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ORIGINAL ARTICLES

Comparative Study of the Effects of Air Pollution on Pulmonary Function between Smokers and Non-Smokers

R Chakrabortty[1], GSLH Bhuiyan[1], KS Bennor[2], KH Jessy[2], MA Hossain[3] J Islam[2], MA Qayyum[2], MM Hiron[3]

Abstract:

This study was conducted to see the effects of air pollution on pulmonary function among the smokers and non-smokers in industrial and residential areas. This cross sectional study was conducted in Tejgaon industrial area and Dhanmondi residential area among smokers and non-smokers for a period of two years. The main objective was to elucidate the effects of air pollution among smokers and non-smokers residing in Tejgaon industrial area and Dhanmondi residential area.

Total number of enrolled subjects was 909 on the basis systematic random sampling. Among them, 40.7% were smokers and 59.3% were nonsmokers. From Tejgaon industrial area 449 respondents were included where smokers and non-smokers were 36.1% and 63.9% respectively. From Dhanmondi residential area 460 respondents were included where smokers and non-smokers were 46.2% and 53.8% respectively. The mean age was 27.4 ± 7.7 years among male and that of among female was 26.1 ± 7.8 years. A standard questionnaire was prepared for data collection, sociodemographic characteristics, smoking pattern, air pollution level, all were evaluated. Chi square test, unpaired student's t test and ANOVA were used for statistical analysis. A p value of <0.05 was considered as significant.

The level of air pollution such as suspended particulate matter (SPM) in Tejgaon industrial area and residential area was 386.21 microgram/m^3 and 146.97 microgram/m^3 respectively. The concentration of particulate matter (PM2.5), particulate matter (PM10), Carbon monoxide (CO), Sulphur dioxide (SO2), Nitrogen dioxide (NO2) and Ozone (O_3) in Tejgaon industrial area and Dhanmondi residential area were 93 microgram/m^3 & 76.37 microgram/m^3, 91.27 microgram/m^3 & 73.67 microgram/m^3, 334 mg/m^3 83.33 mg/m^3, 23.64 microgram/m^3 & 1.28 microgram/m^3, 22.93 microgram/ m^3 & 40.49 microgram/ m^3 and 0.018 ppm & 0.015 ppm respectively.

Chest diseases, cough., shortness of breath, itching of eye, running nose & chest tightness were significantly higher among the resident stayed in Tejgaon industrial area compared to Dhanmondi residential area (p<0.001). Peak Expiratory Flow Rate (PEFR) reduced both in Tejgaon industrial and Dhanmondi residential area which were 18.20 ± 12.4% and 11.92 ± 7.9% respectively. It also showed that it reduced more among the smokers than non-smokers which was statistically significant (p<0.001). Change of Forced Expiratory volume in first second (FEV1) was also reduced in Tejgaon industrial and Dhanmondi residential areas which was also statistically significant. It was also evident that changes were more among the smokers and industrial area where air pollution level was also high and it was also statistically significant.

In summary, we found a significant association between exposure to high level of air pollution and pulmonary function tests (PEFR, FEV1 and FVC) in both smokers and non-smokers, and most important we demonstrated that air pollution has significantly greater effects on pulmonary function in smokers than in never smokers in industrial area than residential area.

[Chest & Heart Journal 2006; 30(1) : 1-13]

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Introduction:

In Dhaka city pollution of air occurs due to industrial and vehicular sources and mainly from automobile vehicles. Air pollution in Dhaka is serious due to increasing population and associated motorization. From the existing air quality monitoring data it is quite clear that the average ambient concentration of suspended particulate matter and other pollutants are higher than Bangladesh National Air quality standard and much higher than WHO guidelines[1]. Particularly the city's average suspended particulate matter (SPM) was two times higher than the Bangladesh standard 200 microgram/m^3 (24 hours) in commercial area. Severe air pollution is threatening human health and economic growth in Dhaka city. If city's annual average pollutant level were reduced to Bangladesh national standard, it is estimated that taking this action would annually result in 3580 fewer premature deaths, 10 million fewer restricted activity days and 87 million fewer respiratory symptoms days. The economic benefit associated with avoiding these health problems could range from a low estimate of 60 million to a high estimate of $ 270 million, equivalent to 6.7% to 7.5% of the city's gross product[2].

Air pollution survey 1990 found that the major industrial area like Tejgaon in Dhaka was not the main source of air pollution but was also due to vehicles and the brick field built around the city which was responsible for the severe air pollution in Dhaka city[1].

Analysis of ambient air sample of Dhaka city for seven days of the month 1998 shows that near Farmgate police box, suspended particulate matter (SPM) was on average higher than standard value for commercial and residential area that is more than 400 microgram/m^3 and on 10th December 1998 it was 2785.42 microgram/m^3. On the same day nitrogen dioxide (NOx) was 94 microgram/m^3 and sulphur dioxide (SOx) was 153.04 microgram/m^3 which were also more than WHO Guide lines. So the over all air pollution is very alarming as the most recent data shows[1].

Half of all regular cigarette smokers will eventually be killed by their habit. In 1995 in developed countries some two million deaths could be attributed to tobacco, in developing countries one million. Within 30 years these figures are likely to increase to 3 and 7 million respectively. Smoking increases the absolute number of deaths from lung cancer, cancer of the other respiratory sites, chronic bronchitis/emphysema and cor pulmonale. Stopping smoking, even in middle age, reduces the risk of dying from smoking-related diseases and reduces disability. Smoking usually begins for psychosocial reasons, such as parental smoking, curiosity, peer pressure, rebelliousness and assertion of independence. Once it becomes regular the pharmacological properties of nicotine are a major influence on the persistence of the habit, which appears to become advantageous to mood and/or life response[3].

There is strong evidence that air pollution and cigarette smoking have adverse effects on respiratory health, but whether the joint effects of air pollution and personal smoking are additive or synergistic remains undocumented. Of particular public health and clinical importance is whether air pollution confers differential risk for adverse respiratory-health outcomes among smokers versus never smokers. It is biologically plausible that such a synergistic effect may exist. The mechanisms by which inhaled pollutants induce adverse health effects depend on the ability of these pollutants to penetrate and deposit in the lung, as well as on subsequent biological responses to the deposited material. Investigators have reported that smoking affects both airway and pulmonary parenchyma, thereby causing airway inflammatory responses and hypertrophy and hyperplasia of mucus glands, increased airway reactivity, and decreased terminal rate of clearance. These changes may, in turn, impair the airway defense mechanisms that clear the inhaled air pollutants and/or alter the airway responses to the material deposited[4].

A large and growing body of literature has documented acute effects of air pollution on mortality, hospital visits and admissions, and

respiratory symptoms and pulmonary function[5]. There is also convincing evidence about chronic deleterious health effects of air pollution. Investigators have long recognized that active smoking is a risk factor for lung cancer and chronic respiratory diseases. In the 1985 Surgeon General's Report, significant interaction effects between smoking and occupational exposure on chronic bronchitis were documented.

A study on "smoking, air pollution and bronchitis in Britain" (lancet Saturday) the prevalence of respiratory symptoms has been carried out in a large sample of the British population. Prevalence –rates for symptoms rise with increasing level of air pollution independently of cigarette consumption. In smokers, high level of pollution is associated with more frequent respiratory symptoms.

In a study[4] wrote on the "synergistic effects of air pollution and personal smoking on adult pulmonary functions". This particular article shows how air pollution, combined with cigarette smoking has a strong adverse effect on the individuals respiratory health, due to the pollutants in the air, and the materials which penetrate and deposit in the individuals lungs. Smoking combined with pollution causes "airway inflammatory responses and pulmonary parenchyma, thereby causing airway inflammatory and hypertrophy and hyperplasia of mucus glands, increased airway reactivity, and decreased terminal rate of clearance".

Methodology:

This study was carried out in the Dhaka city over a period of two years. Two areas were selected for the study. One are was Tejgaon which is an industrial area and another one was Dhanmondi which is a residential area.

This was a cross-sectional and descriptive type of study. It was conducted to see the effects of air pollution on pulmonary function among smokers and non-smokers in industrial and residential areas.

Initially 1000 populations were selected on the basis of systematic random sampling for the study from two areas. From each area 250 smokers and 250 non-smokers were taken. Among them, 91 data were excluded from analysis due to inconsistent response and incomplete information. So, finally a total of 909 respondents were analyzed in which 449 were from Tejgaon industrial area and 460 were Dhanmondi residential area.

With the help of respiratory Dust Sampler (RDS) air pollution was measured in the two regions. The pollutants that were measured are Suspended Particulate Matter (SPM), Particulate Matter ($PM_{2.5}$), Particulate Matter (PM_{10}), Sulphur Dioxide (SO_x), Nitrogen di oxide (NO_x), and Ozone (O_3).

Inclusion criteria:

- Persons of 15-45 age groups.
- Persons of either sex.
- Persons residing in the particular areas for at least 1 year.
- Persons staying at the particular areas for more than 8 hours per day.

Exclusion criteria:

- Less than 15 year
- More than 45 year (due to diagnostic inconsistency)
- Significantly disabled persons.
- Diagnosed chest disease patients (asthma, COPD, TB)
- Person unable to perform spirometric procedure

For this study the following parameters were recorded

1. Body weight
2. Height
3. Completion of data form
4. Spirometry.

After collection of data from the two regions, air pollutants will be compared in the two regions. Pulmonary functions specially PEFR, FVC and FEV_1 were also be compared among the smokers

and non-smokers in each area and then with two regions.

All the collected data were compiled and tabulated in a master sheet and analyzed statistically using the Statistical Package for Social Science (SPSS) programme, version 12.0, in computer. Chi square test, unpaired student's t test and ANOVA were used to find out the differences of different variables. A two-tailed p value less than 0.05 was considered as significant.

Observations and Results:

The mean family size of the Tejgaon area was 5.02±2.1 and that of Dhanmondi residential area 4.67±2.0. Analysis indicated that the family size significantly higher in Tejgaon area than the Dhanmondi residential area.

To determine the social class of the respondents, Principal Component Analysis (PCA) was done using the household assets of cassette/CD player, Television, VCD or DVD player, refrigerator, computers, motor cycle/car and living in own house or land lord. Index of all parameters was further ranked into very poor class, poor class, middle class and rich. Analysis indicated that the residents from Tejgaon area was poor than the Dhanmondi residential area and the difference was statistically significant ($p<0.001$).

It was evident that the percentage of bronchitis/ COPD was higher among the studied families (10.8%) followed by asthma (6.2%), pneumonia (2.8%) and lowest tuberculosis (2.4%). Analysis also indicated that the proportion of bronchial asthma and tuberculosis was higher in the Tejgaon area whereas bronchitis or COPD and pneumonia was higher in Dhanmondi residential area, but the difference was not statistically significant ($p>0.05$).

Table-I

Distribution of the respondents by family size

Family size	Study area				*Total*		p value
	Tejgaon		Dhanmondi				
	No.	*%*	*No.*	*%*	*No.*	*%*	
1-2	44	9.8	39	10.3	83	10.0	
3-4	147	32.7	159	42.2	306	37.0	
5-6	157	35.0	130	34.5	287	34.7	
e"7	101	22.5	49	13.0	150	18.2	
Total	449	100.0	377	100.0	826	100.0	
Mean±SD	5.02±2.1		4.67±2.0		4.86±2.1		0.016
Range	1-13		1-13		1-13		

Table-II

Distribution of the respondents by social class

Social Class (Score of social class)	Study area				*Total*		p value
	Tejgaon		Dhanmondi				
	No.	*%*	*No.*	*%*	*No.*	*%*	
Very poor (-1.81497—1.33359)	162	36.1	49	13.0	211	25.5	0.001
Poor (-1.01082-.15492)	103	22.9	55	14.6	158	19.1	
Middle class (.35745-.85558)	144	32.1	117	31.0	261	31.6	
Rich (.90034-1.33696)	40	8.9	156	41.4	196	23.7	
Total	*449*	*100.0*	*377*	*100.0*	*826*	*100.0*	

Table-III

Distribution of the respondents by pattern of chest diseases

Pattern of chest disease	Study area						p value
	Tejgaon (n=449)		Dhanmondi (n=377)		*Total (N=826)*		
	No.	*%*	*No.*	*%*	*No.*	*%*	
Bronchitis/COPD	8	9.3	15	11.9	23	10.8	0.550
Asthma	26	5.8	25	6.6	51	6.2	0.608
Pneumonia	2	2.3	4	3.2	6	2.8	1.000
Tuberculosis	12	2.7	8	2.1	20	2.4	0.548
Total	*449*	*100.0*	*377*	*100.0*	*826*	*100.0*	

The mean age of the male respondents was 27.4±7.7 years and that of female patients was 26.1±7.8 years. No statistically significant mean age difference was found between male and female patients ($p>0.05$). Among the male patients, highest percentage were (43.1%) in the range of 25 to 34 years followed by in the range of 15 to 24 years (37.9%) whereas among the female patients highest percentage were in the range of 15-24 years (46.1%) followed by 25 to 34 years (33.9%).

Analysis revealed that respondents from Tejgaon area were more younger (mean age 24.4 years) than the Dhanmondi area (mean age 30.2 years) and the mean age difference was statistically significant ($p<0.001$), however, no statistically significant sex difference was found between two areas ($p>0.05$), though the proportion of male respondents was higher in Dhanmondi area (82.2%) than the Tejgaon area (77.7%). It was evident that the proportion of illiterate respondents was higher in Tejgaon area (8.5%) than the Dhanmondi area (2.0%). Regarding the occupation of the respondents, the proportion of business and laborer were higher in Tejgaon area whereas service holders were more in the Dhanmondi area and the difference was statistically significant ($p<0.001$).

It was evident that the proportion of chronic disease was higher among the respondents stayed in the Dhanmondi (4.3%) and it was 1.6% in the Tejgaon area and the difference was statistically significant ($p<0.01$). Regarding the pattern of disease, cardiovascular and diabetes were higher among the respondents stayed in Dhanmondi area whereas arthritis and tumour were higher in the Tejgaon area. However, no statistically significant difference was found between two areas in terms of night stay ($p>0.05$). The mean duration of stay in the Dhanmondi area was 5.9 years and that of Tejgaon area was 4.9 years and mean difference was statistically significant ($p<0.05$). Similarly a statistically significant mean difference was found between study area and duration of stay in day time ($p<0.001$) indicating that the respondents in Tejgaon area stayed in workplace long time (13.4±6.0 hours) than the Dhanmondi area (11.6±5.1 hours).

Table-IV

Distribution of the respondents by age and sex

Age in years	Sex				Total (N=909)		p value
	Male (n=729)		Female (n=180)				
	No.	*%*	*No.*	*%*	*No.*	*%*	
15-24	276	37.9	83	46.1	359	39.5	
25-34	314	43.1	61	33.9	375	41.3	
35-44	139	19.1	36	20.0	175	19.3	
Mean±SD (yrs)	27.4±7.7		26.1±7.8		27.1±7.7		*0.052*

Table-V

Distribution of the respondents by demographic characteristics and study area

Variables	Study area				Total (N=909)		p value
	Tejgaon (n=449)		Dhanmondi (n=460)				
	No.	*%*	*No.*	*%*	*No.*	*%*	
*Age in years							
15-24	259	57.7	100	21.7	359	39.5	0.001
25-34	122	27.2	253	55.0	375	41.3	
35-44	68	15.1	107	23.3	175	19.3	
Mean±SD(yrs)	24.4±7.7	30.2±6.4	27.0±7.7				
Sex							
Male	349	77.7	380	82.6	729	80.2	0.065
Female	100	22.3	80	17.4	180	19.8	
*Years of schooling							
No schooling	38	8.5	9	2.0	47	5.2	
1-5	88	19.6	25	5.4	113	12.4	
6-10	168	37.4	47	10.2	215	23.7	
11-15	147	32.7	135	29.3	282	31.0	
e"16	8	1.8	244	53.0	252	27.7	
Mean±SD	8.3±3.9	14.6±3.8	11.1±5.0	0.001			
Main occupation							
Unemployed	5	1.1	5	1.1	10	1.1	0.001
Bussines (Indoor)	57	12.7	25	5.4	82	9.0	
Business (outdoor)	12	2.7	8	1.7	20	2.2	
Service (indoor)	188	41.9	316	68.7	504	55.4	
Service (outdoor)	10	2.2	28	6.1	38	4.2	
Day labourer	5	1.1	1	0.2	6	0.7	
Rickshapuller	4	0.9	2	.4	6	0.7	
Housewife	37	8.2	25	5.4	62	6.8	
Student	131	29.2	50	10.9	181	19.9	

Table-VI

Distribution of the respondents by study area and selected variables

Variables	Study area				Total (N=909)		p value
	Tejgaon (n=449)		Dhanmondi (n=460)				
	No.	%	No.	%	No.	%	
Having chronic disease							
No	442	98.4	440	95.7	882	97.0	0.013
Yes	7	1.6	20	4.3	27	3.0	
Name of the disease							
Arthritis	2	28.6	0	0.0	2	7.4	-
Tumour	1	14.3	0	0.0	1	3.7	
Diabetes	0	0.0	4	20.0	4	14.8	
Backache	0	0.0	1	5.0	1	3.7	
Cardiovascular disease	4	57.1	14	70.0	18	66.7	
Gynaecological disease	0	0.0	1	5.0	1	3.7	
Night stay in the area							
Yes	225	50.1	218	47.4	443	48.7	0.412
No	224	49.9	242	52.6	466	51.3	
*Duration of stay (years)							
1-3	247	55.0	165	35.9	412	45.3	
4-6	58	12.9	139	30.2	197	21.7	
7-9	65	14.5	77	16.7	142	15.6	
10-12	53	11.8	40	8.7	93	10.2	
e"13	26	5.8	39	8.5	65	7.2	
Mean±SD	4.9±4.8	5.9±5.0	5.4±4.9	0.003			
*Duration of day stay (hours)							
8-12	219	48.8	302	65.7	521	57.3	
13-16	63	14.0	66	14.3	129	14.2	
16-20	58	12.9	15	3.3	73	8.0	
20-24	109	24.3	77	16.7	186	20.5	
Mean±SD	13.4±6.0	11.6±5.1	12.6±5.7	0.001			

It was observed that the proportion of complaints of cough (32.5%), itching eye (30.7%), running nose (29.2%), difficulty in breathing (13.6%), feeling of tightness of chest (12.7%) and pain throat (5.8%) were significantly high among the respondents stayed in the Tejgaon area compared to Dhanmondi area ($p<0.001$), however no statistically significant difference was found in terms asthma ($p>0.05$), though the proportion was higher among the respondents in Tejgaon area.

The proportion of overall complaints was higher among the respondents of Tejgaon area (48.8%) than the Dhanmondi area (26.3%) and the difference was statistically significant ($p<0.001$). It was found that among the respondents from Tejgaon area these complaints appeared to be new (72.1%) and also increase the previous complaints (18.3%) whereas in the Dhanmondi area it remains as usual or decreased. The respondents from Tejgaon area feel well if he/she moves elsewhere from their workplace ($p<0.001$). But no statistically significant association was found in terms of treatment seeking behaviour ($p>0.05$). Regarding the time exacerbation of symptoms, the respondents from Tejgaon area reportedly mentioned that it increased during night compared to Dhanmondi area and the difference was statistically significant ($p<0.001$). In terms of seasonal variation, the respondents from Tejgaon area mentioned that it significantly increased during summer and also winter ($p<0.001$).

The proportion of smokers were higher among the respondents in Dhanmondi area (46.2%) compared to Tejgaon area (36.1%) and the difference was statistically significant ($p<0.05$). Regarding the smoking other than respondents, a statistically significant difference was found indicated that the proportion of smokers were higher in Tejgaon area (54.6%) compared to Dhanmondi area (38.5%). The proportion of workplace smokers was higher in Tejgaon area (66.6%) than the Dhanmondi area (60.2%), but the difference was not statistically significant ($p>0.05$). On the basis of current and past smokers, it was found that out of 909 respondents, 38.9% were smokers and the rest were non smokers.

It was showed that all the air pollutants were higher than the Bangladesh Natural Air Quality Standard. It was also evident that pollution levels were more in Tejgaon industrial area than the Dhanmondi Residential area.

The following result indicated that both measured and predicted mean PEFR was significantly low among the respondents from Tejgaon area than Dhanmondi area. It was also noted that mean PEFR was significantly low among the smokers than non-smokers ($p<0.001$). Similarly the changes of PEFR was significantly high among the smokers than non-smokers of Tejgaon area ($p<0.001$), however no statistically mean difference was found between smokers and non-smokers of Dhanmondi area ($p>0.05$).

Table-VII

Distribution of the respondents by study area and complaints

Complaints	Study area				Total (N=909)		p value
	Tejgaon (n=449)		Dhanmondi (n=460)				
	No.	%	No.	%	No.	%	
Complaints	219	48.8	121	26.3	340	37.4	0.001
Cough	146	32.5	62	13.5	208	22.9	0.001
Itching eye	138	30.7	70	15.2	208	22.9	0.001
Running nose	131	29.2	62	13.5	193	21.2	0.001
Difficulty in breathing	61	13.6	27	5.9	88	9.7	0.001
Feeling of tightness of chest	57	12.7	26	5.7	83	9.1	0.001
Pain throat	26	5.8	11	2.4	37	4.1	0.010
Asthma	13	2.9	11	2.4	24	2.6	0.636

Table-VIII

Distribution of the respondents by study area and smoking and its pattern

Complaints	Study area				Total		p value
	Tejgaon		Dhanmondi				
	No.	%	No.	%	No.	%	
History of smoking (respondent)							
Yes	162	36.1	174	46.2	336	40.7	0.003
No	287	63.9	203	53.8	490	59.3	
Pattern of smoking							
Cigarette	160	98.8	174	100.0	334	99.4	-
Bidi	2	1.2	0	0.0	2	.6	
No. of sticks/day							
1-5	90	55.6	57	32.8	147	43.8	
6-10	47	29.0	63	36.2	110	32.7	
11-15	9	5.6	30	17.2	39	11.6	
e"16	16	9.9	24	13.8	40	11.9	
*Mean±SD	7.5±6.1		9.6±6.3		8.6±6.3		0.002
Duration of smoking (years)							
<5	66	40.7	32	18.4	98	29.2	
5-9	48	29.6	56	32.2	104	31.0	
10-14	26	16.0	51	29.3	77	22.9	
e"15	22	13.6	35	20.1	57	17.0	
*Mean±SD	7.0±6.5		9.4±5.8		8.3±6.3		0.001
History of smoking (other than respondent)							
Yes	245	54.6	145	38.5	390	47.2	0.001
No	204	45.4	232	61.5	436	52.8	
No. of smokers in the family							
1	190	77.6	108	74.5	298	76.4	
2	34	13.9	15	10.3	49	12.6	
e"3	21	8.6	22	15.2	43	11.0	
*Mean±SD	1.3±0.7		1.5±0.9		1.4±0.8		0.090
Smoker in workplace							
Yes	299	66.6	227	60.2	526	63.7	0.058
No	150	33.4	150	39.8	300	36.3	

Table-IX

Air quality in Dhaka City in the study

Pollutant	Bangladesh Standard (mgm/m^3)	Average time	Dhanmondi R/A (mgm/m^3)	Tejgaon I/A (mgm/m^3)
Suspended particulate matter (SPM)	200	8	146.97	386.21
Particulate matter (PM2.5)	15	8	76.37	93
Particulate matter (PM10)	50	8	73.67	91.27
Carbon monoxide (COx)	$10mg/m^3$	1	83.33	334
Sulpher dioxide (SOx)	80	8	1.28	23.64
Nitrogen dioxide (NOx)	100	8	40.49	22.93
Ozone (O^3)	0.08 ppm	8	0.015322	0.01877

Table-XI

Mean PEFR of the respondents of the study area (Smokers versus non-smokers)

Area	PEFR L/min (Measured)			PEFR L/min (Predicted)		
	Overall	*Smoker*	*Non- smoker*	*Overall*	*Smoker*	*Non- smoker*
Tejgaon	391.79±99.6	357.43±105.9	411.18±90.5	479.37±96.0	465.91±111.1	486.97±85.7
Dhanmondi	469.63±79.6	465.24±70.0	472.78±85.8	533.47±80.5	525.83±73.6	538.94±84.9
Total	431.18±98.1	415.91±103.2	440.92±93.4	506.75±92.5	498.41±97.2	512.06±89.1
p value	0.001	0.001	0.001	0.001	0.001	0.001

Table-XII

Reduction in percentage of PEFR of the respondents of the study area (Smokers versus non-smokers)

Area	Percentage of changes of PEFR			p value
	Overall	*Smoker*	*Non- smoker*	
Tejgaon	18.20±12.4	22.84±13.6	15.59±10.9	0.001
Dhanmondi	11.92±7.9	11.42±6.4	12.27±8.8	0.258
Total	15.02±10.8	16.64±11.8	13.99±10.1	0.001
p value	0.001	0.001	0.001	

From the table it was indicated that both measured and predicted mean FVC was significantly low among the respondents from Tejgaon area than Dhanmondi area($p<0.001$). But within area no statistically significant mean difference was found between smokers and non smokers ($p>0.05$).

Table-XII

Mean FVC of the respondents of the study area (Smokers versus non-smokers)

Area	FVC (Measured)			FVC (Predicted)		
	Overall	*Smoker*	*Non- smoker*	*Overall*	*Smoker*	*Non- smoker*
Tejgaon	2.17±0.6	2.13±0.5	2.19±0.6	3.86±0.7	3.77±0.6	3.92±0.7
Dhanmondi	2.39±0.7	2.37±0.6	2.41±0.7	4.19±0.6	4.18±0.4	4.20±0.6
Total	2.28±0.6	2.26±0.6	2.30±0.7	4.03±0.7	3.99±0.6	4.05±0.7
p value	*0.001*	*0.001*	*0.001*	*0.001*	*0.001*	*0.001*

Table-XIII

Reduction in percentage of FVC of the respondents of the study area (Smokers versus non-smokers)

Area	Percentage of changes of FVC			p value
	Overall	Smoker	Non- smoker	
Tejgaon	42.86±15.3	41.80±17.4	43.47±13.9	0.266
Dhanmondi	42.90±15.0	42.88±15.2	42.91±14.9	0.983
Total	42.88±15.1	42.39±16.2	43.20±14.4	0.429
p value	0.971	0.531	0.561	

It was also found that both measured and predicted mean FEV1 was significantly low among the respondents from Tejgaon area than Dhanmondi area ($p<0.001$). Within area, among the Tejgaon area statistically significant mean difference was found between smokers and non smokers ($p<0.05$), but no statistically significant difference was found in Dhanmondi area ($p>0.05$), however, the mean percentage of changes was higher among the smokers than the non smokers.

Table-XIII

Mean FEV1 of the respondents of the study area (Smokers versus non-smokers)

Area	FEV1 (Measured)			FEV1 (Predicted)		
	Overall	*Smoker*	*Non- smoker*	*Overall*	*Smoker*	*Non- smoker*
Tejgaon	1.79±0.6	1.72±0.6	1.84±0.7	3.23±0.6	3.19±0.7	3.26±0.5
Dhanmondi	2.12±0.7	2.02±0.6	2.19±0.7	3.51±0.5	3.47±0.5	3.54±0.5
Total	1.96±0.7	1.88±0.6	2.01±0.7	3.37±0.5	3.34±0.6	3.39±0.5
p value	*0.001*	*0.001*	*0.001*	*0.001*	*0.001*	*0.001*

Table-IVX

Reduction in percentage of FEV1 of the respondents of the study area (Smokers versus non-smokers)

Area	Percentage of changes of FEV1			p value
	Overall	*Smoker*	*Non- smoker*	
Tejgaon	43.13±17.5	44.73±18.0	41.40±16.2	0.045
Dhanmondi	39.62±16.7	41.17±16.1	38.52±17.1	0.941
Total	41.85±17.3	42.80±17.1	41.25±17.4	0.188
p value	*0.001*	*0.051*	*0.001*	

Discussion:

Tobacco related illness accounts for 16% death in Bangladesh among people aged 30 years and above. Hospital sample shows tobacco related accounts for 29% of all inpatient aged 30 years and above. Investigators have long recognized that active smoking is a risk factor for lung cancer and chronic respiratory illness[6]. Bangladesh is a developing country with limited resources and technological advancement. The problem of air pollution in large cities like Dkaka and Cittagong in Bangladesh is very difficult to tackle mainly because of financial constraints and lack of knowledge of the severity and dreadfulness of air pollution. The situation has worsened because of polluting vehicles drivers.

This study helped us to identify the effects of the present level of air pollution in Dhaka city. It also helped to see the effect of air pollution and smoking on pulmonary function individually and combinely as well as common symptoms associated with air pollution and smoking.

In this study 826 families were visited from where total 909 respondents were studied for this purpose. Among them 449 respondents were taken from Tejgaon industrial area and that of in Dhanmondi residential area areas was 460. Regarding monthly family income the residents of Tejgaon industrial area had lower income than Dhanmondi a residential area. Analysis of social class also indicated that the residents from Tejgaon area were poor than the Dhanmondi area and the differerence was statistically significant. In Tejgaon about 36.1% respondents were very poor and about 41.4% respondents in Dhanmondi were rich .

About 33.4% residents living in Dhanmondi residential area had family history of chest diseases where as about 19.2 respondents in Tejgaon industrial area had family history of chest diseases. This was probably due to awareness about health in Dhanmondi area. Among the pattern of chest diseases it was evident that the percentage of Chronic Obstructive Pulmonary Disease (COPD) was higher among the studied families followed by bronchial asthma and tuberculosis. About 5.79% respondents in Tejgaon industrial area and 6.63% respondents of Dhanmondi area were suffering from bronchial asthma. According to First National Asthma Prevalence Study (NAPS), 1999 the prevalence of bronchial asthma was 5.2%. So it correlates with this study.

Sociodemographic data of the study population were also evaluated. The mean age of male respondents was 27.4+7.7 years and that of female respondents were 26.1+7.8 years. It also stated that mean age of respondents in Tejgaon industrial area was 24.4+7.7 years where as it was in Dhanmondi residential area was 30.2+6.4 years. In Tejgaon male female ratio was 77.7%: 22.3% and that of in Dhanmondi residential area was 82.6% : 17.4% respectively.

It was also showed that the proportion of chronic diseases was higher among the respondents stayed in Dhanmondi residential area (4.3%) where prevalence of cardiovascular and diabetes were higher. The mean duration of stay in the Dhanmondi area was 5.9 years and that of in Tejgaon area was 4.9 years. The duration of stay in workplace is long in Tejgaon area than Dhanmondi area. In a study[7] it was showed that exposure to vehicular emission by living near busy roadway might contribute to symptoms of chronic respiratory diseases. In a study[8] it was showed that particulate air pollution is associated with asthma exacerbation and increased morbidity and mortality from respiratory causes. Ultrafine particles may contribute to these adverse effects because they have a higher predicted pulmonary deposition greater potential to induce pulmonary inflammation, larger surface area and enhanced oxidant capacity when compared with larger particles on a mass basis. In a study[9] showed that the outdoor nitrogen dioxide air pollution may be particularly important for the development of asthma and wheeze among children.

Regarding smoking pattern about 36.1% of respondents in Tejgaon area were smoker where about 46.2% respondents in Dhanmondi residential area were smoker. Among the smoker almost all the respondents from both areas were smoked cigarette. Overall in this study around 40% of respondents were smokerS and 60% of respondents were non-smokerS. This was probably due to amendment of anti tobacco law introduced in March, 2005.

In this study it was also evident that pulmonary function test (PFT) such as Peak Expiratory Flow Rate (PEFR), Forced Expiratory volume in first

second (FEV1) and Forced Vital Capacity (FVC) all were reduced in both Tejgaon industrial area and Dhanmondi residential area. However, it was more reduced in Tejgaon area than the Dhanmondi area. It was also stated that pulmonary function tests (PFT) were more reduced among the smoker than the non-smoker in both Tejgaon industrial area and Dhanmondi residential area which was statistically significant ($p<0.001$). In a study[10] it was showed that cigarette smoking is associated with reduced pulmonary function in adult person. it correlate with this study where pulmonary function was reduced among the smokers in both Tejgaon ad Dhanmondi areas.

Two community-based studies published more than two decades ago presented possible differences in the effects of air pollution on respiratory health between smokers and never smokers. In one of the studies[11] conducted their research on post office employees in London (293 men) and in three country towns (477 men). Investigators found that the London men had more frequent and more severe respiratory symptoms, produced more sputum, and had significantly lower levels of lung function than the men in the country towns. The effects appeared to be more prominent in smokers than in never smokers.

A study[12] showed that there is association between respirable particulate air pollution (PM10) and reduction of pulmonary function tests (FEV1 and FVC) of smokers with mild to moderate airflow limitation. A study[13] also showed exposure to ozone (O3) and other pollutants also causes deterioration of pulmonary functions of adult hikers. In another study[10] showed that smoking causes significant development of respiratory symptoms and deterioration of pulmonary function tests among occupationally exposed group. A study **(Wang et al. 1999)** also showed that difference in FEV! between the urban (more air pollution) and suburban (less air pollution were was reduced which is statistically significant.

In another study[14] it also showed that the subjects living areas with high level of air pollution showed higher prevalence rate of respiratory symptoms and a large decrease of FEV1 compared with those living in areas with low level of air pollution. In terms of increases respiratory symptoms and reduced FEV1 were seen in Tejgaon industrial area where air pollution level was also high. So it also correlates with this study.

In another study[4] it was showed that a significant association between long-term exposure to high levels of total suspended particle (TSP) and sulphur dioxide (SOx) and reduced FEV1 and FVC in both never smokers and smokers, and most important, we demonstrated that total suspended particle (TSP) and sulphur dioxide (SOx) have significantly greater effects on FEV1 and FVC in smokers than in never smokers. In a study[15], it was showed that the association between lung function and ambient concentration of respirable particles, suspended particulate matter (SPM), sulphur dioxide (SOx), ozone (O3). An increase of this air pollutant was associated with decrement in FEV1. A study[16] it showed that reduction of pulmonary function and higher airflow limitation or chronic respiratory symptoms were found among the smokers who were exposed to occupational exposure than those who were not exposed. In our study it showed that FEV1 was significantly reduced in Tejgaon industrial area where most of the above mentioned air pollutants level were higher which correlate with that study.

Conclusion:

In conclusion we found that a significant association between exposure to high concentration of air pollution and reduced pulmonary functions in both smokers and non-smokers and most important that this study showed that air pollution has significantly greater effects on reduction of pulmonary functions in smokers than never smokers.

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Coronary Risk Factor Profile In Patient with Ischemic Chest Pain and Normal Coronary Arteries

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Abstract

This prospective study was carried out at the department of cardiology , BSMMU and CMH, Dhaka , during the period of June 2000 to May 2001. Risk factor profile of 38(25%) patients with normal epicardial coronary arteries (32 males, 6 females, mean age 47.84 ± 8.50 years) out of 152 consecutive patients undergoing coronary angiography was analysed and compared with the risk factor profile of diseased coronary arteries (114 patients, 104 males and 10 females, mean age 50.85 ± 8.20). The mode of presentation in these patients was chronic stable angina (44.74% vs 46.49%), angina equivalents (7.89% vs 1.75 %) , atypical chest pain (34.21% vs 1.75%), unstable angina (5.26% vs 20.17 %) , acute Q wave myocardial infarction (2.63% vs 17.04%), acute nonQ myocardial infarction (2.63% vs 5.26%). Majority of patients had one risk factor but multiple (≥ 2) risk factors were not uncommon. A good number of cases had no risk factors. No significant differences in the number of risk factors were seen. The risk factor profile distributed between groups were dyslipidemia (39.47% vs 37.72%), hypertension (36.84% vs 44.74 %), diabetes mellitus (23.68 % vs 26.31%), smoking - current (39.47% vs 39.47%), smoking-past (26.31%vs 30.70%), BMI obesity (15.79% vs 8.77%), abdominal obesity(28.95% vs 17.54%), overweight (31.58%vs 34.21%), sedentary life style (15.79% vs 17.54%), family history of CAD (5.26% vs 7.89%), Type A personality(5.26% vs 4.38%). There were no significant difference between the two groups. The mechanism of myocardial ischemia in patients with normal coronary arteries is not fully understood. We conclude that approximately one forth of patients with ischemic chest pain and one or more conventional risk factors do not have atherosclerotic changes in their epicardial coronary arteries as seen on coronary angiography.

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Introduction

The concept of " risk factors" and their association with CAD evolved from the prospective epidemiological studies in the united states and Europe in 1957 [1,2]. In 1981, working group on atherosclerosis of National Heart Lung and Blood institute of USA had defined a risk factor as " any habbit or trait that can be used to predict an individual's probability of developing that disease" [3] . Major and independent risk factors for CAD are cigarette smoking, hypertension, high total cholesterol and LDL, low HDL, diabetes mellitus, and advancing age. The quantitative relationship between these risk factors and CAD risk has been

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elucidated by Framingham heart studies and other studies. Other factors are conditional and predisposing risk factors. Predisposing risk factors are those that worsen independent risk factors and these are obesity, abdominal obesity, physical inactivity, F/H of premature CAD and psychological factor. Causative, independent and quantitative contribution of conditional risk factors to CAD have not been well documented . These are high TG, small LDL particles, high serum homocysteine, high Lp(a), fibrinogen and CRP [4] . Several reports have focussed on risk factor analysis in patients with atherosclerotic CAD [5-8] . However similar data in patients with normal coronary arteries is sparse and no data available in Bangladeshi population. Thus in this present study we report our observation on the risk factor profile in patient with angiographically normal coronary arteries and comparison with diseased coronary arteries.

Materials and Methods

This prospective cross sectional study was carried out on 152 patients with clinical suspicion or by noninvasive way of having ischemic chest pain at the department of cardiology, BSMMU and CMH, Dhaka during the period of July 1999 to June 2001.

Patient clinically diagnosed and or documented to have ischemic chest pain who underwent coronary arteriography were taken as study subjects. Study subjects were divided into two groups depending on coronary arteriographic findings. Patients with normal coronary arteries in group I and with diseased or obstructed coronary arteries in group II.

Inclusion criteria : Patients were included in study only if they had one or more objective evidence of CAD.

1. History suggestive of ischemic chest pain
2. Ischemic chest pain presented with chronic stable angina, unstable angina, acute and old MI
3. EKG or echo or ETT evidence of ischemic chest pain.
4. Presentation with angina equivalents and atypical chest pain
5. All ages, both sexes, and who are willing to participate in the study

Exclusion criteria : Patients with congenital coronary anomalies, cardiomyopathy, congenital heart disease and other systemic diseases were excluded from the study

Risk factors

1. Hypertension (Systemic blood pressure $\geq$ 140/ 90 mm of Hg or taking antihypertensive medications)
2. Diabetes mellitus with evidence of hyperglycemia either fasting plasma glucose of 7.8 mmole/L (140 mg/dl) or post prandial 11.1 mmole/l (200 mg/dl) or more or patients taking antidiabetic medications.
3. Dyslipidemia (patient having serum total cholesterol > 200 mg/dl or LDL > 130 mg/dl, HDL < 35 mg/dl or TG > 150 mg/dl)
4. Cigarette smoking- current or past
5. Family history of CAD (premature CAD among first degree relative, male < 55 years and female < 65 years)
6. Obesity (Body mass index- BMI $\geq$ 30 kg /m2, overweight BMI 25-29)
7. Abdominal obesity (waist circumference $\geq$ 102 cm in case of male and $\geq$88 cm in case of female)
8. Sedentary life style
9. Type - A personality

Statistical analysis : Data analysis was done by SPSS. Most of the data were presented by using suitable tables, figures, chart and diagram and expressed as percentage. Parametric data were expressed as mean $\pm$SD in appropriate places.

Results

The mean age of 38 patients with normal coronary arteries was 47.84 $\pm$ 8.50 years (range= 30-75 years). The majority of patients were in the age range of 41-50 years (table-I). 32 (84.21%) were males and 6(15.79%) were females. Mean age of 114 patients with diseased coronary arteries was 50.85 $\pm$ 8.20 (range = 32-70 years) and this was statistically higher than normal coronary arteries group. Normal coronary arteries were relatively more common in 4th decade (21.05 vs 13.16%). Regarding sex distribution normal coronaries have relatively (male 84.21% vs 91.23% and female

15.79 vs 8.77 %) more female preponderence than diseased coronary group.Mode of presentations are summarized in table II . Majority of patients (44.74% vs 46.49%) underwent CAG due to chronic stable angina. Patients with normal coronary arteries presented more with atypical chest pain (34.21% vs 20.17%) and less with unstable angina (5.26% vs 20.17%) and AMI-Q (2.63% vs 17.54%) and the differences were statistically significant between the two groups. The number of risk factors in these patients are shown in table III . Majority (39.47%) of patients had one risk factor. The second commonest was patients with two risk factors (28.95%). Similar distribution was seen in patients with diseased coronary arteries.

Table-I

Age distribution

Age groups(years)	Normal coronaries(n=38)	Diseased coronaries(n=114)	P value
≤ 30	1 (2.63%)	0	
30-40	8(21.05%)	15(13.16%)	P < 0.05
41-50	17(44.74%)	47(41.23%)	P > 0.05
51-60	11 (28.95%)	38(33.33%	P > 0.05
61-70	0	14(12.28%	
>70	1(2.63%)	0	
Mean ± SD	47.84+9.50	50.85+8.20	P < 0.05
Range	30-75	32-70	P > 0.05

Table-II

Clinical presentations

Presentations	Normal coronaries(n=38)	Diseased coronaries(n=114)	P value
Chronic stable angina	17 (44.74%)	53 (46.49%)	> 0.05
Angina equivalents	3(7.89%)	2 (1.75)	> 0.05
Atypical chest pain	13(34.21%)	2 (1.75%)	< 0.001
Unstable angina	2(5.26%)	23 (20.17%)	< 0.05
AMI-Q	1(2.63%)	20 (17.54%)	< 0.05
AMI-NonQ	1(2.63%)	6 (5.26%)	> 0.05
OMI	1(2.63%)	8 (7.01%)	> 0.05

AMI- Acute Myocardial Infarction, OMI- Old Myocardial Infarction

Table-III

Distribution of number of risk factors

Number of risk factors	Normal coronaries(n= 38)	Diseased coronaries(n= 114)	P value
None	6 (15.79%)	13 (11.40%)	> 0.05
1	15 (39.47%)	41 (35.95)	> 0.05
2	11(28.95%)	43 (37.72%)	> 0.05
3	5 (13.15%)	15 (13.15%)	> 0.05
>3	1 (2.63%)	2 (1.75%)	> 0.05

Table-IV
Risk factor profile

Risk factor	Normal coronaries (n=38)	Diseased coronaries (n=114)	P value
Dyslipidemia	15 (39.47%)	43 (37.72 %)	> 0.05
Hypertension	14 (36.84%)	51 (44.74 %)	> 0.05
Diabetes mellitus	9 (23.68%)	30 (26.31 %)	> 0.05
Smoking (current)	15 (39.47%)	45 (39.47 %)	> 0.05
Smoking (past)	10 (26.31%)	35 (30.70 %)	> 0.05
Obesity (BMI)	6 (15.79 %)	10 (8.77 %)	> 0.05
Abdominal obesity	11 (28.95 %)	20 (17.54 %)	> 0.05
Overweight	12 (31.58 %)	39 (34.21 %)	> 0.05
Sedentary life style	6 (15.79 %)	20 (17.54 %)	> 0.05
Family H/O CAD	2 (5.26%)	9 (7.89 %)	> 0.05
Type A personality	2 (5.26 %)	5 (4.38 %)	> 0.05

Table-V
Pattern of dyslipidemia

Pattern of dyslipidemia	Normal coronaries (n=38)	Diseased coronaries (n= 114 0	P value
High TC	6 (15.79%)	39 (37.72 %)	< 0.05
High LDL-c	5 (13.16 %)	32 (28.04 %)	< 0.05
Low HDL- c	11 (28.95 %)	35 (30.70 %)	> 0.05
High TG	14 (36.84 %)	62 (54.38 %)	> 0.05

The risk factor profile in patients with normal coronary arteries and their comparison with diseased coronary arteries is summarized in table-IV. Dyslipidemia, hypertension, diabetes mellitus, smoking and overweight were commonest in both groups with no statistically significant difference (39.47% vs37.42%, 36.84 vs 44.74%, 39.47% vs 39.47%, and 31.58% vs 34.21% respectively). Pattern of dyslipidemia is shown in table- V. High TG and low HDL were more common than high total cholesterol and high LDL. High TC and high LDL were more common in patient with disease coronary than in patients with normal coronary. The most common risk factors encountered were hypertension (36.84%), current and past smoking (39.47% and 26.31% respectively). Abdomonal obesity was more common than BMI obesity in both groups. The mean BMI was 25.53 ± 3.89 and 24.14 ± 2.54 respectively. Mean waist circumference was higher (93.34 ± 10.25 cm) in normal coronary group than in diseased coronary group(87.71 ±8.71). A significant number of patients were overweight in both group of patients(31.58% vs 34.21%). Sedentary lifestyle, positive F/H of CAD and type A personality were present in 6 (15.79%), 2(5.26%), 2(5.26%) patients respectively.

Discussion

Though CAD is said to be multifactorial in origin, there are cases where no coronary risk factor can be found. However few studies have tried to look into the prevalence and profile of risk factors in patients with normal coronaries [5,6,8] .

Among patients referred for cardiac catheterization because of chest pain, 10-30% have either normal coronary arteries or only minor atherosclerosis [9-11]. Moreover 11% of patients referred for catheterization with diagnosis of unstable angina have normal coronary angiogram [12] . Thus patient with angina and normal coronary do constitute an important subgroup among patients undergoing coronary angiography.

In this study 25% of patients were found to have normal coronary arteries. The mode of presentations of these patient were chronic stable angina (45%), angina equivalents (8%),atypical chest pain (34%),unstable angina (5%), AMI-Q (2.5%), AMI-nonQ (2.5%) and OMI (2.5%).

Presentation with chronic stable angina is consistent with other reports. PT Upasani found normal coronary presented with CSA (44%), angina equivalents(20%), atypical chest pain(8.5%), UA (12%), OMI (16%) [13] . Momenuzzaman et al reported 39 % of patient with CSA and 32% of patients with ACP and other mode of presentation were UA(8%), MI(14%) [14] . Presentation of atypical chest pain is common with normal coronaries (1.75% vs 34.21%). This is consistent with analysis done by Diamond GA and Forrester. They found that presence of angiographic CAD to be 90%, 50% and 15% respectively in middle aged adults with history of typical angina, atypical angina or non anginal chest pain respectively [15,16] .

In this study while majority of patients with normal coronary arteries had one or two risk factors, multiple risk factors were not uncommon. However there was only one patient with more than 3 risk factors for CAD. This is in consistent with earlier two studies.

The distribution of risk factors among normal coronaries were dyslipidemia (39%), hypertension(37%), smoking(39%), overweight(31%), abdominal obesity (28.95%). Hypertension and dyslipidemia were also frequent in other studies.

There were no significant difference among the number of risk factors and their profile in normal and diseased coronary arteries. This similar association was also found in an earlier study.

Obesity defined by BMI was not much common in our study (15.79% in normal and 8.77% in diseased coronary artery group) but majority of patient felt into obese group defined by waist circumference. A good number of patients in both normal and diseased wcoronary group were overweight (31.57% vs 34.21%).In a study it was found that BMI of 22 or higher was associated with significant elevation of mortality from subsequent cardiovascular disease [17] .

Kemp et al carried out a follow up study on mortality rate in 200 patients with normal coronary arteries at CAG and concluded that it is no greater than expected for a normal cohort matched for age and sex [9] . Waxler et al in a follow up study of 86 women with normal coronary angiogram and chest pain resembling angina pectoris, found no instance of sudden death or MI and concluded that the syndrome has a benign prognosis [18] .

Despite a good prognosis and beneficial effect of reassurance for many patient, most continues to have chest pain that may result in visit to emergency room, admission to coronary care unit and even repeat cardiac catheterization. Thus an apparently benign condition may have considerable adverse effect on the quality of life , employment and the use of health care resources with attendant expenses [13] . Our present study is lacking such following study.

Several possible causes of chest pain in such patients have been proposed including psychiatric illness [18] , oesophageal dysfunction [19] and coronary microvascular dysfunction including an inadequate coronary vasodilator reserve [20-22] , overlap among the conditions has also been reported. Others have described an exaggerated sensitivity to cardiac and esophageal pain in patients who have chest pain despite normal coronary angiogram [20] . The proposed causes of MI in these patients include coronary artery spasm, coronary thrombosis with subsequent recanalization, platelet aggregation and coronary emboli. None of these can be detected by routine coronary angiogram [23,24] .

ETT was done in 18 (54.54%) patients of normal coronary arteries group, of these 11 (61.11%) patients were found to have positive ETT. This is nearly consistent with the data of previous reports by Waxler EB et al where 100 woman of unexplained chest pain with normal coronaries were analyzed and 44 patients underwent ETT and 16 (36%) were found to have positive ETT [18] . In other report also it was found to have positive ETT in 20% of cases of chest pain with normal coronary angiogram [9] .

Although we found that there were no difference in risk factor profile between normal and diseased coronary arteries still it gave us the importance of coronary angiogram in patient with ischemic chest pain. Uddin J et al found 30 patients of normal coronaries out of 200 patients. They studied the beneficial role of CAG in respect to cost. They assessed drug and hospital cost including urgent and elective consultation with general practitioner for 1 year period before and after CAG. The mean cost of health care per patient before CAG was

15130 TK/year. They found highly significant fall in all indices of resources consumption during 1 year following CAG (1076 TK/month) [25].

Conclusion

About 1/4 th of patient with ischemic chest pain may have normal coronary artery. One or more risk factors are frequently present in both the groups. Neither all patients with conventional risk factors have coronary artery disease nor all patients without any risk factors have normal coronary arteries.

Limitation of the study

Although our study overcome the limitation of comparison of normal and diseased coronaries that was not done in earlier studies still it has some limitations. One is the inclusion of less positive ETT cases and another is the lack of stress thallium to confirm ischemia. Last but not the least is follow up and prognosis of such patients.

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Comparative Study of Montelukast Plus Inhaled Budesonide with Double Dose Inhaled Budesonide in Adult Patients with Asthma

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Abstract

Background : Inhaled corticosteroids (ICS) affect many inflammatory pathways in asthma but have little impact on cysteinyl leukotrienes. This may partly explain persistent airway inflammation during chronic ICS treatment and failure to achieve adequate asthma control in some patients. This comparative 12 week study compared the clinical benefits of adding montelukast to budesonide with doubling the budesonide dose in adults with asthma.

Methods : Patients were randomised to receive montelukast 10 mg + inhaled budesonide 800 mg / day (n=53) or budesonide 1600 mg / day (n=52) for 12 weeks.

Results : Both groups showed progressive improvement in several measures of asthma control compared with baseline. Mean morning peak expiratory flow (AM PEF) improved similarly in the 12 weeks of treatment compared with baseline in both the montelukast + budesonide group and in the double dose budesonide group (33.5 v 30.1 l / min). Both groups showed similar improvements with respect to "as needed" b agonist use, mean daytime symptom score, nocturnal awakenings, exacerbations, asthma free days, peripheral eosinophil counts, and asthma specific quality of life. Both montelukast + budesonide and double dose budesonide were generally well tolerated.

Conclusion : The addition of montelukast to inhaled budesonide is an effective and well tolerated alternative to doubling the dose of inhaled budesonide in adult asthma patients experiencing symptoms and inadequate control on budesonide alone.

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Introduction

Chronic inflammation is recognized as a central component of asthma physiolosy.[1] Invading inflammatory cell in lung tissue release a wide variety of mediators and cytokines that contribute to the clinical characteristics of asthma. The cystinyl leukotriens[LTC4;,D4,E4]released from eosinophil and mast cells are important proinflammatory asthma mediators which give rise to bronchoconstriction,mucus secretion,increased vascular permiabiality,smooth muscle hypertrophy and inflammatory cell infiltration.[2] Inhaled corticosteroid[ICS] affect a variety of inflammatory pathways in asthma and represent a gold standard in anti-inflammatory treatment.However for some patient with persistent asthma ICS as prescribed

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may fail to achieve adequate control. Increasing the inhaled corticosteroid dose is one therapeutic option but clinical trial suggest this option may only help a proportion of patients and concern exist that high dose ICS may be associated with local and systemic side effects like osteoporosis,diabetes mellitus,hypertension,peptic ulcer diseases etc.This issue have led to trials of adding other agents to ICS rather than increasing the dose with results suggesting in the patient groups studied that adding other agents such as inhaled long acting $beta_2$-agonists may achieve at least similar benefits to increasing inhaled steroids.The principle that increasing inhaled steroids is only one option in patients with uncontrolled asthma receiving ICS alone has become accepted in guidelines. Research into the patho physiology of asthma has led to the devolopment of specific anti-inflammatory treatments including montelukast which blocks the interaction of cysteinyl leukotriens with their receptors and resulting down stream events. Since montelukast attenuates leukotrien mediated effects ,combination therapy with montelukast and ICS represents a theoretical alternative to increasing the ICS doses in patients inadequately controlled on ICS alone.[3] Although several study have demonstrated additive effects of monteiukast with ICS, none have compared this effect with higher doses of ICS as has been done with other treatments.[4] A prospective study, therefore can compare the clinical benefits of adding montelukast to inhaled budesonide with doubling the dose of inhaled budesonide in adult patients who are symptomatic on inhaled budesonide alone.[5 6]

Materials And Methods

This was a prospective study conducted among the patients having bronchial asthma who attended Asthma Centre of National Institute of Disease of the Chest and Hospital(NIDCH), Mohakhali,Dhaka.The study period was from January'2004 to December'2005.

Study population

Patients enrolled in the study were non-smokers ex-smokers(Stopped for at least 6 months and < 12 pack year history) diagnosed with asthma for> 1, year aged 18-55 years,who were not optimally controlled as judged by investigators in spite of a regular ICS prescription at doses of 600-1200 ug/ day for budesonide,triamcinolone,flunisolide and 300-800ug/day for fluticasone.Patients were required to have forced expiratory volume in 1 second(FEV1) values > 50% predicted at visits 1 and 3, together with >12% improvement in fev1 after B agonist administration,and symptoms requiring B agonist treatment of at least 1 puff/ day during the last 2 weeks of the run in period.

Patients were excluded if they had other active pulmonary disorders,respiratory infection within 3 weeks of visit 1 or during the run in period,treatment in an emergency setting within 2 months of visit 1, systemic corticosteroid treatment within 1 month,cromones or leukotriene receptor antagonists within 2 weeks,long acting antihistamine within 1 week(astemizole 3 months), or long acting B agonists or anticholinergic agents within 24 hours.The study was approved by the appropriate ethical review committees and each patient gave written informed consent.

A total number of 252 patients were screened in the study. 136 patients were included in the study. But 31 patients were dropped out. We could not contact them. Finally there were 105 patients.

Patients were randomized to two treatment groups for12 weeks . Group A(n = 53) (MON-BUD) received montelukast 10 mg /day (1 tab at bed time) in addition to inhaled budesonide 800 ¼gm/ day and group B(n = 52) (BUD 1600) received inhaled budesonide 1600 ¼gm/day (800 ¼g twice daily). Budesonide in both groups were identical in appearance. Patients were instructed to with hold inhaled $beta_2$-agonist (for 6 hours) and short acting antihistamines (within 48 hours) before followup visits (every 4 weeks).There were total 3 visits. Each visit was 4 weeks interval. Patients were given peak flow chart & were instructed to record the best recording out of 3 in morning and evening. Morning and evening peak expiratory flow (AM & PM PEF) was the prespecified primary end point. Other prespecifiied end points included daytime symptoms, nocturnal awakenings, asthma exacerbations, peripheral blood eosinophil counts and asthma specific quality of life.[7] Patients assessed day time asthma symptoms in the evening before bedtime using a validated diary card containing four questions. Patients also recorded nocturnal awakenings and overnight $beta_2$-agonist use .

Patients were allowed to use short acting $beta_2$-agonist on an "as needed" basis but were encouraged to use only the amount required. At base line and week 12, patients completed a validated self-administered asthma specific quality of life questionnaire. In each visit patients peak

flow chart was evaluated and physical examination was done and evaluated for any adverse effect.

The data collection through the above mentioned procedure were recorded systematically. All the data were collected from questionnaire forms and proforma. These data were then analyzed statistically by standard procedure to arrive at a definitive conclusion in respect to the objectives of the study.

Results And Observations

A total of 105 patients were studied and were divided into two groups. Fifty three patients were treated by montelukast plus inhaled budesonide considered as group A and the rest patients were treated by double doses of inhaled budesonide considered as group B.

Age distribution

The mean age of the patients was 32.52±12.53 years. The mean age of the group A patients was 32.02±12.5 years and group B patients was 33.04±12.7 years. No statistically significant mean age difference was found between two group of patients (p>0.05), the mean age was little bit higher in group B patients compared to group A patients.

Sex distribution

Among group A patients, highest percentage were male (56.6%) and 43.4% female. Whereas among group B patients, highest percentage were female (51.9%) and 48.1% were female, however, no statistically significant sex difference was found between two groups of patients (p>0.05).

Education of the patients

Among the studied patients, highest percentage had school level education followed by 31.4% had college level education and 17.1% had university level education and 8,6% were illiterate. However, analysis found no statistically significant difference between two groups of patients (p>0.05).

Socioeconomic condition

Analysis also found that majority of the patients were middle class socioeconomic status (76.3%) followed by poor (16.3%) and only 7.6% were rich. Analysis did not find any statistically significant difference between two groups of patients (p>0.05).

Table-I

Baseline characteristics of the study patients

Parameters	Study patients				Total (N=105)		*p value*
	Group A(n=53)		Group B (n=52)				
	No.	%	No.	%	No.	%	
Age in years							
<20	11	20.8	11	21.2	22	21.0	
20-29	12	22.6	11	21.2	23	21.9	
30-39	14	26.4	14	26.9	28	26.7	
40-49	11	20.8	10	19.2	21	20.0	
e"50	5	9.4	6	11.5	11	10.5	
Total	53	100.0	52	100.0	105	100.0	
Mean±SD (yrs)	32.02±12.5		33.04±12.7		32.52±12.53		0.679
*Sex							
Male	30	56.6	25	48.1	55	52.4	0.382
Female	23	43.4	27	51.9	50	47.6	
Level of education							
Illiterate	3	5.7	6	11.5	9	8.6	0.621
School	22	41.5	23	44.2	45	42.9	
College	19	35.8	14	26.9	33	31.4	
University	9	17.0	9	17.3	18	17.1	
Socioeconomic condition							
Rich	2	4.9	4	10.3	6	7.5	0.657
Middle class	32	78.0	29	74.4	61	76.3	
Poor	7	17.1	6	15.4	13	16.3	

Group A=treated by montelukast plus inhaled Budesonide
Group B= treated by double doses of inhaled Budesonide
*p value reached from chi square test

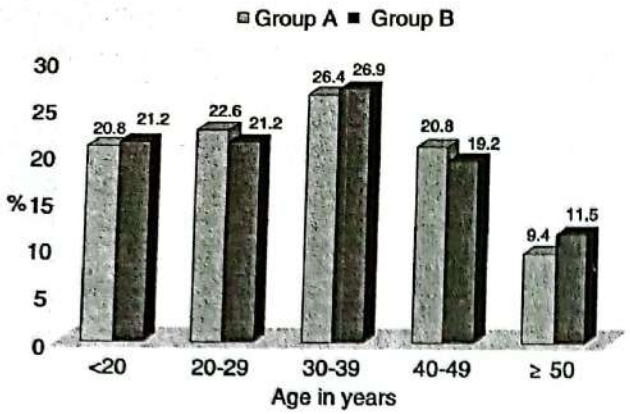

Fig.-1: *Age distribution of the study patients*

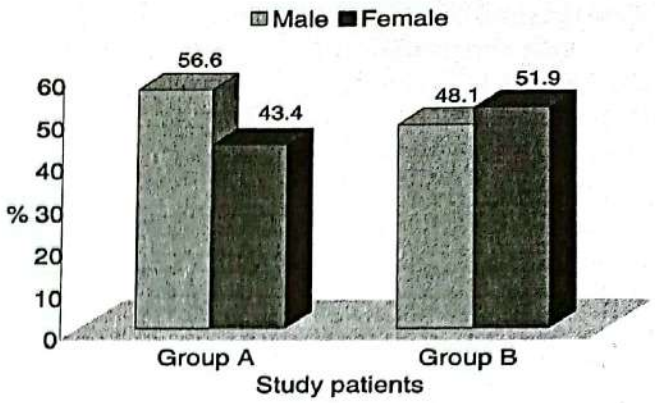

Fig.-2: *Distribution of study patients by sex*

Nutritional status

The mean height of the group A patients was 164.76±5.1 cm and group B patients was 165.26±6.8 cm. The mean weight of the group A patients was 64.65±4.3 kg and the group B patients was 66.12±5.9 kg.

The mean body mass index of the group A patients was 23.99±1.7 and group B patients was 24.51±1.9, however, no statistically significant difference of body mass index was found between two groups of patients (p>0.05).

Family history of asthma and duration of illness

It was found that among group A patients, 22.6% had family history of asthma and in group B patients, 32.7% had family history of asthma, however, analysis found no statistically significant difference between two groups of patients (p>0.05). The mean duration of illness for group A patients was 10.2 years and 11.3 years for group B patients. Analysis found no statistically significant mean difference between two groups of patients (p>0.05).

Table-II

Nutritional status of the study patients

Parameters	Study patients				Total (N=105)		*p value*
	Group A(n=53)		Group B(n=52)				
	No.	%	No.	%	No.	%	
Height in cm							
<155	1	1.9	5	9.6	6	5.7	
155-159	10	18.9	10	19.2	20	19.0	
160-169	32	60.4	24	46.2	56	53.3	
³170	10	18.9	13	25.0	23	21.9	
Mean±SD(cm)	164.76±5.1		165.26±6.8		165.01±6.0		0.666
Weight in kg							
<60	7	13.2	7	13.5	14	13.3	
60-64	23	43.4	12	23.1	35	33.3	
65-69	19	35.8	21	40.4	40	38.1	
³70	4	7.5	12	23.1	16	15.2	
Mean±SD(kg)	64.65±4.3		66.12±5.9		65.38±5.2		0.148
Body Mass Index							
<22	7	13.2	4	7.7	11	10.5	
22-23	18	34.0	14	26.9	32	30.5	
24-25	23	43.4	27	51.9	50	47.6	
³26	5	9.4	7	13.5	12	11.4	
Mean±SD	23.99±1.7		24.51±1.9		24.25±1.8		0.144

p value reached from unpaired student's t test

Table-III

Distribution of patients by family history of asthma and duration of illness

Parameters	Study patients				Total (N=105)		p value
	Group A(n=53)		Group B(n=52)				
	No.	%	No.	%	No.	%	
Family history of Asthma							
Yes	12	22.6	17	32.7	29	27.6	
No	41	77.4	35	67.3	76	72.4	0.249
Duration of illness (yrs)							
<5	19	35.8	17	32.7	36	34.3	
5-9	6	11.3	6	11.5	12	11.4	
10-14	13	24.5	14	26.9	27	25.7	
³15	15	28.3	15	28.8	30	28.6	
Mean ± SD (yrs)	10.2±7.5		11.3±8.4		10.7±8.0		0.457
Range (yrs)	1.50-26.0		1.50-32.0		1.50-32.0		

*p value reached from chi square test

Clinical presentation, persistence of symptoms and provocating factors

No statistically significant difference in terms of symptoms and clinical presentation was found between two groups of patients (p>0.05). Similarly, no statistically significant difference was found between two groups of patients in terms of provocating factors (p>0.05). However, pollen appeared to be the important factors for asthmatic attack.

Previous drug treatment

It was found that all the patients received beta$_2$-agonist and stroid. But 60.4% in group A and 53.8% in group received xanthenes. Analysis found no statistically significant difference between two groups of patients (p>0.05).

Table-IV

Distribution of patients by symptoms, persistence of symptoms and provocating factors

Parameters	Study patients				Total (N=105)		p value
	Group A(n=53)		Group B(n=52)				
	No.	%	No.	%	No.	%	
Symptoms							
Wheeze	53	100.0	52	100.0	105	100.0	-
Chest Tightness	53	100.0	52	100.0	105	100.0	-
Cough	53	100.0	52	100.0	105	100.0	-
Persistence of symptoms							
Whole year	36	67.9	38	74.5	74	71.2	p>0.05
Winter	15	28.3	12	23.5	27	26.0	
Summer	4	7.5	4	7.8	8	7.7	
Provocating factors							
Pollen	47	88.7	47	90.4	94	89.5	p>0.05
Dust	46	86.8	46	88.5	92	87.6	
Cold	27	50.9	29	55.8	56	53.3	
Feather	24	45.3	24	46.2	48	45.7	
Animal	11	20.8	11	21.2	22	21.0	
Smokes	14	26.4	8	15.4	22	21.0	
Food	5	9.4	8	15.4	13	12.4	
Hot	4	7.5	5	9.6	9	8.6	

*Multiple responses

*p value reached from chi square test

Table-V

Distribution of patients by previous drug history

Drug history	Study patients				Total (N=105)		p value
	Group A(n=53)		*Group B(n=52)*				
	No.	%	No.	%	No.	%	
$Beta_2$-agonist	53	100.0	52	100.0	105	100.0	-
Steroid	53	100.0	52	100.0	105	100.0	-
Xanthenes	32	60.4	28	53.8	60	57.1	0.498
Cromolyne	2	3.8	0	0.0	2	1.9	-

*Multiple responses
*p value reached from chi square test

Clinical Characteristics of the asthma patients

The mean asthma score for group A patients was 3.19 and for group B patients was 3.23. Analysis found no statistically significant mean asthma score between two groups of patients (p>0.05).

Pulse, blood pressure and respiration

Haemodynamics analysis of the patients in terms of pulse and blood pressure both systolic and diastolic blood pressure and respiratory rate had no statistically significant difference between two groups of patients (p>0.05).

Peak Expiratory Flow, FEV_1, FVC

The mean peak expiratory flow, forced vital capacity and forced expiratory volume in one second were 386.32±40.25 L/min, 4.18±0.44L, 2.85±0.49L in group A patients respectively and 383.67±38.12 L/min, 4.20±0.49L and 2.92±0.47L respectively in group B patients. Analysis found no statistically significant mean difference between two groups of patients (p>0.05).

Table-VI

Clinical characteristics of the study patients

Parameters	Study patients				Total (N=105)		*p value*
	Group A(n=53)		Group B(n=52)				
	No.	%	No.	%	No.	%	
Daily dyspnoea	47	88.7	47	90.4	94	89.5	0.775
Nocturnal dyspnoea more than two times per month	49	92.5	51	98.1	100	95.2	0.376
Dyspnoea required medications e.g. steroids, nebulize, therapy, aminophylline inj. or hospital admission	49	92.5	50	96.2	99	94.3	0.678
Persistent dyspnoea last six months or more or are you taking steroid tablets for one year or more	5	9.4	5	9.6	10	9.5	1.000
Baseline PEFR <60% of predicted value	9	17.0	5	9.6	14	13.3	0.267
Asthma Score		3.19±1.2		3.23±1.05		3.21±1.14	0.851

*p value reached from chi square test

Table-VII

Changes of pulse, blood pressure and respiration following treatment of the patients

Parameters	Study patients		Total (N=105)	*p value*
	Group A(n=53)	Group B(n=52)		
	Mean ± SD	Mean ± SD	Mean ± SD	
Pulse/minute	82.38±7.4	82.13±2.96	82.26±5.6	0.826
Systolic blood pressure (mmHg)	118.02±8.1	114.04±16.9	116.05±13.3	0.125
Diastolic blood pressure (mmHg)	75.70±5.6	76.27±7.2	75.98±6.4	0.650
Respiratory rate	17.49±2.9	17.48±2.8	17.49±2.8	0.980

p value reached from unpaired student's t test

Table-VIII

Mean distribution of patients by Peak Expiratory Flow, FVC, FEV_1

Parameters	Study patients		Total (N=105)	*p value*
	Group A(n=53)	Group B(n=52)		
	Mean ± SD	Mean ± SD	Mean ± SD	
PEFR (L/min)	386.32±40.25	383.67±38.12	385.01±39.04	0.730
FVC	4.18±0.44	4.20±0.49	4.19±0.46	0.852
FEV1	2.85±0.49	2.92±0.47	2.88±0.48	0.496

p value reached from unpaired student's t test

MINI Asthma Quality of Life Score

Each patient was evaluated by 7 scale questionnaire for Asthma related Quality of Life as 1 for All of the time, 2 for Most of the time, 3 for a good bit of the time, 4 for some of the time, 5 for a little of the time, 6 for hardly any of the time and 7 for none of the time. Total 15 questions were asked to evaluate the current status. Analysis indicated that asthma related quality of life significantly improved following treatment both the treatment modalities ($p<0.001$), however, between the group no statistically significant mean difference was found ($p>0.05$) which is shown as mean score against each question. This indicated that both the treatment modalities are equally effective (Table IXand X)

Morning and Evening variation of PEFR

Pre and post test evaluation of PEFR indicated that it significantly increased from morning level to evening ($p<0.001$). The PEFR increased 5.03% from pretreatment to 12th week of observation in group A patients at morning and it was 4.92% from pretreatment to 12th week at evening. Among group B patients, similar pattern of PEFR was observed. At morning reading, 4.38% increased from treatment to 12th week observation and at evening reading, 5.1% increased from pretreatment to 12th week.

Analysis of PEF L/minute between two group of patients indicated that though the morning evening changes was statistically significant within the group ($p<0.001$), but no statistically significant mean difference was found between two group of patients ($p>0.05$).

Nocturnal and daytime dyspnoea, nocturnal awakening and acute exacerbation

Analysis found that no statistically significant mean difference of different parameters studied ($p>0.05$) though the parameters studied showed a higher preponderance among the patients group B treatment module. It was also found that no patients suffered from acute exacerbation of asthma in the preceding month. Analysis also found that all study parameters were significantly improved following treatment within the group ($p<0.05$), however, no statistically significant difference was found between two groups of study patients ($p>0.05$). It was evident that few patients reportedly mentioned that they suffered from acute exacerbation of bronchial asthma. But no patients reports acute exacerbation of bronchial asthma following treatment.

Table-IX

Mean distribution of patients by MINI Asthma related quality of life score (before and after intervention)

Quality of asthma score	Group A			Group B		
	After	Before	p value	After	Before	p value
Feel short of breath as a result of your asthma	4.55±1.0	4.96±0.8	0.001	4.52±0.9	4.81±0.8	0.001
Feel frustrated as a result of your asthma	4.36±0.8	4.85±0.8	0.001	4.38±0.9	4.81±0.9	0.001
Feel bothered by coughing	4.28±1.0	4.94±0.8	0.001	4.27±1.0	4.75±0.9	0.001
Feel afraid of not having your asthma medication available	4.26±1.0	5.02±0.9	0.001	4.17±0.8	4.88±0.8	0.001
Experience a feeling of chest tightness or chest heaviness	4.40±1.0	4.96±0.8	0.001	4.50±0.9	4.98±0.8	0.001
Feel bothered by or have to avoid cigarette smoke in the environment	4.32±0.9	4.98±0.8	0.001	4.50±0.9	5.12±0.8	0.001
Have difficulty getting a good night's sleep as a result of your asthma	3.77±1.5	4.47±1.7	0.001	3.63±1.5	4.17±1.6	0.001
Feel concerned about having asthma	4.42±0.8	5.00±1.0	0.001	4.46±0.8	5.08±0.9	0.001
experience a wheeze in your chest	4.17±1.2	4.75±1.2	0.001	4.38±1.2	4.69±1.3	0.059
Feel bothered by or have to avoid going out side because of weather or air pollution	4.81±0.9	5.25±0.8	0.001	4.69±0.8	5.17±0.9	0.001
Strenuous activities (such as hurrying, exercising, running up, stairs, sports)	5.70±0.7	6.15±0.5	0.001	5.61±0.9	6.06±0.6	0.001
Moderate activities (such as walking, housework, gardening, shopping, climbing stairs)	4.77±1.2	5.26±0.8	0.001	4.75±1.1	5.29±0.8	0.001
Social activities (such as talking, playing with pets/children, visiting friends/relatives)	4.98±0.9	5.51±0.5	0.001	5.08±0.9	5.46±0.6	0.001
Work-related activities (tasks you have to do at work)	5.49±0.8	6.06±0.6	0.001	5.46±0.7	5.87±0.6	0.001
Feel bothered by or have to avoid dust in the environment	5.64±1.0	6.32±0.6	0.001	5.83±0.6	6.31±0.6	0.001
Composite score	5.3±0.5	4.67±0.6	0.001	5.16±0.5	4.68±0.57	0.001

p value reached from paired t test

Table-X

Mean distribution of patients by MINI Asthma related quality of life score (before and after intervention)

Quality of asthma score	*After treatment*			*Before treatment*		
	Group A(n=53)	Group B (n=52)	p value	Group A (n=53)	Group B (n=52)	p value
Feel short of breath as a result of your asthma	4.55±1.0	4.52±0.9	0.881	4.96±0.8	4.81±0.8	0.339
Feel frustrated as a result of your asthma	4.36±0.8	4.38±0.9	0.874	4.85±0.8	4.81±0.9	0.804
Feel bothered by coughing	4.28±1.0	4.27±1.0	0.943	4.94±0.8	4.75±0.9	0.253
Feel afraid of not having your asthma medication available	4.26±1.0	4.17±0.8	0.602	5.02±0.9	4.88±0.8	0.407
Experience a feeling of chest tightness or chest heaviness	4.40±1.0	4.50±0.9	0.590	4.96±0.8	4.98±0.8	0.905
Feel bothered by or have to avoid cigarette smoke in the environment	4.32±0.9	4.50±0.9	0.289	4.98±0.8	5.12±0.8	0.393
Have difficulty getting a good night's sleep as a result of your asthma	3.77±1.5	3.63±1.5	0.633	4.47±1.7	4.17±1.6	0.358
Feel concerned about having asthma	4.42±0.8	4.46±0.8	0.767	5.00±1.0	5.08±0.9	0.677
experience a wheeze in your chest	4.17±1.2	4.38±1.2	0.347	4.75±1.2	4.69±1.3	0.803
Feel bothered by or have to avoid going out side because of weather or air pollution	4.81±0.9	4.69±0.8	0.465	5.25±0.8	5.17±0.9	0.670
Strenuous activities (such as hurrying, exercising, running up, stairs, sports)	5.70±0.7	5.61±0.9	0.572	6.15±0.5	6.06±0.6	0.391
Moderate activities (such as walking, housework, gardening, shopping, climbing stairs)	4.77±1.2	4.75±1.1	0.916	5.26±0.8	5.29±0.8	0.874
Social activities (such as talking, playing with pets/children, visiting friends/relatives)	4.98±0.9	5.08±0.9	0.589	5.51±0.5	5.46±0.6	0.662
Work-related activities (tasks you have to do at work)	5.49±0.8	5.46±0.7	0.838	6.06±0.6	5.87±0.6	0.095
Feel bothered by or have to avoid dust in the environment	5.64±1.0	5.83±0.6	0.251	6.32±0.6	6.31±0.6	0.915
Composite score	5.23±0.5	5.16±0.5	0.503	4.66±0.6	4.68±0.6	0.851

p value reached from unpaired student's t test

Table-XI

Pre and post test evaluation of PEF following treatment of the study patients from peak flow chart

Parameters	Study patients		% of change (morning-evening)	p value (paired t)
	Morning Mean ± SD	Evening Mean ± SD		
Group A(n=53)				
Pretreatment	384.26±35.9	390.38±37.7	1.56±0.98	0.001
4th week	396.91±39.9	400.66±40.9	0.93±0.37	0.001
8th week	400.53±40.7	404.19±41.5	0.90±0.32	0.001
12th week	403.62±41.5	407.47±42.1	0.94±0.40	0.001
% of changes (before-after)	5.03±4.0	4.92±2.0		
Group B (n=52)				
Pretreatment	381.69±33.5	385.17±34.5	0.89±0.48	0.001
4th week	392.23±35.9	396.63±36.8	1.11±0.53	0.001
8th week	396.63±36.7	400.69±37.9	1.00±0.58	0.001
12th week	400.62±37.9	404.94±38.2	1.08±0.57	0.001
% of changes(before-after)	4.38±3.6	5.11±2.0		

p value reached from paired t test

Table-XII

Changes of PEF following treatment between two groups of patients

Parameters	Study patients				*p value*
	Group A (n=52)		Group B (n=53)		
	Mean ± SD	% of change	Mean ± SD	% of change	
Morning PEFR					
Pre-treatment	384.26±35.9	-	381.69±33.5	-	0.706
4th week	396.91±39.9	3.3	392.23±35.9	2.7	0.530
8th week	400.53±40.7	0.9	396.63±36.7	1.1	0.608
12th week	403.62±41.5	0.8	400.62±37.9	1.0	0.699
Evening PEFR					
Pre-treatment	390.38±37.7	-	385.17±34.5	-	0.462
4th week	400.66±40.9	2.6	396.63±36.8	3.0	0.597
8th week	404.19±41.5	0.9	400.69±37.9	1.0	0.653
12th week	407.47±42.1	0.8	404.94±38.2	1.1	0.748

p value reached from unpaired student's t test

Table-XIII

Changes of clinical parameters following treatment of the study patients

Parameters	Study patients				*p value* (unpaired t test)
	Group A(n=53) Mean ± SD		Group B(n=52) Mean ± SD		
	Pre	Post	Pre	Post	
Nocturnal dysponoea	1.30±1.2	1.13±1.2	1.32±1.2	1.46±1.2	p>0.05
Nocturnal awakening	1.67±1.2	1.13±1.2	1.69±1.3	1.46±1.2	p>0.05
Daytime dyspnoea	3.02±1.0	2.85±0.9	2.96±0.8	2.87±0.8	p>0.05
p value *(paired t test)*	p<0.05	p<0.05			

Changes of Eosinophil count

The mean eosinophil count was 591.13±328.9 in group A patients and 532.60±310.4 for group B patients and the mean difference was not statistically significant (p>0.05). During follow up, the eosinophil count decrease to 529.51±267.4 in group A patients and 483.62±260.3 in group B patients. The mean difference between two groups was not statistically significant (p>0.05). Analysis indicated that the mean percentage of reduction of eosinophil count was 8.53% in group A patients and 7.9% in group B patients, but the difference was not statistically significant (p>0.05).

Table-XIV

Changes of total eosinophil count following treatment of the study patients

Eosinophil count	Study patients		Total (n=105)	*p value*
	Group A (n=53)	Group B (n=52)		
	Mean ± SD	Mean ± SD	Mean ± SD	
Pre-treatment	591.13±328.9	532.60±310.4	562.14±319.7	0.351
Post-treatment	529.51±267.4	483.62±260.3	506.78±263.6	0.375
% of changes	8.53±4.9	7.88±3.9	8.21±4.4	0.456

p value reached from unpaired student's t test

Discussion

Asthma is an important chronic disorder of the airways with significant morbidity and mortality. Around 300 million people in the world currently have asthma. According to first National Asthma Prevalence Study (NAPS) 1999, in Bangladesh about 7 million people (5.2% of the population) are suffering from current asthma (at least three episodes of asthma attack in last 12 months).[8] More than 90% of them do not take modern treatment.

The disease causes physical, emotional and financial sufferings for patients leading to a deleterious effect on the overall socio-economic structure of the country. Asthma accounts for about 1 in every 250 deaths worldwide, although modern management can prevent 80% of such death. The economic cost of asthma is considerable both in terms of direct medical costs (such as hospital admissions and cost of pharmaceuticals) and indirect medical costs (such as loss of work time and premature death).[9 10]

Corticosteroid is the mainstay of treatment in asthma which affect many inflammatory pathways, but in our country there is rampant use of oral salbutamol, injectable aminophy lline and kitotifen in the management of asthma. Use of inhalers by the patients was found to be low and limited only to salbutamol and beclomethasone. [11]

Even though inhaled corticosteroids (ICS) affect many inflammatory pathways in asthma; but have little impact on cysteinyl leukotrienes . This may partly explain persistent airway inflammation during chronic ICS treatment and failure to achieve adequate asthma control in some patients. This issue has led to trials of adding other agents to ICS rather than increasing the dose.[12]

Budesonide, though less used in comparison with that of beclomethasone in our country it is widely used in the west and vastly studied.It can be even used in pregnancy and got brilliant safety profile.[6]

Our study showed no significant difference in response between asthmatics who took double dose inhaled budesonide & who took inhaled budesonide plus leukotriene receptor antagonist , montelukast.

This prospective study was conducted in National Institute of Diseases of Chest and Hospital (NIDCH), Mohakhali, Dhaka for a period of two years starting from January 2004 to December 2005. There were 105 patients. The patients were randomised into two groups. Group A who got low dose inhaled budesonide (800 ¼gm/day) plus montelukast (10mg tab at night) and group B who got double doses inhaled budesonide (1600 ¼gm/ day).

Socio-demographic data of the study subjects were evaluated . Patients within 18-55 years of age were enrolled in this study. This particular age range was considered from the fact that in developing countries the majority of disease and death occurs among the most economically active segment of population, more than75% among 18-55 years of age.[13]

The mean age of the patients were 32.52 ±2.53 years . The mean age of the group A were 32.02 ± 12.5 years and group B patients were 33.04 ±12.7 years .

Statistically significant mean age difference was found between two group of patients(p>0.05),the mean age was little bit higher in group B patients compared to group A patients.Among group A patients,the highest percentage of patients(26.4%) were in age group 30-39 years. Similar age patient was found in the group B patients with highest percentage (26.9%) were in the age group 30-39 years.

This mean age of the patients was consistant with the findings of Hossain& Hasan(1995) where mean age were 33±12.5 and 32±12.53 years respectively.[14]

Analysis of the patients in respect to sex showed male predominance with a male :female ratio of 1.1:1. This finding consistant with the findings of Price(2003) where male:female ratio was 1.5:1. In group A patients male predominated(56.6%) but in group B patients, highest percentage were female (51.9%). However, no statistically significant sex difference was found between two groups of patients (P>0.05).

Among the studied patients, highest percentage(42.9%) had school level education followed by college level education(31.4%) and followed by university level education(17.1). However, analysis found no statistically significant difference between two groups of patients (P>0.05). Educational background is important on giving information to the patients. Comperatively less educated people are becoming more aware of asthma & its management.This finding is consistent with Rahman (2001) where highest percentage of patients(45%) had school level education followed by college level education(34.5%).[15]

Analysis also found that majority of the patients were middle class of origin (76.3%) followed by poor(16.3%).This finding was almost similar to the findings of Rahman(2001) where 72% were middle class origin followed by poor(26.5%). This pattern of distribution reveled no statistically significant difference between two groups of patients (P>0.05).

So from the baseline characteristics of (age,sex,social condition,educational background) patients of both group were homogenous.Analysis did not find any statistically significant difference between two groups of patients (p>0.05).

The clinical information related to the present study was analyzed in detail. The mean body mass index of the group A patients was 23.99±1.7 and of group B patients was 24.51±1.9, however, no statistically significant difference of body mass index was found between two groups of patients (p>0.05). The patients were homogenous in that respect.

It was found that among group A patients 22.6% had family history of asthma and in group B patients 32.7% had family history of asthma, however analysis found no statistically significant difference between two groups of patients (P>0.05).This finding was almost similar to the findings of price(2003) wehere among group A patients 26.5% had family history of asthma and 31% in group B patients.As development of asthma has two distinct bases , hereditary and environmental; family history of asthma is a dominant factor.

The mean duration of illness for group A patients was 10.2 years and 11.3 years for group B patients. Analysis found no statistically significant mean difference between two groups of patients (P>0.05).It revealed that present study patients were suffering from asthma for a substantial period of time. This finding was almost similar to the findings of Sullivan(2003) where the mean duration of illness for group A patients was 12.6 years and 11.9 years for group B patients.[16]

Regarding the persistence of symptoms, 100% in group A and 98% in group B the symptoms persists whole the year, 28.3% in group A and 23.5% in group B during winter.No statistically significant difference of symptoms was found between two groups of patients (P>0.05). Similarly no statistically significant difference was found between two groups of patients in terms of provocation factors (P>0.05). However, pollen appeared to be the important factors for asthmatic attack. Pollen was provocating factor for asthma attack in 88.7% of group A patients and 90.4% in group B patients. Reddel(2005) reported pollen was provocating factor for asthma attack in 89.8% of group A patients and 92.4% in group B patients.[17] This finding was similar with us.

Regarding prior drug treatment, it was found that 100% of the patients received beta agonist & steroids in both group. But 60.4% in group A and 53.8% in group B received xanthines . Analysis

found no statistically significant difference between two groups of patients (P>0.05).

It showed that most of the patient used beta$_2$-agonist, this happened because good number of patients previously diagnosed and registered as suffering from bronchial asthma in asthma center, NIDCH and hence they got a good education regarding asthma medication specially about the reliever drugs . Also people are aware that reliever drugs improve asthma quickly. As those patients are suffering from long period of time, they have learned from practical experience.

Regarding clinical characteristics of the asthma patients, 92.5% patients of group A and 98.1% of group B had nocturnal dyspnoea more than two times per month. This is because we studied patient who were suffering from asthma for a bit of time.This finding is almost similar to Reddel(2000) where 98.5% patients of group A and 92.1% of group B had nocturnal dyspnoea more than two times per month. And we used step care score system,developed at the "National Asthma Center",Mohakhali,Dhaka.The mean asthma score for group A patients was 3.19 and for group B patients was 3.23. Anylysis found no statistically significant mean asthma score between two groups of patients (P>0.05).

Haemodynamic analysis of the patients in terms of pulse and blood pressure both systolic and diastolic blood pressure and respiratory rate had no statistically significant differences between two groups of patients (P >0.05)

Baseline mean peak expiratory flow rate, forced vital capacity and forced expiratory volume on one second were 386.32±40.25 L/min, 4.18±0.44L, 2.85±0.49L in group A patients respectively and 383.67±38.12 L/min,4.20±0.49L and 2.92±0.47L respectively in group B patients.Analysis found no statistically significant mean difference between two groups of patients(P>0.05).These findings were almost similar to the findings of Price(2003) where baseline mean peak expiratory flow rate, forced vital capacity and forced expiratory volume on one second were 387.38±40.35 L/min, 4.28±0.54L, 2.95±0.59L in group A patients respectively and 393.57±48.12 L/min,4.30±0.49L and 2.82±0.57L respectively in group B patients.[18]

In addition to its effect on pulmonary function, asthma affects the physical, social, and emotional aspects of patients lives. Each patient evaluated by 7 scale questionnaire for asthma related quality of life. The composite score of quality of life were 5.23±0.5 and 4.66±0.6 after and before treatment for group A patients respectively. For group B patients, composite score of quality of life were 5.16±0.5 and 4.68±0.6 after and before treatment respectively.

In this study considerable improvement was seen in all domains of an asthma specific quality of life questionnaire (symptoms,activity,emotional function, and environmental stimuli) which were similar in both treatment groups (P<0.001). Analysis indicated that mean percentage of improvement of quality of life was 10.6% for group A patients and 8.92% for group B patients respectively. However between the group no statistically significant mean difference was found(P>0.05). This indicated that both the treatment modalities are equally effective. These findings correlate with findings of Price (2003) where the composite score of quality of life were 5.26±0.6 and 4.76±0.5 after and before treatment for group A patients respectively. For group B patients, composite score of quality of life were 5.26±0.5 and 4.58±0.6 after and before treatment respectively.[18] Mean percentage of improvement of quality of life was 11.1% for group A patients and for 9.7% for group B patients respectively. As those patients were suffering from a long period of time their quality of life also hampered. Proper asthma management is associated with not only improvement of lung function but also quality of life.

Pre and pos test evaluation of PEFR depicated that it significantly increased from morning level to evening (P<0.001). The PEFR increased 5.03% from pretreatment to 12th week of observation in group A patients at morning and it was 4.92% from pretreatment to 12th week at evening . Among group B patients similar pattern of PEFR was observed. At morning reading,4.38% increased pretreatment to 12th week observation and at evening readings,5.1% increased from pretreatment to 12th week.

Analysis of PEF L/minute between two groups of patients indicated that though the morning evening changes was statistically significant within the group (P<0.001), but no statistically significant

mean difference was found between two group of patients(P>0.05). These findings were similar with Price (2003) where the PEFR increased 5.24% from pretreatment to 12th week of observation in group A patients at morning and it was 4.77% from pretreatment to 12th week at evening. Among group B patients, at morning reading,4.59% increased from pretreatment to 12th week observation and at evening readings,5.22% increased from pretreatment to 12th week.

Laboratory finding particularly total blood count and differential is very much nonspecific tests for bronchial asthma. Eosinophils in particular may play a crucial role in asthmatic process. The differential blood count often but not invariably reveals modest eosinophils in patients with asthma.Total eosinophil counts, correlated for age, sex and diurnal variation are usually elevated in untreated symptomatic patients with asthma.

Pre-treatment & post-treatment total peripheral eosinophil count was evaluated. The mean eosinophil count was 591.13±328.9 in group A patients and 532.60±310.4 for group B patients and the mean difference was not statistically significant (p>0.05). During follow up, the eosinophil count decreased to 529.51±267.4 in group A patients and to 483.62±260.3 in group B patients. The mean difference between two groups was not statistically significant (p>0.05). Analysis indicated that the mean percentage of reduction of eosinophil count was 8.53% in group A patients and 7.9% in group B patients, but the difference was not statistically significant (p>0.05).These findings were similar with Pizzichini (1998) where pre-treatment mean eosinophil count was 581.23±338.9 in group A patients and 542.60±312.4 for group B patients and after treatment the eosinophil count decreased to 527.51±267.4 in group A patients and 488.62±260.3 in group B patients.[19] The mean percentage of reduction of eosinophil count was 8.23% in group A patients and 7.6% in group B patients.

Nocturnal dyspnoea, daytime dyspnoea and nocturnal awakening were evaluated in both groups of patients. There was clear improvement in pre & post treatment evaluation. Analysis found that no statistically significant mean difference of different parameters studied (P>0.05).

Regarding acute exacerbation, it was found that no patients suffered from acute exacerbation of asthma in the preceding months, it contrasts to Price (2003) where median days with asthma exacerbations were 2.1 and 2.4 days in the first 4 weeks; 2 and 2.1 in the second 4 weeks ; 1.9 and 1.8 in the final 4 weeks respectively in group A and group B patients.[18]

One explanation for this difference is that our study population might have had less severe asthma & improved lung function inspite of asthma and also they had proper control.

Both treatment approaches in this study achieved clinically significant control of asthma as evidenced by improvement in morning and evening PEF; less nocturnal and daytime dyspnoea, nocturnal awakening, improvement of quality of life and reduction of peripheral blood eosinophil count.

Both montelukast plus inhaled budesonide and inhaled double dose budesonide were generaly well tolerated. The incidence and type of adverse reactions reported for montelukast were consistent with the generally favourable tolerability profile of this drug in children and adults.[20]

This study was neither designed nor powered to observe differences in infrequent adverse events including those related to higher doses of ICS.[21]

Though overall cost of the study was not done, specific drug cost was calculated for both group. For group A , monthly cost was Taka 840.0 and for group B, monthly cost was Taka 580.0.It seems that cost is a bit higher in group A, but as long term use of higher doses of ICS is associated with various adverse events and lower doses of ICS plus montelukast are very safe in the long run, perhaps cost of drugs can be viewed less stringently.

Limitation

One potential limitation of the present study is that; study population is limited in number. More the number of patients,more accurate the result.[22] In application of result from a small group of patient to a vast community there always stands a caution.

Another limitation of the present study is the absence of a placebo group. Random table method is not applied in randomization of patients.[23]

Another limitation of the present study is that, it is a non blind study.[24]

In the present study all patients previously received inhaled steroid but asthma was not optimally controlled. So there may be the question of whether those patients were suffering from steroid resistance asthma. As this phenomena was not evaluated, this seems to be another limitation. Steroid resistant asthmatics do not show desirable response to even higher doses of prednisolone.

But in the present study, in the long run, all the patients of both group showed overall improvement on the basis of all pre-specified outcome.

So, it can be reiterated that steroid resistance issue does not stand strongly.

Conclusion

The data showed that both groups improved in respect of prespecified end point in similar degree.So,in conclusion leukotrine receptor antagonist montelukast plus inhaled budesonide is equally effective as double dose inhaled budesonide in adult patients with asthma.

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Outcome of vitamin- A and Zinc supplementation in the Treatment of Smear Positive Pulmonary Tuberculosis Patients (New cases)

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Abstract

Tuberculosis is one of the major health problems throughout the whole world. With the effective chemotherapy, smear conversion usually starts after second week and most patients become culture negative during the second month of treatment, a long duration during which patients may remain infectious and may favor acquired drug resistance. Malnutrition is frequently observed with the disease that leads to deficiency of many micronutrients which are involved directly or indirectly with the immune activity of the body against the invading organisms. Role of vitamin A and zinc in type IV hypersensitivity reaction and immunity to tuberculosis and their antioxidant properties make them unique for research in the field of treatment of tuberculosis. This research may contribute to lessen the treatment failure rate by addition of vitamin A and zinc in the regular regimen of antituberculosis medication ,to evaluate early smear conversion in micronutrient supplementation group and to ascertain earlier improvement of clinical and laboratory parameters in the micronutrient group. It was a randomized, controlled, prospective study carried out in the department of respiratory medicine, NIDCH, Mohakhali, Dhaka during the period from January 2004 to December 2004. 119 smear positive pulmonary tuberculosis patients (New untreated cases) admitted in NIDCH during the study period were taken as study population fulfilling the inclusion and exclusion criteria. They were divided into two groups as micronutrient group and non micronutrient group by random sampling method. Study time was initial 2months for each patient. A total of 111 patients had completed the study. Relevant investigations were done in each case. Each patient of both groups received CAT-1 antituberculosis medication. Micronutrient group in addition also received vitamin A (5000 iu / d) and zinc (15mg / d) supplementation in initial two months. DOTS strategy was strictly followed. Proper monitoring was ensured with clinical and laboratory parameters. At the end of first week, smear conversion was found in micronutrient group (3.7%) though not statistically significant ($p>0.05$) when compared with non-micronutrient group (0%).But after 2nd week up to 7th week, a statistically significant difference was found between two groups of patients ($p<0.05$). Smear conversion was earlier, rapid and higher in micronutrient group (94.4%) than in non-micronutrient group (82.5%). Radiological improvement of opacities was statistically significant in micronutrient group ($p<0.001$) after 2months of treatment. Resolution of cavities was higher in micronutrient group than in non-micronutrient group. Anthropometric parameters showed more favorable changes in micronutrient group than non-micronutrient group of patients with treatment which in most cases were statistically significant ($p<0.05$). Rise of Hb %, fall of ESR & CRP were statistically higher in micronutrient group. Post 2months serum retinol was higher in micronutrient group than in non-micronutrient group which was statistically significant ($p<0.001$). But the rise of serum Zinc was a bit higher in micronutrient group than in non-micronutrient group ($p>o.o5$). Serum albumin showed slightly higher increase in micronutrient group than in non-micronutrient group after 2months ($p>0.05$). The effectiveness of antituberculosis treatment was improved during first two months by vitamin A and Zinc supplementation with earlier elimination of Mycobacterium tuberculosis bacilli from the sputum with considerable early improvement of other clinical and laboratory parameters.

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Introduction:

Tuberculosis is one of the major health problems throughout the whole world especially in developing countries. It is highly prevalent in Bangladesh. Over 300000 people develop the disease each year of whom 70,000 die[1]. Nearly one third of the global population i.e. two billion people are infected with Mycobacterium tuberculosis and are at risk of developing the disease. More than eight million people develop active tuberculosis every year and about two million die. More than 90% of global TB cases and death occur in the developing world, where 75% of cases are in the most economically productive age group (16-54 years) [2]. Tuberculosis, one of the major health problems throughout the whole world is caused by Mycobacterium tuberculosis spread mainly by droplet infection[3]. With the effective chemotherapy, most patients become culture negative during the second month of treatment, a long duration during which patients may remain infectious and may facilitate mutation of bacilli favoring acquired drug resistance[4]. Further measures are needed to augment the effectiveness of the drugs to overcome the delay in killing bacilli. Malnutrition is frequently observed with the disease that leads to deficiency of many micronutrients which are involved directly or indirectly with the immune activity of the body against the invading organisms. In different studies both serum vitamin A and zinc were found low in patients with active tuberculosis. Role of vitamin A and zinc in type IV hypersensitivity reaction and immunity to tuberculosis by influencing immune system especially on CD4 cells and macrophages and their antioxidant properties make them exceptional for research in the field of treatment of tuberculosis. Different studies have shown that vitamin A has an immuno-protective role against human tuberculosis[5].This finding has historical basis in that cod liver oil, which is rich in vitamin A and D was used regularly for the treatment of tuberculosis before the introduction of modern chemotherapy [6]. Zinc deficiency was reported in patients with pulmonary tuberculosis in India and China [7]. Studies in animal and human have shown that zinc deficiency impairs the synthesis of retinol binding protein and reduces plasma retinol concentration which improves with supplementation of zinc [8] .Moreover, zinc acts as co-factor in the synthesis of enzymes that regulate vitamin A absorption and function. Zinc participates in absorption, mobilization, transport and metabolism of vitamin A. It helps in oxidative conversion of retinol to retinal (Retinaldehyde) via zinc-dependent retinol dehydrogenases enzymes. So concomitant use of vitamin A and zinc with conventional anti-tubercular medications may promote the efficacy of anti-tubercular drugs by enhancing immune mechanism [9].

Objectives

This research may contribute to lessen the treatment failure rate by addition of vitamin A and zinc in the regular regimen of antituberculosis medication

to evaluate early smear conversion in micronutrient supplementation group.

to ascertain earlier improvement of clinical and laboratory parameters in the micronutrient group

Methodology: It was a randomized, controlled, prospective study carried out in the department of respiratory medicine, NIDCH, Mohakhali, Dhaka during the period from January 2004 to December 2004. 119 smear positive pulmonary tuberculosis patients (New untreated cases) admitted in NIDCH during the study period were taken as study population fulfilling the inclusion and exclusion criteria

Inclusion criteria

- Patients of 16 – 55 years of age of either sex with sputum smear positive at least two of the three consecutive samples by bacterial index (BI).
- Patients with clinical and radiological signs consistent with active pulmonary tuberculosis.
- No history of previous anti TB treatment.

Exclusion criteria

- Smear positive PTB patients with any concomitant immunosuppressive disease/ altered immune state like Diabetes mellitus, CRF, CLD, CCF or any malignant disease or pregnancy or lactation or h/o use of steroid, supplements containing Vitamin A, zinc or iron during the previous months.

- Extra pulmonary TB patients.
- PTB patients with moderate to severe injury or surgery during the previous months. PTB patients who did not take their medication regularly, missing even a day in first two months were dropped out from the study.
- Drug resistance at baseline if available
- PTB patients who had developed severe adverse drug affect should be excluded from the study.

They were divided into two groups as micronutrient group and nonmicronutrient group by random sampling method. Study time was initial 2months for each patient. A total of 111 patients had completed the study. Relevant investigations were done in each case.

Each patient of both groups received CAT-1 antituberculosis medication. Micronutrient group in addition also received vitamin A (5000 iu/d) and zinc (15mg/d) supplementation in initial two months.

DOTS strategy was strictly followed. Proper monitoring was ensured with clinical and laboratory parameters including sputum smear weekly, CXR at 4th week and then 2weekly, Hb%, ESR and CRP 2wkly, serum retinol, serum zinc and albumin after 8th week of treatment. BMI (Body mass index) and MAC (Mid arm circumference) were recorded 4weekly interval.

Results and observations

Among 119 patients a total of 111 had completed the study which included fifty four patients in micronutrient group and fifty seven in nonmicronutrient group.

Table-I

Age distribution of the study patients

Age in years	Study subjects				Total		p value
	Micronutrient		Non-micronutrient				
	No.	%	No.	%	No.	%	
<20	8	14.8	6	10.5	14	12.6	
20-29	21	38.9	28	49.1	49	44.1	
30-39	16	29.6	15	26.3	31	27.9	
³40	9	16.7	8	14.0	17	15.3	
Total	54	100.0	57	100.0	111	100.0	
Mean±SD(Range)	29.1±9.9(16-54)		29.2±9.5(16-54)		29.2±9.6(16-54)		0.949

P value reached from unpaired student t test (p>0.05)

Table-II

Changes of micronutrient status of the studied patients

Study subjects	Pre-treatment	Post- treatment	% of improvement
Serum retinol (mmol/L)			
Micronutrient (n=54)	0.62±0.38	1.23±0.65	167.3±191.9
Non-micronutrient (n=57)	0.56±0.29	0.79±0.22	73.82±96.48
p value	0.341	0.001	0.002
Serum Zinc (mmol/L)			
Micronutrient (n=54)	8.85±1.82	9.99±2.16	16.55±32.83
Non-micronutrient (n=57)	8.62±2.04	9.50±1.40	13.81±20.45
p value	*0.537*	*0.161*	*0.597*

*Figure in parenthesis indicate range p value reached from unpaired student's t test

Table-III

Pre and post treatment changes of nutritional status of the studied patients

Parameters	Study subjects		p value
	Micronutrient (n=54)Mean ± SD	Non-micronutrient (n=57)Mean ± SD	
Body weight (kg)			
Pretreatment	40.37±6.22(27-52)	42.97±6.81(31-58)	0.038
At the end of 4th week	42.62±5.82(30-53.5)	44.61±6.61(34-60)	0.095
At the end 8th week	45.52±6.13(33-57)	46.35±7.10(25-62)	0.511
% of improvement	13.23±5.85(2.86-33.33)	9.33±3.9(3.77-21.21)	0.001
Body mass index (BMI)			
Pretreatment	16.04±2.30(11.25-20.31)	17.44±2.41(13.31-25.62)	0.002
At the end of 4th week	16.94±2.14(12.5-21.37)	18.11±2.34(14.11-26.22)	0.007
At the end of 8th week	18.08±2.19(13.21-22.71)	18.81±2.54(10.41-27.41)	0.109
% of improvement	13.23±5.85(2.86-33.33)	9.39±3.94(3.77-21.21)	0.001
Mid Arm Circumference (cm)			
Pretreatment	18.41±2.46(13-24)	18.33±2.49(13-22)	0.860
At the end of 4th week	19.57±2.46(14-25)	19.47±2.54(14-24)	0.819
At the end of 8th week	21.03±2.46(15-26)	20.78±2.38(16-25)	0.586
% of improvement	14.59±5.40(3.33-29.41)	13.78±4.17(4.55-23.08)	0.376

*Figure in parenthesis indicate range; p value reached from unpaired student's t test

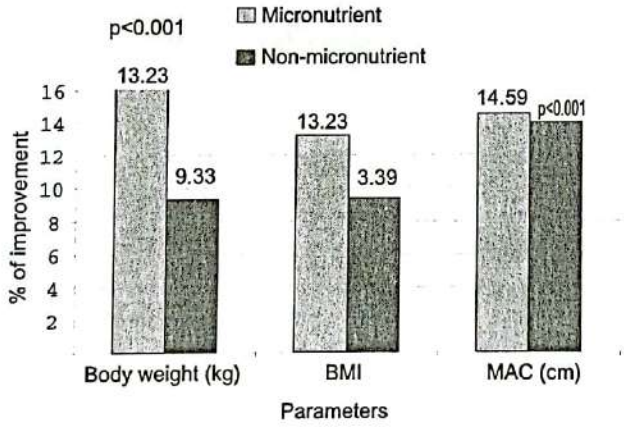

Fig.-1: *Changes of nutritional status of the studied patients*

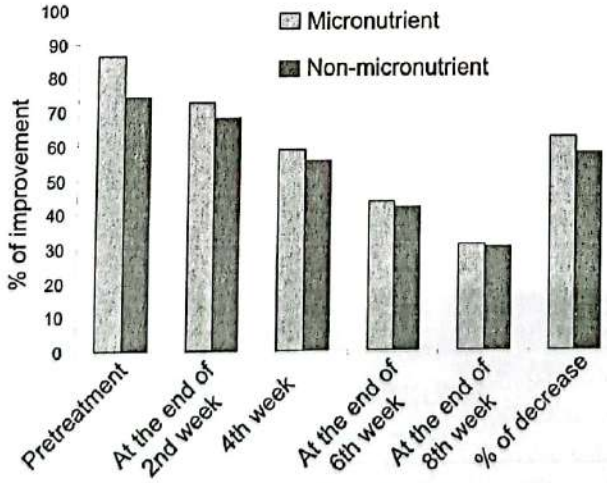

Fig.-2: *Changes of ESR of the studied patients*

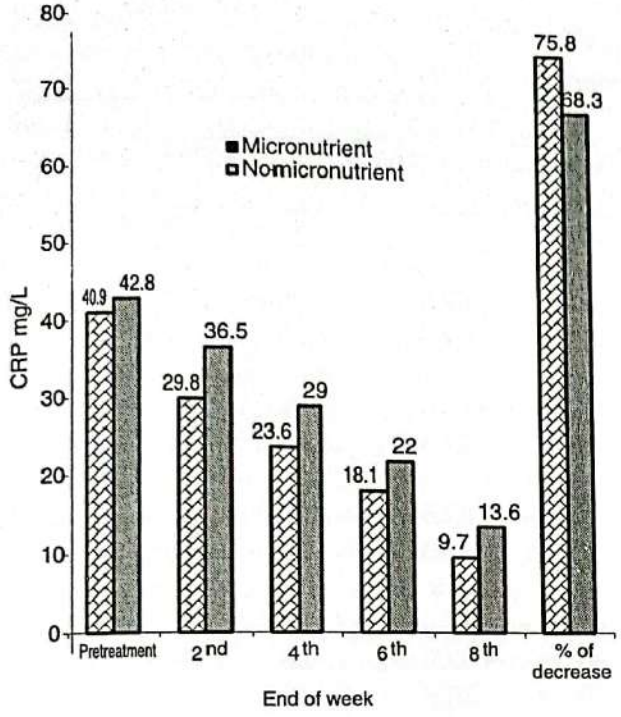

Fig.3: *Changes of CRP of the studied patients*

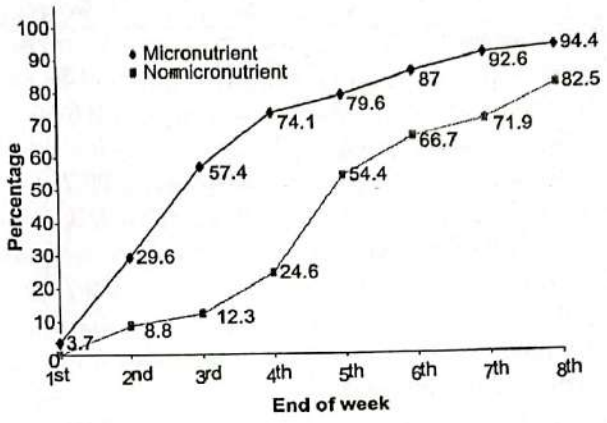

Fig.-4: *Pattern of sputum smears conversion*

Table-1V

Pattern of X- ray changes (Opacity)

X-ray changes	Study subjects						p value
	Micronutrient (n=54)		Non- micronutrient (n=57)		Total (N=111)		
	No.	%	No.	%	No.	%	
Pretreatment Opacity	54	100.0	57	100.0	111	100.0	1.000
At the end of 4th week							
Opacity	37	68.5	54	94.7	91	82.0	0.001
Improved	17	31.5	3	5.3	20	18.0	
At the end of 6th week							
Opacity	3	5.6	41	71.9	44	39.6	0.001
Improved	51	94.4	16	28.1	67	60.4	
At the end of 8th week							
Improved	22	40.7	47	82.5	69	62.2	0.001
Total resolution	32	59.3	10	17.5	42	37.8	

p value reached from chi square analysis

Table-V

Pattern of X- ray changes (cavitations)

X-ray changes	Study subjects						p value
	Micronutrient (n=54)		Non-micronutrient (n=57)		Total (N=111)		
	No.	%	No.	%	No.	%	
Pretreatment							
No cavity	49	90.7	47	82.5	96	86.5	0.202
Cavity	5	9.3	10	17.5	15	13.5	
At the end of 4th week							
No cavity	49	90.7	47	82.5	96	86.5	0.202
Cavity	5	9.3	10	17.5	15	13.5	
At the end of 6th week							
No cavity	49	90.7	47	82.5	96	86.5	0.414
Cavity	3	5.6	7	12.3	10	9.0	
Improved	2	3.7	3	5.3	5	4.5	
At the end of 8th week							
No cavity	49	90.7	47	82.5	96	86.5	0.390
Improved	4	7.4	9	15.8	13	11.7	
Total resolution	1	1.9	1	1.8	2	1.8	

p value reached from chi square analysis

Table-V1

Pre and post treatment changes of serum albumin of the studied patients

Study subjects	Pre-treatment	Post- treatment	% of improvement
Serum albumin (gm/L)			
Micronutrient (n=54)	32.96±4.08(22-46)	38.61±4.13(23-49)	17.70±9.12(4.55-43.48)
Non-micronutrient (n=57)	31.52±1.90(29-35)	36.31±2.47(32-42)	15.33±6.64(2.94-37.93)
p value	0.018	0.001	0.119

Figure in parenthesis indicate range p value reached from unpaired student's t test

Discussion

This study is the first to report an effect of supplementation of vitamin A and zinc on the treatment outcome of new cases of smear positive pulmonary tuberculosis in Bangladesh. Probably worldwide, it is the second to focus such effect after an Indonesian study conducted on 2002 [6]. Actually smear positive cases are the main source of transmission of Mycobacterium tuberculosis as drcplet infection to other persons. So the effective treatment of smear positive cases with early smear conversion is the most practical point of breaking transmission of the infection and thereby limiting as well as eliminating the disease as a whole.

Sputum smear positivity pattern in both groups showed that pretreatment values had no statistically significant difference between two groups of patients (p>0.05). . In baseline observation, sputum smear grading showed that sputum was of ++ (+2) for AFB in >50% cases in both groups. This was not similar to Karyadi et al 2002 study where around same percentage of patient in either group showed + (+1) for AFB in sputum smear direct microscopy. But their system of grading was different. They followed Bronkhorst scale of grading [10]. Our microbiology department followed the national technical guide of direct smear microscopy for TB and Leprosy [11]. Actually bacilli excretion in sputum depends on bacilli load

in the lesions. As low as 5000 organisms/ ml sputum is needed for a sample to become positive [12]. Sputum smear conversion started in the study early in the micronutrient group. Even at the end of first week 3.7% patients were found sputum smear negative in micronutrient group but no patient showed smear conversion in non-micronutrient group in this period. Subsequent follow up of sputum smear conversion rate ranged between 29.6% in the 2nd week and 94.4% in the 8th week in micronutrient group whereas in nonmicronutrient group the same rate ranged between 8.8% and 82.5% from 2nd to 8th week. So micronutrient group showed significant improvement (Fig. no.11) This early and more total percent of smear conversion observed in this study was consistent with the Indonesian study [6]. The early and more total percent of smear conversion in micronutrient group of patients may reflect the positive outcome of micronutrient supplementation in treatment of smear positive pulmonary tuberculosis By X-ray chest, it revealed that opacities in micronutrient group showed higher rate (59.3%) of resolution in initial phase than that of (17.5%) non-micronutrient group of patients ($p<0.001$). Pattern of resolution of cavities was slightly higher among the patients of micronutrient group (1.9%) than that of nonmicronutrient group (1.8%) but the difference was not statistically significant in comparison with non-micronutrient group patients ($p>0.05$). The over all radiological improvement seen in studied patients with micronutrient supplementation was consistent with the finding of Karyadi et al 2002.Micronutrient may effect early radiological improvement when given with conventional antituberculosis therapy. In our studied patients, cavities were in less number of patients than that was in Indonesian study of 2002 but opacities were present in all patients that were consistent with that study.

Pre and post treatment micronutrient concentrations in micronutrient group of patients were 0.62± 0.38¼mol/L and 1.23±0.65¼mol/L respectively. In non-micronutrient group the values were 0.56±0.29¼mol/L and 0.79±0.22¼moi/L respectively. Normal value of serum retinol is 0.699-2.796¼mol/L.Pretreatment values had no statistically significant difference ($p>0.05$) between two groups though the both levels were low than normal. But post treatment values showed that there was significant rise in serum retinol level in patients of both groups but the rise in micronutrient group was more than that of non-micronutrient group and mean difference was statistically significant ($p<0.001$). Analysis revealed that the percentage of improvement was significantly high in micronutrient group patients (167.3%) compared to non-micronutrient patients (73.8%). These findings had wide similarity with that of the Indonesian study by Karyadi et al in 2002 where baseline and after 2 months initial phase, the serum retinol was in micronutrient group 0.82-0.04¼mol/L &1.14±0.05¼mol/L respectively and in non micronutrient group 0.90±0.04¼mol/L &1.08±0.04¼mol/L respectively. The cause of pretreatment hyporetinaemia may be impairment of hepatic release of vitamin A as a result of the reduced synthesis of the retinol binding protein which is a negative acute phase protein. C In addition urinary loss of retinol may also play a role. Patients with pneumonia and sepsis lose up to 50% of their daily requirement of vitamin A in urine and children with shigellosis lose 15% of their daily requirement of vitamin A[6]. Vitamin A supplementation resulted in an acute phase shift in hepatic protein synthesis as indicated by the greater increase in plasma retinol concentration in micronutrient group which was consistent with the finding of study of Karyadi et al 2002.

Normal serum Zn level is 9.18-18.36¼mol/L [13]. Baseline pretreatment serum Zn was 8.85±1.82¼mol/L and 8.62±2.04¼mol/L for micronutrient group and non-micronutrient group respectively. Both values were low than normal. But no statistically significant mean difference was found between two groups of patients ($p>0.05$).After treatment with micronutrient supplementations with zinc, the value slightly raised to 9.99±2.16¼mol/L in micronutrient group. This is just at the lower limit of normal value of serum Zn. But in non-micronutrient group the rise was rather less and 9.50±1.4¼mol/L. Mean difference between the two groups was not statistically significant ($p>0.05$).Above all, with analysis it was obvious that the percentage of improvement was high in micronutrient group of patients (16.6%) compared to non-micronutrient group of patients (13.8%) though not statistically significant ($p>0.05$). This slight rise from baseline may correlate indirectly to the finding of Karyadi et al 2002 where

with treatment serum Zn level was found to fall in both groups during initial 2 months but finally raised after 6 months of treatment. Explanation for such slight rise, even fall with treatment in both groups in initial part may be due to diversion of Zn to the site of infection for proper function of macrophages and other immune cells and increased urinary loss by Ethambutal [6].

At the end of 4th week, there occurred weight gaining in both groups but was of no statistically significant difference ($p>0.05$). At the end of 8th week, weight gaining in both groups was considerably much with % of improvement high in micronutrient group which was statistically significant ($p<0.001$).Weight loss is attributed to the effects of cytokines notably TNF-±, IL-3, IL-6 and IFN-[3]. However, although plasma IL-6 & IFN-[3] concentration decrease rapidly during treatment of severe pulmonary tuberculosis plasma TNF-± level increases transiently early in the treatment. This transient rise may be associated with an initial fall in weight prior to the sustained increase which occurs with ongoing antituberculosis treatment[14]. But in our study whatever the extent, weight gaining was found in all patients of both groups at the end of 4th week and onwards which was consistent with the Indonesian study by Karyadi et al. 2002. Mean body mass index was initially below normal in both groups with statistically significant ($p<0.01$). BMI in non-micronutrient group was higher (17.4 ± 2.4 kg/m^2) than that of micronutrient group (16.0 ± 2.3 kg/m^2).At the end of 8th week of treatment the mean percentage of improvement showed significant weight gain in micronutrient group (13.2%) than non-micronutrient group (10.4%) with $p<0.001$.These trends of weight gaining and BMI improvement were consistent with Karyadi et al. study 2002 with the exception that weight gaining was similar in both groups in that study. This difference in weight gaining in our study may be due to the fact that baseline body weight was less in our study patients especially in micronutrient group or it may be taken as positive effect of micronutrient though there are variable opinion of different studies regarding effect of vitamin A and Zn on growth [8].

Nutritional status in terms of mid arm circumference (MAC) showed no statistically significant mean difference between the two groups of patients ($p>0.05$). However the mean MAC was increased a little bit high in micronutrient group of patients (14.59%) than non-micronutrient group of patients (13.78%).This finding was consistent with the finding of Indonesian study by Karyadi et al.2002.

Baseline hemoglobin level showed that mean value was less than normal- 9.65 ± 1.17 Nutritional status of the studied patients were assessed by measuring body weight, mid upper arm circumference and body mass index (BMI) pretreatment, at the end of 4th week and at the end of 8th week. Pretreatment body weight was 40.37 ± 6.22 kg and 42.97 ± 6.81 kg in micronutrient and non-micronutrient groups respectively. Baseline mean body weight of two groups of patients showed no statistically significant difference ($p>0.05$).

gm/dl and 10.22 ± 1.01gm/dl for micronutrient and non-micronutrient groups respectively. Thus at pretreatment level a statistically significant mean hemoglobin difference was found between two groups of patients ($P<0.01$). After 2months of treatment, analysis revealed that mean percentage of blood hemoglobin increase was more in micronutrient group (21.7%) than non-micronutrient group (17.8%) and mean difference was statistically significant ($p<0.01$). Analysis of repeated measure ANOVA showed that blood hemoglobin increased from previous level significantly ($p< 0.001$) at the end of 2nd week between two groups of patients but was not statistically significant at subsequent follow up ($p>0.05$). Hemoglobin rise with treatment was consistent with Lawn et al study on West African pulmonary tuberculosis patient 2000. But early response in micronutrient group as well as more increase of total hemoglobin concentration after 2months in this group may reflect effect of micronutrient. Total increase more in micronutrient group which had been statistically significant was consistent with study of Karyadi et al.2002.

Initially a statistically significant mean ESR difference was found between the two groups of patients ($p<0.01$) indicating that mean ESR was higher in micronutrient group patients (86.2 ± 27.8) than non-micronutrient group patients (74.5 ± 19.3) . Subsequent follow up showed that the mean ESR decreased in both the groups but between the two

groups no statistically significant mean difference was found (p>0.05). At the end of 8th week follow up, the percentage of decrease of ESR was significantly high in micronutrient group (62.8%) than non-micronutrient group (58.1%) with p value <0.01. Repeated measure analysis revealed that after treatment the ESR decreased significantly from previous measurements (p<0.001) in both groups of patients. Still ESR was higher than normal in both groups of patients after 2 months of treatment. Fall of ESR showed same trends as that seen in West African study by Lawn et al ,2000. Karyadi et al 2002 also noted that ESR did not return to normal with 2months treatment in either group. But considerable fall in micronutrient group may be correlated as positive effect of micronutrient. ESR is affected by the concentration of fibrinogen and other acute phase proteins in the blood which increase in inflammatory condition. Half-life of fibrinogen is much longer than that of many other acute phase proteins. So with treatment return of ESR to normal takes longer time in general [15]

C-reactive protein is an abnormal serum glycoprotein produced by the liver during inflammation- called an acute phase reactant. Because it disappears rapidly when the inflammation subsides, its detection signifies the presence of inflammation. Normal value is <2mg/L [16]. Initially no statistically significant mean difference of CRP level was found between the two groups of patients (p>0.05). During follow up the mean CRP level decreased in both groups of patients (p<0.001) and analysis also found that the mean percentage of decrease was more in micronutrient group patients (75.8%) compared to non-micronutrient group patients (68.3%). The difference of decrease was statistically significant (p<0.001) at the end of the initial phase. Repeated measure analysis revealed that after treatment the CRP significantly decreased from pretreatment value (p<0.001) in both groups of patients but at the end of 4th week and onward follow up no statistically significant difference was found between the groups of patients (p>0.05). This trend of CRP fall was consistent with the study of Karyadi et al 2002. Rapid fall of CRP in general with antikochs is due to quick fall of IL-6, the principal cytokine that induces CRP in inflammation. Further more CRP itself has a very short half-life in the circulation [15]. But the more fall of CRP in micronutrient group was consistent with the study of Timothy et al 2003 [17].

In micronutrient group, Pretreatment serum albumin was 32.96±4.08 gm/L and that in non-micronutrient group was 31.52±1.90 gm/L. Post treatment rise was 38.6±4.13gm/L and 36.31±2.47gm/L in micronutrient group and non-micronutrient group of patients respectively. Analysis revealed that a statistically significant mean difference was found between the two groups of patients in terms of serum albumin both pretreatment and post initial phase (p<0.05) .But mean percentage of changes of serum albumin showed no statistically significant difference between the two groups (p>0.05). None the less, the mean increase of serum albumin was higher among the patients of micronutrient supplementation group (17.7±9.12 gm/L) compared to that of non-micronutrient group (15.33±6.64 gm/L). Most of our patients had low serum albumin concentration at baseline. After 2months of treatment, it raised to normal in all patients. In Karyadi et alstudy 2002, baseline serum albumin was found with in normal range. But our studied patients showed hypoalbuminemia and response with treatment of tuberculosis by rise of serum albumin to normal level was more marked in micronutrient group though the percentage of improvement was not statistically significant. This increase in serum albumin in micronutrient group of patients may well be correlated with overall anthropometric improvement found more in micronutrient group of patients in the study. This trend of outcome was similarly observed in Indonesian study by Karyadi et al 2002 especially in initial phase of treatment

Regarding limitation of the study it is fact that the sample size is small. It was not possible to reach the exact sample size during the study period because of poor availability of smear positive fresh cases of patients fulfilling inclusion and exclusion criteria .The study was conducted in one centre only as far approved protocol. Due to difficulty in arranging placebo, double blind controlled study was not done.

Even that the sample size was far more than the minimum number for a study. It was also a bigger

size than that of Indonesian study by Karyadi et al 2002 where total eighty patients finally completed the study.s The sample was duly randomized. It was a controlled study, prospective in nature having both experimental and control groups Thus present study showed that the effectiveness of antituberculosis treatment was improved during first two months by vitamin A and zinc supplementation with early.

Conclusions

The effectiveness of antituberculosis treatment is improved during first two months by vitamin A and zinc supplementation with early sputum smear conversion and radiological resolution with relatively greater improvement of anthropometric and other laboratory parameters

Recommendations

- We recommend routine use of vitamin-A and zinc as supplementation with conventional anti TB medication.
- Combined formulation of vitamin-A and zinc if feasible to enhance patient compliance

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Study on Histological Patterns and Smoking Habits of Lung Cancer Patients

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Abstract

This analytical, prospective & cross sectional study was conducted at the National Institute of Diseases of Chest & Hospital, Dhaka with a view to find out the relation of major histological types of lung cancer with smoking habit. A total number of 370 consecutive patients suspected of having lung cancer were selected purposely. On the basisi of history, clinical and radiological findings. Of them 24 patients were dropped from initial screening who could not fulfill the criteria and had some exclusion criteria. Out of 346 patient, 303 patients were diagnosed histologically and cytologically and were ultimately included in the final analysis. Most of the patients belong to the age 55-64 year.

Squamous cell carcinoma was more frequent along smokers (91%) followed by small cell carcinoma (30%), Adenocarcinoma (13%) and large cell carcinoma 9%. Among non smokers, highest percentage was squamous cell carcinoma (47%), adenocarcinoma (31%) followed by small cell carcinoma (19%), large cell carcinoma (10%). Among the smokers mean dose of smoking was around 40 peak-year. The mean dose of smoking was higher among the squamous cell carcinoma nearly 40 peak-years.

[Chest & Heart Journal 2006; 30(1) : 47-62]

Introduction

A direct association between smoking and various histologic types of lung cancer has been observed for measures of intensity, duration and dose. Studies concluded in USA, Western Europe and China observed a higher smoking related risk of squamous cell carcinoma and small cell carcinoma than of adenocarcinoma of the lung.[1] The largest of these study suggested that intensity of cigarette exposure has less distinct effect on all cell type than duration of use with duration more strongly associated with SQCC and SMCC than adenocarcinoma[2].

The distribution of lung cancer by histological type differs between smokers and non-smokers and even among smokers, is different for man and woman. In both sexes adenocarcinoma are much more common among non-smokers than smokers. But regardless of smoking status, squamous cell carcinoma is much more common among men and adenocarcinoma more common among women[3].

Lung cancer is a major public health problem in our country. Incidence is increased day by day. The clinical behaviour and aggressiveness among different histological types of lung cancer varies. Accurate cancer cell typing is essential for selecting appropriate therapies, such as surgical procedures or anticancer chemotherapeutic regimens, as well as for making prognosis of the disease[4]. Cigarette smoking is associated with all histological types of lung cancer. However, the dose response relationship between smoking and adenocarcinoma differed clearly from that observed in squamous and small cell carcinomas. In the latter histological types the gradient of risk was much stronger as the number of cigarettes smoked or duration of smoking increased. There are several studies in Western Europe, America and China, showing that lung cancer histology varied with smoking status. Differences in histological type also exist between smokers and non-smokers and between male and female[5].

No such type of study has been done in our country. So, it is of consideration interest important to know smoking history and histologic pattern among he lung cancer patients in our country context.

Materials and Methods

Type of Study:

Cross-sectional and descriptive study.

1. Registrar, National Institute of Diseases & Chest Hospital, Dhaka
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3. Professor of Respiratory Medicine, National Institute of Diseases & Chest Hospital, Dhaka
4. Director-Cum-Professor of Respiratory Medicine, National Institute of Diseases & Chest Hospital, Dhaka

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Place of Study:

The study was conducted in the Institute of Diseases of the Chest & Hospital (IDCH), Mohakhali, Dhaka and National Institute of Cancer Research & Hospital (NICR&H), Mohakhali, Dhaka. The IDCH and NICR&H are the main referral center for chest diseases patients. So, these centers were selected for collection of cases.

Period of Study:

The study was carried out during the period from July'1999 to June2001.

Study Population:

All patients both smoker and non-smoker of either sexes having a suspicious radiological shadow in the chest X-ray fulfill the inclusion and exclusion criteria were initial cases and histologically or cytologically diagnosed primary lung cancer cases were the final study population.

Inclusion Criteria

Clinical features suggestive of carcinoma of the lung:

- cough
- Haemoptysis
- Chest pain
- Dyspnoea
- Fever
- Anorexia and weight loss
- Hoarseness
- Clubbing of fingers
- Chest radiograph suggestive of neoplasm

Persistent or gradually increasing peripheral radiologic shadow, measuring at least 3cm and more in diameter that failed to resolve after a variable period of antibiotic therapy with or without above symptoms or signs.

Mass or cavitary lesion with or without fluid level in spite of 2 weeks of broad-spectrum antibiotic therapy.

- Prominence of hilar shadows
- Complete or partial collapse.
- Segmental emphysema
- Consolidation

Exclusion Criteria

When detailed history, clinical examination and roentgenographic findings raised the possibility that the lung cancer is a secondary one as opposed to primary tumour.

- Very old patients with bad physical condition.
- Major concomitant diseases i.e. recent MI, CVD, serious cardiac dysrythmias, unstable angina etc.
- Poorly controlled bronchial asthma.
- Sputum positive for acid-fast bacilli (AFB).
- Patient was on anti TB drugs and lesion was improving.
- Bleeding diathesis.

Basis for selection of the patient

A standard proforma with questionnaire was designed and filled to select patients with suspected primary lung cancer. The patients were identified according to the predetermined criteria as well as inclusion and exclusion criteria. A detailed history and thorough physical examination followed by following investigations were performed for inclusion criteria and to rule out exclusion criteria. Blood for: total count of WBC, differential count of WBC, ESR, Haemoglobin concentration, bleeding time and clotting time, platelet count, X-ray chest PA view and lateral view, sputum for AFB, blood urea, serum creatinine.

Sample Size

A total number of 370 consecutive patients suspected of having lung cancer were selected purposively on the basis of history, clinical and radiological findings. Of them 24 patients were dropped from initial screening who could not fulfill the inclusion criteria and had some exclusion criteria. Out of 346 patients, 303 patients were diagnosed histologically and cytologically and were ultimately included in the final analysis.

In each case informed written consent from the patient was obtained after discussing the patient about the study procedure

Data recording by a Standard proforma (History and physical examination)

After completion of interview, the patients were examined physically and sent for routine laboratory investigations.

Establishment of histological diagnosis after selection of the patients', initially flexible fibreoptic bronchoscopy was done in patients having suspected central lesions as per standard procedure. Bronchial biopsy, bronchial brushing and in some cases BAL was taken. Slides and materials were immediately sent to the laboratory. FNAC was done in patients as per standard procedure slides were immediately sent to the laboratory. A second opinion was asked for any reports, which seems to contradict with clinical and radiological findings. FNAC or biopsy (in some cases) of the cervical lymph nodes was done in patients who presented with lymphadenopathy. Pleural fluid cytology and pleural biopsy was done in indicated cases. The results of histological or cytological diagnosis were collected from the laboratory and then completed the Data Sheet.

Then presentation of Data and Statistical Analysis of Data was done.

Results and Observations

This was a cross sectional study conducted in National Institute of Diseases of the Chest and l-Hospital (NIDCH), Dhaka. A total of 303 patients with bronchial cancer were studied with a view to assess the pattern of lung cancer and also to find out the relationship of lung cancer with tobacco smoking.

The mean age of the patients was 57.5±11.3 years. it was 57.7±11.2 for male and 56.2±11.2 years for female. It was evident that no statistically significant age difference was found between male and female patients (p>0.05).

Table-I

Age and sex distribution of the study subjects

Age in years	Sex		Total	P Value
	Male	Female		
<45	28 (10.3)	5(16.1)	33(10.9)	0522^{NS}
45-54	58(21.3)	5(16.1)	63(2.8)	
55-64	94(34.6)	14(45.2)	108(35.6)	
65-74	76(27.9)	6(19.4)	82(27.1)	
³75	16(5.6)	(1(3.2)	17(5.6)	
Total	272(89.8)	31(10.3)	303(100.0)	

NB. Figure in parenthesis indicate percentage
Mean±SD= 57.5±11.3 years (Range 25-82 years)
Mean±SD (Male)=57.7±1 1.2 years (Range 25-82 years)
Mean±SD(Female)=56.2±1 1.5 years (Range 28-80 years)
Male: Female ratio= 8.8:1
P value reached from chi square analysis
NS = Not significant (p>0.05)

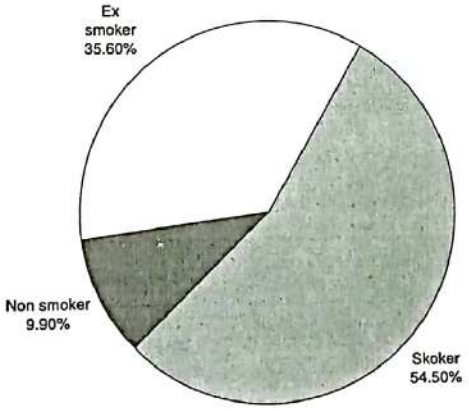

Fig.-1: *Percentage distribution of the study subjects by smoking status*

Table-II

Distribution of study subjects by age and smoking status

Age in years	Smoking status				Total	P value
	Smokers			Non smokers		
	Current	Ex.	Sub-total			
<45	15(9.1)	6(5.6)	21(7.7)	12(40.0)	33(10.9)	0.001^{S}
45-54	41(24.8)	14(13.0)	55(20.1)	8(26.7)	63(20.8)	
55-64	61(37.0)	40(37.0)	101(37.0)	7(23.3)	108(35.6)	
65-74	44(26.7)	36(33.3)	80(29.3)	2(6.7)	82(27.1)	
³75	4(2.4)	12(11.1)	16(5.9)	1(3.3)	17(5.6)	
Total	165(54.5)	108(35.6)	273(90.1)	30(9.9)	303(100.0)	

Table 2 The mean age of the current smoker was 56.9±9.8 years and that on ex smokers was 61.5±10.5 years. So, the overall mean age of the smokers was 57.5±11.3 years. It was also observed that the mean age of the non smokers was 47.0±13.9 years. A statistically mean age difference was found between smokers and non-smokers (pcO.05).

Table-III

Distribution of study subjects by sex and smoking status

Sex	Smoking status				Total	P value
	Smokers		Sub-total	Non-smokers		
	Current	Ex.				
Male	162(98.2)	99(91.7)	261(95.6)	11(36.7)	272(89.8)	0.001[S]
Female	3(1.8)	9(8.3)	12(4.4)	19(63.3)	31(10.2)	
Total	165(54.5)	108(35.6)	273(90.1)	30(9.9)	303(100.0)	

Table 3 shows the percentage distribution of smoking status by sex of the patients.

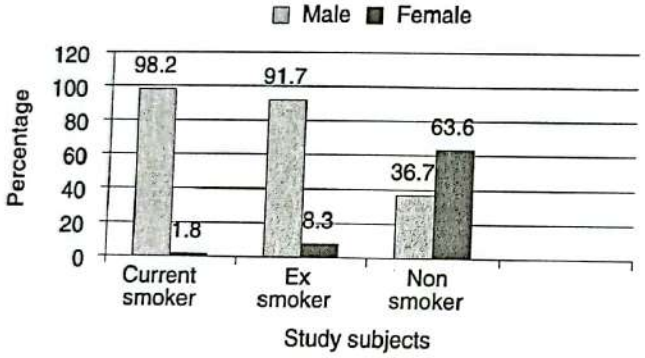

Fig.-2: *Distribution of study subjects by sex and smoking status*

Table-IV

Distribution of study subjects by occupation and smoking status

Occupation	Smoking status				Total	P value
	Smokers		Sub-total	Non-smokers		
	Current	Ex.				
Farmer	71(43.0)	40(37.0)	111940.7)	4(13.3)	115(38.0	0.001[s]
Service	13(7.9)	17(15.7)	30(11.0)	3(10.0)	33(10.9)	
Housewife	3(1.8)	9(8.3)	12(4.4)	19(63.3)	31(10.2)	
Business	16(6.7)	18(16.7)	34912.50	2(6.7)	36(11.9)	
Labourer	46927.9)	15(13.9)	61(22.3)	2(6.7)	63(20.80	
Others	16(9.7)	9(8.3)	25(9.2)	0(0.0)	25(8.3)	
Total	165(54.50	108(35.6)	273(90.1)	30(9.9)	303(100.0)	

Table 4 shows the percentage distribution of smoking status by occupation of the patients. It was among the smokers highest percentage were farmer 111(4.7%). Whereas among non smokers, highest percentage were housewife 19(63.3%).

Table-V

Distribution of study subjects by level of education and smoking status

Level of education	Smoking status				Total	P value
	Smokers		Sub-total	Non-smokers		
	Current	Ex.				
Illiterate	88(53.3)	47(43.5)	135(49.5)	11(36.7)	146(48.2)	0.022[s]
Primary	31(18.8)	15(13.9)	46(16.8)	2(6.7)	48(15.8)	
Secondary	38(23.0)	35(32.4)	73(26.7)	14(46.7)	87(28.7)	
Higher secondary	6(3.6)	8(7.4)	14(5.1)	2(6.7)	16(5.3)	
Graduate	1(0.6)	2(1.9)	3(1.1)	0(0.0)	3(1.0)	
Masters & above	1(0.6)	1(0.9)	2(0.2)	1(3.3)	3(1.0)	
Total	165(54.5)	108(35.6)	273(90.1)	30(9.9)	303(100.0)	

Table 5 shows the percentage distribution of smoking status by level of the education of the patients. It was observed that among the smokers highest percentage were illiterate 135(49.5%). Similar pattern of education was found among the non smokers with highest percentage had 14946.7%) had secondary level of education.

Table-VI

Distribution of study subjects by place of work and smoking status

Place of work	Smoking status				Total	P value
	Smokers		Sub-total	Non-smokers		
	Current	Ex.				
Indoor	23(13.9)	28(25.9)	51(73.3)	22(73.3)	73(24.1)	0.001[s]
Outdoor	131(79.4)	63(58.3)	194(71.1)	6(20.0)	200(66.0)	
Both	11(6.7)	17(15.7)	28(10.3)	2(6.7)	30(9.9)	
Total	165(54.5)	108(35.6)	273(90.1)	30(9.9)	303(100.0)	

Table 6 shows the percentage distribution of smoking status by place of work of the patients. It was evident from table that highest percentage of smokers 194(71.1%) were engaged in outdoor works. Whereas among the non smokers highest percentage were engaged in indoor 22(73.3%) works.

Table 7 shows the percentage distribution of smoking status by socioeconomic status of the patients. It is observed that among the smokers 175(64.1%) were poor. Whereas among the non smokers, highest percentage were 19(63.3%) average socio economic condition.

Table 8 shows the percentage distribution of status and presenting symptoms of the patients.

Table 9 Shows the percentage of smoking status and clinical signs of the study patients. It was found that among the smokers 135(49.5%) has mild anaemia followed by 93(34.1%) moderate and 21(7.7%) had severe anaemia, whereas among non-smokers, highest percentage has moderate anaemia 13(43.3%) followed by 12(40.0%) had mild anaemia and 3(10.0%) severe aneamia, but the difference was not syatistically significant (p>0.05). It was observed that among the smokers, 118(43.2%) has clubbing and among non-smokers 9(30.0%) had clubbing, but the difference was not statistically significant (p>0.05). Similarly, no statistically significant difference was found between smokers and non smokers in terms of neck vein, lymph node and bony tenderness (p>0.05).

Table 10. Shows the distribution of laboratory investigations in terms of TLC of WBC, differential count of WBC, haemoglobin, ESR, bleeding time, clotting and. It was found that no statistically significant mean difference was between smokers and non-smokers (p>0.05) in terms of laboratory investigations.

Table 11. Shows the pattern of chest skiogram between smokers and non-smokers. Among the smokers, highest percentage had 108(39.6) pulmonary mass followed by perihilar opacity 66(24.2%), hilar enlargement 26(9.5), consolidation 21(7.7%), pleural effusion 20(7.3%). Among non-smokers, highest percentage has peripheral pulmonary mass 15(50.0%) followed by 9(3.3%) perihilar opacity, pulmonary nodule 1(3.3%), hilar enlargement 1(3.3%) etc.

Table 12. Shows the pattern of diagnostic procedure applied among the smokers and non-smokers. It was observed that among smokers highest percentage of patients were diagnosed by Fine Needle Aspiration Cytology (FNAC) of lung tissue 151(55.3%) followed by Fibreoptic bronchoscopy 68(24.9%).

Table 13. shows the pattern of bronchial carcinoma among the studied subjects. It was found that highest percentage had squmous cell carcinoma 144(47.5%). The difference was statistically significant (pc0.05) indicating adeneocarnoma was higher among non smokers whereas among smokers highest percentage of bronchial carcinoma was squmous cell carcinoma.

Table 14 shows the distribution of study subjects by histologic patterns of bronchial carcinoma and smoking status. It was found that mean number of stick/day smoked was 21.1±0.6/day.

Table 15 shows the distribution of study subjects by histologic pattern and smoking status. It was found that among the non-smokers adenocarcinoma was significantly higher whereas squamous cell carcinoma and small cell carcinoma was higher among smokers (p<0.05).

Table 16 Among the smokers, the mean dose of smoking was 39.7±1.2 pack year. Although the mean dose of smoking was higher among the squmous cell carcinoma (40.8±1.8 pack year) compared to other variety of carcinoma, but the mean difference was not statistically significant (p>O.OS).

Table 17 It was observed that mean age of starting of smoking was earlier among the patients of adenocarcinoma (17.6±0.6 years) compared to large cell carcinoma and others (1 8.4±0.8 years) and the mean difference was not statistically significant (p>0.05).

Table 18 shows the distribution of study subjects by histologic pattern of lung cancer and smoking status in terms of year since quitting of smoking. Among the patients of squmaous Cell carcinoma, 91(63.2%) were current smokers.

Table 19. It was found that among squmous cell carcinoma highest percentage were in the age group 54(37.5%), similarly highest percentage 24(36.9%) and 7(30.4%) in the same age groups, whereas among the patients of small cell carcinoma highest percentage were in the age group of 65-74 years.

Table 20. shows the percentage distribution of study subjects by histologic pattern and sex of the patients. It was found that the proportion of squmous cell carcinoma(93.1%), small cell carcinoma(97.2%) and large cell carcinoma and others (100.0%) were higher in male subjects whereas adenocarcinoma (29.2%) were proportionately high among female subjects and the difference was statistically significant (p<O.O5).

Table 21. shows the percentage distribution of study patients by histologic pattern and place of works.

Table 22. It was found that highest percentage of squmous cell carcinoma 86(59.7), small cell carcinoma 56(78.9%) were among the patients of poor class whereas large cell and other carcinoma

13(56.5%) were in average social class and adenocarcinoma in rich patients and the difference was statistically significant (p<0.05).

Table 23. It was found that highest percentage of patients smoked both Cigarette and bidi 142(52.0%) followed by cigarette 66(24.2%) and lowest bidi 65(23.8%). It observed that no statistically significant difference was found in terms of different histologic pattern of bronchial carcinoma and pattern of tobacco smoked (p>O.05).

Table 24. It was found that percentage of cigarette smokers were higher among the rich 5(45.5%), whereas percentage of bidi smokers were poor 65(29.7%) and combination of cigarette and bidi 54(62.1%) among average socioeconomic status of the patients and the difference was statistically significant (p<O.05)

Table-VII

Distribution of study subjects by socioeconomic condition and smoking status

Socioeconomic status	Smoking status				Total	P value
	Smokers		Sub-total	Non-smokers		
	Current	Ex.				
Rich	6(3.6)	5(4.0)	11(4.0)	1(3.3)	0.001[s]	
Average	41(24.8)	46(42.6)	87(31.9)	19(63.3)	106(35.0)	
Poor	118(71.5)	57(52.8)	175(64.1)	10(33.3)	185(61.1)	
Total	165(54.5)	108(35.6)	273(90.1)	30(9.9)	303(100.0)	

Table-VIII

Distribution of study subjects by symptoms and smoking status

Symptoms	Smoking status				Total	P value
	Smokers		Sub-total	Non-smokers		
	Current	Ex.				
Dyspnoea						
Yes	87(52.70	50(46.3)	137(50.2)	16953.3)	163950.5)	0.743[NS]
No	78(47.3)	58(53.7)	136(49.8)	14946.7)	150(49.5)	
Nature of Dyspnoea 9n=163)						
Paroxysmal	23(26.4)	13(26.0)	36(26.3)	5(31.3)	41(26.8)	0.899[NS]
Continuous	8(9.2)	3(6.0)	11(8.0)	1(6.3)	12(7.8)	
Exertional	56(64.4)	43(68.0)	90(65.7)	10(62.3)	100(65.4)	
Fever						
No fever	84(50.9)	57(52.8)	141(51.6)	18(60.0)	159(52.5)	0.641[NS]
Continous	12(7.3)	5(4.6)	17(6.2)	1(3.3)	18(5.9)	
Intermittent	27(16.4)	28(25.9)	55(20.1)	4(13.3)	59(19.5)	
High grade	4(2.4)	1(0.9)	5(1.8)	1(3.3)	6(2.0)	
Low grade	38(23.0)	17(15.7)	55(20.1)	6(20.0)	61(20.1)	
Body weight						
Loss of body weight	90(65.5)	65(60.2)	155(56.8)	12(40.0)	167(56.1)	0.079[NS]
Unchanged	75(45.5)	43(39.8)	118(43.2)	18(60.0)	136(44.9)	
Appetite						
Loss of appetite	80(48.5)	50(46.3)	130(47.6)	12(40.0)	142(46.9)	0.427[NS]
No loss of appetite	85(51.5)	58(53.7)	143(52.4)	18(60.0)	161(53.1)	
Associated Complains						
No complaints	131(79.4)	72(66.7)	203(74.4)	17(56.7)	220(72.6)	0.039[NS]
Neck/facial swelling	3(1.8)	2(1.9)	5(1.8)	2(6.7)	7(2.3)	
Dysphagia	3(1.8)	4(3.7)	7(2.6)	2(6.7)	9(3.0)	
Hoarseness of voice	8(4.8)	8(7.4)	16(5.9)	2(6.7)	18(5.9)	
Bone pain	4(2.4)	5(4.6)	9(3.3)	4(13.3)	13(4.3)	
Weakness	16(9.7)	15(13.9)	31(11.4)	3(10.0)	34(11.2)	
Numbness of legs and arms	0(0.0)	2(1.9)	2(0.7)	0(0.0)	2(0.7)	
Associated disease						
No disease	152(92.1)	94(87.0)	246(90.1)	30(100.0)	276(91.1)	0.125[NS]
COPD	7(4.2)	8(7.4)	15(5.5)	0(0.0)	15(5.0)	
Pulm. Fibrosis	4(2.4)	4(2.8)	8(2.9)	0(0.0)	8(2.7)	
DM	2(1.2)	2(1.9)	4(1.5)	0(0.0)	4(1.4)	

Table-IX

Distribution of study subjects by sings and smoking status

Signs	Smoking status				Total	P value
	Smokers		Sub-total	Non-smokers		
	Current	Ex.				
Anemia						
No anemia	16(9.7)	8(7.4)	24(8.8)	2(6.7)	26(9.6)	0.686^{NS}
Mild	78(47.3)	57(52.8)	135(49.5)	12(40.0)	147(48.5)	
Moderate	56(33.9)	37(34.3)	93(34.1)	13(43.3)	106(35.0)	
Severe	15(9.1)	6(5.6)	21(7.7)	3(10.0)	24(7.9)	
Clubbing						
Present	75(45.5)	43(39.8)	118(43.2)	9(30.0)	127(41.9)	0.164^{NS}
Absent	90(54.5)	65(60.2)	155(56.8)	21(70.0)	176(58.1)	
Neck vein						
Engorged	5(3.0)	3(2.8)	8(2.9)	3(10.0)	11(3.6)	0.0.04^{NS}
Not engorged	160(97.0)	105(97.2)	265(97.1)	27(90.0)	292(96.4)	
Lymph node						
Not palpable	136(82.4)	89(82.4)	225(82.4)	25(83.3)	250(82.5)	0.900^{NS}
Single	9(5.5)	5(4.6)	14(5.1)	1(3.3)	15(5.0)	
Multiple	10(6.1)	12(11.1)	22(8.1)	4(13.3)	26(8.6)	
Matted	2(1.2)	1(0.9)	3(1.1)	0(0.0)	3(1.0)	
Fixed	8(4.8)	1(0.9)	9(3.3)	0(0.0)	9(3.0)	
Bony tenderness						
Yes	4(2.4)	5(4.6)	9(3.3)	0(0.0)	9(3.0)	
No	161(97.6)	103(95.4)	164(96.7)	30(100.0)		

Table-X

Distribution of study subjects by laboratory investigations and smoking status

Lab. Findings (Variables)	Smoking status				Total	P value
	Smokers		Sub-total	Non-smokers		
	Current Mean±SE (Range)	Ex. Mean±SE (Range)	Mean±SE (Range)	Mean±SE (Range)	Mean±SE (Range)	Mean±SE (Range)
TLC of WBC	9532.7±182.2 (5000-18000)	9746.3±250.5 (4000-16000)	9617.2±148.0 (14000-18000)	10230.0±410.0 (6500-16000)	9677.9±139.6 (4000-18000)	0.330^{NS}
Polymorph	65.7±0.5 -50.89	67.2±0.6 (51-85)	66.3±6.4 -50.86	67.9±1.0 (56-85)	66.5±0.4 (50-89)	0.053^{NS}
Lymphocytes	26.6±0.5 (10-44)	25.5±0.5 (12-44)	26.2±6.0 (10-44)	24.9±0.9 (12-44)	26.1±0.3 (10-44)	0.168^{NS}
Eosinophils	4.9±0.2 (2-10)	4.8±0.2 (2-10)	4.8±2.1 (2-10)	5.0±0.4 (2-10)	4.9±0.1 (2-10)	0.809^{NS}
Basophils	0.30±0.05 (0-2)	0.2±0.04 (0-2)	0.2±0.8 (0-0-2)	0.0±.00 (0-0)	0.2±0.03 (0-2)	0.113^{NS}
Monocytes	2.5±0.08 (1-6)	2.2±0.08 (1-5)	1.4±1.0 (1-6)	2.2±0.08 (1-4)	2.3±0.05 (1-6)	0.092^{NS}
Haemoglobin	10.4±0.1 (5.3-14.0)	10.3±0.2 (6.0-13.0)	10.3±1.8 (5.3-14.0)	10.2±0.3 (7.0-13.6)	10.3±0.01 (5.3-14.0)	0.857^{NS}
ESR	65.5±2.7 (10-150)	64.4±3.5 (10-130)	65.1±34.9 -10.15	69.1±6.0 (12-130)	65.4±2.0 (10-150)	0.804^{NS}
Bleeding time	4.7±0.08 (2.0-7.0)	4.9±0.10 (30.-7.0)	4.8±6.0 (2-7)	4.7±0.2 (3.0-7.0)	4.7±0.06 (2.0-7.0)	0.499^{NS}
Clotting time	7.0±0.08 (5.0-11.0)	7.2±0.1 (4.0-11.0	7.1±0.07 (4-11)	7.1±0.2 (5.0-10.0)	7.1±0.07 (4.0-11.0)	0.148^{NS}
Platelet count	2.2±0.04 (1.20-3.9)	2.3±0.05 (1.2-3.7)	2.3±0.03 (1.2-3.9)	2.3±0.10 (1.2-3.9)	2.7±3.5 (1.2-3.9)	0.768^{NS}

Table -XI

Distribution of study subjects by X-ray findings and smoking status

X-ray Findings	Smoking status				Total	P value
	Smokers		Sub-total	Non-smokers		
	Current	Ex.				
Hilar enlargement	15(9.1)	11(10.2)	26(9.5)			
Pulm. Nodule	0(0.0)	2(1.9)	2(0.7)			
Perihilar opacity	41(24.8)	25(23.1)	66(24.2)			
Pulmonary mass	63(38.2)	45(41.7)	108(39.6)			
Collapse	8(4.8)	6(5.6)	14(5.1)			
Rib erosion	3(1.8)	1(0.9)	4(1.5)			
Broadening mediastinum	3(1.8)	1(0.9)	3(1.1)			
Pleural effusion	11(6.7)	9(8.3)	20(7.3)			
Consolidation	15(9.1)	6(5.6)	21(7.7)			
Cavitary lesion	6(3.6)	3(2.8)	9(3.3)			

Table-XII

Distribution of study subjects by diagnostic procedure and smoking status

Diagnostic procedure	Smoking status				Total
	Smokers		Sub-total	Non-smokers	
	Current	Ex.			
Sputum cytology	3(1.8)	2(1.9)	5(1.8)	1(3.3)	6(2.0)
Bronchial biopsy	47(28.5)	21(19.4)	68(24.9)	6(20.0)	74(24.4)
Bronchial brushing	6(3.6)	1(0.9)	7(2.6)	1(3.3)	8(2.6)
Bronchial washing	1(0.6)	1(0.9)	2(0.7)	0(0.0)	2(0.7)
FNAC Lung	84(50.9)	67(62.0)	151(55.3)	21(70.0)	172(56.8)
FNAC lymph node	19(11.5)	14(13.0)	33(12.1)	0(0.0)	33(10.9)
Pleural tissue biopsy	2(1.2)	2(1.9)	4(1.5)	1(3.3)	5(1.7)
Pleural fluid cytology	3(1.7)	0(0.0)	3(1.1)	0(0.0)	3(1.0)

Table-XIII

DIstribution of study subjects by histological pattern and smoking status

Histological pattern	Smoking status				Total	P value
	Smoker		Sub total	Non-smokers		
	Current	Ex.				
Squamous cell carcinoma	91(552)	47(43.5)	138(50.5)	6(20.0)	144(4L5)	0.0010
Small cell carcinoma	50(30.3)	19(17.6)	69(25.3)	2(6.7)	71(23.4)	
Aldenocarcinoma	13(7.9)	31(28.7)	44(16.1)	21(70.0)	65(21.5)	
Large cell carcinoma	9(5.5)	10(9.3)	19(7.0)	0(0.0)	19(6.3)	
Adennosquamous carinoma	0(0.0)	1(0.9)	1(0.4)	0(0.0)	1(0.3)	
Alveolar cell carcinoma	1(0.6)	0(0.0)	1(0.4)	1(3.3)	2(0.7)	
Fibrocytoma	1(0.6)	0(0.0)	1(0.4)	0(0.0)	1(0.3)	

Table-XIV

Distribution of study subjects by histologic pattern and smoking status (No. of Stick/day)

Smoking statusPattern Carcinoma					Total	P value
	SQCC	SCC	AC	LCC & others		
No. of stick/day						
Non-smokers	6(4.2)	2(2.8)	21(32.3)	1(4.3)	30(9.9)	0.001
<15	29(20.1)	17(23.9)	5(7.7)	7(30.4)	58(19.1)	
15-24	44(30.6)	15(21.1)	2(3.1)	5(21.7)	66(21.8)	
³25	65(45.1)	37(52.1)	37(56.9)	10(43..5)	149(49.2)	
Total	144(47.5)	71(23.4)	65(21.5)	23(7.6)	303(100.0)	
Mean±SE	20.8±0.8	20.9±1.0	20.1±1.4	20.2±2.2	21.2±0.6	
(Range)	-9.45	-6.42	-6.4	-6.6	-6.6	

Table-XV

Distribution of study subjects by histologic pattern and smoking status (Duration of smoking)

Smoking status	Pattern Carcinoma				Total	P value
	SQCC	SCC	AC	LCC & others		
Duration of smoker (years)						
Non-smokers	6(4.2)	2(2.8)	21(32.3)	1(4.3)	30(9.9)	0.001^{S}
<25	25(17.4)	8(11.3)	4(6.2)	6.(26.1)	43(14.2)	
25-34	24(16.7)	8(11.3)	5(7.7)	3(13.0)	40(13.2)	
35-44	35(24.3)	18(25.4)	20(30.8)	6(26.1)	79(26.1)	
³45	54(37.3)	35(49.3)	15(23.1)	7(30.4)	111(36.6)	
Total	144(47.4)	71(23.4)	65(21.5)	23(7.6)	303(100.0)	
Mean±SE	38.0±0.9	42.0±1.0	39.9±1.5	35.9±2.5	38.9±0.6	0.215^{NS}
(Range)	(17-61)	(18-54)	(11-61)	(15-52)	(11-61)	

Table-XVI

Distribution of study subjects by histologic pattern and smoking status (Age of starting of smoking)

Smoking status	Pattern Carcinoma				Total	P value
	SQCC	SCC	AC	LCC & others		
Dose of smoking						
Non-smokers	6(4.2)	2(2.8)	21(32.3)	1(4.3)	30(9.9)	0.001^{S}
<20	9(6.3)	6(8.5)	2(3.1)	0.(0.0)	17 (5.6)	
20-29	19(13.2)	15(21.1)	6(9.2)	7(30.4)	47(15.5)	
30-39	17(11.8)	5(7.0)	6(9.2)	3(13.0)	31(10.2)	
³50	62(43.1)	35(49.3)	29(44.6)	8(34.8)	134(44.2)	
Total	31(21.5)	8(11.3)	1(1.5)	4(17.4)	44(14.5)	
Mean±SE	144(47.5)	71(23.4)	65(21.5)	23(7.6)	303(100.0)	
(Range)	40.8±1.8	37.9±2.3	39.3±3.2	38.6±4.1	39.7±1.2	0.215^{NS}
	(9.0-94.5)	(9.0-96.6)	(4.4-150)	(6.0-84.0)	(4.4-150)	

Table-XVII

Distribution of study subjects by histologic pattern and smoking status (Age of starting of smoking)

Smoking status	Pattern Carcinoma				Total	P value
	SQCC	SCC	AC	LCC & others		
Age of starting smoking						
Non-smokers						
	6(4.2)	2(2.8)	21(32.3)	1(4.3)	30(9.9)	0.001[S]
	18(12.5)	9(12.7)	12(18.5)	2(8.7)	41 (13.5)	
<15	58(40.3)	38(53.5)	15(23.1)	12(52.2)	123(40.6)	
15-19	62(43.1)	22(31.0)	17(26.2)	8(34.8)	109(36.0)	
³20	144(47.5)	71(23.4)	65(21.5)	23(7.6)	303(100.0)	
Total	18.6±0.2	17.9±0.4	17.6±0.6	18.4±0.8	18.2±0.2	
Mean±SE	(12-26)	(12-25)	(12-26)	(12-28)	(12-28)	0.215[NS]
(Range)						

Table-XVIII

Distribution of study subjects by histologic pattern and smoking status (Year since quitting)

Smoking status	Pattern Carcinoma				Total	P value
	SQCC	SCC	AC	LCC & others		
Year since quitting						
Non-smokers						
	6(4.2)	2(2.8)	21(32.3)	1(4.3)	30(9.9)	0.001[S]
<5	14(9.7)	5(7.0)	3(4.6)	4(17.4)	26 (8.6)	
9-May	3(2.1)	0(0.0)	2(3.1)	2(8.7)	7(2.3)	
14-Oct	2(1.4)	2(2.8)	4(6.2)	0(0.0)	8(2.6)	
³15	28(19.4)	12(16.9)	22(33.8)	5(21.7)	67(22.1)	
Current smokers	91(63.2)	50(70.4)	13(20.0)	11(47.8)	165(54.5)	
Total	144(47.5)	71(23.4)	65(21.5)	23(7.6)	303(100.0)	

Table-XIX

Distribution of study subjects by histologic pattern Age of patients

Smoking status	Pattern Carcinoma				Total	P value
	SQCC	SCC	AC	LCC & others		
<45	16(11.11)	5(7.0)	9(13.8)	3(13.0)	33(10.9)	0.001[S]
45-54	29(20.1)	15(21.1)	13(20.0)	6(26.1)	63 (20.8)	
55-64	54(37.5)	23(32.4)	24(36.9)	7(30.4)	108(35.6)	
65-74	35(24.3)	25(35.2)	15(23.1)	7(30.4)	82(27.1)	
≥75	10(6.9)	3(4.2)	4(6.2)	0(0.0)	17(5.6)	
Total	144(47.5)	71(23.4)	65(21.5)	23(7.6)	303(100.0)	

NB.
SQCC= Squamous Cell Carcinoma
SCC= Small Cell Carcinoma
AC= Adenocarcinoma
LCC & others= Large Cell Carcinoma and others

Table-XX

Distribution of study subjects by histologic pattern and sex of the patients

Sex	Pattern Carcinoma				Total	P value
	SQCC	SCC	AC	LCC & others		
Male	134(93.1)	69(97.2)	46(70.8)	23(100.0)	272(89.8)	0.001^{S}
Female	10(6.9)	2(2.8)	19(29.2)	0(0.0)	31(10.2)	
Total	144(47.5)	71(23.4)	65(21.5)	23(7.6)	303(100.0)	

Table-XXI

Distribution of study subjects by histologic pattern and place of work

Place of work	Pattern Carcinoma				Total	P value
	SQCC	SCC	AC	LCC & others		
Indoor	35(24.3)	7(9.9)	27(41.5)	4(17.4)	73(24.1)	0.001^{S}
Outdoor	93(64.6)	63(88.7)	32(49.2)	12(52.2)	200(66.0)	
Both	16(11.1)	1(1.4)	6(9.2)	7(30.4)	30(9.9)	
Total	144(47.5)	71(23.4)	65(21.5)	23(7.6)	303(100.0)	

Table-XXII

Distribution of study subjects by histologic pattern and socioeconomic condition socioeconomic condition

Socioeconomic condition	Pattern Carcinoma				Total	P value
	SQCC	SCC	AC	LCC & others		
Rich	4(2.8)	1(1.4)	7(10.8)	0(0.0)	12(4.0)	0.001^{S}
Average	54(37.5)	14(19.7)	25(38.5)	13(56.5)	106(35.0)	
Poor	86(59.7)	56(78.9)	33(50.8)	10(43.5)	185(61.1)	
Total	144(47.5)	71(23.4)	65(21.5)	23(7.6)	303(100.0)	

Table-XXIII

Distribution of study subjects by histologic pattern and pattern of tobacco used tobacco used

Tobacco used	Pattern Carcinoma				Total	P value
	SQCC	SCC	AC	LCC & others		
Cigarette only	27(19.6)	19(27.5)	16(36.4)	4(18.2)	66(24.2)	0.001^{SN}
Bidi only	30(21.7)	30(21.7)	9(20.5)	5(22.7)	65(23.8)	
Both	29(42.0)	29(42.0)	19(43.2)	13(59.1)	142(52.0)	
Total	138(50.5)	69(25.3)	44(16.1)	22(8.0)	273(100.0)	

Table-XXIV

Distribution of study subjects by economic status and pattern of tobacco smoked

Tobacco used	Socioeconomic status			Total	P value
	Rich	Average	Poor		
Cigarette only	5(45.5)	21(24.1)7	40(22.9)	66(24.2)	0.008^{S}
Bidi only	1(9.1)	12(13.8)	52(29.7)	65(23.8)	
Both	5(45.5)	54(62.1)	83(47.4)	142(52.0)	
Total	11(4.3)	87(31.9)	175(64.1)	273(100.0)	

Discussion

Tobacco smoking is widely prevalent in both developed and developing countries. It is one of the important preventable causes of premature death. In developing countries, it has been estimated that nearly 50% of men are dependent on some form of tobacco use whereas less than 50% of women are smokers. The main objective of the present study was to assess whether age of starting, dose and duration of smoking habits differ among smokers and non smokers, among smokers of different categories. The study also assesses the differences of histological types of lung cancer with smoking status. This was a cross sectional study conducted in NIDCH and NICR&H, Dhaka. A total of 303 histologically proven primary lung cancer patients were included in the study.

Of them 272 (89.8%) were male and 31(10.2%) were female.

Male Female ratio was 8.8:1. The numbers of female patients are small in this study which can be explained by the fact that in our country females are dependent on husband and or guardian, religious and social grounds, above all bronchogenic carcinoma is uncommon in female in our country. The finding was consistent with Qayyum (2000), But Crofton and Douglas (1989) have shown that the ratios being approximately 5:1 in the USA and in the U.K., the male/female ratio was approximately 5:1 in 1970, but fell to around 2.5:1 in 1982, Limsila et al (1994) showed male/female ratio 13.7:1 in their series of 1600 patients of lung cancer[6]. These findings are not consistent with the present study. This might be due to fact that tobacco smoking in women of those countries became increasingly popular.

Among both sexes most of the patient in the present series belongs to 55-64 years age groups Male, 94(34.6%), Female 14(45.2%) which is similar to Qayyum's study (2000). This finding is also consistent with the finding of Mahmud et al.[7]

In this study it was found that among current smokers most of the patients 61(37%) and among ex-smoker 40(37.0%) belongs to the age range of 55-64 years. Similar pattern of age ranges were reported by Limsila et al. (1992), Chute et al. (1985) where most of the smokers were in 51-60 years of age group and 50-69 age groups respectively.[8]

Among non-smokers most of the patients belongs to 55-64 years of age 7(23.3%) which is similar to Limsila et al.(1994) where they showed most of the non-smokers were in the 51-60 years age group 103 (29%). Among the smokers most of the patients were male 273(90.1%).[9]

Among 303 patients, 273(90.1%) were smokers and 30(9.9%) were non smokers. Similar was found by Qayyum (2000). Male and female ratio among smokers was 22:1 and 0.6:1 among non smokers, but Limsila et. at. (1994) found a male and female ratio 13:1 among smokers and 0.4:1 among non smokers. Huhi et al. (1980) found 37:1 male and female ratio among smokers and 0.16:1 among non-smokers.[10]

Farmers were the predominant in the present study. It was found that among smokers higher percentage were farmers 111(40.7%), this is due to more than 70% of the population belongs are cultivators groups, whereas among the housewives, 19(63.3%) highest percentage were non smokers considering overwhelming proportion of non smokers among female and an expected observation considering that smoking is a socially unacceptable behaviour among female in our sociocultural milieu. Analysis of smoking habit by the educational status showed that highest frequency of smokers among the illiterate groups, whereas non-smoker were prevalent among the patients having education secondary and above. This might be due to the development of awareness among the educated groups regarding bad effects of smoking. Considering the smoking status and place of works, it was evident that nonsmokers were found to be engaged in indoor works whereas smokers were more in outdoor works. This might be due to fact that in this study most of the patients working in indoor were housewives, whereas outdoor workers are mainly farmers or labourer etc. Comparing the socioeconomic status and pattern of tobacco used, it was found that most of the smokers habituated to both cigarette and bidi and almost equal percentage of patients habituated either cigarette or bidi. A statistically significant difference was found between socioeconomic and pattern of tobacco used ($p>0.05$) indicating poor peoples were habituated with bidi whereas the average socioeconomic groups were habituated to both bidi and cigarette.[11]

Regarding the symptoms, most frequent was cough among smokers. The finding were similar to Qayyum (2000), were 90% of the patients had cough. Huhti et al. (1980) showed 4 to 6% and Chute et al. found 45% their study. The finding is not consistent with the present study. This might be fact that dissimilar in study and or sample size also. But Straus (1998) reported 60% cough in their patients with bronchogenic carcinoma and similar in the present study. Among non-smokers, cough was present in 70%, but no statistically significant difference was found in terms of different presenting symptoms and smoking status.[12]

It was found that 64.4% of the smokers' complaints of chest pain and 66.7% among non-smokers, but the difference were not statistically significant. Qayyum 2000 showed 55 (57.9%) cases of chest pain in his study, similar with the present study. Huhti et al.(1980) reported 30% cases of chest pain in his study, Chute 1985, reported 25 % chest pain in their study, Strauss 1998, reported 38% cases of chest pain (25-50. Ahmed et al. (1999), showed 83.8% of the cases presented with chest pain, this finding s are not consistent with the present study. No statistically significant difference was found between smokers and non-smoker in terms of nature and severity of chest pain 163(50.5%) patients complained of dyspnoea.[13] Among smoker this percentage was 137(50.2%) and among non-smokers 16% (53.3%) have complained of dyspnoea, but no statistically significant difference was found between smoker and non-smoker in terms of dyspnoea, this is very similar with that of Mohiudddin (1998). Chute et al.(1985) found 37% cases of dyspnoea in their study. In Nadel series 12% patients reported with lung cancer.[14]

It was observed that among smoker 131 (48.0) had history of haemoptysis and among non-smoker 16(53.3%) suffered from dyspnoea. No statistically significant difference was found between smokers and non smokers. Qayyum (2000) showed 47(49.5%) haemoptysis which is closely similar with the present study. Strauss (1998) reported haemoptysis in 25-57 cases; this is similar to present study. Chute et ai, (1985) also found similar (27%) result in their study. Weight loss has been reported by 167(55%) cases, Qayyum (2000) showed 62(65.31%) which is similar to the present study, Strauss (1998) reported (8-68%) of the cases in their study complained of weight loss which is also similar to the present study grouping respect of weight loss.[15] Chute et al.(1985), reported 46% cases of weight loss and Christopher noted 32% cases of weight loss out of 446 patients. Clubbing was present in nearly 42% cases. This was similar to the Qayyum (2000) study where he found 40% case with clubbing.[16] Ahmed et al. reported 40% cases of clubbing in their study. Mohiuddin (1998) reported 40% cases very consistent with the present study. Murray and Nadel (1994) observed clubbing in 1% cases but not similar with the present study.[17] Among smoker it was around 43% and among non-smoker it around 30%.[18]

Palpable lymph was found in 17.6% cases, this finding was consistent with the findings of Qayyum (2000). He found palpable lymph node in 22.6% cases. No statistically significant difference was found in terms of nature of dyspnoea fever, loss of appetite, and associated diseases ($p>0.05$). [19]

X-ray was done in all patients; among the smokers highest percentage of patients had pulmonary mass lesion (39.6%) followed by pen hilar opacity (24.2%). Among non smoker highest percentage of patients has mass lesion (50%) followed by perihilar opacity (30%).[20]

Regarding procedure of final diagnosis, it was observed that among smokers highest percentage of patients were diagnosed by Fine Needle Aspiration Cytology (FNAC) of the lung (55.3%), followed by Fibreoptic Bronchoscopy (24.9%), FNAC of lymp node (12.1%). On the other hand highest percentages of non-smoking patients were diagnosed by FANG (70%). The 2 main diagnostic procedures cover more than 85% of tissue diagnosis in lung cancer.[21]

It was observed that out of 303 study subject, highest percentage had Squamous cell carcinoma (47.5%) followed by small cell carcinoma (23.4%), Adenocarcinoma (21.5%), large cell carcinoma 6.3%) and others such as bronchioloalveolar carcinoma, fibrocytoma etc. (1.3%) Crofton et al. (2000), found SQCC (40-60%), SCC (7-25%), ACC (10-25%) and LCC (5-15%). This findings are similar to this findings, Strauss (1998), observed SQCC (30%- 40%), Large cell (10%), Small Cell (25%). Barbone et al.(1997) showed SQCC (35%), 5CC (29%), AC (21%) and LCC (12%) and other histologic

types (3%).[22] These findings are almost similar with the present findings. The SQCC in few study has lesser amount may be due to the changing smoking habits in the western world.[23]

Limsila et al. (1994) in a series of 1600 histologically diagnosed lung cancer cases showed SQCC (29%), AC (29%), LCC (24%) and SCC (13%). The findings are not similar with the present study. Gil et al.(1999) observed (51.7%) SQCC, 5CC (21.2%), ACC and others (16.9%), these findings are consistent with the present study group. Jedrychowski et at. (1992) described 50CC (54.7%) SCC (24.1%) and AC (16.9%) LCC and others (4.3%), these findings are closely consistent with the present study. Above finding strongly suggests that smoking is related to all major histological types of lung cancer.[24]

From the present study it was observed that highest percentage of bronchogenic carcinoma was SQCC (50.5%) among the smokers (Ex- & current) followed by SCC (25.3%), AC (16.1%)and lastly large cell carcinoma. Where as among non smoker highest percentage was Adenocarcinoma (70%).Followed by SQCC (20%) and the difference was statistically significant ($p<0.05$) indicating AC was higher among non-smokers. On the other hand as mentioned earlier among smokers highest percentage of bronchial carcinoma was SQCC. [25]

Intensity of smoking in terms of number of sticks of cigarettes used by the smokers it was observed that mean number of stick used by smokers was 21.2/day. The mean number of stick/day was 20.2/ day for LCC, 20.8/day for SQCC, and 20.9/day for SCC and 20.1/day for AC and the mean difference was not statistically significant It is evident that heavy (intense) exposure is almost equally important for the major histologic types of lung cancer

Highest no of patients in all histologic categories smoked more than >25 stick per day. It was almost similar to the observation of Barbone et at. (1997) where they observed that 30.3% of the squamous cell carcinoma group, 31.19% of small cell, 26.6 Large cell & 27.2% adenocarcinoma group smoked between 20 to 29 stick/day and similar pattern of carcinoma was found in relation with smoking habit in the present study. Jedrychowski et al. (1992) found a higher percentage of patients with SQCC(45.1%), SCC (46.62%),& AC (52.52%) used 20-29 cigarettes /day in their study.

In case of adenocarcinoma, majority of the patients (56.9%) used more than 25 stick/day, but Barbone et al. (1997) found most of the patients of Adenocarcinoma (27.2%) had used 20-29 stick/day. Jedrychowski et at. (1992) found 49.0% of adenocarcinoma smoked 20-29 stick/day. In large cell carcinoma, also a higher proportion of patients (43.5%) smoked more than 25 stick/day. Barbone et al. (1997) found (26.7%) in their study.[26]

Differences in duration of smoking habits has been observed among the different histologic pattern of lung cancer. In the present study majority of patients of SQCC, SCC, and LCC had as duration of smoking more than 45 years (Table.17) and similar was found by Jedrychowski et al. (1992) where majority of the patients smoked between 30-50 years. Barbone et al. (1997) also observed majority of the patients having major histologic types of lung cancer continued their smoking habit for more than 50 years.

Dose (ie, life time cigarette consumption) was calculated multiplying intensity (packs packs of 20 cigarettes per day) by total duration (years). It was calculated also easily by the following formula: Dose= no. of stick used per day X duration of habits in years/ 20. Pack year is as unit equivalent to 7300 cigarettes. In this study duration of smoking habit was measured by substracting the age of starting smkoing from the current age (in years) in case of current smoker, where as in case of ex-smoker, by adding the quitting year/years with the age of starting smoking then substracting the two from the current age.[25]

Among smokers mean dose of smoking was 39.7 pack year. It was slightly higher for SQCC, 41 pack years which was not statistically significant. From the present observation It evident that all major histological types of lung cancer require almost equal amount of exposure to smoking. Barbone et al found more than 40% of the patient of all histological categories smoked 45-89 pack year.[23]

Number of the patients in the present study is small it is evident that intensity of smoking in terms of pack year is strong among SQCC, SCC, and adenocarcinoma as well as Large cell carcinoma. It is also evident that SQCC are fore frequent among smokers and incidence of

adenocarcinoma was higher among non smokers and females. Similar observation was made in a study of 480 Chinese patients of Cantonese descent in Hongkong, where 43% of the female patients had adenocarcinoma and 61% of them were nonsmokers (Lam. e t al 1983).Given the high prevalence of adenocarcinoms among female nonsmoker, it is possible that a factor other than smoking is operating among female patients or small sample size inference can not be drawn, warranting further investigation.[21]

Limitations

Total sample size was small and among them the proportion of non-smokers are also minimum, so comparison among the groups was not justified statistically in all situation. The histological diagnosis of the patients was not uniform, and all the diagnosis was not reviewed by second opinion. Majority came from lower socioeconomic condition and illiterate, so they could not give the smoking details clearly.[20]

Conclusion

Data of the present study confirmed a marked relationship between smoking and all histological types of lung cancer under study and also showed that squamous cell carcinoma is more frequent among male smokers and adenocarcinoma in nonsmoking females. However, the association of smoking and adenocarcinoma remain unclear at the moment. Further work in this field should be encouraging.

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REVIEW ARTICLE

Management of Tuberculosis- in the Newborn and pregnancy A Review

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Introduction

Tuberculosis, pulmonary scourge, present in the bone remnants of prehistoric man, observed as Pott's disease in Egyptian mummies, written about by greats such as Hippocrates and Gale, called consumption due to its ravaging effects on the body, dubbed the "Captain of the Man of Death" by Bunyan in his "The Life and Times of Mr. Badman," has been the center of investigation for thousands of years.[1] Once the leading cause of death in civilized countries, improved diagnostic capabilities, careful case investigations, and the development of multiple drugs with which to treat it, have reduced its potential as a threat to the health of the world's population. However, during the last decade, this ancient disease, "phthisis," as it was named by the Greeks, has reemerged as an increasingly dangerous and difficult pathogen. Multiple reasons exist for this, not the least of which is the human immunodeficiency virus (HIV) epidemic. Whereas once, authorities wrote about the triumph over tuberculosis being on the horizon, the development of multiple drug-resistant organisms, increasing homelessness and poverty, the HIV epidemic, and shrinking healthcare reserves have propelled tuberculosis back into the position of a prominent and serious health hazard.

As old as tuberculosis is, it is no older than pregnancy, and over the millennia, investigators have studied the interactions between the two. The myriad of ways that these two conditions interact has been examined extensively. Originally thought to be beneficial to the course of pregnancy, the belief that tuberculosis was detrimental to the point of recommending abortion for the pregnant evolved. This pessimistic view was not substantiated over time, and even before effective chemotherapy developed, it appeared that if not beneficial, tuberculosis was at least inconsequential to the course of pregnancy in the mother. The development of effective chemotherapy, that could be safely employed in the pregnant patient, has perhaps lulled today's physicians into believing that tuberculosis in pregnancy is no longer a serious or significant problem.

The diagnosis of tuberculosis (TB) in pregnancy is of utmost importance to both the mother and the fetus since untreated disease carries much greater risk to both. One third of the world's population is infected with Mycobacterium tuberculosis.[1] It is expected that the incidence of tuberculosis among pregnant women would be as high as in general population. The clinical and laboratory diagnosis, and therapy during pregnancy and postpartum period, deserve special attention. Also untreated pulmonary tuberculosis in a pregnant woman would be a definite risk for transmission of disease to the new born.

Limitation in the diagnosis of tuberculosis during pregnancy, safety of antituberculosis therapy and the need for prophylaxis must be in the knowledge of all physicians giving care to pregnant women.

Effect of tuberculosis on pregnancy and childbirth

From the maternal point of view, there is no evidence to suggest that tuberculosis affects or complicates either the course of the pregnancy or the type of delivery required[2] If proper and adequate chemotherapy is given to pregnant women with TB, they are not at higher risk than non-pregnant women with TB[3].

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Effect on Neonate

The fetus may be at risk if maternal disease is untreated. For example congenital infection can occur by hematogenous spread via the infected placenta, via tuberculosis endometritis or infected amniotic fluid.[4] Fortunately congenital TB is rare, as there is a high mortality of around 50%.[5] The risk of neonatal infection is greater postpartum with transmission via the respiratory tract, especially if the mother has smear-positive, acid-fast bacilli in her sputum and the condition remains undiagnosed.

Congenital TB may occur when there is hematogenous spread of tubercle bacilli through the umbilical vein from the placenta to the fetal liver, or when tubercle bacilli are ingested or aspirated from infected amniotic fluid.[6-9] The diagnosis of congenital TB is somewhat controversial. Historically, the diagnosis was made when the primary TB complex was present in the fetal liver and all other mechanisms of TB acquisition had been excluded. More recently, Cantwell et a1[6] suggest that the diagnosis of congenital TB should be based on one of the following factors: (1) demonstration of a primary hepatic complex or caseating hepatic granulomas by percutaneous liver biopsy at birth, (2) infection of the maternal genital tract or placenta, (3) lesions noted in the first week of life, and (4) exclusion of the possibility of postnatal transmission by a thorough investigation of all contacts, including attendants.

Diagnosis

It is recommended that all patients undergo TB screening during pregnancy[10]. The most effective test is the Mantoux test (Fig. 1). For patients at risk for anergy, such as patients with HIV infection or severe immunosuppression, control antigens (candida, mumps, or tetanus toxoid) also should be placed. Data from a study comparing TB rates of HIV- positive pregnant and nonpregnant women revealed that 30% of pregnant women and 49% of nonpregnant women were anergic[11]. Although anergy was associated more commonly with CD4+ cell counts less than 0.5 x I 09/L, 27% of women with higher counts were also anergic. The purified protein derivative (PPD) is 90% to 99% sensitive for the diagnosis of TB exposure. The tine test (multiple puncture test) is not advised due to its low sensitivity.

For individuals who have received bacilli CalmetteGuerin (BCG) vaccine, the Mantoux test still should be planned unless their skin tests are known to be positive. Over time, tuberculin reactivity caused by BCG is likely to wane.[10] Therefore, one should consider TB infection and preventive therapy in an individual with a skin test reaction of 10 mm or more induration if that individual received the BCG vaccine more than 10 year earlier.[12]

An approach to management of a positive PPD is outlined in Figure 2. The radiologic findings suggestive of active disease include adenopathy, multinodular infiltrates (especially in the upper lobes), cavitation, loss of volume in the upper lobes, and upper medical retraction of hilar markings. After a suspicious or positive chest radiograph, three early morning sputum samples should be obtained for TB culture. Sterile pyuria in the setting of a positive PPD may be an indication of renal TB. Likewise, liver or lymph node biopsy for TB stain and culture may be necessary to make the diagnosis of extrapulmonary TB.

In general, if a mother has active untreated TB at the time of delivery, she should be placed in respiratory isolation and separated from her infant. If she has been treated with appropriate antituberculosis therapy longer than 2 weeks, isolation may not be necessary.

Mantoux test (0.1 ml of PPD)(must raise a wheal [6-10 mm] subdermally)

|

Read of 48 72 hours

|

= 5 mm induration = negative

= 5 mm is positive for HIV infected individuals, close contact of infectious cases, those with fibrotic lesions on CXR

= 10 mm is positive for "high-risk" groups

= 15mm is positive for persons not at "high-risk"

Figure 1 : Algorithm describing the Mantoux test. Asterisk indicates "high-risk", which is defined as: HIV-negative injection drug users, individuals with medical disorders that increase the risk for reactivation of latent TB (e.g., silicosis, gastrectomy, jejunoileal bypass surgery, =10% below ideal body weight, chronic renal failure, diabetes mellitus, high dose steroid or immunosuppressive therapy), some reticuloenclothelial disorders (e.g., leukemia), foreign-born persons from areas where TB is endemic, residents of long-term care facilities or shelters, persons from medically underserved low-income populations, and healthcare workers who provide services to aforementioned patient populations, PPD = purified protein derivative.

Drug treatment

Treatment of pregnant women with active tuberculosis

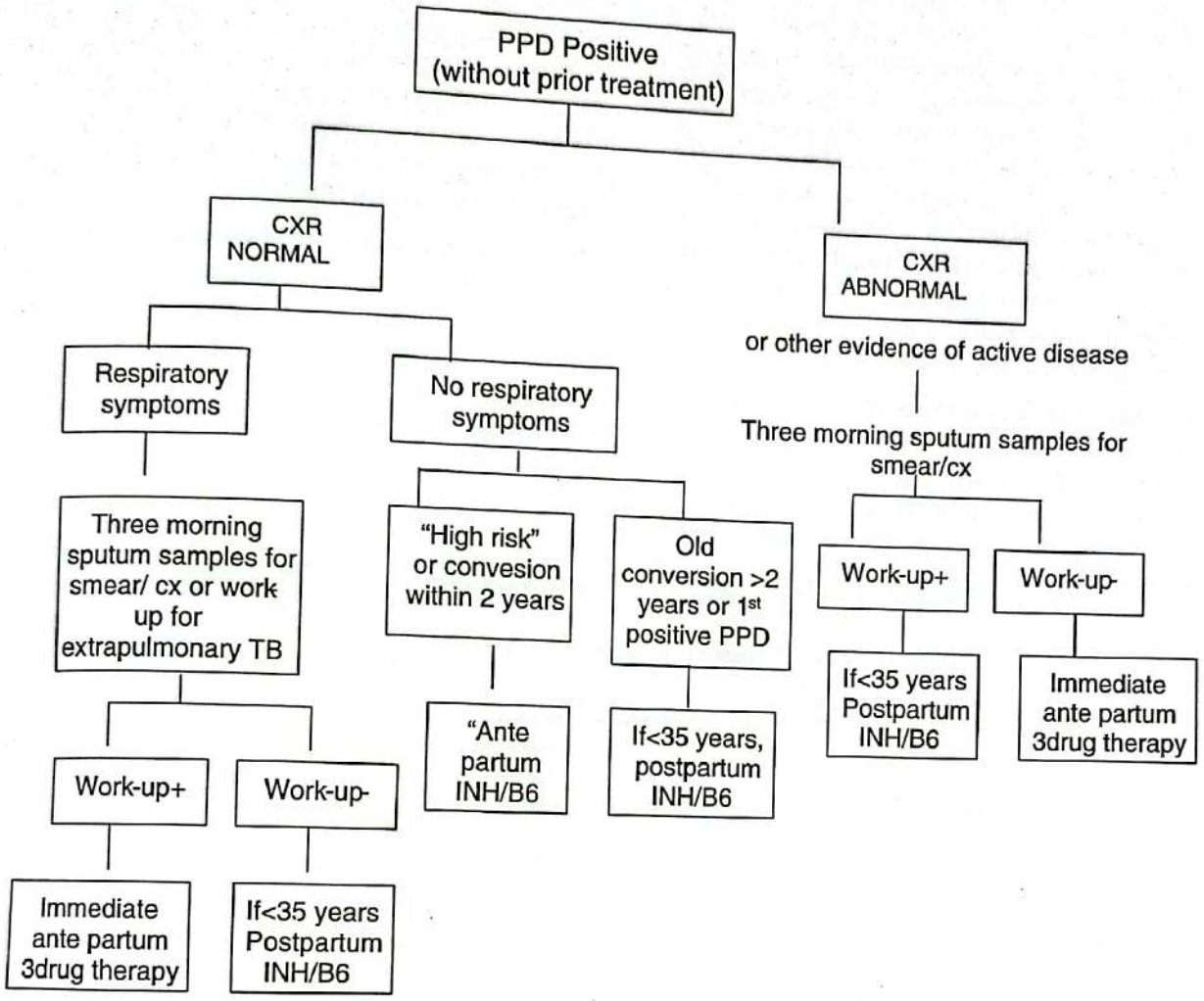

Fig.-2: *Algorithm for the management of a positive PPD.*

The indications for treatment of active tuberculosis in a Pregnant women are the same as for a non-pregnant women. Treatment should be initiated without delay. Several factors can affect the selection and dosage of TB drugs including hepatic and renal impairment, pregnancy, duration of disease before treatment, and extent of debilitation.[13]

Review of published data reveals that INH is safe during pregnancy. Although it crosses the placental barrier, it is not teratogenic even when administered in the first trimester.[14] Only one percent incidence of abnormalities was reported in infants of mothers treated with INH, which falls below the 1.2-6% incidence of fetal malformations cited in the population at large. The rate of congenital malformations in infants who received rifampicin was 3.35% in a study and included limb reduction, CNS lesions and hemorrhagic complications postulated to be due to inhibition of DNA dependent RNA polymerase,[14] However, the incidence falls within the safety limits and hence rifampicin is also considered to be safe. Ethambutol is the next commonly used drug in pregnancy with an incidence of malformations reported at two percent. Although it was feared that ethambutol might interfere with opthalmological development, this was not observed in doses of 15-25 mg/kg body

weight/day". Pyrazinamide, the bactericidal drug used in most first-line regimens, does not have sufficient studies to ensure its safety during pregnancy. Although some international organizations recommend its use, it may be avoided due to inadequate data on teratogenecity. Streptomycin has been proved to be potentially teratogenic throughout pregnancy causing fetal malformations and eighth nerve paralysis with deficits ranging from mild hearing loss to bilateral deafness. Other aminoglycosides including kanamycin, amikacin and capreomycin are also contraindicated during pregnancy.

Para-aminosalicylic acid (PAS) was commonly used in conjunction with INH during the 1 950's, and 60's and did not appear to increase the malformations in infants but caused gastrointestinal side effects, which were difficult to tolerate during pregnancy. Little is known about the safety of cycloserine, ethionamide or fluoroquinolones like ciprofloxacin and ofloxacin during pregnancy. There are no existing guidelines for the treatment of pregnant women with drug resistant tuberculosis and it has been suggested that elective abortion may be considered while treating a pregnant women with MDR-TB.[15]

ERH is a safe regimen. Pyrazinamide should be avoided and streptomycin should be discontinued if the patient becomes pregnant. There is no indication for therapeutic abortion except if MDR-TB is established. A contact study should be considered on a case-to-case basis. In the postpartum period it is important to look for drug induced hepatitis, which is common in these patients.

Table

Drugs commonly Used to Treat Tuberculosis With Dosage and Side Effects.

Drug Name	Daily Dose	Intermitted Dose	Usual Dose	Side effects	Safety in Pregnancy
Isoniazid	10-20mg/kg po or IM	20-30mg/kg 2x wkly	300 mg qd 900 mg 2x wkly	GI distress, hepatitis, seizures, peripheral neuritis hypersensitivity reactions	Safe
Rifampin	10-20mg/kg po	10-20 mg/kg po	600 mg qd 600 mg2xwkly	GI distress, hepatitis, headache, purpura, febrile reaction, orange secretions	Safe
Ethambutol	15-25mg/kg po	50mg/kg po	2-2.5mg qd 4mg 2x wkly	Altered visual acuity, redgreen disturbance, optic neuritis, skin rash	Use with caution
Pyroazinamide	15-30mg/kg po	50-70mg/kg po	2-2.5mg qd	Hepatitis, hyperuricemia, arthralgias, gout	Use with caution
Streptomycin	15-25mg/kg IM	25-30mg/kg IM	1 mg qd 1.5gm 2x wkly	Ototoxicity, nephrotoxicity	Contraindicated
Paraamino salicylic acid	150mg/kg po		10-12 gm qd	GI distress, myxedeap hepatitis, sodium load, CNS-headache, psychosis, seizures, drowsiness	Use with caution
Kanamycin	15-30mg/kg IM	15mg/kg IM 3-5x	0.75-1 gm IM qd	Nephrotoxicity, ototoxicity, rare vestibular toxicity	Contraindicated
Capreomycin	15-30mg/kg IM	15mg/kgIM 3-5x wkly	0.75-1 gm IM qd	Nephrotoxicity, ototoxicity	Contraindicated
Viomycin	15-30mg/kg IM	1-2 gms IM 2-3x wkly	0.75-1 gm IM qd	Nephrotoxicity, auditory and vestibular toxicity	Contraindicated
Ethionamide	15-20mg/kg po		1 mg qd	GI distress, heapatotoxic hypersensitivity	Use with caution

q.d = daily; PO = Oral; IM= intramuscular, GI = gastrointestinal; CNS = central nervous system.

Treatment of tb in lactating women

The safety of breast-feeding is an important issue. Several studies have measured the concentration of ATT drugs in breast milk.[16-18] INH concentration peaks after three hours reach a concentration of 16.6 mg/l with a 300 mg dose.[16] Rifampicin has a peak milk concentration of 10-30 mg1l with a 600 mg dose.[17] No information on the concentration of ethambutol in breast milk has been published. Streptomycin reaches a concentration of 1.3 mg/I thirty minutes after injection of a I gm dose.[19] There is consensus that breast-feeding should not be discouraged. ATT drugs should be taken preferably after breast-feeding and the next feed could be a bottle-feed. Drug concentration in breast milk is low and has no therapeutic value. If both the mother and infant are taking INH, the drug may reach supratherapeutic doses and in such circumstances bottle-feeding is recommended. Supplemental pyridoxine should be administered to an infant on INH or if the breast-feeding mother is taking INH because pyridoxine deficiency may cause seizures in the newborn.

Chemoprophylaxis

The safety of isoniazid is considered sufficient to recommend its use as preventive therapy in pregnancy, i.e. in those who have a positive tuberculin skin test and who have reasonable grounds for suspecting exposure to tuberculosis, but have not developed the disease. In this group, the life time risk of developing tuberculosis is considered to be 10% and the likelihood of developing tuberculosis within 2 years of a positive skin test is approximately 2%.[21,21]

Preventive treatment can be delayed until after delivery, in view of the general fear of taking any medication during pregnancy. However, those with recent contact or with concurrent HIV infection should take chemoprophylaxis after the first trimester.[22] If preventive treatment was started before pregnancy, it should be continued. Such a person can be reassured that the likelihood of fetal abnormality has not increased.

Conclusion

Tuberculosis has been present for thousands of years, during this time, strides have been made in the diagnosis and treatment of the disease. Once feared during pregnancy, it can now be safely and effectively treated with little harm to mother or fetus. Problems that remain include assuring adequate treatment, patient compliance, HIV epidemic, drug resistance, and decreasing medical reserves with which to treat this old, but persistent pathogen. It should be carefully searched for in all pregnancies to find cases that might not otherwise be discovered, to prevent serious maternal and / or fetal disease, and to prevent spread to others. The initial step should be a careful history and physical examination, followed by a PPD test. Those patients who test positive should undergo a chest radiograph and evaluation for the presence of underlying tuberculosis. Pursuit of recommendations made in this article will decrease the incidence of disease and effectively treat it when present. The reader is urged, when facing difficult decisions, to consult a specialist in the field, especially in this era of drug resistance and the HIV epidemic. If carefully sought and effectively treated, tuberculosis may once again take a back seat to other disorders as a threat to the health of the pregnant patient.

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Chest & Heart Journal
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CASE REPORTS

Congenital Oesophageal Duplication cyst : A Case Report

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[Chest & Heart Journal 2006; 30(1) : 69-72]

Introduction:

Cysts within the oesophageal wall may represent inclusion cysts, retention cysts and developmental cysts. The oesophagus is formed after proliferation and later degeneration and vacuolization of epithelial element of the dorsal foregut. Persistence of one of these vacuoles amid degenerated epithelial masses results in oesophageal duplication cyst[1]. Oesophageal cyst is one of the rarest benign neoplasm of the oesophagus account for 0.5 to 2.5 % of all tumours of oesophagus. Evidence from autopsy series suggests an incidence of 1:8200 for oesophageal cysts, with a 2:1 male predominance. Most of the cysts were reported to arise in the lower oesophagus, with only 23% occurring in the upper third[2]. Majority of oesophageal cysts present as symptomatic lesion in neonate or young child but 25 to 30% are formed in adults[3]. Oesophageal cysts present with compression symptoms of mediastinal structures. Dysphagia is the most presenting symptom. But dyspnoea, pain, cough, wheeze can also occur. Infection within cyst may present with fever, causing cyst fluid purulent otherwise cyst contains brownish cloudy serous fluid. Microscopically luminal epithelium varies cuboidal to ciliated columnar and presence of muscle layers. Malignancy may occur in the cyst. Standard chest radiograph may demonstrate a mediastinal mass. Contrast oesophagogram may reveal focal, smooth compression of the oesophagus. CT scan cannot definitely distinguish oesophageal duplication cysts from benign intramural or paraoesophageal lesion such as abscess, old haematoma, neurofibroma, lipoma, or other foregut cysts[4]. Transoesophageal ultrasound reported successful in diagnosing this type of lesion[5]. Oesophagoscopy also necessary to rule out other oesophageal lesions. Surgery is the treatment of choice in both symptomatic or asymptomatic oesophageal duplication cysts. After successful excision of the cyst recurrence is rare.

Case Report

Master Sujon of 4 years, s/o. Mr Abdur Rahim, hailing from Chenga kandi, Sonargaon, Narayanganj admitted in NIDCH on 28.11.05 with complaints of Dysphagia to solid food for 6 months and Chest pain, Fever and shortness of breath for 2 months. Sujon's mother stated that her son having difficulty in having solid food for six months and for this reason she used to feed meshed food to her baby before that the baby was fed with milk and liquids only. Baby complaints of central chest pain almost all the day for two months, pain increased during and after meal, during bending or leaning forward and relatively relieved at rest. When sujon developed low grade intermittent fever, associated with shortness of breath his parents consulted with paediatricians. Examining the baby meticulously and investigating all haematological, biochemical and radiological investigations they conclude as a case of lymphoma or tuberculosis. Haemoglobin-13.2gm/dl, ESR-32 mm in 1st hour,Total count of WBC 7500/cmm, Differential count: Polymorph-50%, Lymphocyte-40%, Eosinophil-08%. Peripheral blood film: RBC and Platelets-normal, WBC- mature & Eosinophilia. Widal test: Normal, Total bilirubin- 0.5mg/dl, SGPT-14 U/L, SGOT- 10 U/L, Serum total protein-5.0g/dl, Albumin- 4.2g/dl, globulin-0.8g/dl, X-Ray chest P/A view – Enlarged cardiac shadow with suggestive of

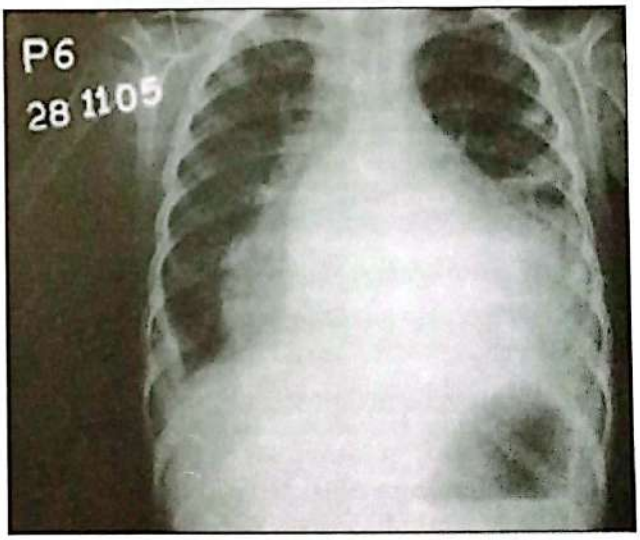

Fig-1: *Showing enlarged cardiac shadow and (L) pleural effusion.*

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left sided pleural effusion (Fig-I).

Pleural fluid aspiration done (L)- Colour-Hazy, RBC-Plenty, TC of WBC-800/cmm, Lymphocyte-85%, Sugar-76mg/dl, Protein-320mg/dl, no AFB, Gram stain reveal no organism, Culture and sensitivity – no growth and negative for malignant cells.

But repeated aspiration reveal turbid pleural fluid and growth of pseudomonas sensitive to Amikacin, Netlemycin, Imipenem. Treated with Amikacin. USG of abdomen- Normal, Bilateral pleural effusion. Colour Doppler Echocardiogram- EF-72%, normal chambers, arterial and venous connection normal, no valve lesions. Moderate pericardial effusion, huge left pleural effusion, Bone marrow examination- Nonspecific findings.CT Scan of chest- Impression 1.

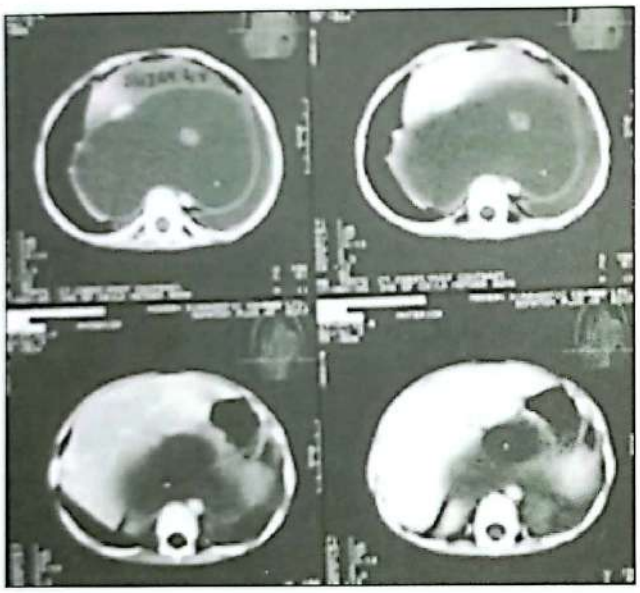

Fig-2: *CT Scan of chest showing mediastinal cystic mass lesion.*

Mediastinal cystic mass lesion (Fig-II).

CT guided FNAC of lesion: 20 cc brownish fluid aspirated, microscopy consisted with Bronchogenic cyst. D/D Mesothelial cyst, Tubercular pleural effusion. Patient than transferred to NIDCH for evaluation and management. With above features and investigation profile we advised a contrast oesophagogram. It revealed oesophagus is compressed from all sides resembling stricture of

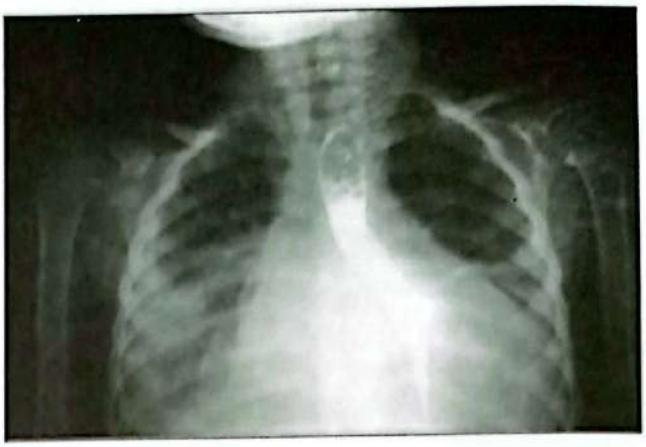

Fig-3:*Contrast oesophagogram showing smooth compressed oesophagus.*

oesophagus(Fig-III).

Re evaluation of contrast enhanced CT Scan of chest and relevant other investigations we decided for thoracotomy.

On 17th December 2005 , Under G/A, Through left standard posterolateral thoracotomy left thoracic cavity entered. Lung found compressed with little effusion, a mass extended from aortic arch to diaphragm & laterally occupying 2/3rd of thoracic cavity. Aspiration revealed straw coloured fluid. Incision made along with long axis of mass. Uni-loculated large cyst encircling the oesophagus found from aortic arch above to lesser curvature of stomach below, covering the cardia, part of fundus and posteriorly part of body of the pancreas. Lateral extension seen into right hemithorax. Cyst was not communicating with

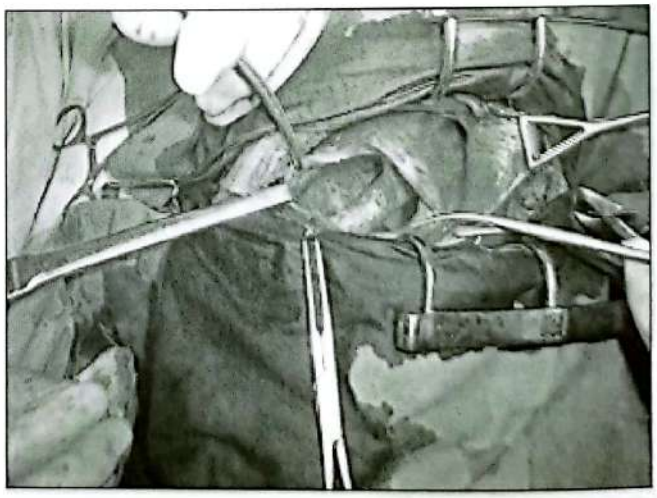

Fig-IV: *Per operative view. Oesophagus encircled by the cyst*

oesophagus (Fig-IV).

After proper delineation of anatomical structures of mediastinum, partial excision of cyst and marsupialization done. With keeping one thoracostomy tube and one nasogastric tube wound closed. Patient was transfused two units of blood. Post operative period was uneventful. On third day all tubes off done and patient allowed to have orally. Stitches off done on 9th postoperative day. Biopsy of cyst wall: Layers of muscles with fibrosis, no malignancy seen. aspirated fluid shown-No growth.

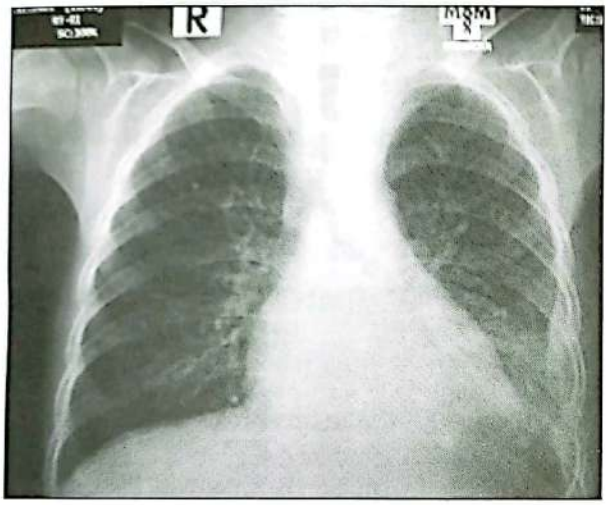

Fig-5: *Follow-up X-Ray chest P/A view showing heart and mediastinal shadow normal.*

Follow up X-Ray chest revealed normal (Fig-V).

Discussion:

Oesophageal cyst is one of the rarest benign neoplasm of the oesophagus. There are no published records related to this type of oesophageal neoplasm in our country.

Location of the cyst mostly in lower oesophagus. Harvell JD and associates found one oesophageal cyst involved at the lower end of oesophagus detected in the abdomen[6]. Matsumura Y and associates experienced 8 cases of oesophageal cysts during the period of 1965 to 1989. In comparison with mediastinal masses operated at that time oesophageal cyst was 2.5%, male predominant (7:1) and mostly occurred in the right side[7]. We found our patient having oesophageal cyst encircling the oesophagus but appeared in the left side.

Age of presentation is mostly neonate and young children but it can be presented in adult age also. Matsumura Y and associates experienced 8 cases of oesophageal cysts where mean age 29.3 years. Kim YW and associates , Laraja RD and associates reported a case of oesophageal duplication cyst in an adult female[8,9]. In our patient it was early childhood presentation.

Presentation of oesophageal cyst varies according to size and compression to surrounding structures. Initial asymptomatic may become symptomatic in the course of time. Dysphagia is the most common encountered symptom. Chest pain, respiratory distress, chronic cough, fever, haemoptysis[10,11,12].

Standard chest radiograph P/A and lateral view is the first investigation we performed to diagnose oesophageal cyst as a mediastinal pathology. Contrast x-ray of oesophagus shows displacement of oesophagus but does not differentiate cystic lesion to intramural leomyoma or other mediastinal pathology. CT scan with contrast material in oesophagus we performed to detect the lesion in oesophagus in relation with other mediastinal pathology. MRI of oesophageal duplication cysts has been advocated but the diagnostic value is equal or better than CT scan[13]. Trans oesophageal ultrasound has a great role in diagnosing oesophageal duplication cysts.

Therapy for oesophageal duplication cysts is complete surgical excision of the cyst and its contents[14]. Small cyst excision is easy but long tubular cyst as we encountered is difficult. The surgical principle for removal of oesophageal duplication cyst is avoidence of oesophageal mucosal injury. Thoracoscopic resection of oesophageal duplication cyst is possible but needs expertise and instruments[15].

After successful removal of the cyst recurrence is extremely rare. We followed up the patient for last 9 months showing no recurrence, reflux or dysphagia. But long term follow up is needed.

Conclusion:

Oesophageal duplication cyst is rare benign disease of oesophagus, presents in neonate and early childhood but adult age presentation also common. Infection within the cyst, malignant transformation can complicate the cyst. After diagnosis at any age, surgical excision is the treatment of choice. After

complete excision recurrence is rare and prognosis is excellent.

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Device Closure of Perimembranous Ventricular Septal Defect (VSD) With Amplazer VSD Occluder: A Case Report

Lt. Colonel Nurun Nahar Fatema, Lt. Colonel SM Mamunur Rahman, Lt. Colonel Syed Asif lqbal, Major Touhid ul Mulk, Major Anisur Rahman

Abstract

A three and half years old boy was diagnosed as a case of perimembranous (PM) ventricular septal defect (VSD) since early infancy. He had failure to thrive with recurrent respiratory tract infection (RTI). He had history of hospital admission several times for RTI. Patient had cardiac Catheterization in June 2005 which showed significant left to right shunt and mild pulmonary arterial hypertension. He was planned for VSD device closure on elective basis. Finally it was performed on 4th April 2006 in Combined Military Hospital (CMH) Dhaka. Echocardiography on next day showed no residual shunt. Patient was discharged from hospital after 72 hours observation.

[Chest & Heart Journal 2006; 30(1) : 73-75]

Introduction:

Device closure of patent ductus arteriosus (PDA) and atria] septal defect (ASD) is now widely accepted and practiced worldwide. Transcatheter closure of ventricular septal defect (VSD) remains challenging and controversial[1]. Most VSD's are accessible surgically and still present time, repair by open heart surgery is regarded as best option in many countries. However there are small group of children with VSD that are difficult to close surgically and involved higher risk, those defects can be closed with devices. But currently pediatric cardiologists would recommend this from of treatment in preference to surgical repair for all VSD's who had no aortic valve prolapse, infundibular stenosis and who are not adjacent to the aortic valve, pulmonary valve and not closely related to the tension apparatus of the mitral and tricuspid valves [1-4].

VSD closure is being available in a small number of centre worldwide. First ever case of perimembranous VSD device closure in Bangladesh was performed in cardiac centre of Combined Military Hospital (CMH) Dhaka on 4th April 2006 which led writing this report.

Case report:

Master S. a three and half years old boy was diagnosed as a case of Ventricular Septal Defect (VSD), perimembranous type since early infancy. He had history of recurrent chest infection. He was on maximum anti failure medication and follow up evaluation was done at three months interval with CXR, ECG and Color Doppler echocardiography. He had cardiac Catheterization in June 2005 which showed QP:QS of > 2:1. His pulmonary artery pressure was 41/16 /8mm Hg. His VSD size was about 06 mm and VSD margin was 08 mm away from the aortic valve. As this patient fulfilled criteria for device closure he was planned for device closure once device and technology would be available in cardiac centre of CMH Dhaka. On his follow up evaluation at three monthly interval his condition was found stable every time. At last device closure was performed on 4th April 2006 when technology was transferred to us by on American pediatric cardiologist.

Procedure:

Equipment's required:

1. Perimembranous VSD device
2. Amplatzer torque delivery system
3. Terumo exchange wire
4. Noodle's wire
5. Arterial and venous sheath.
6. JR-4 catheter
7. Pigtail catheter
8. Snare catheter
9. Standard pediatric drape
10. Echocardiography machine with TEE probe.

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A 6 F sheath was introduced to right femoral vein and a 5 F sheath was introduced to right femoral artery. A pigtail angiography of left ventricle (LV) was performed to locate VSD and measure the size of it. A JR-4 catheter was used with Terumo wire guide to cross VSD. JR-4 was forwarded to main pulmonary (MPA) and terumo wire was changed with noodle wire. Noodle wire was snared from MPA with the help of snare catheter and pulled out through right femoral vein.

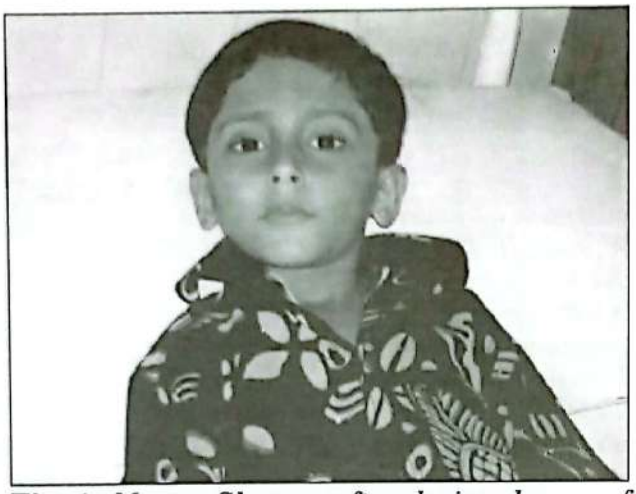

Fig.-1: *Master Shawon after device closure of perimembranous VSD.*

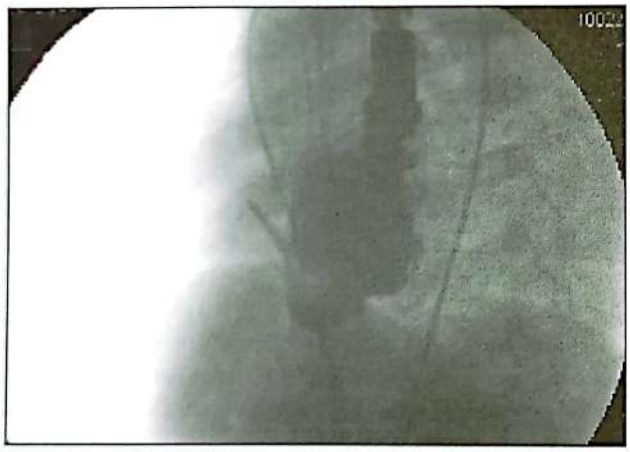

Fig.-2: *LV angiogram showing VSD device in position without any residual shunt.*

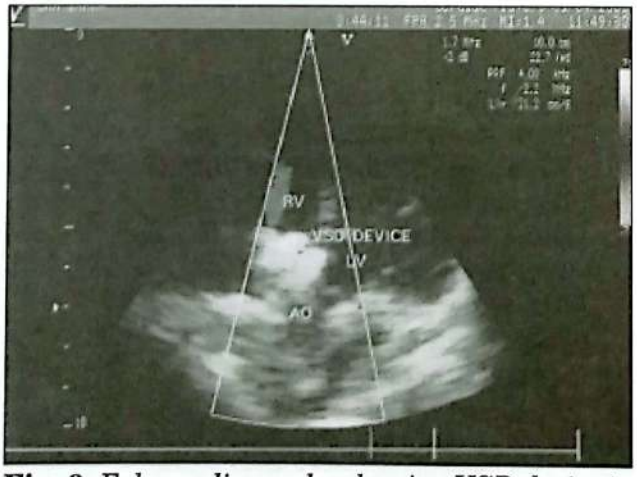

Fig.-3: *Echocardiography showing VSD device in position.*

Amplatzer torque delivery sheath of 7 F size was introduced through right femoral vein over the noodle wire. Delivery sheath was advanced to aorta, than dilator was withdrawn for a short distance and sheath was rotated clock wise and withdrawn backwards to drop it to LV facing towards apex. A 6 mm device was selected for this case and device was loaded to loader with the help of delivery cable and pusher catheter. Delivery system was forwarded to LV. LV disc was released first. Than whole system was withdrawn to RV and RV disc was released. Both fluoroscopy and TEE guide was taken during deployment. Then Pusher catheter was withdrawn backwards and device released by counter clock wise rotation of delivery cable.

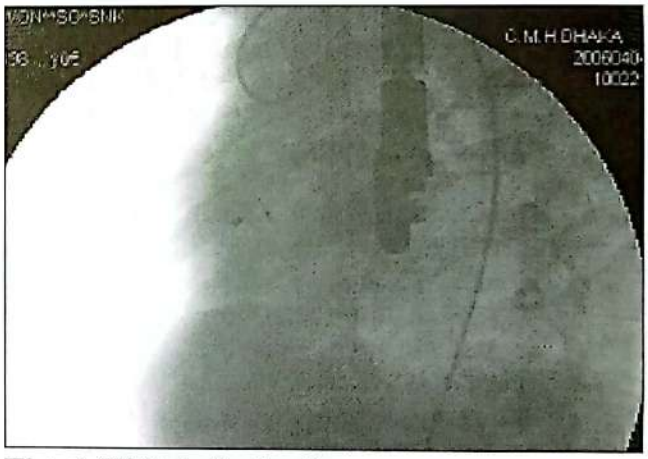

Fig.-4: *VSD device in situ.*

A pigtail LV graphy was done to confirm complete occlusion of VSD. Patient was heparinized with 100 unit / Kg heparin before deployment of device. Injection. Zinacef I S mg / Kg body weight IV was given after deployment of device and was repeated at 8 hourly interval for 24 hours. Echocardiography repeated on next morning, No residual shunt was noticed. Patient was discharged three days after the procedure and follow up appointment was given at 1, 3, 6, 9, 12, 18, 24 months and yearly thereafter.

Discussion:

Non surgical closure of VSD is much less well accepted and can only be regarded as an option for very selected case and available only in very few

centre worldwide. The procedure of VSD was first attempted by Lock et at in 1988 and devices originally designed for closure of other intra cardiac defects like Rashkind umbrella device, lock clamshel, cardioseal, coils, sideris buttoned devices etc were used with a variable success rate and residual shunt[5]. Device closure of perimembranous VSD has been feasible, safe and effective with the new membranous Amplatzer septal occluder[b]. One study was conducted in Sao Paulo, Brazil to see the technical and morphological aspect of Amplatzer membranous VSD occluder[6]. Ten patient had VSD closure. Implantation was successful in all patient. Kinking in the delivery sheath, inability to position the sheath near left ventricular (LV) apex and device prolapse through VSD prompted some modification in the technique of implantation. Device related aortic or tricuspid insufficiency, arrhythmias and embolization were not observed. The study concluded that the Amplatzer membranous septal occluded was suitable to close a wide range of PM VSD sizes and morphologies with good short term outcomes. Another study was conducted to see the immediate outcome of transcatheter closure of perimembranous VSD in Siriraj Hospital, Bangkok, Thailand [7]. The authors demonstrated that transcatheter closure of membranous VSD could be safely and effectively performed in small children. This device also provided an opportunity for closure of VSD in patients with pulmonary hypertension. Another study conducted in University of Delhi, India proved transcatheter closure as safe and efficacious in selected cases of perimembranous and muscular VSD's with good intermediate and immediate results[8].

In CMH Dhaka three cases of perimembranous VSD device closure was done with good immediate result. Now a days hybrid cardiologic procedures are performed in advanced centre where heart is exposed surgicaly and intervention is done [9].

Conclusion

Surgical closure of membranous VSD is performed by open heart surgery with a small but significant morbidity and mortality. Risk of surgery is high specially for infant with pulmonary hypertension and big shunts. Device closure is a good option for those. Even hybrid procedure may be performed in neonate or infant with significant VSD where bypass may be avoided and cardiologist could do the intervention by directly puncturing the heart with the help of a surgeon in operation theatre. This latest technology has reduced morbidity and mortality from open heart surgery specially in neonates and infants.

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