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INSTRUCTION TO AUTHORS ABOUT UNIFORM MANUSCRIPT WRITING

The Chest and Heart Journal is published twice in a year in the months of January and July. The journal publishes original papers, reviews concerned with recent practice and case report of exceptional merits. Papers are accepted for publication with an understanding that they are subject to editorial revision. A covering letter signed by all authors must state that the data have not been published elsewhere in whole or in part and all authors agree their publication in Chest and Heart Journal. All submitted manuscripts are reviewed by the editors and rejected manuscripts will not be returned. Ethical aspects will be considered in the assessment of the paper. Three typed copies of the article and one soft copy in CD or Pen Drive processed all MS Word 6.0 should be submitted to the editor.

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Drug Names

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References should be numbered consecutively in the order in which they are first mentioned in the text. Identify references in text, tables, and legend by Roman numerals in parenthesis. Use the styles of the example below, which are based on the formats used by the US National Library of Medicine (NLM) in the Index Medicus.

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Karalus NC, Cursons RT, Leng RA, et al. Community acquired pneumonia: aetiology and prognostic Index evaluation. Thorax 1991; 46 : 413-12.

c) No author given;
Cancer in South Africa (editorial). S Afr Med J 1994; 84-15.

d) Organization as author
The Cardiac Society of Australia and New Zealand. Clinical exercise stress training. Safety and performance guideline. Med J Aust 1996; 164 : 282-4.

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World Health Organization, Ethical Criteria for Medical Drug Promotion. Geneva: World Health Organization; 1988.

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a) Newspaper article
Lee G. Hospitalizations tied to ozone pollution: study estimates 50,000 admissions annually. The Washington Post 1996, June 21; Sect. A : 3(col. 5).

b) Dictionary and similar references
Student's medical dictionary. 26th ed. Baltimore: Williams & Wilkins; 1995. Apraxia; p.119-20.

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ORIGINAL ARTICLE

Hydrofluoroalkane Beclomethasone Dipropionate (HFA-BDP) Vs Chlorofluorocarbon Beclomethasone Dipropionate (CFC-BDP): A Comparison of Effect in the Treatment of Moderate Persistent Asthma

Jibesh Kumar Pramanik,[1] A. K. M. Mustafa Hussain,[2] Shamim Ahmed,[3] Md. Ali Hossain,[2] Md. Shahedur Rahman Khan,[4] SM. Abdur Razzaque,[4] Md. Khairul Anam,[5] Nihar Ranjan Saha,[5] Bipul Kanti Biswas,[5] Nirmol Kanti Sarker,[5] Abdullah Al Mujahid[5]

Abstract

Background: *The corticosteroid inhaler for the treatment of asthma is an established drug worldwide as it treats the underlying causes of asthma. Beclomethasone is the first inhaled steroid being used in asthma management. The Hydrofluoroalkane-Beclomethasone Dipropionate (HFA-BDP) produces same to or better effect than ChlorofluoroCarbon-Beclomethasone Dipropionate (CFC-BDP) at a lower dose.*

Objective: *The objective of the present study was to compare effects of Hydrofluoroalkane-Beclomethasone Dipropionate (HFA-BDP), 400μg, to Chlorofluorocarbon- Beclomethasone Dipropionate (CFC-BDP), 1000 μg on lung function (FEV_1 & PEFR) and Health Related Quality of Life (HRQoL) with St. George Respiratory Questionnaire (SGRQ) scoring system in treatment of moderate persistent asthma.*

Materials & Methods: *This was a randomized clinical trial carried out in the out patient department (OPD) of National Institute of diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka during the period from July 2010 through June 2011 for one year. All patients were between 18 to 65 years of both sexes suffering from moderate persistent asthma were taken as study population. A total number of 103 patients were enrolled. They underwent a run-in period of initial 7 days when they received 30 mg of daily morning dose prednisolone. But, 6 patients dropped out from the study. Finally, with 97 patients the study was completed.*

Patients presented with moderate persistent asthma were randomized by odd and even number, and divided into two groups. Of them, 49 patients were in group A and 48 patients were in group B. Group A was treated with HFA-BDP and group B was treated with CFC-BDP inhaler for 12 weeks. The patients of either group were evaluated at the end of 4^{th}, 8^{th} and 12^{th} weeks after

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starting the treatment. Health Related Quality of Life (HRQoL) was assessed by using the St. George's Respiratory Questionnaire (SGRQ).

Results: Statistical analysis was performed by using SPSS. Improvements of PEFR and FEV_1 from baseline to subsequent follow ups in both groups were remarkable. But, group A showed better result. Regarding scoring with SGRQ to evaluate health related quality of life (HRQoL), all types of scores (symptom, activity, impact and total scores) showed significant improvement following 12 weeks treatment from baseline in both groups. But group A showed more improvement than group B. All patients had daily daytime symptoms at baseline. Following 12 weeks of treatment about 94% patients from Group A and 83% patients from group B showed no daytime symptoms at all. Nighttime symptoms also improved in the both groups following treatment but group A showed more improvement.

Conclusion:The findings of this study permit to conclude that Hydrofluoroalkane Beclomethasone dipropionate (HFA-BDP) is more effective than Chlorofluorocarbon Beclomethasone dipropionate (CFC-BDP) for the treatment of moderate persistent asthma.

[Chest & Heart Journal 2012; 36(1) : 1-10]

Introduction:

Asthma is a multifactorial and complex chronic disease characterized by variable airflow obstruction and airway hyper-responsiveness.[1] Prevalence of asthma is due to hereditary and changing environmental factors.

Asthma is one of the most common chronic diseases worldwide affecting 300 million people worldwide. In Bangladesh an estimated 7 million people including 4 million children suffer from asthma related symptoms.[2] According to First National Asthma Prevalence Study (NAPS) 1999, in Bangladesh about 7 million people i.e. 5.2% of the population are suffering from current asthma at least three episodes of asthma attack in last 12 months.[2]

However, successful clinical management depends on achieving adequate delivery of the inhaled drugs to the lungs.[3] Targeting of anti-inflammatory agents such as corticosteroids, to the smaller airways appear to be the most promising treatment strategy of the future especially since anti-inflammatory drugs are thought to be most effective when deposited in the smaller airways.[4]

Beclomethasone dipropionate (BDP), an established corticosteroid for the treatment of asthma, has now been reformulated using the new HFA propellant, which has provided the opportunity to significantly improve the delivery of inhaled drugs to the respiratory tract. In contrast to current CFC-BDP products, this new formulation is a solution, rather than a suspension of BDP in propellant with the solution forming an extrafine aerosol of small droplets as the propellant evaporates.[5] Chlorofluorocarbon (CFC) preparations exhibit aerodynamic particle sizes of between 3 to 4 μm, whereas this HFA-BDP formulation has a mass median aerodynamic diameter of approximately 1.2 μm.[6]

HFA-BDP extrafine aerosol changes the standard pattern of drug deposition seen with CFC-BDP formulations, delivering most of the inhaled dose to the airways and depositing in much smaller proportion in the oropharynx.[7] Results of direct radiolabeled deposition studies in both healthy volunteers and patients with asthma show ex-actuator lung deposition to be a51% to 60% with HFA-BDP compared with lung deposition of <10% for CFC-BDP.[8]

The extent of lung deposition is known to be a major determinant of the therapeutic efficacy of inhaled corticosteroids, so, this improved delivery characteristics are likely to provide several important clinical benefits. In particular, the improved lung deposition of HFA-BDP extra fine aerosol compared with CFC-BDP suggests

that lower doses of HFA-BDP may be needed to provide equivalent or better asthma control. So, this study would be undertaken to test this hypothesis.

Hypothesis was, "Hydrofluoroalkane Beclomethasone dipropionate (HFA-BDP) is more effective than Chlorofluorocarbon Beclomethasone dipropionate (CFC-BDP) for the treatment of moderate persistent asthma".

General Objective was to select better standard therapy for patients with moderate persistent asthma in Bangladesh. Specific Objective was to compare the effects of Hydrofluoroalkane-BDP, 400μg, and Chlorofluorocarbon-BDP, 1000 μg on symptom score, lung function (FEV_1 & PEFR) and HRQoL of a patient with moderate persistent asthma.

Materials and Methods:

This was a prospective randomized clinical trial. This study was carried out at the outpatient department (OPD) of National Institute of diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka during the period from July 2010 to June 2011 for one year.

All men and women aged from 18 to 65 years suffering from moderate persistent bronchial asthma attending the OPD of NIDCH, Mohakhali, Dhaka during the specified period, were enrolled after fulfilling the selection criteria. 97 patients were included after taking informed written consent. The diagnosis of moderate asthma was based on Global Initiative for Asthma (GINA) Classification. Patient having daytime symptoms (respiratory distress, cough, wheeze and chest tightness) daily, nocturnal symptoms >1 time a week, diagnosis is confirmed by spirometry. Baseline spirometry showing FEV_1 within 60% to 80% and presence of one of the features of severity was sufficient to place a patient in that category were the criteria.

Sample size was 97. All patients were divided into two groups (A & B) by odd or even number. 49 patients were included in group A and 48 patients in group B.

Inclusion criteria

- Population with moderate asthma (according to GINA classification) who were symptomatic despite current treatment with bronchodilators and inhaled steroid (CFC-BDP)of 500 μg/day
- Age between 18 to 65 years
- Non smokers.

Exclusion criteria

- Acute severe asthma attack
- Refractory asthma
- COPD
- Acute upper or lower respiratory tract infection within 4 weeks before the start of trial
- Patients who received any medication other than for asthma
- A significant diseases other than asthma like Diabetes mellitus, recent history of myocardial infarction (<1 year), heart failure or cardiac arrhythmia requiring drug treatment
- Patients or attendants unwilling to take part in the study.

Study Procedure

The study was out patients hospital based clinical trial which comprised of:

o 7 days Run-in phase- for confirmation of diagnosis and evaluation of eligibility. Each subject was evaluated with history and symptoms regarding the presentation. They were examined and certain baseline investigations were done. Previous investigation reports and all medical records were evaluated thoroughly. During this period they received 30 mg daily morning dose of oral prednisolone to create a baseline.

o 12 weeks Clinical and follow-up phase-management of asthma along with either HFA-BDP inhaler, 400μg/day (100μg 2 puffs twice daily) or CFC-BDP, 1000 μg/day (250 μg 2 puffs twice daily) and to see the effect of the drugs.

The patients were evaluated at 4th, 8th and 12th weeks after starting the treatment. Eligible patients were selected the presence of symptoms, lung function parameters, and bronchodilator usage consistent with a Global Initiative for Asthma (GINA) classification of moderate severity asthma. Patients meeting these criteria and demonstrating a satisfactory technique in using a metered dose inhaler (MDI) with spacer device were randomized to inhaled treatment with HFA-BDP, 400 µg/day (100µg 2 puffs twice daily) or CFC-BDP, 1000 µg/day (250 µg 2 puffs twice daily) for 12 weeks. Medication was assigned according to odd and even number for the patients. Patients were instructed to take their assigned study inhaler medication in the morning and evening at the same time each day. Health Related Quality of Life (HRQoL) was assessed by using the St. George's Respiratory Questionnaire (SGRQ). The SGRQ is a disease specific instrument that assesses 50 items on three subscales (symptoms, activity and impact). Patients were advised to maintain a dairy in which they recorded their symptoms and use of medication. Adherence to the medication protocol was checked by inspection of the dairy and by the amount of medication remaining at each clinical visit. Before entry and the completion of the study, patients had undergone a medical examination and necessary investigations. At each scheduled visit detail of clinical status, adverse events, exacerbations and withdrawals were recorded. The outcome parameters were i) symptoms (Daytime and Nocturnal), ii) spirometry (FEV_1 and PEFR) & iii) asthma related quality of life assessed by St. George's Respiratory Questionnaire (SGRQ) score. Extent of improvements was recorded from the parameters. Statistical analysis was performed by using SPSS (Statistical Package for Social Sciences) for windows version 12.0. 95% confidence limit was taken. Probability value <0.05 was considered as level of significance.

Results and Observations

Group A consists of 49 patients who were treated with HFA-BDP in an amount of 400µg/day and group B consists of the remaining 48 patients who were treated with CFC-BDP in an amount of 1000µg/day.

Table-I

Distribution of age by groups (n=97)

Age (in year)	Groups		p value*
	Group A (n=49) (HFA-BDP inhaler)	Group B (n=48) (CFC-BDP inhaler)	
<25	21 (42.9)	19 (39.6)	
26-35	22 (44.9)	17 (35.4)	
>35	6 (12.2)	12 (25.0)	
Total	49 (100.0)	48 (100.0)	
Mean ± SD	27.49 ± 7.04	27.98 ± 7.86	0.747

*t test was done to measure the level of significance.

Figure within parentheses indicates in percentage.

Table I shows the distribution of age by groups. The difference between two groups was not significant (p=0.747).

Table-II

Distribution of symptoms of disease by groups (n=97)

Symptoms of disease	Groups		Total
	Group A (n=49) (HFA-BDP inhaler)	Group B (n=48) (CFC-BDP inhaler)	
SOB/ Breathlessness	3 (6.1)	0 (.0)	3 (3.1)
Wheeze	1 (2.0)	0 (.0)	1 (1.0)
Cough	0 (.0)	1 (2.1)	1 (1.0)
Multiple	45 (91.8)	47 (97.9)	92 (94.8)
Total	49 (100.0)	48 (100.0)	97 (100.0)

Figure within parentheses indicates in percentage.

Table II shows the distribution of symptoms of disease by groups. In both inhaler groups multiple symptoms were present in majority of cases, 45 (91.8%) cases in group A and 47 (97.9%) cases in group B.

Table III

Distribution of daytime symptoms by groups (n=97)

Daytime symptoms	Groups		Total
	HFA inhaler (n=49)	CFC inhaler (n=48)	
Baseline			
• Daily	49 (100.0)	48 (100.0)	97 (100.0)
1st follow up(at 4th wk)			
• Daily	0 (.0)	2 (4.2)	2 (2.1)
• Weekly	27 (55.1)	42 (87.5)	69 (71.1)
• Monthly	19 (38.8)	3 (6.3)	22 (22.6)
• Nil	3 (6.1)	1 (2.1)	4 (4.1)
2nd follow up(at 8th wk)			
• Weekly	1 (2.0)	28 (58.3)	29 (29.9)
• Monthly	41 (83.7)	17 (35.4)	58 (59.8)
· Nil	7 (14.3)	3 (6.3)	10 (10.3)
3rd follow up(at 12th wk)			
• Weekly	0 (.0)	1 (2.1)	1 (1.0)
• Monthly	3 (6.1)	7(14.6)	10(10.3)
• Nil	46 (93.9)	40(83.3)	86(88.7)

Figure within parentheses indicates in percentage.

Table-IV

Distribution of nighttime symptoms (per week) by groups (n=97)

Nighttime symptoms	Groups		Total
	Group A (n=49) (HFA-BDP inhaler)	Group B (n=48) (CFC-BDP inhaler)	
Baseline			
• 2 times	6 (12.2)	5 (10.4)	11 (11.3)
• 3 times	21 (42.9)	26 (54.2)	47 (48.5)
• 4 times	12 (24.5)	12 (25.0)	24 (24.7)
• 5 times	10 (20.4)	5 (10.4)	15 (15.5)
1st follow up			
• Nil	4 (8.2)	2 (4.2)	6 (6.2)
• 1 time	16 (32.7)	16 (33.3)	32 (33.0)
• 2 times	26 (53.1)	16 (33.3)	42 (43.3)
• 3 times	2 (4.1)	14 (29.2)	16 (16.5)
• 4 times	1 (2.0)	0 (.0)	1 (1.0)
2nd follow up			
• Nil	22 (44.9)	14 (29.2)	36 (37.1)
• 1 time	26 (53.1)	19 (39.6)	45 (46.4)
• 2 times	0 (.0)	15 (31.3)	15 (15.5)
• 3 times	1 (2.0)	0 (.0)	1 (1.0)
3rd follow up			
• Nil	49 (100.0)	42 (87.5)	91 (93.8)
• 1 time	0 (.0)	6 (12.5)	6 (6.2)

Figure within parentheses indicates in percentage.

Table-V

Mean ± SD of PEFR by groups (baseline & during follow up) (n=97)

PEFR	Groups		p value*
	HFA inhaler Gr-A(n=49)	CFC inhaler Gr-B(n=48)	
Baseline	65.45 ± 2.26	65.00 ± 2.38	0.343
1st follow up	74.18 ± 3.56	71.17 ± 2.98	0.001
Difference between baseline and 1st follow up	8.73 ± 3.85 (#p<0.001)	6.17 ± 3.01 (#p<0.001)	0.001
2nd follow up	80.76 ± 3.82	77.06 ± 3.12	0.001
Difference between 1st and 2nd follow up	6.57 ± 3.72 (#p<0.001)	5.90 ± 2.28 (#p<0.001)	0.285
3rd follow up	88.63 ± 4.64	82.58 ± 5.66	0.001
Difference between 2nd and 3rd follow up	7.88 ± 3.39 (#p<0.001)	5.52 ± 3.78 (#p<0.001)	0.002

*t test was done to measure the level of significance.
#Paired t test was done to measure the level of significance.
Data was expressed as Mean ± SD.

Table-VI

Mean ± SD of FEV_1 by groups (n=97)

FEV_1	Groups		p value*
	HFA inhaler Gr-A(n=49)	CFC inhaler Gr-B(n=48)	
Baseline	65.71 ± 5.67	65.75 ± 4.12	0.972ns
1st follow up	77.04 ± 3.83	73.08 ± 4.09	0.001
Difference between baseline and 1st follow up	11.33 ± 5.53 (ap<0.001)	7.33 ± 3.48 (ap<0.001)	0.001
2nd follow up	83.67 ± 3.28	79.19 ± 4.47	0.001
Difference between 1st and 2nd follow up	6.63 ± 3.55 (ap<0.001)	6.10 ± 3.57 (ap<0.001)	0.467 ns
3rd follow up	89.08 ± 4.42	83.71 ± 5.97	0.001
Difference between 2nd and 3rd follow up	5.41 ± 3.55 (ap<0.001)	4.52 ± 3.06 (ap<0.001)	0.191 ns

*t test was done to measure the level of significance.
aPaired t test was done to measure the level of significance.
Data was expressed as Mean ± SD.
ns= not significant

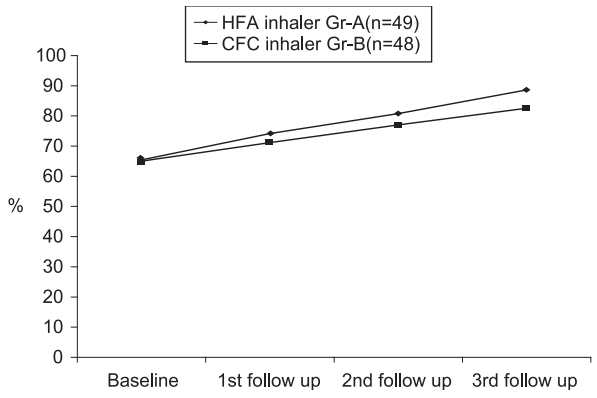

Fig.-1: Line chart of changes of Mean ± SD of PEFR by groups.

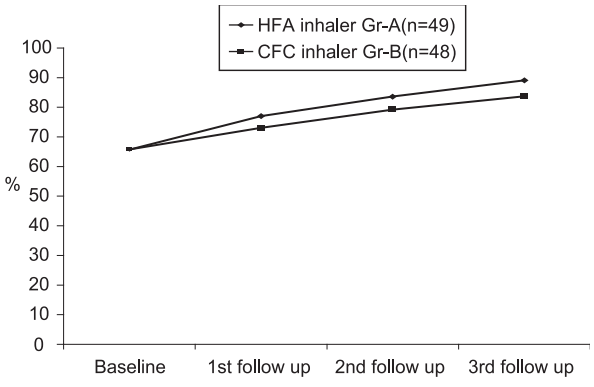

Fig.-2: Line chart of changes of Mean ± SD of FEV_1 by groups (baseline & after treatment)

Table VII

Mean ± SD of SGRQ score at baseline and after treatment by groups (n=97)

SGRQ score	Groups		p value*
	HFA inhaler Gr-A(n=49)	CFC inhaler Gr-B(n=48)	
Before treatment			
Symptom score	82.01 ± 7.51	81.36 ± 6.90	0.659
Activity score	12.20 ± 0.22	12.38 ± 0.38	0.005
Impact score	23.48 ± 2.65	24.34 ± 1.29	0.046
Total score	29.78 ± 2.35	30.19 ± 1.25	0.292
After treatment			
Symptom score	27.39 ± 15.93	50.13 ± 7.55	0.001
Activity score	11.32 ± 0.29	11.62 ± 0.47	0.001
Impact score	13.39 ± 3.02	16.40 ± 3.25	0.001
Total score	14.91 ± 3.89	20.55 ± 2.57	0.001
Difference			
Symptom score	54.62 ± 18.38([a]p<0.001)	31.24 ± 9.31([a]p<0.001)	0.001
Activity score	0.88 ± 0.34([a]p<0.001)	0.76 ± 0.37([a]p<0.001)	0.091
Impact score	10.09 ± 4.11([a]p<0.001)	7.95 ± 2.89 ([a]p<0.001)	0.004
Total score	14.87 ± 4.61([a]p<0.001)	9.64 ± 2.88([a]p<0.001)	0.001

*t test was done to measure the level of significance.
[a]Paired t test was done to measure the level of significance.
Data was expressed as Mean ± SD.
St. George's respiratory questionnaire score (SGRQ)

Table III shows the distribution of daytime symptoms by groups. All patients had daytime symptoms daily at baseline in both the groups. The daytime symptoms were improved gradually during follow ups in different extent in different group. Group A showed more improvement.

Table IV shows the distribution of nighttime symptoms by groups. At baseline every patient had nighttime symptoms >1 times per week. The nighttime symptoms were improved gradually following treatment. But, Group A showed more improvement.

Table V shows the mean ± SD of PEFR by groups at baseline and after treatment. PEFR difference between baseline and 1st follow up, 1st and 2nd follow up, and 2nd and 3rd follow up found in HFA and CFC inhaler group respectively were statistically significant (p<0.001). Changes of

PEFR in the 2nd follow up between two groups were 6.57±3.72 and 5.90±2.28 in HFA and CFC inhaler group respectively which was statistically non-significant (p=0.285). Otherwise, all changes were statistically significant.

Table VI shows the mean ± SD of FEV_1 by groups (baseline and after treament). FEV_1 differences between baseline and 1st follow up were 11.33 ± 5.53 and 7.33 ± 3.48 in HFA and CFC inhaler group respectively. They were statistically significant (p<001). But, FEV_1 changes between 1st and 2nd follow up, and 2nd and 3rd follow up between the two drugs were statistically not significant (p<0.467 & <0.191). So, both the drugs are equally effective in improving FEV_1 in asthma patient

Table VII shows the mean ± SD of SGRQ score before treatment (baseline) and after treatment by groups.

The all subscales of SGRQ scores showed significant improvement following treatment in both groups. But, considering changes in actual values in both groups, those patients who received HFA-BDP inhaler showed more improvement.

Discussion:

The use of corticosteroid aerosols to treat asthma and other diseases is increasing dramatically worldwide owing to the ability of steroids to treat more the underlying causes of asthma and to the contrary â-agonists only treat symptoms.[9]

Beclomethasone Dipropionate (BDP) is being formulated as a solution with the propellant HFA-134a. When the propellant evaporates during dosing, it has been found that much smaller aerosol particles are delivered to the patient than with the CFC–BDP suspension products.[10] So, less amount of drug is needed to control asthma. My study supports this too.

In this study among 97 cases in both groups majority were at or below 35 years of age. Similar result was reported by[11] and mentioned that younger age group are the most prevalent in asthma attack. Schatz et al 2006(12) also found same result in a similar study.

The distribution of daytime symptoms was presented in this study. Daily baseline daytime symptoms were found in 100% cases in both HFA and CFC inhaler groups. They improved gradually following treatment. At the end of 12 weeks therapy only 11% patients had daytime symptoms. About 94% cases from group A and about 83% cases from group B were totally symptom free. So, it is obvious that HFA inhaler group has shown better improvement than CFC inhaler group. The distribution of nighttime symptoms was also shown. At baseline e"3 times nocturnal symptoms per week were found in majority of the cases (89%) in both groups. At the end of 12 weeks therapy (3rd follow up) absence of nighttime symptoms was found in 100% cases in HFA and 87.5% cases in CFC inhaler group. The improvement was remarkable in HFA inhaler group. Similar result was reported by Lanier and Nayak 2008(13) and added that 61% of participants reported nighttime asthma symptoms and 74% reported daytime asthma symptoms with an asthma-related sleep difficulties in approximately 4 times per week in adults. In this study the daytime and nighttime symptoms were improved significantly in both groups, but HFA inhaler group showed better result.

The mean ± SD of PEFR by groups was shown in the study. Baseline PEFR was 65.45 ± 2.26 in HFA inhaler and 65.00 ± 2.38 in CFC inhaler group (p=0.343) respectively. With therapy PEFR was improved gradually in both groups. PEFR difference between baseline and 1st follow up, 1st and 2nd follow up, and 2nd and 3rd follow up found in HFA inhaler group and CFC inhaler group respectively were statistically significant (p<0.001). Changes of PEFR in the 2nd follow up between two groups were 6.57±3.72 and 5.90±2.28 in HFA and CFC inhaler group respectively. These were the only values statistically non-significant (0.285).

From the above result it was shown that the PEFR gradually increased in both groups almost in an almost equal manner. A similar finding was reported by Woodcock et al 2002(14). The significant changes of PEFR occured in HFA-BDP inhaler group with a low dose indicated the good efficacy of HFA inhaler.

The mean ± SD of FEV_1 by groups was shown. FEV_1 differences between baseline and 1st follow

up were statistically significant (p<001). But, FEV_1 changes between 1st and 2nd follow up, and 2nd and3rd follow up between the two drugs were statistically not significant (p=0.467 & 0.191). So, both the drugs were almost equally effective in improving FEV_1 in asthma patient. Woodcock et al (2002)[14] was found a similar result. The significant change of FEV_1 occurred at a lower dose indicated better efficacy of HFA inhaler. Leach et al 1998(9) also performed a similar study and found that Hydrofluoroalkane Beclomethasone dipropionate was produced better lung performance at a lower dose.

The mean ± SD of SGRQ scores before and after treatment were observed. The mean ± SD of symptoms scores were found out. The score change in HFA inhaler group before and after treatment was statistically significant (p<0.001). In CFC inhaler group, before and after treatment, the symptom score showed significant (p<0.001) difference. On the other hand, the impact scores and total scores as well showed similar improvement (p<0.001) following 12 weeks therapy from baseline in both groups. The activity scores in both groups showed significant improvement (<0.001). But mean difference in activity score (p=0.091) between two groups was not statistically significant. Similar result was reported by Leach et al 1998(9). Woodcock et al 2002(14) also reported a similar result and added that an HFA inhaler helps to open the airways of the lungs thereby providing quick relief from wheezing and shortness of breath. Both HFA and CFC inhaler in a statistically significant way increase the lung function. HFA-BDP inhaler acts more effectively than CFC-BDP inhaler at 2.6 time lower dose.

Conclusion:

In conclusion, the findings of this study permit to conclude that the effectiveness of Hydrofluoroalkane Beclomethasone dipropionate (HFA-BDP) is better than Chlorofluorocarbon Beclomethasone dipropionate (CFC-BDP) for the treatment of moderate persistent asthma. The improved lung functions and Health Related Quality of Life (SGRQ) scores were found in Hydrofluoroalkane Beclomethasone dipropionate inhaler group. Therefore, HFA-BDP inhaler can be used as better anti-inflammatory inhaler for the treatment of asthma.

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ORIGINAL ARTICLE

Serum Immunoglobulin E-level Reflects the Severity of Bronchial Asthma

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Abstract:

Bronchial asthma is a major public health concern affecting 100-150 million people worldwide. Elevated total serum immunoglobulin E (IgE) is considered as an objective marker of allergy and has been associated with a number of respiratory disorders. The present study tests the hypothesis that serum IgE levels reflect the severity of asthma. The serum IgE levels were investigated in 132 asthma patients and their severities of asthma were determined by pulmonary function tests. Serum IgE levels were also compared with the severity of asthma by history. The data indicated that 27% patients developed symptoms of bronchial asthma before 30 years of age; 17% patients between 31 to 45 years and only 5% patients developed asthmatic symptoms after the age of 45 years. Serum IgE levels significantly increased in all groups of asthma when compared to control subjects ($p<0.001$). The IgE levels were proportionately higher in patients with more severe airflow obstruction. The present study suggests that the serum IgE level may reflect the severity of bronchial asthma assessed by pulmonary function tests.

Key words*: Immunoglobulin E, Asthma, Atopy and clinical history.*

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Introduction:

Asthma is defined as a chronic disease of the entire lung and asthma attacks may either be immediate delayed or dual in onset. There is a strong association between exposure of allergens and development of asthmatic symptoms. The single most important risk factor for development of asthma is atopy. Atopy is a tendency to produce excessive amounts of IgE antibodies when exposed to allergens.[1] IgE is produced by B-Lymphocytes. Allergic asthma is a complex chronic inflammatory disease of the airways and its etiology is multi-factorial. Bronchial asthma is a type I hypersensitivity reaction where combination of allergens with IgE antibodies produces the airway inflammation and asthmatic symptoms.[2]

IgE is a trace protein and normally accounts for less than 0.001% of total serum immunoglobulin. The concentration of IgE in serum is age dependent and normally remains at levels less

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than 10 IU/ml in most infants during the first year of life. There is a wide distribution of expected serum IgE values in healthy individuals of same age group.[3]

Because IgE is a mediator of allergic response, quantitative measurement of IgE, when integrated with other clinical indicators, can provide useful information for the differential clinical diagnosis of atopic and non-atopic diseases.

Patients with atopic disease, including allergic asthma, allergic rhinitis, and atopic dermatitis have moderately elevated serum IgE levels. However, its serum level, which is within a range of normally expected values, does not rule out a limited set of IgE dependent allergies.[4]

In the absence of parasitic infections, raised IgE is considered as the hallmark of allergy often associated with bronchial hyperresponsiveness and may be linked to reduce FEV_1.[5]

Bronchial asthma is characterized by reversible airflow obstruction. Hence, the most important diagnostic investigation in asthma is the demonstration of airway obstruction by pulmonary function test before and after inhaling brochodilators.[6] Serum IgE levels show association with the degree of airflow obstruction. Based on these observations, the present work was designed to study the serum IgE levels in asthma patients with an objective to determine whether there is any correlation between serum IgE levels and severity of asthma.

Materials and Methods

The study group consisted of 132 patients, who were attending the t department of the Respiratory Medicine, Sir Salimullan Medical College and Mitford Dhaka, Bangladesh from January to December in 2011 with symptoms suggestive of bronchial asthma. The patients who were not on any anti asthma medication in previous one week were included in the study. Patients on medication for asthma will not show the characteristic reversible air flow obstruction in pulmonary function tests and their symptoms are usually relieved with medication; hence, they were not included in the study.

Patient name, age, sex, and duration of symptoms were noted. A detailed history was taken in each patient regarding the duration of asthma symptoms, frequency, and severity of exacerbations. All the subjects were given a respiratory questionnaire. The questionnaire included questions on respiratory symptoms, smoking habits, and previous medical history. Bronchial asthma was defined as (self-reported) doctor-diagnosed asthma. Age and sex matched 30 healthy volunteers were taken as a control group in this study.

Exclusion criterion included smoking, diabetes mellitus, immunosuppression, parasitic infestation, and other lung diseases like pulmonary tuberculosis, lung abscess, brochiectasis, tropical pulmonary eosinophilia, and chest wall abnormalities.

Pulmonary function tests were done in all patients using mini spirometer. Pulmonary function tests were done before and 20 minutes after giving nebulised salbutamol, 5 mg. Peak expiratory flow rate (PEFR), forced expiratory volume within a second (FEV1), forced vital capacity (FVC), and FEV1 / FVC were recorded. An improvement of 12% or more in PEFR and FEV_1 was taken as criterion for diagnosis of asthma. Severity of asthma was assessed by both history and pre-bronchodilator FEV_1 values. Severity of asthma was classified as follows.

1. Mild persistent: symptoms less than once a week, with brief exacerbations; nocturnal symptoms not more than twice a month; FEV_1e" 80%.
2. Moderate persistent: symptoms daily; exacerbations may affect activity and sleep; FEV1 between 60-80%.
3. Severe persistent: symptoms daily with frequent exacerbations; frequent nocturnal symptoms; limitations physical activities; FEV_1d" 60%.

Serum IgE levels were estimated in all the patients 4

Statistical analyses

All values were expressed as mean ± SEM. Statistical analyses were done by one-way analysis of variance (ANOVA) followed by the least significant difference test. P values of less than 0.05 indicated a statistical significance.

Table-I
General characteristics of subjects.

Groups	Control	Severity of asthma by pulmonary function test		
		Mild	Moderate	Severe
Total number	30	36	44	52
Male	16	20	17	23
Female	14	16	27	29
Duration:				
< 1 year	-	2	1	0
1 – 5 years	-	10	10	19
6-10 years	-	6	13	7
> 10 years		18	20	26
Age: 15 – 30 years	2	11	10	16
31 – 45 years	18	17	23	21
46 – 60 years	10	8	11	15
Serum IgE (IU/ml)	127.5 ± 2.9	212.3 ± 9.8	489.2 ± 5.4	1059.6 ± 5.9

Results:

Of the 132 patients in this study, 37 (28%) patients were between 15-30 years, 61 (47%) patients between 31-45 years, and 34 (25%) patients between 46-60 years of age. Three patients had symptoms less than one year, 39 patients for 1-5 years, 26 patients for 6 –10 years, and 64 patients for more than 10 years (Table 1). One hundred and two (27%) patients developed symptoms of bronchial asthma before 30 years of age; 23 (17%) patients between 31 to 45 years and only 7 (5%) patients developed asthmatic symptoms after the age of 45 years. A significant increase in IgE levels was observed in all the three groups of asthmatic patients when compared with normal control subjects ($p<0.001$) (Table 2).

Table-II

Comparisons of serum IgE (IU/ml) with the severity of asthma as predicted by pulmonary

Control	Mild	Moderate	Severe
127.5 ± 2.9	212.3 ± 9.8	489.2 ± 5.4***	1059.6 ± 5.9***

Values are mean±SEM; $p<0.05$, $p<0.01$, $p<0.0001$ when compared to control; *$p<0.05$, **$p<0.01$, ***$p<0.0001$ when compared to mild asthma; $p<0.05$, $p<0.001$, $p<0.0001$, when compared between moderate and severe asthma.

The serum IgE level significantly increased with the severity of asthma predicted by pulmonary function tests ($p<0.001$), i.e., the severe bronchial asthma displayed higher serum IgE than mild or moderate types (Table 3). When the severity was determined by history of the disease, there was a significant increase in the serum IgE level in the moderate persistent and severe persistent asthma, compared to moderate intermittent asthma patients, ($p<0.001$) (Table 3). Thus, the serum IgE level was proportionately higher in patients with more severe airflow obstruction.

Table-III

Comparisons of serum IgE (IU/ml) with the severity of asthma as predicted by the history of patients.

Moderate persistent	Moderate intermittent	Severe persistent
955.6 ± 4.6 ***	785.2 ± 5.1	989.4 ± 4.2 ***

Values are mean ± SEM; *$p<0.05$, **$p<0.01$, ***$p<0.0001$ when compared to moderate intermittent.

Discussion

In the present study, the incidence of bronchial asthma is higher in females than males, being similar to previous reports.[7] Childhood asthma was reported to be more prevalent in boys than in girls.[8] The increased risk for males in childhood is probably related to narrower airways, increased airway tone, and possibly higher IgE in boys,[7,9] which predispose them to enhanced airflow limitation in response to a variety of stimulus. This difference disappears after the age of 10 years when airway diameter/

length ratio is the same in both sexes, because of changes in thoracic size that occurs in puberty in males but not in females. More females than males develop asthma during puberty so prevalence of adult asthma becomes higher in females than males.[7]

More than 70% of the patients in this study had the asthma symptoms before the age of 40 years. This is in accordance with other studies, which have shown that, in the majority of patients with extrinsic asthma, the symptoms develop before the age of 30 years.[10] In the present study, normal levels of IgE itself were relatively higher than those values from western population studies.[11,12] The higher IgE levels in the normal control group may be explained by the higher incidence of parasitic infection and infestation in the patients from this part of the world. When comparing the severity of asthma with serum IgE levels in bronchial asthma, the present data indicated that the more severity of the asthma, the greater is the elevation in serum IgE. The most important risk factor for the development of extrinsic asthma is atopy.[13,14] An atopic individual responds to antigenic stimuli to which normal people will not respond. The basic pathology in bronchial asthma is airway hyper-responsiveness. The airway hyper-responsiveness is an excessive response of the airway epithelium to antigenic stimuli. The airway response in asthma is mediated by T-lymphocytes. Antigenic exposure to T-lymphocytes leads to their differentiation into active T-cells, which secrete a series of biologically active proteins called cytokines.

B-lymphocytes and plasma cells in airways, gastrointestinal tract, and regional lymph nodes produce IgE. The initial formation of IgE antibody depends upon the signals from lymphocytes and IL-4 and IL-13. Patients with clinical symptoms and higher serum IgE levels are likely to be suffering from allergic diseases.[14] The molecular mechanisms underlying immune system activation for allergen-induced asthma include stimulation of Cd4+ Th2 immune response and the subsequent production of IgE antibody. Re-exposure to allergen results in the recruitment of mast cells (via high affinity IgE Fce receptors), eosinophils, and other leukocytes. In particular, mast cells that release the vasoactive amines, histamine, and other ligands from large granules produce a local systemic hypersensitivity reaction.[16] The ensuing inflammation amplifies an individual's hypersensitivity reaction by the recruitment of other cells and perpetuates the clinical symptoms (wheezing, shortness of breath, and chest tightness).[17] In atopic individuals, the IgE receptors, send unusually strong signals when cross-linked, resulting in secretion of abnormally high levels of IL4 from mast cells, which further results in overproduction of IgE antibodies. Mast cells and basophils are the primary initiating cells of IgE-mediated allergic reaction.

Considerable attention has been given in recent years to the possible role of serum IgE in the development of chronic airflow limitation and other respiratory disorders.[1,18,19] IgE is responsible for the release of various inflammatory mediators in asthma, such as histamine, prostaglandins, and leukotriens. These inflammatory mediators increase airway narrowing due to excessive mucus production, airway smooth muscle spasm, and edema of the airway mucosa.[13,20] Bronchial asthma also alters serum levels of other immunoglobulins. Serum IgG and IgA levels increase along with IgE,[21] whereas serum IgM levels decreases in bronchial asthma.[22]

Increased serum IgE levels in asthma may be due to increases in IgE-dependent processes and cellular components of the immune system. The secretion of IgE by lymphocytes defines the allergic state of an individual. The cellular events associated with IgE-dependent processes are very much important in asthma.[23] Higher IgE levels indicate some types of inherent susceptibility and/or presence of a disease process involving airway inflammation.[24,25]

In summary, the present data suggest that serum IgE levels increase significantly in bronchial asthma and reflect the severity of asthma. Degrees of inflammation and the subsequent severity of airway obstruction in bronchial asthma are proportional to the serum IgE levels. Thus, they presumably provide a better clue to atopy and the detection of specific IgE would be a prerequisite for both the definitive diagnosis and the therapeutic strategy for bronchial asthma.

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ORIGINAL ARTICLE

Nebulized Anticholinergic and Sympathomimetic Treatment of Asthma and Chronic Obstructive Airway Disease in the Emergency Room

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Abstract:

Background: *Bronchial asthma and chronic obstructive pulmonary disease (COPD) are multifactorial chronic diseases. Acute exacerbation of both asthma and COPD are emergency condition. The aim of the present study is to establish a safe and effective method of bronchodilatation for patients suffering from acute exacerbation of bronchial asthma and COPD during emergency.*

Method: *This prospective and comparative study was carried out in OPD and emergency room of National Institute of Diseases of the Chest and Hospital, Mohakhali, Dhaka during the period from January 2010 to December 2010 for one year. All men and women aged above 15 years suffering from acute exacerbation of bronchial asthma and COPD attending in OPD and the emergency room of NIDCH, Mohakhali, Dhaka was included in this study. Patients suffering from stable asthma or COPD were excluded from the study. Patients who received a nebulized bronchodilator within 6 hours or if they required with drugs other than specified in the treatment protocol were also excluded from the study. At the time of exacerbation the subjects were randomized into three groups by using table of random number method of which patients of group A were nebulized by Ipratopium bromide and normal saline, patients of Group B were nebulized by Salbutamol and Normal Saline and patients of Group C were nebulized by Ipratopium bromide, salbutamol and Normal saline solutions with a fixed dose formulation (Ipratopium bromide solution 1 ml, Salbutamol solution 0.5ml and Normal saline1.5 ml). Concomitant supportive treatment with intravenous hydrocortisone were administered as per need of the patient. Cardiovascular side effects were monitored by observing heart rate, blood pressure, respiratory rate. Statistical analysis was performed.*

Result: *In this study a total number of 112 patients presented with acute exacerbation of bronchial asthma and COPD of which 32 patients of were in the group A, 37 patients were in the Group B and the rest 43 patients were in*

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the Group C. In the group A maximum were from the age group of 46-55 years (37.5%) (mean ± SD is 43.59 ± 15.39). In the group B maximum were from the age group of 46-55 years (29.7%) (mean ± SD 45.70 ± 15.43). In the group C majority cases were from the age group of 46-55 years (30.2%) (mean ± SD 44.14 ± 13.51). In group A male (84.4%) is predominant than female (15.6%). In the group A majority were service holder (34.4%), cultivator (18.8%), business, (15.6%). In the group B majority were service holder (40.5%). In the group C majority were service holder (51.2%). Smokers were in 18 (56.3) cases, 18 (48.6%) cases and 25(58.1%) cases in group A, group B and group C respectively. In group A the mean ± SD of base line respiratory rate were 27.93 ± 3.10 and 25.67 ± 2.38 in Bronchial asthma and COPD respectively. (p=0.026). After 45 and 90 minutes the mean ± SD of respiratory rate in Bronchial asthma were 23.14 ± 3.39 and 21.07 ± 3.32 respectively. After 45 and 90 minutes the mean± SD of respiratory rate in COPD are 24.00 ± 3.29 and 23.56 ± 4.03 respectively.

Conclusion: *In conclusion, the findings of this study permit to conclude that nebulization combinedly with Ipratopium bromide, salbutamol and normal saline are effective for the management of exacerbation of acute bronchial asthma and COPD.*

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Introduction:

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particals or gases.[1] Bronchial asthma is a chronic, inflammatory disease of large, small and medium airways with typical symtoms (cough, wheezing, breathlessness, chest tightness) and airways narrowing that are partially or completely reversible either spontaneously or by treatment associated with increased airways responsiveness to a variety of stimuli . The largest cause of COPD is smoking, because it produces accelerated decreases in forced expiratory volume in 1 second (FEV1).[2] On the otherhand prevalence of asthma is due to hereditary and changing environmental factors.

Asthma exacerbations are episodes of progressively worsening shortness of breath, cough, wheezing, chest tightness, or some combination of these symptoms.[3] The prevalence of the disease is increasing in industrialized as well as industrializing countries. It is one of the most common diseases worldwide affecting 100 million people with increasing prevalence each year.[4] In the United States alone, approximately 15.7 million adults and 6.7 million children have asthma and in 2004, approximately 3,780 patients died from asthma and its complications.[5] In Indian population the prevalence of asthma is 10%-15% and in semi-urban areas, 29.7% are suffering with chronic bronchitis and 18.8% with asthma.[6] Asthma in Bangladesh appears to be also a substantial public health problem: an estimated 7 million people including 4 million children suffer from asthma related symptoms [7]. Approximately 14 to 20 million people in the United States have COPD, and it is the fourth leading cause of death.[8] Among older adults (65 years or older), approximately 34.1 people per 1000 have COPD.

Chronic obstructive pulmonary disease (COPD), the fifth leading cause of global morbidity [9]. It is a major public health problem. In the past, management and treatment options for COPD were largely ignored because interventions to improve morbidity, mortality, and quality of life were lacking. However, over the last decade, substantial progress has been made in the interventions available, including developments in long-acting bronchodilator drugs and improved ventilation methods, and, reflecting the general shift in medicine towards evidence-based practice, there was recognition that improved, comprehensive management guidelines to evolve and optimize COPD patient care would be valuable.[10]

Allergen mostly the mite, food and animal allergens are the main contributory factors for both the diseases. The most common allergens are house dust, mite, animal dander, pollens, moulds & food stuffs.[11] Patients with asthma tend to have an increase in airway reactivity to a other variety such stimuli, such as exercise, cold air, and viruses.[12] Asthma is an important chronic disorder of the airways with significant morbidity and mortality. Around 300 million people in the world currently have asthma.

The optimal bronchodilator regimen for the treatment of airways obstruction, either acute or chronic, maximizes bronchodilator efficacy while minimizing unwanted side effects. Increasing attention is being given to combination drug regimens.[13] Anticholinergic agents which act through different receptor and biochemical pathways from either sympathomimetic or methylxanthine agents, may be well suited for use in combination bronchodilator regimens.[14] In the treatment of stable asthma, anticholinergic have been shown to increase bronchodilator responsiveness with no significant increase in side effects when added to a regimen of sympathomimetic agents and methylxanthines [15]. Among available anticholinergic agents, ipratopium bromide, a quaternary derivative of atropine, may be best suited to combination bronchodilator regimens, because it is poorly absorbed from airway mucosal surfaces in aerosol form, thereby offering bronchodilatation without unwanted systemic antimuscarinic effect.[16]

Thus, prevention, early detection, and prompt treatment of exacerbations may impact their clinical progression by ameliorating the effects on quality of life and minimizing the risk of hospitalization. This study was undertaken to evaluate the combination therapy and is to find out the superiority of using the either drug alone.

Materials and Methods:

This was a prospective and comparative study.

This was carried out in OPD and emergency room of National Institute of Diseases of the Chest and Hospital, Mohakhali, Dhaka during the period from January 2010 to December 2010 for the duration of one year.

All men and women aged 15-45 years suffering from acute exacerbation of bronchial asthma and COPD aged >45-60 years attending the emergency room of NIDCH, Mohakhali, Dhaka was taken as study population.

A total of 112 patients were enrolled in this study.

The sampling technique was consecutive random sampling and this purposive sampling technique was used as per inclusions and exclusion criteria.

Selection criteria of subjects

Inclusion criteria

- Acute exacerbation of bronchial asthma and COPD attending the OPD & Emergency room of NIDCH
- Patient aged 15-45 years in case of bronchial asthma and >45-60 years in case of COPD
- Patient of both sexes
- Patient with normal ECG
- Participants, who gave consent and willing to comply with the study procedure, were included.

Exclusion criteria

- Patients suffering from stable asthma or, COPD
- Patient presenting with acute dyspnoea but suffering from other than bronchial asthma or, COPD
- Patients suffering from other concomitant medical illness such as pneumonia, pulmonary oedema, acute myocardial infarction or frequent ventricular ectopics.
- Pregnant women
- Nursing mother
- Patients who received a nebulized bronchodilator within 6 hours or if they required with drugs other than specified in the treatment protocol
- Patients who refused to give consent to take medication as advised.

Study Procedure

This study was an OPD and Emergency room based case control study. A total number of 112 patients fulfilling the inclusion and without any exclusion criteria were included in this study attending the OPD and Emergency room of NIDCH, Mohakhali, Dhaka within 24 hours. Data were collected through appropriate questionnaire. At the time of exacerbation the subjects were randomized into three groups by using table of random number method.

- Patients of group A were nebulized by Ipratopium bromide and normal saline.

- Patients of Group B were nebulized by Salbutamol and Normal Saline.
- Patients of Group C were nebulized by Ipratopium bromide, salbutamol and Normal saline solutions.

Dose Formulation

Ipratopium bromide 1 ml solution	(1 ml = 250 microgram)
Salbutamol solution	0.5ml (1 ml =5 mg)
Normal saline	1.5ml

Concomitant supportive treatment with intravenous hydrocortisone will be administered as per need of the patient. Cardiovascular side effects will be monitored by observing heart rate , blood pressure, respiratory rate. Other minor side effects such as eye irritation, sweating and dizziness also be monitored.

Following variables such as pulse, Respiratory rate, Forced Expiratory Volume in 1st Second and SpO2 were selected for both cases of Asthma and COPD. These variables were recorded at baseline and again 45 minutes and 90 minutes after giving salbutamol & ipratomium bromide along with other conventional management. Then the results were evaluated & compared respectively as per study design.

All data were recorded systematically in preformed data collection form and quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. Statistical analysis was performed by using SPSS (Statistical Package for Social Sciences) for windows version 12.0. 95% confidence limit was taken. Probability value <0.05 was considered as level of significance.

No invasive investigation were done. There was no possibility of any physical, social or mental risk of the respondent as this study were carried out with the safest, side effect free Allergen Extract. All information gathered were kept secret and only used for medical research and analysis. Protocol was ethically reviewed and was approved by the Ethical Review Committee of. "National Institute of Diseases of the Chest & Hospital" (NIDCH), Mohakhali, Dhaka."

Results and Observations:

A total number of 112 patients presented with acute exacerbation of bronchial asthma and COPD attending at the OPD & Emergency room of NIDCH were included in this study of which 32 patients of were in the group A, 37 patients were in the Group B and the rest 43 patients were in the Group C who were treated with nebulization by Ipratopium bromide with normal saline, by Salbutamol with Normal Saline and Ipratopium bromide combined with salbutamol and Normal saline solutions respectively.

Table-I

Distribution of study population according to age by groups

Age (in year)	Groups			Total	p value*
	Group A	Group B	Group C		
d"25	8 (25.0)	5 (13.5)	5 (11.6)	18 (16.1)	
26-35	3 (9.4)	6 (16.2)	8 (18.6)	17 (15.2)	
36-45	2 (6.3)	7 (18.9)	8 (18.6)	17 (15.2)	
46-55	12 (37.5)	11 (29.7)	13 (30.2)	36 (32.1)	
56-65	5 (15.6)	4 (10.8)	9 (20.9)	18 (16.1)	
>65	2 (6.3)	4 (10.8)	0 (.0)	6 (5.4)	
Total	32 (100.0)	37 (100.0)	43 (100.0)	112 (100.0)	
Mean ± SD	43.59 ± 15.39	45.70 ± 15.43	44.14 ± 13.51	44.50 ± 14.60	0.821

*ANOVA test was done to measure the level of significance.
Figure within parentheses indicated in percentage.

Table-II

Distribution of study population according to sex by groups

Sex	Groups			Total	p value*
	Group A	Group B	Group C		
Male	27 (84.4)	29 (78.4)	30 (69.8)	86 (76.8)	0.321
Female	5 (15.6)	8 (21.6)	13 (30.2)	26 (23.2)	
Total	32 (100.0)	37 (100.0)	43 (100.0)	112 (100.0)	

*Chi-square test was done to measure the level of significance.
Figure within parentheses indicated in percentage.

Table-III

Distribution of study population according to occupation by groups

Occupation	Groups			Total	p value*
	Group A	Group B	Group C		
Housewife	5 (15.6)	8 (21.6)	6 (14.0)	19 (17.0)	
Student	0 (.0)	1 (2.7)	3 (7.0)	4 (3.6)	
Service	11 (34.4)	15 (40.5)	22 (51.2)	48 (42.9)	0.154
Business	5 (15.6)	3(8.1)	8 (18.6)	16 (14.3)	
Cultivator	11 (34.4)	10 (27.0)	4 (9.3)	25 (22.3)	
Total	32 (100.0)	37 (100.0)	43 (100.0)	112 (100.0)	

*Chi-square test was done to measure the level of significance.
*Figure within parentheses indicated in percentage.

Table-IV

Distribution of chief complaints by groups

Chief complaints	Groups			Total	p value*
	Group A	Group B	Group C		
Respiratory distress	32 (100.0)	37 (100.0)	43 (100.0)	112 (100.0)	Not done
Cough	32 (100.0)	37 (100.0)	42 (97.7)	111 (99.1)	Not done
Sputum	18 (56.3)	17 (45.9)	22 (51.2)	57 (50.9)	0.694
Wheeze	16 (50.0)	26 (70.3)	28 (65.1)	70 (62.5)	0.201
Chest pain	15 (46.9)	12 (32.4)	18 (41.9)	45 (40.2)	0.456
Fever	17 (53.1)	18 (48.6)	22 (51.2)	57 (50.9)	0.933

*Chi-square test was done to measure the level of significance.
Figure within parentheses indicated in percentage.

Table-V

Distribution of study population according to smoking habit

Smoking status	Groups			Total	p value*
	Group A	Group B	Group C		
Smoker	18 (56.3)	18 (48.6)	25 (58.1)	61 (54.5)	0.677
Non smoker	14 (43.8)	19 (51.4)	18 (41.9)	51 (45.5)	
Total	32 (100.0)	37 (100.0)	43 (100.0)	112 (100.0)	

*Chi-square test was done to measure the level of significance.
*Figure within parentheses indicated in percentage.

Table VI shows the mean ± SD of respiratory rate at different follow up in Bronchial asthma and COPD at different treatment. In group A the mean ± SD of base line respiratory rate are 27.93 ± 3.10 and 25.67 ± 2.38 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.026). After 45 and 90 minutes the mean ± SD of respiratory rate in Bronchial asthma are 23.14 ± 3.39 and 21.07 ± 3.32 respectively. After 45 and 90 minutes the mean ± SD of respiratory rate in COPD are 24.00 ± 3.29 and 23.56 ± 4.03 respectively. This is not statistically significant (p=0.476 and 0.072). The percentage of changes that occur from base line to after 45 minutes are 17.22 ± 7.17 and 6.49 ± 9.66 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.002). In group B the mean ± SD of base line respiratory rate are 28.45 ± 3.30 and 25.76 ± 1.82 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.005). The mean ± SD respiratory rate after 45 minutes are 28.45 ± 3.30 and 25.76 ± 1.82 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.371). The mean ± SD respiratory rate after 90 minutes are 19.70 ± 3.81 and 20.47 ± 2.98 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.504). The mean ± SD respiratory rate of percentage of changes that occur from base line to after 45 minutes are 17.64 ± 7.01 and 12.19 ± 7.29 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.027). In group C the mean ± SD of base line respiratory rate are 29.19 ± 3.08 and 26.05 ± 1.56 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001). The mean ± SD respiratory rate after 45 minutes are 22.29 ± 3.12 and 23.27 ± 2.39 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.250). The mean ± SD respiratory rate after 90 minutes are 17.86 ± 3.37 and 21.86 ± 4.66 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.003). The mean ± SD respiratory rate of percentage of changes that occur from base line to after 45 minutes are 23.62 ± 6.69 and 10.57 ± 8.63 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001).

Table-VI

Mean ± SD of respiratory rate at different follow up in Bronchial asthma and COPD at different treatment

	Bronchial asthma	COPD	p value*
Group A			
Base line respiratory rate	27.93 ± 3.10	25.67 ± 2.38	0.026
After 45 minutes	23.14 ± 3.39	24.00 ± 3.29	0.476
After 90 minutes	21.07 ± 3.32	23.56 ± 4.03	0.072
% changes after 45 mins	17.22 ± 7.17	6.49 ± 9.66	0.002
Group B			
Base line respiratory rate	28.45 ± 3.30	25.76 ± 1.82	0.005
After 45 minutes	23.45 ± 3.46	22.59 ± 2.00	0.371
After 90 minutes	19.70 ± 3.81	20.47 ± 2.98	0.504
% changes after 45 mins	17.64 ± 7.01	12.19 ± 7.29	0.027
Group C			
Base line respiratory rate	29.19 ± 3.08	26.05 ± 1.56	0.001
After 45 minutes	22.29 ± 3.12	23.27 ± 2.39	0.250
After 90 minutes	17.86 ± 3.37	21.86 ± 4.66	0.003
% changes after 45 mins	23.62 ± 6.69	10.57 ± 8.63	0.001

*t test was done to measure the level of significance.
Data was shown as Mean ± SD.

Table-VIII

Mean ± SD of FEV_1 at different follow up in Bronchial asthma and COPD at different treatment

	Bronchial asthma	COPD	p value*
Group A			
Base line	29.09 ± 10.93	37.09 ± 8.11	0.024
After 45 minutes	33.09 ± 10.27	39.17 ± 8.35	0.074
After 90 minutes	42.73 ± 14.47	43.92 ± 13.41	0.811
% changes after 45 mins	18.05 ± 23.83	6.29 ± 11.52	0.075
Group B			
Base line	36.75 ± 10.49	40.00 ± 6.79	0.280
After 45 minutes	41.73 ± 11.28	45.32 ± 8.99	0.297
After 90 minutes	50.12 ± 13.25	53.66 ± 11.09	0.389
% changes after 45 mins	15.02 ± 18.58	13.38 ± 13.35	0.764
Group C			
Base line	56.49 ± 7.82	58.80 ± 11.44	0.445
After 45 minutes	79.34 ± 8.57	65.00 ± 7.63	0.001
After 90 minutes	80.21 ± 11.64	70.23 ± 10.00	0.004
% changes after 45 mins	42.37 ± 21.49	13.08 ± 16.67	0.001

*t test was done to measure the level of significance.
Data was shown as Mean ± SD.

Table-IX

Mean ± SD of SpO_2 at different follow up in Bronchial asthma and COPD at different treatment

	Bronchial asthma	COPD	p value*
Group A			
Base line	94.00 ± 3.33	92.33 ± 3.28	0.204
After 45 minutes	97.57 ± 4.03	93.89 ± 3.77	0.001
After 90 minutes	97.33 ± 3.27	92.99 ± 4.86	0.001
% changes after 45 mins	3.80 ± 1.38	1.83 ± 2.57	0.001
Group B			
Base line	93.40 ± 3.41	92.12 ± 3.20	0.056
After 45 minutes	97.60 ± 4.04	93.94 ± 3.21	0.001
After 90 minutes	97.10 ± 3.60	92.88 ± 2.57	0.001
% changes after 45 mins	4.50 ± 2.78	2.09 ± 2.59	0.001
Group C			
Base line	93.19 ± 3.12	91.05 ± 2.24	0.023
After 45 minutes	98.00 ± 2.77	92.41 ± 3.25	0.001
After 90 minutes	98.17 ± 2.76	92.95 ± 5.49	0.001
% changes after 45 mins	5.16 ± 1.29	1.51 ± 0.77	0.001

*t test was done to measure the level of significance.
Data was shown as Mean ± SD.

Table VII shows the mean ± SD of pulse at different follow up in Bronchial asthma and COPD at different treatment. In group A the mean ± SD of base line pulse are 113.50 ± 8.56 and 109.94 ± 8.31 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.245). After 45 and 90 minutes the mean ± SD of pulse in Bronchial asthma are 103.86 ± 10.21 and 94.93 ± 12.12 respectively. After 45 and 90 minutes the mean± SD of pulse in COPD are 109.44 ± 8.11 and 108.11 ± 11.26 respectively. This is statistically significant (p=0.003). The percentage of changes that occur from base line to after 45 minutes are 8.48 ± 5.99 and 0.22 ±

6.66 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001). In group B the mean ± SD of base line pulse are 115.95 ± 10.06 and 109.12 ± 9.41 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.041). The mean ± SD pulse after 45 minutes are 105.30 ± 11.41 and 105.59 ± 7.54 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.930). The mean ± SD pulse after 90 minutes are 96.20 ± 14.65 and 96.00 ± 9.30 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.962). The mean ± SD pulse of percentage of changes that occur from base line to after 45 minutes are 9.19 ± 5.91 and 3.02 ± 4.49 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001). In group C the mean ± SD of base line pulse are 120.14 ± 6.26 and 107.64 ± 7.03 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001). The mean ± SD respiratory rate after 45 minutes are 106.38 ± 7.33 and 104.77 ± 8.70 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.517). The mean ± SD pulse after 90 minutes are 88.86 ± 8.31 and 101.27 ± 13.43 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001). The mean ± SD pulse of percentage of changes that occur from base line to after 45 minutes are 11.48 ± 3.47 and 2.71 ± 3.73 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001).

Table VIII shows the mean ± SD of FEV_1 at different follow up in Bronchial asthma and COPD at different treatment. In group A the mean ± SD of base line FEV_1 are 29.09 ± 10.93 and 37.09 ± 8.11 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.024). After 45 and 90 minutes the mean ± SD of FEV_1 in Bronchial asthma are 33.09 ± 10.27 and 42.73 ± 14.47 respectively. After 45 and 90 minutes the mean± SD of FEV_1 in COPD are 39.17 ± 8.35 and 43.92 ± 13.41 respectively. This is statistically significant (p=0.074). The percentage of changes that occur from base line to after 45 minutes are 18.05 ± 23.83 and 6.29 ± 11.52 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.075). In group B the mean ± SD of base line FEV_1 are 36.75 ± 10.49 and 40.00 ± 6.79 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.280). The mean ± SD FEV_1 after 45 minutes are 41.73 ± 11.28 and 45.32 ± 8.99 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.297). The mean ± SD FEV_1 after 90 minutes are 50.12 ± 13.25 and 53.66 ± 11.09 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.389). The mean ± SD FEV_1 of percentage of changes that occur from base line to after 45 minutes are 15.02 ± 18.58 and 13.38 ± 13.35 in Bronchial asthma and COPD respectively. This is statistically not significant (p=0.764). In group C the mean ± SD of base line FEV_1 are 56.49 ± 7.82 and 58.80 ± 11.44 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.445). The mean ± SD FEV_1 after 45 minutes are 79.34 ± 8.57 and 65.00 ± 7.63 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001). The mean ± SD FEV_1 after 90 minutes are 80.21 ± 11.64 and 70.23 ± 10.00 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.004). The mean ± SD FEV_1 of percentage of changes that occur from base line to after 45 minutes are 42.37 ± 21.49 and 13.08 ± 16.67 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001).

Table IX shows the mean ± SD of SpO_2 at different follow up in Bronchial asthma and COPD at different treatment. In group A the mean ± SD of base line SpO_2 are 84.00 ± 3.33 and 82.33 ± 2.28 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.103). After 45 and 90 minutes the mean ± SD of SpO_2 in Bronchial asthma are 88.57 ± 4.03 and 91.93 ± 3.27 respectively. After 45 and 90 minutes the mean± SD of SpO_2 in COPD are 84.89 ± 3.77 and 86.99 ± 4.86 respectively. This is statistically significant (p=00.014). The percentage of changes that occur from base line SpO_2 to after 45 minutes are 5.54 ± 5.38 and 3.14 ± 4.57 in Bronchial asthma and COPD respectively. This is not statistically

significant (p=0.183). In group B the mean ± SD of base line SpO_2 are 84.40 ± 3.41 and 82.12 ± 2.20 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.023). The mean ± SD SpO_2 after 45 minutes are 87.60 ± 4.04 and 85.94 ± 3.21 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.181). The mean ± SD SpO_2 after 90 minutes are 92.10 ± 3.60 and 89.88 ± 2.57 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.041). The mean ± SD SpO_2 of percentage of changes that occur from base line to after 45 minutes are 3.83 ± 3.78 and 4.72 ± 4.59 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.524). In group C the mean ± SD of base line SpO_2 are 84.19 ± 3.12 and 83.05 ± 2.24 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.173). The mean ± SD SpO_2 after 45 minutes are 90.00 ± 2.77 and 86.41 ± 3.25 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001). The mean ± SD SpO_2 after 90 minutes are 93.67 ± 2.76 and 87.95 ± 5.49 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001). The mean ± SD SpO_2 of percentage of changes that occur from base line to after 45 minutes are 6.94 ± 2.29 and 4.03 ± 1.77 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001).

Discussion:

Bronchial asthma is a multifactorial disease.[12] Like asthma chronic obstructive pulmonary disease (COPD) is also a multifactorial disease and the fifth leading cause of global morbidity.[9] It is a major public health problem. The prevalence is known to be increasing.[17] Acute exacerbation of both asthma and COPD are emergency condition.[3]

Asthma in Bangladesh appears to be also a substantial public health problem: an estimated 7 million people including 4 million children suffer from asthma related symptoms.[7] During an exacerbation of COPD changes occur in the patients baseline dyspnoea, cough, and/or sputum with an acute in onset. In asthma patients with the combination of preventer, reliever and protector drugs and patient education can offer an almost normal life.[18]

Nebulized anticholinergic and sympathomimetic regimens are very effective in acute airways obstruction. The optimal bronchodilator regimen for the treatment of airways obstruction, either acute or chronic, maximizes bronchodilator efficacy while minimizing unwanted side effects. Increasing attention is being given to combination drug regimens.[19] Anticholinergic agents which act through different receptor and biochemical pathways from either sympathomimetic or methylxanthine agents,may be well suited for use in combination bronchodilator regimens.[14] In the treatment of stable asthma, anticholinergic have been shown to increase bronchodilator responsiveness with no significant increase in side effects when added to a regimen of sympathomimetic agents and methylxanthines.[20] Among available anticholinergic agents ipratopium bromide may be best suited to combination bronchodilator regimens as because it is poorly absorbed from airway mucosal surfaces in aerosol form and thereby offering bronchodilatation without unwanted systemic antimuscarinic effects.[16]

In this study, a total number of 112 patients presented with acute exacerbation of bronchial asthma and COPD attending at the OPD & Emergency room of NIDCH were included ,of which 32 patients of were in group A, 37 patients were in Group B and the rest 43 patients were in Group C who were treated with nebulization by Ipratopium bromide with normal saline, by Salbutamol with Normal Saline and Ipratopium bromide combined with salbutamol and Normal saline solutions respectively. The distribution of study population according to age by groups is recorded in this study. Among 32 patients in the group A maximum are from the age group of 46-55 years which is 12(37.5%) cases followed by less than or equal to 25 years, 56-65 years age group and 26-35 years which are 8 (25.0%) cases, 5 (15.6%) cases and 3 (9.4%) cases respectively. Only 2 (6.3%) cases is present in the age group of 36-45 years and more than 65 years in each. The mean ± SD is 43.59 ± 15.39. Among 37 patients in the group B maximum are from the age group of 46-55 years which is 11 (29.7%) cases followed by 36-45 years, 26-35 years and less than or equal to 25 years which are 7 (18.9%)

cases, 6 (16.2%) cases and 5 (13.5%) cases respectively. Only 4 (10.8%) cases is present in the age group of 56-65 years and more than 65 years in each. The mean ± SD is 45.70 ± 15.43. Among 43 patients in the group C majority cases are from the age group of 46-55 years which is 13 (30.2%) cases followed by 56-65 years, and less than or equal to 25 years which are 9 (20.9%) cases and 5 (11.6) cases respectively. Only 8 (18.6%) cases is present in the age group of 26-35 years and 36-45 years in each. The mean ± SD is 44.14 ± 13.51. Similar result was reported by Tarlo et al[21] and mentioned that asthma commonly affects adults and children of all ages and adult asthma may be a continuation of childhood asthma, or new-onset asthma. National Clinical Guideline Centre (2010) has reported that most COPD patients are not diagnosed until they are in their fifties. In another study Renwick and Connolly (1996) reported that patients aged 45 and over have 11% prevalence of non-reversible chronic airflow obstruction which is consistent with the present study. Seamark et al[21] has found a similar result with a prevalence of an abnormal FEV_1 and respiratory symptoms. The reason of high prevalence in aged persons are due to the increases prevalence with increasing age.[22]

The distribution of study population according to sex is recorded in this study. In group A male is predominant than female which is 27 (84.4%) cases and 5 (15.6%) cases respectively. In group B male is predominant than female which is 29 (78.4%) cases and 8 (21.6%) cases respectively. In group C male is predominant than female which is 30 (69.8%) cases and 30 (69.8%) cases respectively. The ratio of male and female is 3.31:1 which is not statistically significant (p=0.321). Asthma is more common in male than female. Similar result was reported by Horwood et al[23] and mentioned that the prevalence of asthma is higher in boys in early life and the sex ratio shifts at puberty and asthma appears predominantly in women in the age group. National Clinical Guideline Centre (2010) has reported that smoking-related diseases like COPD and lung cancer are continuing to increase among women in the United States and are decreasing among men which is dissimilar to the present study. The reason of this may be due to more likely to develop COPD in women or that the severity of COPD in women may be increased compared with men at a similar level of tobacco smoking.[24] Adult women are more likely to both develop and die of asthma than are men.[24]

The distribution of study population according to occupation by groups is recorded. In the group A majority are service holder which is 11 (34.4%) cases followed by cultivator, business and housewife which is 11 (34.4%) cases, 5 (15.6%) cases and 5 (15.6%) cases respectively. In the group B majority are service holder which is 15 (40.5%)) cases followed by cultivator, business, housewife and student, which is 10(27.0%) cases, 3 (8.1%) cases, 8 (21.6%) cases and 1(2.7) respectively. In the group C majority are service holder which is 22 (51.2%) cases followed by cultivator, business, housewife and student which is 4 (9.3%) cases, 8 (18.6%) cases, 6 (14.0%) cases and 3 (7.0%) cases respectively.

Occupation is one of the vital risk factors in the etiology of asthma and COPD. Similar result was reported by Rennard [25] mentioned that in addition to cigarette smoke, occupational exposures, and alfa-protease inhibitor deficiency, etiologies that have been definitely linked to the development of COPD and a number of other factors are likely associated with development of COPD. Buist and Vollmer [26] reported that exposure to the occupational environment is of great influence of the development of COPD and these include air pollution, passive smoke exposure, respiratory virus infection, socioeconomic factors, nutrition, alcohol ingestion, age, gender, poorly defined familial factors, mucus hypersecretion, and airways hyperresponsiveness.

The distribution of study population according to smoking habit is recorded. Smokers are in 18 (56.3) cases, 18 (48.6%) cases and 25(58.1%) cases in group A, group B and group C respectively. Non-smoker is present in 14 (43.8%) cases, 19 (51.4%) cases and 18 (41.9%) cases in group A, group B and group C respectively. The difference between smoker and nonsmoker is not statistically significant (p=0.677). High prevalence is found among the smokers. Similar result was reported by Boschetto et al and

mentioned that cigarette smoking is undoubtedly the main cause of COPD in the population. Fletcher and Peto showed that the average decline in FEV_1 in smokers is faster (60 ml/yr) than in non-smokers (30 ml/yr) . However, smokers who develop COPD have an average decline in FEV_1 of greater than 60 ml/yr, and only 15 to 20% of smokers develop clinically significant COPD. Cigarette smoke is analogous to a mixed inhalation exposure at a workplace because it is a complex mixture of particles and gases .

The mean ± SD of respiratory rate at different follow up in Bronchial asthma and COPD at different treatment is recorded in this study. In group A the mean ± SD of base line respiratory rate are 27.93 ± 3.10 and 25.67 ± 2.38 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.026). After 45 and 90 minutes the mean ± SD of respiratory rate in Bronchial asthma are 23.14 ± 3.39 and 21.07 ± 3.32 respectively. After 45 and 90 minutes the mean± SD of respiratory rate in COPD are 24.00 ± 3.29 and 23.56 ± 4.03 respectively. This is not statistically significant (p=0.476 and 0.072). The percentage of changes that occur from base line to after 45 minutes are 17.22 ± 7.17 and 6.49 ± 9.66 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.002). In group B the mean ± SD of base line respiratory rate are 28.45 ± 3.30 and 25.76 ± 1.82 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.005). The mean ± SD respiratory rate after 45 minutes are 28.45 ± 3.30 and 25.76 ± 1.82 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.371). The mean ± SD respiratory rate after 90 minutes are 19.70 ± 3.81 and 20.47 ± 2.98 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.504). The mean ± SD respiratory rate of percentage of changes that occur from base line to after 45 minutes are 17.64 ± 7.01 and 12.19 ± 7.29 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.027). In group C the mean ± SD of base line respiratory rate are 29.19 ± 3.08 and 26.05 ± 1.56 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001). The mean ± SD respiratory rate after 45 minutes are 22.29 ± 3.12 and 23.27 ± 2.39 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.250). The mean ± SD respiratory rate after 90 minutes are 17.86 ± 3.37 and 21.86 ± 4.66 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.003). The mean ± SD respiratory rate of percentage of changes that occur from base line to after 45 minutes are 23.62 ± 6.69 and 10.57 ± 8.63 in bronchial asthma and COPD respectively. This is statistically significant (p=0.001). The mean ± SD of pulse at different follow up in Bronchial asthma and COPD at different treatment is recorded in this study. In group A the mean ± SD of base line pulse are 113.50 ± 8.56 and 109.94 ± 8.31 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.245). After 45 and 90 minutes the mean ± SD of pulse in Bronchial asthma are 103.86 ± 10.21 and 94.93 ± 12.12 respectively. After 45 and 90 minutes the mean± SD of pulse in COPD are 109.44 ± 8.11 and 108.11 ± 11.26 respectively. This is statistically significant (p=0.003). The percentage of changes that occur from base line to after 45 minutes are 8.48 ± 5.99 and 0.22 ± 6.66 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001). In group B the mean ± SD of base line pulse are 115.95 ± 10.06 and 109.12 ± 9.41 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.041). The mean ± SD pulse after 45 minutes are 105.30 ± 11.41 and 105.59 ± 7.54 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.930). The mean ± SD pulse after 90 minutes are 96.20 ± 14.65 and 96.00 ± 9.30 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.962). The mean ± SD pulse of percentage of changes that occur from base line to after 45 minutes are 9.19 ± 5.91 and 3.02 ± 4.49 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001). In group C the mean ± SD of base line pulse are 120.14 ± 6.26 and 107.64 ± 7.03 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001). The mean ± SD respiratory rate after 45 minutes are 106.38 ± 7.33 and 104.77 ± 8.70 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.517). The mean ± SD

pulse after 90 minutes are 88.86 ± 8.31 and 101.27 ± 13.43 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001). The mean ± SD pulse of percentage of changes that occur from base line to after 45 minutes are 11.48 ± 3.47 and 2.71 ± 3.73 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001). Similarly Lin et al was done a study by administrating of bronchodilator by either continuous or intermittent aerosolization and heart rate were measured before and after two hours and found that an overall significant decrease in heart rate was observed, indicating the lack of significant chronotropic effects.

The mean ± SD of FEV_1 at different follow up in Bronchial asthma and COPD at different treatment. In group A the mean ± SD of base line FEV_1 are 29.09 ± 10.93 and 37.09 ± 8.11 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.024). After 45 and 90 minutes the mean ± SD of FEV_1 in Bronchial asthma are 33.09 ± 10.27 and 42.73 ± 14.47 respectively. After 45 and 90 minutes the mean± SD of FEV_1 in COPD are 39.17 ± 8.35 and 43.92 ± 13.41 respectively. This is statistically not significant (p=0.074). The percentage of changes that occur from base line to after 45 minutes are 18.05 ± 23.83 and 6.29 ± 11.52 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.075). In group B the mean ± SD of base line FEV_1 are 36.75 ± 10.49 and 40.00 ± 6.79 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.280). The mean ± SD FEV_1 after 45 minutes are 41.73 ± 11.28 and 45.32 ± 8.99 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.297). The mean ± SD FEV_1 after 90 minutes are 50.12 ± 13.25 and 53.66 ± 11.09 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.389). The mean ± SD FEV_1 of percentage of changes that occur from base line to after 45 minutes are 15.02 ± 18.58 and 13.38 ± 13.35 in Bronchial asthma and COPD respectively. This is statistically not significant (p=0.764). In group C the mean ± SD of base line FEV_1 are 56.49 ± 7.82 and 58.80 ± 11.44 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.445). The mean ± SD FEV_1 after 45 minutes are 79.34 ± 8.57 and 65.00 ± 7.63 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001). The mean ± SD FEV_1 after 90 minutes are 80.21 ± 11.64 and 70.23 ± 10.00 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.004). The mean ± SD FEV_1 of percentage of changes that occur from base line to after 45 minutes are 42.37 ± 21.49 and 13.08 ± 16.67 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001). Similar result was reported by Cox and mentioned that the overall 10% men and 11% women had an abnormally low FEV_1. Lin et al was done a study by administrating of 30 mg albuterol given over 110 minutes by either continuous or intermittent aerosolization and FEV1, forced vital capacity, heart rate, and systolic and diastolic blood pressures were measured immediately before treatment and then hourly for two hours and found that an overall significant decrease in heart rate was observed, indicating the lack of significant chronotropic effects with this dose of albuterol. Both treatments resulted in significant spirometric improvement without a significant treatment difference for the entire group. A difference was found in the relative rates of FEV1 improvement with the two treatments depending on whether patients had an initial FEV1 less than or more than 50% predicted (P =0.5). A secondary analysis on patients with an initial FEV1 less than percent predicted demonstrated a higher rate of percent predicted FEV_1 increase with the continuously nebulized albuterol group (P = 0.03).

The mean ± SD of hemoglobin oxygen saturation (SpO_2) at different follow up in Bronchial asthma and COPD at different treatment is recorded in this study. In group A the mean ± SD of base line SpO_2 are 84.00 ± 3.33 and 82.33 ± 2.28 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.103). After 45 and 90 minutes the mean ± SD of SpO_2 in Bronchial asthma are 88.57 ± 4.03 and 91.93 ± 3.27 respectively. After 45 and 90 minutes the mean± SD of SpO_2 in COPD are 84.89 ± 3.77 and 86.99 ± 4.86 respectively. This is statistically significant (p=00.014). The percentage of changes that occur from base line SpO_2 to after 45 minutes are 5.54 ± 5.38 and 3.14 ± 4.57 in Bronchial asthma and

COPD respectively. This is not statistically significant (p=0.183). In group B the mean ± SD of base line SpO_2 are 84.40 ± 3.41 and 82.12 ± 2.20 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.023). The mean ± SD SpO_2 after 45 minutes are 87.60 ± 4.04 and 85.94 ± 3.21 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.181). The mean ± SD SpO_2 after 90 minutes are 92.10 ± 3.60 and 89.88 ± 2.57 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.041). The mean ± SD SpO_2 of percentage of changes that occur from base line to after 45 minutes are 3.83 ± 3.78 and 4.72 ± 4.59 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.524). In group C the mean ± SD of base line SpO_2 are 84.19 ± 3.12 and 83.05 ± 2.24 in Bronchial asthma and COPD respectively. This is not statistically significant (p=0.173). The mean ± SD SpO_2 after 45 minutes are 90.00 ± 2.77 and 86.41 ± 3.25 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001). The mean ± SD SpO_2 after 90 minutes are 93.67 ± 2.76 and 87.95 ± 5.49 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001). The mean ± SD SpO_2 of percentage of changes that occur from base line to after 45 minutes are 6.94 ± 2.29 and 4.03 ± 1.77 in Bronchial asthma and COPD respectively. This is statistically significant (p=0.001). Similarly a study was done by Schuh et al [26] with nebulized ipratropium bromide combined with another bronchodilator for asthma. Both therapies resulted in clinically significant improvement.

In another study Raimondi et al [27] reported the response to inhaled albuterol (salbutamol) in 27 adult asthmatics presenting to the emergency department (ED) with an FEV1 <30% predicted. Subjects were treated with one of the following regimens (nine subjects in each group): group A, mean (SD) baseline FEV1 of 0.7 (0.2) L, received albuterol solution, 5 mg, via a nebulizer impelled with oxygen (O2) at 8 L/min; group B, baseline FEV1 of 0.6 (0.15) L, received albuterol, 400 microg, via a CFCMDI attached to a 145-mL valved aerosol holding chamber; and group C, baseline FEV1 of 0.6 (0.17) L, received albuterol , 400 microg. Clinical parameters and FEV1 were recorded on ED admission and 15 min after each dose of albuterol. At the time of ED admission, all patients also received continuous O2 and one dose of I.V. steroids (dexamethasone, 8 mg). FEV1 improved significantly in all patients after the 6 h of treatment. The 6-h area under the curve FEV1 improved similarly with the three delivery methods despite differences in the total dose administered. These data support the view that the three delivery methods appear adequate to treat subjects with acute severe asthma. In another study Lanes et al [27] was performed a study to assess the effect on FEV1 and clinical outcomes of adding ipratropium bromide to salbutamol in the treatment of acute asthma. Patients were randomized to treatment with a combination of nebulized 2.5 mg salbutamol plus 0.5 mg ipratropium bromide, or 2.5 mg salbutamol alone. In the study it was found that treatment groups were comparable at baseline. Comparison of overall improvement in FEV1 at 45 min indicated a better response for patients receiving combination therapy (mean difference=43 mL, 95% confidence interval [CI]=-20, 107). The distribution of change in FEV1 was skewed by a small number of patients with extreme values (38 of 1,064=3.6%) that may have been due to unreliable lung function testing. Removing these outliers produced a larger and more precise estimate of effect (mean difference=55 mL, 95% CI=2,107). Because the distribution was skewed, we performed nonparametric analyses that showed evidence of a beneficial effect of combination therapy. The difference between median values at 45 min is 40 mL (Wilcoxon p value=0.03). In addition, 4.9% (95% CI=-1%, 11%) more patients in the combination group achieved at least 20% of their potential improvement, as measured by the difference between their baseline FEV1 and their predicted FEV1. Patients receiving combination therapy had lower risk for each of three clinical outcomes: the need for additional treatment (relative risk [RR]=0.92, 95% CI=0.84, 1.0), risk of asthma exacerbation (RR=0.84, 95% CI=0.67, 1.04), and risk of hospitalization (RR=0.80, 95% CI=0.61, 1.06). Adding ipratropium bromide to salbutamol in the treatment of acute asthma produces a small improvement in lung function, and reduces the risk of the need for additional

treatment, subsequent asthma exacerbations, and hospitalizations. These apparent benefits of adding ipratropium bromide were independent of the amount of beta-agonist that had been used earlier in asthma and possibly related to a recent upper respiratory tract infection. Confirmatory studies are needed, especially for clinical outcomes.

Karpel et al [28] done a similar study to evaluate the role of inhaled ipratropium bromide in acute asthma, a double-blind study of 384 emergency department patients compared the effect of the combination of ipratropium and albuterol with that of albuterol alone. Patients were randomized to receive nebulizer treatments with either 2.5 mg of albuterol or 2.5 mg of albuterol mixed with 0.5 mg of ipratropium bromide at entry and at 45 min. Spirometry, vital signs, and oxygen saturation were measured before and at 45 and 90 min following the nebulizer treatments.

Karpel et al[28] evaluated a study to determine the optimal treatment interval for administering albuterol metered-dose inhaler (MDI) with a holding chamber to patients presenting to the emergency department (ED) with acute asthma. It was a prospective, randomized, double-blind study. EDs of two affiliated teaching hospitals in the Bronx, NY. One hundred adult patients with acute asthma and FEV1 <60% predicted of normal. At entry (T=0 min), eligible patients all openly received inhaled albuterol (six puffs) via MDI with a spacer. Subsequently, in a double-blind fashion, they received six puffs of albuterol or placebo with new MDIs and spacers at 30, 60, and 90 min such that group 1 (n=34) received albuterol every 30 min, group 2 (n=33) every 60 min, and group 3 (n=33) at 120 min only. FEV1 and vital signs were measured at T=0 and at 15, 30, 60, 90, and 120 min following initial treatment. Potassium levels were measured at T=0 and 120 min.

Garrett reported that routine addition of ipratropium bromide to â-agonist therapy in acute asthma has definite benefit. This study was carried out to evaluate: (1) whether nebulized ipratropium (0.5 mg) plus salbutamol (2.5 mg) (Combivent) confers additional bronchodilation over nebulized salbutamol (2.5 mg) alone in patients with acute asthma and (2) whether adjustment for prognostic indicators of outcome influences any benefit seen with ipratropium. A double-blind, two-center, randomized, single-dose study was performed in 338 patients with asthma, aged 18 to 55 years, who attended the emergency department for treatment of acute asthma. The primary end point was FEV_1 at 90 minutes. The mean absolute difference in FEV_1 at 90 minutes for Combivent compared with salbutamol was 113 ml (SEM ± 48 ml, $p < 0.05$). Independent of the study drug received, a poor response to treatment was predicted by frequent use of inhaled â-agonist before presentation ($p < 0.0001$), severity of the attack ($p < 0.05$), and longer duration of attack ($p < 0.05$). Subjects who had taken more than 10 puffs of inhaled â-agonist through a metered-dose inhaler or who had serum salbutamol levels of greater than 2 mmol/L on presentation demonstrated no benefit from the addition of ipratropium. Patients with an FEV_1 less than 1 L on presentation also responded less well to Combivent, which was explained by the association between severity of attack and greater use of inhaled â-agonist therapy. The study concluded that a single dose of nebulized Combivent confers additional bronchodilation over salbutamol alone ($p < 0.05$) in acute asthma.

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ORIGINAL ARTICLE

Waist-hip Ratio Correlation in Patients with Coronary Disease

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Abstract:

Cardiovascular disease is the commonest cause of death in industrialized countries. In developed world, coronary heart disease accounts for at least one in every five deaths.

Many of these deaths are potentially preventable if we can systematically address known cardiovascular risk factors in populations and in individuals. While some risk factors for cardiovascular disease (such as age, sex and genetic background) are fixed, many others are modifiable. Of these, obesity probably ranks alongside smoking as one of the most important.

In several previous studies, it is documented that obesity is an important risk factor for coronary heart disease either directly or indirectly through intervening risk factors such as hypertension, dyslipidemia and diabetes mellitus.

Body fat distribution can be measured by waist to hip circumference ratio, waist circumference, body mass index, imaging technique such as ultrasound, computed tomography or magnetic resonance imaging.

In Bangladeshi populations, there is no available study about the correlations of these parameters.

In this cross-sectional study a total of 260 samples were taken who underwent coronary angiogram. Ranges of age were 19 to 71 years of which 238 were male and 22 were female. Out of these samples normal coronary arteries - 63, minor CAD - 18, SVD - 64, DVD - 56 and TVD - 58.

Study was performed in Department of Cardiology, BSMMU and Department of Cardiology, CMH, Dhaka. Coronary angiogram and measurement of height, weight, waist circumference and hip circumference were taken in the entire sample excluding patients with hypertrophic cardiomyopathy, valvular heart disease, congenital heart disease, dilated cardiomyopathy and patients with other systemic diseases. Clinical presentations, coronary risk factors and cardiac investigations were noted. In total study, male samples were mainly analyzed. Here numbers of female samples were small for statistical analysis.

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Waist-hip ratio (WHR) with Angiographic features and coronary risk factors were studied among 207 samples of which 22 were in safe group and 185 were non-safe group. In this parameter we got a significant correlation both with Angiographic features and coronary risk factors.

But in the case of waist circumference, we got no significant correlation. Here out of 235 samples, 164 were less circumference group and 74 were more circumference group.

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Introduction:

Cardiovascular disease (CVD) is the commonest cause of death in industrialized countries. In the developed world, for example, coronary heart disease (CHD) accounts for at least one in every five deaths - 2.4 million people each year.

Many of these deaths are potentially preventable if we can systematically address known cardiovascular risk factors, in populations and in individuals. While some risk factors for cardiovascular disease (such as age, sex and genetic background) are fixed, many other are modifiable. Of these, obesity probably ranks alongside smoking as one of the most important. There is compelling evidence that obesity is both an independent risk factor for CVD, and a major contributor - possibly a driving mechanism - behind other risk factors such as hypertension.

Epidemiological studies have shown a strong relationship between obesity and CVD, and between obesity and specific cardiovascular risk factors such as hypertension and hyperlipidaemia.

Many epidemiological studies have attempted to clarify the relationship between obesity and CVD. The simplest form of study is univariate - that is when obesity is considered in isolation, as it had no connection with other cardiovascular risk factors. Such analyses have consistently shown a strong correlation between obesity and CVD.

For example, the univariate analysis included in the Framingham Study found that the incidence of CVD increased steadily with relative weight in both men and women.[1]

However as far as obesity is concerned, univariate analysis does not represent the real-life situation, as obesity is itself a risk factor for other cardiovascular risk factors such as hypertension, and hyperlipidaemia. Multivariate analyses have therefore been conducted to determine whether obesity is an independent risk factor for CVD. The multivariate analysis included in the Framingham Study found obesity was a significant independent predictor of CVD in both men and women.[1]

Body fat distribution can be measured by body mass index, waist circumference, waist to hip circumference ratios, imaging technique such as ultrasound, computer tomography (CT scan) or magnetic resonance imaging (MRI).

Waist circumference measures the fat content in the abdomen, which is considered to be an independent predictor of risks associated with obesity.

Waist hip ratio is an indicator of abdominal fat. Excess fat in the abdomen carries increased health as compared to fat carries elsewhere in the body.

Materials and Methods:

This was a cross-sectional prospective study and was carried out in the department of cardiology, BSMMU, Dhaka and Combined Military Hospital, Dhaka Cantonment, Dhaka during the period of March, 2002 to December, 2002.

Inclusion Criteria: -

- All patients clinically diagnosed or documented to have CAD who required coronary angiogram (CAG).
- Both male and female.

Exclusion Criteria: -

- Samples had ishcaemic heart disease but need not required CAG.
- Valvular heart disease.
- Congenital heart disease.
- Dilated cardiomyopathy.
- Hypertrophic cardiomyopathy.

Criteria for CAD and coronary arteriography:

i) Chronic stable angina pectoris with positive ETT (with or without previous myocardial infarction).

ii) Unstable angina pectoris.

iii) Atypical chest pain with positive ETT,

iv) After acute myocardial infarction (with or without persistent angina),

v) Asymptomatic patients with non-invasive evidence of myocardial ischemia.

Methods:

A. Informed consent was being taken from all patients.

B. Measurement of waist circumference: Accurate measurement was taken by standing up of the sample with fit together and arms at the side. Abdomen was relaxed. A tape was placed around the waist midway between the bottom of the rib and the top of the hip bone. Tape should not be tight and measurement should not be top of the clothes.

C. Hip circumference was determined by standing up straight but relaxed arm at the sides. For men, measurement should be done at the tip off the hip bone for men and at the widest point between the hips and buttocks for women.

D. For lower segment, upper segment measurement was taken by sitting the patient in a chair and it was subtracted from total height.

E. All information regarding history and physical findings and other risk factors for CAD was collected to fill the performed questionnaire.

F. Coronary arteriography and where needed left ventriculography were done in all patients by standard Judking's technique through femoral approach by modified Seldinger technique using non-ionic dye. Multi-angled standard views including antero-posterior (AP), left anterior-oblique (LAO), LAO cranial, LAO caudal (spider) and straight left lateral for left coronary system; and right anterior oblique (RAO),LAO, RAO cranial and LAO cranial for right coronary artery were recorded for analysis; and severity and extent of arterial disease were measured by eye estimation. Prerequisites for CAG were followed according to the hospital protocol.

After processing of all available information, statistical analysis of their significance was done. Body mass index, waist-hip ratio and waist circumference were classified according to the WHO parameters for Asians. Height samples were classified in three equal groups from lower height to higher height. Lower segment were classified in three groups by using standard deviation.

All the analysis was performed using the Statistical Package for the Social Sciences (SPSS) software. Pearson correlation coefficients were calculated between variables and cardiac parameters.

Observations and Results

The prospective study was carried out in the department of cardiology, Bangabandhu Sheikh Mujib Medical University (BSMMU) and Combined Military Hospital (CMH), Dhaka during the period of March to December, 2002.

A total number of 260 samples that underwent coronary angiogram were included in this study of which 238 (91.5%) were male, 22 (8.5%) were female. Age range of male patients was 19 to70 years and means -47.94 years and female patients were 32 to 71 years and mean -47.22 years. Body mass index of male samples were 15.58 to 33.2 and mean -23.26 kg/m square and for female samples 18 to 34.72 and mean -24 kg/m square. Waist hip ratio of male samples were 0.72 to 1.33, mean -0.83 and for female were 0.82

to 1.09, mean -0,77. Waist circumference of male samples were 66 to 124, mean -88.88 cm and for female 71 to 110, mean -86.37 cm. Height of the male samples were 107 to 181, mean -167.17 cm and for female samples 146 to 171, mean -157.59 cm. Lower segment of male samples were 69 to 96, mean -82.52 cm and for female 64 to 84, mean -77.29 cm. These are shown in the following table I and figure 1.

Total features of all the patients:

Table-I

Total features of the entire patient

No. Of Patient	Male 238		Female 22	
	Range	Mean	Range	Mean
Age (years)	19—70	47.94	32-71	47.22
BMI (kg/m2)	15.58-33.2	23.26	18-34.72	24.00
Waist Hip Ratio	0.72-1.33	0.83	0.82-1.09	0.77
Waist circumference (cm)	66-124	88.88	71-110	86.37
Height (cm)	181-107	167.17	171-146	157.59
Lower Segment (cm)	69-96	82.52	64-84	77.29

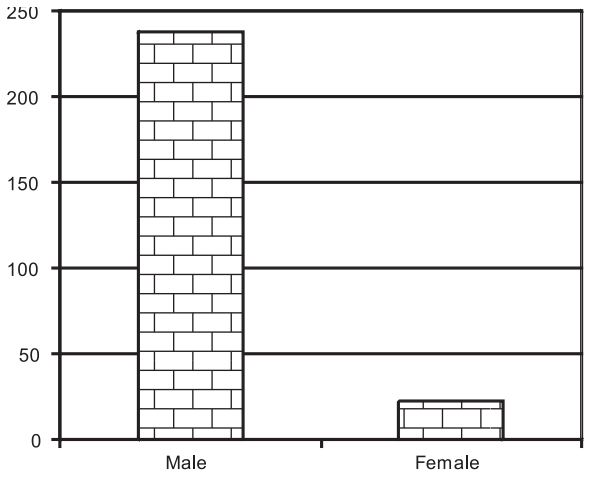

Fig.-1: *Sex distribution of the patients according to percentage, male-91.5%, female-8.5%.*

Total Angiographic features of all the patients:

Out of 259 samples, normal was 63 of which male 50 & female 13, minor coronary artery disease (minor CAD) 18 of which male 15 & female 3, single vessel disease (SVD) 64 of which male 63 & female 1, double vessel disease (DVD) 56 of which male 53 & female 3 and triple vessel disease (TVD) 58 of which male 56 & female 2 and 1 is missing data. These are shown in table II & figure 2.

Angiographic diagnosis of male and female samples:

Table-II

Angiographic features of male and female sample

		Angiographic Diagnosis					Total
		Normal	Minor CAD	SVD	DVD	TVD	
Sex	Female	13	3	1	3	2	22
	Male	50	15	63	53	56	237
Total		63	18	64	56	58	259

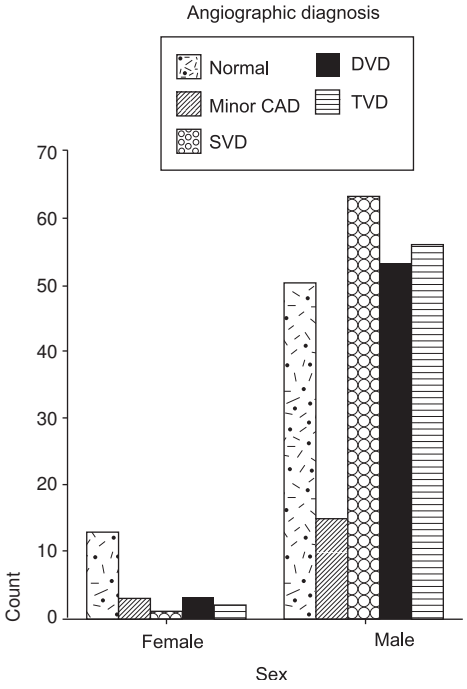

Fig.-2: *Angiographic features of male & female samples.*

Total occlusion:

Out of 259 samples, 63 samples have total occlusion. The number of total occlusion was 10 (15.9%) in single vessel disease, 24 (38.1%) in double vessels disease and 29 (46.0%) in triple vessels disease. Rest of the angiographic feature, total occlusion was absent. These are shown in table III.

Total Occlusion Angiographic features Cross tabulation

Table-III

Relation of Angiographic feature and total occlusion.

			Angiographic Diagnosis					Total
			Normal	Minor CAD	SVD	DVD	TVD	
Total Occlusion	Present (1)	Count			10	24	29	63
		% within Total Occlusion			15.9%	38.1%	46%	100%
	Absent (2)	Count	63	17	55	32	29	196
		% within Total Occlusion	32.1%	8.7%	28.1%	16.3%	14.8%	100%
Total		Count	63	18	64	56	58	259
		% within Total Occlusion	24.3%	6.9%	24.7%	21.7%	22.4%	100%

Waist Hip ratio (WHR):-

According to WHO figures for Asians, WHR for men ratio of <0.9 is safe and for women ratio <0.8 is safe. Out of 207 male sample – 22 (10.6%) were within safe range and 185 (89.4%) were in non-safe range. These are shown in figure 3.

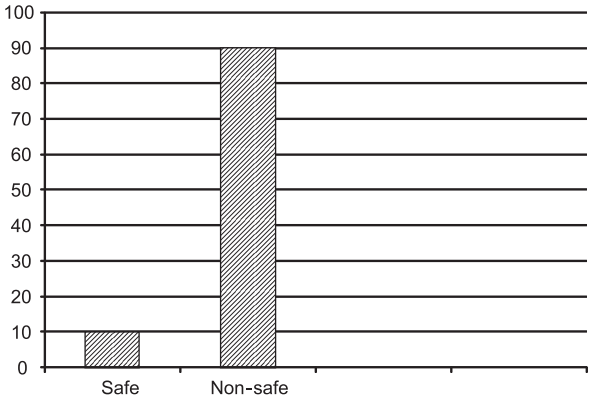

Fig.-3: *Classification of WHR in male.*

Correlation of Waist hip ratio & Angiographic Features in male samples:

In safe group, out of 22, normal was-11(50%), minor CAD-1(4.5%), SVD-6(27.3%), DVD-1(4.5%) and TVD -3 (13.6%).

In not safe group, out of 185, normal was-34(18.4%), minor CAD-11(5.4%), SVD-51(27.6%), DVD-44(23.8%) and TVD -45 (24.3%).

Here the P value was .009, so the correlation was highly significant so that in non safe group there was increased severity of CAD. Showed in table IV & Figure 4.

Correlation of waist-hip ratio and coronary risk factor in male:

Out of 72 samples, 8(11.1%), were within safe group and 64(88.9%) were within not safe group. In safe group, out of 8 smoking- 4(50%),

Classification of Waist hip ratio in male & Angiographic Features Cross tabulation:

Table-IV

Correlation of safe & not safe group of waist-hip ratio with coronary Angiographic findings in male samples.

			Angiographic Diagnosis					Total
			Normal	Minor CAD	SVD	DVD	TVD	
WHR	Safe	Count	11	1	6	1	3	22
		% within WHR	50.0%	4.5%	27.3%	4.5%	13.6%	100.0%
		% within Diagnosis	24.4%	8.3%	10.5%	2.2%	6.3%	10.6%
		% of Total	5.3%	.5%	2.9%	.5%	1.4%	10.6%
	Not safe	Count	34	11	51	44	45	185
		% within WHR	18.4%	5.9%	27.6%	23.8%	24.3%	100.0%
		% within Diagnosis	75.6%	91.7%	89.5%	97.8%	93.8%	89.4%
		% of Total	16.4%	5.3%	24.6%	21.3%	21.7%	89.4%
Total		Count	45	12	57	45	48	207
		% within WHR	21.7%	5.8%	27.5%	21.7%	23.2%	100.0%
		% within Diagnosis	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
		% of Total	21.7%	5.8%	27.5%	21.7%	23.2%	100.0%

Chi-Square Tests: P value = .009

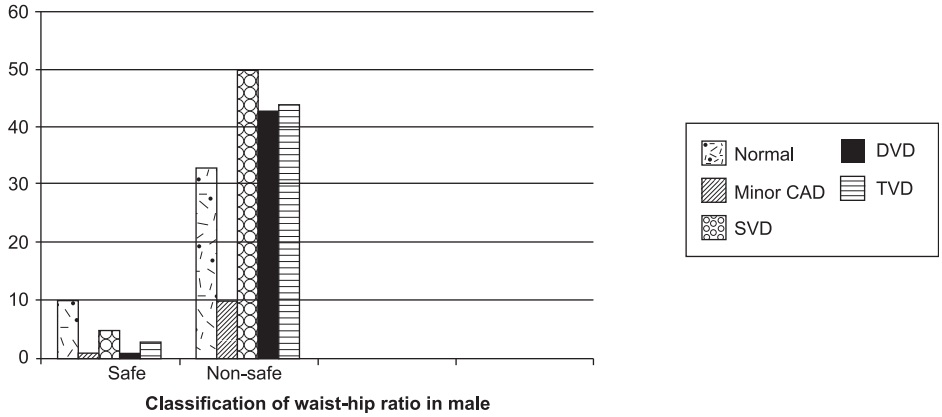

Fig.-4: *Correlation between Waist-Hip ratio and Angiographic features in male samples.*

dyslipidaemia-3(37.5%) and-1(12.5%) of family history of IHD.

In not safe group, out of 64 diabetes mellitus-6(9.4%), smoking-29(45.3), hypertension-17(26.6%) and dyslipidaemia-12(18.8%). Here the P value was .017 which was significant, so there was significant correlation between waist-hip ratio and angiographic risk factors. These are shown in table V and figure 5.

Classification of Waist hip ratio in male & coronary risk factor Cross tabulation:

Table-V

Correlation between waist-hip ratio & coronary risk factors in male samples.

			Coronary Risk Factors					
			DM	Smoking	HTN	Dyslipidemia	Family H/O IHD	Total
WHR	Safe	Count		4		3	1	8
		% within WHR		50		37.5	12.5	100
		% within Risk factor		12.1		20	100	11.1
		% of total		5.6		4.2	1.4	11.1
	Not safe	Count	6	29	17	12		64
		% within WHR	9.4	45.3	26.6	18.7		100
		% within Risk Factor	100	87.9	100	80		88.9
		% of total	8.3	40.3	23.6	16.7		88.9
Total		Count	6	33	17	15	1	72
		% within WHR	8.3	45.8	23.7	20.8	1.4	100
		% within Risk Factor	100	100	100	100	100	
		% of total	8.3	45.8	23.7	20.8	1.4	100

Chi-Square tests: P value = .017

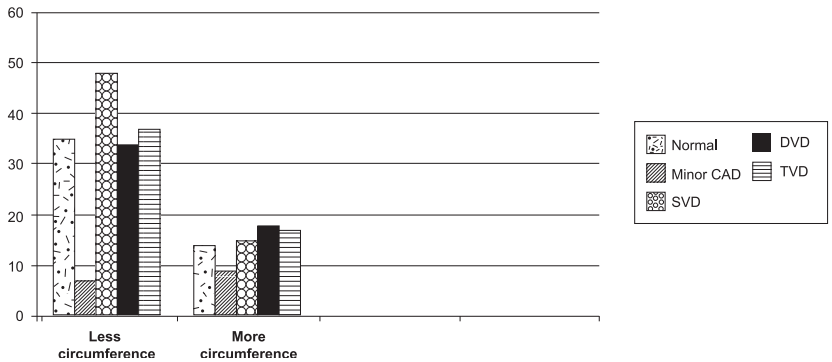

Fig.-5: *Correlation between waist-hip ratio & angiograph risk factors in male sample.*

Waist Circumference:

According to WHO figures for Asians, men with a waist circumference of >90 cm and women >80 cm are considered at risk from obesity related disease. Out of 235 male samples, 164 (69.8%) was within less waist circumference range and 71 (30.2%) was within more circumference range. In less circumference group, normal - 36 (22.0%), minor CAD - 7 (4,3%), SVD - 47 (28.7%), DVD - 35 (21.3%) and TVD - 39 (23.8%). In more circumference group, normal - 14 (19.7%), minor CAD - 8 (11.3%), SVD - 15 (21.1%), DVD - 18 (25.4%) and TVD - 16 (22.5%). Here the P value was not significant. We get no correlation between waist circumference and coronary artery disease in our study. Showed in table VI & Figures 6.

Classification of waist in Male & Angiographic Features Cross tabulation:

Table VI

Correlation between less circumferences & more circumference group of waist circumference and coronary Angiographic findings.

			Angiographic Diagnosis					Total
			Normal	Minor CAD	SVD	DVD	TVD	
Classification	Less circumference	Count	36	7	47	35	39	164
		% within Waist	22.0%	4.3%	28.7%	21.3%	23.8%	100.0%
		% within Diagnosis	72.0%	46.7%	75.8%	66.0%	70.9%	69.8%
		% of Total	15.3%	3.0%	20.0%	14.9%	16.6%	69.8%
-	More circumference	Count	14	8	15	18	16	71
		% within Waist	19.7%	11.3%	21.1%	25.4%	22.5%	100.0%
		% within Diagnosis	28.0%	53.3%	24.2%	34.0%	29.1%	30.2%
		% of Total	6.0%	3.4%	6.4%	7.7%	6.8%	30.2%
Total		Count	50	15	62	53	55	235
		% within Waist	21.3%	6.4%	26.4%	22.6%	23.4%	100.0%
		% within Diagnosis	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
		% of Total	21.3%	6.4%	26.4%	22.6%	23.4%	100.0%

Chi-Square Tests: P value = .251

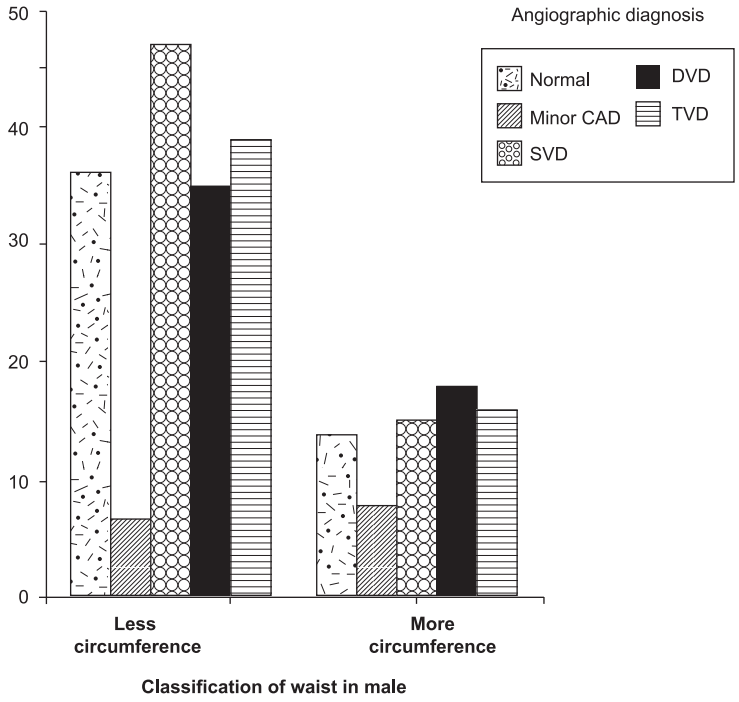

Fig.-6: *Correlation between waist circumference & Angiographic feature in male samples.*

Waist circumference & risk factor correlation:

Out of 78 male samples, less circumference - 60 (77.0%) and more circumferences - 18 (23.0%). In less circumference group of 60 diabetes mellitus - 7 (11.7%), smoking - 40 (40.0%), hypertension - 14 (23.3%), dyslipidacmia - 13 (21.7%) and family history of IHD - 2 (3.3%). In more circumference group of 18 samples smoking -10 (55.6%), hypertension - 3 (16.7%) and dyslipidaemia - 5 (27.8%). Here the P value was .409, which was not significant. So in our study there was no significant correlation between waist circumference and coronary risk factors. These are shown in Table VII & Figure 7.

Classification of waist in Male & Coronary risk factor Cross tabulation:

Table VII

Correlation between waist circumference & coronary risk factors.

			Coronary Risk Factor					
			DM	Smoking	HTN	Dyslipidemia	Family H/O IHD	Total
Classification	Less	Count	7	24	14	13	2	60
	Circumferance	% within WHR	11.7	40	23.3	21.7	3.3	100
		% within Risk factor	100	70.6	82.4	72.2	100	76.9
		% of total	9	30.8	17.9	16.7	2.6	76.9
	More	Count		10	3	5		18
	Circumferance	% within WHR		55.6	16.6	27.8		100
		% within Risk Factor		29.4	17.6	27.8		23.1
		% of total		12.8	3.8	6.5		23.1
Total		Count	7	34	17	18	2	78
		% within WHR	9	43.6	21.8	23.1	2.5	100
		% within Risk Factor	100	100	100	100	100	
		% of total	9	43.6	21.8	23.1	2.5	100

Chi-Square tests: P value = .409

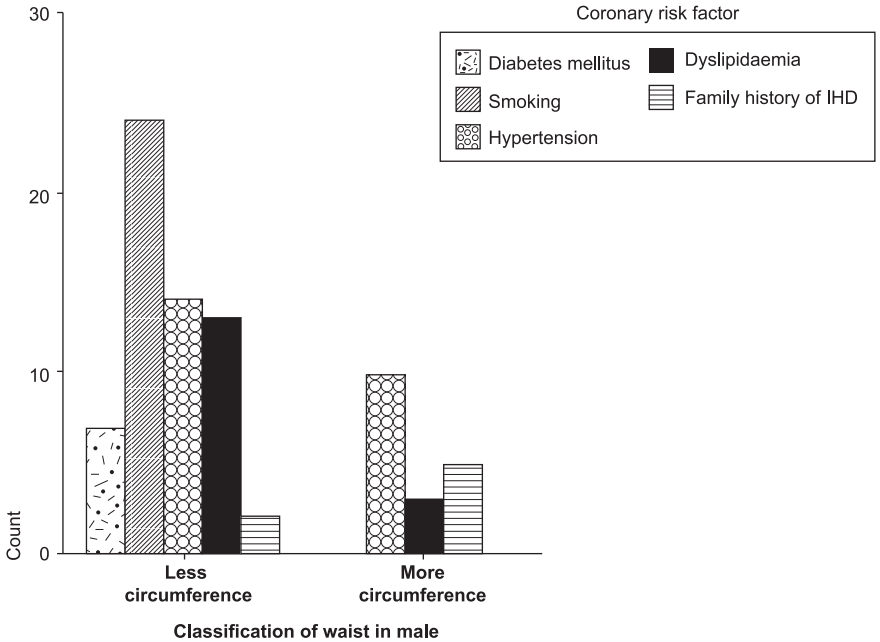

Fig.-7: *Correlation between waist circumference & coronary risk factors in male samples.*

Discussion:

South Asians have more coronary heart disease than Europeans despite apparently lower level of risk factors. Among South Asians, Indians were least and Bangladeshis most disadvantaged in a range of coronary risk factors.[2] Furthermore, in people of South Asian origin the coronary artery disease frequently occurs at an early age and that is diffuse and severe.[3] Of these, obesity probably ranks alongside smoking as one of the most important.

There is compelling evidence that obesity is both an independent risk factor for coronary artery disease and a major contributor- possibly a driving mechanism - behind the risk factor such as hypertension. Extensive prospective epidemiological research has documented that moderate to severe obesity is an important risk factor for coronary heart disease (CHD), either directly or indirectly through intervening risk factors such as hypertension, dyslipidaemia and diabetes.[4] More recently it appears that reduced muscle mass may be another pointer to ill health, which probably accounts for the value for some purposes of measuring the waist hip ratio. The hip circumference indicates mainly muscle mass, while the waist circumference is the best simple indicator of both total bodies fat and intra-abdominal fat.[5]

At present no available data demonstrate correlation of anthropometrical such measurement as obesity (BMI, waist-hip ratio, waist circumference), height, waist-height and lower segment with CAD and coronary angiographic profile in Bangladeshi population.

Currently all overweight and obese adults are considered at risk for developing co-morbidities such as hypertension, dyslipidemia, type 2 diabetes mellitus, and coronary heart disease.

In our study, out of 207 male 22 were within safe range and 185 samples were within non-safe range. Female data was only 18 and insufficient for data analysis but one thing can be mentioned that all were in safe group. In male data, out of 22 safe range patients, 11 were normal coronary arteries, 1 minor CAD, 6 SVD, 1 DVD, 3 TVD. In non-safe range out of 185 samples, 34 normal, 11 minor CAD, 51 SVD, 44 DVD and 44 TVD. Here Chi-Square tests done and P value was highly significant. Out of 72 samples that were associated with coronary risk factor in male only 8 samples were in safe group and 64 samples were in non-safe group. P value was .017, which was highly significant. So there was good correlation between waist hip ratio with coronary artery disease and coronary risk factors.

In case of the female, samples number was only 18. And all were in safe group. The number of sample was too small to get any result. Waist hip ratio is an important tool that helps determine overall health risk. People with more weight around waist are at greater risk of lifestyle related diseases such as heart disease and diabetes than with weight around hips. It is a simple and useful measure of fat distribution. The study of middle age adults showed overall that waist hip ratio and BMI were both moderately strongly associated with incident CHD in women, whereas in men, waist hip ratio showed a somewhat stronger positive association with CHD than did BMI. A useful index of body fat distribution was the ratio of waist girth to hip girth. Elevated levels of this ratio were associated with both an increased risk of diabetes[6] and hypertension.

Subsequently, others have found WHR to be associated with clinical evidence of coronary heart disease. An association has been found between WHR and myocardial infarction.[7] WHR is an important risk factor for CAD that is independent of overall obesity and to some extent independent of the amount of fat in the abdominal area. Body mass index, waist hip ratio and waist circumference all have a role in the identification of those who are obese or overweight.

Most large-scale epidemiological studies of the link between obesity and cardiovascular risk have focused on body weight or BMI. However, it is now clear that risk also varies according to the distribution of body fat. Cardiovascular risk is much higher in men or women with central adiposity (i.e. fat deposited on the trunk rather than on the hips of thigh). Prospective longitudinal studies identifying central obesity as a significant risk factor for CHD include the

Framingham Heart Study,[8] the Honolulu Heart Program,[9] The Paris Prospective Study,[10] the Study of men born in 1913,[11] and the Study of Women in Gothenburg.[12] Since waist circumference relates both to BM1 and to waist hip ratio, it has recently been proposed that simply measuring waist circumference may identify people at increased cardiovascular risk.[13]

Independent of overall obesity, a relative preponderance of abdominal fat is associated with increased risk of CHD.[11] Abdominal obesity is an independent risk factor for coronary heart disease middle-aged men and even more important than overall obesity.

The accumulation of fat in the abdominal region is a well-known independent risk factor for coronary heart disease in both men and women. Angiographic studies have revealed a positive association between clinically significant coronary narrowing and abdominal obesity in both sexes. Out of 235 male samples 164 (69.8%) is within less waist circumference range and 71 (30.2%) is within more circumference range. Out of 235 samples less circumference 164 (69.8%) and more circumferences 71 (30.2%). In less circumference group normal - 36 (22.0%), minor CAD - 7 (4.3%), SVD - 47 (28.7%), DVD - 35 (21.3%) and TVD - 39 (23.8%). In more circumference group normal - 14 (19.7%), minor CAD - 8 (11.3%), SVD - 15 (21.1%), DVD - 18 (25.4%) and TVD - 16 (22.5%). Here the P value was not significant. We got no correlation between waist circumference and coronary artery disease in our study. Out of 78 male samples, less circumference - 60 (77.0%) and more circumference - 18 (23.0%). In less circumference group of 60, diabetes mellitus - 7 (11.7%), smoking - 40 (40.0%), hypertension - 14 (23.3%), Dyslipidaemia - 13 (21.7%) and family history of IHD 2 - (3.3%). In more circumference group of 18 samples, smoking - 10 (55.6%), hypertension - 3 (16.7%) and dyslipidaemia 5 - (27.8%). Here the P value was .409, which was not significant. So it can be conclude that in our study there was no significant correlation between waist circumference and coronary risk factors. In case of the female, sample was only 22, which was insufficient for data analysis.

This study supports our earlier finding that waist circumference action levels identify people with high body mass index and central fat distribution with high sensitivity.[13] In addition the study shows the close relation between waist circumference and cardiovascular risk factors. These results suggest that action levels based on waist measurement may provide a valuable, simple method for alerting people at increased risk of cardiovascular disease who might benefit from weight management. Waist circumference has previously been related to cardiovascular risk factors.[8] In this study waist circumference correlated similarly to BMI and waist to hip ratio with most of the cardiovascular risk factors. Higgins et al reached similar conclusions in the Framingham study,[8] showing that waist circumference was associated with 24-year age adjusted mortality and also that waist circumference gave better risk prediction among smokers. Seidell reviewed anthropometrical methods to assess abdominal fat, concluding that waist circumference alone was probably the most practical measurement for use in health promotion.[5] Waist circumference relates closely to intra-abdominal fat mass[5] and changes in waist circumference reflect changes in cardiovascular risk factors.[14]

Conclusion:

In our study populations, there was significant correlation of waist-hip ratio with coronary artery disease and coronary risk factors. By simple measuring of waist and hip circumference, we can predict about coronary artery disease in our populations and simple measures like lifestyle modifications regarding dietary habit and physical activities and adequate control of other coronary risk factors may reduce the increasing incidence of coronary artery disease in our country.

There were some limitations in our study, such as less number of samples especially female samples and heterogeneous age groups.

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ORIGINAL ARTICLE

Presence of Hepatitis B Surface Antigen Among Tuberculous Patients Receiving Antitubercular Chemotherapy

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Abstract:

This cross sectional study was carried out in the Department of Transfusion medicine, National Institute of Diseases of the Chest & Hospital, Mohakhali, Dhaka, Bangladesh from July 2009 to June 2010 for a period of one year. The aim of the present study is to identify hepatitis B surface antigen among tuberculous patients receiving antitubercular chemotherapy by rapid tests.

A total number of 100 patients who were diagnosed as cases of tuberculosis between age of 5 year to 70 year of both sexes & who were admitted in NIDCH under antitubercular chemotherapy were included in this study.

Maximum age group was 21-30 years 35 (35%) followed by 10-20 years of age group 20 (20%) & 31-40 years group 16 (16%). In this study male is predominant than female which is 62 (62%) cases & 38(38%) cases respectively with a ratio of 1.63:1. Pulmonary tuberculosis was found in 96(96%) cases & extra pulmonary tuberculosis in 04 (0.4%) cases. Smear positive & smear negative tuberculosis were found in 78(78%) cases & 22 (22%) cases respectively. According to degree of anaemia maximum cases were moderately anaemic 76 (76%), followed by severely anaemic 18 (18%) & mildly anaemic 06(6%). Rifampicin was used in all 100 (100%) cases with streptomycin 35 (35%), Isoniazid (INH) 98 (98%) Pyrazinamide 92 (92%) & Ethambutal 99(99%). Nausea, vomiting & high coloured urine were complained by 94(94%) cases, 71 (71%) cases & 22 (22%) cases respectively. Most common blood group was O group which was 37 (37%) cases followed by B group & A group which were 28 (28 %) cases& 26 (26%) cases respectively. AB group was only 09 (9%) cases. Mostly were Rh positive blood group 97 (97%) & 03 (3%) were Rh negative. Among 100 cases 14 (14%) were HBsAg positive & 86 (86%) were HBsAg negative. Previous history of transfusion were present in 04 (4%) cases & were absent in 96 (96%) cases.

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Introduction:

Viral hepatitis is the commonest liver disease in Bangladesh. About one crore people in Bangladesh have been suffering from hepatitis B. A proportion of them are hepatitis B carrier & another proportion is affected by the long standing consequences of this infection. Hepatitis B & hepatitis C infection is a global health problem. HBV is 100 times more infective than human immunodeficiency virus (HIV). It can be transmitted by inoculation with contaminated blood or blood products , by sexual contact, by transplantation of organs from infected donors, by sharing contaminated needles , syringss, razors, blades, tooth brush etc & parentarally from infected mothers. There is no evidence of viral transmission through breast milk.[1] Tuberculosis is a major public health problem in Bangladesh since long. Bangladesh ranks 6th among the 22 high burden countries of tuberculosis globally. Estimates suggests that daily about 880 new TB cases & 176 TB deaths occur in the country. The annual risk of TB infection is 2·14% & proportion of adults infected with TB bacilli is 50%. TB prevalence is (all cases) is 406 per 100000 & the TB mortality is 47 deaths per 100000.[2] Tuberculosis & viral hepatitis are two of the commonest co-infections.

Hepatitis B is a major cause of chronic liver disease & a significant public health issue. Between 350 million to 400 million people worldwide are chronically infected with HBV.[3] The HBV prevalence in Bangladesh is 2.3% to 9.7% with an approximate carrier pool of 10 million.[4] These include healthy adult population 4.4%to 9.7%, healthy children 3%, school girls 2.3%, a rural community 6.4% & slum communities 3.8%. Perinatal or vertical transmission of HBV in Bangladesh is infrequent due to low HBeAg positivity rate (30.1%) among pregnant females with HBV infection.

Among the high-risk population HBV carrier rate that varies widely such as professional blood donors 19% to 29%, family members of HBsAg carrier 20.6%, health care workers 8.7%, parenteral drug abusers 6.2 to 12.0%, truck drivers 5.9%, multiple units of blood recipients13.8%. HBV is an important cause of liver disease in Bangladesh & is responsible for 19 to 35% of acute viral hepatitis, 35.7% of acute liver failure, 33.3 to 40.5% of chronic hepatitis & 46.8% of hepatocellular carcinoma.[5]

Chronic HBV infection is most commonly defined as being present when a person tests positive for HBsAg for at least 6 months.[6]

Most carrier of HBV (as many as 70%-80%) remain in the inactive carrier phase indefinitely. But all affected persons even those who remain in the inactive carrier state are at risk of developing hepatocellular carcinoma (HCC).

After acute HBV infection chronicity develops in 90% of infants infected at birth, 30% of children infected at age 1-5 years& 6% of persons infected after age 5 years. It is estimated that about 15%-20% of patients with chronic hepatitis B develop cirrhosis within 5 years[7] & only 55%-85% of those with active HBV related cirrhosis survive for more than 5 years.[8] Thus it is estimated that over 250000 patients worldwide die annually from HBV-related liver disease.[9,10]

The overall goal of tuberculosis is to reduce morbidity, mortality & transmission of tuberculosis until it is no longer a public health problem. DOTS is the most effective strategy available for controlling tuberculosis epidemic. It was found that HBsAg more frequently detected in patients with impaired cell-mediated immunity.

In this study, the objective is to identify the presence of hepatitis B surface antigen among tuberculous patients who are immuno compromised due to disease process or due to antitubercular chemotherapy. HBsAg is detected by rapid tests among tuberculous patients.

Aims & Objectives

General Objective

1.To identify presence of HBsAg among tuberculous patients who may develop chronic liver disease.

Specific Objective

1. To determine degree of anaemia among tuberculous patients.
2. To identify whether the presence of hepatitis B surface antigen is due to transfusion or due to HBV& TB co-infection.
3. To identify TB patients who may develop chronic liver disease.

Materials & Methods:

It was a cross-sectional study, carried out in the Department of Transfusion Medicine, NIDCH, Mohakhali, Dhaka, Bangladesh.

Study period-From July 2009 to June 2010 (for a period of one year)

Patients who were diagnosed as cases of tuberculosis of both sexes & who were admitted in NIDCH & were under antitubercular chemotherapy, were enrolled in this study.

A questionnaire was developed by using selected variables according to the objectives. Laboratory findings were collected from the record. 5 ml clotted blood & 3 ml of EDTA blood were taken from each patients after fulfilling data sheet.

Statistical analysis was performed by using SPSS for window version 12.0. 95% confidence limit was taken. Probability value<0.05 was considered as level of significance.

Result & Observations:

A total number of 100 patients who were diagnosed as cases of tuberculosis between age 5-70 years of both sexes & who were admitted in NIDCH under antitubercular chemotherapy were enrolled in this study.

Table-I

Distribution of study population according to age

Age(in year)	Frequency	Percent
5-10yrs	4	4.0
11-20yrs	20	20.0
21-30yrs	35	35.0
31-40yrs	16	16.0
41-50 yrs	13	13.0
51-60 yrs	11	11.0
61-70 yrs	1	1.0
Total	100	100.0
Mean + SD (Range)	31.76 + 14.39	4.6-70

Table 1 shows the distribution of study population according to age. Among 100 patients maximum are in the age group of 21-30 yrs which is 35(35%) cases followed by 11-20yr of age, 31-40 yr group,41-50-yr group&51-60 yr group which are 20(20%) cases,16(16%) cases,13(13%) cases&11(11%) cases respectively. Less than or equal to10 yrs age group & more than 60 yrs group are is only 4(4%) cases&1(1%) case.

Table-II

Distribution of the study population according to sex

Sex	Frequency	Percent
Male	62	62.0
Female	38	38.0
Total	100	100.0

Table II shows the distribution of the study population according to sex. In this study male is predominant than female which is 62 (62%) cases &38(38%) cases respectively. The male & female ratio is1.63:1.

Table-III

Distribution of study population according to the degree of anaemia

General appearance	Frequency	Hb%	Percent
Mildly anaemic	6	<10 gm/dl	6.0
Moderately anaemic	76	6-10 gm/dl	76.0
Severely anaemic	18	<6 gm/ dl	18.0
Total	100		100.0

Table IV shows the distribution of uses of antitubercular drug. Rifampicin is used in all 100(100.0%) cases. Isoniazide (INH) is taken by 98(98.0%) cases. Pyrazinamide and Ethambutal are taken by 92(92.0%) cases and 99(99.0%) cases respectively.

Table-V

Distribution of adverse effects among the study population after taking antitubercular drug.

Adverse effect	Frequency	Percent
Nausea	94	94.0
Vomiting	71	71.0
High colored urine	22	22.0

Table V shows the distribution of adverse effects among the study population. Nauses, vomiting and high colored urine are complained by 94(94.0%) cases, 71(71.0%) cases and 22(22.0%) cases respectively.

Table-VI

Distribution of HBsAg positivity among tuberculous patients

HBsAg	Frequency	Percent
Positive	14	14.0
Negative	86	86.0
Total	100	100.0

Table VI shows the distribution of HBsAg positivity .Among 100 cases HBsAg positive are 14 (14%) cases & HBsAg negative are 86 (86%) cases.

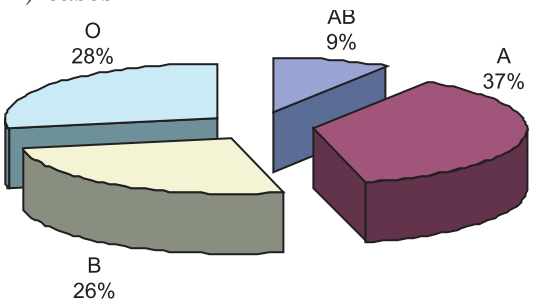

Fig.-1: *Pie chart of study population according to ABO blood grouping.*

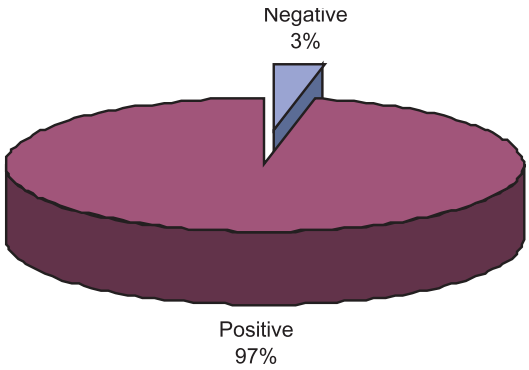

Fig.-2: *Pie chart of study population according to Rh typing of blood grouping.*

Discussion:

The diagnosis of chronic HBV infection typically based on evaluation of serological & virological markers of HBV infection in serum &biochemical and histological markers of liver disease. HBsAg is the first serological marker to appear after infection. Its persistence for >6 months indicate chronic HBV infection. High rates of hepatitis B infection in many South Asian countries are attributed to unsafe blood supply, reuse of contaminated syringe, lack of maternal screeningto prevent perinatal transmission & delay in the introduction of hepatitis B vaccine. India, Pakistan & Bangladesh have the highest rates of infection with prevalence ranging from 2% to 8% in different population group. Prevalence rate in Srilanka are under 1%.[11]

Guideline published in 2003 by American Thoracic Society recommended that tuberculosis patients with epidemiologic factors suggesting a risk for hepatitis B (e.g injection drug use), birth in Asia or Africa or HIV infection) should undergo a serological test for detection of the virus.

Drug induced hepatotoxicity during antitubercular treatment occurred more frequently in HBsAg carriers (8%) . TB treatment in HBsAg positive carriers could be performed in the usual manner, using recommended short course regime containing rifampicin , isoniazid , Ethambutal &/or Pyrazinamide under the condition that monthly liver function tests be performed.[12]

A total number of 100 cases of TB patients of age group between 5-70 years of both sexes were enrolled in this study. In this study maximum are in the age group of 21-30 yrs which is 35(35%). Musellim et al[13] reported a similar result & has shown that patients showed high prevalence of TB in the younger age group like 20-29 yrs of age.

In this study male is predominant than female which is 62 (62%) cases & 38 (38%) cases respectively. The male & female ratio is 1.63:1.A similar result was reported by Borgdorff et al[14] & mentioned that in most countries, TB is diagnosed more often in men than in women, in both routine notifications & prevalence surveys.

The distribution of study population according to blood grouping is recorded in this study. Among 100 cases the most common blood group is O group which is 37 (37%) cases followed by B group & A group which are 28 (28%) & 26 (26%) cases respectively. AB group is only 9 (9%) cases. Similar result was reported by Dean[15]and mentioned that the blood group O is common & group AB is least common.

Among 100 cases 14 (14%) cases were HBsAg positive and 86(86%) cases were HBsAg

negative. Previous history of transfusion were present in 4 (4%) cases & were absent in 96 (96%) cases.Patients who are HBsAg positive ,further follow up to identify the chronicity of HBV should be evaluated. Also this positivity of HBsAg is wheather due to transfusion or not,should be the consideration.

Conclution:

In Bangladesh ,mandatory test for HBsAg among TB patients should be done to continue treatment and patients compliance should be monitored. Awareness building campaigns against HBV infection & availability of vaccine might have contribute to lowering the rate of chronic liver disease due to HBV infection. As HBV infection among TB patients is a major problem in Bangladesh, it may cause fatal liver disease like cirrhosis or hepatocellular carcinoma.

Transmission of HBV is rare because of routine screening tests for HBsAg among donors, deferral of donors who are HBsAg positive & the use of only volunteer donors.

We therefore conclude that HBV infection is still major cause of chronic liver disease in Bangladesh & TB-HBV co-infection is common co-mobidity.

Recommendation:

1. Before starting antitubercular chemotherapy, screening test for hepatitis B surface antigen should be done to explore the cause of hepatitis-whether due to drug or carrier state.
2. To continue treatment without any default by finding the cause of hepatitis.
3. Continuous monitoring if liver function at a regular interval while HBsAg positive patients require antitubercular treatment.

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ORIGINAL ARTICLE

Effect of Bronchial Asthma on Premenstrual Syndrome

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Abstract:

Eighty-Six menstruated women of different ages, where forty three asthmatic and similar number of healthy women, responded to a questionnaire concerning the effect of bronchial asthma on the prevalence of premenstrual syndromes on their reproductive life. The mean age of the asthmatic group was 26.88 ± 5.36 years and that of the non-asthmatic control group was 27.19 ± 5.72 years. The mean duration of bronchial asthma was 13.39 ± 4.46 years. Premenstrual Syndromes almost twice less frequently happened in the Asthmatic women (30.2%) than the non-asthmatic control group (69.8%) (p=.001). Mild form of premenstrual symptoms (69.2%) predominant in asthmatic group while moderate to severe form of PMS in non-asthmatic control group (69.0%) (p=.02). Besides, both groups of respondents had poor health care seeking behavior. Thus, we conclude that bronchial asthma had negative impact on the occurrence of premenstrual syndromes.

Key word: Bronchial asthma, Premenstrual Syndrome.

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Introduction:

Premenstrual Syndrome (PMS) is defined as a cyclic disorder affecting women's physical, emotional and psychological sphere, which occurs in the luteal phase of the menstrual cycle, and does not occur in the follicular phase.[1-3] Several researches have been conducted to uncover the symptoms of PMS and the most common findings include into two different headings, like emotional symptoms (depression, angry outbursts, irritability, crying spells, anxiety, confusion, social withdrawal, poor concentration, insomnia, increased nap taking, changes in sexual desire) and physical symptoms (thirst and appetite changes, breast tenderness, bloating and weight gain, headache, swelling of the hands or feet, fatigue, abdominal pain, skin problems).[1-3] The American College of Obstetricians and Gynecologists (ACOG) defined the criteria for the diagnosis of PMS in 2000[1-3].

This Syndrome (PMS) affects millions of women during their reproductive years. It estimated that its severe from affects from 2.5 to 10% women, mild form-from 25% to even 80% and the girls suffered from it about 5.3-7.8%.[2-4]

The exact cause of PMS is still uncertain. A lots of factors are postulated to have contribution: decreased level of β-endorphins, disturbances in the pulsating release of LH and androgens,

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disturbances of the circadian melatonin rhythm, reduced serotoninergic tone, blood level of serotinin and its platelet uptake, disturbances in all allopregnanolone metabolism, decreased activity of $GABA_A$ receptors, changes in the density of α2 and β2 adrenergic receptors, or decreased kidney secretion of cAMP, PGE2 and PGF2α (1-3). Taking into account the diversity of symptoms and their changeable periodicity, PMS seems to be a result of increased sensitivity of the central nervous system to hormones controlling the menstrual cycle rather than of disturbances in heir peripheral distribution.[2-4]

Bronchial asthma, a chronic respiratory disease, itself a serious public health problem all over the world. About 300 million people, including children and adolescent, suffer from bronchial asthma. In a population of children and adolescents, bronchial asthma occurs with frequency of 5-10%.[5]

PMS has been studied and evaluated extensively in the West and only a hand amount of research studies have been conducted in Asia.[4] However, as per researcher knowledge, no research studies on Premenstrual Syndrome (PMS), especially effect of bronchial asthma on PMS, have been carried out in Bangladesh though there is a significant prevalence of bronchial asthma among the menstruated women. In order to up hold the health and well being of menstrual women who suffer from bronchial asthma, it is essential to make clear whether the bronchial asthma has any influence over the occurrence of PMS in our beloved nation.

Material and Methods:

This is a cross sectional study carried out in Maternal and Child Health Training Institute (MCHTI), Azimpur, Dhaka and Mohammadpur Fertility Services and Training Centre (MFS&TC), Mohammadpur, Dhaka during the period of August 2011 to July 2012 among 86 menstruated women. There were 43 menstruated women treated for bronchial asthma in the Outpatient Units of the two above Institutes (after diagnosed so by a pulmonologist) and a control group consisted of similar number of menstruated women (43 in number), who had no bronchial asthma or any other serious illness.

Data were collected from the study groups according to the questionnaire that was developed for study, which include social and demographic factor (age, place of residence), somatic development (body weight, height), bronchial asthma (duration, family history of bronchial asthma, allergic disease), assessment of the course of menstruation (menarche age, duration of menorrhoea, regularity of menstruation, volume of menstrual blood, pain during menstruation, use of oral contraceptives) and the occurrence and severity of Premenstrual Syndromes.[1-5]

Normal, regular menstrual cycle was defined as menstruation appearing every 28±4 days and lasting for about 5 days, with physiological loss of approximately 30-70 ml of menstrual blood. Menstruation was classified as heavy (Menorrhagia) when blood loss was 80 ml or more during a single cycle and/ or 8 or more sanitary pads or tampons were used (4). Painful menstruation (Dysmenorrhoea) was assessed based on the occurrence of strong pain localized within the lower abdomen during menstruation[4].

PMS was diagnosed as based on the criteria set by the American College of Obstetricians and Gynecologist (ACOG)- (1-4). The diagnostic criteria of PMS require that at least one symptoms should present from the list of six affective symptoms (depression, angry outburst, irritability, anxiety, confusion, social withdrawal) and four somatic symptoms (breast tenderness, abdominal bloating, headache, swelling of extremities), persisting during 5 days before menstrual bleeding and disappearing during 4 days from the beginning of menorrhea in each of the three menstrual cycles. The above symptoms should not observe in the periovulatory phase of the cycle. The above-mentioned symptoms should not be correlated with any drug, hormone therapy or alcohol consumption.

The Severity of the PMS was classified as Mild (when symptoms were present but not a problem

and did not interfere with daily functioning), Moderate (with significant discomfort) and severe (that interfere daily function, such as interpersonal relationship, daily job/day to day performance).[6]

Statistical analysis of the variables chosen in this study was carried out using SPSS with appropriate tests. A value of p<.05 was considered as statistical significant for all performed analysis.

Result:

The mean age of the respondents having bronchial asthma was 26.88 ± 5.36 years and that of the control group was 27.19±5.72 years (table-I).

The duration of bronchial asthma, in the asthmatic respondents, ranged from 4 to 23 years and the mean duration of the asthma 13.39 ± 4.46 years (table-II).

The respondents in the both groups belonged to three categories, like (i) urban, (ii) rural and (iii) slum dwellers groups. About forty four percent dwellers, among asthmatic group, came from slum area and on the other hand, about forty two percent of control group belonged to rural population. There was no significant disparity had been observed in between the both groups in relation to place of residence (p>.05)-(table-III).

Regarding somatic development, it was found that (i) the mean body weight of the asthmatic group was 48.93±7.93 kg and that of the control group was 47.51±6.69 kg and no statistical difference was observed (p>.05), (ii) On the other hand asthmatic group had mean height 150.42±3.35 cm and the mean of the height of the control group was 150.37 ± 3.26 cm. Again there was no positive difference seen among them (p>.05)-(table-#).

In the respondent with bronchial asthma, more frequent incidence of allergic diseases was noticed in comparison to the non asthmatic control group (69.8% and 37.2% respectively) and had significant difference (p<.05)-(table-III).

Use of oral contraceptive pill was slightly less in the asthmatic group than that in the control group (27.9% and 32.6% respectively) but there was no statistical difference was seen in consumption of Oral pill between the groups (p> .05)-(table-III).

Table-I

General profile of the study population

Characteristics	Groups	Mean ± SD	p value
Age of the respondents	Asthmatic group	26.88±5.36	.801
	Control group	27.19±5.72	
Body weight	Asthmatic group	48.93±7.93	.373
	Control group	47.51±669	
Height of the body	Asthmatic group	150.42±3.35	.948
	Control group	150.37±3.26	

Table-II

Duration of the asthma in the asthmatic group

Characteristics	Mean ± SD	Minimum	Maximum
Duration of asthma	13.39 ± 4.46 years	04 years	23 years

Table-III

Socio-demographic characteristics

Characteristics		Asthmatic group	Healthy group	p value
Place of residence	Urban	11 (25.6%)	9(20.9%)	.532
	Rural	13 (30.2%)	18 (41.9%)	
	Slum	19 (44.2%)	16 (37.2%)	
Presence of Allergy	Yes	30 (69.8%)	16 (37.2%)	.002
	No	13 (30.2%)	27 (62.8%)	
Use of Oral pill	Yes	12 (27.9%)	14 (32.6%)	.639
	No	31 (72.1%)	29 (67.4%)	

The study revealed that women suffering from bronchial asthma had their first menstruation by average of 5 months earlier (mean age of menarche in asthmatic group was 10.09±0.75 years) than the control group (the mean age was 10.55±0.76 years) and that was a significant difference (p<.05)-(table-IVa).

On other hand, the mean duration of the menstruation in asthmatic group was 3.79 ± 1.06 days and in control group that was 4.30±0.89 days. This finding marked a appreciable differences between the groups (p<.05)-(table-IVa).

Besides, irregular menstrual cycles were found in fifty eight percent of asthmatic women and almost twice less frequently (25.6%)in the control group (p=.002)-(table-IVb).

The respondents were categorized into three groups, namely (i) normal (ii) oligomenorrhea and (iii) polymenorhoea concerning the amount of blood loss during menstruation. In the both groups, the maximum respondents had either normal blood loss or oligomenorrhoea (table-IVb). No considerable differences was found in between subgroups concerning the amount of blood loss (p=. 394)-(table-IVb).

Further more, painful menstruation was seen about sixty percent of the respondents belonging in the asthmatic group and on the other hand, that was eighty six percent in the control group. These findings exposed a considerable distinction between the two groups in relation to painful menstruation (p=.007)-(table-IVb).

Table-IV a

Menstrual profile of the respondents

Characteristics	Groups	Mean ± SD	p value
Age of menarche	Asthmatic group	10.09±0.75	.006
	Control group	10.55±0.76	
Duration of menstruation	Asthmatic group	3.79±1.06	.017
	Control group	4.30±0.89	

Table-IV b

Menstrual profile of the respondents

Characteristics	Groups	Asthmatic group	Healthy group	p value
Regularity of the menstruation	Regular	18 (41.9%)	32 (74.4%)	.002
	Irregular	25 (58.1%)	11 (25.6%)	
Amount of blood loss	Normal	15 (34.9%)	21 (48.8%)	.394
	Oligomenorrhea	26 (60.5%)	21 (48.8%)	
	Polymenorrhea	2 (4.7%)	1 (2.3%)	
Menorrhagia	Present	26 (60.5%)	37 (86.0%	.007
	Absent	17 (39.5%)	6 (14.0%)	

According to diagnostic criteria, as defined by ACOG, the Premenstrual Syndromes (PMS) was almost twice more frequently happened in the control group than in the asthmatic group (about 69.8% and 30.2% respectively) and it had significant variation (p=.001)-(table-V).

After categorizing the Premenstrual syndromes according to its severity, the mild form of PMS was predominant in the asthmatic group (69.2% vs 31.0%). On the other hand, moderate form of PMS was found more in the control group (48.3% vs 15.4%). The severe form of the PMS was almost similar in the both groups (15.4% and 20.7% respectively)-(table-VI). It was observed that there was distinct variation between the occurrences of various forms of PMS (mild vs moderate to severe variety) among the asthmatic and non asthmatic control groups (p<.02)-(table-V).

Moreover, the study revealed that respondents of the asthmatic group used to visit more frequently to health care facilities, for the treatment of their bronchial asthma, not for premenstrual syndromes (PMS). For the purpose treatment of PMS, below 50% of the both groups reported affirmative (38.8% vs 17.2% respectively) with no distinct relationship. The women reported " no need of treatment" as a reason for not seeking health care (not shown in table). But overall health care seeking behavior was better in comparison to the control group (84.6% and 17.2% respectively) and it was statistically significant (p<.05)-(table-V).

Table-V

The profile of the Premenstrual Syndromes of study population

Characteristics	Groups	Asthmatic group	Healthy group	p value
Premenstrual Syndromes	Present	13 (30.2%)	29 (67.4%)	.001
	Absent	30 (69.8%)	14 (32.6%)	
Severity of PMS	Mild	09 (69.2%)	9 (31.0%)	.02
	Moderate to Severe	04 (30.8%)	20 (69.0%)	
Health care seeking Behavior for PMS	Present	05 (38.5%)	05 (17.2%)	.136
	Absent	08 (61.5%)	24 (82.8%)	
Overall Health Care Seeking behavior	Present	11 (84.6%)	05 (17.2%)	.000
	Absent	02 (15.4%)	24 (82.2%)	

Table-VI

Characteristics of subgroups of Premenstrual Syndromes (PMS) according to the severity

Severity of PMS	Asthmatic group	Control group
Mild	9 (69.2%)	9 (31.0%)
Moderate	02 (15.4%)	14 (48.3%)
Severe	02 (15.4%)	06 (20.7%)

Discussion:

Although a lot of factors might have influenced over the occurrence of Premenstrual Syndromes among the menstruated women, this study was conducted to evaluate only the effect of bronchial asthma on Premenstrual Syndromes (PMS).

As it was a cross sectional study, it might have inherent potential selection bias. More over, there was chance of recall bias in addition. Besides, we came across only few research activities concerning the influence of bronchia asthma over the occurrence of PMS among the menstruated women while reviewing the available literatures.

The occurrence of the Premenstrual Syndromes (PMS) had been observed significantly less in the asthmatic population. This finding has similarity with study done by Skrzypulec V et[4] al as premenstrual syndomes occured 20% of the adolescent girls. On the other hand, the findings of studies done by the Ensom et al[7] and Dorhofer and Sigmon[8] are conflicting with the present study as PMS have been shown a more prevalent in the menstruated women in those studies. How ever the current research can not directly referred to the reports of Skrzypulec V et al[4] where study population belonged to 12-19 year's old girls.

The maximum respondents of asthmatic group suffered more by mild form of Premenstrual syndromes. On the other hand, the healthy menstruated women had experienced more of the moderate to severe forms of the PMS. Besides, this findings are directly opposite to the study findings of the research done by Mirdal et al[9], Chong and Ensom[10] and Lane T et al[11] where the appearance of symptoms of PMS (mainly affective symptoms) makes the course of bronchial asthma more severe.[9] and did not confirm any any positive influence of the asthma on PMS[10] and mild form of PMS occurred only 20-30% of women[11].

Moreover, the study revealed that respondents, from the both asthmatic and non asthmatic groups, less frequently need the medical support for their problems regarding premenstrual syndromes (PMS) and no need of treatment was the most common reason for not seeking health care. These findings have similarity with the research activities done by Balasubramanian[12] and Rehman et al[13]. But the respondents of those studies seek medical help for their reproductive illness while the respondents seek that for the Premenstrual Syndromes affected by bronchial asthma in the current study.

Conclusion:

According to the findings of the present study, it is evident that bronchial asthma has somehow negative influence over the occurrence of the Premenstrual Syndromes among the menstruated women. Besides, the menstruated women were unaware about the effect of the PMS that can be reduced by medication.

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ORIGINAL ARTICLE

Endobronchial Ultrasound – An Innovation in Bronchoscopy in Bangladesh

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Abstract:

Technical development in last two decades has made it possible for pulmonologists to do endobronchial ultrasound (EBUS).[1] With EBUS mini-probe, the multilayered structure of the tracheobronchial wall can be analyzed better than any other imaging modality. Instead of fluoroscopic guided biopsy, EBUS can be used to biopsy peripheral lesions.[2] EBUS-transbronchial needle aspiration has proved valuable for sub-carinal hilar and mediastinal lymph nodes.[2] In National Institute of Diseases of the Chest & Hospital, Dhaka we have introduced EBUS for the first time in Bangladesh. So far, we have done EBUS in 20 patients and our result is very much conclusive in comparison with conventional modalities of diagnostic procedure which we used to do previously (e.g. conventional bronchoscopy, CT-Guided FNAC, etc.). Studies have shown that EBUS is cost-effective as it reduces[3] the need for more morbid and costly invasive procedure like mediastinoscopy or thoracotomy. Prospective studies are needed in Bangladesh to see how EBUS will help in populations having lymphadenopathy in Chest X-ray, where other procedure does not give conclusive diagnosis.

[Chest & Heart Journal 2012; 36(1) : 55-58]

Introduction:

Bronchoscopy has become the most commonly performed invasive procedure by pulmonologists.[1] In Bangladesh fiberoptic bronchoscopy has been performed since 1985s. Since then it has been increasingly employed in the diagnosis of variety of pulmonary diseases. Patients with mediastinal lymphadenopathy or suspected lung cancer required accurate diagnosis to determine optimal treatment.[4] For these patients, mediastinal nodal sampling is often necessary and has traditionally been performed by mediastinoscopy or anterior mediastinotomy.[5]

Real-time endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) is a new technique that combines endoscopic visualization with high frequency ultrasound imaging, which is used to obtain cytological and histological samples of lesions adjacent to the tracheobronchial tree.[4] This makes it easier to locate the lymph nodes to be sampled. As Yasufuku and colleagues[4] reported, EBUS-TBNA had a sensitivity of 94.6%, specificity of 100% and diagnostic accuracy rate of 96.3%, which seemed to be superior to those of mediastinoscopy. However, whether EBUS-TBNA can be applied as the first-line procedure for diagnosis of mediastinal lymphadenopathy is still controversial, because of its false negative rate to some extent.

Moreover, there is few studies reported comparing the relationship of diagnostic accuracy and number of passes or size of lymph nodes.

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Methods:

Patients having mediastinal lymphadenopathy or with mediastinal or hilar lesion suspected of lung cancer detected on enhanced thoracic CT were included in this study. Between June to November 2012, 15 patients in NIDCH meeting the inclusion criteria and undergone EBUS-TBNA (Table 1).

Table-I

Patient characteristics and pre-operation diagnosis

Patient characteristics	
Patients	N=20
Male	12
Female	8
Median age	52.3 yrs (25-75)
Pre-operative diagnosis	
Suspected for lung cancer	N=16
Mediastinal and hilar lymphadenopathy	N= 4

EBUS-TBNA procedure

EBUS-TBNA was performed under local anaesthesia. Patients were monitored with pulse oximetry, and blood pressure with the presence of an anesthesiologist. A flexible bronchoscope containing an ultrasound probe was inserted via the oral route to the trachea and the bronchial tree towards the appropriate area of the mediastinum. The targeted lymph nodes or masses were identified using bronchoscopic visualization and ultrasound imaging. A needle extended from the bronchoscope through the bronchial wall was used to puncture the lesion and to aspirate tissue. A lymph node or mass could be punctured three to four times to gain an adequate sample, and several lymph nodes could be punctured during the same session. The aspirates were then smeared on slides and simultaneously sent to pathology laboratory for subsequent cytology. The cytology sample was considered adequate if it contained malignant cell or a large number of lymphoid cells confirmed by the cytologist, and then the operation was terminated. The lymph nodes punctured were grouped according to the puncture site: the upper paratracheal (2R, 2L), the subcarinal station, the lower paratracheal and hilar station (4R, 4L, 10R, and 10L), the right paraesophageal (8R) and the interlobar station (11L,11R).[6]

Results:

Patient characteristics: We studied consecutively all the patients who underwent EBUS-TBNA for the evaluation of mediastinal and/or hilar lymph nodes and mediastinal/hilar lesion on an inpatient basis between June to November 2012. A total of 20 patients with a mean age of 45 years (range, 40-65) were enrolled in this study, including 12 males and 8 females (Table 1). Clinically, among these patients, all the patients were suspected for lung cancer. All patients were followed up for at least 2 months.

Operation parameters: Details of lymph node stations and masses punchured are shown in Table 3). All the lymph nodes were punctured more than once (range, 2-5). Diameter of lymph nodes ranged from 0.6 cm to 10.5 cm with a median diameter of 2.04 cm. No procedure related complications such as pneumothorax, pneumomediastinum or excessive bleeding ever occurred in this study (Table 2).

Table-II

Operational parameters

Operation Parameters	
Number of lymph nodes punchured	N=65
Mean period of each TBNA pass (min)	5.8
Mean stay length in hospital (day)	No
Complications	2

Table-III

Location of Lymph node station and number of EBUS-TBNA passes of each lymph node station

Right upper paratracheal (2R)	N=2	Left upper paratracheal (L)	N=1
Right lower paratracheal (4R)	N=12	Left lower paratracheal (4L)	N=12
Subcarnial (7)	N=18	Right paraesophageal (8R)	N=0
Right hilar (10R)	N=13	Left hilar (10L)	N=7
Right interlobar (11R)	N=0	Left interlobar (11L)	N=0
		Total	N=65

Diagnostic yield: According to the cytological results, 17 malignant tumors and 3 benign diseases were confirmed. Of these, 7 cases of adenocarcinoma, 4 cases of squamous carcinoma, 3 cases of small cell lung cancers, 3 cases of lymphoma, 2 cases of tuberculosis, one case of nonspecific infection (Table 4).

Table-IV
Final cytological results

Malignancy (N=17)	
Adenocarcinoma	N=7
Squamous carcinoma	N=4
Small cell lung cancer	N=3
Lymhoma	N=3
Benign diseases (N=3)	
Tuberculosis	N=2
Non-specific infection	N=1

Discussion:

For many years surgical biopsy - principally mediastinoscopy - has been regarded as the "standard procedure" for sampling mediastinal lymph nodes. However, mediastinoscopy can only sample nodal stations 1-4, 7 accesses to hilar nodal stations could be difficult and may require thoracoscopy and on occasion a thoracotomy.[6] Moreover, it cannot be repeatedly operated on the same patient. Contrarily, EBUS-TBNA is a simple procedure and also can be performed repeatedly. In our procedure, 65 lymph nodes of 10 stations of mediastinal and hilar nodes were punctured.

Moreover, nearly every lymph nodal group had been checked. A total number of 65 TBNA passes of lymph nodes were conducted. On the other hand, mediastinoscopy is more invasive than EBUS techniques and results in a neck scar which may be cosmetically unacceptable to some patients. Unfortunately it does have a 2% risk of morbidity and 0.08% mortality.[7] In this study, 20 patients received EBUS-TBNA. The mean period of each EBUS-TBNA was 5.8 minutes and mean stay length in hospital was 2 days, which seemed to be more minimal invasive, compared with those parameters of mediastinoscopy.

Furthermore, though viewed as the gold standard for mediastinal nodal assessment, the diagnostic sensitivity of cervical mediastinoscopy is only 78-81%, which is inferior to that of EBUS-TBNA, as reported in two recent systematic reviews.[7]

Another unsettled point is that whether EBUS-TBNA can replace mediastinoscopy as first-line procedure for diagnosis benign mediastinal diseases such as sarcoidosis, tuberculosis, etc. As Nakajima and colleagues reported in 2009, EBUS-TBNA should be added to conventional diagnostic modalities for patients with suspicious stage-I sarcoidosis on chest roentgenogram.[8]

Conclusions:

EBUS-TBNA Is an accurate and safe tool in diagnosis of mediastinal lymphadenopathy and lung cancer. Surely EBUS-TBNA cannot completely replace mediastinoscopy so far, it may indeed reduce the number of mediastinoscopy procedures. .It is cost effective and is a preferred procedure for hilar and mediastinal lymphadenopathy. In patients with positive lymph nodes suspected by enhanced thoracic CT and PET/CT, it can necessarily be the first-line procedure before mediastinoscopy.

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ORIGINAL ARTICLE

Surgical Treatment of Eventration of the Diaphragm with Inverted Plication Technique – Study of 7 Cases

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Abstract:

Eventration of diaphragm is defined as abnormal elevation of diaphragm. Failure of muscularization of developing diaphragm leads to formation of fibrous eventred diaphragm. It is rare. This prospective Observational study carried out in National Institute of Diseases of the Chest and Hospital (NIDCH) and some private centres in Dhaka during the period of January 2008 to October 2012. patients were presented with respiratory and bowel symptoms. Eventration of diaphragm diagnosed radiologically. Total 7 male patients age ranging from 2years to 35 years underwent surgical management with described inverted plication technique with excellent improvement symptomatically and radiologically. Follow up of the patients going on.

[Chest & Heart Journal 2012; 36(1) : 59-62]

Introduction:

Eventration of diaphragm is defined as abnormal elevation of hemidiaphragm. It refers to congenital form as a result of failure of muscularization of the foetal diaphragm. Acquired forms refer to elevated diaphragm due to phrenic nerve palsy. Diaphragm is derived from four embryonic precursors: the septum transversum, right and left pleuroperitoneal membranes and the dorsal mesentery of the oesophagus and body wall. Completion of early fibrous diaphragm occurs during the seventh week of gestation. Final component necessary to complete the diaphragm is the musculature, which migrates from the third, fourth and fifth cervical myotomes of the body wall. Congenital diaphragmatic defects are the result of faulty development and/or fusion of various embryonic components[1].

The leading symptom of Eventration of diaphragm are respiratory problems. Mostly dyspnoea and orthopnoea; less commonly cough, epigastric or retrosternal pain.

In most patients, elevation of the diaphragm is primarily detected on chest radiography. Further confirmation and evaluation of the underlying mechanism may be gained by CT scan. MRI rarely needed, it is useful in detecting paradoxical motion.[2]

Eventration and permanent phrenic nerve injury are the indications for diaphragmatic plication in symptomatic patients.

In general, the routine surgical procedure is plication of the diaphragm without incision of the diaphragmatic membrane.[3]

Diaphragmatic plication is intended to decrease lung compression, to make the thoracic base and

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mediastinum more stable, and to strengthen the respiratory action of the intercostal, perithoracic, and abdominal muscles.[4]

Trans Thoracic Plication can be done in various techniques. Flag plication, Accordation Plication and inverted Plication; No definite data reveal superiority among techniques. But inverted placation reveal easy, less time consuming, with less morbidity. Post operative X-ray chest show a clean diaphragmatic contour.

Video Assisted Thoracoscopic placation of diaphragm having most acceptable results.[5]

Materials and Method

Prospective Observational study carried out in National Institute of Diseases of the Chest and Hospital (NIDCH) and some private centres in Dhaka during the period of January 2008 to October 2012.

Inclusion criteria: All symptomatic patients diagnosed as diaphragmatic eventration.

Exclusion criteria: Patients having diaphragmatic pathology other than eventration

Method:

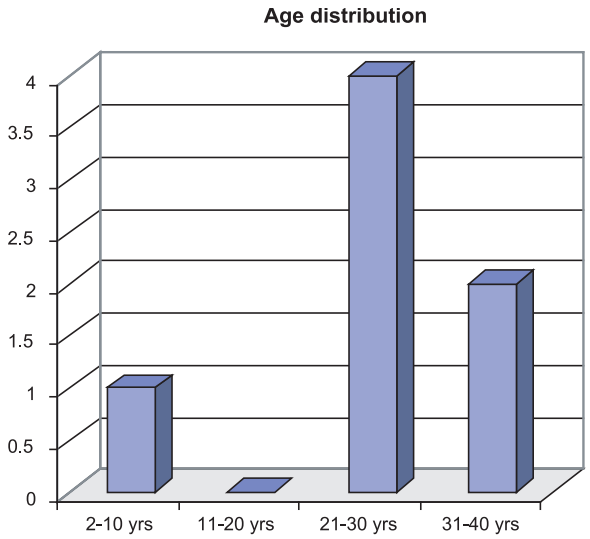
Patients evaluated from history, clinical and radiological examinations. Related haematological, biochemical, spirometric examinations and cardiac evaluation carried out. Patients subjected to operative intervention. Under General anaesthesia with one lung ventilation lateral thoracotomy done along with upper border of 8th rib ± nicking of rib. Diaphragmatic contour assessed and plication planned at assumed normal inspiratory position of diaphragm. Plication done in two layers with monofilament prolene No 0 round bodied suture material with inverted plication technique. Small aperture made at the top of the dome prior plication to prevent any collection of fluid. One water seal chest drain kept in chest cavity. Chest physiotherapy and breathing exercise advocated. Chest drain usually removed on 4th post operative day. All stitches or staples removed on 9th post operative day and patients discharged there after with advices. Routine follow up scheduled after 3 months, 6 months, 12 months.

Observation and Results:

*In this prospective observational study total 7 patients underwent operative intervention.

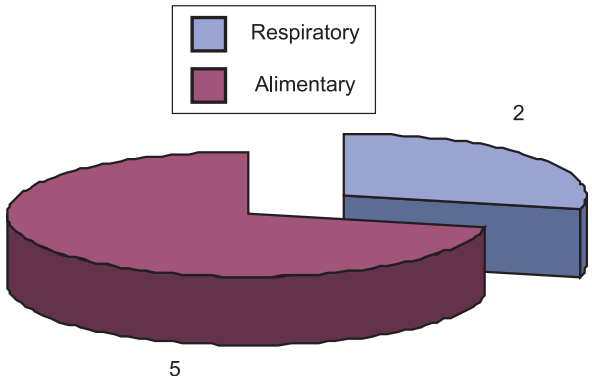
*All patients were male

*Age ranges from 2 years to 35 years.



*Left sided complete eventration.

*Presented with complaints of shortness of breath in 5 patients and bowel problem in 2 patients.



*Diagnosed with x-ray chest P/A and lateral view. CT scan of chest done in 2 patients. Barium meal X-ray of stomach with Trendelenberg position done in 2 patients.

*No other congenital anomaly detected.

*Per operative and post operative period was uneventful. No transfusion needed. Time consumed 1:30 to 2 hours. No abdominal compartment syndrome observed.

*Mild Thoracotomy pain and paresthesia was evident and treated with analgesic, gabapentin.

*Follow up going on. So far followed up excellent symptomatic and radiological improvement seen.

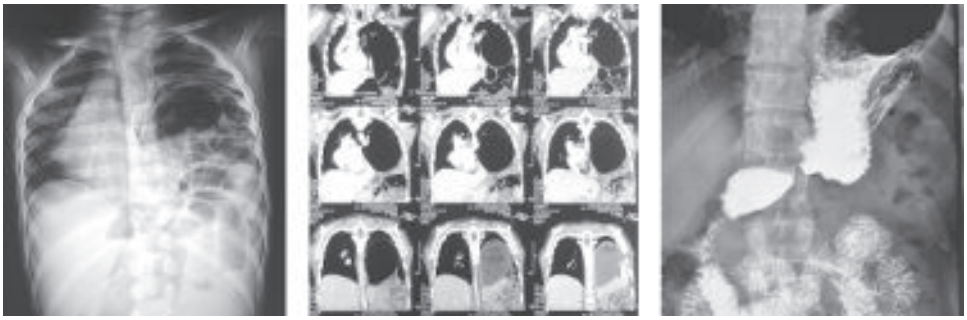


Fig.-1,2&3: *Left sided Diaphragmatic eventration evident by X-Ray Chest P/A view, CT Scan of Chest and Contrast X-Ray of Stomach.*

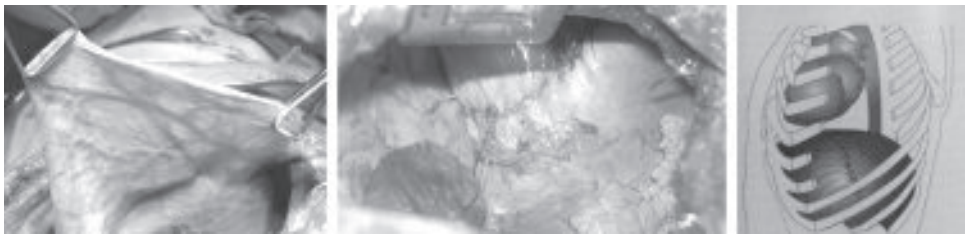


Fig.-4,5&6: *Diaphragmatic eventration. Pulled part showing fibrous diaphragm. Diaphragmatic eventration plicated with inverted plication technique.*

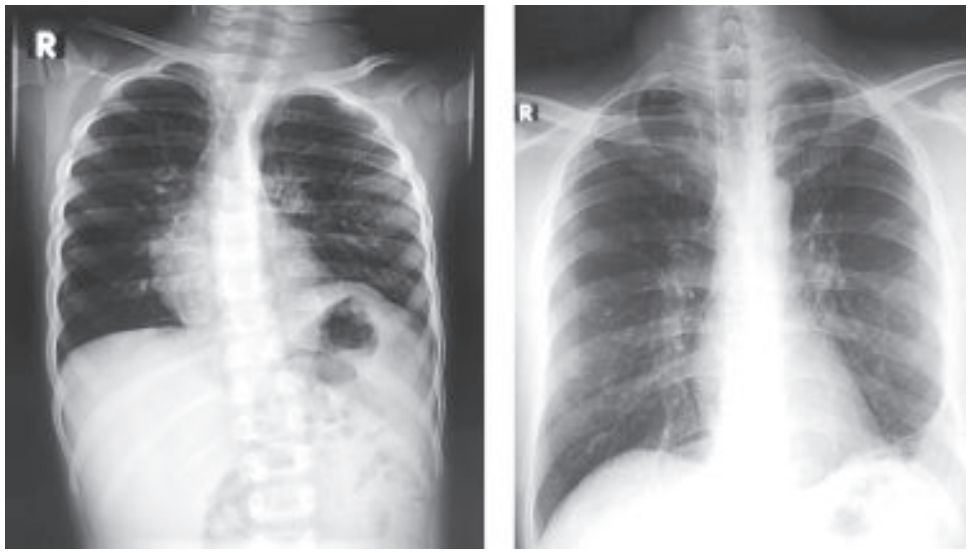


Fig.-7&8: *Post operative chest radiograph of left sided eventration of the diaphragm.*

Discussion:

Eventration is a congenital anomaly of the diaphragm characterized by muscular aplasia and subsequent abnormal elevation of an intact hemidiaphragm. Pathologically, a totally eventrated hemidiaphragm consists of a thin membranous sheath attached peripherally to normal muscle at points of origin from the rib cage. Eventration of the diaphragm is known to cause severe respiratory distress in infants and children. When seen in adults, it is more common in males and the left dome of the diaphragm is most frequently affected.[6] Complete eventration almost invariably occurs on the left side and is

rare on the right.[7] In this series all seven cases were left sided eventration. Symptoms may be present in obese patients as a result of raised intra-abdominal pressure. These symptoms, related to gastrointestinal tract, respiratory embarrassment, and rarely cardiac dysfunction, have been attributed to the anomaly.[8] Tsugawa and co workers, found 4 patients asymptomatic, 17 patients with respiratory and 3 patients having GI symptoms.[9] In this series patients having respiratory and abdominal symptoms.

Wood classically credited with idea of wrinkling the diaphragm in order to reduce the diaphragmatic cupola.[10]

Video-assisted thoracoscopic repair of eventration of the diaphragm in 3 adults was described by Mouroux and colleagues[5] in 1996, using two superimposed transverse back-and-forth continuous sutures. The diaphragm was invaginated before suturing, the first suture line held the diaphragm down and retained the excess within the abdomen, the second suture line placed the desired tension on the diaphragmatic dome. In this series we have done same procedure, opening left thorax, invaginating the diaphragm within abdomen.

Graham and coworkers [11] described that all of their patients showed both subjective and objective improvement, and the effect of initial improvement continued for 5 or more years after placation. In Our series patients recovered well with very little morbidity.

Conclusion:

Eventration of diaphragm is a rare congenital defect. Occurs mostly on the left side. Presentation varies from respiratory distress to abdominal discomfort. It can be diagnosed by X-Ray chest, Fluroscopy, CT scan, some times with MRI. Symptomatic patients need surgery. Plication is the choice of treatment. Flag Plication, Accordation Plication, Inverted Plication all bear good result. Inverted Plication is safe, easy, with less morbidity, less time consuming, can be done by thoracotomy or by thoracoscopy.

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REVIEW ARTICLE

Quest for HIV/AIDS Vaccine: A Global Requirement

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Abstract:

Luc Montagnier and Francoise Barre-Sinoussi shared the 2008 Nobel Prize in Medicine for their discovery of the human immunodeficiency virus (HIV), the causative agent for acquired immunodeficiency syndrome (AIDS). More than 27 years into the HIV/AIDS epidemic, still there is no end in sight to this serious pandemic. The number of new cases of HIV/AIDS continues to climb, particularly in the less developed world. Although short term preventive measures are important, availability of vaccines is more important and crucial if the spread of HIV/AIDS is to be effectively contained and finally eradicated. Since the principle of vaccination was established by Edward Jenner in 1876, many vaccines have been developed and are successfully in use all over the world. Why does an effective HIV/AIDS vaccine remain elusive then? Why such an important task is taking so long? In this review article attempts were made to give a short account about the current status in the quest for HIV/AIDS vaccine.

[Chest & Heart Journal 2012; 36(1) : 63-69]

Introduction:

We were inspired to write this article after learning that Luc Montagnier and Francoise Barie-Sinoussi conferred with the 2008 Nobel Prize in Medicine for their discovery of the human immunodeficiency virus (HIV), the causative agent for acquired immunodeficiency syndrome (AIDS). HIV/AIDS is the most serious pandemic of the world at present.[1,2,3] More than 27 years into the HIV/AIDS epidemic, there is still no end in sight to this dreadful disease. The number of new cases of HIV/AIDS continue to climb, particularly in the less developed world. A two-pronged approach is needed to deal with the devastation being caused all over the world by HIV/AIDS: (i) Short-term preventive strategy stopping further spread of the virus, treating individuals who are infected and mitigating the societal consequences; (ii) long-term preventive strategy – including creating the tools needed to end the epidemic entirely: female-controlled barrier methods and microbicides, diagnostics to improve treatment and control of sexually transmitted diseases and HIV/AIDS vaccines.

Although Bangladesh is a low prevalence country, it has no reason to be complacent and factors around us pose great danger altogether about possible increased cases of HIV/AIDS. A preventive vaccine is the most important way we would be able to contain and finally eradicate the epidemic of HIV/AIDS from this planet. Since the principle of vaccination was established by Edward Jenner in 1876 in England, many successful vaccines have been development and are in use all over the world.[3,4] The vital question then arises: Why does an effective HIV/AIDS vaccine remain elusive? Why such an important task is taking so long? In attempting to answer these questions one must know about the HIV, HIV/AIDS and their epidemiology. The objectives

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of this write up were to (i) highlight these points in brief and (ii) give a short account of present status in the quest for HIV/AIDS vaccine.

HIV/AIDS: History, Definition & Diagnosis

In 1981, the first cases of a new disease syn-drome were recognized by Center for Disease Control (CDC), Atlanta, USA. The victims of this new disease died of a variety of rare infections and malignancies, among them a pneumonia caused by the protozoan "Pneumocystis carini" and a cancer of the skin, Kaposi's sarcoma. They also suffered from other opportunistic infections caused by microorganisms that are ubiquitous but ordinar-ily not able to cause diseases. This new disease, as it ap-peared, killed the victims by destroying their immune sys-tem. All these patients were previously healthy and had no known underlying cause of immunodeficiency. Hence, this new disease syndrome was named as acquired im-munodeficiency syndrome (AIDS).[5,6] Subsequently, cases of AIDS have been reported from Europe, Africa and many other parts of the world including India, Pakistan and Bangladesh. Depending on the se-verity and patterns of the disease, AIDS is classified into various chronological stages as shown in Figure-1.[5,6]

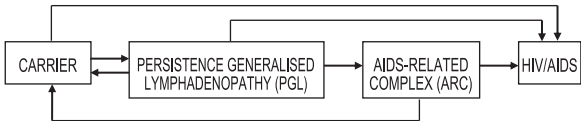

Fig.-1: *Stages of HIV/AIDS.*

In 1983, Ro-bert Gallo's group at the National Institute of Health (NIH), Bethesda, USA isolated a retrovirus from patients with AIDS and PGL which was characterised as human T-cell lymphothropic virus (HTLV).[7] Two retroviruses HTLV-I and HTLV-II, were already linked with acute and chronic T-cell leukemia of adults and termed as human T-cell leukemia viruses. The causal agent of AIDS isolated and characterised by Gallo et al was morphologically and genetically dissimilar to HTVL-I and HTLV-II and so they named it as HTLV-III.[7] At about the same time Luc Montagnier's group at the Institute of Pasteur, Paris, France isolat-ed a new retrovirus from a patient with PGL and named this agent as lymphadenopathy associated virus (LAV).[8] Both Gallo et al and Montagnier et al were reluc-tant to have the name of this virus changed from HTLV-III and LAV. Therefore, the subcommittee empowered by the International Committee on the Taxonomy of Viruses pro-posed in 1986 that the AIDS retrovirus be officially called as the human immunodeficiency virus type 1 (HIV1).[9]

Table-I

The disease and laboratory tests included in the CDC definition of AIDS/ARC/PGL/HIV1 carrier[5,6]

A. Diseases Included In The Definition Of AIDS
a. Opportunistic infections with laboratory confirmation
(i) Protozoal and Helminthic g Isosporiasis (Chronic diarrhoea), toxoplasmosis (pneumonia or cerebral), cryptosporiodiosis (intesti-nal), strongyloidosis (systemic)
(ii) Fungal g Pneumocystic pneumonia, Candidiasis (oesophageal, bronchial or pulmonary), Histoplasmosis (disseminated)
(iii) Bacterial g Atypical mycobacteria (disseminated)
(iv) Viral g Cytomegalovirus (Pulmonary, gastrointestinal or central nervous system), Herpes simplex virus (mucocutaneous with ulcers for more than one month), Progressive multifocal leucoencephalopathy.
b. Malignancies (Histologically confirmed) Kaposi's sarcoma, B-cell lymphoma, cerebral lymphoma, High-grade non-Hodgkin's lymphoma of unknown immunological phenotype

table continued

B. Sings and Symptoms Included In The Definition of AIDS-Related Complex (ARC)Pyrexia of unknown origin for two months or more: Chronic di-arrhoea; Weight loss (10% of body weight), Malaise and lethargy, Persistent generalised lymphadenopathy, Hepato-splenomegaly, Hairy leukoplakia, Minor oral infections (e.g. Oral candidiasis, herpes zoster).

C. Persistent Generalized Lymphadenopathy (PGL)Unexplained lymphadenopathy in at least two extra-inguinal sites for more than three months; The lymphadenopathy may persist un-changed for years and the patient with PGL are generally well; Nearly all patients will have HIV1 antibody; Occasionally seroconversion takes place within two years of the development of PGL.

D. Disease Which May Be More Prevalent In HIV1- Carrier Skin diseases (Seborrhoeic dermatitis, Folliculitis, Acne vulgaris, Xeroderma, Fungal infections, Herpes simplex, lmpetigo); Malig-nancies (Hodgkin's lymphoma, Anorectal carcinomas); Pneumonia (Pneumococcal, Staphylococcal, Tubercular).

E. The Laboratory Tests Included in The Definition of AIDS/ ARC/ PGL/HIV1-Carrier Isolation of HIV1 by culture; Detection of HIV1 antibody by ELISA-screening test and confirmed by western blot technique; Lymphopenia; Leukopenia; Anaemia, Thrombocytopenia, Raised erythrocyte sedimentation rate; Raised serum cholesterol; Raised immunoglobulins; Low CD4: CD8 cell ratio; CD4+ cell count < 200/ìl of blood.

According to centre for disease control (CDC), USA, the criteria for diagnosis of HIV/AIDS are that the patients (a) must have two or more of the diseases indicative of cellular immunodefi-ciency, (b) has no known underlying cause of cellular immunodeficiency, nor any other cause of reduced resis-tance, which might predispose to the disease or diseases, (c) must be positive for two or more laboratory indicators of immunodeficiency including HIV1 isolation or HIV1 anti-body positive plus CD4+ T-cell count <200/µl (Table-1); the sera which are positive for HIV1 anti-body by enzyme-linked immunosorbent assay (ELISA) must be confirmed by western blot tech-nique. The diagnosis of AIDS in a patient is excluded if all the laboratory indicators of immunodeficiency and HIV1 infection are negative.[5-7] The isolation of the virus by culture is tedious, time consuming and expensive. On the contrary rapid, sensi-tive, specific and reliable laboratory tests for the detection of HIV1 antibody are available and most widely used for diagnos-ing exposure to HIV1. The discovery and development of polymerase chain reaction (PCR) technique, particularly reverse transcriptase (RT)-PCR, has revolutionized diagnosing the exposure to HIV.[5,6]

Transmission & Epidemiology of HIV/AIDS

HIV has been isolated from peripheral blood lymphocytes, bone-marrow cells, spinal fluid and brain tissue, lymph nodes, cell free plasma, saliva, tears, semen and vaginal fluid[5]. In theory exposure to any of these body fluids, if contaminated with the virus, represents probable risk of infection. In practice, however, the risk of transmission of the infection seems to depend heavily on the route of ex-posure. The most probable routes for transmission of AIDS are considered as homosexual practice, heterosex-ual practice, intravenous drug abuse, prostitution, blood and blood products, vertical or perinatal transmission and occupational exposure. Transmission through sexual con-tact has remained the predominant mode of transmission, and laboratory and epidemiological studies have failed to demonstrate possible transmission of HIV1 through biting or blood-sucking insects.[10]

Regarding epidemiology, HIV/AIDS is one of the major pandemics (global) and epidemic (regional) that have devastated large population almost all over the world. It is now the seventh leading cause of death among 1-4 year olds, sixth among 15-24 year olds and 1st among 25-44 year olds.[1,11] The joint United Nations Programme on HIV/AIDS (UNAIDS) and WHO report in 2005 revealed that over 40 million people are living with HIV worldwide. More than 25 million of them in sub-saharan Africa and 10 million of them are young people aged 15 to 24 years. Some

15 million children have already been orphaned by HIV/AIDS. In central Bangladesh, comprising mainly of Dhaka city, overall HIV prevalence among intravenous drug users (IDUs) has increased from 1.4% to 4.9% between 2001 and 2005 with one small pocket showing an even higher rate of 8.9% in 2005.[2] The situation worldwide indicates that we are really failing to prevent this pandemic in most parts of the world, despite various intensive preventive measures and treatment programmes in developed as well as in developing countries.[7] WHO's treatment guidelines expand the number of people recommended for HIV treatment for an estimated 10 million to an estimated 15 million. The cost needed for HIV treatment in 2010 will be about US $9.0 billion according to the Joint United Nations Programme on HIV/AIDS (UNAIDS).[12]

In rural and impoverished urban areas of low-income countries, particularly in sub-Saharan Africa, a group of 13 neglected infectious diseases (NIDs) cause massive suffering, although they receive little or no scientific or mass-media attention.[1,13] These 13 NIDs, including Buruli ulcer (Mycobacterium ulcerae), cholera (Vibrio cholerae), cysticercosis, dracumculiasis (Guenea worm), trematodal infections, hydatidosis, leishmaniasis, lymphatic filariasis (elephantiasis), onchocerciasis (river blindness), schistosomiasis, helmenthiasis, trachoma (Chlamidia trachomatis), and trypanosomiasis (African sleeping sickness, Chagas disease), affect over one billion people representing to a sixth of the world's population. Little has been done to specifically address the complex issue of immunity during co-infections with AIDS, malaria, tuberculosis and NIDs. Recent advances in immunological research indicates that a vaccine for the developed world might not give the same result in populations already exposed to a number of different NIDs and this is a major challenge for vaccinology towards development of a successful HIV/AIDS vaccine.[13,14]

Quest for the HIV/AIDS Vaccine

Towards the development of a successful vaccine, scientists are confronted with a number of perplexing problems. Most important of them is that patients infected with HIV develop antibodies that inactivate the virus in laboratory tests, yet they become sick and die away. Why don't these patients' antibodies work against the virus in vivo? HIV is one of the most complex viruses ever identified, and it is extremely good at evading any immune mediated strategy directed against it (Figure-2).[15] HIV is already genetically diverse – there are currently nine genetic subtypes (or classes) of HIV1, the most prevalent strain - and new forms are emerging all the time. HIV mutates rapidly so scientists are trying to hit a constantly moving target.[16,17] Despite inherent enormous problems in constructing a vaccine, particularly without knowing what kind of immune response will be protective, scientists have attempted to design and develop vaccines against HIV/AIDS by using attenuated virus and genetically engineered subunit of the virus particles.[17,18]

Since the first injections of an experimental HIV/AIDS vaccine were given in the USA in 1987, no researched vaccine reached the phase-III clinical trial as yet.[16,17,19] Despite opposition from USA, in 1996 WHO initiated large-scale trials of HIV/AIDS vaccine in Uganda and Thailand, but the results were not so encouraging and an effective HIV/AIDS vaccine has remained ellusive.[3,4,20] In 2003, after more than a decade of work, VaxGen (a biotechnology company) announced with disappointment that their product 'AIDSVax containing synthetic monomeric envelope glycoprotein 120 (Gp 120)' did not prevent HIV infection in the study cohort as a whole.[4]

About 30 HIV/AIDS vaccines are in clinical trials worldwide, but only a dozen have moved to phase II trial according to AIDS vaccine advocacy coalition (ADVAC).[20] International AIDS Vaccine Initiatives (IAVI) partnering with Trangene (a French biopharmaceutical company) has developed another vaccine that uses an adenovirus type 35 (Ad 35) vector to deliver HIV antigens into the body. National Institute of Allergy and Infectious Diseases (NIAID), USA in collaboration with Merk (a German biopharmaceutical company), has developed a vaccine being tested in phase II trial containing replication defective adenovirus type 5 (Ad 5), a vector that transmits the HIV genes (gag, pol, nef) which code for internal HIV proteins and

may stimulate cellular immunity and this vaccine looks promising[4,21]. Italian researchers have announced that they have completed a phase I trial of a HIV/AIDS vaccine which targeted TAT, a protein that allows HIV to replicate. The vaccine is safe and well-tolerated in all subjects with much better immunogenicity as all the volunteers produced HIV-specific antibodies. The researchers plan to conduct phase II trials of the vaccine in Africa, but they need US $ 477 million to bring it to the market by the year 2010[21]. Recently, a promising truly global HIV/AIDS vaccine phase II trial, known as HVTN 204, has been initiated by the National Institute of Health (NIH). This vaccine combines synthetically modified elements of four HIV genes found in subtypes A, B and C which represents 85% of the worlds HIV cases. The US military and overseas researchers are coordinating the trials with NIH. Kenya AIDS vaccine institute (KAVI), NIAID, NIH and IAVI announced recently the start of a clinical trial of a candidate AIDS vaccine designed to prevent HIV/AIDS caused by multiple subtypes of HIV[22,23].

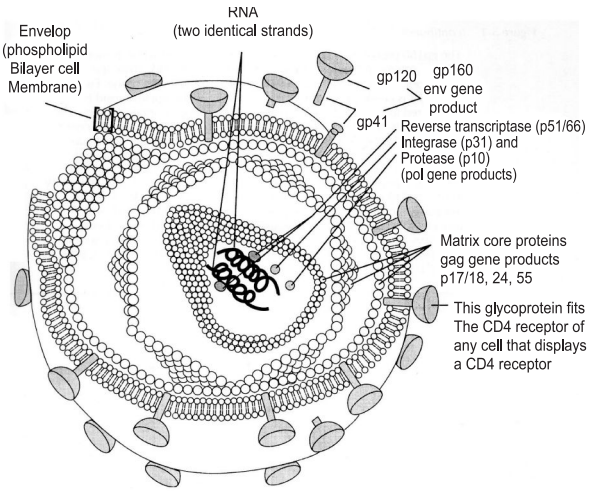

Fig.-2: *HIV is a complex sphere measuring about 1000A in diameter. The external viral membrane contains glycoprotein 160 (gp 160) each appears as spike consisting of two parts, gp41 and gp120. Within the cone-shaped core, there are two identical strands of ribonucleic acid (RNA), each 9749 nucleotide bases long), reverse transmission integrase (p31), protease (p10) and ribonuclease. Matrix core antigens (proteins) are p7, p15, p17/18, p24, p55, etc[15].*

As research for an HIV vaccine is under-funded, the IAVI recently has released a new policy brief "advanced market commitments (AMCs): Helping to accelerate HIV/AIDS vaccine development" to provide economic incentives to the investing commercial companies to support the development of HIV/AIDS vaccine.[22,24,25,26] The belief in an HIV vaccine is so powerful that the search is fast becoming a global research industry. Most of the money spent to date has come from the public sector (with the US giving the lion's share), with regular top ups from the Bill and Melinda Gates Foundation.[27] The enterprise estimates that to fully implement its strategy will cost $1.2bn (£600 m: • 900m) a year.[28]

HIV vaccine research has come a long way since the wildly overoptimistic predictions made by desperate politicians in the mid-1980s. The world waited over a century for a vaccine against typhoid once the causative agent had been identified. Later, it took nearly half a century to develop vaccines against polio and measles.[3,4] "The search for an AIDS vaccine is a far greater challenge than sending a man to the moon," wrote Mike Powell and Mitchell Warren, president and executive director of the AIDS Vaccine Advocacy Coalition (AVAC) in their 2006 report. "When it came down to the space race, we knew where we were; we knew where the moon was; and we knew roughly, how to get there. It was, essentially, an engineering problem. When it comes to an AIDS vaccine, we don't know where the moon is – yet. But that doesn't stop us from aiming for the heavens".[17,29,30]

Conclusions:

In conclusion, the progress made over the past years towards the development of HIV/AIDS vaccine has not been so disappointing. Among the daunting obstacles to develop effective (protective or therapeutic) HIV/AIDS vaccine, there remains one Himalayan obstacle: the remarkable pathogenic power of HIV itself. The scientists even do not know as yet the specific types of immune responses that an effective HIV/AIDS vaccine must stimulate in order to prevent or cure the infection. Immunity in co-infections with NIDs & others is an extremely complexed issue and immunological research is

very expensive. So, all these difficulties have to be overcome before an effective (protective or therapeutic) HIV/AIDS vaccine is available for use. The message for policy makers, therefore, is that investing in HIV/AIDS vaccines makes sense because it affects public health and availability of effective vaccine is the only way we would to be able to end the HIV/AIDS pandemic (global) and endemic (regional) from this planet. We are cautiously optimistic and are in favour of counseling optimistic patience towards the availability of HIV/AIDS vaccines within the next ten years from now, i.e. hopefully by the year 2020 as the scientists casually and optimistically predicted. In fact no scientific achievement, however relevant, could succeed in being applied without a proper context of social acceptability, feasibility and affordability in low-income countries. Thus, research and development of vaccines and therapies for HIV/AIDS must go together with capacity building, local empowerment and social awareness.

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REVIEW ARTICLE

Air Pollution and Chest Diseases – A Threat to Global Health

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Abstract:

Since the begining of the industrial revulation 200 years ago,man has been rather blithly belching ever incerasing quantities of a staggering variety of noxious fumes into the surrounding atmosphere and breathing the stuff every day.It was assumed that the great outdoor atmosphere was a limitless sea which could render harmless by dilution anything thown into it. However it is now clear that the impurities in community air may reach highenough so that they may indeed cause diseases and even death of the people. The major causes of the air polllution in developed countries are nitrogen dioxide from combusion of fossil fuel,ozone from the effect of sunlight on nitrogen dioxide and hydrocarbon and suspended solid and liquid particles.Bimass fuel is important sourse of indoor particulate matter in developing countries.Eniromental tobacco smoking is another important source of indoor air pollution. Ambient air pollution has been found to be associated with a wide range of effects on human health, including increased mortality risk, increased rates of hospital admissions and emergency department visits, exacerbation of chronic respiratory conditions (e.g., asthma),and decreased lung function. Air pollution is a complex mixture composed of both solid particles and gaseous pollutants. Identification of the specific pollutants contributing most to the health hazard of the air pollution mixture may have important implications for environmental and social policies, and for local government in taking steps to protect population health. Although the strongest evidence linking air pollutants with adverse health Air pollution remains a major, global, public health issue. The World Health Organization estimates that outdoor air pollution contributes to 5% of death world-wide (1.3 million deaths per year), and indoor air pollution contributes to 2 million premature deaths in developing countries. Whilst legislation to control air pollution has vastly improved air quality in many regions of the world, still remain many countries with heavily polluted cities and increasing vehicle exhaust emissions. Key outdoor air pollutants of concern are particulate matter, ozone and nitrogen dioxide. In many developing countries, biomass fuels commonly used for cooking and heating lead to indoor air pollution and similarly pose a major risk to respiratory health.

Keywards: *Air Population, Lung Health, Chest Diseases*

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Introduction

Defining "air pollution" is not simple. One could claim that air pollution started when humans began burning fuels. In other words, all man-made (anthropogenic) emissions into the air can be called air pollution, because they alter the

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chemical composition of the natural atmosphere. The increase in the global concentrations ofgreenhouse gases CO2, CH4 and N2O can be called air pollution using this approach, even though the concentrations have not found to be toxic for humans and the ecosystem. [1]

Primary and Secondary Pollutants

Pollutants can be classified as primary or secondary. Primary pollutants are substances that are directly emitted into the atmosphere from sources. The main primary pollutants known to cause harm in high enough concentrations are the following:

- Carbon compounds, such as CO, CO2, CH4, and VOCs
- Nitrogen compounds, such as NO, N2O, and NH3
- Sulfur compounds, such as H2S and SO2
- Halogen compounds, such as chlorides, fluorides, and bromides
- Particulate Matter (PM or "aerosols"), either in solid or liquid form, which is usually categorized into these groups based on the aerodynamic diameter of the particles-

1. Particles less than 100 microns, which are also called "inhalable"10 since they can easily enter the nose and mouth.
2. Particles less than 10 microns (PM10, often labeled "fine" in Europe). These particles are also called "thoracic" since they can penetrate deep in the respiratory system.
3. Particles less than 4 microns. These particles are often called "respirable" because they are small enough to pass completely through the respiratory system and enter the bloodstream.
4. Particles less than 2.5 microns (PM2.5, labeled "fine" in the US).
5. Particles less than 0.1 microns (PM0.1, "ultrafine").[2]

Sulfur compounds were responsible for the traditional wintertime sulfur smog in London in the mid 20th century. These anthropogenic pollutants have sometimes reached lethal concentrations in the atmosphere, such as during the infamous London episode of December 1952. Secondary pollutants are not directly emitted from sources, but instead form in the atmosphere from primary pollutants (also called "precursors"). The secondary pollutants known to cause harm in high enough concentrations are the following:

- NO2 and HNO3 formed from NO
- Ozone (O3) formed from photochemical reactions of nitrogen oxides and VOCs
- Sulfuric acid droplets formed from SO2 and nitric acid droplets formed from NO2
- Sulfates and nitrates aerosols (e.g., ammonium (bi) sulfate and ammonium nitrate) formed from reactions of sulfuric acid droplets and nitric acid droplets with NH3, respectively
- Organic aerosols formed from VOCs in gas-to-particle reactions

In the 20th century, it was recognized that petroleum products are responsible for a new type of "smog", photochemical summertime smog composed of secondary.[3]

Air pollution: a burning concern for **global health**

Air pollution remains a major, global, public health issue. The World Health Organization estimates that outdoor air pollution contributes to 5% of death world-wide (1.3 million deaths per year), and indoor air pollution contributes to 2 million premature deaths in developing countries[4]. Whilst legislation to control air pollution has vastly improved air quality in many regions of the world, there still remain many countries with heavily polluted cities and increasing vehicle exhaust emissions. Key outdoor air pollutants of concern are particulate matter, ozone and nitrogen dioxide. In many developing countries, biomass fuels commonly used for cooking and heating lead to indoor air pollution, and similarly pose a major risk to respiratory health.[5] To address this global health concern, Respiralogy commissioned a series of eight reviews of air pollution and lung health in 2012 which have provided valuable insight into the pathogenesis of air pollution effects on the lung, impact on respiratory diseases, and avenues for preventing the harmful effects of air pollution.[6]

Gene-environment interaction

High levels of air pollution have adverse effects across the population, so goals to lower air pollution levels to safe levels are essential in all communities. However, there is inter-individual variability in the response to inhaled air pollutants (e.g. to ozone 2), which could be determined by genetic susceptibility and gene-environment effects. Different studies recently explain the potential genetic and epigenetic factors involved in lung injury from air pollution.[7]

Mechanism of toxicity

The exact mechanism of injury caused by air pollutants is not yet fully understood. Biological pathways involving inflammation and oxidative stress (e.g. leading to disruption of the lung's protective epithelial barrier) have been implicated in lung injury from air pollution. Surface area and adsorption of organic compounds can increase toxicity, leading to inflammation, oxidative stress and also activation of the innate immune system.[7,8] Clearly a better understanding of the mechanisms of toxicity of air pollutants is needed, to develop preventive strategies against harmful effects. Newer classes of particles should also be recognised for their potential health effects. Michaela Kendall and Stephen Holgate introduce the concept of engineered nano particles of size <100 nm, used in medical and dental applications, and industrial and commercial products. The toxicological effects of nano materials in the lung depend on their size, shape, surface and corona (adherent proteins). Engineered nano sparticles can translocates across tissue barriers, and therefore need closer study for their adverse effects, especially with the emergence of newer everyday products containing Nan materials. In their review of air pollution and COPD, Fanny Ko and David Hui provide substantial evidence for outdoor air pollution as a trigger for COPD exacerbations.[9] Furthermore, outdoor air pollution levels have been linked with mortality rate in COPD. On the other hand, cigarette smoking is by far the predominant cause of COPD, and there seems to be little substantive evidence to date for air pollution in the development of COPD.Biomass fuels are biological materials used as fuel for cooking and heating e.g. wood, charcoal, dung and crop residue, leading to high concentrations of particulate matter in indoor settings. Wei-Yen Lim and Adeline Seow cite 21 epidemiological studies of exposure to biomass fuels and risk of developing lung cancer. [10] Their report indicates highly suggestive but not conclusive links with lung cancer. Although there is *in vitro* evidence for carcinogenicity of biomass fuels, the authors raised methodological issues limiting the interpretation of current epidemiological studies, including concomitant exposure to other pollutants (e.g. coal burning at the same time), interaction with smoking history and genetic susceptibility.[10,11] On the other hand, the International Agency for Research on Cancer has now classified diesel engine exhaust as a grade 1 carcinogen, notably for a relationship with lung cancer development. [11]

Monitoring, prevention and public health measures

Early warning systems are in place in some countries, to advise the public in real time about excessive air pollution levels. Frank Kelly and co-authors describe innovative approaches to using national air quality indices, to rapidly inform the general community about excessive air pollution events. [12] Alert services could then provide valuable information to at-risk individuals about potential risks of prolonged outdoor activity and effects on lung disease. Finally, prevention of the respiratory effects of air pollution is addressed by Martha Sierra-Vargas and Luis Terán in their timely review. They propose a range of initiatives to reduce sources of outdoor air pollution e.g. green vegetation areas in urban settings, reduction of traffic pollution through technological improvements in vehicles, and greater use of alternative energy sources. [13] Multi-pollutant strategies are now needed to be legislated by governments. Until we can achieve lower air pollutant levels globally, we need to continue to address adverse health effects of air pollution, to aim to protect our communities and improve lung health.

Air pollution is a major environmental health problem worldwide. The World Health Organization (WHO) considers that air pollution

is damaging the resources that are needed for the long-term sustainable development of the planet. [14] The sources of air pollution fall into three broad categories:

(1) Mobile sources, which include combustion-engine vehicles such as gasoline-powered cars, diesel powered vehicles, motorcycles, and aircraft;

(2) Stationary sources, which include rural sources such as agricultural production, mining, and quarrying; industrial sources such as manufacturing; and community sources such as the heating of homes and buildings, municipal waste, and incinerators; and

(3) Indoor sources, which include combustion, tobacco smoking, and biological sources; and emissions from indoor materials or substances such as volatile organic compounds, asbestos, and radon. [15]

Specific air pollutants

Air pollutants are usually classified into suspended particulate matter (dusts, fumes, mists, and smokes), gaseous pollutants (gases and vapours), and odours.

Suspended particulate matter

Suspended particulate matter (PM) consists of finely divided small particulates with diameters of less than10 ?m (PM10). Suspended particulate matter comprises a wide variety of substances, which include inorganic and organic carbon (containing polycyclic aromatic hydrocarbons), acidic or neutral sulphates and nitrates, fine soil dust, residues of lead and other metals,asbestos and other fibres. [15,16] Exposure of laboratory animals to fine particles has been shown to lead to inflammation of the airways and lungs. Most of these particulates are smaller than 1 ?m and remain suspended for hours or days. Particles that are smaller than 2.5 ?m in diameter (PM2.5) arise mainly from combustion processes, whereas larger particles are generated by grinding and other mechanical or agricultural processes. Small particles efficiently penetrate indoors, where levels are typically 70% to 80% of outdoor levels in the absence of indoor sources. In locations with indoor sources (eg cooking or tobacco smoke), indoor levels may be much higher than those outdoors.Acid aerosols are a subset of fine particles. Atmospheric oxidation of sulphur dioxide (SO2) may produce sulphuric acid and partially neutralized sulphate salts. The formation of acid aerosols is hastened by humidity and photochemical processes. When individuals with asthma are exposed to acid aerosols, bronchoconstriction is more likely to develop. [16]

Sulphur dioxide

Sulphur dioxide is released into the atmosphere primarily as a result of the industrial combustion of coal and oil. A small proportion is produced by vehicular sources due to sulphur contained in the fuel. Sulphur dioxide is oxidized to sulphuric acid in a humid environment.

Indoor levels are typically lower than outdoor levels,owing to the reactivity of SO2 with indoor surfaces.It is an irritant gas that elicits bronchoconstriction individuals with asthma are more sensitive to this effect. [17]

Oxides of nitrogen

Oxides of nitrogen are most frequently produced by the combustion of fossil fuels. Nitric oxide (NO) may be oxidised to nitrogen dioxide (NO2), the precursor of ozone in photochemical smog. In addition to NO2 itself, potentially harmful NO oxidation products include nitric and nitrous acid. In indoor environments without combustion sources, indoor levels of NO2 are lower than levels outdoors. [17,18] Homes with unvented gas combustion devices, such as gas stoves, generally have higher NO2 levels than outdoors during cooking. In experimental exposure studies, no consistent effects on lung function have been documented for NO2. However, exposure of asthmatic individuals to high levels of NO2 (0.2-0.5 ppm) has been shown to increase nonspecific airway hyper responsiveness and an enhanced specific airway response to inhaled allergens such as house dust mite allergens.[18]

Photo-oxidants

Photo-oxidants are produced by photochemical reactions in air containing oxides of nitrogen and reactive hydrocarbons. Ozone (O3) is the most important photo oxidant.Photochemical pollution causes eye irritation and small temporary changes in lung function, particularly among children or people exercising vigorously.

Because O3 is highly reactive, indoor concentrations are significantly lower than outdoor levels. In both healthy subjects and asthmatic individuals, exposure to O3 causes a reproducible decrease in lung function and an increase in non-specific airway hyper responsiveness.[19] The dose-response curve may be non-linear and there is no threshold effect. Exposure of people with asthma to ozone has been shown to increase the specific response to inhaled allergens. Ozone exposure causes inflammation of the nasal mucosa and broncho alveolar lining, thereby resulting in a reduction in lung function, which is worse in those with asthma. [20]

Volatile organic compounds

Examples of volatile organic compounds (VOCs) arealkanes, alkenes, alkynes, aromatics, aldehydes, ketones, alcohols, esters, benzene, and some chlorinated hydrocarbons.The major sources of VOCs come from the burning of fossil fuels and industrial processes involving solvents. Benzene is emitted from motor vehicle exhausts and/or from evaporated petrol. Indoor levels of VOC are usually much higher than outdoor levels, because VOCs are present in many building materials,such as paints, adhesives, and sealants. Volatile organiccompounds are also released from laser printers and

photocopiers. In the indoor environment, exposure to low levels of VOC may result in headache and irritation of the eyes and nose. Some VOCs have been shown to be carcinogenic. [19,20]

Carbon monoxide

Carbon monoxide (CO) is produced by the incomplete combustion of fossil fuels. Concentrations in urban areas depend on traffic density, topography, and weather conditions. In the absence of indoor combustion devices, indoor levels may be close to outdoor levels. Unvented combustion devices may produce additional CO indoors. The health hazards of CO exposure are related to the binding of this gas to haemoglobin. An increase in carboxyhaemoglobin of 3.6% over baseline levels reduces the time to angina and leads to electrocardiographic changes in exercising men with coronary artery disease. [20]

Impairment of lung function

Long-term exposure to O3 has been found to be associated with a lower level of lung function and a faster rate of decline in lung function. Furthermore, the combination of O3 and acid sulphate may be more important than the effects of O3 alone. In Germany, children aged 9 to 11 years living in areas with the greatest amount of urban traffic had significantly poorer lung function than those living in areas with less traffic. [21]

Clinical impact on Asthma, COPD, lung cancer and lung infection

Understanding mechanisim of injury from air pollutants may have implications for reducing susceptibility to and severity of lung disease.Whilst high levels of air pollution can trigger asthma exacerbations, the question of air pollution as a possible cause of asthma is much less certain. Air pollution is known to be associated with acute asthma exacerbation. The relationship is strongest with particulate and O3; the higher the pollution, the higher the number of asthma patients with acute exacerbation. There has been a general increase throughout the industrialized world in the prevalence of asthma and allergies in children. The reason for this increase is not known and there is no clear evidence that air pollution is causally related.[22]However, there are now several experimental studies showing that diesel particles, SO2, and O3 can act as an adjuvant, which enhance the production of immunoglobulin- antibodies and possibly increase the prevalence of atopic sensitization and asthma.

These reviewers conclude that there is suggestive evidence, from observational studies, for association of asthma incidence in people living close to busy roads with a lot of truck traffic. However, studies at a population level did not find any increased risk of asthma with ambient air pollution levels. Known or suspected carcinogens, such as benzene and other polycyclic aromatic hydrocarbons are detectable in vehicle emissions. Attempts have been made to quantify the cancer risk from vehicle emissions.[23] Recently, the body of evidence on associations between indoor air pollutants (IAP)

and TB has grown significantly. The potential impact of any causal relationship between TB and IAP is very large, particularly in Africa and South East Asia, where the prevalence of both IAP exposure and TB is high.[23, 24]

Preventive measures:

Primary prevention includes abrogating the risk factor before illness strike, banning of certain hazards eg two stroke scooters .Secondary prevntion denotes measures to prevent further deterioration and identification of risk groups. Tertiary prevention includes activities that attempt to slow progression or prevent anticipated complications of previous exposure or of disease that is already established. In the United States, the Environmental Protection Agency (US-EPA) has

established air quality standards to protect public health, including the health of" sensitive" populations such as children, older adults and people with Asthma[25].US-EPA also sets limits to protect public welfare. This includes protecting ecosystems, such as plants and animals, from harm, as well as protecting against decreased visibility and damage to crops, vegetation, and buildings. US-EPA has set National Air Quality Standards (NAAQS)for six principal airpollutants: nitrogen oxides (expressed as NO2), ozone, sulfur dioxide, PM, carbo monoxide (CO) and lead (Pb).The United States Clean Air Act provides the principal framework for national,state, tribal, and local efforts to protect air quality. Improvements in air quality are

the result of effective implementation of clean air laws and regulations, as well as efficient industrial technologies. [26] Under the Clean Air Act, the US-EPA has a number of responsibilities, including the following:

- Conducting periodic reviews of the NAAQS for the six principal pollutants that are considered harmful to public health and the environment.
- Ensuring that these air quality standards are met (in cooperation with the state, tribal, and local governments) through national standards and strategies to control air pollutant emissions from vehicles, factories and other sources.
- Reducing emissions of SO2 and NOX that cause "acid rain".
- Reducing air pollutants such as PM, SOX, and NOX, which can reduce visibility across large regional areas, including many of the nation's parks and wilderness areas.[27]

Conclusion: Air pollution at present is an alarming concern for health all over the world. People should bring change in attitude and should strictly abide by the "Environment Proctection and Biodiversity Conservation Act-1999 and the "Environment Conservation Rules 1997". We may even follow the US-EPS and Clean Air Act.Industrialized nations should have a big share regarding minimization of the air pollution. Awareness programs should be taken through mass media. Concerted efforts should be organized involving multi-discipline peoples.

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REVIEW ARTICLE

Pulmonary Rehabilitation: A Review

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Introduction:

The major goal of treatment of any chronic and irreversible disorder is to allay symptoms and minimize the impact of the illness by enhancing the individual performance of the desired activities. Pulmonary rehabilitation is an effective therapeutic intervention that can be employed to achieve this goal.[1]

Among numerous respiratory conditions, patients with COPD frequently have the most chronic debilitating symptoms which are not completely eliminated or controlled by medications and other traditional medical treatments. Because of the severity of dyspnea associated with increasing activity in patient with COPD, this disease frequently impairs the patient's ability to engage and participate constructively in daily activities.

Comprehensive pulmonary rehabilitation has also been successfully employed in patients with Cystic Fibrosis and respiratory insufficiency associated with neuromuscular disorders.[1]

As COPD is the most common chronic respiratory disease and because patients with COPD are the most common recipients of pulmonary rehabilitation, this review will particularly emphasize on COPD.[2]

Definition

Pulmonary Rehabilitation is defined as "an art of medical practice wherein an individually tailored, multidisciplinary programme is formulated which through accurate diagnosis, therapy, emotional support, and education, stabilizes or reverses both the physio- and psychopathology of pulmonary diseases and attempts to return the patient to the highest possible functional capacity allowed by his pulmonary handicap and overall life situation (The ACCP Definition).[1]

Pulmonary Rehabilitation is defined as "a multidimensional continuum of services directed to persons with pulmonary disease and their families, usually by an interdisciplinary team of specialists , with a goal of achieving and maintaining the individual's maximum level of independence and functioning in the community (The NIH Definition).[1, 2]

Key components of comprehensive pulmonary rehabilitation

- Medical evaluation and management
- Initial assessment and goal setting
- Therapeutic modalities
  - Smoking cessation
  - Exercise training
  - Psychosocial counseling
  - Breathing retraining
  - Daily activity performance and energy management
  - Nutritional counseling
- Outcome evaluation
- Maintenance programe

Medical evaluation and management

Medical evaluation should be done by a physician who plays an integral role in pulmonary

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rehabilitation. The physician should explain the rationale and benefits of this programe for successful adherence of the patients.

An appropriate diagnosis and optical medical treatment of the patient with respiratory disease are prerequisite for the initiation of pulmonary rehabilitation. The goal of evaluation and management by the physician is to minimize the medical impact of the disease on the patient and maximize the patient's ability to benefit from the pulmonary rehabilitation programme.[3]

Table-I

Medical evaluation and management component of pulmonary rehabilitation

Evaluation
Respiratory diagnosis
Severity of respiratory diseases
Other conditions potentially interfering wit pulmonary rehabilitation
Arthritis
Osteoporosis
Cardiac disorders
Oxygenation at rest and during activity
Management
Reduce airflow limitation
Minimize pulmonary secretions
Eliminate or reduce medication adverse effects
Promote collaborative self-management
Provide plan to address changes in symptoms
Reduce impact of other conditions on participation in rehabilitation programe
Provide plan for maintaining continuity of medical care

Initial assessment

Initial assessment is the most important element of pulmonary rehabilitation which culminates in the development of goals to guide the rehabilitation process and coordinate the actions of all team members.[4] The goal of assessment is to

- Determine the individual needs
- Develop short-term goals
- Provide a baseline for future assessment
- Develop long-term goals for continuing management.

Therapeutic modalities

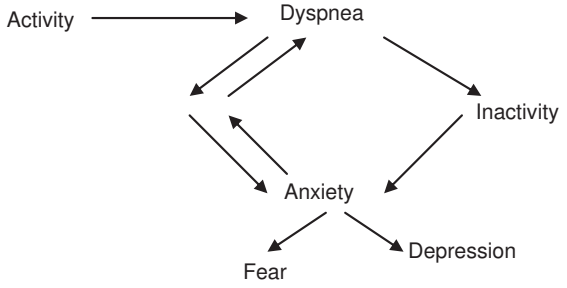
Smoking cessation

The physician should play a key role to promote, encourage and implement a smoking cessation programe. Smoking cessation should be considered as a part of comprehensive pulmonary programe and sometime it may be the primary goal for some patients enrolled in pulmonary rehabilitation.

Exercise training

The most important aspect of pulmonary rehabilitation is exercise training, and the most important training method is endurance training of the lower extremities.

Exercise capacity in COPD



Training

There are multiple potential mechanisms to explain the beneficial effect of exercise training in patients with respiratory disease including increased efficiency in activity performance, enhanced motivation, desensitization to the sensation of dyspnea, improved cardiovascular function, improved muscle function, and increased aerobic activity.[1, 5]

Lower extremity aerobic exercise training is the cornerstone of exercise training during pulmonary rehabilitation.

Exercise intensity, training session duration, training frequency, training programe duration, upper extremity training, strength training, ventilatory muscle training should be organized according to guideline and may be individualized

Psychosocial counseling

Psychological aspect in COPD

Patient with COPD frequently exhibit emotional and psychological concern related to their illness. Anxiety, depressive symptoms, sexual function

and neuropsychological deficits should be properly addressed.

Psychosocial Interventions

Psychosocial Interventions include

Exercise training

Antidepressant medications

Psychosocial support

Breathing retraining

The goal of breathing retraining is to reduce dyspnea and to improve respiratory parameters such as improving oxygenation, slowing the respiratory rate, increasing tidal volume, decreasing air trapping, and reducing work of breathing. These procedures can be practiced during exercise or during daily activities and when patients experience shortness of breath.[1, 6] These are

Pursed-Lip breathing

Diaphragmatic Breathing

Controlled Breathing

Daily activity performance and energy management

Based on the patient assessment, appropriate treatment goals for improving performance of daily activities may include

Reducing shortness of breath with basic ADL

Applying regular coordinated breathing patterns

Increasing functional endurance

Using energy and time management method

Using adaptive equipment

Obtaining assistance from others particularly from family members, and

Enhancing performance at work

Energy management includes employing energy conservation techniques, improving work efficiency, using proper body mechanics, incorporating time management, pacing, and careful planning.

Nutritional counseling

Adequate nutritional intake mut be assured in a person enrolling in pulmonary rehabilitation programe. Weight excess should be treated, and weight loss should be avoided.

Maintenance programe

The patient should be advised to continue exercise and pulmonary rehabilitation programe to achieve long term goal of this programe.

Potential outcome of Pulmonary Rehabilitation

Outcomes of pulmonary rehabilitation are important for three aspects. First, benefits can be evaluated by the patients, by the referring doctors and by medical benefit providers. Second, it can be used as guideline programe in a particular community. Third, it can be used as a guide to develop and ongoing evaluation of comprehensive programe.[1, 7]

Table-II

Potential outcomes of pulmonary rehabilitation

"Medical" factors
Mortality
Morbidity
Respiratory symptoms
Physiological indices
"Nonmedical" factors
Functional capacity
Neuropsychological function
Health-related behaviours
Health-related Quality of life
Physical health
Mental/emotional health
Social health
Role of function
Perception of general well-being
Ability to work
Caregiver burden
Use of assistive technology
Patient satisfaction
Costs

Tools to assess quality of life outcomes

One of the major goals of pulmonary rehabilitation is to enhance in quality of life, so assessment of quality of life is very important to assess the programme.[1, 8] This can be done by

General Quality-of- Life Tools

SF-36 Health Survey

Quality of Well-Being Scale

Sickness Impact Profile

Respiratory Disease-Specific Quality-of-Life Tools

Chronic Respiratory Diseases Questionnaire

St. Georges Respiratory Questionnaire

Outcomes of Pulmonary Rehabilitation

Improvement in many of the important outcome domains have been demonstrated following pulmonary rehabilitation in patients with COPD.[1, 9, 11] These are

Respiratory symptoms

Lower extremity exercise training

Quality of life

Upper extremity exercise training

Ventilatory muscle training

Survival

Morbidity

Functional Capacity

Exercise Capacity

Strength Training

Psychosocial and education

Health care utilization

Ability to work

Conclusion:

Comprehensive pulmonary rehabilitation programe can improve physiological measures of exercise capacity, functional capacity and health-related quality of life. Because of variety, diversity and the number of potential outcomes, this programe should be focused on individual's need. Periodic assessment of the outcomes should be done to modify the programe with an aim to improve outcomes and thus enhancing patient care.[1, 10]

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REVIEW ARTICLE

Managing Asthma in SMART Fashion: A Review

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Abstract:

Single Maintenance and Reliever Therapy (SMART) for asthma involves the patient using a single inhaler containing budesonide and formoterol for both regular maintenance treatment & additional rescue use. This is a patient focused management approach trying to improve asthma control and reducing the future risk of exacerbations. The simplicity, ease of use and evidence from large scale clinical trials showing better improvements in several outcomes has made it popular to the patients and clinicians. Recently the strength of evidence has been critically reviewed and further research in this field was advocated. The current review focuses evolution of SMART, observations of published trials and controversies.

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Introduction

The combination of a long acting â$_2$ agonist (LABA) with inhaled corticosteroid (ICS) is now considered the most effective means of controlling asthma in the majority of patients[1]. This approach reduces exacerbation risk and increases the likelihood of controlling asthma more often, more rapidly and at a lower dose of ICS than is seen with ICS therapy alone[2,3,4]. The traditional approach has been to prescribe an ICS/LABA combination inhaler on a fixed dose (FD) basis with an additional rapid acting â$_2$ agonist inhaler for rescue use[5]. Periodic fluctuations in symptoms and airway inflammation are characteristics of asthma, which means treatment requirements especially reliever use can vary over time[6]. So it is desirable to have a single inhaled medication that can be used as both reliever and controller; formoterol is likely to be one such agent as it has both rapid onset and long lasting action[7].

The LABA formoterol has an onset of effect that is comparable with that of salbutamol[8] and when used as a reliever therapy has proven to be superior to terbutaline & salbutamol in improving asthma control and preventing asthma exacerbations[9 - 11]. A recent development in the management of asthma is the use of a combination inhaler containing a corticosteroid (budesonide) & a LABA (formoterol) that can be used for regular maintenance and additional rescue treatment in place of short acting â$_2$ agonist (SABA). This single maintenance and reliever therapy (SMART) simplifies treatment for both patients and clinicians by providing effective asthma control using a single inhaler[12]. A number of clinical studies have substantiated that managing asthma in the SMART fashion

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results in improved asthma control and a reduction in exacerbation frequency compared with traditional approaches.[6,13-16] But recently, the clinical trials of SMART therapy have been appraised critically and have been the subject of Cochrane reviews highlighting the study limitations.

Evolution of SMART

Long term anti inflammatory treatment with inhaled corticosteroids (ICS) is the corner stone of therapy in persistent asthma.[17] The available evidence indicates that low doses of ICS can often provide ideal asthma control and reduce the risks of severe asthma exacerbations in both children and adults with mild persistent asthma and should be the treatment of choice.[1] If disease control is not achieved with a low to moderate dose of ICS[2, 3, 18, 19] maintenance monotherapy, greater benefit is achieved by the addition of an adjunctive agent such as a long-acting β_2 agonist (LABA) than with further increases in the dose of ICS. The use of LABAs without concomitant ICS is of concern as studies have reported increased risk of asthma related mortality and serious adverse events with LABA monotherapy.[20] International guidelines recommend against monotherapy with LABA in the management of asthma. However, adding a LABA to an ICS has been shown to have a favourable safety profile.[21-23]

Fixed combination inhalers of ICS & LABA in one device with different formulations are now available in the market.[24] The combinations available for clinical use are – budesonide combined with formoterol, fluticasone combined with salmeterol and beclometasone combined with formoterol.[1] Most recent ICS/LABA combination therapy is mometasone furoate combined with formoterol.[25]

Due to its unique properties, formoterol/ budesonide is currently the only ICS/LABA combination that is approved to be used as maintenance and relief in one inhaler. This is because the onset of effect of formoterol/ budesonide is faster than salmeterol/ fluticasone[26] and comparable with traditional relievers such as salbutamol[27] and both budesonide and formoterol show a clear dose response.[28] The combination product containing LABA salmeterol such as fluticasone/salmeterol combination inhaler is unsuitable as a rescue therapy due to slower onset of action[29] and lack of dose response[28]. Inhalation treatments to control asthma are usually delivered by a fixed-dose daily maintenance regimen with short-acting β-agonist (SABA) therapy for the quick relief of symptoms on an as needed basis. Studies in unselected populations have shown that, as an exacerbation develops, patients increase the dose of rescue inhalers but not usually the dose of ICS.[29] This observation led to the evaluation of immediate administration of additional anti-inflammatory medication – combined ICS and β_2-agonist – in response to an increase in symptoms, an approach that has been shown to be safe and effective in regaining symptom control and reducing the risk for progression to exacerbation.[6,13-16]

Considering all limitations of the traditional approach of managing moderate to severe persistent asthma, Astra Zeneca launched a new product, Symbicort turbuhaler in 2001 containing two active ingredients delivered via a single inhaler: Budesonide and Formoterol. With the introduction of Symbicort, a novel treatment approach known as Symbicort/Single Maintenance and Reliever Therapy (SMART) or Single Inhaler Therapy (SIT) was focused.

SMART

When patients use ICS/LABA formulations containing formoterol (a quick onset LABA) the maintenance inhaler could also be used for occasional quick relief purposes. This strategy implemented with combination budesonide/ formoterol inhalers has become widely known as SMART (Single Maintenance and Reliever Therapy) or SIT (Single Inhaler Therapy).[30] The acronym has been used in a previous study too (Salmeterol Multicenter Asthma Research Trial) when Salmeterol was used as LABA in usual asthma pharmacotherapy.[31]

The effectiveness of this treatment regimen is thought to be the result of a rapid increase in ICS dose at the earliest onset of symptoms[32]. ICS delivered in combination with formoterol reliever therapy, targets the underlying inflammation of asthma and provides rapid control of symptoms.[1] In this strategy, patients

step up their controller medication by using budesonide/formoterol for relief of breakthrough symptoms. Once control is regained, patients step down treatment by using budesonide/ formoterol for daily maintenance treatment only, without additional as-needed inhalations.[6]

Since its introduction SMART strategy has attracted attention of the clinicians and patients. The efficacy and safety has been assessed by a number of randomized double - blind clinical trials[6, 13-16, 33] and randomized open label parallel group active comparator controlled multi centred trials of six or twelve months duration in patients with asthma.[6, 34-36] Clinical studies show that patients using formoterol and budesonide experience fewer daily symptoms, less night - time awakenings and have fewer severe exacerbations compared with traditional fixed maintenance doses of inhaled corticosteroid ICS/LABA combination therapies plus as needed SABA.[6,14]

This approach of managing asthma has been incorporated in Global Initiative for Asthma (GINA) guidelines in 2008.[37] Its use is also recommended, in 2009, by British Thoracic Society/Scottish Intercollegiate Guidelines Network (BTS/SIGN) guidelines on the management of asthma for selected adult patients who are poorly controlled at step 2 or step 3.[38]

Key to Success

Good communication between the physician and the patient is an integral part of management of asthma using SMART fashion. If the patient can identify the signs of a forthcoming exacerbation, SMART allows patients to increase the dose during worsening of symptoms[39] and a potentially life threatening asthma attack can be prevented. Adults starting the SMART need to be trained in its use and they need to demonstrate good inhaler technique with the turbuhaler device.[40] They should be warned about the maximum recommended dose (up to 8 puffs of the medication daily) prior to seeking medical help. Ideally this approach needs a clear action plan that should be reviewed annually, as part of a structured process of asthma education.[41]

Benefits

The striking benefit is best described in terms of GINA guidelines statement. "The use of the combination of a rapid and long acting β_2 agonist (formoterol) and an inhaled glucocorticosteroid (budesonide) in a single inhaler both as a controller and reliever is effective in maintaining a high level of asthma control and reduces exacerbations requiring glucocortisteroids and hospitalization (Evidence A)".[37]

Managing asthma in SMART fashion is a safe and simplified approach to asthma management[12] and provides rapid relief of symptoms, alleviating the need for a separate SABA inhaler with every dose being accompanied by additional anti-inflammatory therapy.[6] It can improve compliance because it is simpler for the patient to use.[29] SMART is a cost effective strategy;[42] reduction in severe exacerbations results in overall health care saving.[29]

Control of Asthma with SMART

Published large scale randomized clinical studies have reported that SMART compared with higher maintenance doses of ICS & similar or higher maintenance doses of ICS/LABA all with a separate SABA as needed provides at least a similar level of current control, achieved at a lower total overall steroid load.[6, 13-16,33,36]

There is consistent evidence from randomized clinical trials that SMART reduces the number of severe exacerbations when compared with higher maintenance doses of ICS and similar or higher maintenance doses of ICS/LABA therapy, all with a separate LABA as needed.[6, 13-16,33,36] Compared with a 2-4 times higher maintenance dose of budesonide plus SABA as needed, SMART has been shown to significantly prolong the time to first severe exacerbation and significantly reduce the risk of having a severe exacerbation requiring medical intervention and the need for hospitalizations/emergency room treatments.[6,13,33]

Adverse Effects

In trials of SMART therapy the regimen appeared to be well tolerated in comparison to other strategies with no suggestion of an increased rate of unwanted effects in those using SMART. Also no new safety issues emerged.[43]

Limitations

Single inhaler therapy has been shown to be effective in children aged 4 – 12 years, but has not yet been approved by regulatory authorities for use in them.[29] This strategy is not suitable for patients who overuse their rescue inhalers or who find it difficult to recognize if their asthma is worsening.[29] A recent study has shown higher sputum and bronchial biopsy eosinophil counts after 1 year in patients using budesonide/ formoterol in SMART fashion when compared with traditional constant dose budesonide/ formoterol.[44] A possible concern with SMART is that inadequate anti – inflammatory treatment may be given to (at least some) patients resulting in persistent inflammation and increased bronchial hyper responsiveness (BHR).[5] But Riemersa *et.al*'s primary care study of patients with mild to moderate asthma for 12months has shown that despite a 59% lower dose of ICS, BHR and other clinical outcomes remained stable during SMART treatment while PEF values improved.[17] A study on the effect of SMART on airway remodelling in patients with moderate asthma has shown that Formoterol/ budesonide might interfere in chronic inflammation and remodelling in airways as well as relieve asthmatic symptoms.[45] Whether other combination inhalers containing a fast acting LABA, formoterol can be used in SMART fashion is still not clarified.[5]

Controversies

All the published trials of SMART were funded by Astra-Zeneca, the pharmaceutical company that markets Symbicort. Indeed, there is little non-commercially funded research in this area, and the role of SMART continues to cause controversy.[46,47] When recommendations are being made in favour of SMART strategy, the study limitations of the clinical trials have recently been highlighted.

According to Chapman K R *et. al*[46]:

- Attempts to compare budesonide/formoterol SMART therapy with regular combination ICS/LABA dosing using other compounds has been confounded by a lack of blinding and unspecified dose adjustment strategies.
- Guideline-recommended asthma control is rarely achieved in published SMART trials, in contrast with the reported reduction of severe exacerbations
- In some studies, the conventional (used as control) remained undefined
- Electronic monitoring of medication use in the SMART trials has not been used to test the hypothesis that SMART therapy may encourage compliance
- The potential benefits in partially controlled asthma have not been assessed (All studies with SMART have been conducted in patients with uncontrolled asthma)
- SMART studies have not been reported asthma control using a composite index of symptom variables to categorize patients as having achieved adequate control, but have reported some individual symptom control parameters selectively
- The use of action plans has not been clarified
- The importance of discordant relationship between perception and true airway obstruction has not been addressed
- The SMART strategy has not been tested against equivalent or higher doses of bud/form given in symptom-prevention fashion
- Sufficient information on long term out comes is lacking

Cochrane reviews (recognized as the gold standard in evidence-based health care) suggested further research after two reviews[48,49] and concluded after the third[50] "…..SMART can reduce the risk of asthma exacerbations needing oral corticosteroids in comparison with fixed dose maintenance inhaled corticosteroids….. . SMART has not been demonstrated to significantly reduce exacerbations in comparison with current best practice". But Demoly and colleagues showed that budesonide/formoterol maintenance and reliever therapy was well tolerated and was associated with a greater likelihood of improving overall asthma control, reducing exacerbations and improving symptoms compared with local conventional best practice.[51]

In a systematic review evaluating the effects of the combination of LABA and inhaled corticosteroids versus a higher dose of inhaled

corticosteroids on the risk of asthma exacerbations, the authors concluded that in children there was no significant reduction, but rather a trend towards an increased risk of oral steroid-treated exacerbations and hospital admissions.[52]

Conclusion:

In adult patients, budesonide/formoterol maintenance and reliever therapy is a safe and simplified approach to asthma management, using a single inhaler. Published double blind trials show that budesonide/formoterol therapy delivered in SMART fashion provide better improvements in several outcomes with lower ICS dosing than the traditional combination therapy approach of constant maintenance dosing with a separate reliever. This approach has already been approved by International Guidelines and its use is currently recommended in over 90 countries worldwide.[51] However controversy persists; the clinical trials of SMART have been reviewed critically highlighting the limitations in the study and further research is justified.

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CASE REPORT

Pleural Endometriosis: A Case Report

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Abstract

Pleural endometriosis is a rare condition caused by transdiaphagmatic extension of uterine endometrial tissue to the pleura or haemotogenous implantation of endometrial cell in the lung.[1,2] We present a patient of pleural endometriosis who was referred to our hospital with a massive, loculated right pleural effusion accompanied by significant ascites. Aggressive medical therapy was subsequently initiated but hysterectomy with bilateral oophorectomy was required due to poor symptom control and inability to rule out a neoplastic process.

[Chest & Heart Journal 2012; 36(1) : 88-89]

Case Report:

A 38 years old woman was admitted with dyspnea and right chest pain of two weeks duration. She has a history of dysmenorrhoea and infertility. 10 months before admission laparoscopy revealed extensive pelvic endometriosis, 5 month prior to admission the patient complained of intermittent mild right chest pain especially during menstruation. Physical examination on admission to the hospital revealed diminished breath sound to the right lung field and distended abdomen with ascites. Her hemoglobin was 11.0 gm/dl, white blood cell count, electrolyte, creatinine and liver function test were normal.

Initial chest radiograph obtained at the time of admission showed pleural effusion. Diagnostic thoracocentesis shows a thick old blood like aspirate without any microorganism, negative for malignancy & endometrial cells. Her CA-125 level was normal. The CT scan revealed multiple loculated fluid collection compromising the right lung and displacing the heart into the left hemithorax, ascites, a complex left adnexal cyst, an abnormal soft tissue mass in right adnexa.

A laparotomy disclosed 800ml of bloody fluid with old clots in peritoneal cavity. Total abdominal hysterectomy and bilateral salpingo oophorectomy was performed and pathologic examination revealed multifocal endometriosis of both adnexa, the omentum, the intestinal wall, outer surface of the uterus, post operative recovery was unremarkable. She has been treated with leuprolide for control of her residual endometrial disease. 9 months after her initial presentation she is well, pain free and denies dyspnea and other respiratory symptoms.

Discussion:

Pleural endometriosis causes catamenial pneumothorax or hemothorax or both. Although endometriosis is usually limited to pelvic organ, extra pelvic endometriosis is also recognized.[1] Thoracic endometriosis typically affects women in their mid 30s, with preferential involvement of right hemithorax in greater than 90% of cases.

The differential diagnosis of pleural endometriosis include metastatic adeno-carcinoma as well as a variety of mesothelial proliferative disorders.[2] After the diagnosis is established and the presenting symptoms have been addressed treatment is usually directed at hormonal suppression to prevent recurrence.

Massive bloody ascites is rarely secondary to endometriosis, and is more likely encountered in the setting of hepatic tumors, carcinomatous

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peritonitis or cirrhosis of the liver. In the absence of liver disease, ascites due to endometriosis is commonly mistaken for ascites caused by ovarian neoplasms and therefore this entity is seldom recognized before surgical exploration of the abdomen. The tumor marker for ovarian neoplasms, CA-125, can be elevated in endometriosis.[2]

As in Meig's syndrome, ascitic fluid can reach the pleural cavity by transdiaphragmatic lymphatics.[3] We suggest that in this particular case, endometrial implants on the parietal pleural itself may have been responsible for the associated pleural effusion.

Hormonal treatment is often tried as initial therapy, but surgical intervention is often mandated in order to exclude malignancy. In addition, it is unlikely the loculated effusion in the present cases would have responded to medical therapy alone. Given her residual endometrial disease, our patient has been maintained on hormonal suppressive therapy to prevent recurrence of effusion.

Conclusion:

Hormonal therapy should be incorporated into the treatment regimen to minimize recurrence. If associated with ascites, the similarity to neoplastic pelvic pathology in a young population mandates increased awareness and aggressive diagnostic intervention.

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CASE REPORT

Ewing's Sarcoma with Pulmonary & Bony Metastasis During Treatment : A Case Report

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Abstract

The Ewing's sarcoma family of tumours (ESFT) is an aggressive form of childhood cancer.

It is the second most common primary bone tumor and accounts for 5% of all child and adolescent cancers.

A teenaged boy presented with pain & swelling in the lower side of right buttock for last 1 yrs, which was dull & intermittent in nature, localized, often radiates to rt thigh. Along with this, he also developed low grade irregular fever, loss of appetite and gross emaciation during this period of illness. He had neither history of contact with known case of TB nor history of trauma to the affected site. No history of malignancy among members of the family. X-ray pelvis showed bony -destruction with periosteal reaction forming codman's triangle. X-ray chest reveals normal. Biopsy shows Ewing's sarcoma (ES) & appropriate treatment started. As his symptoms worsened despite of 6 cycle of chemotherapy & radiotherapy reevaluation was done, X-ray pelvis shown sclerotic & lytic areas with expansion & periosteal reaction in proximal metadiaphysis of rt femur with healed pathological fracture. X-ray chest shows, plural effusion with mass in rt lung field. CT chest pulmonary metastasis with large rt plural effusion with shifting of mediastinum. CT guided FNAC showed metastatic ES. We continue the therapy. subsequently he also complaints of back pain & constipation. MRI of lumbro-sacral spine with contrast suggestive of metastasis in lumber vertebra & pelvis. As it is rare to develop both pulmonary & bony metastasis during receiving adequate dose of chemotherapy & radiotherapy so we want to report this case.

Key word- Ewing's sarcoma, Pulmonary metastasis

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Case Reppot:

13 yrs male, child hailing from Mirzapur, Pabna was admitted to National Institute Cancer Research & Hospital (NICRH) with the complaints of pain in the lower side of right pelvis for last 1 yrs, dull & intermittent in nature, localized, often radiates to right thigh. He also developed swelling in the same region for 2 months. Along with this, he also developed low grade intermittent fever, loss of appetite and

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became emaciated during this period of illness. He had neither history of contact with diagnosed case of tuberculosis nor history of trauma to the affected site. No history of malignancy among members of the family. His life before this illness was uneventful. He was the only issue of his non consanguineous parents. He was treated by local qualified physician for several months but as the condition was deteriorating so he was referred to NICRH for further management. Among initial investigation, X-ray pelvis showed bony destruction in proximal metaphysic of right femur with periosteal reaction forming Codman's triangle. X-ray chest revealed right hilar lymphadenopathy, chest CT unremarkable. Biopsy report was Ewing's sarcoma (ES). Patient was admitted under Paediatric oncology unit in NICRH. Tumor board decided to give chemotherapy including ifosfamide—etoposide —. vincristine—doxorubicin—cyclophosphamide (VAC/IE) in the INT-0091 study protocol. Plans were to give total 17 cycle of chemotherapy, as VAC/IE every 2 wkly, for 6 cycles then review for radiotherapy then another 11 cycle of chemotherapy.

After giving 6 cycle of chemotherapy both clinical & radiological evaluation was done. X-ray pelvis shown sclerotic & lytic areas with expansion & periosteal resection in proximal metadiaphysis of right femur with healed pathological fracture. X-ray chest finding was normal. Then he received radiotherapy in right anterior hemi pelvis & right posterior hemi pelvis total therapeutic dose received 5000 cGY in 25 fractions from 06.03.12 to 15.04.12. As radiotherapy was completed rest 11 cycle of chemotherapy was restarted. During continuation of chemotherapy patient developed respiratory distress. Re-evaluation was done. X-ray chest showed plural effusion with right sided mass lesion. Chest CT showed pulmonary metastasis with large right plural effusion with shifting of mediastinum. CT guided FNAC showed metastatic Ewing's sarcoma. We continued the therapy, but subsequently he also complained back pain & constipation. At that time, MRI of lumbosacral spine with contrast suggested metastasis in lumber vertebra & pelvis. In the aim of relieving cord compression palliative radiotherapy was given locally. Now he is on palliative care.

Discussion:

There is currently no internationally recognized risk classification scheme for patients with ES. Early chemotherapy trials found that patients with pelvic primary sites or metastases at diagnosis had a higher risk of relapse and death than others. Our patient also presented with pain & swelling in the lower side of right pelvis & diagnosed as a case of ES of right pelvis.

Treatment modality in case of ES is surgery followed by chemotherapy & radiotherapy. Surgery in pelvic sites is particularly controversial, as excision may be very difficult. An analysis of 75 patients with pelvic tumor in INT-0091 showed that local relapse occurred in 25% of patients treated with surgery or radiation alone, and only 10·5% of patients treated with surgery and radiation, but the difference was not statistically significant (p=0·46). Event-free survival was also not significantly affected.[1]

The subsequent Children's Cancer Group-Pediatric Oncology Group (CCG-POG) cooperative study (INT-0091, 1988—92) showed that ifosfamide and etoposide (IE), alternating with the standard regimen of vincristine, doxorubicin, cyclophosphamide (VAC), markedly improved both overall and event-free survival (69% *vs.* 54%, p=0·005, and 72% *vs.* 61%, p=0·01, respectively) for patients with localized tumours.2 The addition of ifosfamide—etoposide (IE) to vincristine—doxorubicin—cyclophosphamide (VAC) in the INT-0091 study did not improve the outcome for patients with metastases.[2] There has not been significant progress in the treatment of patients with metastases. Our pt also represents this finding. In spite of giving (VAC/IE) schedule of chemotherapy no significant response occurred.

In case of metastasis or relapse, increasing the doses of doxorubicin, cyclophosphamide, and ifosfamide by 20%, 83%, and 56%, respectively, in the same protocol also produced no improvement, rather greatly increased acute toxicity and the incidence of secondary leukaemia and myelodysplasia.[3]

Survival after metastasis of ES is also poor, with only about 10% of patients event free at 5 years.[4,5] Patients whose primary tumors are excised might survive more often, although the

prognostic influences of site and size complicate the analyses.[6] Our finding also agree with the above results.

Conclusion:

In country like Bangladesh where tuberculosis is very prevalent, it comes as the first diagnosis of pain in pelvis. But one should always consider the differential diagnosis, so that less prevalent diseases like bone tumor will not be under diagnosed. As early diagnosis is established & subsequent proper treatment initiated 5 year survival approximates to 75%.

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