attempt to minimize the size of the delivery sheath and reduce complications that can arise from device embolization[3]. The Amplatzer Septal Occluder (ASO) for occlusion of ASD is the latest of these devices. The final decision to implant the device is largely based on the balloon sizing of the ASD during cardiac catheterization[4]. Only the subjective criteria of ASD size and the measurement of septal rims on echocardiography have been used before catheterization[4]. In this study 20 cases were selected from the non invasive cardiac laboratory (NIC lab) of Combined Military Hospital (CMH), Dhaka and 10 cases were taken into the catheterization laboratory according to the appointment given to them from the admission section of NIC lab. Two cases were postponed after balloon sizing and 8 cases had successful deployment of the device.

Materials and Methods

Selection of patient was started from June 2001. Twenty children were selected till June 2003 from pediatric cardiology out patient clinic and NIC lab of CMH Dhaka. Eight cases were performed so far and two were postponed after balloon sizing in the cath lab.

Inclusion criteria were:

(1) Body weight of more than 10 Kg.

(2) Centrally located ASD secundum with superior and inferior rim of more than 7 mm.

(3) Those who had indication for surgical closure also (evidence of Right ventricular volumes overload, QP:QS>2).

(4) Margin of ASD must be 5mm away from the coronary sinus, Tricuspid and Mitral valve (TV, MV) right upper pulmonary vein (RUPV) and superior Vena Cava (SVC).

Exclusion criteria were:

(1) Association with other congenital heart disease, which can not be treated by catheter intervention.

(2) Right or left ventricular decompensation.

Careful echocardiography was done in subcostal four chamber long axis (SC-LAX), subcostal short axis (SC-SAX) and apical four chamber (AP-4C) views. Color flow mapping of left to right shunting across the ASD was also performed. The GE-system-5 software was used to measure the

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dimensions. ASD size was measured in millimeters, from these same view the length of the atrial septum, size of the superior and inferior rim were measured. Finally ASD size was measured with sizing balloon in the cath lab and ASO size more than 2 mm than the balloon size were used for the patients. Patients were kept in observation in pediatric cardiology ward for 24 hours and were discharged with advice of first follow up after one month of the procedure. Next follow up were given at 3,6,9,12,18 and 24 months and yearly thereafter.

Procedure

Equipments required:

(1) Delivery sheath with touhy brost adaptor.
(2) Dilators.
(3) Delivery coil.
(4) Loading device.
(5) Sizing plate.

A routine diagnostic catheterization procedure was done first to see that ASD was suitable for closure. Transesophageal / trans-thoracic echo assessment of size of the defect and proximity of defect to RUPV, MV, TV, coronary sinus and superior venae cava (SVC) to defect repeated.

To size the ASD, ASD occlusion balloon was passed through the sheath across septum from right atrium to left atrium and inflated with dye to know the volume and was withdrawn across septum until it meets with some resistance. This volume was equal to the stretched diameter of ASD and size was determined via the metal template. The sheath size and the ASD occlusion device was chosen accordingly.

The sheath was than advanced through the guide wire to LA through ASD. The patient was heparinized with 50-100u/Kg heparin. The Amplatzer device was threaded through the loader and the occlusion device was screwed to the tip of the delivery cable using a clockwise rotation. The device and loader were than immersed in non heparinized saline and the device was pulled slowly back into the loader. The loading device was than introduced through tuohy brost adaptor into transeptal sheath with continuos flush. The device was than delivered into the sheath by pushing. Under fluoroscopy and echo guide left atrial disc was advanced to LA. Maintaining gentle pressure, the sheath was pulled back and right atrial disc was deployed. The device was detached from the delivery coil by anti-clockwise rotation. Cefuroxime 15mg/Kg IV was given on deployment and then at 8 hourly interval for 24 hours. Aspirin 5mg/Kg everyday was advised for six months.

Results

From June 2001 to June 2003, twenty children were selected for ASD device closure. First ten were taken into the catheterization laboratory after completing precatheterization evaluation and investigations. Two of them were postponed after balloon sizing as size was found too big and obstructing superior vena cava and right upper pulmonary vein. These two cases were referred to cardiac surgeon for surgical closure.

Table I showed age of the patient during diagnosis. Three cases were diagnosed in infancy, 4 cases between 1-5 years, two cases between 5-10 years and one case at the age of 11 years.

Table II showed symptoms on presentation of the already done cases. Six patients had history of recurrent respiratory tract infection (RTI), 8 had failure to thrive (FTT) and two were asymptomatic. These two patients reported to the pediatrician for other reason and a murmur was detected incidentally.

Table III showed patients data and procedure result. Patients age varied from 3 years to 11 and half years. Weight of the patients varied from 13-45 Kg. Lowest size of ASD was 11mm and highest size was 22mm. Lowest device size was 15mm and highest device size was 26mm. Complications not observed in any of the cases.

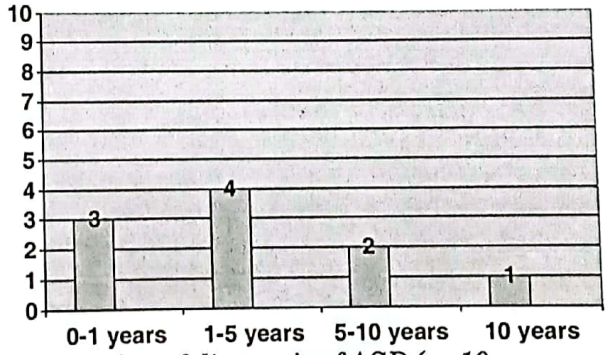

Fig.-1 : *Age of diagnosis of ASD (n=10*

Table I

Principal symptoms on presentation (n = 10)

Symptoms	No	Percentage
Recurrent RTI	6	60
Failure to thrive (FTT)	8	80
Asymptomatic	2	20

* Some patients had more than one mode of presentation.

Table III

Patient data and Procedure results

Case No	Age in Years	Weight in Kg	Date of procedure	SD size A in Echo (mm)	Superior rime in echo (mm)	Inferior rime in echo (mm)	Total length of atrial septum (mm)	Ballooning size of ASD in cath lab (mm)	Device size (mm)	Residual shunt	Emboli-ztion of device	Obstruction to RUPV, MV, TV
1	11.5	45	9.4.02	22	15	16	52	24	26	Nil	Nil	Nil
2	4	14	26.6.01	14	7.2	7.4	28.6	21	24	Nil	Nil	Nil
3	3	13	28.6.01	16	11	12	39	21	22	Nil	Nil	Nil
4	5	15	14.5.02	18	7	8	33	26	Postponed	-	-	-
5	7	18	2.7.02	20	8	10	38	29	Postponed	-	-	-
6	6	17	14.7.02	13	16	22	40	16	20	Nil	Nil	Nil
7	4	15	2.7.02	12	10	13	34	14	16	Nil	Nil	Nil
8	4..5	18	19.6.03	11	12	13	36	13	15	Nil	Nil	Nil
9	5.5	13	23.6.03	12	10	12	34	15	16	Nil	Nil	Nil
10	4	14	30.6.03	15	13	14	42	17	20	Nil	Nil	Nil

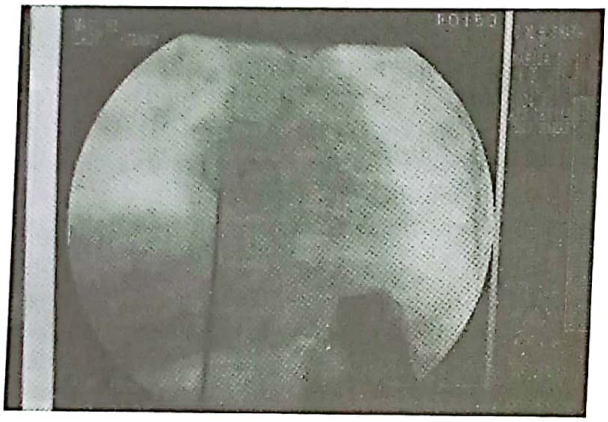

Fig.-1 : *ASD device is visible on both side of artial septum*

Discussion

Transcatheter techniques for closure of ASD's have been available for almost two decades, yet the approach has not achieved widespread uses. In 1976 King et al reported the first transcatheter closure of a secundum ASD with a double umbrella device in humans. [2,5]. Another device was Rashkind Atrial Septal defect occluder and was recommended for isolated ASDs of 18 mm or less in diameter. [6]. Then came Bard Clamshell occluder in 1989[7]. It was the first device with wide clinical testing in USA and Canada [1]. A different type of device was introduced by Sideris et al [8]. This buttoned device can provide effective closure of secundum ASD <25mm in diameter, with effective clinical closure in 79% of cases attempted and 98% of patients the devices were successfully implanted [9]. Many other studies also showed that effective ASD occlusion can be accomplished with buttoned device inspite of possibility of residual shunts, endocarditis, thromboembolism and unbuttoning in some cases. [10-13]. Other new devices like atrial septal defect occlution system (ASDOS) and Amplatzer septal occluder (ASO) are the latest [14]. These devices are promising. The most important advantage of ASO is that it can be delivered through small sheath and it can be used for larger defects also. Chance of Embolization is also less. Echocardiography is a good investigation to select cases for device closure and also to do the follow up on already done cases. [14, 15]. In this study eight cases were finally selected for ASD device closure. All the patients had nice results. None of them had any residual shunts or embolization of device. No evidence of RUPV, SVC, MV, TV, coronary sinus obstruction noticed in these cases in follow up echo. All patients left hospital only 24 hours after the procedure. No morbidity was noticed in follow up. Patient with isolated ASD has few symptoms. But untreated patients have an increased incidence of arrhythmia's and paradoxical emboli. The development of transcatheter closure alleviates a lot of apprehension for patients and families as it decreases the requirements of risky Open Heart Surgery.

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Risk Factors Profile of Coronary Artery Disease - A Study on Acute Anterior Myocardial Infarction

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Abstract:

A prospective study was carried out in the department of cardiology in National Institute of Cardiovascular Diseases, Dhaka during the period of April 2002 to December 2002. A total of 200 patents with first time acute ST segment elevated anterior myocardial infarction who present within 12 hours of onset of symptoms, were enrolled with some inclusion and exclusion criteria to evaluate risk factors of ischemic heart disease. The age range of the study patients was 28 to 67 years with mean age of 49.2 ± L 3 years. The mean age of the male patients was 47.9 ± 10.8 years and it was 57.3 ± 11.3 years for female patients. l he highest number of patients (66%) was in the age group from 40 to 59 years. 87.0% were male and 13.0% were female and the male and female ratio was 6.69:1. It was evident that commonest risk factor was smoking 63.3 % followed by hyperteansive 45%, diabetic 24%, dyslipidaemic 13 and family history of IHD present in I I % patients .The mean -+- SD of composite risk factors were 1.56± 0.9.

[Chest & Heart Journal 2004; 28(2) : 50-54]

Introduction:

Coronary artery disease is the commonest form of heart disease and the single most important cause of premature death in the developed world[1]. Approximately 800,000 people in the United States experience AMI annually, of these about 213,000 die. Of those who die, approximately one-half do so within 1 h of the onset of symptoms, before reaching a hospital 2,3 Ischemic heart disease becomes an important health hazard in the Bangladesh- One survey by Malik[4] detected the prevalence of IHD as 3.3 per thousand and in 1985 it was 14 per thousand'. in 1996, the prevalence of ischemic heart disease in urban population was found about 10 percent[6]. In 1998, one study showed prevalence of ischemic heart disease was 8.14 percent'. AMI has been recognized both in young and elderly in recent years in our country. Khandaker et al.[8] found that AMI is the leading cause of death in Bangladesh in the fourth decade of life.

The major cause of myocardial infarction is atherosclerotic disease of the epicardial coronary arteries. Atherosclerosis is the result of multiple and complex gene-environment interactions. Genetic factors alone may cause symptomatic atherosclerosis, but it is rare [9]. Three factors most consistently correlate with the extent of atherosclerotic lesions per se at autopsy in men are high total cholesterol, low HDL cholesterol and high blood pressure [10]. Several major and independent risk factors for clinical manifestation of atherosclerosis have been identified, including elevated serum total (and LDL) cholesterol, low serum HDL cholesterol, cigarette smoking, elevated blood pressure, diabetes mellitus and advance age "Only a single absolutely necessary and truly independent etiologic agent for atherosclerosis is a high level of serum LDL cholesterol. Atherosclerotic events are rare in population with total cholesterol less than 4 mmol/ L even in the presence of other major risk factors

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[9]. Acute emotional reactions have been implicated as triggers of acute coronary syndromes. It is recommended as secondary prevention to identify and treat depression and anxiety in patients with CHD[12] A certain blood cholesterol level is necessary to initiate and drive the disease, but cholesterol alone is rarely enough for the development of symptomatic atherosclerotic lesions. Although many risk factors are not atherogenic on their own, they accelerate the process. Clinically it may be more rewarding to treat accelerator than initiator, hypercholesterolemia. Maximum benefit, of course, is achieved by treating both [9].

Anterior myocardial infarction was highest location in the left ventricular infarction. Brown et al.[13] and Zaher et al.[14] found acute anterior MI in 52% and 53.12% cases respectively. Anterior wall infarction is usually larger than inferior and lateral wall infarction and has a substantially worse prognosis [15,1'5].

Materials and Methods:

It was a prospective study done in department of Cardiology, National Institute of Cardiovascular Disease (NICVD), Dhaka, Bangladesh during the period of April 2002 to December 2002. During this period 200 patients of first time acute ST segment elevated anterior myocardial infarction present within 12 hours of onset of symptoms were included in the study. Acute myocardial infarction was diagnosed according to ESC/ACC MI Redefined 2000[17].

In this study ST-segment elevated myocardial infarction defined as new or presumed new ST segment elevation of the j-point in two or more contiguous leads with the cutoff points ≥ 0.2mV in leads V_1 V_2 or V_3 and ≥ 0.1 mV in other leads in appropriate clinical setting[17]. Anterior myocardial infarction defined as characteristic ECG change ≥ 2 adjacent leads from V_1 to V_6 with or without I and aVL[18,19].

Elevation of serum enzymes was considered to be due to myocardial infarction when the level was more than two fold elevation in a single sample or increase in CK-MB activity >50% between two samples separated by 6 hours in the appropriate clinical setting [20].

Smoking indicates smoking within one month of the admission or stopped smoking between one month and one year before the admission.

Hypertension indicates blood pressure greater than 140 mmHg systolic or 90 mmHg diastolic on at least two occasions or history of diagnosed hypertension and treated with antihypertensive medication, diet and /or exercise.

Diabetes Mellitus indicates history of Diabetes need for antidiabetic agents or a fasting blood sugar greater than 7 mmol/L.

Dyslipidaemia indicates history of dyslipidaemia diagnosed and/or treated by a physician. National Cholesterol Education Program criteria include documentation of the following:

1. Total cholesterol greater than 200 mg/dl.

2. Low density lipoprotein (LDL) greater than or equal to 130 mg/dl. Or

3. High-density lipoprotein (HDL) less than 40 mg/dl.

Treatment is also indicated if LDL is greater than 100 mg/dl in patients with known coronary artery disease and this would qualify, as hypercholesterolemia.

Family history of IHD indicates CHD in a male relative (1st degree relatives like parents, siblings, children) with onset at age 55 or less or a female relative with onset at age 65 or less[12].

All data were analyzed by using computer based SPSS program.

Observations and Results:

A total of 200 patients of acute ST segment elevated anterior myocardial infarction were enrolled with some inclusion and exclusion criteria to evaluate risk factors of IHD.

The mean age of the patients was 49.2 ± 11.3 years ranging from 28 to 67 yeas (Table-I). The highest number of patients (66%) was in the age group from 40 to 59 years.

Table-I

Age distribution of the patients

Age in years	No of patients (N=200)	Percent
<30	10	5.0
30-39	20	10.0
40-49	74	37.0
50-59	58	29.0
≥60	38	19.0
Mean±SD	49.2±11.3	

Table-II shows the distribution of sex of the patients. The mean age of the male patients was 47.9±10.8 years ranging from 28 to 65 years and it was 57.3±11.3 years for female patients with ranging from 38 to 67 years. Out of 200 patients, 174(87.0%) were male and 26(13.0%) were female and the male and female ratio was 6.69:1.

Table-II

Sex distribution of the patients

Sex	No of patients	Percent
Male	174	87.0
Female	26	13.0
Total	200	100.0

Table-III shows the occupational status of the study subjects. Regarding occupation of the patients, 118 (59.0%) were service holder followed by businessman 52(26.0%), housewife 24(12.0%) and cultivator 6(3.0%).

Table-III

Occupational status of the patients

Occupation	No of Patients	Percent
Service	118	59.0
Business	52	26.0
Housewife	24	12.0
Cultivator	6	3.0
Total	200	100.0

Figure -1 show the percentage distribution of major risk factors associated with cardiovascular diseases of the study subjects. Out of 200 patients, 126(63.3%) were smoker followed by hypertension 90(45.0%), diabetes mellitus 48(24.0)%, dyslipidaemia 26 (13.0%) and family history of ischemic heart disease 22(11.0%). The mean ±SD of composite risk factors were 1.56± 0.9.

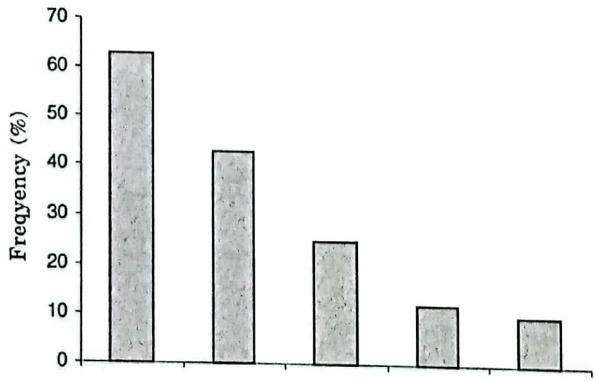

Fig- 1: *Bar diagram will be given here.*

Discussion:

The percent study attempted to assess the modifiable and non-modifiable risk factors associated with ischemic heart disease.

Markedly different CHD rates may be observed between socioeconomic groups of the population. 85% of this study patient was service holder and businessman. As a group becomes affluent, its members use their wealth to purchase high fat and high salt foods, tobacco products and automobiles. In this group of patient role of personality, environment, social support, social contact, stress and lack of control at work, and depression have all been associated with increased risk for CHD.

Age is the non-modifiable risk factor for AMI. Increasing age is associated with higher incidence of atherosclerotic coronary artery disease. CHD incidence rates in men are similar to those in women 10 years older [21]. The age range of the study patients was 28 to 67 years with mean age of 49.2 ± 11.3 years. The mean age of the male patients was 47.9 ± 10.8 years and it was 57.3 ± 11.3 years for female patients. The highest number of patients (66%) was in the age group from 40 to 59 years. Similar patters of age group were reported by Hague MT[22], Rahman MM et al.[23] and Malik A[4]. Age is a strong and independent risk factor for CHD, increases markedly with age up to an age of about 65 [9].

It was observed that 87 percent of the study patients were male. Male and female ratio was 6.69:1. In the previous studies: Amanullah M et a1.[5] found 89 percent, Begum F[24] 90 percent and Rahman MM et al.[23] reported 92 percent were male, these are also consistent with the present study. Estrogen may be the most obvious factor responsible for the protection against CHD in cases of female [25]. Coronary lesions appeared to progress faster in males than in females, evident by the presence of much more advanced plaque in 30 to 34 year old men compared with age matched women [26].

It was evident that 63.3 percent of the study patients were smoker followed by hypertension 45 percent, diabetes mellitus 24 percent, dyslipidaemia 13 percent and family history of IHD 11 percent. Similar patterns of risk factors observed by Sayemi A[27]. The author reported that 72 percent smoker, 34 percent hypertensive, 33

percent diabetic, 37 percent dyslipidaemic and 19 percent had positive family history of IHD. Studies done by Rahman MM et al.[23], Haque MT [22] also reported comparable data.

Cigarette smoking increases risk two to three folds and interact with other risk factors to multiply risk. There is no evidence that filters or other modification of the cigarette reduce risk [28]. Several major prospective epidemiologic studies have found that both systolic and diastolic hypertension have a strong, positive, continuous, and graded relationship to CHD[12]. Diabetes mellitus is an independent risk factor for CHD, increasing risk by two and four times for men and women, respectively. CHD is the leading cause of death among diabetics, and approximately 25% of MI survivors have diabetes [29] A strong recommendation that siblings and children of early CHD patients be screened for CHD risk factors[12]. At high cholesterol levels smoking, hypertension, low HDL cholesterol and diabetes mellitus promote development of coronary atherosclerosis and predispose individuals to CHD[9]

Conclusion:

Acute anterior myocardial infarction was commonly encountered in male of forth and fifth decade. Commonest risk factors were smoking, hypertension and diabetes mellitus. Dyslipidaemia and family history of IHD were less common risk factors.

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Prevalence of Tuberculosis in Garments Workers of Bangladesh

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Abstract

TB among garments workers is a challenging problem now. The prevailing isituation in many garments presents an ideal environment for transmission of TB. So garments works are at increased risk of Mycobaeterium TB infection, but information on these risks remains scarce, especially in developing countries like Bangladesh. This prospective study was designed to assess the prevalence of TB in garments workers of Bangladesh. The study was carried out in general workers of three garment industry of Dhaka, Bangladesh in the year 2002. The sample of the responders (n=755) invited to complete an occupationalhisttory question naive and to perform sputum examination, chest X-ray and MT. Garments TB was defines as having work-relate TB if they answered positivly the questions. :Have you ever had cough, haemoptrysis, loss of weight, evening temperature and others symptoms of TB in relation to this work ? "Of 755 works, 70 had garments related PT, and 20 non-garments related TB. Of 70 patients sputum tests showed 10% AFB +ve by microscopic examination, 60% patients had Mt position and 90% had chest X-ray lesions suggestive of Pt. The prevalence of garments TB was 11.9% in this population. The prevalence of work-relates TB was twice as high in men as in women and did not differ significantly with age or between smoking groups. Garments-related TB amounts to a significant proportion of total TB in population. This should be taken into account by helath policy markers as it is by definition a preventable and curable disorder.

[Chest & Heart Journal 2004; 28(2) : 55-58]

Introduction:

TB infection has a worldwide distribution with great variation in the prevalence being, the lowest in the developed and highest n the developing countries. The overall prevalence of TB, in a population is strongly correlated with the poor socionomic status[1]. The infection is usually acquired by droplet infection[2]. Poor hygiene, overcrowding, malnutrition and undernatrition are added factors[3]. Recently HIV infection has become a threat for TB both in developed countries[4,5,6]. Recently years there have been increasing evidence that Garments airborne exposure may be an independent risk factor for TB in Bangladesh[7]. They are usually overcrowded, somethimes extremely so, with poor hygiene and inadequate ventilation, creating excellent conditions for airborne transmission. Several community surveys

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in Europe and the United States have shown that occupational airbrone exposure is widely distributed in the general population, varying between 25% and 26% in men, between 8% and 20% in women[8]. The object of this study is to assess the prevalence of TB in garments workers by sex, age and smoking habits.

Materials and Methods:

The study was a prospective randomized open study to detect the prevalence of TB performed in Dhaka conducted in the year 2002 in three garments industries by open questionnaire survey. The eligible of the study included 755 those who responded to the questionnaire survey. These 755 subjects were invited for sputum test. chest X-ray and NIT between January 2002 and June 2002. The attendees answered a working history questionnaire, and underwent clinical examination and pathological test as mentioned earlier. Garments TB symptoms was defined as a positive response to questions. "have you ever had TB symptoms (cough, night fever. sweating weight loss. haemoptysis in relation to your work?" Smoking habits were divided into three groups. non-smokers. ex-smokers and smokers.

Data Analysis

Prevalence estimates in test and table are representatives of the garments as they took into account the different sampling: fractions of the study. Difference between prevalence was tested by X2· As significance level of P=0.05 wits used in all analyses.

Result:

Dernogyaphic and clinical Characteristics of the studied population were comparable (tables). Of The study sample majority (92.15%) were female & 13.24% male. Male and female ratio w was 1:11.75. Of the 755 subjects, 70 had Garments related TB. 20 had non-garments related TB and that is they were suffering from PT prior to joining the garments industry and the disease had no relation with garments. 53 Patients were experiencing work-related respiratory symptoms without having physician's diagnosis of the disease. Mean age did not differ between the two TB groups, The prevalence of respiratory symptoms in those with garments related TB and those with garment related respiratory symptoms did not vary significantly. The prevalence of TB in this study population in three garments industries was 11.9%. "The prevalence of garments related TB was twice as high in rnen as in women. The prevalence of garmants I'll did not vary significanlty by age in the sample of the exposed subjects. In neither sample did garments TB differ between the smoking & non-smoking groups.

Table – I

Presenting symptoms of subject with TB and non - TB

Variable	Garments Related TB n-70	Non Garments related TB n-20	Garments-related respirotry symptoms n-53	None of the respiratory disorders n-612	P Value
Cough %	67	46	48	15	0.177^{NS}
Evining Trmp %	27	22	23	6	0.641^{NS}
Night sweating %	47	43	39	15	0.34^{NS}
Loss of Weight %	27	22	23	6	0.781^{NS}
Breathlessness %	27	43	12	19	0.896^{NS}

Table – II

Characteristics of subject with Garments TB, non-Garments related TB, Garments related respiratory systoms, and of subject without any of these disorders. This study 2001-2002(n=1275)

Table – II

Total Sample

Variable	N	Garments related TB %	Non-Garments related TB %	Garments-related respiratory symptoms %	P Value
Men	100	(1.3)	(3.2)	(13.2)	
Women	655	(0.6)	(3.3)	(5.3)	
Age (Yearss)					.522 NS
12-18	240	(0.7)	(2.8)	(12.4)	
19-25	225	(0.6)	(3.6)	(10.6)	
26-40	290	(1.6)	(3.5)	(3.3)	
Smoking habits				0.235 NS	
Non-smokers	550	(0.7)	(3.2)	(7.9)	
Ex-smokers	38	(1.0)	(4.2)	(9.2)	
Current Smokers	50	(1.0)	(2.9)	(10.0)	
Total	755	(0.9)	(3.2)	(9.1)	

Table-III

Laboratory Test

Total Workers = 755, Total TB Patients = 70

	Men	women	P Value
Garments TB Patients 70	6	64	0.001
Sputum AFB +ve 10%	1	6	
MT +ve 60%	5	37	
Definite Lessions in X-ray P/A View	5	58	
	Men	omen	P Value
Non Garments TB Patients	2	18	
Sputum AFB + ve	1	4	
MT+ve	2	12	
Definite Lesions in X ray P/A view	2	19	

Table -IV

Education. Nutrition & Weight Status

Uneducated 80	80%	524
Education 20	20%	131
Malnutrition 40	40%	262
Average Nutrition	10%	65
W eight below 50kg	80%	524
Weight 50kg - above 20	20%	131
B. C. G. Vaccinated 10	10%	65

Discussion :

Pulmonary TB is the most important recognized criminal agent responsible for chronic disability- & chronic respiratory distress. In Bangladesh garments industries play a splendid role in the development of economic condition by earning lot of foreign currency. But unhealthy atmosphere prevail in almost all the garments industries. This surgery was concluded in examine prevalence of garments PT. In garments workers sample by SC

X. age and smoking habits. It was observed 67% of the TB patients in this study had experiences worsening of their disease in relation to occupational exposure III the garments industries. The number of female patients In this study was much higher than the males. because inost of the garments workers in Bangl[a]desh are females. Mortality and morbidity front TB in increasing probably due: to large: expansion of garments industries. The goal of this study was to determine the extent c of prevalence of "113 among the garments workers. Such type of studies are required to cover the whole garments workers in our country at present time.

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"High Plasma Fibrinogen Level - A Risk Factor for Coronary Artery Disease" - A Study in NICVD, Dhaka

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Abstract

Coronary heart disease (CHD) is the commonest cause of morbidity and mortality worldwide. Total 100 consecutive patients underwent coronary angiogram (CAG) for evaluation of coronary artery disease (CAD) during the period of October 1998 to May 1999 were included in this prospective case control study. Angiographically significant CAD was present in 80 (80%) patients, 20 (20%) patients had no coronary artery disease.

Among the risk factors, smoking (68.8% vs 50%) was followed by hypertension (40% vs 30%), family history (23.8% vs 15%) in our cases and control population.

58.8% of our cases presented with myocardial infarction, 23.8% presented with unstable angina and 17.5% presented with chronic stable angina. Single vessel involvement was 13 %, double vessel involvement was 33% and triple vessel involvement was 34%. Left anterior descending artery was the commonest artery involved (83.75%). Mean plasma fibrinogen level in patients with myocardial infarction, unstable angina and stable angina were-458 mg/dl, 476.63 mg/dl and 467.86 mg/dl respectively. Mean total plasma fibrinogen level among the cases (n = 80) was 464.15 mg/dl. Mean plasma fibrinogen level among the control group was 253.00 ± 53.03 mg/dl and significant difference was observed between the case and control (P< 0.005). Maximum coronary artery lesion score was 13 and minimum 3. Range was 10 and mean score was 7.45 ± 2.43. It was evident that the increased in the coronary lesion score, there was increased mean plasma fibrinogen level and significant positive correlation was observed along with the increased coronary artery lesion score (r = + 0.190).

By multiple regression analysis, it was observed that plasma fibrinogen level significantly correlated with coronary artery lesion score indicating plasma fibrinogen level increased with the severity of coronary artery disease. Our results demonstrate a significant positive relation of fibrinogen to the presence and severity of CAD. The results, therefore, lend support to the hypothesis- "Plasma fibrinogen remains elevated in patients with coronary artery diseas e, which has a positive correlation with the severity of CAD"

[Chest & Heart Journal 2004; 28(2) : 59-66]

Introduction

Coronary heart disease (CHD) is a major health problem in the world now. Contrary to the popular belief, CHD is indeed common in the Indian subcontinent. Although there are no large population based data on the incidence, prevalence or the mortality of CHD from this part of the world, several small-scale reports have suggested that the occurrence of CHD in this subcontinent is similar to that found in some of the developed countries and the prevalence of coronary artery disease (CAD) has increased from 1.05% percent in 1960 to 8.67% percent in 1995 in urban population[1].

In 1994 the incidence of ischaemic heart disease (IHD) in Bangladesh was 14 per thousand[2].

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By different prospective epidemiological studies conducted over the last four decades, the relation of five established major risk factors in causation and progression of CAD is well established. Some investigator, both in the field of epidemiology and that of clinical cardiology have described the concept of the epidemiology and that of clinical cardiology have described the concept of the risk factors and their values in identifying the high risk patients as well as extent of CAD. Modifications of established major risk factors reduce the morbidity and mortality of CAD patients significantly. At present time some new risk factors have attracted the researchers and fibrinogen is one of them.

Some prospective studies in Western countries showed a direct, independent and statistically significant association between fibrinogen level and incidence of IHD. This association being as strong as the relation between cholesterol and IHD. The fibrinogen level is also associated with the recurrence of IHD in those who have survived a myocardial infarction and with the onset and recurrence or progression of cerebrovascular disease[3]

On the basis of the concordant results of various epidemiological studies, fibrinogen is increasingly recognized as an important cardiovascular risk factor (The confirmed association of fibrinogen level with the incidence of ischaemic coronary events suggests that fibrinogen contributes to the critical thrombotic component of CAD. However, fibrinogen may also be involved in earlier stages of atherosclerotic plaque formation, a notion that is supported by cross-sectional studies demonstrating a significant positive association of fibrinogen levels with the presence, extent or severity of coronary atherosclerosis More recent studies have revealed that fibrinogen level measured during stable phases in patients with manifest CAD areaalso positively related to subsequent cardiovascular events and mortality[4].

The study was done

To define the plasma fibrinogen level as a coronary risk factor in hospital admitted patients.

To correlate the elevated plasma fibrinogen level with the angiographically determined severity of coronary artery disease (CAD).

To see the relationship of plasma fibrinogen level with known coronary risk factors in patients with CAD.

Fibrinogen is the first coagulation factor. It is a glycoprotein of molecular weight approximately 2,40,000 Dalton, present in plasma at a concentration in the range of 2-4 g/L (200-400 mg/dl). It is synthesized in the liver (1.7-5.0 g/day) and by megakaryocytes.

Fibrinogen is an important cofactor in platelet aggregation. ADP activated platelets bind fibrinogen, which then binds to glycoprotem receptors (GP lib-IIIa) on adjacent platelets, forming a link that enhances platelet aggregation.

Materials and Methods:

A prospective case control study was carried out in national institute of Cardiovascular Disease (NICVD). Oshek During the perior October, 1998 to May, 1999. Total 100 consecutive patients undergoing cornary angiogram (CAG) for evaluation of coronary artery disease (CAD). In patient Group, 80 case was included who were patients diseased coronary artary and in control group 20 patients with normal coronary artery.

Inclusion criteria's:

Patients with myocardial infarction at least one month after attack

Patients with stable and unstable angina.

Exclusion criteria's

Patients within one month of acute attack of myocardial infarction

Patients received thrombolytic therapy for any indications < 1 month,

Patients having acute infection at the time of blood collection for fibrinogen

Patients with rheumatic valvular heart disease

Patients with non-cardiac stressful conditions, like cerebrovascular accident and others.

Quantitative determination of fibrinogen level was done by the clotting method of Clauses by kits "Fibri-Prest" of Diagnostic Stage with coagulometer.

Test principle

In the presence of an excess thrombin, the clotting time of a diluted plasma has a direct bearing on the level of plasma fibrinogen.

Kit reagents

- Reagent 1: Freeze-dried titillated human calcium thrombin.
- Reagent 2: Buffer solution, pH 7.35. The reagent 2 contains sodium azide as a preservative.

Specimen collection and treatment

- Blood 9 volume (1.8 ml) was collected in sodium-citrate anticoagulant 1 volume (0.2 ml).
- Centrifugation - for 10 minutes at 2500 revolutions/ min.
- Plasma storage - for 8 hours at 20^0 C.

Procedure

- Plasma diluted with reagent 2 at the dilution of 1 : 10 (1 volume plasma + 9 volume buffer). This was the test sample.
- Test sample -0.2 ml taken in a container, incubated at 37^0C for 2 minutes. Reagent 1 prewarmed at 37^0C, added 0.2 ml with the previous test sample. Finally, clotting time was noted. Finally, quantity of fibrinogen was estimated by comparing the clotting with the clotting time in the schedule chart and found out quantity of fibrinogen as g/L or mg/dl.

Collected data were edited and coded manually. Then, it was statistically analyzed using computer-based SPSS+ Windows 7.5 version programmed. A value < 0.05 was considered significant.

Results

The number of cases and contrat and distribution of subject by age in very shows in Table-I

Table-I

Distribution of subjects by age in years (n = 100)

Subjects	N	Mean ± SD (years)
Case	80	50.10±9.05
Control	20	42.75±7.71
Total	100	48.63±9.25

Fig.-1 : *Sex distribution of case (n=80) and control (n=20) subject.*

Table-II

Distribution of subjects by IHD status (N=100)

LHD status	Case (n-80)		Control (n = 20)		Total (n = 100)	
	No.	%	No.	%	No.	%
Myocardial infarction	47	(58.75)	0		47	(47.00)
Unstable angina	19	(23.75)	4	(20.00)	23	(23.00)
Stable angina	14	(17.50)	16	(80.00)	30	(30.00)
Total	80		20		100	

Table-II shows that out of 80 cases, myocardial infarction, unstable angina and stable angina were present in 47 (58.75%), 19 (23.75%) and 14 (17.5%), respectively. Among the control group, unstable angina was present in 4 (20%) and stable angina in 16 (80%).

Table-III

Number of coronary artery involved (n=100)

Vessel involved	No. of patients	Percentage
0	20	20.0
1	13	13.0
2	33	33.0
3	34	34.0

Table- III shows, among the cases, single vessel involvement was 13 (13%), double vessel was 33 (33%) and triple vessel was 34 (34%) and 20 (20%) had no lesion.

Table - IV

Individual vessel involvement (n = 80)

Name of vessel	No. of patients	Percentage
LM	5	6.25
LAD	67	83.75
LCx	55	68.75
RCA	60	75.00

Table –IV shows, LAD was the commonest artery involved (83.75), followed by RCA (75%), LCx (68.75%) and LM (6.25%).

Table -V

Distribution of subjects by selected risk factors

Risk Factors	Case (n - 80)		Control (n - 20)		Total (n - 80)		P value
	No.	(%)	No.	(%)	No.	(%)	
Diabetes mellitus							
Present	25	(31.3)	2	(10.0)	27	(27.0)	0.056**
Absent	55	(68.8)	18	(90.0)	73	(73.0)	
Hypertension							
Present	32	(40.0)	7	(35.0)	39	(39.0)	
Absent	48	(60.0)	13	(65.0)	61	(61.0)	0.682
Diyslipidemia							
Present	26	(32.5)	2	(10.0)	28	(28.0)	
Absent	54	(67.5)	18	(90.0)	72	(72.0)	0.045
Smoking							
Present	55	(68.8)	10	(50.0)	65	(65.0)	
Absent	25	(31.3)	10	(50.0)	35	(35.0)	0.116*
Family history							
Present	19	(23.8)	3	(15.0)	22	(22.0)	
Absent	61	(76.3)	17	(85.0)	78	(78,8)	0.398*

** Significant (< 0.05) with Chi-square analysis

* Not significant (P> 0.05)

The prevalence of risk factors in both case and control are shown in Table-VIII. Smoking, hypertension, dyslipidemia, diabetes mellitus and family history were considered to be the major risk factors for this study. No significant association was observed between case and control group in the selected risk factors except diabetes mellitus and dyslipidemia (P<0.05) indicates diabetes mellitus and dyslipidemia were to be high among the cases.

Table –VI

Distribution of subjects by selected variables (case = 80, control = 20)

Risk factors	Mean ± SD	P value[a]
Height (cm)		
Case	165.41 ± 7.27	0.469[NS]
Control	164.10 ± 7.01	
Weight (kg)		
Case	64.45+7.57	7.57 0.677[NS]
Control	63.65+8.02	
Body mass index (kg/M^2)		
Case	23.52+2.09	0.850[NS]
Control	23.63+2.54	
Total cholesterol (mg/dl)		
Case	197.61 ± 24.83	0.244[NS]
Control	207.60 ± 58.53	
HDL (mg/dl)		
Case	44.49±7.73	0.001***
Control	50.20±7.51	
LDL (mg/d 1)		
Case	122.23 ± 24.13	0.392[NS]
Control	118.55 ±15.34	
TG (mg/dl)		
Case	269.41 + 98.49	0.175[NS]
Control	302.05 ± 82.84	
Fibrinogen (mg/dl)		
Case	464.15 + 61.99	0.025*
Control	253.15 ± 53.03	
DM (mg/dl)		
Case	126.92 ± 29.59	0.001***
Control	110.70 + 23.96	

[a]P value reached from unpaired Student's 't' test, *** Highly significant (P<0.001), ** Significant (P<0.02)
[NS] Not significant (P>0.05)

Table - VII

Coronary lesion score

Parameters	Total score
Mean	7.45
SD	2.43
Range	10
Minimum	3
Maximum	13

Table - VII shows that the mean coronary lesion score was 7.45 with standard deviation of 2.43. The minimum score was 3 and maximum score was 13.

Mean fibrinogen levels in myocardial infarction was 458.00 + 68.5 mg /dl, in unstable angina 476.63 ± 60.79 mg/ dl and stable angina 467.86 + 35.08 mg/dl and that of control was 253.15 ± 53.03 mg/ dl. Significant mean difference were found between control group with three groups of cases myocardial infarction, unstable angina and stable angina) (P<0.001)

Table-X shows plasma fibrinogen level is higher among the cases and significant difference observed between case and control (P<0.005).

Table - IX shows plasma fibrinogen level increased from 396.00 ± 49.11 mg/dl) to 515.91 ± 41.98 mg/dl as the vessel involvement increased from single vessel to triple vessel and there was significant difference between two groups-case and control (P<0.005).

Table - VIII

Comparison of plasma fibrinogen level among different subsets of ischaemic heart disease patients with control group (n = 100)

Subsets of IHD and Control	N	Plasma fibrinogen level (mg/dl) (Mean ± SD)	P value
Myocardial infarction	47	458.00 + 68.50	0.001***
Control	20	253.15 + 53.03	
Unstable angina	19	476.63 ± 60.79	
Control	20	253.15 + 53.03	0.001***
Stable angina	14	467.86 ± 35.08	
Control	20	253.15 + 53.03	0.001***

*** Highly significant (P<0.001) with unpaired Student's 't' test

Table –IX

Relation of plasma fibrinogen level with the number of blood vessels involved (n =100)

Number of vessels	N	Plasma fibrinogen level (mg/dl) (Mean ± SD)	r value	P value
No vessel involvement	20	253.00 ± 53.03		
Single vessel Involvement	13	396.00 ± 49.11		
			0.894	0.005*
Double vessel Involvement	33	437.00 ± 36.55		
Triple vessel Involvement	34	515.91 ± 41.98		
Total	100	421.95 ± 103.95		

* P value < 0.005 (Significant)

Table – X

Comparison of plasma fibrinogen level between case and control (N = 100)

Fibrinogen Level (mg/dl)	Case (n = 80)	Control (n = 20)	P value
Range	312-605	176-350	
Mean + SD	464.15 ± 61.99	253.00±53.03	0.005*

*P value significant (P<0.005)

Table-XI

Multiple regression analysis of plasma fibrinogen with selected risk factors

ANOVA analysis

1.

	Sum of Square	Df	Mean Squares	F ratio	P value
Regression	905133.765	4	226283.441	130.936	
Residual	164178.985	95	1728.200	0.005	
Total	1069312.750	99			

II

Risk factors	B coefficient	T value	P value
Age (years)	0.737	1.543	0.126
Total score	19.448	4.998	0.005**
Number of vessels	21.082	1.666	0.099
Number of risk Factors	-3.698	-1.010	0.315

*Dependent variables- Plasma fibrinogen level

*Predictors variable - Age in years, total score, number of vessels, composit risk factors

It was observed from Table - XI that plasma fibrinogen level significantly correlated with total score indicating plasma fibrinogen level increased with severity of coronary artery disease (P< 0.005).

Discussion:

Mean plasma fibrinogen level in patients with myocardial infarction, unstable angina and stable angina were 458 mg/dl, 476.63 mg/dI, and 467.86 mg/dl respectively. Mean plasma fibrinogen level among the cases (n =80) was 464.15 mg/dI and among the control group was 253 ± 53.03 mg/dl.

The study was done on the basis of coronary artery lesion score. Maximum coronary artery lesion score was 13 and minimum score was3, range was 10 and mean score was 7.45 + 2.43. This result is more or less similar with Akhter et al[5]. where mean score in their population was 7.66 ± 1.63. With the increase in the coronary artery lesion score, there was increased mean plasma fibrinogen level and significant positive correlation was observed along with increased coronary artery lesion score (r = + 0.910).

In this study, high plasma fibrinogen level (>400 mg/dl) showed a significant positive correlation with the selected risk factors of age, coronary artery lesion score, number of vessels involved, composite risk factors (P<0.01). But no correlation was observed among the BMI< blood sugar and serum LDL level. In one study by Bolibar et al.[6] showed significant correlation of high plasma fibrinogen level with the selected coronary artery disease risk factors.

Finally, in this study, those predictor variables which are significantly correlated with plasma fibrinogen level in bivariate correlation analysis, then enter into multiple regression analysis . It was observed that plasma fibrinogen level significantly correlated with total coronary artery lesion score indicating plasma fibrinogen level in increased with the severity of the CAD. Similar study was done by Ernst reschid[7] and proved that mean fibrinogen levels had a progressive positive association with incresaing angiographically defined coronary vessels involvement and total coronary lesion score.

Conclusion

Our study suggest that association of plasma fibrinogen level with CAD was of greater magnitude and was statistically more significant. We demonstrated a graded increase in fibrinogen with the severity of coronary stenosis. The positive association of fibrinogen levels with the presence, extent or severity of coronary atherosclerosis. The study was done in hospital-admitted patients. If it is confirmed in a wider population across the country, this factor needs to be included in our risk factor modification schedule.

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REVIEW ARTICLE

Sarcoidosis – A Review

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Abstract :

Sarcoidosis is a disease of unknown etiology presenting with bilateral hilar adenopaty, pulmonary infiltration, and skin or eye lesions. The diagnosis is established most securely when clinical or radiological findings are supported by histological evidence of widespread noncaseating epithelord granutoma in more than one organ or by a positive Kveim siltzbach skin test. Immunological feature are depression of delayed type hypersensitivity, suggestive improved cell mediate immunity and in creased or abnormal immunoglobulin. This may be hypercalciuria with or without hypercalcemia. The course and prognosis may correlate with mode of onset. An acute onset with ery them a nodosum heralds a self-limiting course and spontaneous resolution where as an insidious onset may be followed by relentless progression corticosterods relieve symptom and suppress inflammation and grnnuloma formation.

[Chest & Heart Journal 2004; 28(2) : 67-75]

Introduction:

Sarcoidosis is a multisvstem granulomatous disease It is common in colder climates (Scandinavian countries) commonly affecting young adults. The lung is affected in over o 90^{0}/o of cases. While the aetiology of sarcoidosis remains uncertain, it is associated with imbalance between subsets of T lyrnpliocytes and other disturbances of cell-mediated immunity, but the relation between these phenomena and sarcoidosis has not yet been explained. The lesions are histologically similar to tubercles follicles, apart. from the absence of caseation and tubercle bacilli, but there is no convincing evidence that the disease is caused by any of the myobacteria- Most patients usually present with bilateral hilar lymphadenopathy that is often detected by routine chest x-ray. The prevalence in the UK is approximately 19 in 100,000 of the population But there is no data regarding its incidence or prevalence in our country.

In West Bengal', which is our neighbouring state of India, sarcoidosis is seen with almost similar frequency as in the West. It was largely due to lack of awareness and non-availability of investigations for diagnosis that the disease was reported to be rare in the past[1].

The problem in this sub-continent is the similarity of tuberculosis with sarcoidosis in a few aspects. Both involve mainly the lung and there is formation, of tubercle Many patients diagnosed as tuberculosis possibly suffering[2]. However absence of mycobacterium and of caseation in the histological specimens and presence of skin anergy to tuberculin help make a diagnosis

Definition: The 7th international Conference of Sarcoidosis was held in 1976 in London. In that conference, a descriptive paragraph on sarcoidosis was published till now, It is used as working definition of sarcoidosis- "Sarcoidosisis is a milltisystem granulomatous disorder of unknown

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aetiology most commonly affecting young adults and presenting most frequently with bilateral hilar lymphadenopathy, pulmonary infiltration and skin or eye lesion. The diagnosis is established most securely when clinico-radiographic findings, are supported by histological evidence of wide spread non—caseating epithelioid granulomas in more than one organ or a positiveKveim-Siltzbach skin test. Immunoligical features are depression of delayed type hypersensitivity, suggesting impaired cell mediated immunity, and raised or abnormal immunoglobulin "There may also be hypercalciuria with or without hypercalcaemia. The course and prognosis may correlate with the mode of onset. An acute onset with erytheama nodosum heralds a self-limiting course and spontaneous resolution, while an insidious onset may be followed by relentless progressive Fibrosis. Corticosteroids relieve symptorns and suppress inflammation and granola formation:

History

1) The term 'sarcoid' was introduced by Beck because of a superficial resemblance of a skin lesion to sarcoma[4].
2) Hutchinson in 1898 described skin lesions that principally affected the face, arms and hands and which, were referred to for a long time as "Mortimer's; Malady"
3) Schulman first noticed the clinical similarity of sarcoidosis with tuberculosis and favoured a tubercles aetiology In the 1940s the term 'Sarcoidosis' was universally accepted as the name for this condition

Epidemiology

Incidence and Prevalence

The prevalence of sarcoidosis is from 10 to 40 per 100,000 In USA and Europe.

A recent case-control etiological study of sarcoidosis (ACCESS) shows similar results". In India, sarcoidosis is seen in different parts with almost similar frequency' as in the West. It was largely due to lack of awareness and non-availability of investigations for diagnosis that the disease was reported to be rare in the pas! [5]

Age and Sex Incidence

Most studies have shown the highest incidence to be in the third and fourth decades with a variable female predominance [21] The disease is uncommon at the extremes of life.

Ethnic Factors

Sarcoidosis is 16 times more common in black compared white.

Familial Factors

Familial clustering of sarcoidosis is a reported phenomenon Sarcoldosis, has been observed in twins, more commonly in monozygotic than in dizygotic pairs.

Human Leukocyte Antigens

It is now clear that the HLA region is strongly implicated in the development of sarcoidosis. HLA-DR residue is an important protective marker in sarcoidosis HLA-DQBI*Oa marker is associated with good prognosis, HLA-DQBI*0601 is primarily associated with the development of cardiac sarcoidosis6

Smoking

Unlike many diseases, in which the lung is involved, sarcoidosis favours non smoker.

Occupation

Exposures to numerous toxins, wood dust increases the incidence of developing sarcoidosis.

Aetiology

The cause of sarcoidosis is unknown. A number of aetiologies, including exposure to pine pollen, or beryllium and infection with mycobacterium, viruses and fungi, drugs, have been suggested but there is no absolute Proof that any specific agent is responsible. However, all available evidence is consistent with the concept that the disease results from an exaggerated cellular immune response (acquired, inherited, or both) to a limited class of persistent antigens or self antigens[7] Both environmental and genetic factors seem to play a role.

Role of an Transmissible Agent

Though there is speculation that cell wall defective forms (CWDF) of acid-fast bacteria is associated with sarcoidosis, it needs further validation.

Mineral fibre exposure - The association of metabolic dust exposure, such a beryllium and aluminium, and sarcoid like pulmonary disorders is well known.

Recently, it was observed that MMMF exposure might be related to sarcoid like granulomas similar to chronic beryllium disease

Genetics

Sarcoidosis occurs in genetically susceptible person but it is not an autoimmune disease. In contrast to some autoimmune disorders, a clear association between human leukocyte antigen (HLA) and sarcoidosis is still not evident. There is however, a general agreement that some HLA genes are related to phenotypic variations of the disease[8].

Immunology

The granulomas of pulmonary sarcoidosis are now thought to be the consequence of activation of lymphocytes and macrophages with in the lung, will resultant release of potent mediators that play a critical part in the pathogenesis of the disease. The stimulus for activation is unknown, although the state of activation of lung mononeuclear cells is characteristic of that due to antigen stimulation and it may he that an unknown antigen is involved. The total number of cells recovered at BAL is increased, with striking increases in the absolute numbers of macrophages and lymphocytes.

Important Cytokines in Sarcoidosis

1. IL-1: a protein produced mainly by macrophage, it stimulates helper T cells to differentiate and produce IL-2,
2. IL-12: produced by macrophages and promotes the development of Th-1 cells from raise T lymphocyte.
3. IL, 18: recently identified as an interferon-gamma (IFN-y) inducing factor, and it plays an important role in T helper 1(Th-1) respanse[9].
4. Tumor necrosis factor (TNT): This plays the central role in the pathogenesis in sarcoidosis. It is produced by activated macrophage.. Recent trend is to block this factor by pharmaceutical manipulation.
5. IL-2: a protein produced mainly by helper T cells that stimulates both helper and cytotoxic T cells to grow.

Lung Lymphocytes

Activated T cells release a number of lymphokines which, in turn, induce further T cell activation and replication. Such activated T cells release other lymphokines that produce polyclonal B-cell activation and increased immunoglobulin production resulting in hyperglobulinaemia.

Lung Macrophage

The macrophage population in the lung is increased in active sarcoidosis and consist of alveolar macrophages and young macrophages that are probably freshly]; recruited monocytes. In addition, the release of interferon-Y, Fibronection and alveolar macrophage-derived growth factor may Promote fibroblast recruitment, attachment and proliferation and lead to fibrosis.

Blood

In striking contrast to the findings in the lung, peripheral blood in sarcoidosis usually shows a lymphopenia with a lower than normal ratio of T-helper; T-suppressor cells

Pathophysiology and Immunopathognesis

The first manifestation of the disease is an accunmlation of phagocytes, affected organs - This inflammatory process is followed by the formation) of granulomas, aggregates of macropliages and their progeny', epithelioid cell and multinucleated giant cells. The typical sarcoid granuloma is a compact of all of mononuclear phagocytes surrounded WS a rim of C1) 4-V lympho^{c}ytes, and, to a far lesser extent, B lymphocytes. The overall structure is relatively discrete and is interspersed with fine collagen fibrils, presumably remnants of the underlying- connective tissue matrix[10].

Organ dysfunction in sarcoidosis results mostly from the accumulated inflammatory-; cells distorting the architecture of the affected organ. The disease is suppressed, either spontaneously or with therapy, the mononuclear inflammation is reduced in intensity and the number of granulomas is reduced.

In chronic cases, the mononuclear cell inflammation persists for up to four years. If the intensity of the inflammation is sufficiently high for a sufficient period, !he derangement's to the affected tissues result in extensive damage,. lead to fibrosis, and permanent loss of organ function.

ii) The disease results from an inadequate suppresser arm of the immune response, such that TH I cell processes can not be shut down in a normal.

iii) The disease results from inherited (and/or acquired) difference in immune response genes, such that the response to a variety of antigen is an exaggerted, TH I cell process.

In the involved organs, the ratio of CD4+ to CD8+ T cells may be as high as 10:1 compared to the ratio of 2:1 found in normal tissues or in the blood of affected individuals68· Together with cytokines such as interleukin (IL)-12 and others released locally, these mediators recruit blood monocytes to the affected organs and activate them, providing the building blocks for the formation of the granuloma. The histological features of the sarcoid lesions are not specific and may occur in tuberculosis as well as leprosy, tertiary syphilis, brucellosis, primary billiary cirrhosis, hypogammoglobulinaemia, fungal infection and berillosis,

Modes of Presentation

Sarcoidosis is a systemic disease, and thus the clinical manifestations may be generalized or focused on one or more organs. The diversity of the possible clinical manifestations is such that a practitioner in almost any branch of medicine may be called upon to make the diagnosis. All kinds of combinations of organ involvement are possible. Because the lung is almost always involved, most patients have symptoms referable to the respiratory system.

Sarcoidosis can be serious, because a) it can affect vital organs, with the development of irreversible fibrosis resulting in functional impairments, (b) involvement of the eyes can lead to blindness and (d) death can occur from cardiac, respiratory or renal failure. Sarcoidosis is occasionally discovered an a complerely symptomatic individual

Thoracic Sarcoidosis

Clinical features : The hilarglands and the lungs are the organs most commonly affected in sarcoidosis. Thoracic sarcoidosis is classified in four stages on the basis of the appearances of the chest radiograph" Stage I represents hilar adenopathy; stage II hilar adenopathy plus pulmonary opacities and stage III pulmonary opacities only. Stage IV represents the development of irreversible pulmonary fibrosis.

Hilar lymphadenopathy

Enlargement of hilar lymph glands with or without paratracheal lymphadenopathy is the commonest manifestation of sarcoidosis. Usually, the glands are bilaterally and symmetrically involved. The hilar lymph adenopathy may be asymptoma.tic and it may be associated with erythema nodosum. Other presenting symptoms may include cough, chest pain, loss of weight, malaise, or excessive fatigue.

Possible Presentations of Sarcoidosis

Chest physicians
- Hilar glands
- Diffuse pulmonary opacities
- Breathlessness

Ophthalmologist
- Uveitis: anterior and posterior
- Conjunctivitis
  - Non specific
  - Phlyctenular
- Keratoconjunctivitis
- Enlarged lacrimal glands
- Sjogren-like syndrome (when salivary glands involved)
- Glaucoma

Neurologist
- Peripheral neuropathy
- Eye change Meningitis
- Isolated cranial nerve lesions
- Space- occupying lesions
- Pituitary involvement (usually posterior)
- Transverse myelitis

Rheumatologist
- Subcutaneous tissue swellings
- Polyarthralgia
- Bony cysts

Gastroenterologist
- Hepat0 splenomegaly

Dermatologist
- Erythaema nudism
- Plaques
- Papules Nodules Lumps Scars

Cardiologist
- Pulmonary heart disease
- Myocarditis and congestive cardiac failure
- Conduction disorders

General Surgeon
- Diagnostic lymph node biopsy

ENT surgeon
- Nasal granuloma
- Laryngeal granuloma

General practitioner
- All above for sorting out'
- Atypical mumps
- Hypercalcaemia
- Renal calculi
- Impaired renal function

The hilar lymphadenopathy syndrome with or without erythaema nudism is most commonly a benign manifestation. The average time for the chest film to become normal is about 8 months. The older the age at onset, the greater the chance of chronicity. Haemoptysis is rare, as is production of sputum. Distal atelectasis can result from endobronchial sarcoidosis or from external compression from enlarged intrathoracic nodes.

Bronchial Sarcoidosis

The bronchi may be involved in sarcoidosis through external compression by glands, resulting in atelectasis in a very few cases.

Pleural Sarcoidosis

Pleural sarcoidosis is uncommon but has been reported. The pleura is involved in 1 to 5% of cases, almost always manifesting as a unilateral pleural effusion[78]. Superior vena cava obstruction and hydro pneumothorax has been reported[81] but is extremely rare.

Extrathoracic Sarcoidosis

Lymphatic system

The lymph nodes most frequently affected in saracoidosis are those of the hilar and paratracheal groups. Among extra thoracic nodes, the right scalene group are most commonly affected.

Eye

The eyes should be examined routinely, preferably with a slit lamp, in all cases since mild asymptotic eye involvement may be commoner (25%) than is suspected.

Skin

The most common skin manifestation in sarcoidosis is erythema nudism, which 'in severe cases may be associated with prolonged fever. Maculopapular eruptions, subcutaneous nodules, plaques and lupus pernio are other lesions that may be found[12]. Women are more vulnerable.

Upper respiratory tract

Sarcodosis may affect the nose, nasopharyngel mucosa and larynx Disease of the laryngeal and pharyngeal mucose may coexist with or be independent of nasal lesions. Hoarseness, cough, dysphagia and dyspnoea secndary to upper airway obstructions may occur

Alimentary system

Involvement of the salivary glands and liver is common while affection of the pancreas and gastrointertinal tract is rare.

Uveparotid fever

Uveoparotid fever was first described by Heerfordt in 1909[13]. As febrile illness characterized by uveitis and swelling of the parotids, accompanied frequently by facial palsy.

Haemopoietic system

Enlargement of the spleen is relatively common in sarcoidosis and is usually symptomless. Sarcoidosis of the marrow is reported in 15 to 4% of patients, but it rarely causes haematological abnormalities.

Kidney

Clinically apparent primary renal involvement in sarcoidosis is rare, although, tubular, glomerular, and renal artery diseases have been reported. More commonly, there is a disorder of calcium metabolism with hypercalcauria, with or without hypercalcauria.

Nervous and endocrine systems

Sarcoidosis affecting the nervous system by infiltration or sarcoid deposits may result in a variety of clinical pictures including: Peripheral neuropathy or mononeuritis multiplex, bilateral facial nerve palsy, Lymphocytes meningitis. Meningo-encephalitis, space-occupying lesions, epilepsy.

Cardiovascular system

Extensive pulmonary fibrosis can lead to cor-pulmonary, while actual involvement of the myocardium may result in dysarrhythmias, conduction disorders, heart failure or sudden death. Pericarditis has been recorded.

Investigations

Pulmonary Function Tests

The most frequent and earliest abnormalities in pulmonary function in patients with sarcoidosis

are reduction in lung volumes (restrictive lung disease) and impaired diffusing capacity (decrease in DLO) Expiatory flow rate may be reduced which indicates airway obstruction. PFT may be normal. Arterial hypoxernia occurring at rest suggests more advanced disease Hypercapnia occur only in patients with advanced disease.

Radiology

Because the lung is involved so commonly, the routine chest film is almost always abnormal.

Table-I

Chest X-Ray staging system.

Stage	Characteristics
Stage 0	Normal CXR
Stage I	BHL
Stage 11	BHL and infiltrates
Stage III	Infiltrates alone
Stage W	Fibrosis

The hilar adenopathy is almost always bilateral, but unilateral node enlargement, can be seen. Nodes are also common in the paratracheal region.

Kveim Test

Initially Kvein Test was regarded as a reliable and clinically useful aid to diagnosis. Unfortunately, shortage of suitable tissue and fears of transmission of viral infection have caused the test to be abandoned in most centres.

Tuberculin testing

Tuberculin test is helpful in diagnosing sarcoidosis in the developing countries where the two are associated with granulomas formation Numerous studies have shown that about two-thirds of patients with active sarcoidosis fail to react to 100 TU about one-quarter react to 100 TU; less than one-tenth to 10 TU and less than 1 in 20 to TU.

Serum Angiotensln-Converting Enzyme

Serum ACE has been reported to be elevated in 75% of patients with active sarcoidosis. Sensitivity and specificity as a diagnostic test is limited; 60 and 70%, respectively[14] . Decisions on treatment should not be based on the ACE level alone.

Gallicim-67 Scanning

It is an expensive investigation involving a substantial radiation dose to the patient and can not at present be justified in the routine investigation of the disease. It is more valuable in the diagnosis of atypical cases of sarcoidosis.

Bronchoalveolar Lavage

Bronchoalveolar lavage (BAL) is used in the diagnosis of pulmonary sarcoidosis, This is used to support but not prove a diagnosis of sarcoidosis[15]. BAL fluid from patients with pulmonary sarcoidosis contains increased numbers of T lymphocytes, with a high ratio of CD4 to CD8 T cells and increased macrophages in comparison with control fluid. Most of the T lymphocytes found in broncho-alveolar lavage are members of the activated TH 1 subset of CD4+ T lymphocyte.

Measurements in Blood, Urine and Sputum

Serum calcium should be measured as well as 24 hour urinary calcium. Serum globulins may be elevated. Routine examination of the peripheral blood is of no value in diagnosis, but common abnormalities in the blood include lymphocytopenia, an occasional mild eosinophilia and increased erythrocyte sedimentation rate. Other serum abnormalities relate involvement of specific organs such as liver, k˙idney, or endocrine glands. If sputum production is a feature, acid fast bacilli should be sought by direct smear or culture.

CT, MRI

CT scan of the thorax is usually unnecessary in sarcoidosis. It may be of value, when used with contrast, in differentiating hilar enlargement due to lymphadenopathy from enlargement of the pulmonary vessels.

Other Investigations

It depends upon the extra thoracic organ involvement. In case of neurosarcoidosis, other than CT or MRI CSF fluid analysis is vital. EMG/ Nerve conduction studies can be used to confirm neuropathy. Endocrine studies should be performed whenever involvement of the pituitary-hypothalamic axis is suspected.. Creatine kinase, erythrocyte sedimentation rate and aldolase may be useful in cases of myopthy.

Antineutrophil cytoplasmic antibody (C-ANCA) titres may be needed to differentiate from Wegener's granuiomatosis. ECG monitoring is indicated yearly for cardiac involvement.

Tissue Biopsy

Tissue biopsy is often crucial to the diagnosis of sarcoidosis. When typical clinical and radiographic findings are supported by histological proof of the sarcoid granulomatous process and tuberculosis has been excluded by the tuberculin test and by bacteriology, the diagnosis of sarcoidosis can be confidently made.

The tissues found to be useful for biopsy in sarcoidosis linclude superficial lymph nodes, mediastinal glands, skin, palate, bronchus, lung liver-conjunctiva, gastrocnemius muscle, bone marrow. A recent study[16] shows that the impressive sensitivity of asymptomatic gastrocnemius muscle biopsy. Transbronchial biopsy of lung and bronchial wall via the flexible fibreoptic bronchoscope is the procedure of choice in the diagnosis of diffuse pulmonary abnormality of probable sarcoid aetiology.

A minimum of four lung biopsies by transbronchical method optimizes the chances of securing a diagnosis.

Treatment

With better understanding of genetics and immunology, the treatment of sarcoidosis has improved in the last decade Most patients (>75)%) require only symptomatic therapy (Nonsteroidal anti-inflammatory drugs. While 15% of patients require treatment for persistent pulmonary disease. Cytokines play a pivotal role in the inflammation of sarcoidosis and anti-cytokine therapy is now corning forward, especially in chronic sarcoidosis. Decisions regarding treatment must be individualized and are best based on individual manifestations of the disease

Corticosteroids

There is no consensus on which patients should receive treatment how patients should be monitored, and the dose of corticosteroid once the decision to treat has been made. Long term glucocortocoids are associated with number of toxic side effectst. These are:Osteoporosis,cataracts, glaucocma, diabetesmellitus, electrolyte abnormalities, metabolic abnormalities, suppression of inflammatory and immune responses leading to opportunistic infections, cushingoid features, growth suppression in children hypertension, avascular necrosis of bone, myopathy alterations in mood psychosis peptic ulcer disease, pancreatitis.

Treatment of sarcoidosis can be divided into i) Thoracic sarcoidosis Ii) Extrathoracic sarcoidosis

Thoracic Sarcoidosis

initial treatment can be medical but lung transplantation may be required in those who are refractory to medical treatment and present with chronic lung failure

A. Medical treatment:

a. Gluco corticoids
b. Steroid sparing agent like methotrexate and azathioprine
c. Newer anti-cytokines: infliximab, pentoxifylline
d. Other alternatives: hydroxychloroquine, thalidomide, cyclosporine-

B. Surgical:
Lung or heart lung transplantation.

• Patients with stage I disease are often asymptomatic and usually have normal or near normal pulmonary function. They should be carefully observed with serial chest radiographs and pulmonary function tests initially every three months if disease progress radiographically or pulmonary function significantly declines treatment with steroid should be initiated • Patients with stage l I or stage l l l disease with normal or near normal pulmonary function and minimal symptoms should be followed serially And treated if they progress as described for stage I patient , Patients presenting with significantly abnormal pulmonary function warrant an empiric trial of steroids , • Patients presenting with fibrobulous disease (advance stage III or IV) also warrant an empiric trial of steroid .

Glucocorticoids

Phases of steroid application and side effects have been mentionedd above.

There is no universal agreement about the indications for corticosteroid therapy in stage II and stage III thoracic sarcoidosis. Treatment, when required, is initiated with prednisolone 20-40 mg, in daily or alternate day regimens and is continued for 3-6 months, whith a slow and graduated reduction in dosage may be attempted while clinical, radiographic and functional status is

monitored. If relapse is to occur, it is commonly seen when the prednisolone dose is reduced below 7.5-15 mg. This necessitates a return to a higher dose and further period (6-12 months) on a continuing maintenance dose commonly 10 mg daily, before further reduction in dosage is attempted. There is no need to continue the drug for more than 2 years whatever might be the Outcome [17] Despite treatment, some progress relentlessly to chronic pulmonary fibrosis.

Steroid Sparing Agent

Methotrexate

Methotrexate has been used in chronic sarcoidosis. A recent study shows that it can be a steroid sparing agent even in acute sarcoidosis

Azathioprine

It is an antimetabolite that inhibits purine synthesis. Azathioprine may provide a safe alternative to corticosteroids.

Cyclosporin

Cyclosporin acts by suppressing T helper lymphocyte. There has been, report of successful treatment of pulmonary sarcoidosis by cyclosporin Newer agents

Mycophenolate mofetil: A recent study shows that this novel drug cast be a steroid sparing agent in the treatment of pulmonary sarcoidosis Anticytokines : Tumor necrosis factor-alpha (TNF-a) plays an important role in the caseation of sarcoidosis. New agents pentoxifylline,thalidomide, and infliximab have proved useful in selected cases-

Lung Transplantation

Lung transplantation is a viable alternative for end-stage lung disease secondary to pulmonary sarcoidosis.

Extra Thoracic Sarcoidosis

Other than symptomatic relief, immunosuppression is the principal method of controlling the disease, and corticosteroids are the cornerstone of therapy spontanious remission has been observed but long term therapy often is required.

Ketaconazole, an imidazole anti-fungal, has got role in the treatment of refractory hypercalcaemic sarcoidosis[19]. Renal, CNS, symptomatic muscle and myocardial sarcoidosis are all indications for corticosteroid therapy. In case of endocrine organ failure, hormone replacement therapy is indicated,

Prognosis

Overall, the prognosis in sarcoidosis is good. Most individuals who present with the acute disease are left with no significant sequelae. Approximately half of all patients have chronic permanent organ dysfunction, but for most this is mild stable, and rarely progressive. In <IS to 20°10 of patients, the disease remains active or recurs intermittently [20].

Although corticosteroids are used for symptom relief and remain the mainstay of therapy, their efficacy is sometimes unpredictable- The best study up to date has been the recently completed multicentre trial from Britain sponsored by the British Thoracic Society. In this nonrandomized study, 55 patients were selectively observed treated, with corticosteroids[20].

Table-2

Results of multicentre trial sponsored by the British Thoracic Society. [20]

Characteristics	GroupL*	Group S*	P
Dyspnoea score(range1-4)	0.24	0.47	NS
Fibrosis score (range 0-16)	0.83	1.47	NS
FBV1-(%predicted)	95.9	86.9	0.05
VC (% predicted)	99.8	90.8	‘0.02
DLCO (% predicted }	84.3	77.7	NS
Weight gain (Kg)	+ 126	+0.99	0.02

* Long-term steroids
# Short bursts of steroids
NS = not significant

Conclusion

There are no data on incidence and prevalence of sarcoidosis in Bangladesh, but is seems that it is present almost in similar frequency as in the west. As there is often clinically confusion between sarcoidosis and tuberculosis, tuberculin test is an important diagnostic tool in developing countries. In our country, when a patient is diagnosed as having tuberculosis but not responding to antikoch's therapy sercoidosis should be considered.

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Tetralogy of Fallot (TOF) with Pectus Excavatum (PE): Total Correction for TOF and Ravitch Procedure for PE done - A Case Report

Kazi Shariful Islam[1], SAM Sabur[2], M. Alimuzzaman[3]

Abstract :
A fifteen years old boy was admitted in the department of cardiac surgery, National Institute of Cardiovascular Diseases (NICVD), Dhaka, with the diagnosis of Tetralogy of Fallot (TOF) with Pectus Excavatum (PE) deformity with mental retardation. Total correction for TOF was done through mid sternotomy under cardiopul monary bypass (CPB). Patient was weaned from CPB and Ravitch procedure was done for PE deformity. Patient recovered uneventfully except mild superficial wound infection at the lower end of the sternotomy skin incision which improved after adequate treatment. Patient was discharged from hospital with the advice to consult with psychiatrist for mental retardation and come after 4 weeks later for follow up. Subsequent follow up showed that marked symptomatic improvement for TOF with reasonable correction of PE deformity with good wound healing. This is for the first time in the operative history of cardiac surgery at NICVD, Dhaka that such a Ravitch procedure with total correction of TOF was done in the same sitting.

[Chest & Heart Journal 2004; 28(2) : 76-78]

Introduction:

Pectus excavatum is the most common congenital deformity of the sternum, occurring in as many as 1 in 300 to 400 live births.' The currently accepted cause of pectus excavatum is an excessive, misdirected growth of the lower costal cartilages, which form congenitally in a concave manner because of rapid growth and create a depressed sternum.[2,3] The first and second ribs as well as the corresponding costal cartilages, are often uninvolved, with the most severe depression just above the xiphoid process and continuing cephalad to the sternomanubrial junction. As the prevertebral space is reduced, the heart is usually depressed to the left. Although this deformity is usually present at birth, sporadic cases have occurred as late as adolescence.[4] A familial incidence of pectus excavatum has been desoribed.[5,6]

Most infants and young children with pectus excavatum are asymptomatic. When questioned carefully older children and teenagers may become aware that they do not have the same respiratory reserve as their peers. This finding is most noticeable when heavy and continuous exercise is performed. In some patients serious cardio-respiratory problems improve after surgical correction [7]. Frequent and recurrent lower respiratory tract infections and asthma may be seen in as many as 32% of patients with this deformity.[8] Scoliosis may be found in association with anterior chest wall deformities[9,10]. The abnormality usually involves a single thoracic curve originating between T_4 and T_9 inclusive.11 Mitral valve prolapse has also been observed, either clinically or echocardiographically, in 40 to 65% of patients.[12]

Children with pectus excavatum demonstrated low normal vital capacities that were unchanged by operation; however, total lung capacity and maximal voluntary ventilation significantly improved with corresponding increases in exercise capacity and maximal oxygen consumption.[13] Abnormal pre-operative pulmonary function assed

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by Xenon perfusion and ventilation scintigraphy has also significantly improved with surgical correction.[14]

The increase in right and left ventricular volumes after operation suggests that, if present cardiac compression may be improved by operative correction.[15] As many as two thirds of patients with Marfan's Syndrome may have associated pectus excavatum deformities.[16]

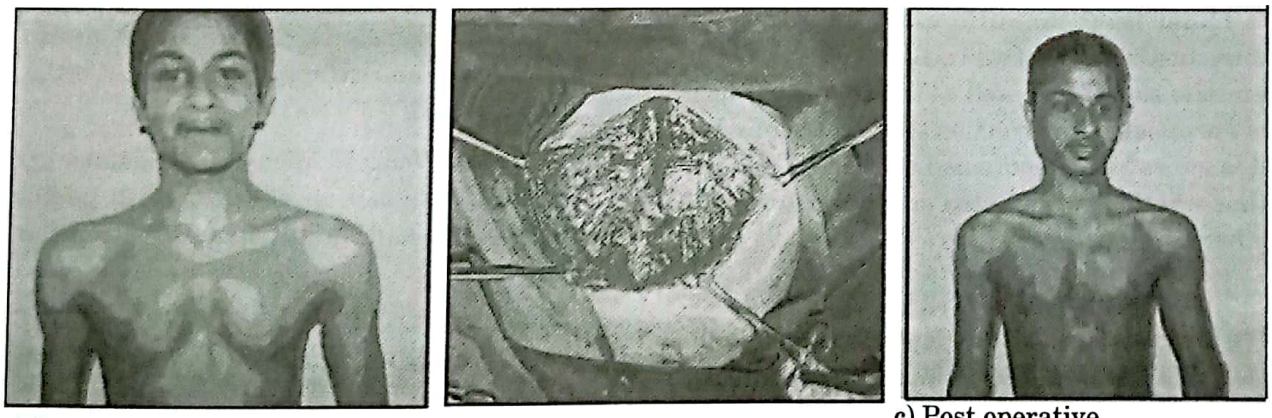
Indications for operation are: a) The desire for cosmetic improvement b) The presence of a pectus excavatum in all but very mild cases is an indication for correction. c) Patients with evidence of respiratory insufficiency, exercise limitation and recurrent respiratory infections also require operation.

Whenever possible, correction should be made before a child reaches school age (approximately 5 years old) to minimize the psychological impact of the deformity. Although surgical correction is possible in patients of any age, the operation technically easier and may have the best results when performed in younger patients.[17]

Case Report:

A fifteen years old boy was admitted in the cardiac surgery department of NICVD, Dhaka, Bangladesh on 22/01/2002 with the complaints of dyspnoea and bluish discolouration of the tongue and lips following moderate to severe exertion for the last 14 years. As per advice of the local doctor he was referred to NICVD for better management. He was mentally retarded and always smiling, cyanotic, Pulse 96/min regular B.P-110/70 mm of Hg with finger clubbing. Liver-not palpable. The central part of the anterior chest wall was depressed. Heart sounds were audible in all the areas, there was a systolic murmur heard in the left parasternal area and pulmonary area. All the relevant investigations were done before operation including cardiac catheterization. Patient was operative on 19/01/2002 under general anaesthesia and cardio pulmonary bypass (CPB). Mid sternotomy was done, CPB was established by bicaval and aortic cannulation. With antegrade intermittent cold cardioplegic arrest of the heart, total correction for TOF (closure of VSD, excision of parietal band of right ventricular outflow tract trans annular pericrdial patch across the annulus of pulmonary artery) was done.

Patient was weaned from CPB and decannulation done. Following it Ravitch procedure for PE was done. All the costal cartilages were removed sub-periosteally from both sides of the sternum starting from third to sixth costal cartilages. Osteotomy was done at the manubrial sternal junction on both sides of median stemotomy. The splitted sternum was approximated by encircling sternal wire. The sternum was elevated by a Kirschner wire under the sternum extending under both pectoralis major muscle. The skin wound was closed in layers keeping mediastinal drain and pacing wire after approximation of splitted sternum with encircling wire. Sub sequent follow up shows good healing of the wound with improvement of the PE defect. Post operatively patient suffered from mild superficial skin wound infection at the lower end. After proper treatment infection was controled.



a) Pre-operative b) Par-operative c) Post operative

Figure : *Ravitch procedure*

Discussion:

Pectus excavatum is quite a common chest wall deformity. From the NICVD registry; the combination of tetralogy of Fallot with PE was not found. For total correction of TOF midsternstomy was done first. In the Ravitch procedure for isolated pectus excavatum deformity, such sternotomy is not done. We removed all the costal cartilages starting from 3rd to 6th/7th on both sides. We apposed the sternotomy by encircling wire. It is some what a modification of Ravitch procedure. The procedure was performed after weaning the patient from CPB. We took around 1.5 to 2 hours to complete the procedure. Post operative recovery was uneventful, except superficial wound infection at the lower end of the skin incision. There are two other techniques for correction of PE deformity e.g. Sternal turnover technique, which was initially proposed by Judet (1954) and Jung (1956). The procedure was madofied and popularized in Japan by Wada and coworkers (1970). Another non operative techniques using orthotic support during childhood have produced satisfactory results in small groups of patients (Haje and Bowen 1992). Although alternative methods exists, most surgeons favour this technique or a modification thereof to correct pectus excavatum deformities.

Conclusion:

Correction of pectus excavatum deformity was done for the first time at NICVD, in combination with an open heart procedure for Tetralogy of Fallot. It is found from the different literatures that correction of the chest wall deformity (PE) improves exercise capacity as well as function of the heart of the patient. So correction should be done where it is indicated as mentioned before and at proper time whether it is isolated or in association with other disease.

Acknowledgements:

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Varied Presentation of Atrial Myxomas: Report of Six Cases

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Introduction :

Myxomas are most common type of primary cardiac tumour, comprising 30 to 50 percent of the total in most pathological series[1-5]. The mean age of patients with sporadic myxomas is 56 years and 70 percent are females. However, myxomas have been described in patients ranging in age from 3 to 83 years and are now not infrequently diagnosed in elderly patients, in whom the symptoms and signs of cardiac tumour may have been attributed to other causes for a substantial time. Approximately 86 percent of myxoma, occur in left atrium, and more than 90 percent are solitary[5,6]. In the left atrium, the usual site of attachment is in the area of the fossa ovalis. Myxomas also may occur in the right atrium and less often, in the right or left ventricle. Several tumors may occur in the same chamber or in a combination of chambers. Myxomas of the mitral and tricuspid valves lave been reported'". The clinical signs and symptoms produced by cardiac myxomas include non specific manifestations, embolization and mechanical interference with cardiac functions. Not surprisingly, the symptoms produced by cardiac myxomas may simulate a wide variety of other cardiac and non cardiac conditions. Myxomas are usually sporadic (90%) but may be familial (10%). Some patients with cardiac myxoma have a syndrome frequently called as "syndrome myxomas" or Carney syndrome- consists of cardiac myxoma, Spotty Skin pigmentation and peripheral and endocrine neoplasms. Some patients have been said to have the NAME Syndrome (Nevi, atrial myxoma, myxoid neurofibroma, ephelides) or the LAMB Syndrome (Lentigines, atrial myxoma, and blue nevi)[9]. A myxoma is neoplastic rather than a thrombotic origin is supported by the ultra-structural characteristics of the tumour, the results of biochemical analysis, the cultural properties of the tumour cell, and DNA analysis of the tumours. Six cases of myxomas are discussed below who have varied way of presentation.

Case Reports:

Case-1

Mrs. S.B., 36 years old from Gaibanda admitted in NICVD in May, 2003 with the complaints of palpitation for 4 months, shortness of breath for 4 months and transient loss of consciousness for 3 times within last 15 days. She has also low grade fever and arthralgia for last 4 months. On examination, patient was dyspnoeic having tachycardia but in sinus rhythms and her blood pressure was low -80/60 mm Hg. Her 1st heart sound was loud & second heart sound was normal. There was a mid - diastolic murmur in the tricuspid area, intensity varies with the change of posture. Her lungs were clear. ECG, CXR and echocardiogram were performed. ECG showed right atrial enlargement. 2-D Echocardiography showed an echogenic cardiac mass in the right atrium which prolapsed into the right ventricle through tricuspid valve during diastole. Mitral valves and Tricuspid valves were normal. The patient was diagnosed as a case of Right atrial myxoma and referred to cardio-thoracic surgery unit for immediate surgical removal.

Case-2:

Md. A.R, 30 years old from Panchagar, admitted in NICVD in December 2002. Patient was initially admitted in Rangpur Medical College Hospital for acute viral hepatitis but on physical examination, a diastolic murmur was found incidentally. Echocardiography was done and diagnosed as a case of left atrial myxoma. This patient had history of prolonged fever, arthralgia and weight loss. Patient was referred to cardio- thoracic surgery unit for immediate removal.

Case-3:

Mr. B.P, 16 years old from Bera, Pabna admitted in NICVD in May, 2003 with the complaints of abdominal and leg swelling for 7 days, shortness of breath for 2 months, repeated history of syncope for 7 months and prolonged low grade fever for I year. On examination, patient was dyspnoeic. His pulse was 120/min. blood pressure was low (90/70

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mm Hg), J.V.P was raised and there was ankle edema. Abdomen was distended and ascites was present. Liver was palpable 2 finger from right costal margin. His l st heart sound was loud and pulmonary component of second heart sound was also loud. There was a mid diastolic murmur at the apical area with variable intensity with changing posture. She had bilateral basal crepitation. Echocardiography (2 D & M-mode) showed left atrial myxoma attached at the inter atrial septum. There was also pulmonary hypertension with mild MR with mild TR. He was diagnosed as case of left atrial myxoma with congestive cardiac failure with pulmonary hypertension. He was sent to cardio- thoracic surgery unit for urgent operation.

Case-4:

Mrs. S, 32 years old from Rajshahi, was admitted in NICVD in November, 2002 with complaints of chest discomfort, palpitation, paroxysmal dyspnoea, dizziness and prolonged low grade fever for seven months. On examination, patient was moderately anaemic, pulse 120/min, B.P. 95/70 mm Hg. Her first heart sound was loud. Second heart sound was normal and there was a mid-diastolic murmur in the apical area. There was no tumor plop. Echocardiography showed left atria] myxoma. He was referred to cardio- thoracic surgery unit for immediate removal.

Case-5:

Mrs. F, 30 years old from Feni, was admitted with swelling of face, leg swelling, abdominal swelling for 5 months, palpitations and shortness of breath for 2 years, generalized weakness with low grade fever for 2 years. On examination, patient had puffy face with engorged vein in the neck. Patient was dyspnoeic and mildly anemic, ascites and ankle edema was present. Pulse was 110/min, and B.P. was 90/70 mm Hg. Her first heart sound was loud and second heart sound was normal. She had mid diastolic murmur in the tricuspid area and its intensity was changing with posture. CXR-P/A view showed cardiomegaly. Echocardiography showed right atrium is hugely dilated with a big mass in the right atrium, attached with inter atria] septum and moderate pericardial effusion. She was diagnosed as a case of right atria] myxoma with congestive cardiac failure (CCF). She was referred to cardio- thoracic surgery department for surgical removal.

Case-6:

Md. A.H, 55 years old admitted in NICVD in August 2003. He had complaints of chest discomfort, palpitation, paroxysmal dyspnoea, dizziness and prolonged low grade fever for several months. He had also history of syncopal attack. On examination, patient was mildely anaemic, pulse 120/min, B.P. 100/70 mm Hg. His first heart sound was loud. Pulmonary component of second heart sound was also loud and there was a mid-diastolic murmur in the apical area. Echocardiography showed large (80x29mm) left atrial myxoma (Fig-1) associated with pulmonary hypertension. He was referred to cardio- thoracic surgery unit for immediate operation. Myxoma was removed successfully (Fig-2) and patient is now symptom free.

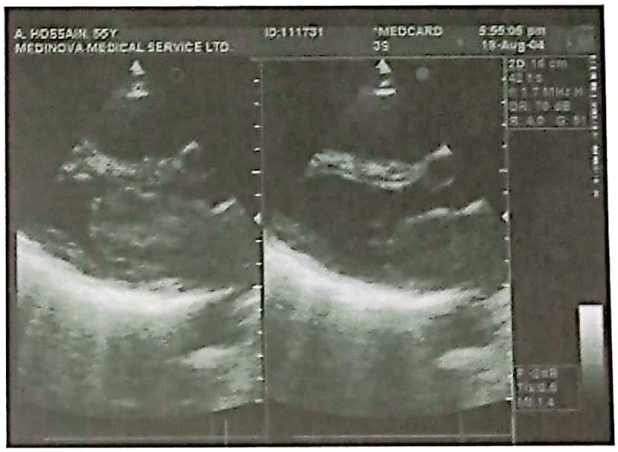

Fig-1: *Two dimentional echocardiogram of a patient with left atrial myxma. The tumour appears as an elongated mass in the left atrial cavity. During diastole (left), the tumour prolapses through the mitral orifice in to left ventricular cavity, completely filling the valve orifice.*

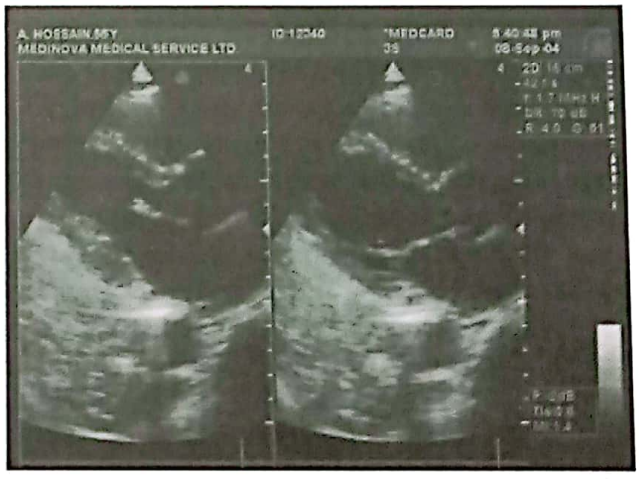

Fig-2: *Two dimentional echocardiogram of the same patient after successful surgery.*

Discussion:

Intracardiac myxoma is the most frequent benign tumour of the heart and constitutes nearly 50 percent of all benign cardiac tumors. About 75 percent of these are located in the left atrium; usually from region of fossa ovalis. Myxoma arise from mural endocardium. A neoplastic rather than a thrombotic origin of myxoma is supported by the ultra-stuctural characteristics of the tumor[10,11]. Primary cardiac tumors may be misdiagnosed as bronchial asthma, mitral stenosis, neurological disorder or pyrexia of unknown origin because history and clinical examination may be inconclusive. But a noninvasive 2-D echocardiogram can give conclusive diagnosis. Patient with the atrial myxoma may remain asymptomatic but generally present with symptoms of triad of manifestations-constitutional, embolic and obstructive. Systemic manifestation which noted in 90% cases- consist of fever, malaise, weight loss, anaemia, high ESR and elevated immunoglobulin level (usually IgG) and likely to be due to the tumor's synthesis and secretion of IL-6. In 50% cases arterial emboli occur involving brain, kidney, heart and extremities. Left atrial myxoma may obstruct either mitral valve or pulmonary venous drainage producing pulmonary venous & arterial hypertension with secondary right heart failure. Symptoms include dyspnoea, orthopnea, paroxysmal nocturnal dyspnoea, pulmonary edema, hemoptysis, dizziness & syncope, and occasionally sudden cardiac death, changes of position may also alter symptoms[12]. Right atrial myxoma frequently produce symptoms of right heart failure, including fatigue, peripheral edema, ascites, hepatomegaly and produce 'a' waves in the jugular vein pulse. Right atrial hypertension may cause right-to-left shunting through a patent foramen ovale, with systemic hypoxia, cyanosis, clubbing and polycythemia. The average time interval from the symptomatic presentation to the correct diagnosis of right atrial myxoma may be years. The murmurs are generally the result of tumor obstruction to tricuspid valve flow or of tricuspid regurgitation caused by tumor interference with valve closure or valve destruction caused directly or indirectly by the tumor. Right atrial myxomas have been misdiagnosed as Ebsteins anomaly of the tricuspid valve, constrictive pericarditis, tricuspid stenosis, carcinoid syndrome, superior vena caval syndrome and cardiomyopathy. Pulmonary embolism and pulmonary hypertension occur and may simulate classic thrombo-embolic disease [13-16]. Finding of loud S, in the absence of a short PR interval or a mitral diastolic murmur should raise the suspicion of a left atrial tumor. In many cases, an early diastolic sound, termed a tumor plop, case be identified. It is thought to be produced as the tumor strikes the endocardial wall or as its excursion is abruptly halted. Tumor plop is frequently confused with the opening snap or the S_3. The ECG and X-ray finings may be normal or like that of mitral stenosis but sinus rhythm is usual. The 2-D echocardiogram is diagnostic & demonstrate its location, origin and movement of intracardiac mass. Trans-esophageal echocardiography has potential advantage of improved resolution of the tumor and its attachmant. Trans-esophageal echocardiography has been used to guide percutaneous biopsy of a right atrial myxoma. Radionuclide ventriculography has a lower rate of resolution with less sensitivity than echocardiography. Computed Tomography has advantage of a high degree of tissue discriminate which may allow definition of the degree of intramural tumor extension, evaluation of the extracardiac structures and the ability to construct images in any place. MRI may be of considerable value in detecting and delineating cardiac tumors and in some cases my depict the size, shape and surface characteristics of the tumor more clearly than two dimensional echocardiography. Because of the risk of embolisation, cardiac catheterization and coronary angiography are only indicated for diagnosis of concomitant cardiac or coronary disease. Treatment of atrial myxomas consists of prompt surgical resection of the tumor with a small rim at the base. Numerous reports document complete cure of left and right atrial myxomas with follow-up periods of 10 to 15 years. In about 1 to 5 percent of cases, a recurrence or second cardiac myxomas has been reported after resection of the initial myxoma. Possible causes of the second tumor include incomplete excision of the original tumor with regrowth, growth from a second "Pretumorous" focus or intracardiac implantation from the original tumor. Laser photocoagulation of a 1-cm area around the stalk attachment site has also been suggested as a way of eradicating pretumorous cells.

So, atrial myxomas are often misdiagnosed as mitral stenosis, pyrexia of unknown origin, ischemic heart disease, thrombo-embolic disorder or neurological disorders clinically. These cases can be diagnosed reliably by echocardiography. Following diagnosis they are to be treated surgically as early as possible to save life of these patients.

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