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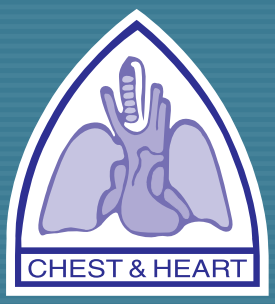

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INSTRUCTION TO AUTHORS ABOUT UNIFORM MANUSCRIPT WRITING

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

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Results should be presented in logical sequence in the text, tables or illustration. Do not repeat in the text all data in the tables or illustrations; emphasize or summarize only important observations.

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Genetic names should generally be used. When proprietary brands are used in research, include the brand name in parentheses in the Methods section.

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Discussion

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

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Chest & Heart Journal
Vol. 40, No. 1, January 2016

ORIGINAL ARTICLE

Effects of Anxiety, Depression and Health Status on Hospitalized COPD Patients: A Study in DMCH

Mohammad Aminul Islam[1], Adnan Yusuf Choudhury[2], Biswas Akhtar Hossain[3], Md. Mohiuddin Ahmad[4], Hena Khatun[5], Md. Osman Goni[6], Biswas Shaheen Hassan[7]

Abstract

Anxiety depression and poor health status is common complaints of COPD patients, not least if they have history of repeated hospitalization for exacerbations. The aim of this study was to analyze the interrelationship between health status, anxiety, depression and physical status in discharged COPD patients after hospitalization. It was a prospective study of 118 patients in the indoor of Dhaka Medical College Hospital. Data included demographic information, lung function and co-morbidity. The hospital anxiety and depression scale and St. George's Respiratory questionnaire (SGRQ) were applied to all patients. Among the COPD patients health status was poor those with anxiety, depression or both. Higher GOLD stages were significantly associated with increasing impairment in health status. In conclusion, patient with psychological disorders have poor health status. Anxiety and depression screening may help to identify patients with poor quality of life and an urgent need for intervention in order to improve their health status.

[Chest & Heart Journal 2016; 40(1) : 1-5]

Introduction

Chronic obstructive pulmonary disease (COPD) is associated with intermittent exacerbations characterized by acute deterioration in the symptoms of chronic dyspnoea, cough and sputum production. These acute exacerbations are the main cause for hospitalization in COPD patients and they are also associated with deterioration in health status and lung function.1 and 2 .Health status is a very important outcome variable. To evaluate health status valuable questionnaires have been developed that are used mainly for research purposes on groups.[3] This has been done in epidemiological studies and in studies on medications and in evaluating the efficacy of new drugs4, 5 and 6 including large trials with inhaled corticosteroids and long-acting anticholinergic medications.6, 7 and 8 Other factors are also important for the well-being of the COPD patient, including psychological status. Depression has been described with increased frequency in patients with COPD.[9] Anxiety is also important in patients with chronic diseases, especially if the disease can be life threatening as is COPD.[10] Anxiety and depression can be evaluated with a questionnaire that is short and easy to administer.[11] A study on

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patients with obstructive lung diseases receiving emergency care found that those with anxiety and depression were at much higher risk of hospitalization or relapse 1 month later.[12] There is limited information on the interrelationships between the measures of health status, anxiety and depression, and physical status. Such knowledge could potentially enable better individual care for patients with COPD.

The aim of this study was to analyze simultaneously in a prospective indoor setting health status, anxiety, depression, physical status and their interrelationships before discharge after hospitalization for COPD exacerbation

Methods:

This is a prospective study of patients hospitalized with acute exacerbations of obstructive airway disease in the indoor of Dhaka Medical College Hospital.

Patients were included provided that they had been admitted with acute exacerbations of COPD during the year 2015-2016. All patients with asthma were excluded and reported are only data from those fulfilling criteria for COPD according to the Global Initiative for Chronic Obstructive Pulmonary Disease (www.GOLDCOPD.com) stage 1 or higher.[2]

The following data were collected at discharge:

1. Questionnaire that included information on smoking history, type of living and family situation (living at home, assisted at home, nursing home, with spouse, alone or with others) in addition to educational level.
2. Spirometry, body weight and height. Predicted values for forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) were calculated .
3. Health status was assessed using the disease-specific St. George's Respiratory Questionnaire (SGRQ). It has three components: symptoms, activity and impact, in addition to the total score.[8]
4. From the patient records, information was collected on treatment during the hospitalization and at discharge. Assessment of co-morbidity was based on the diagnosis used by the treating physician. Diabetes mellitus was considered to be present if medications were used for diabetes. Hypertension, ischemic heart disease or atrial fibrillation were considered to be present when diagnosed by the attending physican and when the patient was using appropriate medications.

Statistics:

The $\div^2$-test, *t*-test and one-way analysis of variation were used in the univariable analyses, whilst multiple linear regression was used in the multiple variable analyses. SGRQ scores were analysed as a continuous variable and then checked for normality. . A *P*-value of <0.05 was considered statistically significant.

Results:

A total of 118 patients with COPD were enrolled in the study. The demographics of the study patients are shown in Table 1. Of those admitted, one-fourth were current smokers but most of the patients in the study had an extensive smoking history in the past. Women had significantly lower life-time tobacco exposure compared with men. Furthermore, women were more likely to be living alone than men.

Spirometry at discharge was performed in all the patients. The mean FEV_1 was low (38.5% of predicted value) suggesting significant disease. Most of the patients were in stages III and IV. There was a non-significant trend that the men had more severe COPD than women (P=0.07). The use of long-term oxygen therapy was relatively high (23.6%) and co-morbidities were common, with nearly half of the patients being diagnosed with cardiovascular disease and 10% having diabetes mellitus. Further details of the study patients are given in Table 1

Almost half of the study population suffered from anxiety and/or depression. Both anxiety and depression were more common in current smokers compared with non-smokers (P<0.001) while no significant relationship was found between psychological status and age, education, living conditions, lung function, LTOT or somatic co-morbidity (Table 2)

Health status

The mean total score on the SGRQ was 58, suggesting overall poor health among these severely affected COPD patients in the study. COPD patients with anxiety, depression or both had significantly higher scores in all domains and the total score of the SGRQ, suggesting a worse

health status than those who did not suffer from psychiatric co-morbidity (Table 3)

Effects of psychological condition on health condition

Lung function and psychological status both have a large impact on health status as measured by the SGRQ (Table 4). A significant impairment in health status was seen with decreasing FEV_1 for all domains except symptoms. Depression alone or anxiety with depression had clinically significant effects on all domains and anxiety alone had effects on all domains except symptoms. The effects were substantial

Table-I

Patients characteristics

	All	Males	Females	*P*-value
Number	128	93	35	<.5
Age (years)	69.4±10.4	71.0±9.4	67.8±11.2	0.001
Smokers (%)	25.8	23.6	28.0	0.32
Pack years smoking	33.7±23.9	38.9±27.0	28.8±19.2	<0.0001
College education (%)	30.7	33.3	28.1	0.25
Living alone (%)	52.1	37.6	66.2	<0.0001
FEV_1 (% of predicted)	38.5±18.2	36.4±16.2	40.5±19.7	0.01
FVC (% of predicted)	61.7±20.3	58.7±17.8	64.5±22.1	0.002
Cardiovascular diseases (%)	45.0	48.3	41.7	0.17
Diabetes (%)	10.6	10.2	10.9	0.82

Table-II

Demographics and psychological disorders.

	None	Anxiety only	Depression only	Anxiety and depression
Number	23	27	41	37
Women (%)	47.0	56.8	38.7	62.0
Age (years)	70.0±10.7	67.9±9.4	72.3±6.6	67.9±11.3
Smokers (%)	19.4	23.5	23.3	43.0
Pack years smoking	33.3±23.4	34.9±21.4	38.0±35.1	31.4±22.9
College education (%)	31.8	35.8	12.9	31.6
Living alone (%)	19.2	56.8	50.0	48.7
FEV_1 (% of predicted)	39.6±18.4	38.4±19.0	36.6±15.9	39.2±16.9
FVC (% of predicted)	61.1±20.5	64.1±20.0	59.5±13.1	62.1±21.1
LTOT (%)	5.3	23.5	35.5	27.8
CV diseases (%)	41.1	49.4	48.4	53.2
Diabetes (%)	10.4	8.6	16.1	10.1

FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; LTOT: long-term oxygen therapy; CV: cardiovascular.

Table-III

Health status and psychological condition.

	All	None	Anxiety	Depression	Anxiety and depression
Number	128	37	28	32	31
SGRQ points					
Symptoms		61.1±20.2	68.0±16.0	69.7±17.4	69.0±17.2
Activity		62.7±23.6	69.3±18.8	70.9±19.3	74.7±16.8
Impact		40.3±19.1	52.1±18.5	55.9±17.8	53.6±17.9
Total		52.3±17.8	61.8±15.0	64.1±14.0	64.2±14.6

Tabl-IV

Relationship between lung function and psychological and health status.

SGRQ components	Symptoms estimate* (95% CI)	Activity estimate (95% CI)	Impact estimate (95% CI)	Total estimate (95% CI)
FEV_1 (% pred)**	"0.59 ("1.74, 0.57)	"4.10 ("5.33, "2.87)	"2.29 ("3.42, "1.16)	"2.59 ("3.56, "1.62)
Anxiety	3.32 ("1.89, 8.53)	5.77 (0.26, 11.3)	9.49 (4.37, 14.6)	7.09 (2.68, 11.5)
Depression	6.04 ("1.71, 13.8)	5.06 ("3.21, 13.3)	14.8 (7.24, 22.4)	10.3 (3.83, 16.8)
Anxiety and Depression	6.02 (0.68, 11.4)	12.0 (6.25, 17.7)	13.2 (8.02, 18.5)	11.9 (7.39, 16.33)

*Estimates are regression coefficients derived from multiple linear regression.

Discussion

The main findings of our prospective study of a small group of COPD patients were that patients being discharged after hospitalization for acute exacerbation had a high prevalence of anxiety and depression and also a poor health status. Women and current smokers were more likely to suffer from more significant anxiety or depression. There was a close relation between health status and psychological condition among these severely affected COPD patients who were close to being discharged from the hospital. Their health status may be expected to improve with increasing time from recovery after their exacerbation[17] but we are not aware of studies on the time course on the interrelationship between health status and psychological condition.

The prevalence of poor health status, anxiety and depression found are in accordance with those of some other studies. In a recent study by van Manen it was shown that the risk for depression in stable COPD patients from general practice was 2.5 times greater in patients with severe COPD (FEV_1<50% of predicted) compared to controls.[18] Living alone, respiratory symptoms and physical impairment were also significantly associated with the risk for depression. In the COPD group, as a whole, 21.6% were depressed compared to 17.5% in the control group. In another study by the same author, where the prevalence of co-morbidity in patients with chronic airway obstruction was studied, depression was found to be more common in the study group than among the controls.[9]Heart disease and diabetes were not more common in the patients with chronic airway obstruction than in the control group. A study from Japan on 218 male patients with COPD of differing severity showed higher scores on SGRQ (worse health status) with increasing severity of disease[19]; and also a correlation between the HAD scale and SGRQ. In another study, patients with COPD reported anxiety with increased frequency and this correlated with severity of disease.[20] In a recent study, GOLD stages II and higher, marked a dramatic worsening of health status as measured by SGRQ, but psychological status was not analysed simultaneously.[21]

Conclusion:

From a clinical point of view, our study underlines how important it is to identify those COPD patients who suffer anxiety and depression at discharge after an acute exacerbation and to pay attention to these commonly encountered complaints. This study shows that special attention needs to be put on females with COPD and current smokers. The HAD scale is a simple and effective way to screen patients for anxiety and depression. It requires only a short time to apply and analyse and is well standardised, all of which makes it attractive for this purpose.11, 14, 15 and 16 Further studies should be conducted evaluating the effect of treatment of anxiety and depression and also to analyse whether simple screening tests such as the HAD scale can be used to select those that could benefit from specific therapy based on future randomised trials.

Source of support : Nil

Conflict of Interest : None declared

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ORIGINAL ARTICLE

Role of FOB (Fiber Optic Bronchoscopy) in Diagnosis of Smear Negative Pulmonary Tuberculosis: A Prospective, Observational Study in a Tertiary Care Hospital in Bangladesh

Adnan Yusuf Choudhury[1], MohammadAminul Islam[1], Biswas Akhtar Hossain [2],Md.Mohiuddin Ahmad[3], Mohammad Billal Hossain[4], Md. Abu Raihan[5], M.M. Hiron[6]

Abstract:

Background: *World Health Organization recommends bacteriological confirmation of pulmonary tuberculosis (PTB) by the detection of acid-fast bacilli (AFB) in respiratory specimens. However about 40-60% of patients with PTB suspected clinically or radiologically may fail to produce sputum, or when it is available, AFB may be negative on repeated smear examination. These sputum smear negative patients and those who fail to produce any sputum can be diagnosed by flexible fiberoptic bronchoscopy.*

Aims: *Our study was an attempt to analyze the role of fibreoptic bronchoscopy in sputum smear negative PTB patients with respect to their association with clinical and radiological profile.*

Materials and Methods:*This prospective , open level, observational study was conducted on 80 suspected sputum/ smear negative PTB cases attending Respiratory Medicine Department of Dhaka Medical College& Hospital. Patients were subjected to bronchoscopic examination after taking informed consent and samples like bronchial aspirate, bronchoalveolar lavage and post bronchoscopy sputum were collected and smear were prepared and culture for MTB done from collected specimens. The data were analysed and results were given in percentage.*

Results: *Out of total 80 patients, overall diagnosis was confirmed in 46 (57.5%) patients. Of these 46 patients, 32 patients were confirmed for PTB whereas 14 had other diagnoses.*

Conclusion: *Our study suggests that fibreoptic bronchoscopy can provide excellent material for diagnosis of suspected cases of pulmonary tuberculosis in whom smears of expectorated sputum do not reveal mycobacteria.*

[Chest & Heart Journal 2016; 40(1) : 6-11]

Introduction

Pulmonary Tuberculosis is a major public health problem worldwide. According to WHO estimates, 12 million people were suffering from active TB disease in 2011 causing 1.4 million death globally.

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The initial diagnostic approach to suspected cases of pulmonary tuberculosis is to demonstrate *Mycobacterium Tuberculosis* in stained smear of expectorated sputum. In most of the tuberculosis centers, even after meticulous search, the bacteriological positive yield from sputum is around 16 to 50% and large portion remain negative in spite of clinical profile and radiological lesions being consistent with diagnosis of pulmonary tuberculosis[5]. Early diagnosis of pulmonary tuberculosis prevents progression of disease, morbidity, spread of disease and permanent damage by fibrosis.

A number of studies confirm the usefulness of fiber optic bronchoscopy in the diagnosis of pulmonary tuberculosis [4-6]. In the series reported by Chan et al [5],34 patients with suspected PTB who were sputum smear negative, were subjected to fiberoptic bronchoscopy. PTB was confirmed in 29 of them. Flexible fiberoptic bronchoscopy with bronchial aspiration and bronchoalveolar lavage under local anaesthesia is a relatively safe procedure and well tolerated by most of the patients [7-10]. Its safety and diagnostic yield have been reported before[11-12]. Complications are known but rare in occurrence [13-14].

Thisstudy was carried out to know the usefulness of bronchoscopy in sputum smear negative pulmonary tuberculosis patients diagnosed on clinical and radiological grounds, by direct visualization of bronchial tree and collecting specimens such as bronchial aspirate, broncho-alveolar lavage and post bronchoscopy sputum and assess the positivity of these specimens through smear examination for AFB by Ziehl-Neelsen staining method and culture of the specimens for Mycobacterium tuberculosis on Lowenstein-Jensen media.

Materials and method

This study was conducted in the Department of Respiratory Medicine, Dhaka Medical College from June 2014 to June 2016. The subjects of the study group was chosen from among the patients attending the outpatient department and those admitted in the wards (under respiratory medicine department and also cases referred from other discipline/departments).

Clinically suspected cases of pulmonary tuberculosis, aged 16 – 75 years, with three sputum smears negative for AFB and a chest radiograph suggestive of pulmonary tuberculosis were included in the study. Patients with bleeding diathesis, history of myocardial infarction or arrhythmia, extra-pulmonary tuberculosis, history of anti tubercular treatment (ATT) for more than one month and those with severe dyspnea were excluded from the study.

A detailed history, clinical examination and routine investigations were carried out on suspected cases of tuberculosis. Three sputum samples (spot, morning and spot) were tested in DOTS corner of DMCH for presence of AFB in smear. In patients with suspected smear negative pulmonary tuberculosis, a sputum sample was sent for sputum culture and the patients were taken for bronchoscopy.Prior to the procedure an informed written consent was obtained from the patient/ patients attendant. The procedure was carried out electively in early morning with the patient fasting overnight. Patients were pre-medicated 30- 45 minutes prior to bronchoscopy with 0.6 mg atropine and nebulization was done with 2%xylocaine via nedulizer. Bronchoscopy was carried out under local aneasthesia.

Bronchial washing was performed by instilling 0.9% isotonic saline at room temperaturethrough the internal channel of the fiberoptic bronchoscope and aspirated into a trap connected to suction tubing. Usually 15-30 ml of fluid instilled with each washing and about one fourth to half of this volume was retrieved in the suction trap. Upto one-fourth of the instilled amount retrieved was considered successful. The bronchial washing was sent for AFB staining, AFB culture, and for cytology and cell count. In cases where an endobronchial growth was seen washing, brushing and biopsy was performed.

After the procedure, the patient was observed for 2 hours in post procedure room for any bronchoscopy related complications. The first sample sputum (post bronchoscopic sputum) was collected and sent for analysis along with bronchial washings.

Results

Bronchoscopy was performed in 80 patients.

Characteristics of the patients were given in Table 1.

Table-I
Patients characteristics

Sex:	
Male	53 (66.3%)
Female	27 (33.7%)
Mean age:	
Total	43.2 ± 14.6
Male	45.2 ± 15.2
Female	39.2 ± 12.9
Mean duration of illness	2.2 months
Symptoms:	
Cough	67 (83.7%)
Expectoration	52 (65%)
Fever	55 (68%)
Constitutional symptoms	59 (73.7%)
Dyspnoea	23 (28.7%)
Haemoptysis	16 (20%)
Chest pain	14 (17.5%)
Asymptomatic	4 (5%)
Chest radiography: Site of lesion	
Right	39 (48.7%)
Left	27 (33.7%)
Bilateral	14 (17.5%)
Type of lesion:	
Cavitory	11 (13.7%)
Non cavitory	69 (86.3%)

The most common bronchoscopic finding was congestion with mild to moderate hyperaemia with whitish plaques of variable size in between, observed in 43 (53.7%). In 14 (17.5%) patient sulceration, erosion or granulation was seen. In all patients with cavitary lesion the mucosa was ulcerated and swollen. In 5 patients ulcerative lesion was observed with extensive areas of pulmonary involvement radiographically. In 16 patients (20%) the segmental opening were narrowed and slightly deformed.Endobronchial growth was seen in 3 (3.8%) patients.

Through bronchoscope Bronchial aspirate (BA) and Bronchoalveolar lavage (BAL) were collected and smeared for ZN staining for AFB. After bronchoscopy Post bronchoscopy sputum (PBS) was taken for ZN staining for AFB.

In study group of 80 patients, 12(15%) patients were positive for AFB by ZN staining from BA, 14(17.5%) patients were positive in BAL smear and 14 (17.5%) patients were positive on PBS smear. 2 smear each was exclusively positive for AFB on BAL smear and PBS smear.

Table-II
Results of microscopic examination of bronchial specimen

Bronchoscopic specimen	Positive specimen N (%)	Exclusively positive specimen (%)
BA smear	12 (15)	0 (0)
BAL smear	14 (17.5)	2 (2.5)
PBS smear	14 (17.5)	2 (2.5)

All specimens collected through bronchoscope were cultured for mycobacteria. BA culture for mycobacteria was positive in 16 (20%) patients whereas BAL culture was positive in 24 (30%) patients and PBS culture was positive in 11 (27.5%) patients. 4 specimens of BA culture was exclusively positive whereas 6 BAL cultures were exclusively positive. No PBS culture was exclusively positive.

Table-III
Culture results of bronchial specimens for Mycobacterial Spp

Bronchoscopic specimen	Positive specimen N (%)	Exclusively positive specimen (%)
BA culture	16 (20)	4 (5)
BAL culture	24 (30)	6 (7.5)
PBS culture	22 (27.5)	0 (0)

When all results were combined together it was found that in the study group of 80 patients, 46 (57.5%) patients could be diagnosed. Out of these 46 patients,32 (40%) patients were diagnosed as a case of pulmonary TB, while 14 (17.5%) patients had a diagnosis other than TB.

Table-IV
Diagnostic yield of bronchoscopic specimens

Diseases diagnosed	N (%)
Total PTB cases diagnosed	32 (40)
With smear (BA + BAL + PBS)	22 (27.5)
With culture (BA + BAL + PBS)	10 (12.5)
Total other diseases diagnosed	14 (17.5)
Malignancy	6 (7.5)
Bacterial pneumonia	8 (10)

No serious complications were encountered during the study, except pneumothorax (less then 10%) in one patients and minimal hemoptysis (less then 10 ml) in six patients. No specific treatment was required to manage these complications.

Discussion:

The WHO Expert Committee on Tuberculosis recommends that patients of pulmonary tuberculosis in whom the disease has not been confirmed bacteriologically should be classified as suspects till the presence of AFB is demonstrated and a patient with persistent symptoms whose sputum does not contain AFB should be followed and anti-tubercular treatment should be given only if the diagnosis can be confirmed bacteriologically [19].

In areas of high transmission, the risk of infectivity of sputum smear negative PTB to young household contacts has been estimated to be quite high [20-22]. Published observations suggest that over 50% of smear negative patients would need treatment by the end of 12 months if left untreated [23,24]. Data from longitudinal surveys in Bangalore district,India[25]indicate that at 18 months follow up, the mortality rate from smear negative,culture positive cases was 14.1% compared with 34.7% observed in smear positive patients. Many patients with PTB who are co-infected with HIV with late stage disease and those who are severely immunosuppressed are more likely to be smear negative [26]. Thus, early diagnosis of active sputum smear negative PTB disease is important.

In the earlier days of rigid bronchoscopy, patients with tuberculosis were seldom subjected to bronchoscopy for diagnostic purpose. With the advent of fiberoptic bronchoscopy, smear and culture for mycobacteriafrom the bronchial aspirate, bronchial brushing, bronchial washing, broncho-alveolar lavage fluid, post-bronchoscopy sputum and biopsy materialhave been used in various studies for diagnosing pulmonary tuberculosis. The main advantage with this instrument is the ability to visualize the bronchial tree and collect samples directly from the bronchial pathology site. Though FOB procedures have some risk of complications like hemoptysis, pneumothorax, it is considered to be a relatively safe procedure [27].

After bronchoscopic examination of 80 patients, the most common bronchoscopic finding was congestion with mild to moderate hyperemia with whitish plaques of variable size in between, observed in 43 (53.7%). In 14 (17.5%) ulceration, erosion or granulation was seen. In all patients with cavitary lesion the mucosa was ulcerated and swollen. In 5 patients ulcerative lesion was observed with extensive areas of pulmonary involvement radiographically. In 16 patients (20%) the segmental opening were narrowed and slightly deformed. Which was comparable to the study of So et al [28] who found endoscopically visible lesions such as localized red swollen mucosa, stenosis or plaques of caseous material in 33 (50.8%) of the 65 patients.

As shown in a number of previous studies, the positivity of smear from BA varies from 13% [29] to 61% [30]. So Syet el [28] obtained a positive yield of 38% in bronchial aspirate while Danek et al [31] observed BA smear positive in 24 cases. Anand reported the diagnostic yield of BA smear to be 28%, BA culture to be 32%, while BA was the exclusive means of diagnosis in 16% patients [30]. In our study BA smear was positive in 12 (15%) patients whereas when both BA smear and BA culture were combined, the positivity increased to 16 (20%) patients. Thus the data generated in our study is comparable to previous studies.

In our study the BA culture was positive in 16 (20%). In previous studies it varied from 4% [29] to 72% [28]. At the end of our study BAL smear was diagnostic in 14 (17.5%) patients which is comparable to previous studies where it was reported to be 12% by Pande et al [33]and 26% by Mohan et al [34]. BAL culture yielded M.tuberculosis in 24 (30%) patients in our study which was comparable to the 25% yield obtained in the study done by Mohamed S.Sawy et al [35].

Combining all the results of bronchoscopic procedures in our study, a definitive diagnosis of tuberculosis was possible in 32 (40%) of the 80 patients. BAL smear was exclusively positive in 2 cases, BAL culture in 6 patients and PBS smear also had 2 patients exclusively positive.PBS smear revealed AFB in 14 (17.5%) patients. In various other previous studies PBS smear revealed AFB positivity ranging from 23 to 37%. 21% positivity was noted by Danek et al [31], 26% by Purohit et al [36], 28% by Anand et al [32] 35% by Wallace et al [29] 37% by So et al [28]and 23% by Kulpati et al [37].

Flexible FOB is a relatively safe procedure with risk such as spread of tuberculosis following bronchoscopy[38, 39],iatrogenic transmission of other infections by bronchoscope [40], hemoptysis and pneumothorax. However transmission of infection through bronchoscope can be prevented by following proper disinfection guidelines like double disinfection technique [41].

Major advantage of bronchoscopy in suspected patients with negative sputum smear examination for AFB, is the isolation of mycobacteria at an early stage when the destruction of lung tissue is minimal and the risk of spreading disease to contacts can be decreased by early diagnosis and treatment.

The study concludes that flexible bronchoscopy is a useful tool in diagnosis of pulmonary tuberculosis in sputum smear negative patients. Bronchoscopy reveals a higher bacteriological confirmation of diagnosis in patients with strong clinical and radiological evidence suggestive of pulmonary tuberculosis and those having more risk factors.

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ORIGINAL ARTICLE

The Sputum Smear Conversion Rate of Pulmonary Tuberculous Patients after Initial Phase of Treatment

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Abstract:

The sputum smear conversion rate (SCR) is an operational indicator for the directly observed treatment short course (DOTS) strategy of national tuberculosis control programme. This study was undertaken to determine the smear conversion rate among the sputum smear positive pulmonary tuberculous patients undergoing DOTS.

Methods: *This prospective study was conducted on pulmonary tuberculous patients at the selected DOTS centers in Dhaka city during March 2007 to June 2007. Study place was selected purposively. Data were collected from the respondents by face to face interview, from their TB registrar books, TB treatment cards, using structured questionnaire and check list.*

Result: *A total of 122 registered TB patients were enrolled in the study. Among them 75 (61.7%) were male and 47 (38.35%) were female. Mean age of the respondents was 33.42 years (SD ± 13.68). in this study populations 76 (62.29%) were found smear positive and 46 (37.7%) sputum smear negative at the beginning of anti TB treatment. Of them 76 (62.3%) were taking category -1 anti-TB regimen. At the end of 2nd and / 3rd months of DOTS treatment regimen 15 (12.3%) were remain sputum positive and 107 (87.70%) sputum negative and the sputum smear conversion rate was found 80.29%.*

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Introduction:

Tuberculosis is an infectious disease, caused by bacilli called mycobacterium tuberculosis. Pulmonary tuberculosis is the most common form and occurs in 80% of cases[1]. Tuberculosis was declared a Global Emergency by the WHO in 1993. Every year 8 million new cases of TB (pulmonary and extra-pulmonary) occur, of which about 95% are in developing countries. Of the 1.7 billion people estimated to be infected with TB bacilli, 1.3 billion live in developing countries. About 1 to 2 million peoples die of TB every year, constituting 26% of avoidable deaths worldwide. The greatest burden of the mortality and morbidity is borne by adults of 15-60 years who constitute the

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most productive members of society[2]. Tuberculosis is a major public health problem in Bangladesh. It is estimated that 300,000 new cases crop up each year, of which about half of them are infectious. It is further estimated that about 70,000 people die every year[3]. In 1993,World Health Organization (WHO) recommended a standard strategy for control of the disease that since 1993, is known as the Directly Observed Treatment Short Course (DOTS) strategy. Bangladesh introduced this strategy in 1993 and had expanded at all upazilas in collaboration with the partner NGOs by June 1998[1]. However, poor adherence to TB medication regimens is a common problem. Development of drug resistant TB and the possibility of death are the fatal consequences of irregular treatment[4]. Approximately 425000 new cases of MDR-TB are identified each year, and alarming rates of XDR-TB have recently been reported[5].

The standardized TB treatment regimens

There are many different possible anti-TB treatment regimens. The World Health Organization (WHO) and the International Union Against Tuberculosis and Lung Disease (UATLD) recommend standardized TB treatment regimen. National TB control programme (NTP) in the country recommends which regimens to use. Treatment regimens have an initial (intensive) phase of 2 months and the continuation phase of 4-5 months after initial phase[6].

Sputum smear at the end of initial phase

The vast majority of patients have a negative sputum smear at the end of the initial phase. If the sputum smear is still positive at the end of the initial phase, the initial phase treatment with the same 4 drugs is to be continued for 4 more weeks. It is unlikely still to be positive after the 3 months of initial treatment[6].

Sputum conversion rate

The sputum conversion rate (SCR) is the percentage of smear positive pulmonary TB cases registered in a specified period that converted to smear negative status after the standard two months of the intensive phase of treatment. WHO recommends its use as a useful indicator for TB control programs in monitoring the TB program performance, and as a trigger for rigorous assessment in patients with still positive smears[7]. Smear conversion rate at two months of intensive phase and at three months of extended intensive phase is a significant operational indicator as it shows the capacity of the programme to maintain the patients on treatment. It also provides an objective evidence for the patient response to therapy and hence the treatment outcome[8].

Objectives

To find out the sputum conversion rate after completion of initial phase of anti TB treatment of pulmonary TB patients under DOTS in some selected DOTS centers of Dhaka city.

Maerial and Methods:

A prospective cohort study was carried out among category-1 sputum smear positive pulmonary tuberculosis patients registered at the DOTS centers of Gandaria, Wari, Shampur and Dhaka National Hospital in Dhaka city. A total 122 pulmonary TB patients were registered at their respective DOTS center during March 2007 to June 2007. Among them 76 patients were found sputum smear positive. Sputum result and treatment outcome were recorded from TB register and patient's treatment cards. All the study subjects were interviewed using a pre-design semi-structured interview schedule within two months of their registration at the DOTS centers. Subsequent visits to the DOTS centers were made to collect the information on sputum results at 2^{nd} / 3^{rd} months of initial phase. Sputum Conversion Rate was defined as per operational guidelines under the National TB Control Programme (NTCP). Sputum conversion rate= (no of sputum smear positive before treatment - no of sputum positive after treatment)/(no of sputum smear positive before treatment) X 100.

After data collection, data were checked, cleaned, edited, and analyzed with SPSS Windows software version 12.

Result:

Socio-demographic information such as age, sex and socio-economic status were summarized in table-1. The mean age of the respondents was found 33.42 years (SD ± 13.68 years). In this study male were 76 (62.30%) and female 46 (37.70%). Among the respondents married 78(63.93%) and 30 (24.59%) were illiterate, 51 (46.72%) had primary education. In the study group 40(32.79%) were service holder, and 30(24.59%) house worker. Among study respondents 48 (39.34%) had less than 3000 TK monthly income, 70(57.38%) in-between 3001-5000 Tk , 46(37.71%) lived in kancha house, 58 (47.54%) in semipacca house.

As shown in table-2, among the study population 76 (62.30%) were found sputum smear positive at

the beginning of treatment. The table -3 showed, among the respondents 118 (76.62%) received category-1, 13(08.44%) category-2 and 23 (14.93%) category-3 treatment regimen. Among the respondents 67(54.92%) were adherent to treatment and 55(45.08%) non-adherent as showed in table-4. Among the 76 sputum smear positive patients 15(19.74%) remain sputum smear positive and 61 (80.26%) converted to negative after initial phase of category-1 treatment. And sputum conversion rate was found 80.26% after the completion of initial phase of treatment as shown in table-5.

(Sputum conversion rate= (no of sputum smear positive before treatment-no of sputum positive after treatment)/(no of sputum smear positive before treatment)X 100.
= 76-15/76 X 100
=80.26%.)

Table-I

Distribution of demographic characteristics of the respondents.

Variable	Frequency	Percent
Age groups		
0-14 years	3	2.46%
15-44 years	90	73.77%
≥45 years	29	23.77%
Mean age ±SD	33.42 ±13.68 years.	
Sex		
Male	76	62.30%
Female	46	37.70%
Marital status		
Married	78	63.93%
Unmarried	40	32.79%
Divorce	04	03.28%
Education		
Illiterate	30	24.59%
primary	51	46.72%
Secondary	25	20.49%
Higher secondary	07	5.74%
Graduate	03	2.46%
Occupation		
Servicemen	40	32.79%
Students	20	16.39%
housework	30	24. 59%
Businessmen	17	13.93%
Unemployed	15	12.30%
Economical status		
Monthly income <3000 TK	48	39.34%
Monthly income 3000-5000 TK	70	57.38%
Monthly income >5000 TK	46	37.71%
Housing status		
Kancha house	46	37.71%
Semipacca house	58	47.54%
Pacca house	18	14.75%

Table-II

Distribution of patients according to sputum smear test at the beginning of treatment (n=122).

Variables	Frequency	Percent
Sputum smear test		
Smear positive	76	62.30%
Smear negative	46	37.70%

Table-III

Distribution of patients according to their category of anti TB drugs treatment (n=122).

Variables	Frequency	Percent
Category- 1	76	62.30%
Caegory-2	13	10.66%
Category-3	33	27.04%

Table-IV

Distribution of patients according to adherence to treatment (n=122).

Variables	Frequency	Percent
Adherence to treatment		
Adherent	67	54.92%
Non-adherent	55	45.08%

Table-V

Distribution of patients according to sputum smear test at the end of initial phase of treatment (n=76).

Variables	Frequency	Percent
Sputum smear test		
Smear positive	15	19.73%
Smear negative	61	80.26%
Sputum Conversion Rate= (76-15)/76 X 100 =80.26%.		

Discussion:

In our study sputum smear conversion rate was found 80.26%. Falix R Kayigamba etal from Rwanda found sputum conversion rate 80% in his study, which was consistent with our study[9] . Rieder etal from Paris (1996) showed sputum conversion of 75% with a range from 61.7% to 90.9% in patient with initially strongly and weakly positive smear

respectively after the 2 months intensive phase[10]. Lienhardt etal from Gambia (1998) observed sputum smear conversion at the end of two month after the start of treatment was 90%[11]. Singla et al from New Delhi (2005) reveals sputum conversion at the end of 2 months were 76 .8% and at the end of 3 months 89.5%[12]. Bwirie R et al from India(2008) found sputum conversion at the end of 1st months 71% and at the end of 2nd month 84% and at the end of 3rd month 92%[13]. Simmi Tiwari at el from India (2006) showed sputum conversion after 2 months intensive phase was 71.6%[14].

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ORIGINAL ARTICLE

A Study on Clinical Presentation of Primary Lung Cancer

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Abstract:

Background: *To improve the current understanding about clinical presentation of primary lung cancer, a study was carried out on 50 consecutive lung cancer patients.*

Method: *Total 70 cases were prospectively included in the study on the basis of clinical presentation and radiological findings. Out of 70 cases 50 cases were confirmed by lympnode biopsy/FNAC and CT guided FNAC of lung lesion. 18 cases could not be confirmed due to lack of available diagnostic facility like FOB and pleural biopsy. Two cases were dropped out during the study period. This was a single-center prospective study held in the department of medicine of Sylhet MAG Osmani Medical College hospital between July 2007 and June 2008.*

Measurements and results: *Of the 50 primary lung cancer patients, 84% were men and 16% were female with male female ratio was 5.25: 1. Among the lung cancer patients 34% were cultivator, 22% were business professional, 18% were day laborer, 10% were service holder. A tobacco smoking history was present in 90% of patients. 37.80% patients had the smoking habit of 31 to 40 pack year, 33.30% was 21 to 30 pack years, 13.30% 41 to 50 pack year. 68% of primary lung cancer patients had cough, 64%, had dyspnea, 60% chest pain, 56% loss of weight, 54% loss of appetite, 30% fever, 24% hemoptysis, 18% hoarseness of voice, 10% dysphagia, 6% pain in limbs and 4% had the lower limb weakness. Signs of primary lung cancer patients had clubbing 76%, anemia 62%, Mass lesion 60%, palpable lymphnode 18%, pleural effusion 16%, features of Superior venacaval obstruction 10%, jaundice 4%, hepatomegaly 2%, Pancoast syndrome 2% and Horner's syndrome 2%. Histological types of primary lung cancer 62% was Squamous cell carcinoma, 24% was Adenocarcinoma and 14% was Small cell carcinoma.*

Conclusion: *Clinical presentation of primary lung cancer is characterized by a specific sings and symptomatic pattern. Updating of these knowledge of this pattern may help to improve the rate of early diagnosis.*

Key words: FNAC- Fine Needle Aspiration Cytology, FOB- Fiber Optic Bronchoscopy

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Introduction:

Lung cancer is the leading cause of cancer deaths worldwide[1]. Also it's the leading cause of cancer-related death in the United States. In 2006, the disease caused over 158,000 deaths—more than colorectal, breast, and prostate cancers combined[2]. Approximately 85% of all lung cancers occur in current or former cigarette smokers[3]. Although death rates have begun to decline among men in the United States, the lung recently surpassed the breast as the most common origin of fatal cancer in women.[4] Because one fourth of adults smoke, lung cancer will remain a problem for many years.[4] Despite advances in lung cancer therapy, the average five-year survival rate is only 15 percent.[5] Adenocarcinoma has surpassed squamous cell carcinoma as the most common histologic type of lung carcinoma,[6,7] and early metastasis has become increasingly common.

Like many other countries in the world cancer in Bangladesh is one of the major killer diseases. The National Institute of Cancer Research and Hospital (NICRH), Dhaka, started a cancer registry in 2005 for the first time in Bangladesh with technical assistance from the World Health Organization (WHO). Confirmed diagnosis of cancer could be made available for 18829 cases. Among them 10.847 (57.6%) were male. Lung cancer was the leading cancer (17.3%), followed by cancers of breast (12.3%) for sexes combined in all ages. 25.5% males were diagnosed lung cancer among them[8].

Methods:

Study design:

A total 70 cases were prospectively included in the study as per inclusion criteria on the basis of clinical presentation and radiological findings. Out of 70 cases 50 cases were confirmed by lympnode biopsy/FNAC and CT guided FNAC of lung lesion. 18 cases could not be confirmed due to lack of available diagnostic facility like FOB and pleural biopsy. Two cases were dropped out during the study period. This was a single-center prospective study held in the Department of Medicine of Sylhet MAG Osmani Medical College Hospital between July 2007 and June 2008. The study was approved by the Ethical committee of the institution and the informed consent were taken from every prospective patient.

Data collection:

The patients who had been admitted in the department of medicine on basis of clinical presentation and radiological findings suggestive of primary lung cancer were included. During the study clinical data including age, gender, smoking history, signs-symptoms, co morbidities, radiological findings, results of histopathological report of lymphnodes and of lung lesions were compiled and analyzed.

Result:

Patient characteristics:

During the study period, 50 patients with lung cancer who presented with pulmonary radiological findings and confirmed by histopathology were identified. Their age was ranging from 40-75 years. Of the 50 primary lung cancer patients, 84% were male and 16% were female. The male female ratio was 5.25: 1.

Table-I

Demographic characteristics of the patients with lung cancer

Characteristics	Subject n	Median (range)	Frequency	Percentage
Age years	50	57(40-75)		
Male sex y/n	50		42/08	84%/ 16%
Current smokers y/n	50		45/05	90%/10%
History of other cancers y/n	50		0/50	0/100%
Occupation	50			
Cultivator			17	34%
Businessman			11	22%
Day laborer			09	18%
Service			05	10%
Housewife			04	08%
Retired			02	04%
Others			02	04%

They came from different occupational background. Among the lung cancer patients 34% were cultivator, 22% were business professional, 18% were day laborer, 10% were service holder, 8% was housewife, 4% were retired and 4% others. In 90% of patients had tobacco smoking history with different time span. In the only male patients were smokers. Highest (37.80%) number of patients had smoking habit of 31-40 pack years, 33.30% had 21 to 30 pack years, 13.30% had 41 to 50 pack years.

Table-II

Smoking habit of the patient with primary lung cancer (n=45)

Smoking habit	Frequency	Percentage (%)
10-20 Pack years	04	8.9%
21-30 Pack years	15	33.3%
31-40 Pack years	17	37.8%
41-50 Pack years	06	13.3%
51-60 Pack years	03	6.6%

All patients were presented with some signs and symptoms. All of them had more than one complaints or presentation at a time. 68% of primary lung cancer patients had cough, 64% , had dyspnea, 60% chest pain, 56% loss of weight, 54% loss of appetite, 30% fever, 24% hemoptysis, 18% horsness of voice, 10% dysphagia, 6% pain in limbs and 4% had the lower limb weakness. Signs of primary lung cancer patients had clubbing 76%, anemia 62%, Mass lesion 60%, palpable lymphnode 18%, pleural effusion 16%, features of Superior venacaval obstruction 10%, jaundice 4%, hepatomegaly 2%, Pancoast syndrome 2% and Horner's syndrome 2%.

All the case were confirmed by histopathological examination and were classified on the basis of findings. Histopathological findings of primary lung cancer 62% was Squamous cell carcinoma, 24% was Adenocarcinoma and 14% was Small cell carcinoma.

Among the 50 primary lung cancer patients radiologically presented with more than one findings. Collapse and Pleural effusion were found more common presentation on the chest 54% and 23% whereas in CT scan raveled 62% and 29% respectively.

Table-III

Clinical presentation of the patients with primary lung cancer

Presentation	Subject n	Percentage
Symptoms	50	
Cough		68%
Dyspnea		64%
Chest pain		60%
Loss of weight		56%
Loss of appetite		54%
Fever		30%
Hemoptysis		24%
Hoarseness of voice		18%
Dysphagia		10%
Limb pain		6%
Lower limb weakness		4%
Signs	50	
Clubbing		76%
Anemia		62%
Mass lesion		60%
Palpable lymphnode		18%
Features of pleural Effusion		16%
Features of SVC obstruction		10%
Jaundice		4%
Hepatomegaly		2%
Pancoast Syndrome		2%
Horner's syndrome		2%

Table-IV

Radiological findings primary lung cancer n =70

Presentation	X Ray chest Percentage	CT scan of chest Percentage
Collapse	54%	62%
Pleural Effusion	23%	29%
Mass lesion	17%	21%
Mediastinal widening	11%	17%
Cavitary lesion	4%	9%
Others	2%	5%
Rib's erosion		
Elevated hemidiaphragm		
Pericardial effusion		

Table-V

Histopathological types of primary lung cancer

Type	Subject (n=50)	Frequency	Percentage (%)
Squamous cell carcinoma		31	62%
Adenocarcinoma		12	24%
Small cell carcinoma		07	14%

Discussion:

Among the primary lung cancer patients male were 84% and smoker were 90%. In socioeconomic background 34% were cultivator who were suffering from primary lung cancer. As in Bangladesh the cultivator comes off a low socioeconomic status most of them have got the smoking habit from very early age. So they got the history of smoking for long time. The incidence of lung cancer has been increasing in parallel with the increasing proportion of older persons. Long time smoking habit causes smoking associated respiratory diseases. Older persons may have serious comorbidities such as chronic obstructive pulmonary disease, pulmonary fibrosis, or cerebrovascular diseases and often develop pulmonary bacterial infections such as aspiration pneumonia.[9]

Eleven symptoms and ten signs were found associated with the primary lung cancer. All the symptoms shown to be associated with lung cancer. This reflects the high frequency of respiratory symptoms in the general population and illustrates the difficulty of doctors have in selecting which patients require investigation. Among those symptoms Cough, Dyspnea, Chest pain, Loss of weight, Loss of appetite, Fever, Hemoptysis, Hoarseness of voice were main features. Among the symptoms cough, dyspnea, chest pain and loss of weight were found very common and most of the patients were suffering from these complaints. Loss of appetite, loss of weight, dyspnoea, chest pain, fatigue and cough individually posed a low risk for lung cancer. However, as with haemoptysis, when more than one symptom was present the risk of cancer rose. This finding supports a retrospective study which reported that dyspnoea was the initial complaint in 17% of lung cancer patients[10] and an interview study in which patients reported symptoms of their cancer for a median of 12 months before diagnosis.[11] In the cases reported here, dyspnoea was rarely an isolated symptom. This accords with research from clinics for investigation of isolated dyspnoea which very rarely identified lung cancer.[12] This suggests that investigation of isolated dyspnoea should concentrate on non-malignant causes such as heart failure, and only if a second symptom is reported should lung cancer become the focus of investigation. Cough is the most common symptom seen in primary care.[13] It is also the most common symptom in lung cancer, occurring in 68% of cases in this study. Re-attendance with cough was also very common in cases. The risk of lung cancer increased with each attendance. However, cough is the first symptom of cancer in nearly a quarter of patients, so it should not be readily dismissed as a predictor of lung cancer.[10] These symptoms were ignored due to lack of awareness and social status. Among signs clubbing, anemia, mass lesion, palpable lymphnode, features of pleural effusion, features of SVC obstruction etc. were the main signs. Clubbing, anemia, mass lesion were predominant among the lung cancer patients. These signs take time to cause any other problem and is nearly impossible to detect by the patient himself or herself. Because these signs can only be detected by the physicians. The patients were referred from primary and secondary level to tertiary level hospitals like this hospital. Only from low and lower-middle socioeconomic background peoples avail the service from Government health care facilities. Other economically solvent peoples avail the private healthcare facilities in our country and abroad. That's why the people from low economic status suffer more and our findings also representing the similar scenario.

Limitations of the study

Small sample size is one of the limitations we faced along with limited time frame. Investigation facilities were not available like FOB and pleural biopsy during the study period.

Conclusion:

When a patient presents with cough, both doctor and patient can afford to wait a short time to allow the diagnosis to become clearer. It is highly unlikely that a delay of a few days in diagnosing lung cancer will have a material impact on the chance of survival. It is therefore reasonable to suggest a chest radiograph for a re-attendance with unexplained cough that has persisted for 3 weeks or more. This guidance would help some patients with a slow recovery from an upper respiratory infection would be clear.

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ORIGINAL ARTICLE

Role of flexible Bronchoscopy in the Diagnosis of Intrabronchial Mass Lesions

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Abstract:

Background: *Variety of benign and malignant lesions of respiratory system presents as intrabronchial mass lesions. Present study was carried out to study the spectrum of intrabronchial lesions and role of flexible flexible bronchoscopy in their diagnosis.*

Methods: *Retrospective study of case-records of patients with intrabronchial mass lesions diagnosed by flexible bronchoscopy, bronchial washings and bronchial biopsy between January 2015 and July 2016.*

Results: *Out of the 696 flexible bronchoscopies done during the study- period, intrabronchial mass lesions were evident in 74 patients (10.6%) (age range 21-86 years; 60 males). Fifty (68%) lesions were malignant, eighteen (24%) lesions were benign while six (8%) lesions were inconclusive. Diagnostic yield was about 92%; repeat bronchoscopy for inconclusive results improved the diagnostic yield.*

Conclusions: *Though malignant lesions are common, benign lesions remain important causes of intrabronchial mass lesions. Bronchoscopy with adequate sampling is an essential diagnostic modality for confirming the diagnosis of such lesions.*

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Introduction:

A significant number of patients presenting with an abnormal chest radiograph and/or computed tomography (CT) requires further investigation in the form of bronchoscopy as a part of their diagnostic work-up. With the advance imaging techniques, intrabronchial mass lesions can be diagnosed with accuracy Pulnionologists come across significant number of intrabronchial mass lesions on bronchoscopy. Clinical and radiological features of these lesions may not discriminate between different aetiologies, and sampling is required to distinguish benign from malignant lesions. However, limited information is available from Bangladesh on the spectrum of diseases causing intrabronchial mass lesions and its epidemiology.

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The present study was undertaken to study the spectrum of the diseases presenting with intrabronchial mass lesions and epidemiology of such lesions and describe the utility of flexible bronchoscopy in diagnosing intrabroncha mass lesions.

Material and Methods:

This was a retrospective study conducted at a tertiary care hospital in North Bangladesh between January 2015 and July 2016. All patients who presented to the hospital for flexible bronchoscopy were included. Written consent was taken from all the patients who underwent bronchoscopy. Information of demographic details (age and gender), indication for bronchoscopy, findings of bronchoscopy, relevant investigations (radiology, reports of bronchoalveolar lavage and biopsy) of each patient with intrabronchial mass lesion was recorded. These lesions were further sub-grouped according to the diagnosis; patients with intrabronchial mass lesions were then grouped into those with benign and malignant lesions. Repeat bronchoscopy was done for inconclusive results. Percentage of all groups, subgroups and diagnostic yield of the bronchoscopy were calculated.

Results:

Six hundred and ninety-six patients underwent flexible bronchoscopy during the study period and 74 (10.63%) patients showed intrabronchial mass lesions. Of the 74 patients, 50 (68%) had malignant lesions and 18 (24%) had benign lesions while the results were inconclusive in six (8%). The main clinical indications of bronchoscopy in 74 patients with intrabronchial mass lesions in our study were: unexplained chronic cough with localised clinical finding; unexplained lung collapse; non-resolving pneumonia; diagnosis and staging of lung carcinoma; aspiration of foreign body; etc. Prominent clinical symptoms at presentation are shown in table I. Radiological findings in patients with malignant lesion were mass lesions, collapse or non-resolving pneumonias. Patients with benign lesions showed mainly non- resolving pneumonias, collapse or lymphadenopathy as shown in table II.

Table-I

Prominent clinical symptoms at presentation in 74 patients presenting with intrabronchial mass lesions

Symptom*	No. (%)
Dry cough	39 (53)
Haemoptysis	16 (21)
Dyspnoea	11 (15)
Hoarsness of voice	6 (8)
Chest pain	2 (3)

· Patients presented with combination of symptoms

Table-II

Radiological findings in patients with benign lesions

Radiological Finding	No. (%)
Consolidation	9 (50)
Collapse	5 (28)
Lymphadenopathy*	4 (22)

Their median age was 65 years (range 21-86 years); there were 60 males (male:female = 4.3:1). Patients with malignant lesions had median age of 62 years (range 45-84 years) while patients with benign lesions had median age of 69 years (range 21- 86 years). Among patients with malignant lesions (n=50), male:female ratio was 9:1. Among patients with benign lesions (n=18), male:female ratio was 2:1. Distribution of various malignant and benign lesions are shown in table 3. In one patient bronchoscopy detected carcinoma larynx extending to the trachea. One patient had adeno carcinoma on bronchial biopsy but bronchial washings were positive for acid- fast bacilli (AFB). Three foreign bodies included betel nut, ciprofloxacin tablet and a screw were found. Inconclusive results were due to inadequate sample size, necrotic material, non-specific finding or normal mucosa on histopathology with inconclusive bronchial washings.

Repeat flexible bronchoscopy was done in three patients with inconclusive results. In two patients malignancy was diagnosed while one remained undiagnosed. Three patients with inconclusive results were lost to follow-up.

Diagnosis was made on bronchoscopy in 68 cases of the 74 cases in the first attempt; the diagnostic yield.

Table-III

Distribution of various intrabronchial mass lesions

Type of Lesion	No. (%)
Malignant Lesions (n=50)	
Squamous cell carcinoma	22 (44)
Adenocarcinoma	9 (18)
Small cell carcinoma	12(24)
Large cell carcinoma	2 (4)
Non-small cell carcinoma	2 (4)
Others*	3 (6)
Benign Lesions (n=18)	
Tuberculosis	7 (39)
Foreign body	3 (17)
Nocardia	4 (22)
Bronchial adenoma	1 (5.5)
Arteriovenous malformation	1 (5.5)
Broncholith	2 (11)

* Others included infiltrating lesions from oesophagus and larynx

* Foreign bodies included betel nut, tablet and screw being 92 percent. Diagnostic yield improved further to 94.6% on repeat bronchoscopy.

Discussion:

Malignant lesions are common but benign lesions also contribute significantly to the intrabronchial mass lesions. Intrabronchial mass lesions were seen in all age groups. Benign lesions showed greater age range as compared to the malignant lesions. While malignant lesions are seen in middle-age to elderly- age group, benign lesions occurred in all age groups. Both benign and malignant intrabronchial mass lesions were predominantly seen in males as compared to females. The male preponderance was much more in malignant lesions as compared to benign lesions.

Though adenocarcinoma is the most common form of lung cancer, in our study squamous cell carcinoma and small cell carcinoma were common. This could probably be due to central location of these tumours which are better assessed with bronchoscopy; adenocarcinomas because of their predominantly peripheral location are not visualised on bronchoscopy. One patient who presented with fever and an opacity in the right middle zone on the chest radiograph was found to have anintrabronchial mass lesion that on biopsy was found to be an adenocarcinoma. Bronchial washings of this patient revealed AFB. This was attributed to coincidental finding in which patient had gradual clinical improvement after antituberculosis treatment though radiological opacity persisted. The number of case reports of benign lesions that mimic malignant lesions indicates the importance of the benign lesions. Infections that are reported to cause intrabronchial mass lesions include tuberculosis,1 nocardiasis2 and mucormycosis.3 Among benign lesions, tuberculosis was most common, possibly due to endemic nature of this disease in our country. Bronchial foreign bodies with granulomatous reactions leading to the complete obstruction of the airways may simulate endobronchial malignancy.4 Foreign bodies are mainly seen in children and elderly population, but, may be seen in young- to middle-age group adults also. Sometimes organised blood clots or mucus plugs may simulate intrabronchial mass lesions but these get cleared by aspiration or coughing. Rare entities, like mycotic pulmonary artery aneurysm5 or vascular lesions may also present as intrabronchial mass lesion.6 We also found an intrabronchial vascular lesion that simulated malignancy; diagnosis was confirmed on histological examination of the pneumonectomy specimen.

Computed tomography or virtual bronchoscopy can also diagnose intrabronchial mass lesions with good morphological correlation between CT and bronchoscopic findings (89% for discrete nodule, 80% overall).7 Virtual multi-slice CT bronchoscopy can add important information about intra-luminal tumour and its relation to surrounding structures.8 These modalities are non-invasive but do not permit obtaining samples for diagnostic testing and cannot distinguish benign lesions from malignant lesions. According to a study,9 CT failed to detect endobronchial tumours in 11 of 64 patients (17%). So, bronchoscopy can sometimes detect radiographicaily occult lesions. In an another study of 98 patients,'° bronchoscopy was diagnostic for cancer in 88 (89.8%) patients. Forceps biopsy gave results in 82.7% cases, transbronchial needle aspiration (TBNA) in 68.6%, brushing in 68.4% and washings in 31.6 percent. Cytological examination does not increase the diagnostic yield of biopsy spechnens" but increases the yield by 16.9%, when

intrabronchial lesions are not visible.1' Diagnostic yield of TBNA is high when endoscopically visible bronchial anomalies suggesting neoplasm are evident, particularly when the lesion is due to extrinsic compression, submucosal infiltration or exophytic growth with necrosis.'2 False-positive results of bronchoscopy are low. Sometimes results are inconclusive due to inadequate sample size or non- specific changes, so repeat bronchoscopy may be required in such cases for the diagnosis. According to the American Thoracic Society / European Respiratory Society (ATS/ERS)," diagnostic yield of bronchoscopy should be more than 90%, but in our study diagnostic yield was about 92 % on first attempt which improved to

94.6% on second attempt to diagnose inconclusive results. Recently, the role of endobronchial ultrasound (EBUS) during bronchoscopy as the diagnostic tool for lung cancer has emerged. According to a study,14 under EBUS guidance, the diagnostic yield of transbronchial lung biopsy in peripheral lung cancer by bronchoscopic examination was significantly improved without difference in the complication rate.

Bronchoscopy has the advantage of detecting lesions in the upper airways, as seen in one case in the present study, in which carcinoma larynx extending to the trachea could be identified. Disadvantages of bronchoscopy include its limited approach to distal airways and only proximal airways upto subsegmental level bronchi can be approached. It is invasive procedure and it has high cost apart from various other complications of bronchoscopy and biopsy. Moreover, it cannot be used for mass screening of malignancy but fluorescence endoscopy might be useful to detect early bronchial lesions, especially in smokers with heavy occupational exposure to asbestos.'5

In conclusion, malignant lesions are a common cause of intrabronchial mass lesions but benign lesions also contribute significantly to such lesions. Benign lesions can mimic malignant lesions on visual impression, and thus, adequate sampling is a must. However, good histopathology and microbiology laboratories should support bronchoscopy for obtaining high yield. In spite of advances in imaging techniques, bronchoscopy stillremains an essential tool for the diagnosis of centrally located mass lesions.

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Antibiogram and Extended Spectrum Beta-lactamase (ESBL) production among *Klebsiella pneumoniae* isolated from sputum

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Abstract:

Background & Aims: *Klebsiella pneumoniae is one of the major causes of respiratory tract infection. It has been found that this organism is being increasingly resistant to broad spectrum antibiotics especially â- lactam antibiotics mediated by extended Spectrum â-lactamase (ESBL) enzymes. The present study was undertaken to determine the antibiogram and the incidence of ESBL production among Klebsiella pneumoniae strains isolated from sputum.*

Materials & Methods: *sputum specimens from patients were subjected to culture as per Clinical Laboratory Standard Institute (CLSI) guidelines. All specimens were inoculated on to Blood agar, Chocolate agar and MacConkey agar plates. Klebsiella pneumoniae were identified by the standard biochemical procedures. Detection of ESBL production by isolated Klebsiella pneumoniae strains was done by Double Disc Synergy Test which is a phenotypic confirmatory test for ESBL production. Antibiotic susceptibility testing of isolates was also done and described as per CLSI guidelines. The study was conducted from 1st August, 2014 to 31st July, 2015.*

Result: *A total of 124 Klebsiella pneumoniae strains were isolated of which 40 (32.25%) isolates were ESBL producers. Susceptibility of isolates to Cephalosporins tested except Ceftriaxone , was not satisfactory. All isolates were sensitive to Imipenem. More than 80% sensitivity was found only to Gentamicin (83.89%), Tazobactam- Piperacilin combination (82.25%) and Doxycyclin (81.45%). Moderate number of isolates were sensitive to Colistin and Ciprofloxacin.*

Conclusion: *A high prevalence of respiratory tract infections by Klebsiella pneumoniae was observed in our hospital setting and the rate of ESBL production was moderately high. Bacteria is gaining resistance to many commonly used antibiotics.*

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Introduction:

The discovery and development of antibiotics was one of the greatest advances of modern medicine. But antibiotic resistant bacteria has emerged as a threat to this advancement. Antibiotics are among the most commonly used and misused of all drugs. The inevitable consequence of this has been the emergence of antibiotic resistant pathogens[1].

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Klebsiella pneumoniae is gram negative, non motile, encapsulated, lactose fermenting bacteria belonging to Enterobacteriaceae family. They are ubiquitously present and reported worldwide[2]. In recent years *Klebsiella pneumoniae* has become an important pathogen for both nosocomial and community acquired infections. In addition to causing various extra-pulmonary infections, it is one of the predominant organism of primary pneumonia[1,2]. Extensive use of broad-spectrum antibiotics especially Penicillin and Cephalosporin in hospitalized patients has led to both increased carriage of *klebsiella pneumoniae* and the development of multidrug resistant (MDR) strains[3]. Evidence from researches have proved that multidrug resistant *Klebsiella pneumoniae* are emerging world-wide causing serious infections which are difficult to eradiate using available antibiotics. This situation is alarming in both developing as well as developed countries which has led clinicians in the state of paucity of antibiotics to treat the organism[1, 4, 5 6]. Pharmacological industries are trying to combat this by producing large number of newer antibiotics. Microorganisms develop resistance to these newer antibiotics even. In Gram negative bacteria like *Klebsiella pneumoniae*, production of Extended spectrum â-lactamase (ESBL) is perhaps one of the most important causes of such resistance pattern. ESBLs are plasmid mediated enzymes that cause hydrolysis of â- lactam antibiotics, like Penicillin, Cephalosporins, Monobactams conferring resistance to these drugs. ESBL enzymes have been identified in large number in various *Klebsiella pneumoniae* strains[3]. On the other hand plasmids carrying genes of ESBL enzymes also carry resistance genes to other antibiotics including Aminoglycosides, Sulphonamides, Trimethoprim, Tetracyclin, Ciprofloxacin[7]. As plasmids are mobile genetic material so they can carry resistance genes against a number of antibiotics between bacteria. As such ESBL producing strains are associated with resistance to other non â-lactam drugs also. Infection with such multidrug resistant bacterial strains leads to increased patient mortality and morbidity when antibiotics inactive against the strain are used[8]. Also ESBL producing organisms are threat to infection control and there is a potential for transfer of such organism to other patients[8]. The microbiology laboratory plays a central role in the decision to select a particular antibiotic by appropriate identification of causative organism of infection and by rational selection of class of antibiotic likely to work on the patient[1]. The present study was therefore conducted with a view to see the antimicrobial susceptibility profile and the prevalence of ESBL production among *Klebsiella pneumoniae* isolated from sputum.

Materials and Methods:

This prospective observational study was carried out in the Department of Microbiology, DNMCH, Dhaka for a period of one year from 1st August, 2014 to 31st July, 2015. Total 896 sputum specimens from 896 patients with suspected respiratory tract infection were collected which included both indoor and outdoor patients. For sputum collection, patients were asked to take a deep breath & then expel the expectorate directly into a sterile leak-proof plastic container. The specimens were inoculated on to Blood agar, Chocolate agar and MacConkey agar plates and incubated overnight at 37°c. *Klebsiella pneumoniae* isolates were identified by their morphology and biochemical characteristics like Gram staining, negative indole test, positive citrate utilization test, positive urease test, acid and abundant gas production from glucose, lactose, sucrose[9]. Antimicrobial susceptibility testing: Antimicrobial susceptibility testing of the isolates was carried out using various antimicrobial disks (shown in table I) by Kirby-Bauer disk diffusion method[10]. Inoculum of 0.5 McFarland standards turbidity was prepared in a nutrient broth from isolated colony of *Klebsiella pneumoniae* selected from 18-24 hour agar plates. Within 15 minutes, a sterile cotton swab was dipped into the inoculum suspension. The swab was rotated several times and pressed firmly against the inside wall of the tube above the fluid level and inoculated on the dried surface of Mueller – Hinton agar plate by streaking the swab over it. For even distribution of the inoculum, the swab was streaked two more times at 60° angle over the surface. After 3-5 minutes antibiotic disks were applied and pressed down to ensure complete contact with agar surface. The disks were distributed evenly to ensure a minimum distance of 24 mm from centre to centre. Within 15 minutes the plates were inverted and kept in incubator for

aerobic incubation at 37°c. The diameter of zone of inhibition for individual antimicrobial agent was measured in millimeter with the help of a ruler and described as sensitive, intermediate & resistant according to CLSI 2012 guideline[11]. Detection of ESBL: Isolated *Klebsiella pneumoniae* were tested for ESBL production by Double Disk Synergy test (DDST), which is a phenotypic confirmatory test of ESBL production. For this, a lawn culture of isolated bacteria was made on Mueller Hinton Agar and disks containing 30ìg Ceftriaxone and 30ìg Ceftazidime were placed with a disk of Amoxicillin-Clavulanic acid (20 ìg /10 ìg) in between. The distance between the disks was 30mm centre-to-centre. The plate was incubated overnight. A clear extension of the edge of any Cephalosporin inhibition zone toward the disk containing Clavulanic acid was interpreted as synergy, indicating the presence of ESBL[8].

Result:

During the study period a total of 896 sputum specimens were processed. Sputum samples from patients of all age group of both sexes were processed. 247 sputum specimens were couture positive. (Table II). Table III shows different organisms isolated from sputum specimens. *Klebsiella pneumoniae* is the most frequent isolate (46.10%), which is followed by *Pseudomonas spp.* (20.44%), *Staphylococcus aureus* (11.15%), *Moraxella catarrhalis* (9.29%) and other organisms like *E. coli, Acinetobacter spp.*, *S. pneumoniae*, *H. influenzae*, *Candida spp.* Isolation rate of *Klebsiella pneumoniae* is highest (34.69%) among 46-60 years age group patients and least (2.41%) among patients <16 years of age. 32% of *Klebsiella pneumoniae* isolates were ESBL producer. ESBL production is highest in isolates obtained from sputum specimen of patients of more than 60 years of age. From Table V we observe that *Klebsiella pneumoniae* are most sensitive to Imipenem (100% sensitivity) followed by Gentamicin (83.87%), Tazobactam+Piperacilin combination (82.25%), Doxycyclin (81.45%) and Amikacin (72.58%). It is seen that the organism is moderately sensitive to Ceftriaxone, whereas sensitivity to other Cephalosporins is not at all satisfactory. *Klebsiella pneumoniae* is moderately sensitive to Colistin and Ciprofloxacin.

Table-I

Antimicrobial disc used & their zone diameter interpretative for Klebsiella pneumoniae

Antimicrobial disc	Disc potency	S	I	R
Imipenem	10µg	≥23	20-22	≤19
Amikacin	30µg	≥17	15-16	≤14
Gentamicin	10µg	≥15	13-14	≤12
Ciprofloxacin	5µg	≥21	16-20	≤15
Ceftriaxone	30µg	≥23	20-22	≤19
Ceftazidime	30µg	≥21	18-20	≤17
Cephradine	30µg	-		- -
Cefixime	5µg	≥19	16-18	≤15
Cefuroxime	30µg	≥18	15-17	≤14
Trimethoprim+ Sulphamethoxazole				
25µg	≥16	11-15	≤10	
Doxycycline	30µg	≥14	11-13	≤10
Tazobactam+piperacilin				
10/100µg	≥21	18-20	≤17	
Colistin	10µg	≥11	-	≤10

Note: S=Sensitive, I= Intermediate, R= Resistant

Table-II

Number of culture positive specimen among different age groups

Age in years	No. of specimens	No. of culture positive specimen(%)
<16	58	12 (20.69)
16-30	266	41 (15.41)
31-45	218	68 (31.20)
46-60	234	79 (33.76)
>60	120	47 (39.17)
Total	896	247 (27.57)

Table-III

Organisms isolated from sputum specimen

Organism	Number of organism isolated
Klebsiella pneumoniae	124 (46.10)
Pseudomonas spp.	55 (20.44)
Staphylococcus aureus	30 (11.15)
Moraxella catarrhalis	25 (9.29)
Others	35 (13.02)
Total	269 (100)

Table-IV

Frequency of Klebsiella pneumoniae isolation & ESBL production in different age groups

Age in years	No. of *Klebsiella pneumoniae* isolated (%)	No. of ESBL producer (%)
<16	3 (2.41)	00 (00)
16-30	22 (17.74)	04 (18.18)
31-45	31 (25)	07 (22.58)
46-60	43 (34.69)	13 (30.23)
< 60	25 (20.16)	16 (64)
Total	124 (100)	40 (32.25)

Table-V

Antimicrobial susceptibility of isolated Klebsiella pneumoniae

Antimicrobial agents	Sensitive (%)	Resistant (%)
Imipenem	124(100)	00 (00)
Amikacin	90(72.58)	34(27.42)
Gentamicin	104(83.87)	20(16.13)
Ceftriaxone	81(65.32)	43(34.68)
Ciprofloxacin	75(60.48)	49(39.52)
Cephradine	26(20.96)	98(79.04)
Ceftazidime	45(36.29)	79(63.71)
Cefixime	71(57.25)	53(42.75)
Cefuroxime	44(35.48)	80(64.52)
Trimethoprim+ Sulphamethoxazole	24(19.35)	100(80.65)
Doxycyclin	101(81.45)	23(18.55)
Tazobactam+ Piperacilin	102(82.25)	22(17.75)
Colistin	84(67.74)	40(32.26)

Discussion

Antibiotic resistance is an important issue affecting public health drastically[12]. In case of Gram negative bacteria one important cause of antibiotic resistance is production of ESBL enzymes. During the past decade, ESBL producing *Klebsiella pneumoniae* have emerged worldwide as causative pathogen for serious infections in both hospital and community settings[1]. So, rapid detection of antimicrobial resistant organisms, especially those producing ESBL, in clinical laboratories is essential[12]. In this study an attempt was made to understand the antimicrobial sensitivity pattern and epidemiology of ESBL production of *Klebsiella pneumoniae* isolates in sputum. This study results revealed that *Klebsiella pneumoniae* was the predominant isolate in sputum constituting more than 46% of all isolated organism, followed by *Pseudomonas aeruginosa*. A previous study in Bangladesh showed predominance of *Klebsiella pneumoniae* isolation from sputum in diabetic patients, with isolation rate of 19.1%[13]. In Indian studies rate of *Klebsiella pneumoniae* isolation was in range of 10-39%[1,14,15,16], though some of these studies[15,16] revealed *S. pneumoniae* as the predominant isolate. Some patient factors like old age, smoking, concomitant illness such as COPD and Diabetes impair pulmonary defense and predispose to infection by Gram negative bacilli like *Klebsiella pneumoniae*[16]. This may be the reason of our finding. Infact, we found *Klebsiella pneumoniae* infection was most predominant among 46-60 years age group patients. The occurrence of ESBL production among clinical isolates of *Klebsiella pneumoniae* vary greatly world wide and geographically[12]. We found 32% of *Klebsiella pneumoniae* isolates were ESBL producer. A retrospective study in Saudi Arabia (year 2004-2005) reveals this rate as 13.7% and 3.1% among indoor & outdoor specimens respectively[4]. On the year 2013 in Europe, the rate of ESBL positive *Klebsiella pneumoniae* was 18.4%[17]. On contrary much higher rate of ESBL positive *Klebsiella pneumoniae* isolates were found in a tertiary care hospital in tehran, Iran (77%)[18]. Our finding of most frequent ESBL production in patients at the higher extreme of age is also in contrast to that study where high prevalence of ESBL was found in patients at the lower extreme of age. Prolonged hospital stay, poor nutritional status, previous use of broad spectrum antibiotics may be the risk factors for the high prevalence of ESBL among this age group patients as has been reviewed by Paterson & Bonomo[8]. Based on our in vitro findings, Imipenem was the most effective antibiotic against *Klebsiella pneumoniae* (100% sensitivity). 100% sensitivity to Imipenem was found in a previous study in Bangladesh also[19] and even ESBL producing strains were reported to be 100% sensitive to Imipenem by different research groups like Jones et al[20]. Many investigators prefer Imipenem and Meropenem as drugs of choice for life- threatening infections due to ESBL producing

Enterobacteriaceae. However, to preserve the therapeutic value, the use of these drugs should be restricted[18]. Rather based on institutional pattern of susceptibility results, Tazobactam-Piperacilin combination, Fluoroquinolones or an Aminoglycoside would be preferable. In fact, with more than 80% sensitivity we found Gentamicin (83.89%), Tazobactam- Piperacilin combination (82.25%) and Doxycyclin (81.45%) to be moderately active against *Klebsiella pneumoniae* in our study. On the other hand we found only 60% isolates were sensitive to Ciprofloxacin. Such susceptibility pattern to Ciprofloxacin was comparable to previous studies[1,18,19]. Report has shown a close association between ESBL production and Ciprofloxacin resistance[3]. Though we found moderate activity of Gentamicin, some studies showed much less activity [1,2,18]. A previous study in Bangladesh also showed lesser sensitivity to Gentamicin[19]. In contrast to our finding of moderate sensitivity to Tazobactam- Piperacilin combination (82.25%), studies from Iran[18] and India[21] showed striking resistance to this drug. In fact, it is to be noted that therapeutic failure with this antibiotic combination have already been documented[3] and thus in vitro susceptibility may not necessarily predict in vivo efficacy. A moderately higher resistance to Amikacin (27.12%) and Colistin (32.20%) was observed in this study. There are reports covering high levels of resistance of *Klebsiella pneumoniae* to these antibiotics in other studies also[2]. But a study from India showed more than 92% sensitivity to Amikacin[1]. We found Ceftriaxone has better sensitivity (more than 65%) among Cephalosporins. Sensitivity to other Cephalosporins like Cephradin, Ceftazidime and Cefuroxime was disappointing. This finding is in accordance with previous studies [1,17]. This high resistance rate may be due to the production of â-lactamase enzymes which cause the hydrolysis of â- lactam rings resulting in inactivation of â-lactam drugs. In the present study with a sensitivity rate of as low as 19%, Trimethoprim+ Sulphamethoxazole combination has shown to be of no value in the treatment of infections by *Klebsiella pneumoniae*.

As the available treatment options are becoming limited, antibiotic control policies together with implementation of infection control measures remain of high importance. Due to the changing nature of ESBL enzymes, clinicians should be familiar with the clinical significance of these enzymes and clinical laboratories should adopt a technique most appropriate to them for their detection.

Conclusion:

High antibiotic resistance of *Klebsiella pneumoniae* towards commonly used antibiotics are the major reason for prolonged infections, increased hospitalization, increased cost of therapy and enhanced morbidity and mortality rates. Regular surveillance of antibiotic susceptibility pattern may help to overcome the indiscriminate use of antibiotics which is the major cause of emergence of drug resistance among pathogens and to develop antibiotic policies. The data of this study may be used to determine trends in antimicrobial susceptibility to formulate local antibiotic policy and thus may assists clinicians in the rational choice of antibiotic therapy.

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ORIGINAL ARTICLE

Association between Body Mass Index and Outcomes after Pulmonary Resectional Surgery in Lung Cancer

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Abstract

Objective: *Obesity has been thought to predispose patients to excess morbidity after lung resection because of decreased diaphragm excursion, reduced lung volumes and relative immobility. We assessed the relationship of body mass index (BMI) to acute outcomes after major lung resection.*

Methods*: We enrolled 46 consecutive patients undergoing lobectomy and pneumonectomy for NSCLC at the Department of Thoracic Surgery, National Institute Institute of Diseases of the Chest and Hospital, Dhaka, from July 2014 to June 2015. To determine the influence of preoperative body mass index (BMI) on postoperative complications, patients were classified into two groups: (1) BMI e" 23 kg /m²; n = 22 (47.8%); and (2) BMI 18.5 to 22.9 kg/ m²; n = 24 (52.2%). Data on sex, age, cigarette smoking, HTN, Diabetes, Duration of operation, and histology and pathological stage were collected. Information on total postoperative complications, 30-day mortality rate, specific pulmonary and other complications, intensive care unit (ICU) admission and hospital stay was collected and analysed for the BMI group.*

Results*: Fifty-two percent (24 of 46) were nonobese, and 48% (22 of 46) were overweight & obese. Preoperative variables were similar in the overweight & obese and nonobese group. Overall mortality was 6.5% (3 of 46) and was not different between groups (p = 0.466). Length of hospital stay (p = 0.708) were similar. Complications occurred in 25% (6 of 24) of nonobese and 22.7% (5 of 22) of overweight & obese patients (p = 0.856). Respiratory complications occurred in 8.3% (2 of 24) of nonobese and 18.2% (4 of 22) of overweight & obese patients (p = 0.290). Significant difference was found in duration of operation at nonobese 2.6±0.6 and 3.2±0.8 at overweight & obese patients (p = 0.05); type of operation (p = 0.045). No association was found between risk factor and complication.*

Conclusions: *Being overweight or obese does not increase the risk of complications after major lung resection in contrast to patients who are normal weight. A large sample size is needed for further evaluation.*

Keywords: *Lobectomy; Pneumonectomy; Lung cancer; Body mass index*

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Background

Obesity is defined as 'abnormal or excessive fat accumulation that may impair health[1]. Obesity is currently the most common metabolic disease in the world[2] with more than 1.6 billion overweight adults worldwide of whom at least 400 million are obese[1]. Obesity and overweight are classified by the body mass index (BMI, kg/m^2) devised by Lambert Adolphe Quetelet (1796—1874) in 1835. Body mass index is highly correlated with body fat and is therefore one of the easiest and most effective measures in clinical assessment and epidemiological studies[2]. The World Health Organization (WHO) has estimated that around 2.3 billion adults will be overweight and more than 700 million obese by 2015[1].

According to WHO classification of BMI for south Asian countries; BMI (kg/m^2) was categorized as underweight (<18.5 kg/m^2), normal healthy person (18.5 to 22.99 kg/m^2), overweight (23 to 26.99 kg/ m^2) , obese (> 27 kg/m^2)[3].

Epidemiological studies have suggested a significant inverse relationship between BMI and the incidence of lung cancer but it has only been with the recent epidemic of obesity that significant numbers of patients presenting for resection of non-small-cell lung cancer (NSCLC) have been overweight or obese[4].

Body mass index (BMI) intuitively influences the technical aspects of lung cancer surgery and its outcome[5]. Surgeons traditionally welcome the easily discerned internal anatomy of thin patients, while reluctantly facing challenges that obese patients present[5]. The greater technical and physical demands engendered by substantial girth and excess mediastinal fat are associated with increased operating time for lung resection [6]. Obesity intuitively increases the peri-operative risks of lung surgery owing to associated co morbidities such as diabetes, hypertension and coronary artery disease, and physiological impairment of ventilation[5].

Results of recent reports on acute outcomes of lung resection in obese patients are mixed: some reports substantiate this increased risk[7,8], while others demonstrate no increase in risk[4,5,9,10,11].

As complete anatomic resection remains the mainstay of attempted curative therapy for NSCLC in patients with locoregional disease [4], it is quite common nowadays for thoracic surgeons and anaesthesiologists to manage overweight or obese patients eligible for standard or major curative lung resections in stage I,II,IIIA disease[7].

The aim in our study was to explore the relationship of BMI, particularly over weight and obese with normal weight status, undergoing major lung resection for curative therapy of NSCLC, on postoperative respiratory and overall complication.

Materials and methods

The study was conducted in the Department of Thoracic Surgery, National Institute of Diseases of the Chest and Hospital, Dhaka, between the periods of July 2014 to June 2015. It was a prospective, observational study.

A Study population

Patients who were diagnosed as a case of operable (stage- I, II, & IIIA) NSCLC, lobectomies and standard pneumonectomies were performed. Standard pneumonectomy was defined as the removal of the entire lung, associated with mediastinal lymph node dissection without any resection of mediastinal, chest wall or diaphragmatic structures. A total of 46 cases of NSCLC were taken and they were divided in two groups, Group - I, 22 patents (i.e; BMI e" 23 kg/ m^2) and Group - II, 24 patients (BMI 18.5 kg/ m^2 to 22.9 kg/ m^2).

B Selection of sample:

Sample was selected from the inpatient department of NIDCH of either sex. Patients who got admitted in NIDCH and underwent major lung resection (lobectomy, bilobectomy pneumonectomy) for NSCLC at stage-I, II and IIIA disease, undergoing lung resection for NSCLC for the first time and with inducton chemotherapy was included in the study. Patients with NSCLC who has been suffering from active respiratory disease, previously treated with induction radiotherapy, with renal failure, symptomatic heart disease, with BMI <18.5 kg / m^2 was excluded in the study. Sampling was done by convenience sampling.

C Patient selection and management

Operability and staging procedures was determined by standard clinical examination, some laboratory

investigations and radiographic procedures such as complete blood count, liver funtion test, renal function test, blood glucose level, chest X-Ray P/A and lateral view, computed tomography (CT scan) of chest, both flexible and rigid bronchoscopy, ultrasonography of whole abdomen including chest, bone scan, nuclear imaging [whole-body 18F-fluorodeoxyglucose (FDG)-positron emission tomography (PET scan)] as appropriate. Final staging was done after histopathology report. Preoperative respiratory function was assessed routinely by spirometry and occationally blood gas analysis (ABG) if needed. Preoperative cardiac function evaluation was routinely performed by echocardiography with left ventricular ejection fraction (EF) and pulmonary artery pressure (PAP) was estimated. Diabetes was well controlled preoperatively and postoperatively by short acting insulin. Hypertension was well controlled preoperatively and postoperatively by antihypertensive drug. Smoking was stopped at least two weeks before surgery. Patient with any abnormality of these investigation sort out properly, if correctable/manageable, managed properly or excluded from this study..

Postoperative analgesia was achieved, in conjunction with anaesthesiologists, using a combination of epidural analgesia (when technically feasible and not contraindicated), and oral and parenteral adjuncts as needed to improve pulmonary and physical therapy.

Patients were instructed preoperatively regarding incentive spirometry. Postoperatively, they received two assisted sessions of chest physiotherapy daily, starting on the first postoperative day, and were asked to repeat the physiotherapy programme six times during the day until discharge. Therapeutic bronchoscopy was instituted early, based on clinical findings and correlation with chest films.

D Postoperative complications

Postoperative death was defined as the 30-day mortality rate or longer if mortality occurred during the index hospitalisation. Complications were classified as: a) respiratory and b) other complications. Respiratory complications were classified as follows: I) Major complications: (i) acute respiratory failure; (ii) adult respiratory distress syndrome (ARDS); (iii) acute lung injury (ALI); (iv) pneumonia; (v) pulmonary embolism; and (vi) pulmonary oedema vii) bronchopleural fistula. II) Minor complications: (i) sputum retention and (ii) atelectasis not requiring toilette bronchoscopy.

b) Other complications included: i) haemothorax, ii) empyema, iii) chylothorax,iv) cardiac dislocation v) wound infection vi) neurological complications; and vii) abdominal / urinary tract complications.

E Body mass index

Height and weight were measured preoperatively: BMI was calculated as patient weight in kilograms divided by the square of patient height in metres (kg / m^2). The WHO BMI classification for south asian people was used as follows: underweight (BMI < 18.5 kg/ m^2); normal weight (BMI from 18.5 kg/ m^2 to 22.9 kg/ m^2); overweight (BMI 23 kg/ m^2 to 26.9 kg/ m^2) and obese (BMI e" 27 kg/ m^2) [3].

Patients were then classified into two groups: Group- I, BMI e" 23 kg/ m^2; and Group- II, BMI 18.5 kg/ m^2 to 22.9 kg/ m^2. Group- I, BMI e" 23 kg/ m^2 were divided into two subgroups: overweight patients (BMI: 23 kg/ m^2 to 26.9 kg/ m^2); obese patients (BMI: e" 27 kg/ m^2).

F Follow up

All patients with satisfactory outcome were discharged. After discharge patients were followed up at one month interval for two times. In follow up patients were evaluated clinically, and radiologically, for any evidence of complication. If complication was detected, he/she was admitted and treated accordingly.

G Statistical methods

Statistical analyses was carried out by using the Statistical Package for Social Sciences version 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA). A descriptive analysis was performed for all data. The mean values was calculated for continuous variables. The quantitative and qualitative observations were indicated by frequencies, percentages. Chi-Square test and Odds ratio with 95% CI was used to analyze the categorical variables, shown in cross tabulation and unpaired t-test was used to analyze the continuous variable and expressed as mean (±SD) and further analyzed using logistic regression analysis for their possible independent association. A P-value was considered

to be statistically non significant if >0.05 and statistically significant if d" 0.05.

Observations and Results

During the study period, 46 patients underwent major lung resection for NSCLC. Patients were devided into two group. In Group-I, BMI e"23 included overweight and obese were 22 patients and in Group-II, BMI 18.5 - 22.9 included normal weight were 24 patients, of them 35 (76.1%) were male and 11(23.9%) were female. The female sex was comparatively more frequent in the high BMI group than normal. The mean age was (55.6±11.3) years (range: 25—80) are listed in Table-I. No statistically significant difference between the two groups was evident in terms of age (p=.054) and sex(p=.228). As many as 30 patients (65.2%) were smokers or former smokers at the time of diagnosis of whom13(59.1%) in group - I and 17(70.8%) in group -II. Total 15(32.6%) patients were diabetic and 12(26.1%) patients were hypertensive are listed in Table-II. No statistically significant difference between the two groups was evident in terms of smoking(p=0.403), diabetes (p=0.602) and hypertension(p=0.396).

In case of tissue diagnosis, 30(65.2%) patients were squamous cell carcioma, 14(30.4%) were adenocarcinoma and 2(4.4%) were large cell carcinoma. Lobectomy was done in 42(91.3%) patients and pneumonectomy was done in 4(8.7%) patients. It was observed that in diagnosis, squamous cell carcinoma was found 14(63.6%) in group I and 16(66.6%) in group II. Adenocarcinoma was found 7(31.9%) in group I and 7(29.2%) in group II. Large cell carcinoma was found 1(4.5%) in group I and 1(4.2%) in group II. The difference was not statistically significant (p<0.05) between two groups are listed in table III. In type of operation, lobectomy was found 22(100.0%) in group I and 20(83.3%) in group II. The difference was statistically significant (p<0.05) between two groups are listed in table III.

Mean duration of operation was found at all patients were 2.9±0.7 (2-5) hrs , and 3.2±0.8 hrs in group I and 2.6±0.6 hrs in group II. In pathological staging, stage- I was 7(15.2%) patients, stage- II was 30(65.2%) patients and stage-IIIA was 9(19.6%) patients. Mean duration of operation was statistically significant (p<0.05) between two groups. Pathological staging was not statistically significant (p>0.05) between two groups that is listed in table IV. Mean duration of operation was found 3.2±0.8 hrs in group I and 2.6±0.6 hrs in group II. In pathological staging, stage II was found 14(63.6%) in group I and 16(66.7%) in group II. Mean duration of operation was statistically significant (p<0.05) between two groups

Mean duration of hospital stay was found at all patients were 31.9±6.2 (25-52)days. It was observed mean duration of hospital stay was found 30.0±5.7 days in group I and 32.8±6.7 days in group II. The mean duration of hospital stay was not statistically significant (p>0.05) between two groups(Table-V). Total 3(6.5%) patient needed ICU support. Two patients in group-I and one patient in group-II. One patient recovered from ICU and two patients were died. No statistically significant difference between the two groups was evident in terms ICU admission (p = 0.499). Four patients (18.2%) received induction chemotherapy in group-I but not found in group in group II. Induction chemotherapy was statistically significant (p<0.05) between two groups. Five patient(10.9%) was resection margin positive of whom 2/22(9.1%) in group -I and 3/24(12.5%) in group -II. The resection margin positive was not statistically significant (p=0.550) between two groups.

Three patients (6.52%) died within the first 30 days of operation. One patient belonged to the group with normal BMI and died at 6th POD. Causes of death was respiratory failure due to pneumonia with septic shock,. Two deceased patients belonged to the high BMI group; one of them died at 6th POD after respiratory failure due to pneumonia with septic shock, another patient died at home on 18th POD, 4 days after discharge with respiratory distress. This patient suffered postoperatively with bronchopleural fistula and collapse of remaining lobe(Table -VI, VlI). No statistically significant difference between the two groups was evident in terms mortality (p = 0.466).

Respiratory complications were more frequent in the high BMI group (18.2% vs 8.3%, crude OR = 2.44; 95% CI: 0.32-22.09; p=0.290) but not statistically significant between the two groups (Table -VI, VlI). In the 'normal weight' group, we observed 2/24 pulmonary complications (8.3%); one of them developed pneumonia with ARDS with respiratory failure.He died at ICU on 6th POD. Another patient developed prolong air leak with IT collection. After discharged patient was readmitted for post pneumonectomy space infection. After tube thoracostomy patient was recovered . In the higher BMI group we observed

4/22 pulmonary complications (18.2%); they were pneumonia in one case that resolved after conservative treatment; pneumonia with ARDS with respiratory failure in one case, who died on at ICU; bronchopleural fistula and collapse of remaining lobe with respiratory failure in two cases, one who recovered after treatment at ICU and another patient died at home 4 days after discharge on 18th POD.

Non respiratory complications were more frequent in the normal BMI group(16.7% vs 4.5%, crude OR = 0.24; 95% CI: 0.01-2.65; p=0.201) but not statistically significant between the two groups (Table -VIII, IX). In the 'normal weight' group, we observed 4/24 non pulmonary complications (16.7%);

Respiratory complications were more frequent in the high BMI group (group I) (18.2% vs 8.3%, crude OR=2.44; 95% CI: 0.32 to 22.09%).

At first follow up one month after discharged, three patients developed metastatic lesion. One patient in thoracic vertebrae, one patient in brain and another patient developed two metastatic lesion in opposite lung. At second follow up two months after discharged, this patient developed pleural effusion in same hemi thorax needed tube thoracostomy At the second follow up, one month after first follow up, one patient developed pleural effusion needed readmission and tube thoracostomy. In the high BMI group, we observed 1/22 non pulmonary complications (4.5%). (Table -Vlll).

Table-I

Distribution of the study patients by age and sex (n=46)

	Group-I (n=22)		Group-II (n=24)		Total (n=46)		P value
	n	%	N	%	N	%	
Age (years)							
≤50	9	40.9	5	20.8	14	30.4	
51-60	6	27.3	11	45.9	17	37.0	
>60	7	31.8	8	33.3	15	32.6	
Mean±SD	52.2	±12.0	58.7	±10.0	55.6	±11.3	[a]0.054[ns]
Range (min-max)	25	-77.0	32	-80.0	25	-80.0	
Sex							
Male	15	68.2	20	83.3	35	76.1	[b]0.228[ns]
Female	7	31.8	4	16.7	11	23.9	

Group I- Over weight & obese
Group II- Normal BMI
ns= not significant
[a] p value reached from unpaired t-test
[b] p value reached from chi square test

Table-II

Distribution of the study patients by risk factors (n=46)

Risk factors	Group-I (n=22)		Group-II (n=24)		Total (n=46)		P value
	n	%	N	%	N	%	
Smoking							
Yes	13	59.1	17	70.8	30	65.2	0.403[ns]
No	9	40.9	7	29.2	16	34.8	
DM							
Yes	8	36.4	7	29.2	15	32.6	0.602[ns]
No	14	63.6	17	70.8	31	67.4	
HTN							
Yes	7	31.8	5	20.8	12	26.1	0.396[ns]
No	15	68.2	19	79.2	34	73.9	

ns=not significant
P value reached from chi square test1

Table-III

Distribution of the study patients by diagnosis and type of operation (n=46)

	Group-I (n=22)		Group-II (n=24)		Total (n=46)		P value
	n	%	N	%	N	%	
Diagnosis							
Squamous cell carcinoma	14	63.6	16	66.6	30	65.2	0.977^{ns}
Adenocarcinoma	7	31.9	7	29.2	14	30.4	
Large cell carcinoma	1	4.5	1	4.2	2	4.4	
Operation							
Lobectomy	22	100.0	20	83.3	42	91.3	0.045^{s}
Pneumonectomy	0	0.0	4	16.7	4	8.7	

s=significant; ns=not significant
P value reached from chi square test

Table-IV

Distribution of the study patients by duration of operation and pathological staging (n=46)

	Group-I (n=22)		Group-II (n=24)		Total (n=46)		P value
	n	%	N	%	N	%	
Duration of operation (hrs)							
Mean±SD	3.2	±0.8	2.6	±0.6	2.9	±0.7	^{a}0.005^{s}
Range (min-max)	2.0	-5.0	2.0	-4.0	2.0	-5.0	
Pathological staging							
I	4	18.2	3	12.5	7	15.2	^{b}0.860^{ns}
II	14	63.6	16	66.7	30	65.2	
IIIA	4	18.2	5	20.8	9	19.6	

s=significant; ns=not significant
^{a}P value reached from unpaired t-test
^{b}P value reached from chi square test

Table-V

Distribution of the study patients by duration of hospital stay (n=46)

Duration of hospital stay (day)	Group-I (n=22)		Group-II (n=24)		Total (n=46)		P value
	n	%	N	%	N	%	
dd30 8	36.4	12	50.0	20	43.5		
>30 14	63.6	12	50.0	26	56.5		
Mean±SD	30.0	±5.7	32.8	±6.7	31.9	±6.2	0.135^{ns}
Range (min-max)	25.0	-52.0	26.0	-45.0	25.0	-52.0	

ns= not significant
P value reached from unpaired t-test

Table-VI

Distribution of the study patients by resection margin and pre operative chemotherapy (n=46)

	Group-I (n=22)		Group-II (n=24)		Total (n=46)		P value
	n	%	N	%	N	%	
Resection margin							
Positive	2	9.1	3	12.5	5	10.9	0.542[ns]
Negative	20	90.9	21	87.5	41	89.1	
Pre operative chemotherapy							
Yes	4	18.2	0	0.0	4	8.7	0.028[s]
No	18	81.8	24	100	42	91.3	

s=significant; ns=not significant
P value reached from chi square test

Table-VII

Distribution of the study patients by ICU admission (n=46)

ICU admission	Group-I (n=22)		Group-II (n=24)		Total (n=46)		P value
	n	%	N	%	N	%	
Yes	2	9.1	1	4.2	3	6.5	0.499[ns]
No	20	90.9	23	95.8	43	93.5	

ns=not significant
P value reached from chi square test

Table-VIII

Distribution of the study patients by post operative complication (n=46)

Post operative complication	Group-I (n=22)		Group-II (n=24)		Total (n=46)		P value
	n	%	N	%	N	%	
No complication	17	77.3	18	75.0	35	76.1	0.856[ns]
Complication	5	22.7	6	25.0	11	23.9	
Respiratory complication	4	18.2	2	8.3	6	13.0	0.290[ns]
Non respiratory complication	1	4.5	4	16.7	5	10.9	0.201[ns]
Death	2	9.1	1	4.5	3	6.5	0.466[ns]

ns=not significant
P value reached from chi square test

Discussion and limitations

Obesity is associated with an increase in cancer risk and cardiovascular disorders, and is accompanied by decreased life expectancy and impaired quality of life in the general population [13]. Excess body weight/mass has been explored as a predictor of postoperative outcomes after a variety of surgical procedures[5]. A recent review of the link between excess BMI and outcomes after nonbariatric general surgery identified mixed results, with increased morbidity and mortality associated with extreme obesity, whereas being overweight or moderately obese did not confer an increase in perioperative risk[5,14]. Similar mixed findings have been reported for outcomes from cardiovascular surgery[5]. In contrast, underweight is consistently associated with increased risk of operative morbidity and mortality in noncardiac[5] surgery.

Nutritional status is known to influence postoperative morbidity in patients undergoing gastrointestinal surgery, oesophageal surgery and lung cancer surgery[9]. Although several investigators have demonstrated that weight and relative weight are inversely associated with the

risk of lung cancer[10,15], recent studies found a low incidence of low BMI in operable lung cancer [9,15] and the majority of operable lung cancer patients were over- rather than underweight [9]. This finding is most likely due to two conditions: (i) operable patients are often in the early and mainly not-advanced stages of lung cancer rather than the late cachectic stage; and (ii) with the recent epidemic of obesity in industrialised countries, significant proportions of patients presenting for the resection of NSCLC are overweight or obese[4,7].

Obese patients do suffer from more comorbidities such as diabetes, renal impairment, deep vein thrombosis and stroke, preoperatively; therefore, postoperative complications after surgical intervention are expected to increase with obesity[10]. But in our study we found no significant difference between risk factors with BMI groups. We also found no significant association between risk factors and perioperative complications probably due to selection of patient, well control of risk factor and special care for this patients.

Saina Attaran et al.2012 found in Group A (patients with BMI e"30), postoperative histology showed 161(48.5%) patients with squamous cell cancer, 138 (41.6%) with adenocarcinomas and 27 (8.1%) with other cancer types, excluding small cell and carcinoid tumours[10]. Our result was also similar with this result. In this group, postoperative staging showed 96 (28.9%) patients as stage I(a), 120 (36.1%) as I(b), 10 (3.0%) as II(a), 58 (17.5%) as II(b), 39 (11.8%) as III(a) and 9 (2.7%) as III(b)[10]. Our result was not similar with this result, we found more patient in stage-II disease. Postoperative histology showed that resection margins were positive in 19 (5.7%) patients in Group A and 16 (4.8%) in Group B[10]. we found 2 (9.1%) in group-I and 3 (12.5%) in group-II patients.

Obesity is associated with increased operating time [6]. We also found similar result. But whether obesity is associated with increased risk is uncertain based on recent clinical reports [5,6]. The growing obesity epidemic mandates that surgeons understand the implications of the extremes of BMI for perioperative and long term outcomes after major lung resection[5,7]. We explored the interactions of BMI and outcomes after major lung resection. we found no increase in perioperative risk with normal weight vs overweight and obese status.

F Petrella et al. clearly suggest that overweight and obese patients present a higher pulmonary complication rate than do normal weight patients: increased intra-operative difficulties, frequent bleeding complications, co-morbidities and impaired preoperative pulmonary function may justify this result[7].

Although intuitive, it has not hitherto been demonstrated that pulmonary complications are fivefold more frequent in overweight patients[7]. Several mechanisms have been proposed to explain pulmonary abnormalities in obese patients: obesity-induced abnormal respiratory system mechanics, impaired central responses to hypercapnia and hypoxia, sleep-disordered breathing and neurohormonal abnormalities such as leptin resistance[17]. Obesity imposes a significant mechanical load leading to a reduction in total respiratory system compliance, increased lung resistance and a relative state of respiratory muscle weakness leading to increased work of breathing[17].

S. Attaran et al.2012 did not show the same trend after lung resection for lung cancer[10]. The main reason for that could be the low rate of complications after lung resection in general. When comparing patients with normal weight with the ones who have a higher BMI, an improved survival rate has been observed in patients with a high BMI. Surgical resection for lung cancer, survival is significantly higher in patients with a BMI of e"30 compared with those with a BMI of <30 [10]. No similar study has ever shown an obesity survival paradox after resection for lung cancer. Theoretically, it can be expected that cancers, which result in weight loss, may be more aggressive in nature and a rapid weight loss after developing cancer can negatively affect cell regulatory systems resulting in progression of the cancer [10]. Moreover, overweight patients have shown biochemical evidence for better nutrition than the normal weight patients [18]. They have more adipose tissue, therefore are less likely to suffer from energy deficits [18] and may have a better tolerance rate for further postoperative treatment.

However, a recent meta-analysis failed to establish a positive correlation between high BMI and increased postoperative complications or mortality rates [19]. Similarly, in our study, we did not observe any difference between the postoperative complications in terms of morbidity and mortality between patients with high and normal BMI.

Morbidity and mortality after resections for NSCLC are lower now than in the past . Although reported perioperative mortality rates have ranged widely in individual series, a large registry report of nearly 8,000 patients demonstrated 3.1% 30-day mortality. A recent multi institutional prospective trial of more than 1,100 patients reported 1.4% 30-day mortality. *Francesco Petrella et al.2011* found 6% mortality[7]. Our 6.5% mortality rate is, therefore, well within accepted standards. Most studies report at least one aspect of TNM staging to be related to prognosis [20]. Performance status is a well-known prognostic indicator in many diseases, including NSCLC[20].

Low BMI was recently identified by Thomas et al. as an independent risk factor for increased complications after major lung resection, including pulmonary complications and death[11]. Low body weight is often associated with low serum albumin, and the latter has been shown to adversely influence postoperative morbidity and mortality following thoracic surgery in general and pneumonectomy in particular [21]. There are a number of potential explanations for these findings. Adipose tissue, particularly nonvisceral adipocytes, secretes cytokines that regulate inflammation, endovascular homeostasis and insulin sensitivity. Adipose tissue is capable of scavenging inflammatory toxins, and lipoproteins that are often increased in the obese can bind to and neutralize endotoxins [14]. In contrast, low BMI may not be a specific cause of increased risk, but instead may be a result of other acute or chronic processes that themselves increase risk such as smoking and chronic obstructive pulmonary disease (COPD). Extreme loss of muscle mass (sarcopenia) may be related to decreased effectiveness of muscles of respiration and relative inactivity, both of which may contribute to increased perioperative risks, especially for pulmonary complications. Sarcopenia is common in patients with COPD and in those with lung cancer[22].

This study is unable to draw conclusions regarding resource utilization or costs associated with evaluating and managing obese patients with NSCLC. Even in the absence of more complications, obese patients require heavy resource utilization for preoperative evaluation and perioperative care. Increased use of staff and specialized equipment, such as patient lifts and specially designed operating room and floor beds, leads to increased cost. Obese patients require longer times in the operating room owing to challenges in airway management, positioning, and the technical performance of the procedure . Obese patients also have greater medication requirements. Thus, while not fully explored by this study, it is likely that lung resection in the obese patient is an expensive and labor-intensive endeavour.

Another limitation of this study is that tumour biomarkers such as epidermal growth factor receptors were not tested for our patients. This may have resulted in a confounding bias, which should be addressed in future studies.

Conclusions and Recommendations:

Respiratory complications after lobectomy and pneumonectomy for curative resection of NSCLC are not frequent in overweight and obese patients than in subjects with normal weight patients. No statistical difference was observed regarding nonrespiratory complications and 30-day mortality rate. The operative time was observed increased significantly in overweight and obese patients than in subjects with normal weight patients. Our results suggest that it is unwarranted, based on current knowledge, to avoid surgical intervention in obese patients who are otherwise appropriate candidates for resection of NSCLC.

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ORIGINAL ARTICLE

Chemical Pleurodesis for Secondary Spontaneous Pneumothorax – A Comparative Study between Talc and Teracycline Pleurodesis

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Abstract:

Background: *Secondary spontaneous pneumothorax is a significant problem in the area of management of the chest diseases. An estimated recurrence rate of primary/secondary spontaneous pneumothorax is about 23-50% after the first episode and higher after the first recurrence. (Tschopp, 1997)[1]*

Early interest in the development of pleural symphysis resulted from the desire of surgeons to produce adhesions between visceral and parietal pleura. To achieve this desire, various agents (such as- silver nitrate, tetracycline, talc, bleomycine fibrin glue etc.) were tried but were found to be of limited value. The indications for pleurodesis have expanded over the years to include the treatment in prevention of recurrence of pneumothoraces. More recently, it is also used to assist in the closure of persistent bronchopleural fistula and the treatment of benign and malignant pleural effusion. (Kennedy and Sahn, 1994)[2]. Because of its excellent record of successful pleurodesis and low cost, talc has received substantial attention recently. The purpose of this study is to review the chemical properties, efficacy and safety of talc as a pleurodesis agent.

Objective: *To compare the efficacy of the talc pleurodesis and tetracycline pleurodesis for the treatment of secondary spontaneous pneumothorax, find out a standard and cost effective treatment for better outcome, complications following instillation and length of hospital stay.*

Methods: *Since January 2012 to December 2013, 60 patients meeting the enrolled criteria were included. Patients were divided into two groups – Group A: Talc pleurodesis& Group B: tetracycline Pleurodesis. Selective variables were studied. Statistical analysis of the results was obtained by using SPSS-16. The result was presented in tables & diagrams.*

Result: *Chemical pleurosis with talc is effective and reduces the hospital stay & cost of patient suffering from secondary spontaneous pneumothorax.*

Conclusion: *Chemical Pleurodesis with talc and tetracycline are equally effective in clinical aspects for the management of secondary spontaneous pneumothorax. But talc pleurodesisreduces hospital stay & cost during management of secondary spontaneous pneumothorax.*

Keywords: *Pleurodesis, Secondary Pneumothorax, Talc.*

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Introduction:

Pneumothorax is a condition where there is accumulation of air within the pleural cavity with secondary lung collapse.Source of air in the pleural space are rupture of visceral pleura with secondary air leak from lung, loss of integrity of the parietal pleura (e.g; trauma), loss of integrity of the mediastinal pleura, rarely by gas forming organisms etc.

A spontaneous pneumothorax is either primary or secondary and occurs because of parenchymal lung disruption. Primary spontaneous pneumothorax arise in healthy people without any pre-existing lung disease. Secondary pneumothorax arise in subjects with underlying lung disease and recur (Almind, et al.,1989)[3].The choice of treatment is influenced by the size of the pneumothorax, clinical symptoms, local practices, technical possibilities and the presumed recurrence rate (Almind, et al., 1989). Spontaneous pneumothorax is a frequent management problem for the chest physicians and thoracic surgeons in our country.

Pleurodesis is a procedure to obliterate the pleural spaces by apposition of visceral & parietal pleura by initiating a sterile inflammation. This procedure prevents recurrence of pneumothorax. This procedure is commonly accomplished by removing air from the pleural space when present, followed by either a mechanical procedure (i.g; abrasion or partial pleurectomy) or instillation of a chemical irritant into the pleural space which causes inflammation and fibrosis.

At the present time, the most popular pleurodesis agents are talc all over the world. The reason for this popularity of talc are that its instillation procedure either in a suspension (slurry) or by insufflation, effective, inexpensive, widely available and associated with minimal side effects in most reports (Light, 2002)[4]. In case of the spontaneous pneumothorax, the success rate of the recurrence prevention by talc is 91% and approximately 67% for tetracycline, which is mostly used procedure in our country now a days (Sahn, 2000)[5].

Materials & Methods:

Place of study: The study was conducted in the Department of Thoracic Surgery, National Institute of Diseases of the Chest and Hospital, Dhaka.

Study design :It was a prospective, randomized, single blinded, controlled trial .

Period of study:The study was conducted between the periods of January 2012 to December 2013.

Study population: All secondary spontaneous pneumothorax patients in NIDCH, Mohakhali, Dhaka.As NIDCH is the only referral centre in Bangladesh and patients are coming from every corner of the country, the patient selected from NIDCH represent to some extent the whole Bangladesh.

Sample size: A total of 60 cases of secondary spontaneous pneumothorax were taken and they were divided in two groups, one for group A (i.e; talc pleurodesis) and another for group B(i.e; tetracycline pleurodesis).

Selection of sample:

Sample was selected from the inpatient department of NIDCH of either sex.

a) Inclusion criteria:

i Patients who are admitted in NIDCH and diagnosed as secondary spontaneous pneumothorax of different aetiology with tube thoracostomy.

ii Should have radiological and clinical evidence of complete expansion of underlying lung after tube thoracostomy.

b) Exclusion Criteria:

i. Patients with incomplete expansion of underlying lung.
ii. Patients with broncho-pleural fistula.
iii. Empyema thoracis
iv. History of previous chemical pleurodesis.
v. Patients who are not willing to be included in the study.

Randomization of the Patients: Was done by lottery method.

Talc Slurry Pleurosis:

I. When lung became completely expanded.

II. Then we introduced injection 1% lignocaine 20 ml or 2% lignocaine 10 ml diluted with 10 ml normal saline and introduced through the IT tube.

III. Tube was clamped and waited for 15 minutes for local anesthesia.

IV. Then a 5gm dose of talc was mixed with sterile saline solution of 50ml in a 50 cc. syringe to create a "slurry". The drain was clamped and the syringe was connected to the drain. The slurry was injected and the drain was re-clamped.

V. Then the patient would be placed in a series of positions by the nursing staff one side first, then the other, with the head up followed by head down- each position for 10 minutes. This distributed the talc slurry over the surface of the lung and the ribs.

VI. After an hour or so the drain became unclamped to allow excess talc and saline to drain out. The drain is usually removed the following day after a check x-ray of the chest to get information about air leak, repexpansion of the affected lung.

Tetracycline pleurodesis:

I. Tetracycline pleurodesis done when lung was expanded.All air was came out.

II. Then we introduced injection 1% lignocaine 20 ml or 2% lignocaine 10 ml diluted with 10 ml normal saline and introduced through the IT tube.

III. Tube was clamped and waited for 15 minutes for local anaesthesia.

IV. Then we introduced injection tetracycline hydrochloride at a dose of 35 mg/kg body weight.

V. Finally 20 ml normal saline is introduced to flush the tube.

VI. The IT tube is clamped for 6-8 hrs and advised the patient to change his posture hourly.

VII. Unclamped the tube after 6-8 hrs and allowed drainage.

Measures of variables :

1. Demographic variables: Age, Sex, Weight (in kg).
2. Presence of risk-factors :Diabetes,Mellitus,HeartFailure,Smoking.
3. Variables related to disease:
   i. Cause of secondary spontaneous pneumothorax.
   ii. Pre-pleurodesis complaints :Chest pain, Cough, Fever, Dyspnoea
4. Immediate post pleurodesis side effect: Pain, Fever,Dyspnoea .
5. Post pleurodesis complications : Wound infection , ARDS
6. Post pleurodesis death
7. Post pleurodesis X-ray findings
8. Duration of IT tube remained
9. Total hospital stays

Statistical analysis of data:

Statistical analysis of the results was obtained by using window based computer software devised with Statistical Packages for Social Sciences (SPSS-16) (SPSS Inc., Chicago, IL, USA). The results were presented in tables and diagrams. During analysis frequency distribution for all the variables were worked out and produced in tabular form. ?2 tests and unpaired't' was used to compare proportions. A two-sided p value 0.05 will be considered significant at 95% level.

Result:

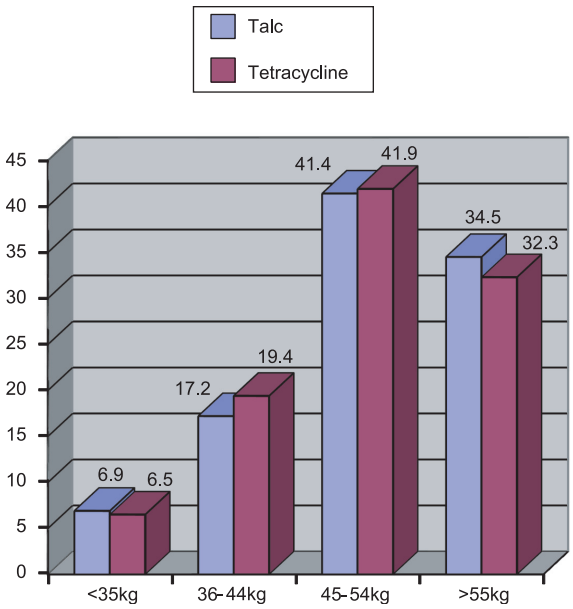

Fig.-1: *Distribution of weight of the patients by groups.*

Table-I

Distribution of risk factors by groups

Causes of secondary spontaneous pneumothorax	Groups		p value#
	Talc n=29	Tetracyclinen=31	
COPD	28 (96.6)	28 (90.3)	0.334
Tuberculosis	01 (3.4)	03(9.7)	
Total	29(100.0)	31 (100.0)	

Table-II

Distribution of causes of secondary spontaneous pneumothorax

Causes of secondary spontaneous pneumothorax	Groups		p value#
	Talc n=29	Tetracyclinen=31	
COPD	28 (96.6)	28 (90.3)	0.334
Tuberculosis	01 (3.4)	03(9.7)	
Total	29(100.0)	31 (100.0)	

Table-III

Distribution of pre pleurodesis complaints by groups

Pre pleurodesis complaints	Groups		p value#
	Talcn=29	Tetracyclinen=31	
Chest pain			
Present	23 (79.3)	23 (74.2)	0.640
Absent	06 (20.7)	08 (25.8)	
Cough			
Present	20 (69.0)	27 (87.1)	0.088
Absent	09 (31.0)	04 (12.9)	
Fever			
Present	04 (13.8)	09 (29.0)	0.152
Absent	25 (86.2)	22 (71.0)	
Dyspnoea			
Present	29(100.0)	29(00)	
Absent	00(oo)	00(00)	

Table-III

Distribution of immediate post pleurodesiscomplaints by groups:

Post pleurodesis complications	Groups		p value#
	Talcn=29	Tetracycline n=31	
Wound Infection			
Present	00 (00)	2 (6.5)	0.164
Absent	29 (100)	29 (93.5)	
ARDS			
Present	02 (6.9)	00 (00.0)	0.137
Absent	27 (93.1)	31 (100.0)	
Death			
Present	2 (6.9)	1 (3.2)	0.514
Absent	27 (31.0)	30 (96.8)	

Table-IV

Distribution of X-ray findings before discharge:

Post pleurodesis X-ray findings	Groups		p value#
	Talc n=29	Tetracycline n=31	
Expanded	27(93.1)	30 (96.8)	0.514
Not expanded	2 (6.9)	1 (3.2)	
Total	29 (100.0)	31 (100.0)	

Table-V

Distribution of Duration of IT tube by groups

Duration of IT tube remained	Groups		p value#
	Talc n=29	Tetracyclinen=31	
< 5 days	26(88.4)	19(61.29)	0.022*
6-10 days	01(3.4)	09(29.03)	
> 10 days	02(6.8)	03(9.67)	
Total	29(100.00)	31(100.00)	
Mean ± SD	2.37±3.46	5.22±4.09	

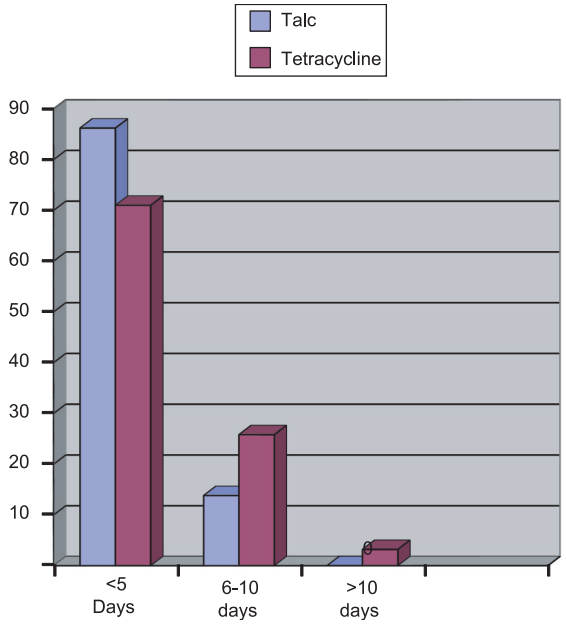

Fig.-3: *Distribution of hospital stay of the patients by groups*

Table-VI

Distribution of hospital stay (days) by groups

Hospital stay (days)	Groups		p value#
	Talc n=29	Tetracycline n=31	
Mean ± SD	3.27±2.03	4.93±2.22	0.004*

Discussion:

In the present study out of 29 patients in talc group about half of the patients of the talc group were in age group of 41 to 50 (44.8%) years followed by 31 to 40 years (24.1%). Five (17.2%) patients were in the age group of 61 to 70,Three (10.3%) patients were 51 to 60 and one (3.4%) patient was less than 30 years. Out of 31 patients in tetracycline group highest number of patients was in the age group of 41 to 50 years (38.7%) followed by 61 to 70 years age group (29.0%). Five (16.1%) patients of the tetracycline group were in the age group of 31 to 40 years and four (12.9%) patients of the tetracycline group were in the age group of 51 to 60 years and rest 1 (3.2%) were in the age group of more than 70 years. Mean ± SD of age of the talc group and tetracycline group were 47.48 ± 11.26 years and 53.52 ± 12.61 years respectively (Table-1). There is no statistically significant difference in the age between the groups (p>0.05). In the present study the age range of patients were 29-80 years. Almind, et al.,1989 in a study of ninety-six patients of spontaneous pneumothorax found the age range of 18-88 years. (Almind , et al.,1989)

In the present study out of 29 patients in the talc group 28 patients (96.6) had COPD and one patient (3.4%) had pulmonary tuberculosis. Out of 31 patients in tetracycline group 28(90.3%) patients had COPD and 3(9.7%) patients had pulmonary

tuberculosis. There is no statistically significant difference in the groups (p>0.05).

The clinical symptoms associated with secondary pneumothoraces are more severe than those associated with primary pneumothoraces, and most patients with a secondary pneumothorax complain of breathlessness which is out of proportion to the size of the pneumothorax . (Henry, Arnold and Harvey, 2003)[6] Chest pain , cough, and fever are most often found in secondary spontaneous pneumothorax patients with underlying pulmonary tuberculosis than in secondary spontaneous pneumothorax patients without tuberculosis.(Michael,2000) In the present study pre-pleurodesis complaints by groups were evaluated. Most of the patients in the present study were presented with typical symptoms associated with secondary spontaneous pneumothorax include dyspnea, cough and chest pain. In the present study out of 29 patients in the talc group, all the patients (100.0%) were presented with dyspnoea, followed by chest pain (79.3%) and cough (69.0%). Four (13.8%) patients in this group presented with fever. In tetracycline group all the patients(100.0%) were presented with dyspnoea, followed by cough (87.1%) and chest pain (74.2%). Nine (29.0%) patients in this group were presented with fever. There is no statistically significant difference in pre pleurodesis complaints of dyspnoea, cough, chest pain and fever between the groups (p>0.05).

In the talc group post pleurodesis complaints of local pain, fever and dyspnoea were present in 100%, 82.8% and 62.1% respectively. In tetracycline group post pleurodesiscomplaints of local pain and dyspnoea were present in 96.8% and 93.5% respectively and 87.1% patients in the tetracycline group were presented with post pleurodesis fever (Table 7). There is no statistically significant difference in post pleurodesis complaints of local pain and fever between the groups (p>0.05) but statistically significant difference observed in post pleurodesis complaint of dyspnoea between the groups (p<0.05). The local pain, dyspnoea and fever were easily controlled with routine medications. Chest pain and fever are the most common adverse effects of all pleurodesis agents (Sahn, 2000).Well-documented complaints of talc pleurodesis are fever (16-69%) and chest pain (7%). But Milanez et al.,1994 found that local pain associated with talc pleurodesis is less than that associated with tetracycline pleurodesis.(Milanez et al.,1994)[7].

In the present study out of 29 patients in talc group In talc group post pleurodesis complications of wound infection, ARDS and death were present in 00%,6.9%, and 6.9% respectively. In tetracycline group post pleurodesis side effects of wound infection, ARDS and death were present in 6.5%,00% and 3.2% respectively. There is no statistically significant difference in post pleurodesiscomplications of wound infection, ARDS and death between the groups (p>0.05) In case of ARDS,we tried to manage according to ARDS management protocol. After intrapleural administration as slurry or insufflation, serious pulmonary complications, including acute pneumonitis, acute respiratory failure and ARDS with different incidences ranging between 0% and 33% have been reported (Gozubuyuk et al.,2010[8]; Andres et al.,2000[9]).

The incidence of ARDS has varied markedly from series to series. The mechanism by which talc produces acute lung injury is unknown. (Light,2000). A possible cause of the lung injury is a systemic inflammatory response secondary to extra-pleural dissemination of talc, the severity of which is dependent on the particle size and the dose used for the procedure. Aetiology of ARDS is thought to be related to dose and particle size of talc. In the future, the safety of talc for pleurodesis will need close attention (Andres et al.,2000)[9].

In the present study out of 29 patients in the talc group 27(93.1%) were expanded and 2(6.9%) were not expanded . Out of 31 patients in the tetracycline group 30 (96.8%) were expanded and 1 (3.2%) were not expanded.There is no statistically significant difference in X-ray findings before discharge between the groups (p>0.05).

From duration of IT tube remained in the present study, out of 29 patients in the talc group highest number 26(88.4%) patients of the talc group were in 5days and below group followed by 02(6.8) patients were in above 10 days. 01(3.4) patient was within 6 to 10 days group. Highest number 19(61.29%) patients of the tetracycline group were in 5days and below group followed by 09(29.03%) patients were within 6 to 10 days group . 03(9.67%) patients were in above 10 days group. Mean ± SD

of duration of IT tube remained of talc group and tetracycline group were 2.37±3.46 days and 5.22±4.09 respectively. There is statistically significant difference in duration of IT tube remained between the groups ($p>0.05$).

From hospital stay in the present study, out of 29 patients in the talc group highest number 25(86.2%) of patients of the talc group were within 5 days followed by 6 to 10 days group 4(13.8%).Highest number 22(71.0%) of patients in the tetracycline group were within 5 days followed by 6 to 10 days group8 (25.8%). 1(3.2%) patients were in above 10 days group. Mean ± SD of hospital stay of talc groupand tetracycline group were 3.27±2.03 days and 4.93±2.22 respectively. There is statistically significant difference in hospital stay between the groups ($p<0.05$).

Conclusion:

From the present data it may be concluded that chemical pleurodesis with talc and tetracycline are equally effective in clinical aspects for the management of secondary spontaneous pneumothorax. But talc pleurodesis reduces hospital stay and cost during the management of secondary spontaneous pneumothorax.

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ORIGINAL ARTICLE

Prediction of Contrast Induced Nephropathy Following Percutaneous Coronary Intervention

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Abstract:

Background: *Contrast induced nephropathy (CIN) is associated with significant morbidity and mortality after percutaneous coronary intervention (PCI). The aim of this study is to evaluate the collective probability of CIN in Bangladeshi population by prediction of several identified risk factors in patients undergoing PCI.*

Methods: This was a prospective single center study of 118 consecutive patients who underwent PCI from November 2014 to October 2015. CIN was defined as an increase of serum creatinine by e"25% and/or e"0.5 mg/dl at 48 hours after PCI when compared to baseline value. Top most independent predictors of CIN was identified using univariate followed by multivariate logistic regression analysis among identified risk factors including amount of contrast, diabetes mellitus, hypotension, peripheral vascular disease (PVD) & Chronic Kidney Disease (CKD). A predictive score was then developed to identify the probability of CIN using the logistic regression equation.

Results: *Amongst 118 patients included in our study, maximum patients (72.0%) were above 60 years, mean age was 61.88±9.12 years. 74.6% of the patients were male and 25.4% were female. So male were predominant in our study. Prevalence of diabetes mellitus, hypertension, smoker, hypotension, Heart failure, CKD & cerebrovascular accident were 56.8%, 50.0%, 29.7%, 5.9%, 3.4%, 8.5%, & 2.5% respectively. 16 (13.56%) patients developed CIN. Univariate logistic regression analysis for prediction of risk factors in CIN revealed that Age, CKD, Diabetes mellitus, Hypotension, Hypertension, LV dysfunction, Heart failure (HF), Cerebrovascular accident (CVA), PVD and Contrast volume are the individual risk factors for the development of CIN. Multivariate analysis revealed CKD, contrast volume, Diabetes mellitus, PVD, HF and hypotension as the predictors for development of CIN.*

Conclusion: *A simple prediction model can be employed to predict the probability of CIN following PCI, applying it to each individual. More vigilant preventive measures can be applied to the high risk candidates.*

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Introduction:

Radiologic procedures utilizing intravascular iodinated contrast media injections are being widely applied for both diagnostic and therapeutic purposes. This has resulted in an increased incidence of procedure related contrast induced

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nephropathy (CIN).[1] Although the risk of renal impairment associated with radiologic procedures is low in the general population, it may be very high in selected patient subsets, especially in cardiac procedures.[2]

Contrast induced nephropathy (CIN) is defined as a e"25% increase in serum creatinine from the baseline value, or an absolute increase of serum creatinine at least 0.5 mg/dL (44.2 mmol/L), 48 to 72 hours after the administration of radiographic contrast media that is not attributable to other causes.[3,4] CIN is the acute kidney injury caused by contrast media and is a common cause of hospital-acquired acute renal failure. It is associated with increased morbidity and mortality as well as prolonged duration of hospital stay, need for renal replacement therapy and major cardiac events.[1] At least two significant processes are known to be involved in the pathophysiology of CIN: vasoconstriction resulting in medullary hypoxia and direct toxicity caused by the contrast media to renal tubular cells. The mechanisms that have been implicated in these processes are dehydration, decreased prostaglandin and nitric oxide induced vasodilatation, impaired endothelial function, increase in renal adenosine concentration, increase in oxygen free radicals in response to hyperosmotic load, increased intratubular pressure owing to contrast induced diuresis, increased urinary viscosity and obstruction of the tubules.[5]

Percutaneous coronary intervention (PCI) is a lifesaving procedure in the management of acute coronary syndrome and improves the quality of life in patients with stable coronary artery disease. However, PCI poses a risk of CIN due to the exposure to contrast media during the procedure.[6] There are several types of contrast media used during PCI e.g.- Ionic contrast media, Non-ionic contrast media, High-osmolar, Low- osmolar & Iso-osmolar contrast media. Different types of contrast media poses various magnitude of CIN. Amount of contrast media is also important. Amount of contrast media needed for PCI depends on complexity of coronary artery lesion, number of arteries diseased, number of lesion, morphology of lesion, location of lesion, presence of chronic total occlusion as well as operator's expertise. Various risk factors were identified based on studies conducted previously. Advanced age, female gender, anemia, pre-existing renal impairment, diabetes mellitus, reduced intravascular volume, congestive cardiac failure, presence of hypotension, presence of cardiogenic shock, use of intra-aortic balloon pulsations (IABP), type of contrast media, large volume of contrast media, co-administration of nephrotoxic drugs such as angiotensin-converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARB), proteinuria (including nephrotic syndrome), multiple myeloma, hypercholesterolemia, hyperuricaemia, hypercalcemia, sepsis, atopic allergy are some of the recognized risk factors.[7,8]

Although many individual risk factors for the development of CIN have been reported, combination of two or more risk factors is rather common in daily practice. Therefore, cumulative risk of several variables on renal function is more important & more informative. So, prediction of contrast induced nephropathy following percutaneous coronary intervention by assessing cumulative effects rendered by individual risk factor can prognosticate the high risk patients for CIN after the exposure to the contrast.[9]

This study aimed to develop a risk score model to predict development of CIN following PCI in Bangladeshi population rendered by cumulative effect of several risk factors.

Though there were various risk scoring systems available for prediction of CIN, the risk factor profile and their cumulative effect in Bangladeshi patients had never been considered, to our knowledge. On the other hand, Bangladeshi people are different in terms of biophysical profile, food habit & nutritional status, geographical position, ethnicity and environmental & toxin exposures. So, risk scoring system developed elsewhere may or may not be applicable in our country. This had prompted us to conduct this prospective study with an aim to predict CIN in our sample population, to detect the incidence of CIN, to identify the predictors and to determine their collective effect in the development of CIN in patients undergoing PCI in our institution.

Materials & Methods

Aims

- To evaluate the collective risk of CIN in Bangladeshi population by several identified risk factors, in patients undergoing PCI.

Objectives

- To determine the incidence of CIN in the study group following PCI.
- To identify the risk factor profile for CIN in Bangladeshi patients.
- To estimate the cumulative risk rendered by individual risk factors and to develop a simple risk score model to predict CIN.

Study population: Consecutive 118 patients who underwent PCI during this period in the Department of Cardiology, University Cardiac Center, BSMMU.

Study protocol: Consecutive 118 patients were selected who got admitted in the department of cardiology, BSMMU to undergo PCI on the basis of inclusion & exclusion criteria. Informed written consent was taken from every patient in a preformed consent form . Patients' age & sex were noted from patients' demographic data. Medical history including diabetes mellitus, hypertension, cerebrovascular accident (CVA), congestive heart failure (CHF), chronic kidney disease (CKD) were noted. History was taken from patient and from patient's authentic medical documents. Detailed clinical examination was done for all patients. All data were noted in the preformed "data collection sheet".

A vigilant checkup was done to reveal the variables. The key variables were as follows

- Age (>70 yrs.),
- Male gender,
- Smoking,
- Diabetes mellitus,
- Cerebrovascular accident (CVA),
- Congestive heart failure
- Hypertension,
- Hypotension,
- Peripheral vascular disease (PVD),
- Anemia,
- LV dysfunction,
- Chronic kidney disease (CKD),
- Pre-PCI GFR &
- Amount of contrast.

Patients' smoking status was assessed from Patients' & their attendants' statement. Patients who had smoked at least 100 cigarettes in their lifetime were labelled as smoker. Those smokers who didn't smoke even for a single time in last 6 months were labelled as ex-smokers.[10]

Patients were enrolled as CKD who had the estimated GFR <60 ml/mt/1.73 m^2 or baseline serum creatinine e" 1.5 mg/dl.[11] Patients with diabetic nephropathy were also included in the CKD group.

History of cerebrovascular accident was sought from patient's authentic medical documents. Patients were examined for higher psychic function with speech, cranial nerves with optic fundi, cerebellar system, motor & sensory system to find out any focal neurological deficit.

Patients who were diagnosed case of diabetes mellitus previously were treated as per guidelines. RBS (Random Blood Sugar) was done for rest of the patients who were non-diabetic or didn't know whether they were diabetic or not. If RBS was < 5.5 mmol/L, no further action was taken, if it was 5.5 – 11.0 mmol/L then Oral glucose tolerance & HbA_1C were done. Those patients who had RBS e" 11.1 mmol/L were treated as per guidelines.

Patients who were diagnosed as hypertension were noted. Intake of antihypertensive medications were confirmed by checking patients' medical records & medicine box. Blood pressure was measured in all patients ideally. All patients were remained seated at rest for more than 5 minutes before taking the blood pressure. Avoidance of caffeinated products such as coffee, cola, or tea as well as activities such as smoking and exercising for at least 30 minutes prior to measuring the blood pressure was confirmed. Blood pressure was measured by aneroid sphygmomanometer keeping the patient's hand supported with arm at the level of the heart. Korotkoff phase I was used for systolic blood pressure & Korotkoff phase V for diastolic blood pressure measurement; but if there was a 10 mmHg or greater difference between Korotkoff phase IV and phase V then the pressure reading at phase IV was recorded as the diastolic blood pressure. Blood pressure was measured in both arms & highest value was taken if there were any discrepancy.

Authentic medical documents were searched for any previous diagnosis of PVD. Presence of intermittent claudication, blackish discoloration &/or gangrene of tip of toes and ankle-brachial pressure index < 0.9 were suggestive of PVD. Presence of PVD was confirmed using Doppler ultrasound if the clinical history & physical examination was suggestive of the diagnosis.

Congestive heart failure cases were enrolled from previous medical records as well as from bedside diagnosis. Clinical features suggestive of congestive heart failure were dyspnea, orthopnea, engorged jugular venous pressure, tender hepatomegaly, ascites, dependent edema, bilateral pulmonary basal crepitation & 3rd heart sound. Biomarkers including BNP (B-type natriuretic peptides) & NT-proBNP (N-terminal pro *B-type natriuretic peptide*) were measured in unresolved cases.

Hemoglobin was assessed before the procedure by standardized tests in our laboratory.

2 D & M-mode echocardiography was done for all patients. Left ventricular ejection fraction was measured by Teichholz M-mode method routinely. If any patient had left ventricular regional wall motion abnormalities, then Simpson's method was used.

Detailed drug history including ACEI, ARB, Metformin, NSAIDs were noted. Metformin, NSAIDs were withheld and doses of ACEI, ARB & other drugs including lipid lowering agents were adjusted as per guidelines.

Patients with pre-existing end-stage renal disease requiring dialysis and other contrast exposure within two week or less from the index procedure, patients treated with PCI for acute myocardial infarction, and patients in shock were excluded from the analysis. Patients underwent PCI according to current guidelines after informed written consent was obtained. Routine hydration was performed with 1 ml/kg/h of Normal saline for 4 to 12 h before PCI and 18 to 24 h after PCI. All patients received antiplatelet drugs as per guideline.

All PCIs were done by Iohexol 350; a non-ionic low osmolar contrast media; as per our hospital protocol. Iohexol 350 contain 350 mg of Iodine per mL of contrast media with an osmolality of 823 mOsm/Kg. Amount of contrast media used during the procedure was recorded in mL. PCI complicated by perforations of coronary arteries, development of cardiac tamponade, rupture of abdominal &/or thoracic aorta, acute myocardial infarction associated with PCI, development of cardiac arrest &/or development of cardiogenic shock were excluded from the study.

Serum creatinine was measured before the procedure and 48 to 72 hours after the procedure. GFR was calculated from S. Creatinine & body weight using the Cockcroft-Gault formula {GFR = (140 - Age in years) × Weight in kg × (0.85 for female) / 72 × serum creatinine in mg/dl} both pre & post procedure.

To get eligible 118 sample, a total of 132 patients were needed to enroll. 14 patients were excluded from the study due to late appearance of exclusion criteria, patients' denial & irrelevant data. Variables from eligible 118 sample collected in raw data sheet was then entered into master data sheet (SPSS 22 for Windows).

The outcome variable was Contrast Induced Nephropathy (CIN) which was defined as a e"25% increase in serum creatinine from the baseline value, or an absolute increase of serum creatinine e"0.5 mg/dL (44.2 mmol/L), 48 to 72 hours after PCI. Total 16 patients were found who developed CIN which were identified from SPSS by sorting ascending for CIN. Then, association of CIN with each of 14 variables were assessed by 2 X 2 contigency table in univariate analysis. 11 variables were found to be significantly associated with CIN. These significant 11 variables were then assessed in the multivariate analysis in a stepwise selection procedure where 6 variables were found to be significantly associated. The strength of association was determined by the OR (Odds Ratio) which was more simplified by giving an integer 1 for each 1 OR. The sum of integer of each variable of individual patient was his or her score. Scale of this score was then further divided into 4 groups. Incidence of CIN was then determined in each group.[12]

Inclusion criteria

- All consecutive patients who underwent PCI in Bangabandhu Sheikh Mujib Medical University Hospital from November 2014 to October 2015 were enrolled into the study.

Exclusion criteria

- Patients with renal failure on regular dialysis,
- Acute renal failure before PCI,
- Cardiogenic shock,
- Patients who exposed to contrast media within last 14 days of PCI,
- Patients requiring intra-aortic balloon pump (IABP) support and
- Patients who developed PCI related complications.

Statistical Analysis

- Statistical analyses were carried out by using the Statistical Package for Social Sciences version 22.0 for windows software (SPSS Inc., Chicago, Illinois, USA).
- Quantitative variables were expressed as the minimum, maximum, mean, standard deviation (SD)
- Qualitative variables were expressed as frequencies and percentage.
- Univariate and multivariate analyses were performed to identify individual risk factors.
- The results were presented in tables, figures, diagrams
- 'p' value <0.05 was considered statistically significant.

Risk score development. Eligible patients from the entire data were tabulated on master dataset. The risk score development dataset was initially used for identifying univariate associations between 14 variables from baseline clinical and key procedural characteristics and CIN. Cut off value for age was considered 70 yrs.[7] Cut off value for GFR was considered 50 ml/min/m^2.[12] Other variables were entered into dataset as present (yes) or absent (no). These variables were

- Age (>70yrs),
- Male gender,
- Smoking,
- Anemia,
- Diabetes mellitus,
- Hypertension,
- Hypotension,
- Peripheral vascular disease (PVD),
- LV dysfunction,
- Congestive heart failure
- Cerebrovascular accident (CVA),
- Chronic kidney disease (CKD)
- Pre-PCI GFR,
- Amount of contrast.

11 variables were found to be significantly associated with CIN in univariate analysis, these variables were:

- Age (>70yrs),
- Diabetes mellitus,
- Hypertension,
- Hypotension,
- Peripheral vascular disease (PVD),
- Heart failure,
- LV dysfunction,
- Cerebrovascular accident (CVA),
- Chronic kidney disease (CKD)
- Pre-PCI GFR,
- Amount of contrast.

Variables that were significant in univariate analysis were included in the final multivariate model. Multivariate logistic regression analysis was then performed to identify independent predictors of CIN and to estimate odds ratios (ORs). Risk factors that were significant in the multivariate analysis were available for selection in the final model; for each sample, a stepwise selection procedure was used to choose independent predictors of CIN. Significant risk factors in the multivariate analysis were:

- Diabetes mellitus,
- Hypotension,
- Peripheral vascular disease (PVD),
- Heart failure,
- Chronic kidney disease (CKD) &
- Amount of contrast,

Then the regression model was created based on the baseline serum creatinine value. The six

variables in the final model with $p < 0.05$ were assigned a weighted integer coefficient value. For this purpose, the estimated ORs from the logistic model were used, giving an integer of 1 to each 1.0 value of OR; the integer of 1 was given for each 100-ml increment in contrast media administered during the procedure. The final risk score represented the sum of integer coefficients (Mehran et al. 2004). Based on the attained score, patients were further divided into low, moderate, high, very high risk groups as score of 0-5, 6-10, 11-15 & e"16 and then the incidence of CIN in each risk group was assessed.[12]

Operational Definitions

Anemia: Anemia was defined as hemoglobin <13 g/dl in men and, <12 g/dl for women.[13]

Cardiogenic shock: Cardiogenic shock was defined as prolonged hypotension (systolic blood pressure <90 mm Hg) with evidence of decreased organ perfusion caused by severe left ventricular dysfunction, right ventricular infarction, or mechanical complications of infarction and not due to hypovolemia, bradyarrhythmias, or tachyarrhythmias.[14]

CIN (Contrast Induced Nephropathy): CIN was defined as an increase of ≥25% and/or ≥0.5 mg/dl in serum creatinine at 48 hours after PCI when compared to the baseline value.[15]

CKD (Chronic Kidney Disease): CKD was defined as the estimated GFR <60 ml/mt/1.73 m2 or baseline serum creatinine ≥1.5 mg/dl.[11]

CVA (Cerebrovascular Accident): Cerebrovascular accident was defined as diagnosed case of stroke or patients with focal neurological deficit.[8]

Diabetes mellitus: Diabetes mellitus[16] was defined as presence of any of-

1. Patient is taking antidiabetic drugs
2. Fasting blood sugar ≥7.0 mmol/L
3. Blood sugar 2 hours after breakfast ≥11.1 mmol/L
4. HbA_1C ≥7.0 %

Hypertension: Hypertension was defined as systolic blood pressure ≥140 mm Hg (≥150 mm Hg ≥60 yrs. older patients) or diastolic blood pressure ≥90 mm Hg or patients who are taking antihypertensive drugs.[17]

Hypotension: Hypotension was defined as systolic blood pressure <100 mm Hg for at least 1 hour within 24 hours peri-procedurally.[12]

PCI related complications[18] includes-

- Perforations of coronary arteries
- Cardiac tamponade
- Ruptured abdominal &/or thoracic aorta
- Development of cardiac arrest
- Development of cardiogenic shock
- Development of myocardial infarction associated with PCI

GFR (Glumerular Filtration Rate): GFR was calculated using the Cockcroft-Gault formula[19]:

GFR = (140 - Age in years) × Weight in kg × (0.85 for female) / 72 × serum creatinine in mg/dl

LV dysfunction: Left ventricular dysfunction was defined as Left ventricular ejection fraction <50%.[20]

Smokers[10]:

Former Smokers (Ex-Smokers) – Adults who had smoked at least 100 cigarettes in their lifetime, but didn't smoke even for a single time in last 6 months.

Nonsmokers – Adults who didn't smoke even for a single time in last 6 months & either never smoked or had smoked less than 100 cigarettes in their lifetime.

Smokers (Current Smokers) – Adults who have smoked 100 cigarettes in their lifetime and currently smoke cigarettes every day (daily) or some days (nondaily) or smoked at least once in last 6 months.

Results:

Distribution of demographic characteristics of the study subjects:

Baseline demographic characteristics of the study population are summarized in Table-I & Table-II. Amongst 118 patients included in this study, maximum patients (72.0%) were above 60 years, mean age was 61.88±9.12 years.

Distribution of demographic characteristics of the study subjects:

Table-II showed that 74.6% of the patients were male and 25.4% of patients were male. So male were predominant in this study.

Distribution of the patients by variables from medical history

Table-III shows the medical history of the patients: 57.8% patients had diabetes mellitus, 50.0% patients had hypertension, 29.7% patients were smoker, 3.4% patients had heart failure, 8.5% patients had CKD and only 2.5% patients had cerebrovascular accident.

Distribution of the patients by variables from clinical parameters

Table-IV shows the clinical examination of the study patients, mean systolic blood pressure were 125.5±17.9 mmHg and mean diastolic blood pressure were 78.26±12.5 mmHg;

Distribution of the patients by variables from pre-procedure laboratory & procedural parameters

Table-V shows mean Hemoglobin level was 12.04±1.40 (g/dl). Mean LVEF was 60.25±7.65 (%) & mean contrast volume used was 150.85±43.95 (ml). pre-procedure mean Serum creatinine was 1.14±0.23 (mg/dl) with mean eGFR 64.64±17.54 (ml/min).

Post procedure Serum creatinine & eGFR

Table-VI shows post-procedure mean Serum creatinine was 1.2668±.35497 (mg/dl) with mean eGFR 59.7088±16.91982 (ml/min).

Comparison of pre & post procedure Serum creatinine & eGFR and rise in Serum creatinine in those patients who developed CIN.

Table-VII shows pre procedure Serum creatinine & eGFR as well as post procedure Serum creatinine & eGFR in those patients (n =16) who developed CIN. The absolute rise in S. Creatinine (mg/dl) & percent rise in S. Creatinine Post-PCI from Pre-PCI baseline S. Creatinine were also shown.

Univariate analysis for predictors of CIN

In Table VIII, Univariate analysis for prediction of risk factors in CIN. Age (e"70 yrs), CKD, Diabetes mellitus, Hypotension, Hypertension, low GFR, LV dysfunction, CHF, CVA, PVD and Contrast volume are the individual risk factors for the development of CIN.

Multivariate logistic regression analysis for prediction of risk factors of CIN

Table IX provides an overview of the multivariate analysis for development of CIN. Logistic regression analysis (Table VII), had shown that CKD, DM, contrast volume, Heart failure, Peripheral vascular disease and hypotension as a predictor for the development of CIN.

Integer scores of variables that were significant in multivariate logistic regression analysis:

Table-X shows the Integer scores depending on the Odds Ratio, the assigned Integer is 1 for OR of each 1.0 for CKD, PVD, Hypotension, DM, CHF & 1 for each 100 mL of contrast dye used.

Risk score group of CIN with their incidence

Table-XI shows the risk score of CIN with their incidence, 49 patients were found in mild risk group (0 – 5) and there was no incidence of CIN, moderate risk group (6-10) had 53 patients and 6(11.3%) cases developed CIN, high risk group (11-15) had 12 patients and 7(58.3%) cases developed CIN. Very high risk group (>15) had 4 patients and CIN developed in 3(75.0%) cases.

Table-I

Distribution of the patients by variables from medical history (n =118)

Variables	Frequency (no)	Percentage (%)
Diabetes mellitus	67	57.8
Hypertension	59	50.0
Smoking	35	29.7
Congestive Heart failure	4	3.4
Chronic kidney disease	10	8.5
Cerebrovascular accident	3	2.5
Peripheral vascular disease	3	2.5

Data are presented as Percentage (%)
n = Number of study population

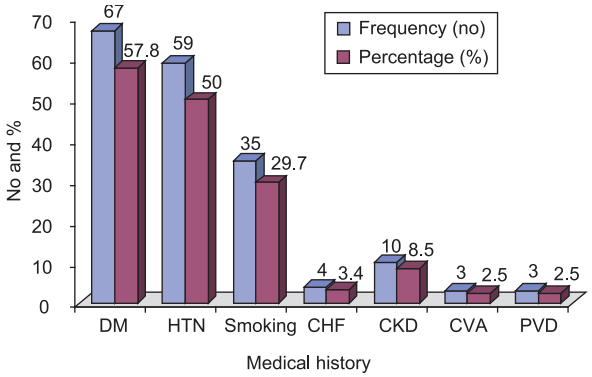

Fig.-1: *Bar diagram showing frequency & percentage (%) of variables present in the study population (n = 118). Here, DM = Diabetes Mellitus, HTN = Hypertension, CHF = Congestive Heart Failure, CKD = Chronic Kidney Disease, CVA = Cerebrovascular Accident, PVD = Peripheral Vascular Disease*

Table-II

Distribution of the patients by variables from pre-procedure laboratory & procedural parameters (n =118)

Variables	Mean±SD
Hemoglobin level (g/dl)	12.04±1.40
LVEF (%)	60.25±7.65
Contrast volume	150.85±43.95
Serum creatinine (mg/dl)	1.14±0.23
eGFR (ml/min)	64.64±17.54

Data were presented as mean±SD
SD =Standard deviation
eGFR= Estimated glomerular filtration rate
LVEF= Left ventricular ejection fraction
n = Number of study population

Table-III

Post procedure Serum creatinine & eGFR (n =118)

Variables	Mean±SD
Serum creatinine (mg/dl)	1.2668±.35497
eGFR (ml/min)	59.7088±16.91982

Data were presented as mean±SD
SD =Standard deviation
eGFR= Estimated glomerular filtration rate
n =Number of study population

Table-IV

Comparison of pre & post procedure Serum creatinine & eGFR and rise in Serum creatinine CIN group (n =16)

Sl No.	Code No.	Pre-PCI		Post-PCI		Increase in S. creatinine	
		S. Creatinine (mg/dl)	eGFRS. (ml/min)	S. Creatinine (mg/dl)	eGFR (ml/min)	Absolute Increase (mg/dl)	% Increase
1	5	1.20	53.26	1.80	35.51	0.60	50.00
2	16	1.55	45.17	2.20	31.82	0.65	41.90
3	43	1.95	25.67	2.65	18.89	0.70	35.90
4	48	0.90	60.52	1.40	38.91	0.50	55.60
5	56	1.83	41.00	2.30	32.62	0.47	25.70
6	64	1.00	80.28	1.85	43.39	0.85	85.00
7	66	0.90	61.52	1.60	34.61	0.70	77.80
8	69	1.20	56.88	1.90	35.92	0.70	58.30
9	72	1.80	24.67	2.60	17.08	0.80	44.40
10	77	1.60	43.13	2.05	33.67	0.45	28.12
11	83	0.95	81.05	1.45	53.10	0.50	52.60
12	88	1.62	38.45	2.10	29.67	0.48	29.63
13	90	1.20	47.40	1.70	33.46	0.50	41.70
14	97	1.20	63.89	1.80	42.59	0.60	50.00
15	109	1.90	26.64	2.50	20.25	0.60	31.60
16	117	1.20	37.73	1.75	25.87	0.55	45.80

eGFR= Estimated glomerular filtration rate
Code no= Code number of patients in the study
Pre-PCI= Before Percutaneous Coronary Intervention
Post-PCI= 24-72 hours after Percutaneous Coronary Intervention
% Increase = % Increase in Post-PCI S. Creatinine from Pre-PCI baseline S. Creatinine

Discussion

Coronary artery disease has reached epidemic proportions in Asia including in Bangladesh. Percutaneous coronary intervention is a lifesaving procedure for many patients and occupies a significant place in the practice of interventional cardiology. As the number of coronary interventions increase, so do the consequent complications such as CIN. CIN contributes to significant morbidity and mortality after PCI. Hence, identification of high risk patients for CIN by risk stratification is indispensable.[18]

Prior studies have reported varying levels of incidence of CIN: 13.1% in the study conducted by Roxana Mehran[12], 9.7% in the study conducted by Suma M. Victor [18], and 5.5% in the study conducted by Amal[21]. In an analysis by McCullough et al, the incidence of CIN in patients undergoing PCI was 14.5% (in the derivation set of 1826 patients)[22]; it was 13.56% in this study which is similar with other studies.

Various factors have been identified as risk markers for CIN in different studies. Diabetes mellitus is proven to be a strong predictor for CIN.[12, 22. 23] Diabetes significantly influences the outcome of CIN in this study also. This may be because of the higher association of diabetes in the development off CIN.

In this study, older age (age >70 years: 17.9%) is an independent predictor for CIN in univariate analysis that is similar to the studies done by Roxana Mehran[12] & Dangas[23]. But unlike other studies[21.24], female gender is not independent predictors for CIN that is similar to the study conducted by Suma M. Victor[18] . Male patients were predominant in this study population (female gender: 25.4%) that is also similar to the study conducted by Suma M. Victor. This may be due to the under representation of this subgroup in this study. This is not uncommon in the context of Bangladesh where females receive fewer coronary interventions[20] and those who do receive usually belong to the higher economic strata. Other established risk factors like peripheral vascular disease[25, 26]. Hypotension[23], renal impairment[22, 26] and high contrast volume[27] form the rest of the components of this risk scoring system that are similar to other relevant studies. Unlike other studies, Anemia[28] was not an independent predictors for CIN in this study. This may be due to stringent exclusion of anemic patient in our hospital and small study sample may be another cause.

Similar risk prediction models have been published previously.[12, 21, 25] Mehran et al. developed and validated a scoring system in 8357 patients with eight variables consisting of hypotension (5 points), IABP (5 points), heart failure (5points), chronic kidney disease (4 points), diabetes (3 points), age 75 years (4 points), anemia (3 points), and volume of contrast (1 point for each 100 cc).[12] Based on the attained score, patients were further divided into low, moderate, high, very high risk groups, and the incidence of CIN, risk of RRT and mortality were calculated for each group. Risk scoring system of this study differs from this in few aspects. IABP patients were excluded in this study as IABP use itself may precipitate renal dysfunction either by releasing atheroembolic milieu to renal circulation or by impeding the renal blood flow if placed low in the aorta and thus making it difficult to differentiate it from CIN. Our risk scoring system allows risk calculation pertaining to each individual rather than to a cluster. It also allows the actual values of the variables to be entered in to the formula rather than group them further, hence it is convenient to use, even when there is lack of standardized definitions pertaining to Bangladeshi population for diagnosis, as in the case of anemia. However, no formula to calculate individual risk of RRT or mortality was developed in this study. Thus, the scoring system proposed in this study is formed by easily available clinical, laboratory and procedural variables and allows identification of high risk groups for developing CIN, allowing prophylactic measures to be employed early.

Finally, patients were grouped into four groups on the basis of total integer score as mild, moderate, high & very high risk group. Risk of development of CIN was increased with increase in integer score that is increase in the order of risk group. This finding is very relevant & is similar to other studies.

Conclusion:

CIN is a frequent complication following PCI, and is associated with complicated hospital stay and high mortality rate. The risk factor profile in Bangladeshi population as determined by this study

is unique to the subcontinent and may also be applicable to other countries across the world. Individual patient risk for CIN after PCI can be predicted based on the easily available clinical and procedural information to predict the probability of CIN following PCI. High risk groups can be identified using this risk scoring system and more vigilant preventive measures can then be applied for the prophylaxis of CIN. This CIN risk prediction can be used for both clinical and investigational purposes.

Study Limitations

1. This is a study involving a single center in Dhaka, hence multicentric validation across the country is required to authenticate this scoring system.
2. The sample size is also small, so it requires similar study in large scale.
3. There are many other risk factors as well that were not included in this study.
4. Although the rise in serum creatinine occurs within the first 24 h after exposure to contrast media in 80% of the patients, the absence of data on serum creatinine later than 48-72 h after PCI in the present study might result in the slight underestimation of CIN (McCullough & Sandberg 2003).
5. Sampling is purposive sampling, not a random one.
6. We did not use creatinine clearance value based on 24-h urine collection during a true baseline clinical condition, and our eGFR calculation is subject to limitations due to the formula used and the possibility that patients may not be at their true baseline condition before PCI because of dehydration or cardiac illness; however, we believe that the assessment of CIN risk based on the utilized cutoffs of serum creatinine and eGFR is fairly accurate for the clinical purposes of this study and certainly more practical and readily available than direct measurement of creatinine clearance.

Recommendations

1. Studies with larger sample size and longer duration with long term follow up could overcome some of the shortcomings that this study had.
2. A multicentric study can be done across the country with more risk factors analysis.
3. A further validation study should be done to validate this study.

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REVIEW ARTICLE

Bronchiectasis

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Abstract:

Bronchiectasis is characterized by dilatation of bronchi, airflow limitation and chronic infection/inflammation.Patients with bronchiectasis have chronic cough and sputum production, and bacterial infections develop in them that result in the loss of lung function.The diagnosis of bronchiectasis is made by high-resolution CT scans. Patients with bronchiectasis may have predisposing congenital disease, immune disorders, or inflammatory disease. The treatment of bronchiectasis is multimodality, and includes therapy with antibiotics, antiinflammatory agents, and airway clearance. Resectional surgery and lung transplantation are rarely required. In this comprehensive review, the etiology, pathogenesis, clinical presentation, appropriate investigations and management of bronchiectasis have been discussed.

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Introduction:

Bronchiectasis is a condition where destruction and damage of bronchioles lead to chronic airflow obstruction and typically copious expectoration. It is characterized by permanent dilation of bronchi and bronchioles caused by destruction of the muscle and elastic tissue, resulting from or associated with chronic necrotizing infection[1] . This was first described by Laennec in 1819 and identified tuberculosis and pertussis as the most likely causes[2] .

Today's most common cause in developing countries is the post infectious route. The development of antibiotic treatments and vaccines has resulted in a continuous decrease in the number of cases of bronchiectasis with post infectious causes in industrial countries[3] . Currently, congenital causes of bronchiectasis are seen more observed than postinfectious causes.In Europe, bronchiectasis is common in patients with cystic fibrosis (CF) [4] .This article aims to provide a comprehensive discussion about the etiology, pathogenesis, clinical presentation, appropriate investigations and management of bronchiectasis.

Prevalence:

Because high-resolution computed tomography (HRCT) scanning is more commonly used nowadays, bronchiectasis is diagnosed earlier and

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at earlier stages. This has resulted in a seeming increase in the prevalence of bronchiectasis.[3]

Very few data on prevalence are currently available.In the United States, the rate was reported to be as high as 52/100 000 .[5]

One in 1,800 UK hospital admissions is a result of bronchiectasis as the primary condition, and bronchiectasis patients occupy around one in every 1,000 hospital bed days.[6]Data from UK primary care suggests an incidence of 1/1000 or higher in older age groups.[7]

Pathogenesis of bronchiectasis:

The common feature among all the conditions that lead to bronchiectasis, is that they either lead to alteration in the pulmonary defense mechanisms, or are associated with inflammation.[8] The end result, is that the individual becomes susceptible to bacterial colonization and infection. Regardless of the initiating event, any damage to the airways that results in loss of the mucociliary transport, renders the airways susceptible to microbial colonization. Infection leads to inflammatory response and progressive lung damage.[9] Neutrophils are thought to play a central role in the pathogenesis of tissue damage that occurs in bronchiectasis.[10] The progressive nature of bronchiectasis is thought to result from a continuous "vicious circle" of inflammation and tissue damage.[11]

Pathological types of bronchiectasis:

Pathologically, bronchiectasis can be divided into four types.[12] The first type, cylindrical bronchiectasis, is characterized by uniform dilatation of bronchi, that extends into the lung periphery, without tapering. The second type is called varicose bronchiectasis and is characterized by irregular and beaded outline of bronchi, with alternating areas of constriction and dilatation. The third type is called cystic or saccular bronchiectasis and is the most severe form of the disease. The bronchi dilate, forming large cysts, which are usually filled with air and fluid. The fourth type of bronchiectasis is called follicular and is characterized by extensive lymphoid nodules within the bronchial walls. It usually occurs following childhood infections.[13]

Etiology:

Up to 50% of cases of bronchiectasis are idiopathic, with no identified underlying cause. This aetiology may have better outcomes than bronchiectasis that is associated with COPD or rheumatoid arthritis. There are some known causes of bronchiectasis (see box 1) and several conditions have been associated with bronchiectasis without a clear understanding of the aetiology.[14]

Infections

Many infections have been implicated to cause bronchiectasis. Measles, pertussis, adenovirus 21, tuberculosis, aspergillosis and human immunodeficiency virus (HIV), may all lead to permanent airway damage.[16] Immunizations against measles and pertussis have led to marked reduction in the incidence of bronchiectasis, caused by these two infections.[17] Tuberculosis was among the most important causes of Bronchiectasis. Currently, the incidence of bronchiectasis, secondary to mycobarium tuberculosis, is declining due to effective antituberculous treatment. Lately, mycobarium avium-intracellulare complex (MAC), has been recognized to cause bronchiectasis. Allergic bronchpulmonary aspergillosis is associated with airway damage and bronchiectasis.[18]

Immune dysfunction

Immunodeficiency syndromes such as immunoglobulin deficiency, complement deficiency and chronic granulomatous disease, are associated with bronchiectasis.[19]Deficiency of IgG, IgM and IgA, put the patient at increased risk of recurrent pulmonary infections, that eventually end in bronchiectasis.[20]

Cystic fibrosis

Cystic fibrosis is well known to cause bronchiectasis, as a result of recurrent respiratory tract infections with Staphylococcus aureus and mucoid pseudomonas aeruginosa.[21] In addition, the gene responsible for cystic fibrosis (CF), the cystic fibrosis transmembrane regulator (CFTR), is shown to occur in high frequency in children with idiopathic bronchiectasis.[22]However, CFTR mutations alone cannot be responsible for bronchiectasis, as the heterozygotes for this gene mutation were not found to be at increased risk of bronchiectasis.[23]It is suggested that CFTR

Bronchiectasis : Etiology and pathogenes[15]

Pathogenic mechanisms	Etiology
Primary infective insult	Bronchitis/brnchiolitis Pertussis Measles Adenovirus Pneumonia Tuberculosis
Primary impairment of Mucous clearance Genetic,biochemical Genetic,ultrastructural	 Cystic fibrosis Primary ciliary dyskinesias
Immunodeficiency syndrome, Congenital and acquired	Common varied Immunodeficiency Selective immunoglobulin deficiency Functional immune Deficiency Secondary Hypogammaglobulinaemia Human immunodeficiency Virus infection
Hyperimmune response	Allergic bronchopulmonary mycoses
Infection secondary to bronchial Obstruction Intraluminal Extraluminal	 Slow-growing tumour, Aspirated foreign body Lymphadenopathy
Miscellaneous inflammation Autoimmune disease	 Inflammatory bowel disease Coeliac disease Systemic lupus erythematosus Rheumatoid disease Cryptogenic fibrosing alveolitis Primary biliary cirrhosis Thyroiditis Pernicious anaemia
Inhalation/aspiration injury	Toxic fumes Gastric contents
Developmental defects Structural	 Pulmonary agenesis Sequestrated segment Tracheobronchomegaly Bronchomalacia
Biochemical	α_1-Antitrypsin deficiency

mutation acts with other factors (genetic, environmental) to contribute to bronchiectasis.[22]

Immotile Cilia syndrome/Kartagener's syndrome

Inherited as an autosomal recessive disease, immotile cilia syndrome can lead to bronchiectasis, as a result of recurrent pulmonary infections due to retained secretions.[17]Approximately 50% of patients with immotile cilia syndrome, have Kartagener's syndrome. It consists of sinusitis, bronchiectasis and situs inversus.[24]

Chronic obstructive pulmonary disease

Patients with advanced chronic obstructive pulmonary disease (COPD) may have

bronchiectasis; the literature reports rates between 30% and 50% .[25] These patients more often suffer from dyspnea and show poorer lung function. CT-morphologically, bronchiectasis in COPD differs from classic bronchiectasis, since theectasis is less pronounced but the peribronchial infiltration is more pronounced.[3] With the rising global prevalence of COPD, bronchiectasis is of increasing importance.

Rheumatoid arthritis

The association between rheumatoid arthritis and bronchiectasis, has recently received considerable interest. Bronchiectasis can occur, before or after the onset of Rheumatoid arthritis.[26]It has been suggested that, if bronchiectasis occurs before the onset of Rheumatoid arthritis, that chronic suppurative infection leads to triggering an immune response to the synovial membrane, causing rheumatoid arthritis.[27]In contrast, those patients who develop bronchiectasis after the onset of rheumatoid arthritis, may have increased susceptibility to respiratory infections caused by rheumatoid arthritis itself or its treatment. The recurrent pulmonary infections eventually lead to airway damage and bronchiectasis. This association is still controversial.[28]The combination of rheumatoid arthritis and bronchiectasis carries a poor prognosis.

Inflammatory bowel disease

Pulmonary involvement in inflammatory bowel disease is uncommon.[29]Interestingly, some patients with inflammatory bowel disease, develop bronchiectasis after colectomy.[30]It has been suggested, that bronchiectasis in inflammatory bowel disease, is due to an autoimmune process and infection has a minor role in its pathogenesis. This may explain the occurrence of bronchiectasis, post-colectomy, as the inflammatory and autoimmune processes shift from the bowel to the lung.[31]

Clinical features:

Patients with bronchiectasis complain of chronic cough, sputum production, and lethargy. Hemoptysis, chest pain, weight loss, bronchospasm, dyspnea, and impaired physical performance have also been observed.[32] The often mentioned three-layer sputum consisting of a foamy upper layer, mucous middle layer, and viscous purulent bottom layer is pathognomonic, but does not always occur.[3] Some patients are

symptom free in everyday life and become clinically conspicuous only during exacerbations.[3] Mild cases of bronchiectasis often have no abnormal physical signs. When the disease is sufficiently developed, the characteristic finding is that of persistent early and mid-inspiratory crackles.[15] Clubbing of the fingers and/or toes is a feature of gross disease with prolonged bronchial infection.[33] Nowadays finger clubbing in

bronchiectasis, other than that associated with CF, is uncommon in more developed countries.[15] Signs of collapse and fibrosis may be present in advanced cases.[15]

Exacerbation is defined as the presence of four or more of the symptoms listed in Box 2.[34]

Box 2

Symptoms of exacerbation
• Increase of sputum with cough
• Increased dyspnea
• Raised temperature >38° C
• Increased wheezing
• Lowered physical resilience
• Fatigue
• Deterioration in lung function
• Radiological signs of infection

A minimum of 4 symptoms are the defining criteria foran exacerbation

Complication:

Complications of bronchiectasis includes (Box-3)

Complications

- Hemoptysis
- Cor-pulponale
- Resoiratory Failure
- Amyloidosis
- Secondary visceral abscess at distant sites (i.e Branin)

Investigation:

1.CT Scan - High resolution CT scan of the chest is the confirmatory test for diagnosis of bronchiectasis. Findings include bronchial wall thickening with dilatation of bronchi to a diameter greater than that of accompanying arteriole (signet ring sign), lack of normal tapering of bronchi on sequential slices and visualization of bronchi in the the outer 1-2 cm.[35]Cases of allergic bronchopulmonary aspergillosis have central bronchiectasis while cystic fibrosis cases have upper zone bronchiectasis. (Fig- 1)

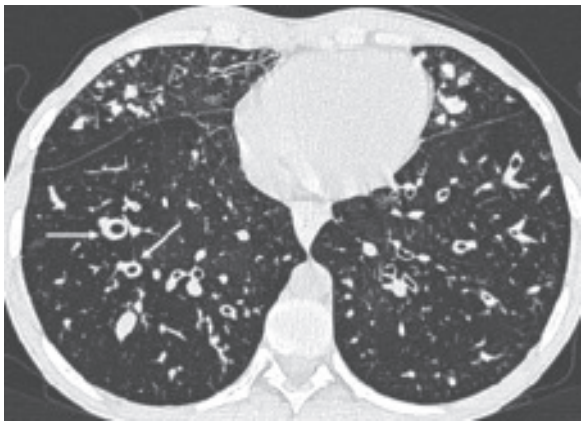

Figure- 1

2. Chest X-ray - This is useful as a baseline to monitor disease progression and at times of exacerbations. X-rays may show tram

lines or ring shadows[36] (Fig- 2).

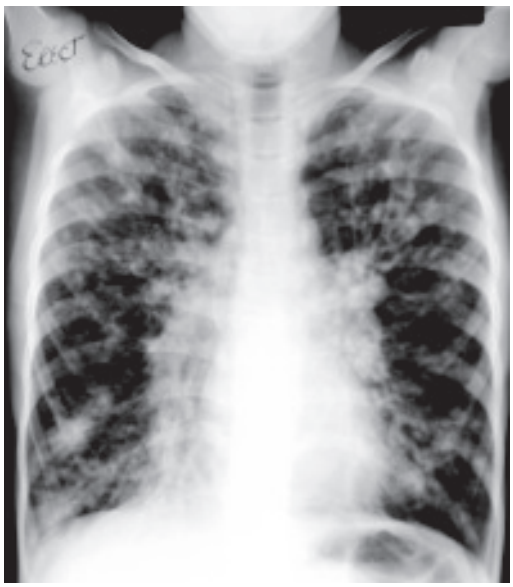

Figure- 1

3. Blood tests - Full blood count may show anaemia (of chronic disease). IgE levels may be raised in cases of allergic broncho-pulmonary Aspergillosis associated bronchiectasis. Aspergillus precipitin tests, Immunoglobulin levels and subclasses, Alfa 1 anti trypsin levels are other tests done to investigate etiology of brocnhiectasis.

4. Sweat tests and genetic tests may be done if cystic fibrosis is suspected. Other specific genetic tests and tests of ciliary functions are requested in appropriate clinical contexts.

5. Sputum examinations: Routine cultures are helpful in finding the colonizing bacteria e.g. *H influenza, S pneumonae and Pseudomonas aeruginosa*. AFB cultures are done to exclude *Mycobacterium tuberculosis* and also to consider the possibility of infection by Environmental Mycobacteria.

6. Lung function tests - These are useful in assessing severity of airflow obstruction and in monitoring disease progression.

Management:

The aims of treatment for bronchiectasis are:

- Improving mucociliary clearance or drainage of secretions
- Treating the infection
- Treating airway obstruction
- Treating the chronic inflammation that leads to disease progression.
- Treating the underlying disease.[3]

Draining secretions

Breathing therapy and physiotherapeutic measures are the basic treatments for bronchiectasis, to improve drainage of secretions and deal with dyspnea. The mainstay of treatment is sufficient administration of fluids for secretolytic purposes. This can be supported by inhalation of hypertonic saline solution. Especially inhaling hyperosmolar solutions has been found to be beneficial.[3] Studies using 7% saline for inhalation by CF patients have shown improved lung function and secretion clearance .[37]

In contrast to other hyperosmolar solutions, mannitol has the advantage of a longer half life within the airways. In an open label, non-

controlled study over 12days, quality of life, lung function, and sputum viscosity were notably improved.[38] A disadvantage of mannitol is the fact that hyperresponsiveness increases during inhalation. Currently, further studies are being conducted in order to gain licensing approval for the substance. Evidence base for n- Acetyl cysteine is very limited. Dornase-alfa may be harmful in non cystic fibrosis bronchiectasis althogh it is well established in cystic fibrosis.[39]

Vaccinations:

Influenza and pneumococcal vaccination are recommended as per national schedules

Antibiotics:

Antibiotics are the mainstay of treatment in exacerbations caused by infections. Choice of antibiotics depends on previous and current sputum culture results. Intravenous antibiotics may be used in cases with severe exacerbations or in cases not responding to oral antibiotics. Treatment with maintenance antibiotics in bronchiectasis can be directed at simply reducing the increased bacterial load, since chronic colonisation has been found to coincide with enhanced inflammation and worse clinical outcome.[40]

Macrolides, because of their anti-bacterial and anti-inflammatory properties, have long been thought ideal to intervene in the vicious circle of infection and inflammation that underlies bronchiectasis.[40]

Inhaled antibiotics are standard treatment for patients with CF who have been colonized with *Pseudomonas aeruginosa* [41] .Since 25% of patients with non-CF bronchiectasis are colonized with *Pseudomonas aeruginosa*, this therapeutic principle may offer an advantage in this setting. Significant clinical improvement has been shown, with a reduced density of pathogens and eradication of *Pseudomonas aeruginosa* in up to 35% of cases [42] .Choice of antibiotics depends on previous and current sputum culture results. Intravenous antibiotics

may be used in cases with severe exacerbations or in cases not responding to oral antibiotics.Box provides an overview of inhaled antibiotics.

Anti-obstructive therapy:

If a patient's airways are obstructed, anti-obstructive treatment similar to COPD should be considered. Parasympatholytics and beta-sympathicomimetics constitute the treatment of choice. Long-acting substances (tiotropium bromide or salmeterol/formoterol) seem

superior to short-acting substances.[3]

Inhibiting inflammation:

Oral corticosteroids are often administered in acute exacerbations of bronchiectasis. For inhaled steroids, long-term usage seems to confer benefits. [3]

Treating the underlying disease:

If possible, the underlying disease should be treated first. This primarily applies to immunodeficiency syndromes.[3]

Allergic bronchopulmonary aspergillosis

Allergic bronchopulmonary aspergillosis (ABPA) is arare but typical complication in bronchiectasis.

Box4: *Selection of the most researched inhaled antibiotics*

Substance	Results	Source
Tobramycin	Eradication in 13-35%,reduction of pathogenic load, improved lung function	42 43
Colistin	Rise in FEV1,eradication in 3 of 18 cases,fewer exacerbations,reduction of pathogenic load	44 45
Aztreonam	CF:improved lung function,longer interval to exacerbation	46
Liposomal ciprofloxacin Ciprofloxacin	Reduction of pathogenic load Reduction of pathogenic load	47 48
Gentamycin	Fewer exacerbations,improved quality of life Eradication of P.a. in 30.8% improved quality of life	49 50

Bronchiectasis can be a sequela of ABPA, but it can also predispose to ABPA. Acute exacerbation of ABPA usually requires treatment with systemic steroids for a long period of time [51].In order to prevent recurrence, long-term oral therapy with itraconazole is indicated in patients with pulmonary colonization; several studies have shown the effectiveness of this treatment in CF. Inhaled amphotericin B is the subject of studies. Individual reports have documented successful treatment with a monoclonal antibody against IgE (omaluzimab).[3]

Surgical therapy

Surgery is the method of choice in unilateral and localized bronchiectasis. Several studies have shown that resection of the bronchiectasis improved symptoms.[52]In the different studies, mortality varied from 1% to 8.6%.[33] Complications included pneumonias, postoperative hemorrhage, atelectasis, bronchopulmonary fistula, and wound infection. In particular cases, the resection of bilateral bronchiectasis may be the aim,but the lesions should be limited and completely resectable.[52] In severe complications, such as life threatening hemorrhage or fungal infection, surgical therapy can be used as the method of last resort.Hemoptysis, which is mostly caused by bleeds from hypertrophied vessels of the inflamed mucosa, can becontrolled by bronchial artery embolization (coiling) if required. This should only be done in specialized centers.

Lung transplantation in advanced disease

Lung transplantion can be a useful intervention in very advanced non-CF bronchiectasis. It is of vital importance to identify the right time for putting the patient on the transplant list. In accordance to the guidelines, the following criteria should be met:

- FEV1 < 30 % and an exacerbation with inpatient admission to intensive care, or
- More than three exacerbations per year, or
- Recurrent pneumothorax, or
- Hemoptysis requiring—and receiving—intervention .[53]

A double lung transplant is the method of choice in more than 90% of cases. In case only one lung is transplanted, there is a risk that pathogens are transferred from the native lung into the transplanted lung. Experiences from large centers have shown that he long-term prognosis does not differ much from that of other indications, with 5-year survival rates between 55% and60% .[55]

Conclusion:

Bronchiectasis is still, one of the frequently seen chronic lung diseases, that can affect the life quality and expectancy of the affected person. Multiple conditions are associated with the development of bronchiectasis, but all require both an infectious insult plus impairment of drainage, airway obstruction and/or a defect in host defense. Treatment of bronchiectasis is aimed at controlling infection and improving bronchial hygiene. Surgical extirpation of affected areas may be useful in selected patients.

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CASE REPORT

A Paradox of Pleural Effusion

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Abstract:

Paradoxical response is referred to an unusual expansion or formation of a new lesion during successful anti-tuberculous chemotherapy (ATT).In general tuberculosis is the most common cause of pleural effusion but development of pleural effusion during successful anti-tuberculous chemotherapy is uncommon.In our case, a young man was diagnosed as sputum smear negative pulmonary tuberculosis and ATT was started. He responded to treatment but 12 days later he developed right sided pleural effusion. A paradoxical pleural effusion was suspected. We continued ATT with addition of oral corticosteroid and the patient was under observation. Pleural effusion subsided over time and the patient was recovered completely without any further complication. Development of pleural effusion in patient getting ATT may be due to a paradoxical response having an immunological basis, and does not necessarily require nay modification in chemotherapy. Strong suspicion is needed to diagnose such case.

Key words: *Anti-tuberculous chemotherapy (ATT), Paradoxical effusion.*

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Case Report

A 35-year-old male Muslim from urban residency presented to us with the complaints of cough and fever for 2 months and heaviness in chest for 5 days. The patient stated that he had cough for 2 months which was present throughout day and night. Cough was mostly dry with occasional expectoration of sputum which was yellowish in colour.He also noticed low grade continued fever for last 2 months, more marked at evening and associated with night sweats. Cough had no diurnal variation. There was no history of wheeze, shortness of breath, hemoptysis, chest pain or palpitation.He had no history of contact with active TB patient. He consulted a chest physician and was diagnosed as a case of smear negative pulmonary tuberculosis.

Category-I anti TB drug was started. His fever and cough subsided within 07 days.On 12th day he felt heaviness on right side of chest and according to his physician's advice he got admitted into specialized hospital (NIDCH) for further

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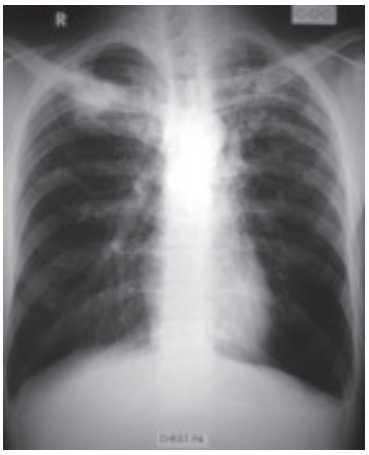

Fig-1: *A non- homogenous opacity in right upper zone.*

evaluation. He gave no history of weight loss, joint pain and abdominal pain, alteration of bowel habit, oral ulceration, hair loss, skin rash, and dryness of eye or mouth. He was normotensive and non-diabetic. His bowel and bladder habit and sleep pattern was normal. There was no significant history of past illness.

He was a businessman with middle-class family. He smoked cigarette with a history of 24 pack-year. He was alcoholic 06 years back. For last 1 year he used to take methamphetamine (as tab. Yaba).He was unmarried and gave history of multiple sexual exposures. His father died of geriatric diseases.

On examination, he was anxious and ill-looking with average body built. His pulse rate was 92/minute, blood pressure 110/70 mmHg, and respiratory rate 22/minute, temperature99^0F. There was no palpable lymph node or organomegaly. Chest examination revealed movement restricted on right side. Breath sound, vocal fremitus and vocal resonance diminished on right lower chest and percussion note dull over the same area. Examination of other systems revealed no abnormality. A clinical diagnosis of right-sided pleural effusion was made.

After admission at NIDCH, diagnostic procedures were done. His WBC count was 8500/cmm with 66% neutrophil, total platelet count 350000/cmm, ESR 25 mm in 1st hour and haemoglobin count 12gm/dl.Urine routine examination revealed trace albumin with 0-5 pus cell/HPF and no RBC. Random blood sugar 93mg/dl, serum creatinine 0.7mg/dl, serum albumin5.0gm/dl, SGPT 35U/L. Sputum AFB and GeneXpert was negative and Mantoux test revealed 12 mm induration. Chest radiograph showed right-sided pleural effusion with consolidation in right upper zone.

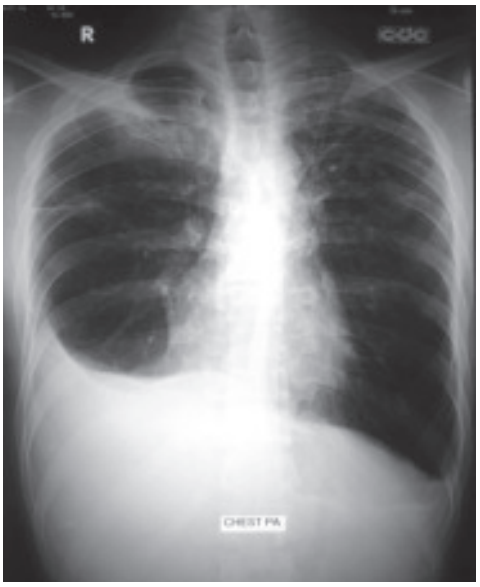

Fig-2: *Dense homogenous opacity with curvilinear upper border in right hemithorax with non-homogenous right apical shadow.*

Development of new pleural effusion in a patient getting ATT may be due to different phenomena. This may be an immunological response or drug induced hypersensitivity most likely INH. Keeping in mind the possible causes, further investigations were done. CT scan of chest revealed consolidation in right upper lobe with small right-sided pleural effusion. We decided to do diagnostic thoracentesis. About 80 cc pleural fluid was aspirated. Aspirate was straw colored, with 80mg/dl glucose and 5.3mg/dl protein. Total count 130/cmm with 92% lymphocytes. As there was small effusion, pleural biopsy was not taken. HBsAg and HIV screening was negative. ANA and anti-ds DNA was also negative.

Anti-Histone antibody was not done. Spirometry and echocardiography was normal. Surgical consultation was taken regarding pleuroscopy and decided against any intervention. We continued treatment with ATT and added short course oral corticosteroid and followed-up the patient. His

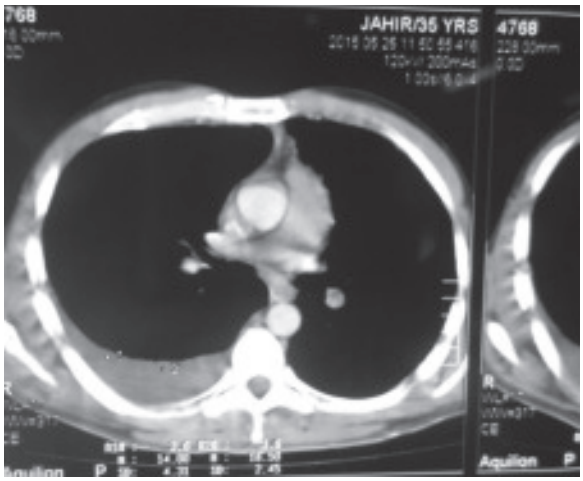

Fig-3: *CT scan of chest showing right-sided pleural effusion.*

condition was improving. Chest X-ray on 23rd day showed resolution of effusion. Further intervention was not done. Patient was discharged with ATT and tapering dose of oral corticosteroid. The clinical diagnosis of paradoxical pleural effusion was established. On subsequent follow-up, he was doing well without any new symptom.

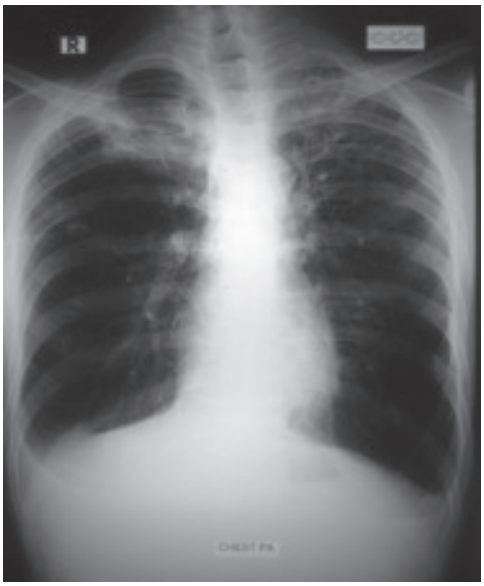

Fig-4: *Chest X-ray on 23rd day.*

Discussion:

Tuberculosis is one of the most common causes of pleural effusion andcan occur in any formof pulmonary tuberculosis. But development of new effusion in a patient on anti-tuberculous chemotherapy is a rare phenomenon. The first case of development of pleural effusion in a patient on ATT was reported by Trocme[1] on 1950. This may be due to a paradoxical response or drug-induced hypersensitivity. In most of the reported cases, pleural effusion developed between three to eight weeks of starting ATT[1-9]. The term "paradoxical response" refersto enlargement of old lesions or unexpectedappearance of new lesions during anti-tuberculoustherapy. Re-crudescence of fever, enlarging lymphadenopathies, worsening of pulmonary infiltrates,pleural effusion, ascites and appearance ofintracranial tuberculomas have all been described. An incidence of 16% of paradoxical worsening oftuberculous effusion following the start of antituberculoustreatment has been observed[6,10].

During active pulmonary tuberculosis, signs of both immune depression and immune activation are concomitantly present[11]. It has been observed that mycobacterial products induce the production of

tumour necrosis factor-alpha (TNF-á) which is involved in the expression of many of the local and systemic toxicities evident in tuberculosis. Kaplan *et al*[12]have recently shown that cytokines in newly diagnosed tuberculosis patients falls with ATT, except TNF, which increases to a maximum at 7-14 days. This temporary rise in TNF is associated with a transitory clinical deterioration. Interleukin-2 (IL-2) is also known to cause development of pulmonary infiltrates and pleural effusion[13]. The possible mechanism of development of pleural effusion during ATT seems to have an immunological basis. The possibility of a local hypersensitivity reaction to tuberculoprotein is further supported by Gupta and colleagues[14] who studied twenty nine cases of tuberculosis developing pleural effusion after starting ATT. Among them, 79.3% cases showed negative pleural fluid smear and/or culture for *M. tuberculosis* and 15 cases showed negative pleural biopsy for tuberculousp[athology.

Our patient developed pleural effusion on 12th day of starting ATT and subsided spontaneously after addition of stroid and continuing anti-TB drugs. Similar observation is noted by Gupta *et al* [14]. However, Al-Majed reported six patients who developed massive PE with respiratory distress requiring therapeutic aspiration and oral corticosteroid[6]. Endo *et al* [9]reported a case where recovery occurred after stopping all drugs and adding steroids.

Hypersensitivity reaction to isoniazid has also been implicated in development of pleural effusion during ATT. Isoniazid (INH) is known to be associated with lupus pleuritis causing chest pain, fever and arthritis[15]. The development of PE during ATT could be due to either INH-induced pneumonia's or INH induced lupus pleuritis[5,6].

There have been few cases of INH-induced pleural effusion documented in the literature.5 INH-induced pleural effusion usually begins 3 to 12 weeks after starting the medication and regresses after a change of therapy or introduction of steroids, or both[8].While the exact pathogenic mechanism ofINH-induced pleural effusion remains unclear, this indicatesthat the disease entity may have an underlying inflammatory component. Khattri S *et al*reported a case of INH-induced pleural effusion and lupus erythematosuswhere pleural fluid was eosinophilic and effusion subsided after discontinuing INH and addition of corticosteroid[16].

Development of tuberculouspleuritis or effusion during the early stages of chemotherapy does not imply failure of the current therapeutic regimen and no change in therapy is indicated unless there are other reasons, like progressive paraenchymal infiltrates or an unfavourable bacteriological response or drug-induced reaction[2]. In our case, we continued ATT with addition of corticosteroid and the patient recovered fully. Thus, there is no need to change drugs or increase treatment duration when pleural effusion occurs as a paradoxical response to ATT.

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CASE REPORT

Pleural lipomatosis: An unusual CT Chest Feature

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Abstract

Intrathoracic benign neoplasm can develop from any tissue; inside the thoracic cavity, however, pleural lipomatosis is unusual diposition of adipose tissue in the pleural and subpleural layer. Asymptomatic presentation may be proven commonly and revealed by unintended radiology with a measured Hounsfield scale "100 to -50. We report this case of pleural lipomatosis by radiological finding though thoracoscopic finding is the ideal for diagnosis and with. pathological examination of the specimen confirmed the diagnosis of lipomatosis. A radiological diagnosis of pleural lipomatosis can be made by computed tomography, transthoracic ultrasound as a diagnostic investigation because of their characteristic fat attenuation. Medical thoracoscopic biopsy provides a more accurate and confirmed diagnosis. Pleural lipomatosis is a rare clinical pleural dilemma that needs suspicious sense and a feasible radiological diagnosis as soon as a strong evidence of malignant transformation is excluded.

Excessive unencapsulated infiltrative fat deposition is known as mediastinal lipomatosis (Fig 5). Lipomatosis is commonly associated with obesity and exogenous steroid administration.

Keywords: *Hounsfield unit, lipomatosis, medical thoracoscopy*

[Chest & Heart Journal 2016; 40(1) : 74-77]

Introduction

Lipomatosis is a benign but unusual and excessive deposition of adipose tissues that can develop all over the body. Lipomatosis can develop in fat-containing tissues such as the mediastinum, diaphragm, bronchus, lung, or thoracic wall; however, atypical localization can be noticed in the pleura as pleural lipoma or lipomatosis. 1,2.

These lesions are thought to originate from the submesothelial layers of the parietal pleura, extending into the subpleural, pleural, or extrapleural space. Pleural lipomatosis are excessive deposition of fat with a slow growth rate. Pleural lipomatosis is found by the way on a chest radiograph or a computed tomography (CT) examination of the chest for patients presented with complains other than pulmonary problems.

Extrapleural fat is fat deposition outside the parietal pleura in the chest wall. It is a component of the loose connective tissue of the endothoracic

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fascia and is most abundant along the posterolateral aspects of the fourth through eighth ribs bilaterally 3,4. The resulting soft-tissue shadow that is produced can be confused with pleural thickening at conventional radiography. Pleural plaques may calcify, whereas extrapleural fat does not. When this finding is not present, secondary features are used to differentiate between these two entities. Extrapleural fat is typically bilateral, symmetric, and located along the midlateral chest wall. Pleural plaque is asymmetric, is randomly distributed, and spares the apices and costophrenic angles. Definitive diagnosis is made at CT when the lesion in question shows fat attenuation of approximately "100 HU.

Radiographic features

Plain radiography

- well defined, convex lesions forming obtuse angles with the pleura
- normally vertically orientated in relation to the chest wall
- no rib erosion
- appears denser than fat because of interface with air in the lung

Cross sectional imaging

- homogeneous fat density or fat signal intensity
- no enhancement
- Definitive diagnosis is made at CT when the lesion in question shows fat attenuation of approximately "100 HU.

Differential diagnosis

The principal differential diagnosis is encysted pleural effusion. Ct chest typical fat attenuation and pleural diagnostic tap reveal the diagnosis.

Extrapleural fat represents fat outside the parietal pleura. It is part of the loose connective tissue of the endothoracic fascia, most abundant along the posterolateral aspects of the 4^{th} through 8^{th} ribs. Extrapleural fat is typically *bilateral, symmetrical*, and located along the mid-lateral chest wall [1].

Presentation of case

A 28-year-old house wife was admitted after she was incidentally found her abnormal x-ray for medical fitness. She had no significant respiratory constitutional symptoms. He had no previous history of chest troubles or cardiac disorders. Chest radiography was performed and indicated bilateral encysted moderate pleural effusion. Transthoracic ultrasound examination was performed for localization and as guidance for aspiration, which showed pleural fluid with simple anechoic criteria of about 2600 ml in volume with few pleural-based nodules. Pleural aspiration was tried and revealed dry tap. Other routine laboratory tests of complete blood count, and liver and kidney function tests were of normal range. Collagen profile was done which was normal. Tuberculosis profile was normal. Cardiac evaluation was doneand found normal. A CT of the chest reveals that non dense homogenous opacity all over the anterior chest wall and from 8^{th} rib posterior chest wall.

Patient was counseled and medical thoracoscopy was advised but declined for the procedure because of financial constrains. FOB done to see endobronchial lesion, which reveal that shiny mucosal swelling. Preplanned biopsy taken. Histopathological examination of the biopsy with staining of block with hematoxylin and eosin indicated well-differentiated mature adipocytes, with no pleomorphism, necrosis, or mitotic activity, suggestive of lipomatosis Finally CT chest report was reviewed and discussed with radiologist which showed Hounsfield unit -100 which is fat attenuation unit for diagnoses of lipomatosis.

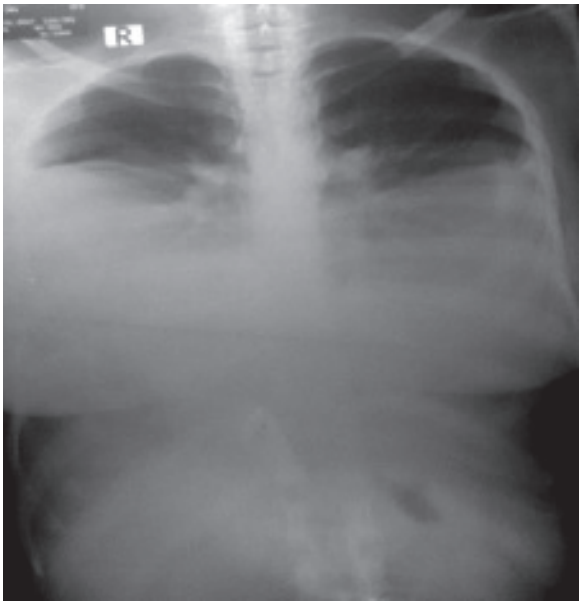

Fig.-1: Chest x-ray PA view

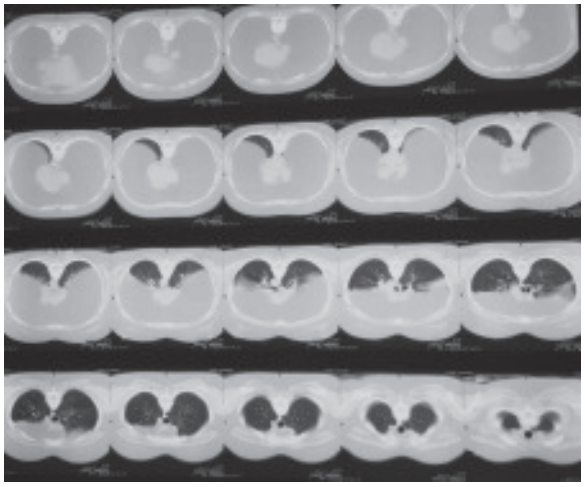

Fig.-2: CT scan chest

Fig.-3: CT scan chest

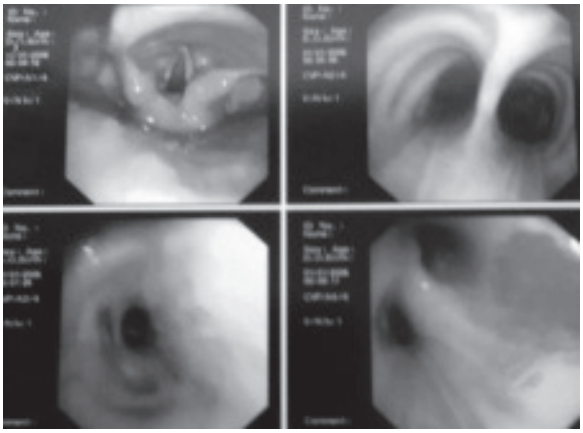

Fig.-4: Fibre optic bronchoscopy

Discussion:

In general, lipomatosis is benign mesenchymatous adiposes that develop all over the body composed of mature adipocytes presenting just about half of soft tissue tumors and 80% of benign fat-containing neoplasms. Ordinary lipomatosis may be found all over the body, but they are rarely found in the thoracic cavity. Consistent with classifications established by Keeley & Vana and Williams & Parsons, they can be divided into two classes:

Along with their origin, they are classified as follows:

i. Endobronchial lipomatosis originating from the submucosal fat of the tracheobronchial tree,

ii. Parenchymal lipomatosis originating from interstitial adipocytes and located peripherally,

iii. Pleural lipomatosis originating from the submesothelial layer of parietal pleura,

iv. Mediastinal lipomatosis and

v. Pericardial lipomatosis 1,2,4..

vi. Pleural lipomatosis are usually multiple and have no association with other extrathoracic locations; they involve both sides with the same frequency, but there is no malignant conversion.

They are most commonly detected between the ages of 30 and 50 years, often associated with obesity. Lipomatosis is commonly associated with obesity and exogenous steroid administration.

The pleural lipomatosis observed originated in the submesothelial layer of parietal pleura and showed hemispherical sessile lesions distributed widely all over the costal pleural surface4,5. From the clinical point of view, no specific signs or symptoms of this kind of lesion were detected apart from conventional pulmonary symptoms such as dyspnea and dry cough until they attained a large size, and once it spreads over the wide costal surface, it may induce compression symptoms such as persistent dry cough, chest pain, increased dyspnea, or chest heaviness sensation. In 11% of cases as part of Pierre Marie's syndrome, clubbing was observed, which disappeared after surgical resection of lesion1. In a study by Zidane *et al.* 2, accompanying signs were occasional; bone erosion, cortical thickening, and hyperostosis secondary to extrinsic pressure, and periosteal irritation have been documented.

CT chest provides essential information to differentiate between benign and malignant pleural disease, and determine the location and extent of disease; it occasionally enables characterization of tissue on the basis of signal attenuation The radiological diagnostic criteria are as follows: a well-defined nodular appearance composed of homogeneous fat (-50 to "150 HU), not enhanced by an injected contrast medium, with obtuse angles with the chest wall and displacing adjacent pulmonary parenchyma and vessels 1,2,6,7 However, differentiation between malignant liposarcomas and benign lipomatosis may be challenging on CT images. The typical characteristics of a malignant tumor include invasive growth, infiltration of surrounding structures, rather than displacement, inhomogeneous enhancement after intravenous contrast medium application, attenuation values greater than -50 HU, poor delineation of the lesion, and occurrence of metastases 1,2,7 Ultrasound of the thoracic wall may facilitate the diagnosis, confirming the pleural origin of the tumor 1,8. If there is doubt in radiological diagnosis by CT, MRI may be useful. Its main value is its ability to differentiate between lipomatosis and liposarcoma. Pathological examination is the definitive diagnosis by which differentiation between these two tumors can only be achieved only by, which should differentiate between these two tumors. No definitive lines of a management strategy for pleural lipomatosis have been established as yet. A close monitoring policy with clinical and radiological follow-up may be suitable for patients, especially in those with small and asymptomatic lesion 2,4,7. However, a surgical excision is considered to be the treatment of choice. Sometimes, intracavitary radiotherapy can be, to some extent, valuable, fearing of recurrence. Infiltration of lipomatosis to the surrounding structures can cause severe symptoms, such as for example invasion to intercostal spaces, and induce rib destruction 1,2. Thoracoscopic surgery has become a more common technique for thoracic tumor operations, being an effective, well-endured procedure that is associated with less morbidity and mortality than that with conventional surgery 1,5,9. Surgical resection can be performed easily by an open thoracotomy to provide relief of symptoms and to confirm diagnosis.

Conclusion:

Pleural lipomatosis, however, is a rare pleural lesion; concern should be put in mind for lipomatosis as being one of the possible etiologies before stating the case as idiopathic effusion. The clinical scenario usually does not involve a neoplastic course as well as a thoracoscopic view; hence, transthoracic ultrasound and/or CT assessment by Hounsfield unit represent important noninvasive diagnostic tools that have the advantages of decreased surgical morbidity, not as much pain, and a reduced duration of hospital stay

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CASE REPORT

Colon interposition for Esophageal Replacement in Corrosive Stricture through Transhiatal Route – First time in Bangladesh

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Abstract:

Stomach is the most common conduit used after esophageal resection. However, stomach may not be feasible all the time to use as a conduit. In that setting, colon is an alternative conduit with several advantages. In this article, we are reporting a patient who had underwent multiple dilatation of esophagus for corrosive stricture esophagus but his symptoms of dysphagia did not subsided. Also patient's stomach could not be used as a conduit, as he had undergone gastro-jejunostomy for gastric outlet obstruction. Hence colon was preferred in this case as a conduit after esophagectomy.Transhiatalapproach for esophageal resection and colon interposition was performed in our case which was firstever documented procedure in Bangladesh,so we are reporting this case of colon interposition via transhiatal route.

[Chest & Heart Journal 2016; 40(1) : 78-81]

Introduction

Corrosive esophageal injuries of the esophagus are caused by the ingestion of strong acid or alkali. Ingestion of corrosive agents could be either accidental or suicidal. Accidental ingestions are mostly common in children and with acid since it is colorless as water. But suicidal ingestions are mostly common in adults and with alkali. Ingestion of acid produces coagulation necrosis limiting the depth of injury, whereas ingestion of alkali produces liquefaction necrosis and increased depth on injury[1].Transhiatal approach for esophageal resection is safe and sufficient and in times has many advantages[2]. Other most commonly performed techniques for esophageal resection are one-stage, two-stage or three-stage esophagectomyand minimally invasive techniques. Each of the techniques has their own advantages and disadvantages.

Case report:

A 25 years old gentleman, Mr.Porimol Kumar Das, hailing from Bogra presented to Thoracic Surgery Unit, NIDCH with complaint of difficulty on swallowing for 3 years. His problem started after he had suicidal attempt with ingestion of acid 3 years back. Immediately after ingestion of acid, he had excessive salivation and bleeding orally with burning pain and painful swallowing for which he was managed primarily in SZMCHospital, Bogra. After two days of this incident, he was started on liquid diet orally and gradually solid food was being started. However he experienced difficulty on swallowingeven for liquid food and was referred to our hospital, NIDCH for further management.After all pre-operative preparation, rigid esophagoscopy and esophageal dilatation was done (stricture was found at 17cm from upper incisor teeth and dilatation done up to 34Fr). After

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this procedure, he was apparently alright and he could take solid food. One month later, he developed cough and severe vomiting. Vomitus contained food particles which were taken several hours back. He was diagnosed with gastric outlet obstruction due to pyloric stenosis, which was corrected by Gastro-jejunostomy.

About 9 months of the initial dilatation, he again presented with difficulty on swallowing. This time he underwent rigid esophagoscopy and dilatation twice. During the second attempt of dilatation, esophageal perforation occurred and he was managed conservatively with tube thoracostomy. He gradually started on liquid and then solid diet, which he tolerated well.

In next one year, he had esophageal dilatation for two more times. Everytime after dilatation he could take food for few months and then he again developed difficulty on swallowing. Then he was admitted for surgical correction of the condition.

On physical examination, he was ill-looking, emaciated, with poor nutritional status. BMI was 14.02 (weight=41kg, height=1.71m). He was

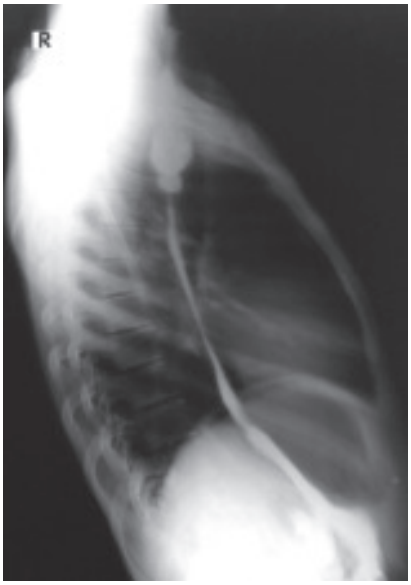

Fig.-1: *Long segment stricture esophageal.*

moderately anemic, but cyanosis, icterus, clubbing, koilonychia, edema absent and accessible lymphnodes were not palpable. JVP not raised and thyroid gland not enlarged. His pulse was 80bpmregular, BP was 110/80mmHg, RR 18/min and he was afebrile. Abdominal examination revealed that abdomen was scaphoid in shape, well healed upper midline scar was present and umbilicus was centrally placed. Abdomen was soft, no any mass was palpable and organomegaly was not found. Tympanic on percussion and normal bowel sound was heard on auscultation. Other systemic examination reveals normal findings.

Investigation revealed hemoglobin 11.2gm/dl (after three units of whole blood transfusion), ESR 27mm in 1sthr, TC 8600, neutrophils 60%, lymphocytes 30%, monocytes 06%, and eosinophil 04%, blood group "O" positive, Na 138mmol/L, K 3.5mmol/L, Cl 103mmol/L, RBS 100mg/dl, Urea 28mg/dl, S.Creatinine 1.0mg/dl, HBsAg/Anti-HCV-negative, sputum for AFB-negative and ECG and Echocardiography revealed normal study. Barium study showed persistent narrowing of almost whole length of the esophagus with passage of dye to stomach and then to jejunum bypassing the duodenum.

After all pre-operative preparation, patient underwent restoration of esophago-gastric continuity by colon interposition and feeding jejunostomy via transhiatal approach on 9th July,2014. With all aseptic precaution,draping done. Abdomen opened with upper midline incision. Transverse colon and adjoining parts of ascending and descending colons were mobilized. Right, middle and left colon artery were identified. Transverse colon was chosen for the conduit and prepared after ligation and transaction of middle colic artery, keeping the ascending branch of left colic artery as the principle blood supply of the graft. Oblique incision was made on left side of the neck, then cervical esophagus was mobilized and healthy part of the esophagus for proximal anastomosis was identified. Transverse colon was freed after the resection proximal to the hepatic flexure, which was later anastomosed proximally with the cervical esophagus. The distal resection was done near the splenic flexure and anastomosed distally to the anterior part of the body of stomach. This pedicle colon graft was taken to the neck through the trans-hiatal route. The colonic continuity was restored by colo-colic anastomosis using circular GI stapler. Rest of the anastomosis was done by hand-sewn technique. Feeding jejunostomy was performed and abdomen was

closed in layers keeping one drain tube in situ and also the cervical incision was closed in layers keeping another drain tube in situ. On 7th POD, patient developed colo-colic anastomosis leakage, for which initially conservative management was tried but patient deteriorated with fecal matter spreading along the fascial plane of anterior abdominal wall giving rise hyperemia and patchy cutaneous gangrene. On 13th POD, re-exploration laparotomy was done and loop colostomy was performed. With debridement and daily dressing followed by skin grafting, the complication was managed well. On subsequent follow-up after 3 months, patient can swallow satisfactorily and his all wounds were healthy and had functioning loop colostomy in situ . Barium study was satisfactory. His loop colostomy was closed after this follow-up and now he is passing stool normally.

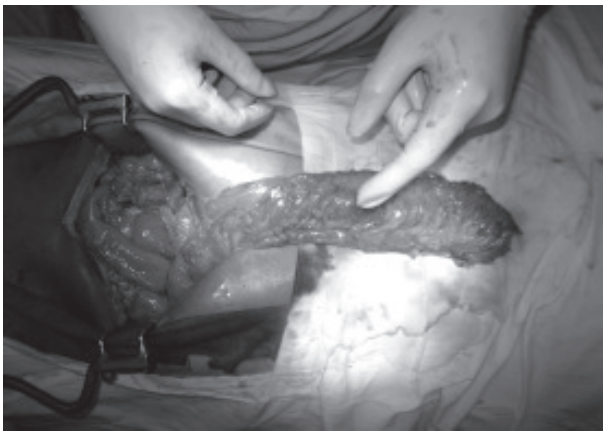

Fig.-2: *Free colon graft.*

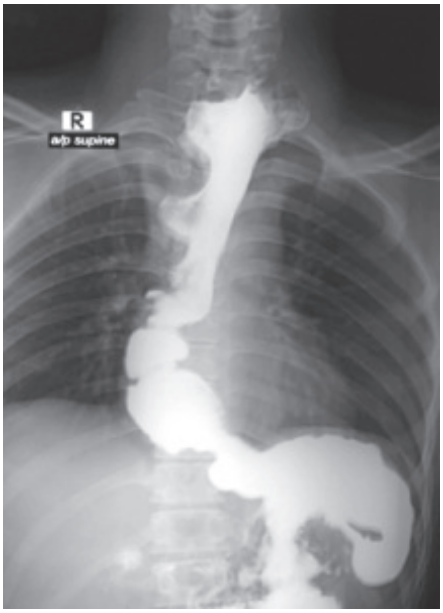

Fig.-3: *Showing colon interposed in esophageal position.*

Discussion:

Trans-hiatal approach for esophageal resection is indicated for benign esophageal disease for which complete lymphadenectomy may not be necessary and also in a patient with poor pulmonary function (FEV_1<800ml or <35% predicted) and pleural symphysis, which would favour technique that avoids thoracotomy[3].Also the transhiatal route is the most anatomical and had shortest distance between the cricoesophagus and gastroesophageal junction.Complications like transient recurrent laryngeal nerve palsy, anastomotic leakage and stenosis occurred in acceptable number of patients showing that transhiatal route for esophageal resection is safe and satisfactory procedure for benign obstructive condition of the esophagus.[2]Our patienthas a benign condition (corrosive esophageal stricture) that doesn't necessitate lymphadenectomy but his pulmonary reserve is up to the mark. Hence transhiatal approach was done.

Although the stomach is the most commonly used conduit for esophageal replacement after esophageal resection, colon has multiple advantages compared to stomach as a conduit. Resistance to acid, sufficient length of graft, consistent and robust blood supply, and potential for wide gastric resection margin for cancer of gastroesophageal junction are the main advantages. However, need of preoperative evaluation with colonoscopy, barium enema +/- colonic vessels angiography, pre-operative bowel preparation, more time consuming to mobilize and to do 3 anastomosis and increase late redundancy requiring re-operation are the disadvantages of colonic interposition compared to the gastric pull-up.[5] Also colonic interposition is technically demanding and often used only in specialized centers. As our setting is also specialized center with potential surgeons and also the stomach had been used previously for gastro-jejunostomy, colon was primarily selected in our case.

Anastomotic leakage, graft necrosis and post-operative stricture are the known complication after the esophageal resection. In one study, graft

necrosis and or anastomosis leakage occurred in about 10% and stricture occurred in about 22% of the patient and also anastomotic leakage and stricture are more common and the strictures are more severe after gastric pull-up compared with colon interposition.[2] In our case, esophageal anastomosis had no leakage or stricture on follow-up but he developed the leakage from the colo-colic anatomotic site leading to hyperemia and patchy necrosis of the anterior abdominal wall, which was managed bydefunctioning loop colostomy and regular debridement and dressing of the necrosed part, and later the split-skin grafting. It was also seen that only the colo-colic anastomosis was done by the circular GI anastomosis, whereas other two anastomosis (i.e.esophago-colonic and gastro-colic anastomosis) was done with the hand-sewn technique. It shows that our surgeons are professional in traditional hand-sewn techniques.

In conclusion, colon interposition after esophageal resection is suitable for young patient with benign condition requiring the esophageal replacement. The long-term result is good as the stomach has been preserved,hence the reservoir function is intact and also had less chance of aspiration. Therefore the quality of life is good as compared to gastric pull-up. This operation had been performed for the first time in our centre and had uplifted the confidence for the surgeons but the long-term efficacy of this procedure is yet to be known by performing multiple number of cases.

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