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CONTENTS

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CONTENTS

Chest & Heart Journal
Vol. 27, No.-2, July 2003

ORIGINAL ARTICLES

Prednisolone as Therapeutic Adjunct in Tuberculous Pleural Effusions

**Shah Md. Saifur Rahman[1], Md. Abdul Qayyum[1], Mirza Mohammad Hiron[2]
Md. Mostafizur Rahman[3], Md. Rashidul Hassan[4], Md. Ali Hossain[4], Md. Atiqur Rahman[5]**

Abstract :

Tuberculous pleural effusions remain an important treatable cause of exudative pleural effusions. It results significant morbidity by producing cough, fever, chest pain and / or chest heaviness and breathlessness. If untreated or improperly treated extensive pleural thickening may result from pleural adhesion and fibrosis. Latter there are also chance of developing pulmonary parenchymal tuberculosis.

Treatment of tuberculous pleural effusions requires anti-tuberculous chemotherapy. Prednisolone acts as a therapeutic adjunct to produce significant beneficial effect by rapid symptomatic improvement in a large number of patients with quicker absorption of fluid from pleural space, thus reducing the development of adhesion between pleural surface and formation of thickened pleura.

A total number of 120 subjects were selected finally in this study. They were divided into two treatment groups by simple random technique. Treatment group A (n=57) and treatment group B (n=63). Group A patients were treated with anti-tuberculous drugs only which included Rifampicin, INH, Ethambutal and pyrazinamide. Group B patients were treated with anti-tuberculous drugs along with prednisolone in a dose of 40 mg / day for initial 4 weeks then tapered gradually.

Their clinical improvement, change in lung function, radiological clearance of pleural fluid and development of any complication were noted. In this study patients of treatment group B showed better clinical and radiological improvement when compared with patients of group A. These results were statistically significant hence suggesting the use of prednisolone along with antituberculous drugs while treating patients of tuberculous pleural effusions.

[Chest & Heart Journal 2003; 27(2) : 64-69]

Introduction :

Tuberculous pleural effusion is the most common cause of exudative pleural effusions in many parts of the world. In the USA approximately one in every thirty cases of tuberculosis is of tuberculous pleurisy[1]. In Bangladesh, 6 million people are estimated to be suffering from tuberculosis. Approximately a quarter million new cases and 80 thousands deaths occur annually[2]. Though there is no epidemiological data regarding pleural tuberculosis but a larger proportion of our hospital admission due to tuberculosis are cases of pleural effusions. The effusion results from actual infection of pleura by tubercle bacilli and tuberculin

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hypersensitivity plays an important role in potentiating the reaction[3]. The clinical presentation of tuberculous pleurisy covers the spectrum from acute illness simulating bacterial pneumonia to an indolent disease first suspected on a chest radiograph in a patient with minor constitutional symptom. The acute illness is charecterised by cough and pleuritic type of chest pain in about 75% of cases. The chronic form presents with low grade fever, weakness and weight loss. Breathlessness due to respiratory insufficiency occurs in cases of pleural effusions and sometimes may be severe. Breathlessness is mostly attributable to reduced diaphragmatic movement. Extensive pleural fibrosis from long standing pleural effusions may produce severe ventilatory impairment with subsequent death from respiratory failure[4]. WHO recommended anti-tuberculous treatment regimens are suitable for treating patients with tuberculous pleural effusion. This regimen consists of standard six months short course chemotherapy with an initial phase of two months rifampicin, isoniazid ethambutal or streptomycin and pyrazynamide followed by a four months continuation phase of rifampicin and isoniazid[5]. This treatment results absorption of pleural fluid along with healing of tuberculous lesion. Corticosteroid have definitive role in the treatment of tuberculous pleural effusion. It is generally accepted that the longer an effusion is present the greater the likelihood of extensive fibrin deposition on pleural surface with later development of adhesion between the leaves of the pleura. The use of Prednisolone along with WHO recommended antituberculous chemotherapy results more rapid clinical improvement along with quicker absorption of pleural fluid. Thus sign symptoms of pleural effusion disappear earlier along with diminished chance of development of pleural fibrosis.

Materials and Methods :

This was a prospective case control study carried out in the National institute of diseases of the chest and hospital (NIDCH), Mohakhali, Dhaka, during the period of January 1998 to December 1999. A total number of 146 patients of pleural effusion were selected consecutively in this study on the basis of clinical and radiological findings. Among them 120 patients were eligible for final analysis who fulfilled the inclusion criteria and had no exclusion criteria. To be included in this study following criteria were considered essential: (a) Symptoms of pleural effusion; (b) Clinical evidence of pleural effusion; (c) Radiological evidence of pleural effusion; (d) Pleural fluid analysis suggestive of tuberculous pleurisy, and/or pleural biopsy showing granuloma consistent with tuberculousis. Exclusion criterias for this study were (a) History of taking anti-tuberculous drugs; (b) Diseases association where steroid and anti-tuberculous drugs are contraindicated; (c) Extremes of ages (<10 and > 70 years); (d) Poor cooperation of patient. Informed written consent was obtained in each case and a proforma with questioner was filled and signed by every patient. They were divided into two treatment groups by simple random technique. Group A were treated with antituberculous drugs which included rifampicin, isoniazide, ethambutal and pyrazinamide. Rifampicin and isoniazide was given for six months with ethambutal and pyrazinamide for initial two months. Group B were treated with prednisolone along with antituberculous drugs. Prednisolone was given in a dose of 40 mg/ day for initial four weeks and then tapered gradually. Following investigations were done: (1) Chest X-ray: a) P /A view, to see the presence of pleural effusion; its site, side and approximate amount. Effusions were considered small when it occupied one-third of hemi-thorax; moderate, when less than two-third of hemi-thorax were occupied; and large, when two-third or more of a hemi-thorax were occupied by effusion. Postero-anterior film was also taken to see pulmonary parenchymal lesion associated with pleural effusion. b) Lateral decubitus view to detect small effusion and thickened pleura. (2) Sputum examination: Sputum was examined for acid-fast bacilli, for gram staining, for malignant cell and for culture / sensitivity. (3) Tuberculin test: By montoux method, 10 TU of purified protein derivative; contained in 0.1 ml of normal saline was injected intradermaly into the flexor surface of one forearm. Area of induration 10mm or more after 72 hour were considered positive. (4) Thoracentesis, pleural fluid examination and pleural biopsy Aspiration : of pleural fluid relieved dyspnoea, fluid was sent for biochemical analysis and cytological examination including those for malignant cells.

Pleural biopsy was done for histo-pathological examination. (5) Pulmonary function test, Principal pulmonary function parameter was FEV_1, FVC and FEV_1/FVC ratio. Ventilatory impairments were classified as obstructive, restrictive or mixed pattern. Restrictive impairments were further classified as mild, moderate and severe when FVC was reduced from normal to 66-80%, 50-65% and less than 50% of the predictive value respectively.

All patients were treated with anti-tuberculous chemotherapy which included Rifampicin Isoniazid Ethambutal and pyrazinamide in adequate dosages. Group B patients were treated with prednisolone as an adjunct. Regular follow up was done and in each day patients were asked if they noticed any change in their condition compared with pre-treatment state. This was recorded as worse than usual, same as usual, or better than usual.

Pulmonary function test were repeated after two weeks of treatment and changes in pulmonary function were noted for both group of patient. For every patient chest X--ray was done monthly during their hospital stay and then on every follow up visit. Evidence of complete radiological clearance or development of thickened pleura were noted. Heeling of pulmonary parenchymal lesion were also noted in both group of patients to see any difference between the two treatment group.

Each patient was observed daily for any side effect of anti-tuberculous drugs or steroid. Necessary measures were taken to overcome the side effects of drugs.

Results :

Symptom and symptomatic improvement in two treatment group are shown in Table 1. Major symptoms in both treatment group A and treatment group B were cough, fever, chest pain and/or chest heaviness and dyspnoea. In treatment group A cough was present in 47 patients, fever in 39 patients, chest pain and/or chest heaviness in 41 patients and dyspnoea in 38 patients. In treatment group B, cough was present in 48 patients, fever in 47 patients, chest pain and/or chest heaviness in 46 patients and dyspnoea in 45 patients. Chest x-ray showed pleural effusion in all 120 patients. Seventy seven patients had right sided and 43 patients had left sided effusion. In treatment group A, 21 (36.84%) patients had small effusions, 32 (56.14%) patients had moderate effusions and 4 (7.01%) patients had large effusions. In treatment group B, 25 (39.68%) patients had small effusions. 31 (49.20%) patients had moderate effusions, and 7 (11.11%) patients had large effusions (Table II).

Sputum smear examination showed 82.5% patients were sputum negative for acid fast bacilli (AFB). Tuberculin test showed induration of varying diameter after 72 hours. It was <10mm in 15.87%; 10-20 mm in 46.03% and >20mm in 38.09% patients. Pleural fluid analysis showed protein >50gm/dl in 80.75% and glucose 50--60 gm/dl in 71.42% patients. Predominant cells were lymphocytes in 80.95% patients. Pleural biopsy showed caseating granuloma in more than 80% cases. Pulmonary function test showed restrictive pattern of impairment in all 120 patients.

Two weeks after starting treatment, symptomatic improvement was noticed in both group of patients. In group A, 19 patients out of 47 who complained of cough initially were free of this symptom where as it was 33 out of 48 patients in group B who were free of cough by this time. Fever was absent in 15 patients out of 39 in group A and in 32 patients out of 46 in group B after fourteen days of treatment. During this period 11 patients in group A and 32 patients in group B were free of chest pain and chest heaviness and 10 patients in group A and 29 patients in group B were relived from dyspnoea.

Complete radiological clearance of effusion was observed in some patients of both treatment groups after 8 weeks of treatment.12 (21%) patients in group A and 27 (42.5%) patients in group B showed complete radiological clearance of effusion during this period (Table III).

Pulmonary function test (PFT), after 14 days of treatment, showed return to normal in some patients of both treatment groups. During this period PFT became normal in 12 (21.05%) patients in group A and 31 (49.2%) patients in group B. In group A, 14 (24.56%) patients showed mild restriction; 28 (49.12%) patients showed moderate restriction and 3 (5.26%) patients showed severe restriction. In group B, 18 (28.57%) patients showed mild restriction; 11 (17.46%) patients showed moderate restriction and only 1 (1.58%) patient showed severe restriction (Table IV).

During follow-up, chest x-ray was done regularly to detect pleural thickening or any other complications. Thickened pleura was detected in 8 (15%) patients in group A and in only 1 (<1 %) patient in group B (Table V).

Table -I

Symptoms and Symptomatic improvement in different treatment group

Symptoms	Treatment Groups	Symptomatic Improvement		P-Value
		Improved	Not Improved	
Cough	A (n=47)	19	28	S P=<0.01
	B (n=48)	33	15	X^2=7.77
Fever	A (n=39)	15	24	S P=<0.01
	B (n=47)	32	15	X^2=7.52
Chest pain and heaviness	A (n=41)	11	30	S P=<0.01
	A (n=46)	30	16	X^2= 12.82
Dyspnoea	A (n-38)	10	28	S P=<0.01
	B (n=45)	29	16	X^2=7.18

Table -II

Amount of pleural effusion

Extent of effusion (Chest-X-ray)	No. of cases in treatment groups				
	Group A (n= 57)	Percentage (%)	Group 8 (n=63)	P-value Percentage (%)	
Small effusion	21	36.84	25	39.68	NS P>0.05 (Z= 0.52)
Moderate effusion	32	56.14	31	49.20	NS P>0.05 (Z= 0.78)
Large effusion	4	7.01	7	11.11	NS P>0.05 (Z= 0.75)

Table - III

Complete Radiological clearance in different treatment groups

Treatment Group	Complete Radiological Clearance (8 Weeks)	
	Cleare	Cleare
Group A	12	45
Group B	27	36
χ^2 = 6.49, df = 1	P=< 0.02	

Table IV

Results of PFT in two treatment groups

Impairment type (Restrictive) (n = 120)	Treatment group				P-value
	Group A (n= 57)	Percentage (%)	Group B (n=63)	Percentage (%)	
Mild restriction	14 (n = 20)	24.56	(n = 21)	28.57	-
Moderate restriction	28 (n = 33)	49.12	11 (n=35)	17.46	S P<0.001 Z= 3.88
Severe restriction	3 (n = 4)	5.26	1 (n = 7)	1.58	-
Normal	12 (n = 0)	21.05	31 (n = 0)	49.20	S P<0.001 Z= 3.89

Table-V

Detection of Thickened Pleura (End of treatment)

Treatment Group	Thickened Pleura on Chest X- Ray	
	Present	Absent
Group A	8(15%)	49(85%)
Group B	1 (<1%)	62 (>99%)

χ^2= 5.02 (after yates correction) df=1 P=<0.05

Discussion :

In this study the clinical and demographic profile shows that in group A age distribution of patients range from 16 years to 46 years and the mean age was 27.06 years. In group B, the age range from 16 to 45 years and the mean was 26.41 years. This age distribution showed that tuberculous pleural effusion affected mainly young and middle aged peoples. 54% cases in this study were in the range of 26-35 years. This result coincides with the study of Teklu where 50% patients were young and middle aged[6]. No of male patient in group A were 41 and female 16. Male female ratio in this group was 2.5:1. In group B the number of males were 45 and that of females were 18. Here the male female ratio was also 2.5:1. In the previous study by Lee et al; male female ratio were 1.7, where the sample size was much smaller[7]. Patients included in this study came from different occupations. Workers, farmers; house wives, service holders, students and businessmen all were included and they came from all six divisions of Bangladesh. Regarding socioeconomic status, majority of patients in this study were poor who in group A they were 56.17% and in group were B 52.38%; next were the middle class whose percentages were 31.17% and 34.92% in group A and group B respectively. Rich were very few in this study, 7 (12.28 %) patients in group A and 8 (12.69 %) patients in group B were rich only. This result also coincide with previous study where most of the patients were poor[8].

Tuberculin test was positive in 101 patients (84%) in this study. only 19 patients were tuberculin negative. Pleural fluid cytology revealed that lymphocytes were predominant cells in 47 (82.45 %) patients in group A and 51(80.95 %) patients in group B. These findings were consistent with previous reports where in 80% cases tuberculin test was positive and the 80% of the predominant cells in pleural fluid cytology were lymphocytes[9].

In this study major symptoms of patients of both treatment group A and group B were cough, chest pain or chest heaviness, fever and dyspnoea. These symptoms were also present in cases of pleural effusions studied previously by several researchers. After starting chemotherapy symptomatic improvement occurred in both group of patients

but more rapid improvement was noticed in group B who took prednisolone along with antituberculous chemotherapy. Prednisolone used as a therapeutic adjunct in tuberculous pleural effusion followed the dose regimen as advised previously in the treatment of tuberculosis. It was 40mg per day for initial four weeks and then gradually tapering the dose[10,11]. Comparison of symptomatic improvement between group A and group B showed that after two weeks of treatment with prednisolone along with anti-tuberculous drugs cough were absent in 33 (68.75%) patients out of 48 in group B, whereas it was absent only in 19 (40.42%) patients out of 47 in group A who were treated with anti-tuberculous drugs only. This result of better improvement in group B is statistically significant (p = <0.01). Fever was present in 39 patients in group A and 47 patients in group B. After two weeks treatment 15 (38.46%) patients in group A and, 32 (68.08%) patients in group B were free of this symptom. Here also significant improvement was noticed in group B who were treated with prednisolone as an adjunct along with anti-tuberculous drugs (p=<0.01). Chest pain and/or chest heaviness was present in 41 patients in group A and 46 patients in group B. 11 (26.82%) patients in group A and 30 (65.21%) patients in group B were free of this symptom after two weeks of treatment. This shows statistically significant improvement in group B (p=<0.01) who were treated with prednisolone as a therapeutic adjunct. Dyspnoea was relieved in 10 (26.31%) patients, out of 38, in group A and in 29 (64.45%) patients, out of 45, in group B. The improvement in patients of group B was statistically significant (p=<0.01).

Rapid fluid absorption from pleural space to show complete radiological clearance was noticed in patients of group B in whom prednisolone was added along with anti-tuberculous drugs. Here 12 (25.53%) patients in group A and 27 (42.86%) patients in group B showed complete radiological clearance after 8 weeks of treatment. The difference of improvement is statistically significant (p=<0.02).

In this study, pulmonary function test showed restrictive impairment in all 120 patients before starting treatment. After pleural fluid aspiration and starting of chemotherapy lung function improved in both group of patients with return to normal. 12 (21.05%) patients in group A and 31 (49.20%) patients in group B showed normal lung function. This result also coincides with the study of others and is highly significant (p=<0.001).

After completion of treatment 8 (15%) patients in group A and 1 (<I%) patient in group B showed pleural thickening on chest x-ray, which indicates significant (p=<0.05) prevention of fibrogenic process in patients of pleural effusion who are treated with prednisolone along with anti-tuberculous drugs.

Side effects of anti-tuberculous drugs or prednisolone was minimal in different studies. In our study, epigastralgia was the principal complaints in few patients which was properly managed conservatively.

References:

1. Mehta J.B, Dutt A, Harvill L, Mathews K. M. Epidemiology of extra pulmonary tuberculosis. Chest. 1991; 99 : 1134-1138.
2. Bennoor. K. S, Mahmood A. M, Huq S. Multi drug resistant tuberculosis; Problem on the rise. Abstract book of chest and heart association. 1998; 1: 3.
3. Stead W W, Bates J H, Evidence of silent bacilemia in primary tuberculosis. Ann Inter Med. 1955; 74: 559-561.
4. Berger H W, Mejia E, Tuberculous pleurisy. Chest. 1973; 63 : 88-92.
5. Smith M H, Mastaniotis N, Treatment of tuberculous pleural effusion with particular reference to adrenal corticosteroid. Chest. 1958; 10: 1075-1087.
6. Teklu B, Symptom of pulmonary tuberculosis in smear positive cases. Tubercle. 1993; 74: 126-128.
7. Lee C H, Ian W J, Tasai Y H, Chiang Y C, Corticosteroid in the treatment of tuberculous pleurisy. Chest, 1988; 94: 1254-1259.
8. Dubos R J, Biologic and epidemiological aspect of tuberculosis. Am Rev of Tuberc. 1953; 68, 1: 1-7.
9. Yam L T, Diagnostic significance of lymphocytes in pleural effusions. Ann of Int Med. 1967; 66, 5: 972-982.
10. Seaton A, Seaton D, Leitch A G, Crofton and Douglass respir dis. 1990; 4(edn) : 15, 423-435.
11. Dutt A K, Dory R M, Stead W W, Short course chemotherapy for pleural tuberculosis. Chest. 1986; (90) 1: 112-115.

Chest & Heart Journal
Vol. 27, No.-2, July 2003

Effect of Beta Carotene on Acute Respiratory Infection in a Girls School of Dhaka City

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Abstract :

Vitamin A deficiency has been associated with increased rates of morbidity among young children. Some recent studies stated that vitamin A deficiency is related to acute respiratory infections. The aim was to investigate whether Vitamin A supplementation can reduce the attack rate of ARI in adolescent girls. A cross-sectional case control study was carried out among randomly selected 150 students aged 13 – 15 years (100 study and 50 control) of class IX and X of Sher-e-Bangla Nagar Govt. Girls High School in Dhaka. Base line data about socio-economic information, food habit and disease history of ARI was collected through a structured questionnaire. Height, weight and MAC of the girls were measured before and after 3 months intervention. An intervention of four biscuits made by Red Palm Oil containing 1500 mg of b-carotene were fed per girl everyday for 3 months in order to provide about one third of RDA of Vitamin A. ARI attack rate decreased to 17% from 38% at base line in the study group ($p<0.02$) with the reduction of ARI by 55.26%, while in control group ARI increased by 5.56%. Mean intake of vitamin A was not significantly different between the two groups. In the study group mean height, weight and MAC increased significantly ($p<0.001$) after intervention, but in control group although increased but insignificantly ($p<0.05$). Normal BMI in study group increased by 44% after intervention where as in control group by only 2%.

The findings reveal that because of vitamin A intervention there is reduced rate of ARI along with change in various parameters of nutritional status.

[Chest & Heart Journal 2003; 27(2) : 70-76]

Introduction :

Vitamin A deficiency is a major public health problem in many areas of the less industrialized world. Vitamin A deficiency has been associated with increased rates of morbidity among children[1]. In developing countries adolescent girls are worst sufferer form vitamin A deficiency[2]. And it may contribute to severe malnutrition, like growth retardation, under weight, anaemia, ARI and diarrhoea.

In Bangladesh the prevalence of vitamin A deficiency has decreased from 3.6% in 1982-83 [3] to about 1% in 1996 [2]. Intake of vitamin A decreased from 1670 IU in 1962 – 64 [4] to 730 IU in 1975-76 [5] and then increased to 763 IU in 1981-82 [6] which further increased to 1668 IU/person /day in 1995-96. Around 1.7% of children aged between 6-71 months in 1989 were suffering from night blindness[7], when compared with that of 1982-83 [3]. More than one million children (6-71 months) worldwide go blind every year due to chronic vitamin A deficiency and almost half of them die within a year of becoming blind[7]. Vitamin A deficiency has been associated with other morbidities beyond classic deficiency symptom. In recent studies, it has been found that vitamin A deficiency is related to ARI.

Early reports stated that children who went blind during chronic debilitating illness like encephalitis and tuberculosis, were complicated by severe pneumonia, diarrhoea and emaciation[8]. Early clinical reports also suggested that severe vitamin A deficiency has been associated with respiratory tract infections,[9-15]. Lower respiratory disease was

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associated with vitamin A deficiency in 8 of the cross-sectional clinic and population based studies[16]. Vitamin A is an important antioxidant vitamin which has the property of protecting infectious diseases. Scrimshaw et al, stated that "no nutritional deficiency is more consistantly synergestic with infectious disease than that of vitamin A[17].

Previous studies have been carried out primarily based on clinical examination for signs of vitamin A deficiency but how to solve vitamin a deficiency have been studied in a limited way. For a long term measure to solve vitamin A deficiency, a food based approach is of utmost importance. Red palm oil is the richest natural sources of b-carotene (pro-vitamin A) may be an easy solution to this problem. Because palm oil contains a large number of carotenoids which are the precursor of vitamin A. Red Palm Oil (RPO) supplementation has also been used successfully to elevate vitamin A status of lactating mothers in some developing countries. Thus PRO would be ideal for use in food-based strategies to prevent vitamin A deficiency in countries where the nutritional disorder is still a serious public health problem[18].

While suffering from ARI Bangladeshi people use to consume seven seas cod liver oil. But now people are using Red Palm Oil as a source of vitamin A supplementation which is cheap and devoid of smell. The present study was designed and conducted among adolescent girl students of a secondary school in Dhaka city to investigate whether vitamin A supplementation (b-carotene supplementation) can reduce the prevalence of ARI or not.

Materials and Methods :

A cross sectional case control study was conducted in 150 (100 study group and 50 control group) girl students aged 13 - 15 years of class IX and X of Sher-e-Bangla Nagar Govt. Girls High School in Dhaka city with due permission of the Headmistress. The students also signed on informed consent form. The study was carried out during the period from February to April, 2001.The height, weight and MAC were measured before starting intervention. Data regarding socio-economic, food habit and disease history about ARI were collected by interviewing the girls through a structured questionnaire. After collection of baseline data intervention of 4 biscuits per girl were fed every day for 3 months. Data collection and biscuit feeding progromme was conducted by five trained paramedics under supervision of a doctor. The biscuits were made by Red Palm Oil (RPO) at a rate of 1 tea spoonful (5 gm) for 4 biscuits. These 4 biscuits contained 1500 mg of B- carotene equivalent to 250 mg of retinol equivalent i.e. 832 I.U. The goal of RPO containing biscuits supplementation was to provide one third of the RDA of vitamin A (retinol equivalent) to the girls beyond their usual intake of vitamin A through daily food consumption. The composition of one biscuit was as follows:

Carbohydrate -59.8%, Protein - 9.1%, Fat-17.1% , and b-carotene -375 mg.

After 3 months intervention height, weight and MAC of the girls were again measured and recorded. After necessary editing collected data were analyzed in computer using SPSS software package with appropriate statistical tests as needed.

Results :

A total of one fifty adolescent girls students were included in the study of whom 100 and 50 respectively constituted study and control group. Table-1: shows that majority of the girls were between 14 and 15 years of age in both study and control groups. The mean age was 14.27 $\pm$ 0.68 in study group and 14.28 $\pm$ 0.648 in control group.

Table 2 shows that mean vitamin A intake of study and control groups were 748.52 $\pm$ 625 and 776.98 $\pm$ 725 respectively. By age group, the mean vitamin A intake of 13, 14 and 15 years old girls of study group were 625.25 $\pm$ 281, 730.16 $\pm$ 878 and 890.15 $\pm$ 368 I.U. respectively, the corresponding figures for control group were 680.52 $\pm$ 291, 744.26 $\pm$ 974 and 906.17 $\pm$ 408 I.U. respectively. The mean intake in both groups were not significantly different.

Table-3 Shows that the total food intake of study group (609.96+158) was less than control group (620.18$\pm$17).Mean intake of all the nutrients in study group were lower in comparison to those in control group. But the differences were not significant between two groups.

Table-4 shows that before intervention 30% of the study girls had average growth, while the rest 70%

were below average including 42% short girls. After intervention the proportion of girls having average growth increased to 45%. On the other hand, in control group 27% girls had average growth at the begining which remained unchanged after intervention.

In respect of weight for age, 30% girls of study group had average weight for their ages including 1% having above average weight, while in control group the proportion of girls having average weight was also 30%. After intervention of the proportion of study girls with average weight increased to 65% including 1% having above average weight, while in control group the proportion of girls having average weight remained unchanged (Table 5).

Figure-1 & 2 show that baseline height and weight of the study group were positively correlated with the height and weight obtained after 3 months intervention ($r=0.80$, $p<0.001$ and $r=0.68$, $p<0.001$) but no significant correlation were observed in case of control group.

Body mass index (BMI) of the study girls showed that 30% had normal BMI, while 64% were malnourished, the corresponding figures for control group were 28 and 68% respectively. After intervention normal BMI in study group increased by 44% from 30 to 74 %, while that increased in control group by only 2% from 28 to 30% (Table 6).

Table-7 shows that in study group ARI was 38% at baseline and after 3 months intervention it significantly reduced to 17% with a reduction of ARI by 55.26%, while in control group, the corresponding rates were 36% and 40% respectively with ARI attack rate increased by 5.56% indicating that vitamin A has contributed in reducing the risk of deficiency by 2.48 times.

Table-I

Age distribution of all subjects

Age in year	Study gr. (No.=100)		Control gr.(No.=50)	
	No.	%	No.	%
13	13	13.0	5	10.0
14	47	47.0	26	52.0
15	40	40.0	19	38.0
Mean±SD	14.27±0.68		14.28±0.648	
z-test for Equality of Means at 5% level		P>0.05 NS		

Table-II

Comparison of Vitamin A intake between two groups by age

Age in year	Intake of Vitamin A (I.U)				z-test for
	No.	Study group Mean±SD	No.	Control group Mean±SD	Equality of Means
13	13	625.25±281	5	680.52±291	Ns
14	47	730.16±878	26	744.26±974	NS
15	40	890.15±368	19	906.17±408	NS
Overall	100	748.52±625	50	776.98±725	NS

Table III

Comparison of food and nutrients intake between two groups

Food and Nutrients	Study group Mean±SD	Control group Mean±SD	z-test for Equality of Means
Food (gm)	609.96±158	620.18±117	NS
Calorie (Kcal)	1630.40±452	1654.88±406	NS
Protein (gm)	51.01±19	56.52±17	NS
Fat (gm)	22.85±19	28.59±36	NS
CHO (gm)	295.43±83	305.21±72	NS
Fibre (gm)	3.69±1.56	3.91±3.0	NS
Calcium (mg)	313.69±195	327.99±238	NS
Iron (mg)	14.98±8.6	18.66±11	NS
Vitamin A (I.U)	748.52±625	776.98±725	NS
Thiamine (mg)	1.09±0.41	1.18±0.37	NS
Riboflavin (mg)	0.73±0.30	0.74±0.23	NS
Niacin (mg)	17.24±5.7	17.57±4.97	NS
Vitamin C (mg)	61.16±18.1	61.98±56	NS

Table-IV

Height and nutritional status of the study and control group by anthropometric indices

Category	Percentile	Z-score	Study group (N=100)		Control group (N=50)		Growth status[1]
			Baseline (%)	After 3 months (%)	Baseline (%)	After 3 months (%)	
Category I	0.0 to 5.0	Z <-1.650	42.0	34.0	44.0	43.0	Short
Category II	5.1 to 15.0	-1.645<Z<-1.040	28.0	21.0	29.0	30.0	Below Average
Category III	15.1 to 85.0	-1.035<Z<+1.030	30.0	45.0	27.0	27.0	Average
Category IV	85.1 to 95.0	+1.036<Z<1.640	-	-	-	-	Above Average
Category V	95.1 to 100.0	Z>1.645	-	-	-	-	Tall

[1]Growth status defined with reference to sex-specific standards of height.

Table-V

Weight and nutritional status of the study and control group by anthropometric indices

Category	Percentile	Z-score	Study group (N=100)		Control group (N=50)		Weight status[2]
			Baseline (%)	After 3 months (%)	Baseline (%)	After 3 months (%)	
Category I	0.0 to 5.0	Z <-1.650	40.0	21.0	40.0	39.0	Low weight
Category II	5.1 to 15.0	-1.645<Z<-1.040	30.0	14.0	30.0	31.0	Below Average
Category III	15.1 to 85.0	-1.035<Z<+1.030	29.0	64.0	30.0	30.0	Average
Category IV	85.1 to 95.0	+1.036<Z<1.640	1.0	1.0	-	-	Above Average
Category V	95.1 to 100.0	Z>1.645	-	-	-	-	Heavy weight

[2]Weight status defined with reference to sex-specific standards for weight by age.

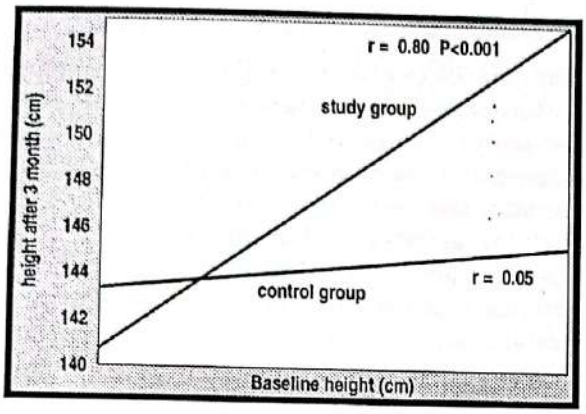

Fig.-1 : *Curvelinear relationship of height between baseline and after 3 months.*

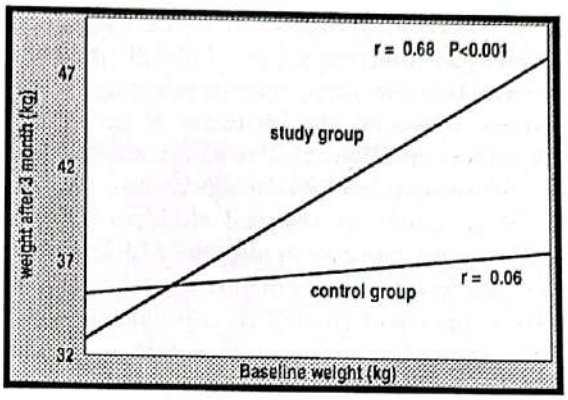

Fig.-2 : Linear trend of weight between baseline and after 3 months

Table-VI

Nutritional status by BMI of both study and control groups

Nutritional status	Baseline				After 3 months			
	Study gr.		Control gr.		Study gr.		Control gr.	
	No.	%	No.	%	No.	%	No.	%
BMI < 20(Malnourished)	64	64.0	34	68.0	20	20.0	33	66.0
BMI 20-24.99(Normal)	30	30.0	14	28.0	74	74.0	15	30.0
BMI 25-30(Obesity)	5	5.0	2	4.0	5	5.0	2	4.0
BMI > 30(Health risk)	1	1.0	0	0.0	1	1.0	0	0.0

Table-VII

Prevalence of ARI among the subjects

Source of variation	Study group (n=100)		Control group (n=50)	
	No.	%	No.	%
Baseline	38	38.0	18	36.0
After 3 months	17	17.0	20	40.0
Improvement /No improvement	55.26% reduced		5.56% increased	

Chi-square = 5.12 P<0.02 Odds ratio (OR) = 2.48Relative ratio = 1.72

Discussion :

In the baseline, 38% of study subjects, while 36% of the control group had ARI. After 3 months of intervention incidence of ARI decreased to 17% in the study group showing a reduction of ARI by 55.26% while in control group the rate increased to 40% with an increment of ARI attack rate by only 5.56%. Previous studies of large dose vitamin A supplementation on respiratory morbidity have produced conflicting results in a variety of populations, the influence of malnutrition has not been examined in the majority of these trails. So, a hypothesis has been taken that weekly low-dose vitamin A supplementation would prevent respiratory disease morbidity where malnutrition might influence the efficacy of vitamin A supplementation. In a randomized, double-blind, placebo-controlled field trial of 400 children, 6-36 months of age in a high Andean urban slum, half of the children received 10,000 IU of vitamin A weekly and other half received placebo for 40 weeks. Children were visited weekly at home by physicians and assessed for ARI. The age matched study and control subjects from middle to high

income families were included in this study. Acute respiratory infection did not differ globally or by severity between supplement-treated and placebo groups. However, the incidence of acute lower respiratory infection (ALRI) was significantly lower in underweight (weight-for-age Z score [WAZ] <-2SD) supplement treated children than in underweight children on placebo. ALRI incidence was significantly higher in normal-weight (WAZ>-2SD) supplement treated than in normal weight children on placebo. In Guatemala[19], respiratory disease was more common among children with serum retinol <10mg /dl and in Thailand, an increase of 1 m mol / litre of serum vitamin A was associated with an 80% reduction in respiratory disease[20].

Regarding food and nutrition intake by the study girls, calorie intake was comparable to the national daily calorie consumption for Bangladeshi women. Bangladeshi diet rich in cereals and lack in vegetable (both leafy and non leafy) and also low fat intake have contributed to less availability of vitamin A. The observed availability of vitamin A is one third of national availability as found in nutrition survey of 1995-96. The reason of non-availability of vitamin A, as it is a fat soluble vitamin, might be due to low intake of green leafy vegetables, coupled with low intake of visible and non visible fat. Over and above total food intake is just low (though not significant) between study and control group. Further more, there is deficiency in fiber and calcium intake also and as such height, weight and MAC of the subjects were also low. The study and control group did not differ by Z test when compared with baseline height with that obtained after 3 months but the study group showed positive significant correlation ($r=80$, $p < 0.001$). Weight showed the same pattern in study subjects ($r=68$, $p=0.001$) than control ($r=0.06$) (Fig .1 & 2)

By BMI, 64% of study girls were malnourished but after intervention 20% remained in the malnourished category. At baseline 30% of the study girls were normal, but after 3 months it went up to 74%. These normal 44% came from malnourished group, indicating that vitamin A intake as per recommendation could control the infectious disease attack rate following a sharp increase in nutritional status. Over and above it is the period when maximum growth spurt occurs. The control group did not show the same trend.

Carotenoids (b-carotene and lycopene vitamin E (μ tocopherol) and vitamin C (ascorbate) are naturally occurring antioxidant nutrients that play important roles in animal health by inactivating harmful free radicals produced through normal cellular activity and from various stresses. Vitamins generally enhance different aspects of cellular and non-cellular immunity. The anti-oxidant function of these micro-nutrients could, at least in part, enhance immunity by maintaining the functional and structural integrity of important immune cells. A compromised immune system will result in reduced animal production efficiency through increased susceptibility to diseases, thereby leading to increased animal morbidity and mortality[21].

So because of intervention of beta carotene from red palm oil, there has been 2.4 times increase in disease prevention along with improvement of various parameters of nutritional status.

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References:

1. Sommer A, Tarwotjo, Hussiani G, Susan to D. Increased mortality in children with mild Vitamin A deficiency, Lancet. 1983, 2:585-588.
2. Jahan K and Hossain M. Nature and Extent of Malnutrition in Bangladesh. Bangladesh National Nutritional Survey 1995-96. Institute of Nutrition and Food Science, D.U., July, 1998.
3. Helen Keller International and Institute of Public Health Nutrition. Bangladesh Nutritional Blindness study 1982-83.
4. Nutrition Survey of East Pakistan 1962 – 64, U.S Department of Health, Education and Welfare, Washington D.C, USA , 1966.
5. Nutrition Survey of Rural Bangladesh 1975 – 76. Institute of Nutrition and Food Science, University of Dhaka, 1977.

6. Ahmed K and Hassan N. Nutrition Survey of Rural Bangladesh 1981-82. Institute of Nutrition and Food Science, University of Dhaka, December 1983.

7. Institute of Public Health Nutrition and UNICEF. Night Blindness Prevention Program Evaluation Report 1989.

8. Elliot RH. Night-blindness. In: Tropical Ophthalmology. London: Henry Frowde, Hodder & Stoughton. 1920:75-86.

9. Spicer H. Ophthalmological Society. Keratomalacia in young children. Panophthalmitis following lacrymal abscess. Probable rupture of the optic nerve (editorial). Lancet 1892; 2:1387-1388.

10. Bloch CE. Clinical investigation of xerophthalmia and dystrophy in infants and young children (xerophthalmia et dystropia alipogenetica). J Hygiene (Cambridge) 1921; 19:283-301.

11. Blackfan K, Wolbach SB. Vitamin A deficiency in infants. A clinical and pathological study. J Pediatr 1933;5:679-706.

12. Ten Doesschate J. Causes of blindness in and around Surabaja. East Java, Indonesia Thesis, University of Indonesia, Jakarta 1968:159-241.

13. Sweet LK, K'ang HJ. Clinical and anatomic study of avitaminosis A among the Chinese. Am J Dis Child 1953; 50:699-734.

14. DeHass JH, Posthuma JH, Meulemans O. Xerophthalmia in children in Batavia. Indian J Pediatr 1941; 8:139-157.

15. Reddy V. Vitamin A deficiency and blindness in Indian children. Indian J Med Res 1978; 68:26-37.

16. Sommer A., West KP. Vitamin A Deficiency: Health, Survival, and Vision. New York, Oxford 1996; 64,76.

17. Scrimshaw NS. Taylor CE. Gordon JE. Interactions of nutrition and infection. Geneva: World Health Organization 1968;

18. Nutrition Briefs. MPOPC's Nutrition Publication: Vol.2; 8 Issue: Dec. 2000.

19. Arroyave G. Aguilar JR. Flores M. Guzman MA. Evaluation of sugar fortifivation with vitamin A at the national level. Scientific Publication No 384. PAH. Washington, DC 1979.

20. Bloem MW, Wedel M. Egger RJ, Speek AJ, Schrijver J. Saowkontha S, Schreurs WHP. Mild vitamin A deficiency and risk of repiratory tract diseases and diarrhea in preschool and school children in northeastern Thailand. Am J Epidemiol 1990; 131:332–339.

21. Chew BP. Antioxidant Vitamins Affect Food Animal Immunity and Health. J. Nutr. 1997; 125: 1804 - 1808.

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Clinical Course and Short-term Outcome in Patients with Hypertrophic Cardiomyopathy

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Abstract :

The aim of the study was to describe the clinical course and short-term outcome in patients with hypertrophic cardiomyopathy. Although hypertrophic cardiomyopathy (HCM) is believed to be a relatively uncommon cardiac disease, some of patients got admitted in the hospital for symptomatic treatment. A prospective study of 10 patients with HCM diagnosed in single unit from July, 2000 to December 2001 was performed. Clinical course and short-term outcome were analyzed. In the 10 study patients, age, sex, and the extend of the left ventricular hypertrophy, as well as the diastolic filling abnormalities, subaortic obstruction and arrhythmias, were similar with respect to other studies. Cardiac symptoms, however, were much less severe in the study patients. One atient (10%) had moderate to severe symptom (class IV). During the follow-up period none-died; five patients (50%) were asymptomatic, one patient (10%) developed dizziness due to complete heart block and other developed anginal pain. We concluded that, the majority of patients with hypertrophic cardiomyopathy do not show any detoriation in their functional class and most of them remain asymptomatic during follow-up period.

Keywords : *Clinical course; Hypertrophic Cardiomyopathy.*

[Chest & Heart Journal 2003; 27(2) : 77-82]

Introduction :

Hypertrophic cardiomyopathy (HCM), a complex disease has fascinated and often confused physicians for the quarter of a century since its recognition in the late 1950[1-5]. Although relatively uncommon, this disease has nevertheless been of great interest to clinicians and scientists due to its particularly diverse clinical, morphologic, and pathophysiological manifestations[6,7].

Numerous studies have explained specific facets of this disease, and several have comprehensively received the broader aspects of its clinical profile and course, including the physical findings of patients with the disease, electrocardiographic and radiographic features and haemodynamics[8-12]. This hospital based prospective study was under taken to investigate the clinical manifestations and the short-term outcome in 10 patients with hypertrophic cardiomyopathy.

Materials and Methods :

Selections of patients : Between July 2000 to December 2001, we decided to assemble a population of patients with hypertrophic cardiomyopathy attended in the single unit. Accordingly we identified 10 patients with , hypertrophic cardiomyopathy by clinical features and reviewing the medical records.

In each of the 10 patients, the diagnosis of hypertrophic cadiomyopathy was established by echocardiographic demonstration of a hypertrophied, non-dilated left ventricle in the absence of another cardiac or systemic disease that could produce comparable left ventricular hypertrophy. The presence of obstruction to the left ventricular outflow under basal conditions was assessed from the M - mode echocardiogram on the basis of the magnitude and duration of systolic anterior motion of the mitral valve[3,4]. In each study patient, a clinical assessment of symptoms, echocadiographic measurements of the extent of hypertrophy, and Doppler measurements of diastolic function were obtained by the same investigator.

Electrocardiography (ECG) :

Routine electrocardiographic screening showed more than 80 percent of patients with HCM had

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abnormal ECGs and entirely normal ECG was found in 15 percent patients. The most common abnormalities were ST-segment and T wave abnormalities, followed by a evidence of left ventricular hypertrophy, with QRs complexes that are the tallest in the midprecordial leads[19]. Giant negative T-waves in the midprecordial leads and Q-wave abnormalities were also noted, different types of arrhythmias (ventricular and supra ventricular) were also found in the study populations.

Echocardiography :

The echocardiographic studies were performed in echocardiography laboratory in all study population. The thickness of the anterior ventricular septum and the posterior free wall and the diastolic dimension of the left ventricular cavity were measured according to criteria described elsewhere[14]. The overall extent and distribution of left ventricular hypertrophy were assessed with use of two dimensional echocardiographic index reported elsewhere.[15-17] Serial M-mode and two dimensional echo-cardiograhic measurements were obtained at the time of the initial and the most recent clinical examination in study patients.

The Doppler echocardiographic studies were recorded in 10 study patients. At the time of the Doppler study, 8 patients were taking no cardio-active medications or had discontinued such

medications at least 48 hours before the examination. None of the patients had a clinical history of systemic arterial hypertension. Blood pressure, measured by sphygmomanometers at the time of the Doppler examination, was within the normal range in each patient.

Angiography : During the study period two patients underwent selective coronary and LV angiography for symptoms of myocardial ischaemia. The procedure included the evaluation of coronary artery disease, presence of spade like configuration of left ventricle and assessment of LVOT obstruction.

Statistical Methods :

Data were expressed as means±SD. The mean values for age and the echocadiographic measurements reported in the published studies were pooled and compared with those obtained in our study population. Differences between continuous variables were determined with use of the unpaired Student t-test. Differences between proportions were determined with use of the chi-square test.

Results :

Clinical Findings : The age and sex distributions in our 10 study patients were similar and not significantly different from those reported in the other studies (Table-1). Cardiac symptoms were substantially less severe, however 5 patients (50 percent) were asymptomatic[2], 2 patients (20 percent) had mild symptoms (New York. Heat Association functional Class II), and only 1 patient (10 percent) had moderate-to-severe symptoms (Class IV). Among the mildly symptomatic patients, the most common limiting symptom was dyspnoea after moderate exertion. Less frequent symptoms included palpitations, chest pain, and dizziness, presyncope. None of the patients had episodes of syncope. The only patient with severe symptoms was a 51 year old man with chronic atrial fibrillation and symptoms of fatigue and dyspnoea after mild exertion. Subaortic obstruction under basal conditions, as assessed from M-mode echocardiography, was present in 2 study patients (20 percent). One of these patients had mild cardiac symptoms, and one was asymptomatic.

Left Ventricular Morphology : At the initial examination, the septal and posterior free-wall thickness in our study patients did not differ significantly from the mean values reported in the literature, whereas the diastolic dimension of the left ventricular cavity was 46±5 mm in the study. Two-dimensional echocardiography was used to assess the overall extent and distribution of left ventricular hypertrophy[15-17]. The maximal thickness (Fig-1) of the left ventricular wall was 17±4 mm (range, 15 to 20), and the left ventricular wall-thickness index- a quantitative measurement of the extent of left ventricular hypertrophy derived from the sum of the wall thickness of the anterior septum, posterior septum, posterior free wall, and lateral free wall was 61116 mm. Both values are comparable to the mean values (21 and 65 mm, respectively) reported for these indexes in two previous studies performed at the National Heart, Lung, and Blood Institute in a total of 158 patients with hypertrophie cardiomyopathy28,29 (Table-II).

Electrocadiography : The analysis of ECG recording are presented in Table-I. Increased QRS

activity (30%), ST-T changes (80%), Q-wave (20%), gaint T-wave (30%) and normal (10%) were noted in the study patients Fig-2.

Angiography : Two patients of the study population underwent CAG. One patient showed normal and other showed double-vessels (Left anterior descending and right coronary), disease, with spade like configuration.

Demographic Findings : An echo cardiographic survey of all first degree relatives in the families of the 10 study patients were not performed.

Follow-up : All patients were followed-up from the time presentation for one year. There was no death or major cardiac events except one patient developed complete heart block (CHB)

Table-1

Clinical Data in 10 patients with Hypertrophic Cardiomyopathy (HCM)

Case	Age (yr.)	Sex	Electrocardiographic findings					Echocardiographic findings					
			QRS voltage	ST-T changes	Q waves	GNT	Normal	LVD (mm)	IVST (mm)	PWT (mm)	SAM	Basal LVOT gradient	FS%
1	30	M	0	+	0	0	0	47	17	8	0	0	30
2	42	M	+	+	0	0	0	55	20	12	+	0	39
3	44	M	+	0	+	0	0	43	15	9	0	60	36
4	45	M	0	+	0	+	0	47	16	11	0	0	37
5	47	F	+	+	0	0	0	45	20	12	+	10	42
6	51	M	0	+	+	0	0	42	18	10	0	0	35
7	56	M	0	+	0	0	+	51	19	10	0	0	34
8	62	M	+	0	0	+	0	43	19	12	0	0	39
9	55	F	0	+	0	0	0	45	16	14	0	0	50
10	64	M	+	+	0	+	10	149	120	113	0	0	48

GNT = gaint negative T-waves; LVDd = Left ventricular end deastolic diameter IVS = interventricular, septal thickness; post-wall thickness; SAM = systolic anterior motion of mitral value, LVOT = Left ventricular outflow tract; FS = fractional shortering.

Table –II

Clinical features of patients with Hypertrophic cardiomyopathy al two referral centers and other institutions, as Reported between January 1983 and December 1987.

Feature	National Institutes of Health	Royal postgraduate school	Other Institutions
Patient : No(1)	1898(56)	5 85(17)	921(27)
Age (Yr)	39 ± 7	43 ± 6	46 ± 13
Functional class III or IV-no/no.of patient(%)	710/ 1447(49)	17/ 141(12)	3 0/ 13 3 (23) .
Left Ventricular outflow-tract obstruction no-/no. of patients (%)	651 /1779(39)	3 5/ 146(24)	92/269(34)
Ventricular Septerm (mm)	23±4	not reported	21 ±4
Posterage Wall (mm)	12± 1	not reported	12±3
Left Ventricular internal diastolic diameter (mm)	41 ±3	not reported	3 9±5

Discussion :

Hypertrophic cardiomyopathy is a complex disease, characterized by a broad spectrum of morphologic and functional abnormalities.[16-22] Although some patients with hypertrophic cardiomyopathy may be severely symptomatic or require surgical treatment,[23-24] many others remain asymptomatic and unaware of their disease. In such patients, the diagnosis of hypertrophic cardiomyopathy is often first made in the course of routine examinations. Whenever the clinical presentation of a disease shows such great variability, patterns in patient referral and selection biases may have a major influence on the investigation findings. This may be particularly true in the case of hypertrophic cardiomyopathy, a disease that has been investigated mainly at referral institutions.

The present study reports the clinical, morphologic, and functional findings in a population with hypertrophic cardiomyopathy. Although the age and sex distributions in our study patients were similar to those reported in the studies, their clinical presentation was substantially more favorable.

None of the study patients died of cardiac causes or had severe clinical deterioration during a mean follow-up period of one year. This benign course contrasted with the clinical deterioration and 2 to 4 percent annual mortality rate reported in major clinical investigations.[25-27] Despite this mild clinical presentation, the magnitude of left ventricular hypertrophy in our study patients was comparable to that described in the literature. The only morphologic difference was the presence of a larger left ventricular diastolic cavity- a factor that may have played -a part in determining the lower severity of symptoms in our patients.

The pattern of left ventricular diastolic filling was abnormal in about 40 percent of our patients- a percentage similar to that reported recently in more than 100 patients with hypertrophic cardiomyopathy.[28] This - prevalence of diastolic abnormalities should not be considered inconsistent with the low prevalence of symptoms of cardiac failure observed in our study population, since diastolic abnormalities can frequently identified in asymtomatic patients with hypertrophic cardiomyopathy.[28] Subaortic obstruction under basal conditions was 20 present in percent of our study patients, and atrial fibrillation and ectopics were identified during ECG monitoring in I percent Both figures are similar to those reported in the literature.[29-30]

Although our study population was small, our patients were carefully characterized, and their morphologic features, as well as the prevalence of diastolic filling abnormalities, subaortic obstruction, and arrhythmias, were similar to those reported in the literature. With regard to their clinical presentation, however, our study patients would seem to represent the mild end of the disease spectrum. Although the clinical features of patients with hypertrophic cardiomyopathy have not previously been described; the favorable clinical course identified in our patients is perhaps not surprising, since in many clinical disorders outpatient populations may have more favorable clinical features than the corresponding inpatient populations. Nevertheless, our findings raise the important question of how many patients with hypertrophic cardiomyopathy are never hospitalized and remain free of severe cardiac symptoms and functional limitations.

In conclusion, whereas the large body of studies performed at major referral institutions has undoubtedly increased our understanding of the pathophysiology of hypertrophic cardiomyopathy, Our f ndings in an population suggest that many such patients may have a better clinical course and prognosis than could be inferred from the current literature. This data are likely to influence the counselling and management of patients with hypertrophic cardiomyopathy.

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References :

1. Brock R. Functional obstuction of the ventricle (acquired aortic subvalvular stenosis). Guy's Hosp Rep 1957; 1064 : 221-3 A.
2. Teare D. Asymmetrical hypertrophy of the heart in young adults. Br Heart J 1958; 20;1-8.
3. Bercu BA, Diettert GA, Danforth WH, Jr, Ahlvin RC, Belliveau RR. Pseudoaortic

stenosis produced by ventricular hypertrophy. Am J Med 1958 : 25; 814-8.

4. Goodwin JF, Hollman A, Cleland WP, Teare D. Obstructive cardiomyopathy simulating aortic stenosis. Br Heart J 1960; 22 : 403-14.
5. Morrow AG, Braunwald E. Fuctional aortic stenosis; a malformation characterized by resistance to left ventricular outflow without anatomic obstruction, Circulation 1959; 20 : 181-9.
6. Moron BJ. Gottdiner Js. Epstein SE : Patterns and significance of distribution of left ventricular hypertrophic Cardiomyopathy. A wide angle, two-dimensional echocardiographic study of 125 patients. Am J Cardiol 1981; 48 : 418-4.28.
7. Louic EK, Maron BJ : Apical hypertrophic Cardiomyopathy; Clinical and two-dimensional echocardiographic assessment. Ann Inter Med 1987;106 : 663-670.
8. Simon AL, Ross J Jr, Gault JH. Angiographic anatomy of the left ventricle and mitral valve in idiopathic hypertrophic subaortic stenosis. circulation 1967; 36 : 852-67.
9. Frank S, Braunwald E. Idiopathic hypertrophic subaortic stenosis; clinical analysis of 126 patients with emphasis on the natural history. Circulation 1968; 37 : 759-88.
10. Goodwin JF. Congestive and hypertrophic cardiomyopathy; a decade of study. Lancet 1970;1;731-9.
11. Kaga Y, Itayc K-i, Toshima H,, Prognosis in hypertrophic cardiomyopathy, Am Heart J 1984; 108 : 3 51-9.
12. Epstein SE, Henry WL, Clark CE et al. Asymmetric septal hypertrophy. Ann intern Med 1974; 81 : 650-80.
13. Maron, B.J : HypertopfiC Cardiomyopathy . Curr . Probi . Cardiol
14. Sahn DJ, DeMaria A, Kisslo J. Weyman A, Recommendations regarding quantitation in M-mode echocardiography : results of a survey of echocardiographic measurements. Circulation 1978; 58 : 1072-83.
15. Spirito P, Maron BJ, Charella F, et al. Diastolic abnormalities in-patients with hypertrophic cardiomyopathy : relation to magnitude of left ventricular hypertrophy. Circulation 19 8 5 ; 72 : 310-6 .
16. Spirito P, Maron BJ. Absence of progression of left ventricular hypertrophy in adult patients with hypertrophic cardiomyopathy. J Am Coll Cordial 1987 : 9 : 1013-7.
17. Spirito P, Maron BJ, Bonow RO, Epsein SE, Occurrence and significance of progressive left ventricular wall thinning and relative cavity dilatation in hypertrophic cadiomyopathy, Am J Cardiol 1987;60 : 123-9.
18. Spirito P, Maron BJ, Bonow RO. Noninvasive assessment of left ventricular diastolic function : comparative analysis of doppler echocardiographic and radionuclide angiographic techniques. J AM Coll Cardiol 1986; 7 : 518-26.
19. Mckenna WJ, England D, Doi YL Deanfield ,I, Oakley C, Goodwin JF. Arrhythmia in hypertrophic cardiomyopathy. I. Influence on prognosis. B Heart J 1981; 46 : 168-72.
20. Wigle ED, Heimbecker RO, Gunton RW. Idiopathic ventricualr septal hypertrophy causing muscular subaortic stenosis. Circulation.l 962;26 : 325-40.
21. Braunwald E, Lambrew CT, Rockoff SD, Ross J Jr, Morrow AGr. Idiopathic hypertrophic subaortic stenosis. I. A description of the disease based upon an analysis of 64 patients. Circulation 1964; 30 : Suppl IV : IV-3-IV-119.
22. Wigle ED, Sasson Z, Henderson MA, et al. Hypertrophic cardiomyopathy : the importance of the site and the extent of hypertrophy : a review Prog. Cardiovasc Dis 1985; 28 : 1-83.
23. Maron BJ, Bonow RO, Cannon RO III, Leon MB, Epstein SE. Hypertrophic cardiomyopathy : interrelations of clinical manifestations, pathophysiology, and therapy. N,, Engl J Med 1987; 1 1 : 83-112.

24. Wigle ED, Tremble AS, Adelman AG, Bigelow WG. Surgery in muscular subaortic stenosis. Prog Cardiovasc Dis 1968; 11 : 83-1 1 21.

25. Morrow AG, Reitz BA, Epstein SE, et al. Operative treatment in hypertrophic subaortic .stenosis : techniques, and the results of pre and postoperative assessments in 83 patients, Circulation 1975; 52 : 8-102 .

26. Shah PM, Adelman AG, Wigle ED, et al. The natural (and unnatural) history of hypertrophic obstructive cardiomyopathy. Cire Res 1974; 35 : Suppl II : II-179.

27. Hardarson T, De la Calzada CS, Curiel R, Goodwsin JF. Prognosis and mortality of hypertrophic obstructiv e cardiomyopathy. Lancet 1973; 2 : 1462-7.

28. Maron BJ, Spirito P, Gree KJ, Wesley YE, Bonow RO, Arce J. Noninvasive assessment of left ventricular diastolic function by pulsed doppler echocardiography in patients with hypertrophic cardiomyopathy, J Am Coll Cardiol 1987; 10 : 733-42.

29. Maron BJ, Savage DD, Wolfswon JK, Epstein SE. Prognostic significance of 24 hour ambulatory electrocardiographic monitoring in patiens with hypertrophic cardiomyopathy : a prospective study. Am J Cardiol 1981; 48 : 252-7.

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Clinical and Investigative Characteristics of Fifty-Five Patients with Angiographically Documented Coronary Artery Disease

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Abstract :

This prospective study was carried out in the department of Cardiology, Bangabandhu Sheikh Mujib Medical University (BSMMU) and Combined Military Hospital (CMH), Dhaka, Bangladesh during the period of March 1999 to October 2000. The study was designed to see clinical & investigative characteristics of patients with documented coronary artery disease(CAD). Fifty-five consecutive patients with CAD were included in this study who received treatment percutaneous transluminal coronary angioplasty (PTCA) with and without stent. Among the 55 patients, 40[72.73%(35 male and 5 female)] were in stent group(group A) and 15[27.27%(14 male and 1 female)] in PTCA only group(group B). Mean age of the two groups were 50.85±6.81 years and 46.60±6.45 years respectively (P<0.01). Smoking was the most common risk factor followed by hypertension, dyslipidaemia, diabetes and positive family history of IHD in both the groups. Myocardial infarction was the commonest clinical diagnosis (56.37%), followed by unstable angina (23.63%) and chronic stable angina (20%). Before intervention, 43(78.18%) patients were symptomatic (functional class 11 and 111) and 12(21.82%) were asymptomatic (class 1). No significant difference was observed between the two groups regarding clinical presentations (P>0.05). In addition to angiography, basic clinical and investigative parameters were noted including echocardiography (2D, M-mode & Colour doppler). It was observed that majority of the patients had more than 3-risk factors and most of patients were symptomatic before intervention. Patients who have more risk factors more the involvement of coronary arteries.

[Chest & Heart Journal 2003; 27(2) : 83-86]

Introduction :

Coronary artery disease is the leading cause of death and disability world wide[1] and it is increasing in South Asian countries including Bangladesh[2-3]. Many epidemiological studies conducted over decades firmly established the association of coronary risk factors with the development coronary artery disease[4]. The relationship between the clinical and investigative parameters and the development and severity of angigraphic CAD is less defined in Bangaladeshi patients. This study was done to find out the association between the clinical & investigative characteristics and angiographically documented CAD.

Method :

Fifty-five consecutive patients selected in CMH, Dhaka during the period of Marchl999 to October 2000, and grouped into two groups (Group A and Group B) according to final treatment they received. In group A, 40 patients were included who underwent PTCA with stent and in group B, 15 patients who underwent PTCA only. The study population consisted of patients with chronic stable angina (CSA), unstable angina (UA) after stabilization of symptoms, myocardial infarction, and those who had evidence of provocable ischaemia on exercise tolerance' test (ETT). The specific criterion for intervention was at least 70 percent stenosis. In addition to angiography, baseline clinical characteristics, patients symptoms, basic investigations were noted. Echocardiography (2D & M-mode and Colour doppler) were done to see functional improvement and wall motion changes and to exclude congenital and valvular diseases in all patients before the

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procedure and at 6-month after the procedure.

Statistical analysis : All the parametric values are expressed as mean±one standard deviation (mean±SD) and non-parametric values as percentage(%). Unpaired Students 't' test, Chi-square, and Fisher's exact test were used where applicable. A probability (P) value of <0.05 was considered as significant.

Results :

A total of 55 consecutive patients were included in this study and divided into two groups, group A & group B. Group A included 40(72.72%) patients treated with stent and Group B included 15(27.28%) patients treated with PTCA only. The mean age of group A was 50.85±6.81 years and in group B was 46.6±6.45 years; male patients were significantly higher in both the groups (P<0.01). Smoking (70 vs 66.7%) was the most common risk factor followed by dyslipidaemia(65 vs 60%), hypertension(60 vs 53.3%), diabetes mellitus(35 vs 26.67%) and positive family history of IHD (40 vs 20%) in group A and B, respectively. MI was the commonest clinical diagnosis(55 vs 60%0 followed by UA(25 vs 20%) and CSA(20 vs 20%) in both the groups respectively and no significant difference was observed in two groups(P>0.05) [Table-I]. Majority of the patients had ≥3 risk factors(50 vs 53.33%) in group A and group B, respectively [Table-II]. Before intervention 32(80%) patients in group A and 11(73.33%) patients in-group B were symptomatic (functional class II & 111) and no significant differences were observed regarding clinical presentations (P>0.05)[table-III]. Majority of the patients had positive ECG(ST-T change and Q-wave) changes in both the groups (90% Vs 86.67%) respectively, and ETT was positive in all cases [Table-IV]. Majority of patients had hypokinetic wall motion in both the groups (60% VS 53.33%) before intervention. Most commonly involved wall was LV anterior wall followed by posterior wall. Most of the patients had ejection fraction in between 40-49%, followed by >50% and < 40% but no significant difference was noted in between groups (P>0.05) [Table-V]. Single-vessel disease was present in 33(82.5%) patients in group A and 13(86.67%)patients in group B, double-vessel disease was present in 5(12.5%) and 2(13.33%) patients in group A and B, respectively. Triple-vessel disease was present in 2(5%) in group A only. No significant difference in CAG findings was observed between the two groups (P>0.05) [Table-VI].

Table-I

Clinical characteristics of the study patients

Characteristics	Group A (n=40)	Group B(n=15)
1. Age (years) (mean±SD)	50.85±6.81	46.60±6.45
2. Sex (No./ %)		
Male	35(87.5)	14(93.33)
Female	5(1.25)	1(6.67)
3. Height (cm) (mean±SD)	166±2.63	160.13±623
4. Weight (kg) (mean±SD)	63.90±5.07	65.53±5.94
5. BMI (kg/m2)	23.21±1.73	25.51±0.86
6. Risk factor (No./ %)		
Smoking	28(70.0)	10(66.7)
Hypertension	24(60.0)	8(53.3)
Dyslipidaemia	26(65.0)	9(60.00)
Diabetes Mellitus	14(35.0)	4(26.67)
Family history of IHD	16(40.0)	3(20.0)
7. Clinical diagnosis(No./ %)		
Chronic stable angina	8(20.0)	3(20.0)
Unstabe angina	10(25.0)	3(20.0)
Myocardial infarction	22(55.0)	9(60.0)

Table-II

Risk factors of the patients

Number of risk factors	Group A(n=40)		Group B (n=15)	
	No	(% o)	No	(%)
1	8	20.0	2	13.33
2	12	30.0	5	33.33
3	20	50.0	8	53.33

Table-III

Symptoms of study patients

Variables	Before intervention(N=55)		After intervention(N=48)	
	Gr-A(n=40)	Gr-B(n=15)	Gr-A(n=36)	Gr-B(n=12)
Asymptomatic				
CCS class-I	8(20.0)	4(26.67)	24(66.67)	7(58.33)
Symptomatic				
CCS class-II	20(50.0)	8(53.33)	6(16.67)	3(25.0)
CCS class-III	12(30.0)	3(20.0)	6(16.67)	2(16.67)

Table - IV

Baseline investigation of the study population(N=55)

Investigations	Before intervention(N=55)		After intervention(N=48)	
	Gr-A(n=40)	Gr-B(n=15)	Gr-A(n=36)	Gr-B(n=12)
ECG(No/%)				
Positive for IHD	36(90.0)	13(86.67)	27(75.0)	10(83.33)
Negative for IHD	4(10.0)	2(13.33)	9(25.0)	2(16.67)
ETT(No/%)				
Positive	40(100)	15(100)	30(83.33)	11(91.67)
Negative	0	0	6(16.67)	1(8.33)

Table-V

Echocardiopraphic profile of patients before & after intervention

Variables	Before intervention(N=55)		After intervention(N=48)	
	Gr-A(n=40)	Gr-B(n=15)	Gr-A(n=36)	Gr-B(n=12)
1. RWMA:				
Normal	16(40.0)	7(46.67)	20(55.55)	7(58.33)
Hypokinetic	24(60.0)	8(53.33)	16(44.45)	5(41.67)
Akinetic & Dyskinetic	0	0	0	0
2. Wall involved:				
LV anterior wall±IVS	14(58.33)	5(62.5)	10(62.5)	3(60.0)
LV lateral wall	3(12.5)	1(12.5)	2(12.5)	1(20.0)
LV posterior wall±IVS	7(29.16)	2(25.0)	4(25.0)	1(20.0)
3. Ejection fraction(%)				
<40	6(15.0)	3(20.0)	2(5.55)	1(8.33)
40-49	20(50.0)	8(53.33)	16(44.45)	6(50.0)
>50	14(35.0)	4(26.67)	18(50.0)	5(41.67)
4. Other abnormalities	0	0	0	0

Table-VI

Coronary angiographic finding of the patients

Number of vessel Involved	Group-A(n=40)		Group-B (n=15)	
	No	(%)	No	(%)
Single	33	82.5	13	86.67
Double	5	12.5	2	13.33
Triple	2	5.0	0	0

Discussion :

Fifty-five consecutive patients with CAD who underwent intervention with PTCA with and without stent were included in this study and were divided into two groups. Group A included 40 patients who underwent PTCA with stent and group B included 15 patients who were treated with PTCA only. In this study, symptomatic improvement and echocardiographic profile were analyzed of the patients before and at 6- month follow-up who were treated successfully with PTCA with and without stent. During follow-up, 4 patients from group A and 3 from group B were missed. Among the 55 patients, males were 87.5 & 93.33 percent, and females were 12.5 & 6.67 percent in-group A and B respectively. Sex distribution was not statistically different between the two groups (P>0.05). The mean (±SD) age of the two groups were 50.85±6.81 years and 46.60±6.45 years respectively. Similar sex and age distribution was reported by Rahman et al[5]. Study patients had clinical diagnosis of MI (55vs 60%), UA (25vs 20%) and CSA (20vs20%) in group A & B, respectively. Majority of the patients were symptomatic (functional class II and 111) before intervention (80) (vs 73.33%) in group A & B, respectively. At 6-month follow-up, symptomatic patients were significantly less (33.33%vs 41.67%) in group A & B, respectively (P<0.05). This is similar to the other studies (O'Keefe et al., Bell et al[6,7]. Before intervention, majority patients had hypokinetic wall motion in both the groups (60%vs53.33% respectively) and at 6-months follow-up there were improvement in wall motion in both the group which was significant (P<0.05) (44.45% vs 41.67% respectively). Most of the patient had ejection fraction in between 40-49%, followed by >50% and < 40% but no significant difference was noted in between groups(P>0.05). But at 6-month follow-up there were significant improvement of LV ejection fraction(P<0.001). This finding is comparable with other studies (Fischman et al. 1994; Moussa et al.1998)[8,9].

The study showed that majority of the patients had multiple risk factors had more involvement of coronary arteries.

References:

1. Libby P. Atherosclerosis. In Fauci AS, Braunwald E, Isselbacher KJ, Wilson JD, Martin JB, Kasper DL et al (eds). Harrison's Principles of Internal Medicine, 14th ed; McGraw- Hill inc., New York 1998; 1345-52.
2. Amanullah M. Intravenous thrombolytics in acute myocardial infarction (editorial) Bangladesh Heart J 1994; 9 : 124.
3. Gupta R, Gupta VP. Meta-analysis of coronary heart disease prevalence in India. Indian heart J 1996; 48 : 241-5.
4. Fried LP, Pearson TA. The association of risk factors with angiographically defined coronary artery disease. Am J Epidemiol 1987; 125 : 453-88.
5. Rahman S, Akanda MAK, Azam A, Malik F, Rahmatullah KHI. Clinical and angiographic outcome after PTCA in 100 patients in Bangadesh. Bangladesh Heart J 1998;13 : 65-9.
6. O'Keefe JH, Rutherford BD, McConahay DR, Johnson WL, Giorgi LV, Ligon RW, et al. Multivessel coronary angiography from 1980 to 1989; Procedural result and long-term outcome. J Am Coll Cardiol 1993; 16 : 1097-102.
7. Bell MR, Grill DE, Berger PB, Bresnahan JF, Reeder GS, Baily KR, Homes DR Jr. Initial and long-term outcome of 354 patients after coronary ballon angioplasty of total coronary occlusions. Circulation 1992; 85 : 1003-11.
8. Fischman DL, Leon MB, Balm DS, Schatz RA, Savage MP, Penn I, et al. A randomized comparison of coronary-stent placement and balloon angioplasty in the treatment of coronary artery disease. N Engl J Med 1994; 331 : 496-501.
9. Moussa I, Di Mario C, Moses J, Reimers B, Di Francesco L, Blengino S, et al. Comparison of angiographic and clinical outcomes of coronary stenting of total occlusions versus subtotal occlusions. AM J Cardiol 1998; 81 : 1-6.

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A Study of Twenty Four Hours Ambulatory Electrocardiography Recording for Detection of Cardiac Arrhythmias and Ischaemia

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Abstract :

Introduction : The cardiac events like arrhythmia and myocardial ischaemia which are not detected by ECG, ambulatory ECG recording for 24 hours in various cardiac patients admitted in this University are needed to studied.

Method : Continuous recording of 3 Electrocardiographic leads for a period of 24 hours. This device records the information on a digital flash card. The patient was advice to carry out normal activities during the recording period.

Results : Twenty four hours ambulatory ECG recording of 229 cases was studied in cardiology department of BSMMU during the period of Feb. 2001 to Dec. 2002. Out of 229 cases 141(61.57%) were male, 88(38.42%) were female, with a mean age of 50.83 yrs (age range 13 - 83 years). Among 229 cases clinical characteristics was -76 (33.18%) had palpitation, 64 (27.94%) had chest pain of short duration; 51(22.27%) history of syncope or pre-syncope; 16(7.42% had left bundle branch block ; 9(3.93%) had paroxysmal supraventricular tachycardia (PSVT); 3(1.31%) had right bundle branch block;2(0.87%) bifascicular block; 6(3.05%) had complete heart block; and 2 (0.87%) chest pain with H/O. CABG. After analysis of their 24 hours ambulatory ECG recording - 31 (13.53 %) were diagnosed as PSVT; 46 (20.52%) as multiple ventricular ectopics; 17 (7.42%) as significant ST deviation ; 9 (3.93%) as SSS. Out of total 229 cases 104 (45.41%) were diagnosed as different types of arrhythmia or significant ST deviation, which was not diagnosed from their resting ECG.

Conclusion : Ambulatory ECG recording is important for detection of different types of arrhythmia and ischaemia which were not evident in routine ECG and this method of investigation gives also therapeutic and prognostic information.

[Chest & Heart Journal 2003; 27(2) : 87-90]

Introduction :

Cardiac arrhythmia are one of the important alarming condition in clinical practice . Cardiac rhythm abnormalities are common. Many arrhythmia are benign although some can give early signal for fatal arrhythmia like cardiac arrest or sudden cardiac death. The early detection and quantification of arrhythmia's are important, specially for patients with structural heart disease. Arrhythmia are frequently limited in duration and occurrence and such can not be detected during physical examination and resting

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electrocardiography (ECG). So, resting ECG detect the cardiac events only for a few seconds or a minute. Diagnosis of episodic or non-persistent arrhythmia can be made with longer periods of ECG recording to assess their relationship with symptoms during his or her routine activity.

Astonishingly the prevalence of cardiac arrhythmia is high in general population.[1-A] . Ventricular ectopy occurs in 64-100 % of apparently healthy people[1-B], 40-50 % of young or middle aged people[2,3], supraventricular ectopy and atrial fibrillation also increase with age. Frequent and complex ventricular ectopy in patients with ischaemic heart disease[4,5] or previous acute myocardial infarction[6,7] have been found to predict increased mortality from cardiac causes. However, frequent ventricular ectopy in healthy subjects is commonly accepted as a benign phenomenon without prognostic importance. Frequent ventricular ectopic beats induced by an stress may not predict graveness of condition in apparently healthy Individuals of all ages[8,9]

Hinkle et al observed that in middle aged men with asymptomatic ventricular arrhythmia were associated with sudden death[10]. In five year follow up study elderly people with more than ten (10) ventricular ectopic beats an hour had about double the mortality of those with less frequent ectopy[11]. It is difficult to distinguish between physiological and pathological ventricular ectopic activity as ectopy in apparently healthy subjects may be related to underlying silent ischaemic heart disease. It is important to undertake study for detection of arrhythmias in symptomatic patient with normal resting ECG.

Method :

In Clinical practice there are a large number of patients who come with the complaints of palpitation, history of syncope or pre-syncope, dizziness – but in many cases the cause of those clinical events can not be diagnosed from their resting electrocardiography or other laboratory investigations. Patients admitted in the Cardiology ward with the following complaints have been taken for the study.

Inclusion Criteria :

1. History or complaints of palpitation , chest pain, pre-syncope, syncope, dizziness, vertigo with non-specific resting electrocardiographic changes.
2. Suspicious resting ECG with clinically suspected ishchaemia or arrhythmia.
3. History of syncope, pre-syncope or dizziness with bifascicular block, left bundle branch block (LBBB), right bundle branch block (RBBB) in resting ECG or history of Coronary artery bypass graft (CABG).]
4. Patient of arrhythmia on treatment.

Exclusion criteria :

Patient is on cardiac pacemaker.

This study has been conducted in cardiology department of Bangabandhu Sheikh Mujib Medical University (BSMMU) during the period of February 2001 to December 2002. During these period 229 (two hundred and twenty nine) patients were studied. A clinical history was obtained by personal interview. Before ambulatory ECG recording a complete clinical examination was done including resting ECG, chest radiography and routine biochemical analysis. Diagnosis was established on the basis of history and clinical examination. Previous Acute Myocardial Infarction was recorded if Q wave abnormalities described in the Minnesota code were seen in the ECG[12]. We also asked about smoking habits in the personal interview.

Twenty four continuos ambulatory ECG monitoring was done with a portable three channel recorder (Hillmed brand, made in USA). Total weight of the recorder is 254 grams, this recorder has a digital flash card. Recording is carried out via seven leads placed on the chest to yield three channels of ECG data. After recording the flash card was removed from the device and inserted into the analyzer connected with a computer. It took about five minutes to analyse the findings, then the total twenty four hours recorded ECG was screened in the computer monitor. The patient was instructed to keep a diary to note the time when the symptoms occurred for later correlation with ECG abnormalities. These recordings were also used for measuring how often the arrhythmia occurred, determining if there were any variations by time of day or night.

Results :

During the study period, 229 number of cases were studied . Out of 229 cases 141 (61.57%) were male, 88 (38.42%) were female (Fig-I). Mean age ± SD was 43.80 ± 14.56 in females (The range was from 13 to 80 years). Mean are ± SD was 50.64 ± 15.75 in males years (The range was from 20 to 83 years). Among 229 cases clinical characteristics were -76 (33.18%) had palpitation, 64 (27.94%) had chest pain of short duration; 51(22.27%) had history of syncope or pre-syncope; 16(7.42% had left bundle branch block.

Table-I

Showing clinical characteristics of the study

Clinical characteristics (N=229)	
Palpitation	76 (33.18%)
Non specific Chest pain	64 (27.94%)
H/O Syncope, pre syncope	51 (22.27%)
LBBB	16 (7.42%)
H/O SVT	9 (3.93%)
RBBB	3 (1.31%)
Bifascicular block	2 (0.87%)
Complete Heart Block	6 (3.05%)
H/O. CABG	2 (0.87%)

9(3.93%) had paroxysmal supraventricular tachycardia (PSVT); 3(1.31%) had right bundle branch block; 2(0.87%) bifascicular block; 6(3.05%) Complete heart block; 2(0.87%) chest pain with H/O. CABG. (Table-I) After analysis of their 24 hours ambulatory ECG recording - 32 (13.53 %) were diagnosed as PSVT; 46 (20.52%) as multiple ventricular ectopics; 17 (7.42%) as

significant ST deviation ; 9 (3.93%) as SSS. Out of total 229 cases 104 (45.41%) were diagnosed as different types of arrhythmia or significant ST deviation, which was not diagnosed from their resting ECG. (Table-II)

Table –II

Showing findings of the ambulatory ECG of the study

Findings of Ambulatory ECG	
No significant changes	125 (54.59%)
Significant PVC's	46 (20.52%)
PSVT	32 (13.53%)
Significant ST deviation	17 (7.42%)
Sick Sinus Syndrome	9 (3.93%)

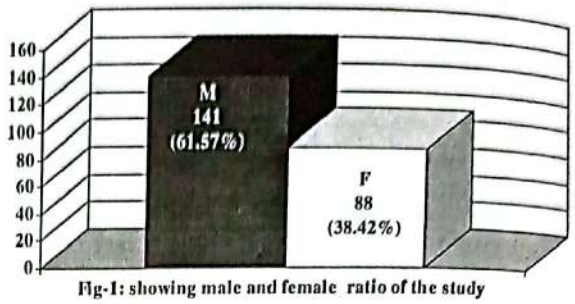

Fig-1: showing male and female ratio of the study

Total number of patient in this study was 229, which gives the diagnosis of the patient's with apparently normal resting ECG. In this study out of 229 number of patients 141 (61.57%) were male and 88 (38.42%) were female (M:F= 1.6:1). In other study of IJ Raiha, SJ Piah, A Seppanen et. al. found M:F = 1.2:1 , total number of patient was 347 [13]; Balmelli N, Naegeli B, Bertel O et al. found M:F = 3:2 total number of patient was 101[14], recruitment of the patient was almost similar. In this study Mean ± SD was 43.80 ± 14.56 in females Mean ± SD is 50.64 ± 15.75 in males. Balmelli N, Naegeli B, Bertel O et al. found Mean ± SD was 47.30 ± 15.46 in females Mean ± SD is 49.24 ± 14.35 in males14, which are quite similar to this study.

Discussion :

Persistent cardiac arrhythmia can be diagnosed easily from resting ECG but when cardiac arrhythmias are paroxysmal or intermittent then it is difficult to detect in the resting ECG. So, twenty four hours holter monitoring or in some situation forty-eight hours to ninety-six hours extended ECG monitoring might help in the diagnosis. In this series 34% of patient showed different (PSVT & significant PVC's) arrhythmias, which were not known earlier . Mc Leod AA, Jewitt DE et al. found 36 % of their study patient's had significant cardiac arrhythmia[15] & Zeldis SM, Levine BJ, Michelson EL et al found 53% of their patients (N=518) had significant srrhythmia[16] – almost similar to this study. Sick sinus syndrome was detected in 3.93% in this study where as IJ Raiha, SJ Piah, A Seppanen et al. found 5.1% which is also quite similar to this study[13]. About significant ST-T changes, in this series there were 7.4% of patients had that changes whereas Preben Bjerregaard, M.D., D.M.Sc., Amr El-Shafei et al. Found 4.5% of their cases had that changes[17] which also statistically almost similar to this study.

Conclusion :
Ambulatory ECG recording is important for dtection of different types of arrhythmia and ischaemia which were not evident in routine ECG and this method of investigation gives also therapeutic and prognostic information.

References :

1.-A. Peter R, Kowet, MD; Dusan Z, Kocovic, MD; Ambulatory electrocardiographic recording, Circulation 2003; 108 : e31

1-B. Kantelip J-P, Sage E, Duchene-Manullaz P: Findings of ambulatory ECG monitoring in subjects older than 80 years, AMJ Cardiol 1986; 57 : 398-401.

2. Brodsky M, WuD, Kanakis C, Rosen, KM. Arrhythmias documented by 24 hours contineous ECG monitoring in 50 male medical students without apparent heart disease. AMJ Cardiol 1977; 39 : 390-5.

3. Savage DD, Levy RJ, Garrison WP, Castelli P, Kligfield JB, Deverson SJ, et al. Mitral valve prolapse in the general population. III. Dysrhythmias: the Framingham study. Am Heart J 1983;106 : 582-6.

4. Vismara LA, Pratt C, Price JE, Miller RR, Amsterdam EA, Mason DT. Correlation of the standard electrocardiogram and continuous ambulatory monitoring in the detection of ventricular arrhythmias in coronary patients. J Electrocardiol 1977; 10 : 299-36.

5. Califf RM, McKinnis RA, Burks J, Lee KL, Harrell FE Jr, Behar VS, et al. Prognostic implications of ventricular arrhythmias during 24 hour ambulatory monitoring in patients undergoing cardiac catheterization for coronary artery disease. Am J Cardiol 1982; 50 : 23-31.

6. Lown B, Wolf M. Approaches to sudden death from coronary heart disease. Circulation. 1971; 44 : 130-42.

7. Moss AJ, Davis HT, DeCamilla J, Bayer LW. Ventricular ectopic beats and their relation to sudden and non-sudden cardiac death after myocardial infarction. Circulation 1979; 60 : 998-1003.

8. Kennedy HL, Whitlock JA, Sprague MK, Kennedy LJ, Buckingham TA, Goldberg RJ. Long-term follow-up of asymptomatic healthy subjects with frequent and complex ventricular ectopy. N Engl J Med 1985; 312 : 193-7.

9. Busby MJ, Shefrin EA, Fleg JL. Prevalence and long-term significance of exercise-induced frequent or repetitive ventricular ectopic beats in apparently healthy volunteers. J Am Coll Cardiol 1989;14 : 1659-65.

10. Hinkle LE, Carver ST, Stevens M. The frequency of asymptomatic disturbances of cardiac rhythm and conduction in middle-aged men. Am J Cardiol 1969; 24 : 629-50.

11. Martin A, Benbow LJ, Butrous GS, Leach C, Camm AJ. Five-year follow-up of 101 elderly subjects by means of long-term ambulatory cardiac monitoring. Eur Heart J 1984; 5 : 592-6.

12. Criteria Committee of New York Heart Association. Nomenclature and criteria for diagnosis and disease of the heart and great vessels. 8th ed. Boston: Little, Brown, 1979 : 188-250.

13. I J Raiha, S J Piah, A Seppanen, P Puukka, L B Sourander ; Predictive value of continuous ambulatory electrocardiographic monitoring in elderly people ; BMJ 1994; 309 : 1263-1267 (12 November)

14. Balmelli N, Nargeli B, Bertel O, Diagnostic yield of automatic and patient triggered ambulatory cardiac events recording in the evaluation of patients with palpitations, dizziness, syncope; Clin Cardio 2003 ;26(4) : 173-6.

15. McLeod AA, Jewitt DE, Role of 24 hour ambulatory ECG monitoring in a general hospital; PMID 638693[Pub-med- indexed for MEDLINE].

16. Zeldis SM, Levine BJ, Michelson EL, Morganroth J, Cardiovascular complaints. Correlation with cardiac arrhythmias on 24 hour electrocardiographic monitoring, PMID 7418465 [Pub-med- indexed for MEDLINE].

17. Preben Bjerregaard, M.D., D.M.Sc., Amr El-Shafei, M.D., Susan L. Kotar, and Arthur J. Labovitz, M.D. ST Segment Analysis by Holter Monitoring: Methodological Considerations : Annals of Noninvasive Electrocardiology ; Volume 8 Issue 3 Page 200 - July 2003 doi:10.1046/j.1542-474X.2003. 08306.x.

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Pattern of Valvular Lesions in Patients with Rheumatic Heart Disease Undergoing, Echocardiography - A Study of 346 Patients

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Abstract : *Three hundred and forty six patients with Rheumatic Heart Disease were undergone echocardiography including 2D-M Mode, colour doppler and in selected cases transesophageal echocardiography. There were 47% male and 53% female. Mean age of the male patients was 31 years and of female patients was 33 years. Among all the cases 60% had isolated mitral valve lesions, 10% had isolated aortic valve lesions and 30% had combined lesions. The mitral valve lesions were significantly higher in female than male and aortic valve lesions significantly predominated in male. Isolated mitral valve stenosis was significantly higher in both sexes*

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Introduction :

Rheumatic fever and its sequel rheumatic heart disease is a major health problem in developing countries. Although it was thought to be nearly eradicated from developed countries but it continues to be a challenge for developing countries like Bangladesh as its prevalence is quite high. Rheumatic heart disease (RHD) causes a significant number of morbidity and mortality in Bangladesh and accounts for 34% – j42% of hospital admission of all cardiac cases[1, 2]. The prevalence of rheumatic fever and RHD in Bangladesh is respectively 4.2 – 6.2 and 2.5 – 3.6 per thousand populations[3,4]. The mitral valve is the most common valve involvement and pure mitral stenosis occupies a great portion of total RHD in Bangladesh[5]. Two-thirds of them occur in female patients[6].

According to Okubo S et al and Islam MN et al, the pure mitral stenosis varies from 54% to 45% respectively in-patients with RHD[7,2]. In contrast, aortic valve lesions in male were significantly higher[8].

In our economically underprivileged country with limited health facilities, the course of this disease is unpredictable and usually malignant; and surgical intervention is eventually required for most of the patients. For proper evaluation, non-invasive technique like two-dimensional and M-mode echocardiography is always preferable rather than invasive methods which is a costly affair and is not without risk. Bangubandhu Sheikh Mujib Medical University Hospital is a multi-disciplinary teaching hospital and academic cases like valvular Heart diseases are referred to this hospital from different regions of the country. So pattern of the valvular lesions is almost a true picture of RHD of our country.

Objective :

To analyze the pattern of different types of valvular lesions in patients with rheumatic heart disease and to evaluate whether this pattern is changing over time. It will help to guide the health planners to mobilize the limited resources to combat the major burns of rheumatic fever sequel.

Materials and Methods :

The study was carried out in the 'Echocardiography Laboratory' (Echo Lab) of the Cardiology Department of Bangubandhu Sheikh Mujib Medical University during the period since July 1995 to June, 2001. Three hundred and forty six patients clinically diagnosed to have rheumatic valvular heart disease on the basis of clinical findings, electrocardiogram (ECG) and chest X-ray examination were included in the study. The findings of these cases were compared with the echocardiographic findings before confirming our diagnosis in the Echo Lab. Regarding mitral

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stenosis all cases were included unless otherwise diagnosed, e.g., mitral annular calcification. Bicuspid aortic valve and degenerative aortic sclerosis were excluded in aortic valve lesion cases. Functional tricuspid regurgitation as a consequence of mitral stenosis were not entitled as a separate rheumatic valve lesion.

In most of the cases, 2-D and M-mode echocardiography was done by Seimens machine and in the later period of the study by colour Doppler Aloka-5000 echocardiography machine. 2.5 to 3.5 MHz probe were used. During echocardiography, patients were in left lateral position in most cases and standard views were taken. Statistical analysis was done in computer and numerical data were expressed in mean ± SD and comparison between same group is expressed by the use of unpaired t test and Z test. P value < 0.05 is taken as highly significant.

Results :

Table-I among 346 patients with rheumatic heart disease, 165 were male (47.7%) and 181 were female (52.3%). Age range of male patients were from 8 yrs to 60 yrs with their mean age ± SD 30.58 ± 13.35; and that of female 4 yrs to 77 yrs and 32.58 ± 14.35 respectively (Table- I).

Table- II among all the cases isolated mitral valve lesions were found in 206 (59.52 %) cases, isolated aortic valve lesions in 33 (9.54 %) cases, combined mitral and aortic valves lesions in 106 (30.64 %) cases and pulmonary stenosis in one (0.30 %) female case.

Table III show the pattern of involvement of mitral, aortic and combined valve lesions in both male and female patients. Isolated mitral valve lesion is common in female which is about 60.7 % and isolated aortic valve lesion is common in male, about 81.8% and combined valve involvement in both male and female is almost equal in number.

Table - IV we show in table IV total pattern of valvular lesion in both sex. Among mitral valve lesion mitral stenosis, mitral regurgitation even mitral stenosis with mitral regurgitation, all types of lesion are more common in female. Regarding aortic valve, aortic stenosis, aortic regurgitation and aortic stenosis with aortic regurgitation are common in male. In combined pattern mitral stenosis with aortic stenosis is most common and which is more in female patients. Mitral regurgitation with aortic regurgitation is more common in male patients.

Table - I

Age and sex distribution of valvular lesions.

Sex	Number	Percentage	Mean age ± SD
Male	165	47.7%	30.58 ±13.35
Female	181	52.3%	32.58 ±14.35
Total	346	100%	

Table II

Pattern of valvular lesions:

Type of lesion	Number	Percentage
Isolated mitral valve	206	59.52
Isolated aortic valve	33	09.54
Comb. Mitral & aortic valve	106	30.64
Pulmonary valve (stenosis)	1	00.30

Table III

Sex distribution of different valve lesions.

Valve involvement	Male No. with %	Female No. with %	P-value
Isolated mitral valve	81(39.3%)	125(60.7%)	0.002
Isolated aortic valve	27(81.8%)	6(18.2%)	0.001
Comb. Mitral & aortic	57(53.8%)	49(46.2%)	0.58 valve

Table-IV

Pattern of different types of valve lesions

Types of valve lesions	Male No. with %	Female No. with %	P-value
Mitral			
Mitral stenosis (MS)	51 (30.9 %)	78 (43.1 %)	0.017*
Mitral regurgitation MR	9 (05.5%)	19(10.5 %)	0.059*
MS with MR	21(12.7%)	28 (15.5 %)	0.317
Aortic			
Aortic stenosis AS	7(4.2%)	1(0.6%)	0.034*
Aortic regurgitation AR	13(7.9%)	4(2.2%)	0.029*
AS with AR	7(4.2%)	1(0.6%)	0.034*
Combined			
MS with AS	13(7.9%)	25(13.8%)	0.052*
MS with AR	7(4.2%)	2(01.1%)	0.096
MR with AR	15(9.1 %)	4(02.2%)	0.012
Other combinations	22 (13.3 %)	18 (09.8 %)	0.527
Pulmonary stenosis PS		1(0.6%)	

Table-V show the age distribution of the mitral stenosis cases. Majority of cases are in 19 - 40 years of age group.

Table V

Age group of mitral stenosis.

Age group(Years)	Number	Percentage
Below 40	87	67.44%
Above 40	42	32.56%
Total	129	100%

Discussion :

In the present study, 346 patients who were diagnosed clinically as Rheumatic heart disease and later on confirmed with investigations, including chest X - ray, ECG, and echocardiogram, and pattern of their valvular lesions were analyzed.

Among the valve lesion mitral valve lesions is the predominant which is about 60% 8 Mean age of the patients is 31.62 ± 13.90 that is the 3rd decade and this is consistent with the findings of wood and glenn et al. who stated to be average age 37.6 yrs[9,10]. But Powik Supriadi et al showed the majority of rheumatic heart disease patients were 20 - 29 years[11]. In total valve lesions male and female ratio1:1 which is almost consistent with Hossain et. al[12]. In our study we see that common age group of mitral stenosis is 19 - 40 years which is consistent with the Zafar et al [8] and 2/3 cases of mitral valve lesions were occupied by female patient[6].

In the aortic valve disease aortic regurgitation is more common than aortic stenosis. As single valve lesion they are making a small percentage of total valvular heart disease. On the other hand pure mitral stenosis made about 40 % of the total valvular lesion[8, 1 2]. Here in aortic valve disease we can see the predominance of the male patients which is almost 5 times the female patient which is consistent with previous study in Bangladesh [8].In combined valve lesion mixed mitral with aortic valvular diseases are making the majority of the, cases.

The bulk of Rheumatic heart, disease is due to mitral valve involvement & mitral stenosis comprises 1/3rd of total Rheumatic heart disease which is common in 3rd decade so to reduce the morbidity and mortality from RHD in this young age group is an alarming point for our country. As this pattern of valvular lesion is not changed over time it is a burning issue for our country wher a good number of patients are undergoing closed mitral commissurotomy(CMC). In last 20 years long term and short term out come of CMC in our country is good. In 13 government medical hospital

of Bangladesh where about 20 cardiovascular surgeons are working and for CMC cost is only ≤100.

Pattern of valvular lesions in patients with Rheumatic heart disease is similar to that of industrialized nations in the early 20th century and in this part of the country 20 years back. The existing information indicates that the magnitude of the problem may not have changed. So proper strategy, manipulation of manpower and health resources for treating in-patients with RHD specially MS may mitigate some problem.

So search should be continued for cost effective modalities of treatment with limited health resources and should be available at peripheral part of the country.

References:

1. Soler JS, Galve E: Valve disease world wide perspective of valve disease. Heart 2000; 83 : 721-725
2. Islam, MN Alimuzzaman M, Zafar A and Malik A: Two dimensional echocardiography analysis of Rheumatic mitral valve disease in Bangladesh, proceedings at 2nd Bangladesh Japan conference on cardiovascular disease 1986;-148.
3. Hossain M, Tokeshi S, Haque S, Razia SM, Arzu S, Jalil Q, Hossain MI, Katsuhiro Y, Kuno Y, Reaul KK, Zafar A, Malik A: Epidemiology of Rheumatic fever and Rheumatic heart disease in urban and rural school : Surgery of 8102 children. 10th APCC 1991, Seoul Korea. p-140 10th Asian Pacific Congress of Cardiology 1991, Korea.
4. Haque KMHSS, Hossain M, Mahmud SM, Tokeshi S, Arzu S, Jalil Q, Hossain M, Yoshitke K, Kuno Y, Zafar A, Malik A: Epidemiology of Rheumatic fever and rheumatic heart disease; observation on 15798 children of rural and urban area. European heart Journal, Volume 13, Abstract suppliment, August 1992, p-105.
5. Taranta A and Mark Owitz,M: Rheumatic fever. MTP press Ltd. England P60, 1981.
6. Braunwald E: Valvular Heart Disease. In: Heart disease : Braunwald 5th ed W.B. Saunders Company 1997; 32 : 1007.
7. OkuboS. Masuday, KawazocK Atobe M Manable H with Japan : Rheumatic heart disease in Bangladesh and Japan : Difference of clinical features including two dimensional echocardiography findings, Proceedings of Bangladesh - Japan Joint conference on cardiovascular disease 1984;1
8. Zafar A, Islam N, Newaz T, Amanullah M, Jalluddin M, Khandaker RK, Malik A. Echocardiogaphc analyzed of 7134 cardiac eases in Bangladesh Proceedings of 2nd Bangladesh Japan conference on cardiovascular disease 1986; 143.
9. Wood P : An appreciation of mitral stenosis 1) clinical features 11) Investigation and results. Br MidJ 1954; 1: 1051-63. with 1113-24
10. Glenn WLL, Calabrese C, Gooyear AVN, Humen, Stansel HC: Mitral Valvolomy. AMJ Surgery 1969; 177 : 493.
11. Powik Supriadi MD : The pattern of Rheumatic heart disease in sub urban area, Malang, Indonesia. 10th Asian pacific congress of cardiology October 1991 Seoul, Korea,p-139
12. Hossain AKMM, Jamil AA, Mamun AA, Haque SA, Majumder AAS, Chowdhury NA, Zaman MA: Clinical Profile of Diagnosed Rheumatic Mitral Stenosis- Study of 50 cases admitted in Dhaka Medical College Hospital. Journal of Dhaka medical college 1995; 4(1): 25 : 29.

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REVIEW ARTICLE

Low birth weight as the Risk factor for cardiovascular Disease-A review

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Introduction :

Low birth weight and cardiovascular risk factor is a growing interest in medical research. A study in Hertfordshire comprising 5600 men born in that place in 1911 and 1930 showed that among men who weighed 8.2 kg or less at one year of age had three times death rates from ischemic heart disease than among those who weighed > 12.3 kg[1]. This study enhance the suspicion that the intrauterine programming place a major role in the development of cardiovascular disease which arose from a series of geographical studies in England and Wales, revealing that the large differences in cardiovascular mortality between different areas of the country are paralled by similar differences in neonatal mortality around 70 years ago[2]. In subsequent years, findings suggested that ischaemic heart disease and associate conditions like hypertension, Type-2 diabetes mellitus, hyper fibrinogenaemia originate through impaired growth and development during foetal life and infancy[3,4,5].

Since the studies done in the above years provided the evidence that association of low birth weight (LBW) with abnormal glucose tolerance, hypertension (HTN) and Coronary artery disease (CAD) separately[6,7] and since hypertension and type 2 Diabetes tends to occur in the same patient , it was remaining to see if subjects with low birth weight(LBW) do have also other abnormalities, including high plasma insulin, high serum triglyceride concentration, low serum HDL concentration, high body mass index and high waist - hip ratio so as to fit in a combination of abnormalities known as syndrome X- (now termed as cardiovascular dysmetabolic Syndrome). In a study in Hertfordshire, the percentage of men with syndrome X fell progressively from 30% in those with birth weight of 2.5 kg or less to 6% in those whose birth weight was more than 4.3 kg. These subjects with syndrome X in comparison to other men in the study had higher 2-hour plasma insulin concentration, lower HDL cholesterol, raised fasting plasma insulin and 32-33 split pro-insulin concentration, raised apolipo-protein and plasminogen activator inhibitor concentration. The study concluded that type 2 Diabetes and Hypertension have a common origin and sub optimal development in utero and that the syndrome X should be renamed as small baby syndrome[8].

In 1994 Phillips et. al. investigated the insulin resistance in the adults by measuring insulin resistance (IR) using insulin tolerance test showing Insulin Resistance was greater in subjects with low ponderal index at births. The highest Insulin resistance was found in those subjects with low PI at birth and high BMI in adults[8]. Studies done from different geographical areas in the world also supported the relationship between LBW and IR including cardiovascular disease[9-15]. Similar report of increased cardiovascular disease was obtained in a study done in the Indian sub-continent showing short birth length and small head circumference at birth being associated with coronary artery disease[16]. In recent years studies have revealed correlation with LBW and endothelial function[17]. Inverse co-relationship between height and coronary artery disease as revealed by coronary angiography has also been reported[18-20]. The association between height and coronary artery disease is merely a reflection of well documented association between birth weight and cardiovascular disease, since adult height is 'correlated to birth weight[21].

The mechanism for the association between low birth weight and cardiovascular disease has not been fully described and documented. Hales and Barker proposed that the poor fetal and early neonatal nutrition imposes mechanism of nutritional thrift upon a growing individual. In the major long term consequences of such thrift is

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impaired development of endocrine pancreas and certain other organ and tissue leading to functional abnormalities seen in later part of life which includes DM, hypertension and also possibly some hyper' lipidaemia and Insulin resistance collectively known as cardiovascular dysmetabolic syndrome. This famous thrifty phenotype hypothesis is also known as Barker hypothesis.

In contrast to the thrifty phenotype hypothesis the basis for susceptibility of IR could be the result of a thrifty gene which promotes fat deposition and storage of calories in times of plenty and provide a positive selective advantage during the period of food shortage and starvation- the thrifty genotype hypothesis[22]. The hypothesis can be translated in a simple way- people who were thin at birth but obese as adult are most resistant to insulin[8].

The thrifty gene confers survival advantage during the regular famine and natural disaster and the fetus carring thrifty gene in an environment of intrauterine malnutrition are more likely to survive in later life with abundance of highly refined foods over stimulates the mechanism of insulin production (which once used to store energy more efficiently) thus leading to hyperinsulinaemia. This hypothesis in which hyperinsulinaemia is the lynch pin also explained the hypertension and atherosclerosis that accompany Diabetes thus constituting cardiovascular dysmetabolic syndrome.

To find out the issue whether a genetic or intrauterine factors are responsible for contribution to the relationship between IR and LBW. Jahan S et al. measured the paternal insulin sensitivity and evaluated the correlation between paternal insulin sensitivity and birth weight.[23] In the study the author hypothesized that if the genetic predisposition to IR is linked to poor early growth then the paternal insulin sensitivity should also be related to the parameters of fetal growth as insulin resistance precede the onset of clinical NID Diabetes by several decades.[24] The result of the study revealed the paternal insulin sensitivity has got no relationship with the parameters of LBW which implies that the link between LBW and IR syndrome in later life is not genetic but may be intrauterine in origin. The author of course cautioned that the study could not exclude the possibility of genetic origin solely because genetic transmission could be due to maternal or could be originated through genetically determined B-cell secretory deficiency rather than Insulin resistance.

The study done by S. Jahan et. al. put Berker hypothesis one step forward by excluding one of the important aspect of genetic link implying that the nutritional care of the mothers during child bearing age may prevent adult disease in later life (thrifty phenotype). There are also alternative explanation provided evidence and proposed that intrauterine programming of the hypothalamic pituitary adrenal axis may be a mechanism of LBW and Insulin resistance syndrome[25]. Later on levitt NS et al, also confirmed that cortical axis activation is an early feature in linking LBW with adult cardiovascular and metabolic diseases[26]. Hypercortisolism may cause cardiovascular abnormality in male directly while in female indirectly through the hyperinsulinasmia and hyperandrogenism, as S Zathmari M et al, showed increased DHEA level in cortisol primed female with Low Birth Weaght babies[27].

With some supportive evidences other proposed mechanism involving link between LBW and hypertension may be due to reduced nephrogenisis with a higher threshold for pressure natriuresis and greater - susceptibility of progressive renal disease, impaired development of endothelium, increased sensitivity to glucocorticoids[28].

Conclusion :

The traditional risk factor for CVD has not been sufficient to explain all the epidemiological variables that occurs with this disease. The increasing CVD in this part of the world along with declining incidence in the western countries may reflect the population at health transition.

This well suits with the concept of intrauterine origin of adult cardiovascular disease- may be the missing link in explaining epidemiological variation of cardiovascular diseases. So considerable work and on going research need to be done to explore the issue further. The issue more relevant specially in this part of the world where LBW is highly prevalent[29] and cardiovascular disease is increasing alarmingly. If intrauterine environmental factor is well established and well explained this may have tremendous impact in cardiovascular diseases prevention by improving the nutritional status and by reducing other factors responsible for low birth weight babies.

References:

1. Barker DJP, Winteen PD, Osmond C, Margetts B, Simmonds SJ. Weight in infancy and death from ischaemic heart disease. Lancet, 1989 : 577-580
2. Barker DJP, Osmand C. Infant mortality, Child hood nutrition and ischaemic heart disease in England and Wales. Lancet 1986; 1077-1081.
3. Barker DJP, Osmand C, Magell SB, Simmonds SJ. Fetal and placental size and risk of hypertension in adult life. Br med J 1990; 301 : 259-262.
4. Hales CN, Barker DJP, Clark PMS, Cox LJ, Fall C, Osmand C et al. Fetal and infant growth and impaired glucose tolerance at age 64. Br. Med J 1991; 303 : 1019--1022.
5. Phipps K, Barker DJP, Hales CN, Fall CHD, Osmand C, Clark PMS. Fetal growth and impaired glucose tolerance in men and women. Diabetologia 1993; 36 : 225-238.
6. Barker DJP, Bull AR, Osmand C, Simmonds SJ. Fetal & plaecntal size and risk of hypertension in later life. Br. Med J 1990; 301 : 259-262.
7. Barker DJP, Osmand C, Simmonds SJ, Weild GA. The relation of small head circumference and thinness at birth to death from cardiovascular disease in adult life. Br. Med J 1993; 306 : 422-426
8. Phillips DIW, Barker DJP, Hales CN, Hirst S, Osmond C. Thinness at birth and insulin resistance in adult life. Diabetologia 1994; 37 : 150-154.
9. Valdez R, Athens MA, Thompson GH, Bradshaw BS, Stern MP. Birth weight and adult health outcomes in a Biethnic population in the USA. Diabetologia 1994; 37 : 624-631.
10. Mc Cance DR, Pettitt DJ, Hanson RL, Jacobsson LTH, Knowler WC, Bennett PH. Birth weight and non-insulin dependent diabetis: Thrifty genotype, thrifty phenotype, or surviving small baby genotype ? Br Med J 1994; 308 : 942-945.
11. Levitt NS, Lambert EV, Woods D, Hales CN, Andrewr, Seckb. Impaired glucose tolerance and elevated blood Pressure, low birth weight, nonobase, young south African adults: early programming of cortisol axis. J clin endocrinol Metab 2000; 85(12) : 4611-8.
12. Loos RJ, Fegard R, Beunen G, Derom C, Vlietinck R.Birth weight and blood pressure in young adults: a prospective twin study . Circulation 2001; 104(14) : 1633-1638.
13. Seidman DS, Laor A, Gale R, Stevenson DK, Mashiach S, Dano YL . Birth weight, current body weight and blood pressure in late adolescence. BMJ 1991; 302(6787) : 1235-1237.
14. Vanclusi F, Alletto M, Busgio A, Fulco G, Pasadiso R, Piangia M . Inverse relationship between fetal Growth and actual pressure in children and adults. Ital Cardiol 1995; 25(7) : 833-841 .
15. Uiter waal CS, Anthony S, Launer LJ, Witteman JC, Trouwbor AM, Hofman A, Grobbee DE. Birth weight, growth and blood pressure : an annual follow up study of children aged 5 Through 21 yrs. Hypertension 1997; 267-271.
16. Stein CE, Fall CHD, kumaran K, Osmond C, Cox V, Barker DJP. Fetal growth & coronary heart disease in South India. Lancet 1996; 348 : 1269-73.
17. Leeson CP, Katten horn M, Morley R, Lucas A, Dean field JE, Impact of low birth weight and cardiovascular risk factors on endothelial function in early adult life. Circulation 2001; 103(9) : 1264-8.
18. Obi N Nwasokwa, Maurice Weiss, Clifford Gladstone, Bodenheimer. Higher prevalence and greater senerity of coronary artery disease in short VS tall men referred for coronary arteriography. American Heart Journal 1997;133 :147-52.
19. Chowdhury AHK, Meshkat Ahmed C, Jamaluddin Mir, Jaman M.A.. Comparison of severity of coronary artery disease in short vs tall men : A study of Bangladeshi patients who under went coronary angiography. In : the proceedings of second international conference of cardiovascular disease 1998.
20. Hoque I, Ahmed QS, Siddique MA, Banerjee S, Ahmed CM, Sayed A et al. Higher

prevalence and greater senerity of coronary artery disease in short VS tall men referred for coronary angiography. In : The proceding of 24th annual general conference of the Chest and heart association of Bangladesh 2002.

21. Brown DC, Byrne CD, Clark PM et al. Height and glucose tolerance in adult subjects. Diabetologia 1991; 34 : 531-533.
22. Neal JV. Diabetes militias : a "thrifty genotype rendered detremental by "Progress"? Am I hum Genet 14:353-362.
23. Jahan S. An investigation into the Genetic contribution to the relationship between insulin resistance and birth weight, MS Gynecology and Obstetrics thesis 1999.
24. Lillioja S, Moot DM, Spraul M, Ferraro R, Foley JE, Ravussin E, et al. Insulin resistance and insulin secretory dysfunction as processors of non insulin dependant diabetes mellitus: Prospectiven studied of pima Indians. N Eng L J Med 1993 ; 329 : 1988-1992.
25. Phillps DIW, Barker DJP, Fall CHD, Seckl JR, Whorwood CB, Wood PJ,et al. Elevated plasma cortison concentrations: A link between low birth weight and the insulin resistance syndrome? J Clin Endocrine Metab 1998; 83 : 757-60.
26. Szathmasi M, Reusz G, Tulassay T. Low birth weight, adrenal and sex hormones and their correlation with carbohydrate metabolism and cardiovascular physiology investigated in young adults. Orv Hetil 2000; 141(36) :1967-73.
27. Lack land DT, Egan BM, Ferguson PL. Low birth weight as a risk factor for hypertension J clin hypertens (Greenwich) 2002; (2):133-6.
28. Hinchlliffe SA. Lynch MRJ, Sargent PH, Howard CV, Van Velzen : The effect of intrauterine growth retardation on the development of renal nephrons. Br. J Obstel Gynaeco1992; 2 : 96-301.
29. Nahar N, Afroza S, Hossain M. Incidence of low birth weight in three selected communities in Bangladesh. Bangladesh Med Res Coun Bull 1998; 49-54.

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Pulmonary Cryptococcosis : Localised and Disseminated Infection - A Review

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Introduction & Etiologic agent

Cryptococcosis, the most common life threatening fungal infection in patients infected with the HIV, is a systemic infection caused by cryptococcus neoformans, the yeast form of the dimorphic fungus Basidiomycete Filobasidiella spp[1] The organism was originally thought to exist as a yeast and the name of this imperfect-form, cryptococcus, has been maintained. The spectrum of disease ranges from asymptomatic pulmonary infection in normal hosts to rapidly fatal meningitis in immunosuppressed individuals. Clinically, the most commonly recognized form of cryptococcal disease is chronic meningitis. [2,3] pulmonary, cutaneous and widely disseminated forms of the infection are also recognized. In some postmortem studies, C. neoformans has presented in the lung and the central nervous system (CNS) with equal frequency[4,5]

This fungus reproduces by budding and forms round, yeast like cells. Within the host and on certain culture media, a large polysaccharide capsule surrounds each yeast cell. The fungus grows well in smooth, creamy-white colonies on Sabouraud's or other simple media at 20° to 37° C. Identification of the organism is based on gross and microscopic appearance, biochemical test results, and growth at 37°C. The results of Nucleic Acid hybridization or the formation of brown pigment on Niger seed agar can also be used for identification.

The fungus has four capsular serotypes, designated A, B, C and D. There are also two mating types - Filobasidiella neoformans var. neoformans for serotypes A and D and F. neoformans var. bacillspora for serotypes B and C. Organisms not cultured under making conditions are designated C. neoformans var. neoformans for serotypes A and D and C. neoformans var. gattii for serotypes B and C; a simple color medium destinguishes the two varieties.

Epidemiology :

Cryptococcosis has been recorded from most countries, although it is most prevalent in the United States and Australia. It is rare before puberty. Cryptococcosis is the most common life-threatening fungal infection in patients infected with the Human Immunodeficiency Virus (HIV) type I and occurs in 5 - 8% of patients with Acquired Immunodeficiency Syndrome (AIDS) [6,7], and Cryptococcosis is and AIDS-defining condition in the 1987 CDC / WHO case definition for AIDS.

With the increased use of immunosuppressive agents and the increasing incidence of Acquired Immunodeficiency Syndrome (AIDS), the incidence of cryptococcal disease seems to be increasing[8]. Before the AIDS epidemic in the United States approximately 50% of cases were said to occur in normal persons. By contrast, in the United Kingdom 85% of cases were found in patients with underlying disorders. The serotype C. neofol·mans vat·. gattii, found specially in Australia and Papua New Guinea, is associated particularly with infection of the immunocompetent, whereas the more widespread variety C. neoformans vat". neoformans is increasingly associated with infection of the immunosuppressed and is a common complication of late infection with HIV[9,10]. Weathered pigeon droppings commonly contain serotype A or D (C. neoformans var. neoformans). C. neoformans var. gattii has been isolated from the litter around some species of Eucalyptus trees. The distribution of this Eucalyptus species in Australia corresponds to the

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distribution of infections due to C. neoformans var. gattii in that country.

The incidence appears to be declining in some areas of the United States, probably as a result of highly active antiretroviral therapy and use of fluconazole for oropharyngeal candidiasis. Patients who have undergone solid - organ transplantation or glucocorticoid therapy and those with sarcoidosis, Hodgkills disease, collagen disease, carcinoma are also at increased risk for infections with C. neoformans var. neoformans. Infections with var. gattii have been rare among AIDS patients and other immunocompromized patients, even in subtropical climates, where var. gattii infection occurs in previously healthy individuals. Evidence for the existence of subclinical infection is provided by the repeated isolation of C. neoformans In Sputum from individuals without evidence of CDC = Centers for Disease control, Atlanta Georgia: WHO = World Health Organization.

disease and by the positive skin test with a skin - test - reagent (used in some pilot studies in the United States) in persons without any overt sign of infection.

Pathogenesis and Pathology :

The organism may be found in the soil, although it is not known whether the yeast or hyphal form is predominant. It is most readily found in bird, especially pegion, droppings and in soils contaminated with such excreta[11]. The yeast form is only about 5um in diameter and therefore potentially respirable; the evidence now strongly suggests that the primary route of infection in pulmonary, neurological and disseminated cryptococcosis in humans and in experimental animals is via the inhalation of the fungus into the lungs. Inhalation of the yeast does not necessarily lead to pulmonary cryptococcosis. There is clear evidence of different degrees of resistance to infection by different species of animals. When disease does occur it appears to be sporadic and there is no evidence of transmission from humans or other animals to humans.

The portal of entry is the lung. Once in the alveoli, the small yeast germinates. The large capsule quickly reappears as the fungus multiplies. The capsular polysaccharide is antiphagocytic. A non-encapsulated cryptococcus is readily ingested and destroyed by neutrophils, whereas an encapsulated one resists phagocytosis and, thus, killing. Killing of ingested cryptococcai is a function of both oxidative and nonoxidative mechanisms within the neutrophils. Patients with chronic granulomatous disease, whose neutrophils have defective oxidative mechanisms, are often infected by this fungus. Infections with C. neoformans are seen in both normal and immunocompromised hosts. The underlying process are Sarcoidosis, Hodgkin's disease, Collagen disease, Carcinoma, the administration of systemic corticosteroid therapy, or AIDS, the commonest predisposition.

Pulmonary infection has a tendency toward spontaneous resolution and is frequently asynlptornatlc. From the lung the organism spreads to involve other organs or sites such as memnges. Silent haematogenous spread to the brain leads to clusters of cryptococci in the perivascular areas of cortical gray matter, in the basal ganglia, and, to a lesser extent, in other areas of CNS. Cell mediated immunity figures prominently in host defense against cryptococci. The central role of the T-helper lymphocyte in protecting against cryptococcal disease has been further underlined by the frequent association of cryptococcosis with AIDS, the most profound form of deprest cell - mediated immunity known[12]. In fact, AIDS is now the major risk factor for disseminated forms of cryptococcosis, including meningitis, and a large majority of all serious cryptococcal infections occur in the setting of AIDS[6].

Cryptococcal infection in the lung in normal hosts is eventually limited by a granulomatous inglamatory reaction[13] In patients with severe suppression of cell mediated immunity, granulomas are not seen and the organisms grow unchecked with predominantly macrophage and giant cell reaction; some plasma cells and lymphocytes may be present but well formed granulomas are not common. In these infected tissues, cryptococcus is seen to be surrounded by a thick capsule of polysaccharide, which may be of value to the organism by preventing its recognition by host defences and by enlarging it sufficiently to be too big for ingestion by macrophages. The organism appears to excite a cell mediated immune response,

although humoral antibodies are also produced[14,15].

The fungus is tropic for CNS, and cryptococcal meningitis is the most common form of extrapulmonary spread. When severe infection occurs, the most dangerous lessions are found in the brain and men inges. It is not known whether the systemic spread of the fungus is a routine event, but presumably the organism is carried to the CNS by the blood stream and,finds appropriate conditions for grow the; it has been shown that cerebrospinal fluid (CSF) is a good culture medium and that inflammatory responses to cryptococcus are delayed or absent in the brain[16] In the more chronic cases a dense basilar arachnoiditis is typical. Cryptococci are best seen in tissues by staining with methenamine silver or periodic acid - Schiff.

Pulmonary Cryptococcosis

Acute or subacute respiratory disease caused by C. neoformans rare in most parts of the world, but is well recognized in the United States and in many cases appears to have been asymptomatic and self-limiting[11,4]. The lungs are important as the site of entry of the organism when it causes neurological or disseminated disease; very occasionally pulmonary manifestations are the dominant or only clinical feature. Even though apparently normal persons occasionally develop cryptococcal disease, the illness is most common in patients with AIDS, those with Hodgkin's disease, organ transplant recipients, and patients receiving corticosteroids. The natural history of pulmonary cryptococcal infection in normal hosts is spontaneous resolution, whereas in immunocompromised patients extra pulmonary spread is the rule[17].

Patients with pulmonary cryptococcosis may be free of symptoms or have non - specific complaints. Fever, malaise, chest pain, and cough occur frequently in symptomatic patients[17]. Pulmonary cryptococcosis causes chest pain in about 40% of patients and cough in 20%. Many patients have no pulmonary symptoms but have infiltrates on routine chest roentgenograms obtained during evaluation for symptoms of chronic meningitis. The chest X-Ray shows one or more dense infiltrates, which are often well circumscribed. Cavitation, pleural effusions, and hilar adenopathy are infrequent. Calcification is not evident, and fibrotic stranding is rarely noticeable. In some patients no treatment is required, and the whole process resolves, although it is probably advisable to give chemotherapy to those with prolonged disease or underlying abnormalities. The laboratory diagnosis is made by biopsy or culture.

Isolated cryptococcal granulomas (cryptococcoma) may present as coin lesions and are removed surgically to exclude carcinoma. Once the correct diagnosis is made, many workers advise a short course of amphotericin B or fluconazole as there is a small risk of dissemination to other organs following surgery.

Disseminated Cryptococcosis :

The best recognized form of extrapulmonary cryptococcosis is meningitis; again most patients of cryptococcosis have meningoencephalitis at the time of diagnosis; also C. neoformans is the most conlnlon cause of meningitis in AIDS patients. Meningitis, the commonest manifestation of cryptococcosis, may occur at any time during the course of HIV infection, either as the initial opportunistic infectious disease or as a later complication in patients with AIDS diagnosed previously on the basis of one or more opportunistic infections or AIDS - related malignancy.

This may present with signs of acute meningism. However, more usually, the features are indolent and less specific. This form of the infection is invariably fatal without appropriate therapy; death occurs any time from 2 weeks to several years after the onset of symptoms. Early manifestations include headache, nausea, staggering gait, dementia, irritability, confusion and blurred vision. Both fever and nuchal rigidity are often mild or lacking. Fever and headache, the most common symptoms, are present in about 80%- 90% of patients. Non specific symptoms, including nausea, vomiting, and malaise, are seen in <50% of patients. Meningismus occurs in only 30%, alteration of mental status in 20%, and photophobia in 19% - 28%. Signs and symptoms Indicating focal neurological disease are uncommon, e.g., seizures occur in <10%. Papilloederna is evident in one - third of cases at the time of diagnosis. Cranial nerve palsies, typically asymmetric, occur in about one - fourth of cases. Other lateralized signs are rare. With progression of the infection, deepening

coma and signs of brianstem compression appear. Autopsy often reveals cerebral oedema in more acute cases and hydrocephalus in more chronic cases. AIDS patients present with disseminated disease. The signs of meningeal involvement may be very subtle and the infection has often spread to other sites such as liver and spleen as well as skin, genitourinary tract, bone marrow and blood. The presence of persistent fever and headache in any member of a high - risk group, any individual with documented HIV infection, or any person with AIDS should signal an evaluation for cryptococcal disease of the CNS. Although multiple infectious and noninfectious diseases may mimic CNS cryptococcosis, the primary diagnostic considerations include neurological disease caused by HIV, toxoplamsosis, and lymphoma, either primary CNS or rrretastatic disease.

Other Sites :

Cryptococci may disseminate to other sites including liver, spleen, kidney, skin or bone. Infection in skin and bone are most often seen in patient with sarcoidosis. It is estimated that about 10% of patients with cryptococcosis have skin lesions, and the vast majority of patients with skin lesions have disseminated infection (e.g.. meningitis). One or a few asymptomatic tiny papular lesions appear and slowly enlarge; they display a tendency towards central softening leading to ulceration. Osteolytic lesions occur in 4% of cases and usually present as a cold abscess. Rare manifestations of cryptococcosis include prostatitis, endophthalmitis, hepatitis, pericarditis, endocarditis, and renal abscess.

Diagnosis :

Fever and headache in a patient with AIDS or with risk factors for HIV infection suggest the possibility of cryptococcosis, toxoplasmosis or CNS lymphoma. Optimally, any patient with proven or suspected HIV infection or AIDS and central neurological dysfunction should first undergo Computerized Tomographic (CT) scanning and /or magnetic resonance imaging (MRI) because of the possibility of space - occupying lesions. The CT scan of the head of patient with toxoplasmosis or lymphoma is likely to reveal striking focal abnormalities such as ring enhancement, solid enhancement, or non-enhancing focal oedema. By contrast, in patients with CNS cryptococcosis, especially meningitis, the CT scan is usually normal or nonspecifically abnormal, e.g., light cortical atrophy or varying degrees of ventricular enlargement without focal lesions or enhancement (18) The incidence of cryptococcal intracerebral mass lesions is unknown. Evidence of focal a lesion on MRI is unusual in cryptococcosis. Most cryptococcal cerebral mass lesions occur in patients infected with C. neoformans var. gattii who also have meningitis. In patients without AIDS, meningitis due to C. neoformans resembles that due to MA-cobacterimn tuberculosis, Histoplasrna capsulaturn, Coccidioidis inrrnitis, or metastatic cancer. Lumbar puncture is the single most useful diagnostic test. Patients who do not have space-occupying lesions on CT scan or MRI Should have a lumber puncture to measure opening pressure and multiple laboratory studies of CSF, including cell count; protein; glucose; cultures of bacteria, mycobacteria, and fungi; India ink preparation; cytology; and various serological tests. An India ink or nigrisin smear (which is used to highlight the capsule) of centrifuged CSF sediment reveals encapsulated yeast in more than half of cases, although artifacts can cause confusion. In patients without AIDS, levels of glucose in CSF are reduced in half of all cases; protein levels are usually increased; and lymphocytic pleocytosis is usually found. CSF abnormalities are less pronounced in patients with AIDS, protein and glucose levels may be normal or mildly abnormal in many patients with AIDS and meningitis, although India ink smear is more often positive, cryptococcal antigen and culture are usually positive. The organism may be cultured on sabouraud medium from sputum within 48 hours, but this is not necessarily diagnostic unless it can be found repeatedly, hence isolation of cryptococcal organisms from sputum must be interpreted continuously, even in the cautiously, even in the presence of a compatible clinical illness. The fungus fr[e]quently colonizes the airways. It is commonly found in the sputum of patients with chronic bronchitis and patients who are immunosuppressed and at high risk for progressive pulmonary and systemic infection (4). Also, many non-neoformans species of non-pathogenic cryptococci can be recovered from sputum. The organism may be cultured from blood, urine, gut or bone marrow, and the CSF. Isolates from . the CNS are always C. neoformans and

always indicate cryptococccal meningitis. As the definite diagnosis of cryptococcal infection depends on the demonstration of a yeast - like organism in the pathological or culture findings, transcutaneous fine needle aspiration cytology under Computed Tomographic guidance (CT - guided FNAC), and transbronchoscopic brushings and biopsy and Broncho-Alveolar Lavage (BAL) are less invasive diagnostic techniques in the establishment of a definite diagnosis.

Cultures of blood for fungi should be obtaipedfrom all patients. In addition, in patients with suspected extraneural disease; specimens of potentially involved sites (e.g., skin, bronchial washings, liver, bone marrow, and urine) should be obtained for culture and histopathology with special stains.

Aside from studies on CSF, analysis of serum for cryptococcal antigen in patients with AIDS and suspected cryptococcal meningitis is probably the diagnostic test that yields the greatest amount of information: the test is usually positive, and cryptococcal antigen titres, which are often greatly elevated, may remain high despite therapy.

Antibodies to cryptococcas may be helpful, and a latex agglutination test has been developed that is specific (in the absence of rheumatoid diseases and IgM antibody has been removed) and reasonably sensitive[19]. An enzyme immunoassay for cryptococcal antigen is also available. Generally, however, diagnosis depends on direct demonstration of the organism in biopsied or aspirated tissue or in CSF, When the doubly refractile cell wall, the presence of budding and the clear capsule (as shown by Indian ink preparation) are characteristic.

Approximately 90% of patients with cryptococcal meningo-encephalitis, including all those with a positive CSF smear, have capsular antigen detectable in CSF or serum by latex agglutination and also by ELISA. Occasional false-positive results in the above tests make culture the definitive diagnostic test and have prevented serum antigen from being a useful screening test in asymptomatic patients with AIDS. The antigen titre has both diagnostic and prognostic value. Initial high (> 100) titres are likely to correlate with relapse following therapy and with a poor prognosis. In AIDS patients, antigen titres over 1:1000 convey poor prognosis and blood cultures are often positive. C. neoformans is often present in urine from patients with meningo-encephalitis. Fungaemia occurs in 10 to 30% of patients and is particularly common among patients with AIDS.

Pulmonary cryptoccosis mimics malignancy with regard to radiographic findings and symptoms. Although radiological findings may be varied widely, Khoury et al. reported that cryptococcal pulmonary disease in immunocompetent patients is predominantly characterized by nodular opacity, whereas the disease in immunocompromised hosts tends to be diffuse infiltration[20]. Sputum culture is positive in 10% of cases and is unreliable, and serum antigen tests are positive in only one-third. So biopsy is usually required for diagnosis and differentiation from malignancy.

Cutaneous cryptococcosis may be mistaken for a comedo, basal cell carcinoma, or sarcoidosis. In patients with AIDS, skin lesions, may be numerous and are sometimes mistaken for molluscum contagiosum. Biopsy reveals myriad cryptococci. Osseous ctyptococcosis resembles tuberculosis.

Treatment:

There is always uncertainty whether or not to treat a patient when C. neoformans is isolated from the sputum. If the patient is a normal host and has no abnormalities on the chest roentgenogram, a lumbar puncture should be done. If the cerebrospinal fluid (CSF) is completely normal, careful observation is appropriate.

Similarly, if the fungus is isolated from the sputum of an imnuinocompetent patient with pneumonia, a lumber puncture should be done. In the past, if the CSF was normal and the patient was not very ill, then no treatment was given because the natural history Of pulmonary cryptococcosis in the normal host is resolution[17]. However while the risk of progression to meningitis is low, it is not zero. Now that fluconazole (oral and nontoxic) being available, in all cases of pulmonary cryptococcosis it is advisable to treat the patient with anti-fungul drugs once the diagnosis has been made in order to prevent both progressive pulmonary disease and involvement of the brain and meninges. Treatment may be withheld in the few patients with minimal pulmonary disease that has been diagnosed by removal of the lesion.

On the other hand when an immunocompromised patient has pulmonary disease, even if the original CSF is normal, antifungal treatment must be given. In patients without AIDS, The therapeutic goal is to cure the infection, not merely to control its symptoms. A single intensive course is given until cultures from all previously positive sites (particularly CSF) become convincingly negative. Normalization of the glucose level in lumbar CSF is desirable, but complete clearing of CSF or serum antigen during therapy is not essential. The clinical response and antigen levels are useful for monitoring progress.

Amphotericin B (0.6 - 0.7mg/kg daily for >_ 10 weeks) is the best-studied regimen. Flucytosine (150 -180 mg/kg daily has been added to IV Amphotericin B to accelerate the culture response, but grave toxicity can result unless flucytosine blood levels are kept below 100 ug/ml. Case reports have described patients without HIV infection who have responded to fluconazole or liposomal amphotericin B, but the dose and duration of treatment required to cure cryptococcal meningitis remain undefined. cryptococcal meningitis usually responds well (75% - 85%>) to the combination of 0.4 pg/kg amphotericin B and 150 mg/kg 5-flucytosine (daily for 6 weeks), in patients without AIDS [21] Whereas even when relapses do Occur, the same course of treatment can be repeated with a good chance of success.

The situation is different in cryptococcal meningitis in AIDS patients because it is seemingly impossible to achieve complete recovery and residual antigen titres are commonplace. Moreover the disease frequently recurs when treatment is stopped. The object of therapy is firstly to induce most rapid remission (Induction Of Remission), secondly to be followed by a life - time maintenance suppressive therapy to prevent relapse (Consolidation). There are various regimens used for induction Of remission. Patients with AIDS and cryptococcosis are treated Initially with IV amphotericin B (0.7 mg/kg daily) for at least 2 weeks and until their clinical condition is stable, thereafter they receive fluconazole. Current evidence suggests that oral fluconazole is the best long-term maintenance therapy. In the era before AIDS, the combination regimen of flucytosine (150 mg/kg daily) and low dose amphotericin B (0.3 mg/kg daily for 6 weeks was equivalent to or better than amphotericin B alone (0.4 mg/kg daily) for 10 weeks, with regards to cures, relapses, and rates of CSF sterilization[21]. In contrast, among patients with AIDS and cryptococcal disease the addition of flucytosine (100 mg/kg daily) to amphotericin B did not alter survival, as compared with amphotericin B alone; in addition about half the patients receiving combination therapy, flucytosine had to be withdrawn because of drug associated cytopenias[6,22]. Now it has been shown that for the initial induction treatment of AIDS - associated cryptococcal meningitis, the use of higher dose amphotericin B (0.7 mg/kg /day) plus flucytosine (100 mg/kg /day) is associated with an increased rate of CSF sterilization and decreased mortality at 2 weeks, and that, when followed by consolidation therapy with oral fluconazole, is safe and effective and should now be considered the treatment of choice for AIDS - associated cryptococcal meningitis[22].

After treatment with amphotericin B, fluconazole (400 mg) is given once daily. Daily doses of 800 mg have been used with marginal changes in toxicity or efficacy. The addition of flucytosine to fluconazole increases gastro-intestinal intolerance. After infection is controlled, treatment with smaller doses of fluconazole (200 mg/day) is continued indefinitely. Although consolidation therapy with fluconazole is associated with a higher rate of CSF sterilization than itraconazole, itraconazole may be a suitable alternative for patients unable to take fluconazole[22]. It is not yet known whether or not patients whose CD4+ T-lymphocyte counts have exhibited a sustained rise in responses to anti retroviral therapy can safely discontinue fluconazole maintenance therapy.

In most patients treated with amphotericin B, nausea, vomiting, headache,febrile reactions may occur. Anaphylactic reactions are rare but it is nevertheless recommended that a test dose is given before the first full infusion of any new course, 1 mg in 10 ml 5% dextrose being infused over 20 minutes and the patient of observed for a further 30 minutes. The most important dose-limiting adverse effects are renal, amphotericin both reducing glomerular filtration rate and causing renal arteriolar vasoconstriction that may lead to renal failure, particularly if used in combination

with other nephrotoxic drugs or in presence of volume depletion or hypotension . Some degree of azotaemia is to be expected in 80% patients. Electrolyte abnormalities such as hypokalaemia and hypomagnesaemia may occur. Mild normocrornic normocytic anaemia may also occur, usually as a result of marrow suppression.

The major problems with flucytosine are bone marrow suppression with leucopenia and thrombocytopenia and nephrotoxicity. The dose must be adjusted in renal impairement according to creatinine clearance. Fluconazole is well tolerated. The commonest adverse effects are nausea and other gastrointestinal symptoms. Rashes, including Stevens-Johnson syndrome, may occur but are uncommon. Hepatic cytochrome P450-dependent enzyme inducer (e.g., Rifampicin) reduces bioavailability of fluconazole and itraconazole, while drugs that are metabolized by cytochrome P450-dependent enzyme system may be potentiated by azoles including fluconazole and itraconazole. Because of this drugs such as terfenadine, astemizole, cisapride are also best avoided with fluconazole inview of the possibility

Sequele & Outcome :

Risk factor for poor outcome despite adequate treatment include AIDS, lymphoreticular malignancy, glucocorticoid therapy, high opening pressure on lumbar puncture, a leucocyte count of less than 20 cells / mm' in CSF, positive India ink smear, isolation of the fungus from an extraneural site, and cryptococcal antigen titre of 1:32 or greater in the CSF.

Hydrocephalus may be the presenting manifestation or a later complication of cryptococcosis. Blindness, dementia and personality change are among the other sequelac. Daily lumbar puncture or CSF shunting has been advocated in the hope of averting permanent blindness- for patients with marked cerebral oedema who have incipient blurred vision.

Patients with extraneural cryptococcosis most often require treatment with IV amphotericin B, with or without flucytosine. Observation or excision of lesions may suffice for some patients who have previously been healthy; who have single focus in lung, skin, or bone; and who have no cryptococci in CSF, urine or blood.

Prevention :

Fluconazole (200mg/day) has been shown to decrease the incidence of cryptococcosis in HIV-infected patients with CD4+ cell counts of <200 / uL and particularly in those with counts of <50 / pL. Weekly fluconazole has not provided this protection. Daily fluconazole has not conferred a survival advantage; in light of its cost and the currently low incidence of cryptococcosis in patients with AIDS in the United States, prophylaxis is strongly discouraged.

References :

1. Kwon-chung KJ. A new genus, Filobasidiella, the perfect state of cryptococcus neoformans. Mycologica 1975; 67: 1197
2. Smilack JD, Bellet RE, Talman WT. Cryptococcal pleural effusion. JAMA 1975; 232: 639-641
3. Hay RJ. Mackenzie DWR. Fungal infections: Oxford Textbook of Medicine, Third edition, Oxford Medical Publications 1996; Vol - 1: 809-810
4. Hammerman KG. Powell KE, Christianson CS et al. Pulmonary cryptococcosis: clinical forms and treatment. Am Rev Respir Dis 1973; 108:1116 - 1123.
5. Lewis JL. Ravinovich S. The wide spectrum of cryptococcal infections. Am J Med 1972; 53: 315-322.
6. Chuck SL, Sande MA. Infections with cryptococcus neoformans in the acquired immunodeficiency syndrome. N Engl J Med 1989; 321: 794 - 799.
7. Saag MS, Powderly WG, Clowd GA et al. Comparison of amphotericin B with fluconazole in the treatment of acute AIDS - associated cryptococcal meningitis. N Engl J Med 1992; 326: 83-89.
8. Duperval R, Hermans PE, Brewer NS, Roberts GD. Cryptococcosis, with emphasis on the significance of isolation of cryptococcus neoformans fr°m the respiratory tract. Chest 1977; 72: 13-19.
9. Mitchell D H, Sorrell TC, Allworth AM et al. Cryptococcal disease of the CNS in imirlunocompetent hosts: influence of cryptococcal variety on clinical manifistations and outcome. Clin Infect Dis 1995; 20: 611.

10. Seaton RA. Clinical and epidemiological features ofcryptococcal meningitis in Papua New Guinea. Neurol Inect Epidemiol 1996; 1: 81.

11. Littman ML waiter JE. cryptococcosis: current status. Am J Med 1968; 45: 922.

12. Mildvan D, Mathur U, Enlow RW et al. Opportunistic infection and immune deficiencies in homosexual men. Ann Intern Med 1982; 96: 700-704.

13. Salyer WR, Salyer DC, Baker RD. Primary complex of cryptococcus and pulmonary lymph nodes. J Infect Dis 1974; 130: 74-77.

14. Graybill JR, Mitchell L, Drutz DJ. Host defense in cryptococcosis. 111. Protection of nude mice by thymus transplantation. J Infect Dis 1979; 140 : 546.

15. Kozel TR, Follette JL opsonizati' on of encapsulated cryptococcas neoforn-lans by specific anti capsular antibody. Infect Immunol 1981; 31 : 978.

16. Igel H.I, Bolande RP. Humoral defense fnecharlisms in cryptococcosis; Substances in normal human serum, saliva and cerebrospinal fluid affecting the growth of cryptococclis neoformans. J Infect Dis 1966; 116 : 75.

17. Kerkering TM, Duma RD, Shadomy S: The evolution of pulmonary cryptococcosis. Ann Intern Med 1981; 94 : 611-616.

18. Dlsmukes WE. cryptococcal meningitis in patients with AIDS. The J Infect Dis. 1988; 157: 624-628.

19. Stockman L, Roberts GD. Correction version. Specificity of the latex test for cryptococcal antigen: a rapid simple method for eliminating interference factors. Clin Microbiol 1963; 17 : 945.

20. Khoury MB, Godwin JD, Ravin CE. Thorasic cryptococcosis: immLfnologic competence and radiologic appearance. AJR 1984; 141 : 893 - 896.

21. Bennettc JE, Dismukes WE, Duma RJ et.al. A comparison of amphotericin B along and combined with flucytosine in the treatment of cryptococcal meningitis. N Engl Med 1979; 301: 126-131.

22. Van der Horst CM et.al. Treatment of cryptococcal meningitis associated with the acquired immuno deficiency syndrome. MAID Mycosis Study Group and AIDS Clinical Trials Group. N Engl J Med 1997; 337 : 15.

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CASE REPORTS

Pleural Effusion In Neurofibromatosis- A Case Report

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Abstract :

A 45-year-old gentleman reported to NIDCH with the Complaints of cough, productive sputum and respiratory distress for 1 month. Physical examination revealed multiple cutaneous nodules of variable size and shape with cafe'-au-lait spots and kyphoscoliosis. History, clinical features and investigations confirmed the diagnosis as neurofibromatosis with left sided pleural effusion. Pleural biopsy revealed the case as neurofibomatosis with sarcomatous change. Pleural effusion in a case of neurofitbomatosis is very uncommon and this is the reason for presenting the case.

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Introduction

Neurofibromatosis is a disorder of autosomal dominant inheritance due to an abnormal gene on chromosome 17 (q.11,2 type I neurofibromatosis, NF1) or 22 (q.12,2 type 2 neurofibromatosis, NF2)[1] . Two types of this condition are recognized, both inherited as an autosomal dominant. Type 1 is V on Recklinghausen's disease and is caused by a mutation on the long arm of chromosome 17q that codes for a GTPase activating protein known as neurofibromin[3,4]. This condition may be complicated by kyphoscoliosis, pheochromocytoma, malignant change in fibromas, pathological bone fractures and mental retardation. Neurofibromatosis-I is a relatively common disorder with a frequency of almost 1 in 3000. Although approximately 50% patients have a definite family history consistent with autosomal dominant transmission, the rest appear to represent new mutations[5]. Neurofibromatosis, type-2, also called acoustic neurofibromatosis, causes mainly bilateral acoustic neuromas and other intracranial lesions such as gliomas and meningiomas, cataracts and retinal abnormalities but may involve spinal nerves. It is causes by a mutation on chromosome 22q coding for a protein called schwanomin[6]. Muttiple fibromatous tumors develop from the neurilemmal sheaths of peripheral and cranial nerves. Most of the lesions are benign but sarcomatous change may occur. Neurofibromatosis type 1 (Von Recklinghausen's disease) is characterized by cafe'-au-lait spots, axillary freckling and neurofibromas of the skin and internal organs. Cutaneous lesions are the result of maldevelopment of neural crest cells. Large plexiform neurofibromas develop along peripheral nerves and involve deeper tissues. Patients with NF2 present with acoustic neuromas, often bilateral and/or other central neoplasm and have fewer, if any,' Cuaneous lesions. A family history of cerebral or spinal tumours should be noted with care, since relative of patients with NF2 may require screening for accoustic neuromas.

Respiratory involvement occurs in 10% to 15% of patients with neurofibromtasis. Although neurofibromatosis is a congenital disorder, the lung involvement does not become evident until adulthood. Upto 20% of patients older than 35 years develop diffuse interstitial fibrosis. Diminished perfusion and ventilation to apices of the lungs has been documented by radionuclide studies in a patient with cutaneous neurofibromatosis. Bullous lung disease may occur alone or in combination with diffuse pulmonary

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fibrosis usually seen in the basal areas of the lungs, whereas the bullous lesions occur predominantly in the apical areas. Cystic lung disease resembling honeycomb lung also has been described. The clinical manifestations are mild usually consisting only of exertional dyspnoea but a restrictive pattern of pulmonary function and diminished diffusing capacity often are observed. Intrathoracic neurofibromas and meningocoeles may be associated with a dermal form of neurofibromatosis but these usually remain undetected because they rarely are symptomatic. When these lesions are situated in the posterior mediastinum, as they commonly are, they may represent the so called dumb-bell tumours with intraspinal extension[7]. Thoracic manifestations are usually confined to chest wall neurofibromas associated with intercostal nerves and which sometimes show the dumb-bell appearance with enlarged intervertebral foramen associated with an extension into the spinal canal. Occasionally, however, the condition is associated with diffuse pulmonary neurofibromatosis and bullous emphysema[8] and may present as pneumothorax. Investigation and treatment is only indicated if there are symptoms of cerebral or spinal involvement or if malignant change is suspected.

Case Report :

A 45- year- old gentleman, a businessman from Narsingdi, reported to NIDCH on 25-6-2002 with the complaints of cough with productive sputum and respiratory distress for one month. There is no history of chest pain. He is a non smoker. He is neither diabetic nor hypertensive. He has no family history of allergy or asthma.

He has two brothers and no sister. Interestingly his father and both the brothers have cutaneous nodules throughout the body. On general examination, he looked ill, kyphoscoliotic and mildly dyspnoeic. There are multiple painless soft cutaneous nodules of variable size and shape throughout the whole body with multiple hyperpigmented patches (cafe'-au-fait patches). There is also axillary freckling. Pulse rate was 92 per minute, regular; blood pressure was 125/85 mm of Hg, Respiratory rate 24/min. He was neither anaemic nor cyanosed. There was no oedema and JVP was not raised. On examination of the respiratory system, there was restricted movement of the left side of the chest. Trachea was deviated to the right. Apex beat was not palpable. Percussion note was dull from 3rd ICS downwards anteriorly in MCL. On auscultation the breath sound and vocal resonance were found to be diminished on the same side. Examination of the skeletal system revealed kyphoscoliosis on the left. Examination of other systems revealed no abnormality.

Investigation revealed Hb-10 gm/dl, ESR-56 mm in 1st hour, TC of WBC - -7000% cmm of blood, DC: Neutrophil-56%, Lymphocyte-38% Monocyte-2%, Eosinophil-4%. FBS-110 mg/dl, Blood urea-24mg/dl, Serum creatinine-0.8 mg/dl, Routine examination of urine was within normal limit. Sputum examination revealed no AFB or malignant cells. ECG was normal. X-ray chest (P/A and left lateral view) showed evidence of pleural effusion on the left side. Spirometry showed moderate restriction. FOB examination detected no endobronchial lesion. Pleural fluid examination revealed protein-5.2 gm/dl and sugar-80 mg/dl. Cytology showed plenty of RBC, no malignant cells, neutrophil-3%, monocyte-70%, TC-1000/cmm. Pleural tissue biopsy was suggestive of benign spindle cell tumour (Neurofibroma) with some atypical cells, which may be suggestive of sarcomatous change. MT was 2mm. Biopsy of the cutaneous nodules showed clusters of spindle shaped wavy cells, suggestive of benign spindle cell tumour (Neurofibroma). Patient was advised to attend NICR & H for further evaluation and management.

Discussion :

Neurofibromatosis, also referred to as Recklinghausen's disease, is an autosomal domimant disease that is recognized, by the appearance of cutaneous cafe'-au-fait spots, subcutaneous neurofibromas, and the lisch nodule in the iris. There are many thoracic manifestations of neurofibromatosis, the most important

of these, interstitial lung disase, occurs in 25% of affected patients and dyspnoea first appears between the third and sixth decades. Lower zone radiographic interstitial infiltrates are the rule, and eventually, bullous changes appear in the upper zones. Physiological testing early in the course of the disease reveals restrictive ventilatory impairment, but with time, obstructive lung

disease supervenes, as the fibrotic process in the lungs involves not only the interstitium but also the small airways. Scar carcinoma has been reported as a carplication of neurofi bromatosis[9]. Nerofibromatosis can involve the mediastinum and pleura which may result in pleural effusion and respiratory failure. Haremorrhagic pleural effusion may occur when neurofibromatosis involves the Pleura with sarcomatous change. Mediastinal and pleural haemorrhage may occur as a result of an eroded thoracic artery.

References:

1. Allen CMC, Lueck CJ. Diseases of the nervous system. Chapter 14, Davidson's Principles and Practice of Medicine. 18th ed. Churchill Livingstone. 1999, 1020.
2. Riccardi VM. Von Recklinghausen's neurofibromatosis. N Engl J Med 1981; 305,1671.
3. Upadhayaya M, Osborn MJ, Maynard J, Kim MR, Tamanoi F, Cooper DN. Mutational and functional analysis of the neurofibromatosis type (NF 1) gene. Hum Genet 1997; 99 : 88.
4. Shin MK Harper PS, Upadhayaya M. Molecular genetics of neurofibromatosis type-1 (NF1). J Med Genet 1996; 33 : 2.
5. Cotran RS, Kumar V, Robbins SL. Genetic disorders. Chapter 5, Robbins' Pathologic Basis of Disease 5th ed. WB Saunders Company 1994, 148.
6. Ruttledge MH, Andermann AA, Phelan CM, et al. Type of Mutation in the neurofibromatosis type 2 gene (NF2) frequently determines severity of disease. Am J Hum Genet 1996; 59 : 331.
7. Prakash UBS. Dermatologic Diseases. Chapter 62. Text book of pulmonary Diseases. 6th ed. Editors Baum JL, Crapo JD, Lippincott- Raven Publishers, 1998, 1228.
8. Massaro D, katz S, Methews MJ. Haggins G. Von Recklinghausen's neurofibromatosis associated with cystic lung disease. Am J. Med. 1975, 38 : 233.
9. Marvin I, Schwarz, Renben M, Cherniack et al. Diffuse alveolar haemorrhage and other infiltrative disorders. Chapter-60, Text book of Respiratory Medicine. 3rd ed. Murray IF, Nadel J.A editors. WB Saunders company. Vol-2, 2000, 1748.

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Primary Tuberculosis of The Male Breast : A Case Report

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Abstract

A case of tuberculosis of the breast is reported in 53 yrs old man. Clinically diagnosis was malignant tumour or gynaecomastia. Histopathological examinnation of the breast lesion revealed caseating and non caseating granuloma. Special stains (Ziehl-Nelseen) revealed numerous acid first bacilli. The patient was treated satisfactorily by anti-tubercular therapy.

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Introduction :

Tuberculosis of the breast is a rare disease. It is uncommon in the breast compared to other organ, as mammary tissue appears to be unsuitable site for survival and multiplication of tubercle bacilli. The overall incidence is 3-4% of all breast tissue in developing countries and less than 1% in developed countries[1,2].

Tuberculosis mastitis of male breast both primary and secondary, are rare. Primary very rare but secondary are rarely reported[1,3-6]. The haematogenous, lymphatic and contagious spread from pleura and chest wall considered the major route of infection.

Case Report :

A 53 yrs old man refered to the surgical out patient department of Bangabandhu Sheikh Mujib Medical University (BSMMU) Hospital with a painless lump in the left breast with a history of 9 months. He had no other symptoms and had not experienced any significant previous illness. He is from low socioeconomic group with alcoholic and smoking habit. On examination he looked average physique but not well nourished. A small, firm, mobile nodule was found in upper and outer quadrant. The nipple and skin were normal. On systemic examination , no significant abnormalities were found. Accessible lymph node are not palpable and liver and spleen were also not palpable. The patient was provisionally diagnosed as either malignancy or gynocomastia and got admission in surgical ward in BSMMU hospital. Lump was excised and sent for histopathological examination. Histopathological study revealed granulomatous inflammation with positive acid fast bacilli. The patient was started on antitubercular 4 drug therapy for six month and recovery was satisfactorily.

Discussion :

Though male breast tuberculosis is exeedingly rare but in developing countries sporadic cases are reported [2,5,7,8]. Sirstely cooper in 1929 was first to report a case of mammary tuberculosis. many factors are considered as predisposing factors for tuberculous mastitis, trauma, lactation, supporative mastitis, poor general health etc. Interestingly, lactation in the presence of poor general health increases susceptibility of tuberculosis. The most probable route of penetration of tubercle bacilli into the breast is through the lactiferous ducts, direct extention from the lung and the chest wall through the lymphatics from the axillary lymph node and blood stream. Clinically tuberculosis of breast is mistaken for neoplasm. At present mammographic studies in addition to the fine needle aspiration cytology studies are not helpfull for the diagnosis of tubercular mastitis[9-10,11]. Confirmation of diagnosis by excision and biopsy. In case of comedo-mastitis where chronic inflammatory cell is found and is similar to tuberculosis demonstration of acid fast bacilli is essential for definite diagnosis. Overall male breast tuberculosis is very rare and only few

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male cases have been reported[4]. In this case may differential diagnosis were considered Gynaecomastia, Breast abscess, acute mastitis, fat necrosis, carcinoma. Histopathological report shows caseating and not caseating granulomas. Acid first (Ziel-neelsons) stain revealed presence of numerous bacilli in this case which helped in the correct diagnosis of tuberculosis. If the bacilli are not seen, the probablity of granulomatous e.g-autoimmune mastitis cannot be ruled out. The management of this lession by excision and biopsy and the anti tubercular therapy.

Tuberculosis should, therefore, always be considered in the differential diagnosis of male breast lumps, specially in developing countries.

References:

1. Haagensen CD : Infections of the breast 2nd ed. Philadelphia : Saunders, 1971 : 335-6.
2. Hamit HF, Ragsdale TH : Mammary Tuberculosis. JR soc Med 1982; 75 : 764.
3. Chaudhuri M, Sen S, Sengupta J: Breast lumps : a study of ten years: J Ind Med Asso 1995; 93 : 455-7.
4. Mende W-Da-s, Levi M, Levi GC; Breast tuberculosis case report and literature review. Rev Hosp Clin Fac Med sanopauo 1966; 51 : 136-7.
5. Shinde SR, chanawarkar RY, Deshmukh SP : Tuberculosis of breast maquerading ascarcinoma: a study of 100 patients. World J Surg 1995; 19 : 379-81.
6. Wilson JP, Caapman SW; Tubercular mastitis. Chest 1990; 98 : 1505-9.
7. Cooper A : Illustration of the diseases of the breast. Part I. London; Longman, Orme, Brown and Green, 1929; 73.
8. Wilson TS, Macgregor JW : The diagnosis and treatment of tuberculosis of the breast. Can Med Assoc 1963; 89 : 1118.
9. Vassilakos P : Tuberculosis of the breast; cytologic finding with fine needle aspiration. ACTA cytologica 1973; 17 : 160.
10. Divan RV, Shinde SR: Tuberculosis of breast. A clinico radiologic study. Indian J Radiol 1980; 34 : 275.
11. Helmer M, Pokieser L, Salmononwithz E; tuberculosis of the female breast; diagnostic clarification, Rontgenblatter 1986; 39 : 357.