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EDITORIAL

Reactive Airways Dysfunction Syndrome and Irritant –Induced Asthma

Md. Khairul Anam

[Chest Heart J. 2022; 46(1) : 1-2]
DOI: http://dx.doi.org/10.33316/chab.j.v46i1.2019644

Reactive airways dysfunction syndrome (RADS) and irritant-induced asthma (IIA) are closely related forms of asthma that result from a single exposure to a high concentration of irritant agents or repeated exposure to moderate to low doses of irritant agents[1].

Irritant-induced asthma is a general term to describe an asthmatic syndrome that results from single or multiple exposures to irritant products that induce bronchial hyperresponsiveness. When symptoms promptly follow a single high-dose exposure to a corrosive gas, vapor or fume, the syndrome is called reactive airways dysfunction syndrome [2].

Acute symptoms associated with RADS include a rapid onset of a burning sensation in the throat and nose, chest pain, dyspnea, cough and wheeze. In IIA, the symptoms are similar, but the onset is less acute than with RADS.

The diagnosis of RADS requires the combination of exposure to a high-dose of an inhalational irritant, onset of symptoms within hours (rarely days), and evidence of reversible airflow limitation (eg, spirometry with bronchodilator reversibility or positive non-specific bronchoprovocation challenge), although a restrictive defect can also be present. A chest radiograph is often obtained to exclude other causes of dyspnea.

The diagnosis of IIA is based upon a history of single or multiple exposures to an irritating inhalational agent, the presence of asthma-like symptoms, and the presence of reversible airway obstruction and/or hyperresponsiveness.

For patients who present with the acute onset of RADS, treatment approach is same used as for acute asthma exacerbations in other settings, including oral glucocorticoids and high dose inhaled glucocorticoids with or without concomitant long-acting inhaled beta-2 agonist [3]. High dose inhaled glucocorticoids are often needed to control symptoms. Inhaled rather than oral glucocorticoids are appropriate initial therapy for patients who present with less severe symptoms.

For patients with persistent symptoms due to RADS or IIA, it is suggested to follow the step-wise approach used in asthma management. In addition, patients are advised to avoid respiratory irritants, including cigarette smoke, and allergens to which they are sensitive.

In general, workers with RADS or IIA are able to return to their working environment with appropriate asthma treatment and safety measures to prevent further high dose exposures. The worker should have ongoing monitoring to detect any deterioration in respiratory status.

The majority of patients with RADS and IIA improve over time, although many continue to have some respiratory symptoms for at least a year and have physiologic abnormalities such as non-specific bronchial hyperresponsiveness for several years.

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ORIGINAL ARTICLE

Sequential Organ Failure Assessment (SOFA) Scores as Predictive Indices for Weanability from Mechanical Ventilation

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Abstract

Background: *Sequential Organ Failure Assessment (SOFA) score was designed for describing the severity of a patient's illness resulted from the affected degree of six organ failure or dysfunction, There was little knowledge about application of SOFA scoring system to predict weanability from mechanical ventilation.*

Aims: *The aim of the study was to determine the SOFA score as a predictive index for weaning of the patients from mechanical ventilation.*

Materials & Methods: *This prospective observational study conducted at the Department of Respiratory Medicine in National Institute of Diseases of the Chest and Hospital (NIDCH) from March 2020 to February 2021 in collaboration with the Department of Respiratory Intensive Care Unit (ICU). A total of 42 critically ill patients admitted to Respiratory ICU of NIDCH were enrolled in this study. SOFA score measured every day and weaning process involved spontaneous breathing trial with a T piece. Statistical analyses of the results were obtained by using windows based computer software devised with Statistical Packages for Social Sciences (SPSS-23).*

Results: *Among the 42 patients with a mean age of 58.5±18.6 years requiring MV, 34(81%) patients were successfully weaned from Mechanical Ventilation. Male patients were predominant 39(92.9%) with male to female ratio was 13:1.The most common reason for ICU admission was acute exacerbation of COPD (AECOPD) with Type 2 Respiratory Failure 7(16.7%). Fifty seven percent patients had DM followed by 21(50.0%) HTN. Among 42 patients, 8(19.0%) patients were died and 31(73.8%) were survived. The mean SOFA score maximum was found 8.0±2.0 with range from 5 to 14. Based on the receiver-operator characteristic (ROC) curves SOFA score maximum had area under curve 0.991. Receiver-operator characteristic (ROC) was constructed by using SOFA score level, which gave a cut off value ≥9.5 with 87.5% sensitivity and 97.1% specificity for prediction of mortality. With cut off SOFA score ≥9.5 mean duration of mechanical ventilation was 6.8±3.3 days. There were no significant association of socio-demographic variables and co-morbidities compared with successful weaning and weaning failure patients.*

Conclusion: *In conclusion, SOFA score may be used as predictive index for weanability from mechanical ventilation.*

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Introduction:

Critical illness is any disease process which causes physiological instability leading to disability or death within minutes or hours. Mechanical ventilation (MV) is commonly needed in critically ill patients for variable periods. Over the last decade there has been an exploration of new ventilator techniques that present a bewildering array of the alternative for the treatment of respiratory failure[1]. Over the past few years our understanding of the detrimental as well as beneficial effects has increases many folds and now majority of the patients requiring mechanical ventilation in the ICU are safely weaned from ventilation within a short period of time. Accurate prediction of MV duration is important for patients and their family members. It is also an essential first step in the allocation of resources and appropriate use of weaning centers

Weaning from mechanical ventilation can be defined as the process of abruptly or gradually withdrawing ventilator support. Weaning from mechanical ventilation usually implies two separate but closely related aspects of care, discontinuation of mechanical ventilation and removal of any artificial airway. A variety of criteria have been used as predictors of weaning outcome. More recently, the respiratory rate (f) to tidal volume (Vt) ratio (f/Vt); CROP index {compliance (thoracic), respiratory (rate), oxygen (arterial), pressure (maximal inspiratory- Pimax); relative inspiratory effort (RIE); and a new weaning index (WI), based on ventilatory endurance and the efficiency of gas exchange have been proposed as predictors of the success or failure of weaning attempts. However, all these weaning indices have been used to predict only the immediate outcome of weaning attempts; they are difficult to apply in daily clinical practice. The SOFA score evaluates the severity of the patient's illness with an assessment of six organ systems[2]. This study would offer an insight into the potential use of SOFA score as predictive index for weaning from mechanical ventilation. By doing so, it would provide clinicians a reliable, convenient, cost effective and routinely measured tool as SOFA score to assess prediction of weaning from mechanical ventilation patients.

Materials and methods The study was designed as prospective cross sectional observational study ,conducted in the Respiratory ICU, National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka from March 2020, to February 2021. Critically ill patients treated with mechanical ventilation were included in the study.

Inclusion criteria

- Patient who were admitted and mechanically ventilated in ICU
- Age ≥18 years.

Exclusion criteria

- Patient with history of Cardiac surgery within last 4 weeks.
- Patient admitted due to traumatic injuries.
- Patient referred from another ICU.
- Patient attendants who refused to be part of study.
- Patients with incomplete follow up.

Operational definition

The SOFA score

Ranges from 0 to 24 and includes points related to six organ systems: respiratory (hypoxaemia defined by low PaO2/FiO2); coagulation (low platelets); liver (high bilirubin); cardiovascular (hypotension); central nervous system (low level of consciousness defined by Glasgow Coma Scale); and renal (low urine output or high creatinine). Sepsis is defined by an increase in the sepsis-related SOFA score of e" 2 points. The baseline score is assumed as '0' if data are not available [3] .

Weaning from mechanical ventilation

Weaning from mechanical ventilation is the process of reducing ventilatory support, ultimately resulting in a patient breathing spontaneously and being extubated. This process can be achieved rapidly in 80% of patients when the original cause of the respiratory failure has improved. The remaining cases will require a more gradual method of withdrawing ventilation[4].

Observations and results

The mean age was 58.5±18.6 years with range from 19 to 90 years. Majority (92.9%) patients were male. Among the admitted patients 7(16.7%) patients were found Acute Exacerbation of COPD with Type 2 Respiratory Failure, 6(14.2%) post TB fibrosis, 5(11.9%) Pneumonia and 4(9.5%) bronchial carcinoma. Regarding co-morbidities 24(57.1%) patients had Diabetes Mellitus followed by 21(50.0%) HTN, 9(21.4%) IHD, 8(19.0%) Cor-pulmonale, 7(16.7%) CKD, 6(14.3%) CVD, 5(11.9%) BEP and 4(9.5%) had pulmonary hypertension.

Regarding duration of mechanical ventilation, 35(83.3%) patients were in mechanical ventilation for ≤7 days. The mean duration of mechanical ventilation was found 6.0±1.9 days with range from 2 to 11 days. In our study it was found that 8(19.0%) patients died, 31(73.8%) were survived and 3(7.1%) were switched to multidisciplinary ICU. Weaning were successful in 34(81%) patients and 8(19.0%) patients had unsuccessful weaning. Low SOFA score ≤6 was found in 9 cases and their mean duration of mechanical ventilation was 4.7±1.2 days. Medium SOFA score 7-10 was found in 28 cases and their mean duration of mechanical ventilation was 6.3±1.7 days. High SOFA score >10 was found in 5 cases and their mean duration of mechanical ventilation was 7.0±2.9 days. The difference was statistically significant ($p<0.05$) among three groups. It was found that 3(37.5%) patients was found SOFA score 7-10 in patents who didn't survive, 2(66.7%) in switched to multidisciplinary facility ICU and 23(74.2%) in survived group. Based on the receiver-operator characteristic (ROC) curves SOFA score maximum had area under curve 0.991. Receiver-operator characteristic (ROC) was constructed by using SOFA score level, which gave a cut off value 9.5, with 87.5% sensitivity and 97.1% specificity for prediction of mortality. It was found that positive predictive value was 87.5% and negative predictive value was 97.1%. It was found that SOFA score ≥9.5 was found in 8 cases and their mean duration of mechanical ventilation were 6.8±3.3 days. SOFA score <9.5 was found in 34 cases and their mean duration of mechanical ventilation were 5.8±1.4 days. The difference was statistically significant ($p>0.05$) between two groups. SOFA score ≥9.5 was found in 7(87.5%) patients who did not survived, 1(33.0%) in switched to multidisciplinary facility ICU and SOFA score cut off was <9.5 those who survived. The difference was statistically significant ($p<0.05$) among three groups.

Table-I

Demographic characteristics of the study patients (n=42)

Demographic characteristics	Number of patients	Percentage
Age (years)		
Mean±SD		58.5±18.6
Range (min-max)		19.0-90.0
Sex		
Male	39	92.9
Female	3	7.1

Table-II

Distribution of the study patients according to co-morbidities (n=42)

Co-morbidities	Number of patients	Percentage
DM	24	57.1
HTN	21	50.0
IHD	9	21.4
Cor-pulmonale	8	19.0
CKD	7	16.7
CVD	6	14.3
BEP	5	11.9
Pulmonary hypertension	4	9.5

Table-III

Distribution of the study patients according to diagnosis (n=42)

Diagnosis	Number of patients	Percentage
Acute severe asthma	3	7.1
Bronchiectasis	2	4.8
Post TB fibrosis	6	14.2
AECOPD with T2RF	7	16.7
Aspiration pneumonia with CVD	3	7.1
Bronchial carcinoma	4	9.5
Pneumonia	5	11.9
Post COVID fibrosis	2	4.8
Sepsis with ARDS	3	7.1
DPLD	3	7.1

Table-IV

Distribution of the study patients according to duration of mechanical ventilation (n=42)

Duration of mechanical ventilation (days)	Number of patients	Percentage
≤7	35	83.3
>7	7	16.7
Mean±SD	6.0	±1.9
Range (min-max)	2.0	-11.0

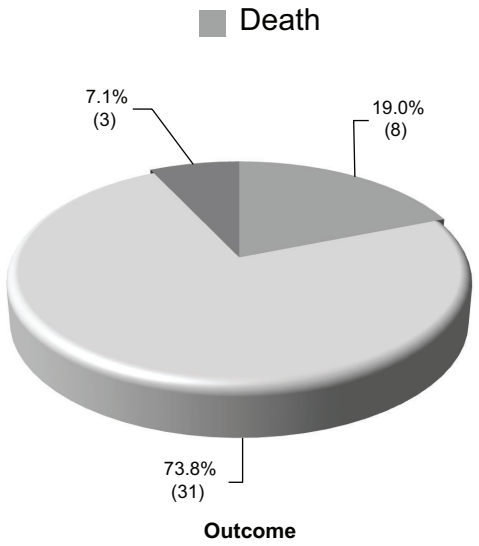


Fig.-1: *Outcome of mechanical ventilation*

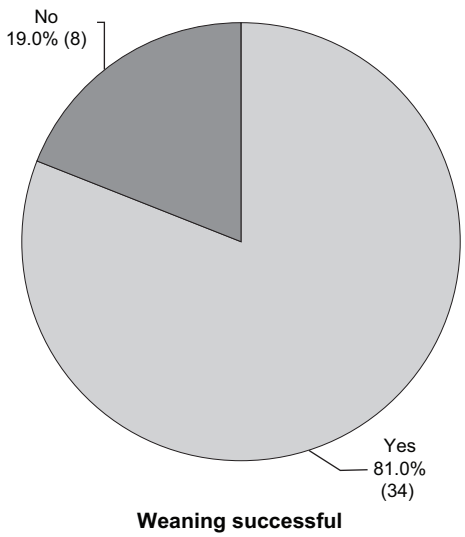


Fig.-2: *Weaning from Mechanical Ventilation*

Table-V

Association between SOFA score maximum with duration of mechanical ventilation (n=42)

SOFA score	Number of patients	Duration of mechanical ventilation (days) Mean±SD	P value
≤6 (Low)	9	4.7±1.2	
7-10 (medium)	28	6.3±1.7	0.04[s]
>10 (high)	5	7.0±2.9	

s= significant

P value reached from ANOVA test

Table-VI

Association of SOFA maximum score with outcome (n=42)

SOFA score	Outcome						P value
	Death (n=8)		Switched to multidisciplinary facility ICU (n=3)		Survived (n=31)		
	n	%	N	%	n	%	
≤6 (Low)	0	0.0	1	33.3	8	25.8	
7-10 (Medium)	3	37.5	2	66.7	23	74.2	0.001[s]
>10 (High)	5	62.5	0	0.0	0	0.0	

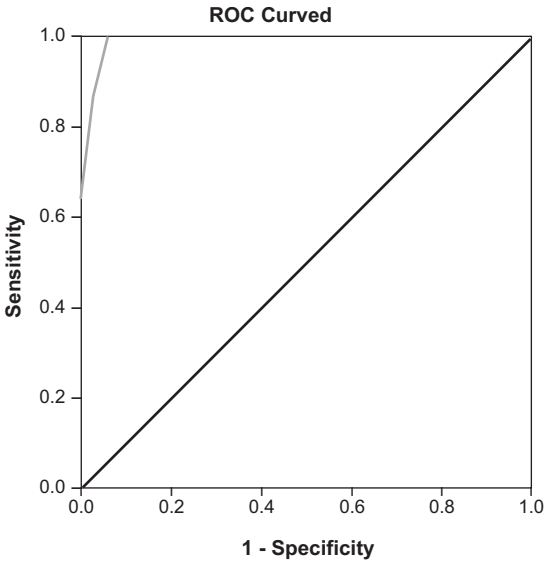
s= significant

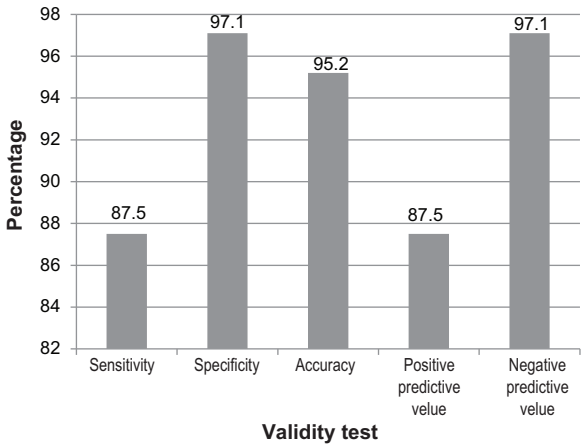
P value reached from chi square test

Table-VII

Receiver-operator characteristic (ROC) curve of SOFA score maximum level for prediction of mortality

	Cut of value	Sensitivity	Specificity	Area under the ROC curve	95% Confidence interval (CI)	
					Lower bound	Upper bound
SOFA score maximum	9.5	87.5	97.1	0.991	0.970	1.000





Receiver-operator characteristic curves of SOFA score maximum.

Table-VIII

Association between SOFA score cut off value with duration of mechanical ventilation (n=42)

SOFA score	Number of patients	Duration of mechanical ventilation (days) Mean±SD	P value
≥9.5	8	6.8±3.3	0.022[s]
<9.5	34	5.8±1.4	

s= significant

P value reached from unpaired t-test

Table-IX

Association between SOFA score cut off value with outcome (n=42)

SOFA score	Outcome						P value
	Death (n=8)		Switched to multidisciplinary facility ICU (n=3)		Survived (n=31)		
	n	%	N	%	n	%	
≥9.5	7	87.5	1	33.3	0	0.0	0.001[s]
<9.5	1	12.5	2	66.7	31	100.0	

s= significant

P value reached from chi square test

Discussion:

In this present study it was observed that 12(28.6%) patients belonged to age 61-70 years. The mean age was found 58.5±18.6 years with range from 19 to 90 years. Almost same study conducted by Anami et al. (2010) where they found patient ages ranged from 18 to 104 years, with a mean (±SD) of 56.7 (±19.1) years[5], supports our current study findings.

In this study it was observed that majority 39(92.9%) patients were male. Dehghani et al. (2016) reported that of the 61 patients in the sample, 46 were males (75.4%) and 15 were females (24.6%)[6]. Lee et al. (2017) had observed that male was 67.0% and female was 33.0%[7].The dominance of the male patients may be due to the fact that most of our patients were COPD patients and COPD is most commonly seen in male in our country.

Regarding co-morbidities in this study it was observed that 24(57.1%) patients had DM followed by 21(50.0%) HTN, 9(21.4%) IHD, 8(19.0%) corpulmonale, 7(16.7%) CKD, 6(14.3%) CVD, 5(11.9%) BEP and 4 (9.5%) were pulmonary hypertension. Almost similar findings were reported in several other studies. Muzaffar et al. (2017) documented that most of them had cardiac co-morbidities (coronary artery disease) (41%) followed by diabetes mellitus (33%), chronic kidney disease (12%), respiratory co-morbidities (chronic obstructive pulmonary disease, asthma, or history of pulmonary tuberculosis) (10%), and both respiratory and cardiac co-morbidities (4%)[8]. Consisted that 49 participants had diabetes mellitus (27%) and 24 patients (13%) had chronic kidney disease[9].

Nearly two-third (73.8%) of patients in our study survived and 19% patients died. Lee et al. (2017) reported that the mortality rate was 23%[7]. Muzaffar et al. (2017) had observed ICU mortality 33.0%[8]. Described the overall mortality seen in the study was 30% (60 patients)[9]. The mortality reported in earlier studies varied from 5 to 20% (Freund et al. 2017)[10]. This dissimilarity in this study may be explained by the fact that this study was conducted at a specialized respiratory ICU and hence a majority of the patients included were cases referred from other centers.

In this study it was observed that in 35(83.3%) patients, duration of mechanical ventilation were ≤7 days. The mean duration of mechanical ventilation was found 6.0±1.9 days with range from 2 to 11 days. In this study it was observed that in 22(64.7%) patients weaning started from more than 3 days. The mean weaning days were found 3.8±0.9 days with range from 2 to 5 days. Several other study findings are almost consistent with our findings. Afessa et al. (1999) documented that 57 patients (48%) were successfully weaned from MV within 3 days of weaning assessment, and 67 (57%) were weaned within 7 days[11]. Muzaffar et al. (2017) also found the median weaning duration was 14 (9.5 - 19) days[8]. However, those are not in agreement with our study result may be due to different multidisciplinary ICU setting.

Regarding SOFA score in this study we have found SOFA score (maximum) 7-10 were in 28(66.7%) patients. The mean SOFA score (maximum) was found 8.0±2.0 with range from 5 to 14. Lee et al. (2017) consisted that the average of SOFA score from the first day of admission of respiratory care center was 5.5±2.3[7]. Our findings almost correspond with the other studies.

In this study based on the receiver-operator characteristic (ROC) curves SOFA score maximum had area under curve 0.991. Receiver-operator characteristic (ROC) was constructed by using SOFA score level, which gave a cut off value 9.5, with 87.5% sensitivity and 97.1% specificity for prediction of mortality and accuracy 95.2%, positive predictive value 87.5% and negative predictive value 97.1%. In a study done by Lee et al. (2017) where they observed the area under ROC curve of SOFA score was 0.645 (P value=0.012). The optimal cut-off point of SOFA score for weaning predict was 4.5 with 72.0 % sensitivity and 54.0% specificity[7]. Dehghani et al. (2016) described the area under the ROC curve was 0.499 in predicting the failure of the first weaning based on the SOFA score at admission and the cut off point for the SOFA score at admission was 5.5. The sensitivity and specificity for predicting in-hospital mortality were 68% and 69%, respectively[6]. Other studies have reported a sensitivity and specificity of 70% and 79%, respectively, which is similar to what was observed in the study[10]. Timing of ICU admission may be an important cause of the different values in different studies. In this respect our results are consistent with other studies.

In our study we found that SOFA score ≥9.5 in 8 cases and their mean duration of mechanical ventilation was 6.8±3.3 days and among them

7(87.5%) patients expired. SOFA score <9.5 was found in 34 cases and their mean duration of mechanical ventilation was 5.8±1.4 days were successfully liberated from mechanical ventilation. The difference was statistically significant (p>0.05) between two groups. Similar study carried out by Afessa et al. (1999) documented that 57 patients (48%) were successfully weaned from MV within 3 days of weaning assessment, and 67 (57%) were weaned within 7 days[11]. This finding is almost consistent with our current study.

A limitation of our study is that it was a single center study. The study period was short. Further multicenter study with long duration may be carried out.

Conclusion:

In conclusion, SOFA score may offer a cut off value 9.5 with successful weaning among mechanically ventilated patients. SOFA score is a better way to predict early weanibility from mechanical ventilation. SOFA scores may be used as an important predictive index for weaning outcome of patients' from mechanical ventilation..Further large scale multicenter study may be carried out.

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ORIGINAL ARTICLE

Association of Metabolic Syndrome with Chronic Obstructive Pulmonary Disease (COPD)

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Abstract:

Background: *Chronic obstructive pulmonary disease (COPD) is thought to have increased association with metabolic syndrome (MS) which represents a cluster of factors that increase the risk of cardiovascular diseases and diabetes mellitus. However, the extent of association of COPD with MS and its individual components are still an unsettled issue, and it is likely to vary from population to population. This study was undertaken to assess association of COPD with metabolic syndrome.*

Methods: *This cross-sectional study conducted at the Department of Respiratory Medicine in National Institute of Diseases of the Chest and Hospital from January 2019–December 2019. A total of 91 patients with chronic obstructive pulmonary disease (COPD) were enrolled in this study.*

Results: *Out of 91 patients with COPD, more than one third (34.1%) patients were belonged to age 51-60 & 61-70 years respectively with mean age 60.4±10.9 years ranging from 42 to 90 years. Majority (85.7%) patients were male. Male to female ratio was 6:1. Twenty seven (29.7%) were service holder and most of the patients 76(83.5%) were smoker. Mean BMI was 20.6±4.0 kg/m^2, mean waist circumference was 86.9±6.8 cm, mean SBP 120.1±17.5 mmHg and mean DBP 76.3±11.1 mmHg. Mean FEV_1/FVC post bronchodilator was 51.2±9.5 percent. Mean triglycerides was 149.9±38.4 mg/dl, mean HDL-C was 39.4±9.8 mg/dl, mean fasting glucose was 104.1±28.0 mg/dl. Metabolic syndrome was found in 19(20.9%) patients. Age, sex, occupational status, smoking, BMI, waist circumference, hypertension, triglycerides, HDL-C, fasting glucose and metabolic syndrome were not statistically significant (p>0.05) when compared grade of COPD.*

Conclusion: *In conclusion, the present study demonstrated that metabolic syndrome present in 20.9% of COPD patients. Age, sex, occupational status, smoking, BMI, waist circumference, hypertension, triglycerides, HDL-C, fasting glucose and metabolic syndrome were not statistically significant when compared grade of COPD. Thus, considering COPD as a systemic disease and screening for components of metabolic syndrome could form a part of routine work-up of these patients.*

Keywords: *Metabolic syndrome (MS), Chronic obstructive pulmonary disease (COPD).*

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Introduction:

The metabolic syndrome (MS) represents a cluster of risk factors that increases the risk for developing diabetes mellitus[1], nonfatal and fatal cardiovascular disease[2]. The common risk factors are raised fasting plasma glucose, abdominal obesity, dyslipidemia, and high blood pressure[3]. This syndrome has outspread as epidemic worldwide[4]. Some studies from USA and Australia found 20–25% of the adult population suffering from MS[5,6]. Different international expert committees developed varied clinical criteria for the diagnosis of metabolic syndrome. Among them, definition prepared by International Diabetic Federation (IDF), National Cholesterol Education Program–Third Adult Treatment Panel (NCEP ATP III), and WHO were wildly accepted[7]. As a gross, all the Expert Committee agreed that obesity, insulin resistance, dyslipidemia, and hypertension are the important markers of MS[8]. The exact pathogenesis of MS is unknown, but it is predicted that obesity, insulin resistance associated with systemic inflammation are the causative factors[9].

Chronic obstructive pulmonary disease (COPD) is a major cause of health care burden throughout the world–wide, and the only leading cause of death that is increasing in prevalence[10]. COPD has a great impact on public health. It is one of the leading causes of mortality and morbidity in Bangladesh. The reduction of mortality and morbidity among COPD patients must remain in public health priority. COPD is a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary components are characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases[11]. COPD is not only a lung disease but also has some systemic effects. With the progression of this disease, systemic inflammation occurred among the COPD patients, and the patients suffered from different symptoms of chronic diseases, for example, dyslipidemia, diabetes mellitus, hypertension, coronary and peripheral artery diseases, anemia, osteoporosis, and rheumatoid arthritis. They are called as the comorbidities of the COPD. The exact pathological way of these systemic inflammation is not known but is believed to be related to enhance systemic inflammation and oxidative stress. These mechanisms may be multifactorial. The association between chronic inflammation and increased insulin resistance may be accounted for disruption of insulin receptor signaling by inflammatory mediators. Usually, insulin resistance occurs in combination with obesity, dyslipidemia, and hypertension. These together make up the "MS" which is a major determinant of cardiovascular morbidity and mortality[12]. Link between metabolic syndrome (MS) and COPD has been observed in several cross sectional and longitudinal studies, and the syndrome has been identified as an independent risk factor for worsening respiratory symptoms, increasing lung function impairment, pulmonary hypertension.

Methods:

This cross-sectional study was conducted in the Department of Respiratory Medicine of National Institute of the Diseases of the Chest & Hospital (NIDCH), Mohakhali, Dhaka, Bangladesh, from January 2019 to December 2019. A total of 91 patients with COPD were selected by purposive sampling who attended in the above mentioned hospital (both outpatients and admitted patients) were included this study according to the inclusion and exclusion criteria of the study. In first phase, the eligible participants were explained the study purpose and written informed consent was obtained from the patients and the relevant socio-demographic characteristics and history of the smoking were collected by face to face interview using predesigned datasheet. After completion of interview the patient was examined physically, all information and findings were recorded in the preformed proforma. The relevant investigations, like- Complete blood count (CBC), Fasting Blood Sugar, Fasting lipid profile, Serum Creatinine, Serum Bilirubin, SGPT, Serum Electrolytes, ECG, Chest X-Ray P/A view, Spirometry with reversibility, USG of Whole abdomen were done and recorded. Patients diagnosed with COPD based on GOLD guidelines, on history, clinical examination, and pulmonary function test (FEV1/FVC <0.7), age >40 years. Presence of asthma or other chronic respiratory diseases, presence of malignancy or serious comorbidities that would

prevent the study completion, patients with active pulmonary tuberculosis and patients with acute exacerbation of COPD requiring ICU admission were excluded from the study.

Results:

A total ninety one patients with COPD were included in this study based on inclusion and exclusion criteria. The findings obtained from data analysis are presented below:

Table-I

Demographic characteristics of the study patients (n=91)

Demographic characteristics	Number of patients	Percentage
Age (years)		
≤50	20	22.0
51-60	31	34.1
61-70	31	34.1
71-80	5	5.5
>80	4	4.4
Mean ± SD	60.4±10.9	
Range (min-max)	42.0-90.0	
Gender		
Male	78	85.7
Female	13	14.3
Occupational status		
Service	27	29.7
Farmer	23	25.3
Business	13	14.3
Shop keeper	9	9.9
Teacher	6	6.6
House wife	5	5.5
Day labour	3	3.3
Rickshaw puller	3	3.3
Clark	1	1.1
Village police	1	1.1
Smoking		
Yes	76	83.5
No	15	16.5

Table-II

Distribution of the study patients according to waist circumference (n=91)

Waist circumference (cm)	Number of patients	Percentage
Abnormal (Male >102 cm; female >88 cm)	3	3.3
Normal (Male ≤102 cm; female d”88 cm)	88	96.7
Mean±SD	86.9±6.8	
Range (min-max)	74.0-104.0	

Table-III

Distribution of the study patients according to blood pressure (n=91)

Blood pressure	Mean±SD
SBP (mmHg)	120.1±17.5
Range (min-max)	90.0-160.0
DBP (mmHg)	76.3±11.1
Range (min-max)	60.0-100.0

Table-IV

Distribution of the study patients according to triglycerides (n=91)

Triglycerides (mg/dl)	Number of patients	Percentage
≤150 (Normal)	59	64.8
>150 (Abnormal)	32	35.2
Mean±SD	149.9±38.4	
Range (min-max)	65.0-311.0	

Table-V

Distribution of the study patients according to HDL-C (n=91)

HDL-C (mg/dl)	Number of patients	Percentage
≥40 (Normal)	41	45.1
<40 (Abnormal)	50	54.9
Mean±SD	39.4±9.8	
Range (min-max)	28.0-78.0	

Table-VI

Distribution of the study patients according to fasting glucose (n=91)

Fasting glucose (mg/dl)	Number of patients	Percentage
≤100 (Normal)	57	62.6
>100 (Abnormal)	34	37.4
Mean±SD	104.1±28.0	
Range (min-max)	78.0-290.0	

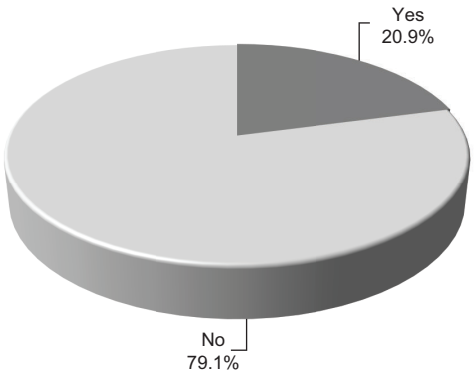

Fig.-1: *Pie chart showing metabolic syndromem of the study patients (n=91).*

Table-VII

Association between demographic characteristics with COPD (n=91)

Demographic characteristics	COPD				P value
	Grade III (n=41)		Grade II (n=50)		
	N	%	n	%	
Age (years)					
≤50	6	14.6	14	28.0	
51-60	12	29.3	19	38.0	
61-70	17	41.5	14	28.0	
71-80	3	7.3	2	4.0	
>80	3	7.3	1	2.0	
Mean±SD	62.8±11.0		58.4±10.6		[a]0.058
Range (min-max)	43.0-90.0		42.0-90.0		
Gender					
Male	37	90.2	41	82.0	[b]0.263
Female	4	9.8	9	18.0	
Occupational status					
Service	10	24.4	17	34.0	
Farmer	14	34.1	9	18.0	
Business	4	9.8	9	18.0	
Shop keeper	5	12.2	4	8.0	
Teacher	5	12.2	1	2.0	[b]0.105
House wife	0	0.0	5	10.0	
Day labour	1	2.4	2	4.0	
Rickshaw puller	2	4.9	1	2.0	
Clark	0	0.0	1	2.0	
Village police	0	0.0	1	2.0	
Smoking					
Yes	37	90.2	39	78.0	[b]0.117
No	4	9.8	11	22.0	

[a]P value reached from unpaired t-test; [b]P value reached from chi square test

Table-VIII

Association between BMI with COPD (n=91)

BMI (kg/m^2)	COPD				P value
	Grade III (n=41)		Grade II (n=50)		
	N	%	n	%	
<18.5	15	36.6	13	26.0	
18.5-24.9	22	53.7	32	64.0	
25.0-29.9	2	4.9	5	10.0	
≥30.0	2	4.9	0	0.0	
Mean±SD	20.0±4.0		21.0±3.1		0.179
Range (min-max)	12.9-33.7		14.9-28.2		

P value reached from unpaired t-test

Table-IX

Association between waist circumference with COPD (n=91)

Waist circumference (cm)	COPD				P value
	Grade III (n=41)		Grade II n=50)		
	n	%	n	%	
Abnormal (Male >102 cm; female >88 cm)	2	4.9	1	2.0	
Normal (Male ≤102 cm; female ≤88 cm)	39	95.1	49	98.0	
Mean±SD	88.1±7.4		85.9±6.0		0.116
Range (min-max)	74.0-104.0		75.0-101.0		

P value reached from unpaired t-test

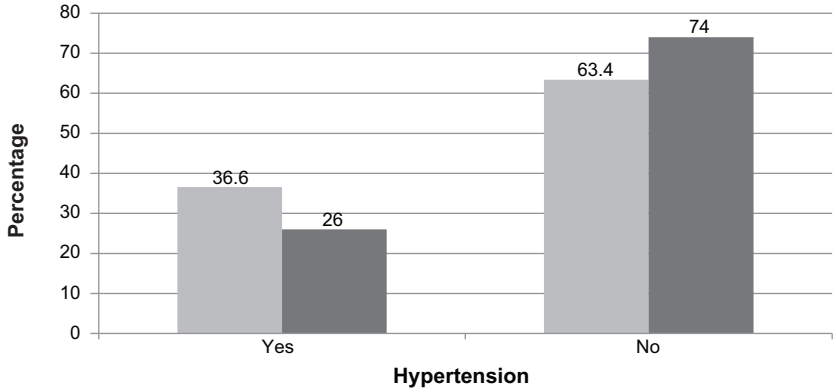

Fig.-2: *Bar diagram showing hypertension of the study patients (n=91)*

Table-X

Association between triglycerides with COPD (n=91)

Triglycerides (mg/dl)	COPD				P value
	Grade III (n=41)		Grade II (n=50)		
	N	%	N	%	
≤150 (Normal)	25	61.0	34	68.0	
>150 (Abnormal)	16	39.0	16	32.0	
Mean±SD	153.7	±42.9	146.7	±34.3	0.385
Range (min-max)	92.0	-311.0	65.0	-260.0	

P value reached from unpaired t-test

Table-XI

Association between HDL-C with COPD (n=91)

HDL-C (mg/dl)	COPD				P value
	Grade III (n=41)		Grade II (n=50)		
	N	%	N	%	
≥40 (Normal)	15	36.6	26	52.0	
<40 (Abnormal)	26	63.4	24	48.0	
Mean±SD	39.3	±11.0	39.4	±8.7	0.959^{ns}
Range (min-max)	28.0	-78.0	28.0	-74.0	

P value reached from unpaired t-test

Table-XII

Association between fasting glucose with COPD (n=91)

Fasting glucose (mg/dl)	COPD				P value
	Grade III (n=41)		Grade II (n=50)		
	N	%	N	%	
≤100 (Normal)	24	58.5	33	66.0	
>100 (Abnormal)	17	41.5	17	34.0	
Mean±SD	108.7	±36.9	100.3	±17.2	0.158^{ns}
Range (min-max)	78.0	-290.0	80.0	-192.0	

P value reached from unpaired t-test .

Table XIII

Association between metabolic syndrome with COPD (n=91)

Metabolic syndrome	COPD				P value
	Grade III (n=41)		Grade II (n=50)		
	N	%	N	%	
Yes	10	24.4	9	18.0	0.456
No	31	75.6	41	82.0	

P value reached from chi square test

Discussion:

This cross-sectional study was carried out with an aim to assess association of COPD with metabolic syndrome.

In this study it was observed that more than one third (34.1%) patients belonged to age 51-60 & 61-70 years respectively. The mean age was 60.4±10.9 years ranging from 42 to 90 years. The reason for the difference of age at presentation in various regions of the world may be due to geographic/ ethnic influence.

In our study it was observed that majority (85.7%) patients were male and 13(14.3%) patients were female. In a study of Pasha et al. (2018) observed that among each group there were forty-three (84.3%) males and eight (15.7%) females.

Our study showed that 27(29.7%) were service holder, 23(25.3%) farmers. This difference across various studies may be due to different demographic and geographic distribution of the population.

In this present study it was observed that 76(83.5%) were smoker. In present study, maximum proportions of smokers were in GOLD stage-3 (70.6%) followed by stage-2 (60%) followed by stage-4 (57.1%) and in GOLD stage-1 smokers were 40% but the difference was not significant (p>0.05).

In our study it was observed that majority (59.3%) patients had BMI 18.5-24.9 kg/m^2. Mean BMI was found 20.6±4.0 kg/m^2 with range from 12.9-33.7 kg/m^2. Mean BMI of study population was 26.22±7.22 kg/m^2.

In this current study it was observed that 3(3.3%) patients were found abnormal (male >102 cm; female >88 cm) waist circumference. Mean waist circumference was found 86.9±6.8 cm with range from 74.0-104.0 cm. Almost similar study conducted by Acharyya et al. (2016) which showed mean waist circumference was 87±17 cm. Kumar et al. (2020) in their found that mean WC of study population was 88.30±14.61 cm.

This study showed that mean SBP was found 120.1±17.5 mmHg with range from 90.0-160.0 mmHg. The mean DBP was found 76.3±11.1 mmHg with range from 60.0-100.0 mmHg.

In this study it was observed that 32(35.2%) patients had triglycerides >150 mg/dl. Mean triglycerides was found 149.9±38.4 mg/dl with range from 65.0-311.0 mg/dl.

In this present study it was observed that 50(54.9%) patients found HDL-C <40 mg/dl. Mean HDL-C was found 39.4±9.8 mg/dl with range from 28.0-78.0 mg/dl.

Our study showed that 34(37.4%) patients had fasting glucose >100 mg/dl. Mean fasting glucose was found 104.1±28.0 mg/dl with range from 78.0-290.0 mg/dl.

Our study showed that metabolic syndrome was found in 19(20.9%) patients. In a study of Pasha et al. (2018) observed that metabolic syndrome was 16(31.4%) patients.

In this study it was observed that age, sex, occupational status and smoker were not statistically significant (p>0.05) between two group.

In this current study it was observed that mean BMI was found 20.0±4.0 kg/m^2 in COPD grade III and 21.0±3.1 kg/m^2 in COPD grade II. The difference was not statistically significant (p>0.05) between two group.

In my study it was observed that mean waist circumference was found 88.1±7.4 cm in COPD grade III and 85.9±6.0 cm in COPD grade II. The difference was not statistically significant (p>0.05) between two group.

In this present study it was observed that 15(36.6%) patients were found hypertension in COPD grade III and 13(26.0%) in COPD grade II. The difference was not statistically significant (p>0.05) between two group.

Our study showed that mean triglycerides was found 153.7±42.9 mg/dl in COPD grade III and 146.7±34.3 mg/dl in COPD grade II. The difference was not statistically significant (p>0.05) between two group.

In this study observed that mean HDL-C was found 39.3±11.0 mg/dl in COPD grade III and 39.4±8.7 mg/dl in COPD grade II. The difference was not statistically significant (p>0.05) between two group.

In my study it was observed that mean fasting glucose was found 108.7±36.9 mg/dl in COPD grade III and 100.3±17.2 mg/dl in COPD grade II. The difference was not statistically significant (p>0.05) between two group.

Our study showed that 10(24.4%) patients was found metabolic syndrome in COPD grade III and 9(18.0%) in COPD grade II. The difference was not statistically significant (p>0.05) between two group. Incidence of metabolic syndrome is not related to severity of COPD. It may increase with any stage of COPD.

Conclusion:

In conclusion, the present study has demonstrated that metabolic syndrome were 20.9% patients. Age, sex, occupational status, smoker, BMI, waist circumference, hypertension, triglycerides, HDL-C, fasting glucose and metabolic syndrome were not statistically significant. Thus, considering COPD as a systemic disease and screening for components of metabolic syndrome could form a part of routine work-up of these patients. These findings suggest that physicians should screen COPD patients for associated metabolic syndrome. Management of these disorders may reduce the risk of overall morbidity and mortality in patients with COPD.

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ORIGINAL ARTICLE

Association of Glycaemic Status (Hba_1c) with FEV_1 and FEV_1/ FVC Ratio in COPD Patients with Type 2 Diabetes Mellitus

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Abstract

Background: *Diabetes mellitus (DM) is an important and common comorbid condition associated with chronic obstructive pulmonary disease (COPD). Diabetes damages major organ systems through disrupted glycemic control and increased inflammation. Reduced pulmonary function has been observed in patients with type 2 diabetes. This functional impairment has been shown primarily through cross-sectional associations between glycemic status (HbA_1c) with FEV_1 and FEV_1/FVC ratio.*

Materials & Methods: *This Cross sectional observational study was conducted in the department of Respiratory Medicine of National Institute of Diseases of the Chest and Hospital (NIDCH) from December 2019 to March 2021. Eighty Two diagnosed cases of COPD with type 2 DM who were treated in NIDCH were enrolled purposefully in this study.*

Results: *Sixty two percent (62.2%) patients had moderate obstruction (FEV_1 79-50 percent) with mean FEV_1 was 56.3±13.1 percent predicted. More than three fourth (76.8%) patients had FEV_1/FVC ratio 60-69 percent with mean FEV_1/FVC ratio was 63.3±4.7 percent predicted. Mean FEV_1 and FEV_1/FVC ratio was significantly lower in uncontrolled glycaemic status (HbA_1C) (p=0.001). In multivariate regression analysis, uncontrolled HbA_1C was found to be an independent predictor for low FEV_1 (<50%).*

Conclusion: *This study concluded that FEV_1 and FEV_1/FVC ratio were significantly lower in uncontrolled glycaemia than controlled glycemic group of COPD patients with type 2 DM. Uncontrolled HbA_1C was found to be independent predictor for low FEV_1 (<50%).*

Keyword: Hemoglobin A_1C (HbA_1C), Forced expiratory volume in one second (FEV_1), Forced vital capacity (FVC), Chronic obstructive pulmonary disease (COPD), Type 2 DM.

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Introduction:

Chronic obstructive pulmonary disease can be described by air flow limitation and chronic inflammatory disorder of lungs which is progressive and partially reversible through treatment and which occurs because of exposure of noxious particles and gases for a long term.[1] When chronic cough and sputum from airways for at least three months in each of two successive years without any other causes of chronic cough; associated with irreversible airflow limitation; then the group of chronic bronchitis and emphysema together defined as chronic obstructive pulmonary disease.[2] It has been associated with various systemic and co-morbid conditions like ishchaemic heart disease, type 2 diabetes, hypertension, osteoporosis, malnutrition, skeletal muscle dysfunction, endocrine disorders, lung cancer and anxiety.[1]

COPD determined as one of the main causes of mortality worldwide. In 2005, globally, COPD was responsible for 5% of all deaths.[3] It has been predicted to become the third leading cause of death worldwide by 2030.[4]

According to World Health Organization (WHO), sixty-five million people suffer from moderate to severe form of chronic obstructive pulmonary disease.

Diabetes mellitus is selected as a chronic condition also and increasing rate of diabetes leads to affect around 600 million people by 2035.[5] Progression of COPD can be increased by type 2 DM which causes COPD-related mortality. Other studies showed that, patients of COPD gained a protective effect from the Diabetes-associated adiposity which can reduce the death of individuals having COPD.[5]

Some studies have showed that, in COPD patient, there are impact on both lung function and quality of life. Many other studies describe that, DM is associated with impaired pulmonary function. Other studies suggest that there are no association between DM and lung function.[4]

Inhaled corticosteroid which is usually prescribed in case of patient of COPD was also related with increased incidence of type 2 DM.[6]

Development of COPD can be caused by Diabetic patients as well as COPD patients are also at risk of developing diabetes mellitus because of sedentary life, smoking, obesity, oxidative stress, increased inflammatory condition and corticosteroid therapy.[4]

90% of diabetes cases represent type 2 DM which results commonly from adiposity and sedentary lifestyle, having genetic predisposition.[7]

Combination of insulin resistance and non-functioning pancreatic beta cells that causes failure of control of blood glucose level of an individual are the characteristic features of type 2 DM. Increased incidence and prevalence of diabetes mellitus specifically in Asians are being alarming day by day.[8]

Respiratory system is affected by hyperglycemia through the induction of oxidative stress, systemic inflammation, hypoxemia, altered gas exchange and structural changes of lung tissue.[5] Diabetes and prior to development of diabetes have associated with obstruction on spirometry.[4] Airflow limitation and reduced lung volume are chronic complications of type 2 DM. Lower forced expiratory volume in 1s (FEV_1) and forced vital capacity (FVC) are the features of diabetic patients also.[5]

In case of diabetic patient, four sources are selected as the origins of lung function impairment: such as (a) non-enzymatic glycosylation of lung elastin and collagen reduces the elasticity of the lung, (b) Reduction of blood volume of pulmonary capillary and diffusing capacity by thickening of alveolar epithelial basal lamina and microvascular changes in pulmonary capillary beds, (c) Reduction of muscle tone of diaphragm can be created by autonomic neuropathic lesion of the phrenic nerves, and (d) Hyperglycemia induced increased bacterial colonization is responsible for frequent acute exacerbations of COPD.[9]

To address these issues, this study was conducted to assess the lung function among the individuals who have both COPD and type 2 Diabetes Mellitus and explore the relationship between lung function and glycaemic control of patients with COPD.

Material and methods:

This cross-sectional observational study was carried out in the outpatient department of Respiratory Medicine of National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka over a period December 2019 to March 2021.

The sample of the study was selected using consecutive sampling technique. From the attendees of outpatient department (OPD), a group of patients with COPD and type 2 DM was selected using a non-probability consecutive sampling technique. The consecutive sampling technique provides the opportunity to choose eligible

participants until the desired sample size were reached. Subjects with exacerbation, asthma, pneumonia, pulmonary TB, bronchiectasis, DPLD, bronchial carcinoma and cardiac disease were excluded in this study.

Glycaemic control was defined according to the HbA_1C target of <7.0% as recommended by American Diabetes Association.[10]

Statistical Package for Social Science (SPSS) version 23 for windows was used to analyze the data. Statistical analysis was done by unpaired 't' test and multiple regression analysis as applicable. P values <0.05 was considered as statistically significant.

Results:

The association of glycaemic status (HbA1c) with FEV_1 and FEV_1/ FVC ratio in COPD patients with type-2 diabetes mellitus. This cross-sectional observational study was carried out in the department of Respiratory Medicine of National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka. A total of 82 patients with stable COPD with type 2 diabetes mellitus were included in this study, who fulfilled the inclusion and exclusion criteria. The findings obtained from data analysis are presented below.

Majority 36(43.9%) patients belonged to age 61-70 years. The mean age was found 59.2±6.5 years with range from 45 to 69 years. Majority 78(95.1%) patients were male with male-female ratio 19.5:1. Thirty five 35(42.7%) were businessman. The mean BMI was found 25.1±2.8 kg/m^2 with range from 20.6 to 30.6 kg/m^2 [Table-I]. 68(82.9%) patients were found HbA_1C e"7 percent. The mean HbA_1C was found 8.2±1.4 percent with range from 6.2 to 12.9 percent [Table-II].

Study shows that 51(62.2%) patients had moderate FEV_1 (79-50 percent). The mean FEV_1 was found 56.3±13.1 percent with range from 27 to 88 percent. More than three fourth (76.8%) patients had FEV_1/ FVC ratio 60-69%. The mean FEV_1/FVC ratio was 63.3±4.7 percent with range from 53 to 69 percent [Table-III].

In this study 43(63.2%) patients were found FEV_1 level 79-50 percent in uncontrolled glycaemic group and 8(57.1%) in controlled glycaemic group. The mean FEV_1 was found 54.1±11.6 percent in uncontrolled glycaemic group and 66.9±14.9 percent in controlled glycaemic group. So, it reveals that the mean FEV_1 (%)was significantly lower in uncontrolled glycaemic group than controlled glycaemic group and the difference was statistically significant (p<0.05) between two groups [Table-4]. Similarly 49(72.1%) patients had FEV_1/ FVC ratio 60-69% in uncontrolled glycaemic group and 14(100.0%) in controlled glycaemic group. The mean FEV_1/FVC ratio was found 62.4±4.8 percent in uncontrolled glycaemic group and 67.3±1.7 percent in controlled glycaemic group. So, here it has been shown that mean FEV_1/FVC ratio (%) is significantly lower in uncontrolled than controlled glycaemic group and the difference was statistically significant (p<0.05) between two groups [Table-V].

In multivariate analysis, uncontrolled HbA_1C was found to be an independent predictor for lowFEV_1 as here p value is low (p<0.05). However, age, male, tobacco use, hypertension and obesity were not found to be independent predictors for lowFEV_1 as in every condition p value is high (p>0.05) [Table-VI]. Multivariate analysis also reveals age, male, tobacco use, hypertension, obesity and uncontrolled HbA_1C were not found to be independent predictors for lower FEV_1/FVC ratio (<60%) because in every conditions p value was high (p>0.05) [Table-VII].

Table-I

Patient demography (n=82)

Variables	Frequency	Percentage
Age (years)		
41-50	13	15.9
51-60	33	40.2
61-70	36	43.9
71-80	0	0.0
Mean±SD	59.2±6.5	
Range (min-max)	45.0-69.0	
Sex		
Male	78	95.1
Female	4	4.9
Occupational status		
Businessman	35	42.7
Service holder	20	24.4
Cultivator	19	23.2
House wife	4	4.9
Shopkeeper	2	2.4
Cook	2	2.4
BMI (kg/m^2)		
<18.5	0	0.0
18.5-24.9	52	63.4
25.0-29.9	23	28.0
≥30.0	7	8.5
Mean±SD	25.1±2.8	
Range (min-max)	20.6-30.6	

Table-II

Distribution of the patients according to glycaemic status based on HbA$_1$C (n=82)

HbA$_1$C (%)	Frequency	Percentage
<7.0 (Controlled)	14	17.1
≥7.0(Uncontrolled)	68	82.9
Mean±SD	8.2±1.4	
Range (min-max)	6.2-12.9	

Spirometric variations of study population (n=82)

Table-III

Spirometric variables of study population (n=82)

FEV$_1$ (%)	Frequency	Percentage
<30 (Very severe)	2	2.4
49-30 (Severe)	22	26.8
79-50 (Moderate)	51	62.2
≥80 (Mild)	7	8.5
Mean±SD	56.3±13.1	
Range (min-max)	27.0-88.0	
FEV$_1$/FVC ratio (%)		
50-59	19	23.2
60-69	63	76.8
Mean±SD	63.3±4.7	
Range (min-max)	53.0-69.0	

Table-IV

Association between FEV$_1$ with glycaemic status of study population (n=82)

FEV$_1$ (%)	Glycaemic status (HbA$_1$C)				t value	P value
	Uncontrolled(n=68)		Controlled(n=14)			
	n	%	n	%		
<30 (Very severe)	2	2.9	0	0.0		
49-30 (Severe)	20	29.4	2	14.3		
79-50 (Moderate)	43	63.2	8	57.1		
≥80 (Mild)	3	4.4	4	28.6		
Mean±SD	54.1±11.6		66.9±14.9		3.57	0.001^s
Range (min-max)	27.0-82.0		40.0-88.0			

s= significant

P value reached from unpaired t-test

Table-V

Association between FEV_1/FVC ratio with glycaemic status of study population (n=82)

FEV_1/FVC ratio (%)	Glycaemic status (HbA_1C)				t value	P value
	Uncontrolled(n=68)		Controlled(n=14)			
	n	%	n	%		
50-59	19	27.9	0	0.0		
60-69	49	72.1	14	100.0		
Mean±SD	62.4±4.8		67.3±1.7		3.75	0.001[s]
Range (min-max)	53.0-69.0		64.0-69.0			

s= significant

P value reached from unpaired t-test

Table-VI

Multivariable Regression Analysis for low FEV_1 (<50%)

	Adjusted OR	95% CI		P value
		Lower	Upper	
Age (≥61 years)	0.501	0.172	1.459	0.205[ns]
Male	2.982	0.431	84.407	0.980[ns]
Tobacco use	1.188	0.197	6.854	0.864[ns]
Hypertension	1.905	0.644	5.635	0.244[ns]
Obesity	0.231	0.026	2.424	0.249[ns]
Uncontrolled HbA_1C	2.668	1.129	6.287	0.023[s]

s= significant, ns= not significant; OR=Odds Ratio

p value reached from multivariate analysis by binary logistic regression analysis

Table-VII

Multivariable Regression Analysis for lower FEV_1/FVC ratio (<60%)

	Adjusted OR	95% CI		P value
		Lower	Upper	
Age (≥61 years)	1.788	0.410	5.968	0.309[ns]
Male	2.112	0.151	88.340	0.989[ns]
Tobacco use	1.174	0.218	8.287	0.738[ns]
Hypertension	0.752	0.368	3.993	0.752[ns]
Obesity	0.272	0.027	2.698	0.266[ns]
Uncontrolled HbA_1C	0.186	0.082	1.097	0.062[ns]

ns= not significant; OR=Odds Ratio

p value reached from multivariate analysis by binary logistic regression analysis

Discussion:

This cross sectional observational study was carried out with an aim to assess the association of glycaemic status (HbA_1c) with FEV_1 and FEV_1/FVC ratio in COPD patients with type 2 DM attending in outpatient department of NIDCH. Out of 82 patients of COPD with type 2 diabetes mellitus who fulfilled the inclusion and exclusion criteria during the period from December 2019 to March 2021 were included in this study.

In this study it was observed that majority 36(43.9%) patients belonged to age 61-70 years. The mean age was found 59.2±6.5 years with range from 45 to 69 years. Almost similar study conducted by Ajit et al.[3] where they found the mean age among study participants was 58.4±11.6 years. Mekov et

al.[4] reported mean age of patients was 65.1±9.9 years. Another study conducted by Adiody et al.[1] where they observed maximum patients were in the age group of 61-70 years showing that COPD commonly affects the elderly population.

Here it has been found majority 78(95.1%) patients were males and 4(4.9%) were females. Male-female ratio was 19.5:1. Almost similar study documented by Ajit et al.[3] where they showed out of 412 patients, 328 (79.6%) were males and 84 (21.6%) females with male-female ratio 3.9:1. Nemagouda[11] described out of 52 patients, males were 30(58%) and females were 22(42%). Mekov et al.[4] also consisted that 71.1% were males, 28.9% were females.

This study revealed almost two third (63.4%) patients were normal body mass index (BMI). The mean BMI was found 25.1±2.8 kg/m^2 with range from 20.6 to 30.6 kg/m^2. In a study done by Ajit et al.[3] where they observed mean body mass index of the participants was 23.47±3.7 kg/m^2. Nemagouda[11] also found the mean BMI was 23±2.4 kg/m^2.

Regarding glycaemic status based on HbA_1C in this study we have found 68(82.9%) patients were found HbA_1C ≥7 percent. The mean HbA_1C was found 8.2±1.4 percent with range from 6.2 to 12.9 percent. In Bangladeshi study conducted by Ali et al.[12] where they observed mean HbA_1C was found 6.48 percent in type 2 DM patients with diabetic duration 5-10 years and 7.21 percent in diabetic duration 10-20 years. Adiody et al.[1] reported mean HbA_1C was found 7.9±1.89 percent. Lecube et al.[13] described mean HbA_1C was found 7.5±1.4 percent. Another study conducted by Nemagouda[11] where they showed the mean HbA_1C was 8.8±1.7 percent.

Among the total 82 study patients 7(8.5%) had mild FEV_1 (≥80 percent), 51(62.2%) patients had moderate FEV_1 (79-50 percent) followed by 22(26.8%) had severe FEV_1 (49-30 percent), and only two (2.4%) had very severe FEV_1 (<30 percent). The mean FEV_1 was 56.3±13.1 percent with range from 27 to 88 percent. In a study of Ajit et al.[3] showed that the prevalence in mild, moderate, severe, and very severe COPD was 14.73%, 18.94%, 36.84% and 29.47%, respectively. Mekov et al.[4] reported that the mean FEV_1 was 55.34±19.5 percent. Lecube et al.[13] consisted the mean FEV_1 was found 88.4±19.7 percent.

Regarding association between FEV_1 with glycaemic status in this study it has been revealed 43(63.2%) patients were found FEV_1 level 79-50 percent in uncontrolled glycaemic group and 8(57.1%) in controlled glycaemic group. The mean FEV_1 was found 54.1±11.6 percent in uncontrolled glycaemic group and 66.9±14.9 percent in controlled glycaemic group. FEV_1 was significantly higher in controlled group than uncontrolled group ($p<0.05$). In the study done by Ajit et al.[3] where they showed that there was a severe decline in lung function (mean FEV_1 45.92±4.22) in people with diabetes as compared to non-diabetics (56.64±3.58) and it was found to be statistically significant ($P = 0.001$). Tanni et al.[14] consisted that the mean percentage of predicted value of FVC and FEV_1 were significantly lower in T2DM than those of control ($p<0.001$). Ali et al.[12] described the mean percentage of predicted values of FVC and FEV_1 in DM group was significantly ($p<0.001$) lower than those of control group. Nemagouda[11] reported the FEV_1, FVC & FEV_1/FVC had statistically significant difference with respect to BMI & HbA1c ($p <0.05$). The severity related to the duration & poor glycaemic control of type 2 diabetes mellitus. Dennis et al.[15] and McKeever et al.[16] in their studies have reported that diabetics with inadequate glucose control have a lower pulmonary function as compared to those with adequate control.

Regarding association between FEV_1/FVC ratio with glycaemic status in this study we have found 49(72.1%) patients had FEV_1/FVC ratio 60-69 percent in uncontrolled glycaemic group and 14(100.0%) in controlled glycaemic group. The mean FEV_1/FVC ratio was found 62.4±4.8 percent in uncontrolled glycaemic group and 67.3±1.7 percent in controlled glycaemic group. FEV_1/FVC ratio was significantly lower in uncontrolled group than controlled group ($p<0.05$). Adiody et al.[1] had observed their study lung function in terms of FEV_1, FVC, FEV_1/FVC, FEF 25-75 were the least in COPD with DM group than DM group. Ali et al.[12] documented that the mean percentage of predicted values of FEV_1/FVC (%) were significantly higher ($p<0.001$) in diabetic duration 10-20 years compared to 5-10 years. El Habashy et al.[17] showed that there was a significant decrease in pulmonary function tests among diabetic patients (FEV_1, FEV_1/FVC%, forced expiratory flow –25%–75%, maximal

voluntary ventilation, and PEF) compared with healthy controls and further proved that decline was exaggerated in poorly controlled DM. Tanni et al.[14] consisted that the difference in FEV_1/FVC between the groups was not significant. Several studies results showed significant lower values of all lung function parameters except FEV_1/FVC ratio strongly suggests impaired lung function in T2DM.[18-20]

In multivariable regression analysis, uncontrolled HbA_1C was found to be independent predictor for air way obstruction low (FEV_1 <50%). However, age, male, tobacco use, hypertension and obesity were not found to be independent predictors for low FEV_1. Another multivariate regression analysis was found age, male, tobacco use, hypertension, obesity and uncontrolled HbA_1C were not found to be independent predictors for lower FEV_1/FVC ratio (<60%). Rana et al.[21] observed that COPD patients had a multivariate relative risk of 1.38 (95% confidence interval [CI]: 1.14–1.67) for new onset type 2 DM. Mekov et al.[4] reported linear regression analysis shows that HbA_1C is a risk factor for lower FVC (R = 0.166, r2 = 0.027, p = 0.041, B = -3.116, 95% CI -6.111-0.122). Peng et al.[22] consisted linear associations of FVC% and FEV1% with risk of T2DM were found (Pnon-linearity > 0.05). Another study conducted by Baba et al.[23] documented that logistic regression analysis revealed that age (>60 years), HbA_1c levels (>5.6%), current smoking, and former smoking were significantly associated with a FEV_1/FVC <70%.

From above discussion in brief, it has been shown that out of 82 study patients of COPD with type 2 diabetes mellitus majority of the study patients were in uncontrolled glycaemic group. Mean FEV_1 (%) & FEV_1/FVC ratio (%) were significantly lower in patients of uncontrolled glycaemia than controlled glycaemic group. There was significant association of FEV_1 (%) & FEV_1/FVC ratio (%) with glycaemic status.

Conclusion:

This study revealed that there was significant association between HbA_1C with FEV_1 and FEV_1/FVC ratio in COPD patients with type-2 DM. Strict glycemic control is an important issue in those patients as uncontrolled glycaemia is associated with low FEV_1 and low FEV_1/FVC ratio.

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ORIGINAL ARTICLE

Pattern of Antibiotic Susceptibility of Bacteria Isolated from Patients of Bronchiectasis in ICU of NIDCH and Identification of Causes of their Antibiotics Resistance

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Abstract

Background and objective*: Antibiotics are usually started empirically in the bronchiectatic patients of ICU. The knowledge of pattern of local bacterial growth and their susceptibility to antibiotics is essential in selecting empirical antibiotic. Appropriate use of antibiotic in patients of bronchiectasis in ICU is crucial for optimal outcome. Antibiotic resistance pattern varies from one country to another even among health centres specially ICU. This study was conducted to know the current organisms and pattern of their antibiotic susceptibility in patients of bronchiectasis in ICU of NIDCH and identification of risk factors for their antibiotic resistance.*

Patients and Methods: *This cross-sectional study was conducted at the Intensive Care Unit(ICU) of National Institute of Diseases of the Chest and Hospital (NIDCH) for 1 years of period from july2019 to june2020. Total 50 patients with bronchiectasis admitted to ICU of NIDCH whose sputum or endotracheal specimen showed bacterial growth were included.*

Results: *Most common pathogen isolated was* Pseudomonas species *(40%), followed by* Acinetobacter species *(28%),* Klebsiella species *(20%),* Staphylococcus aureus *(16%),* Enterobacter species *(12%). Pathogens were sensitive to Colistin (100%), followed by Tigecycline, Amikacin, Levofloxacin, Meropenem, Cotrimoxazol whereas resistant to Ampicillin, Cefuroxime, Cefixim, Cefepime, Amoxicilin+clavulonic acid. Factors for antibiotic resistance found were patients taking antibiotic without doctor's prescription (62%), taking various type of antibiotic (56%), taking antibiotic on increased interval (52%), taking inadequate dose of antibiotics(50%), old age e"60 years (40%)and malnutrition(16%).*

Conclusion: *For patients of bronchiectasis in ICU consider empirical antimicrobial agent that covers Gram negative infection. Patients having risk factors for antibiotic resistance should be also considered during use of antibiotics.*

Key words: *Bronchiectatic patients of ICU,Current Bacterial Antibiotic Susceptibility,Causes of Resistance.*

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Introduction:

Bronchiectasis is described as indelibly dilated airways due to chronic or recurrent infection and chronic bronchial inflammation caused by improper clearance of several microorganisms.[1]

Recurrent attacks are a fundamental cause of morbidity and mortality and may promote significant economic and social costs.[2] Bronchiectasis is a heterogeneous chronic disease. Heterogeneity present both in stable and during exacerbations. Although the scientific community recognizes that bacterial infection is a cornerstone in the development of bronchiectasis exacerbations.[3]

Bacteria most commonly isolated from the airways of patients with bronchiectasis include Haemophilus influenzae, Pseudomonas aeruginosa, Streptococcus pneumoniae, Staphylococcus aureus and Moraxella catarrhalis.[4] These colonizing pathogens commonly show antimicrobial resistance arising from intrinsic resistance mechanisms or frequent exposure to varieties of antimicrobial agents.

Patients with bronchiectasis were frequently exacerbations have been viewed as being exclusively bacterial, those patients treated with intravenous antibiotic therapy had a good clinical response.[5] So identification and appropriate treatment of these organisms is an essential part of the management of bronchiectasis. Dominant bacteria were Pseudomonas aeruginosa and Haemophilus influenza worldwide.[6] But emerging pathogens in the airways of people with bronchiectasis and the geographical and community differences together with ethnic variation warrant further investigation.[7]

Hospitalized patients usually have more severely compromised lung function, and the spectrum of the causative organisms could be different. Furthermore, emergence of resistant bacteria is a potential threat, especially in developing countries.[8] Causes of which may be due to frequent administration of antibiotic by self or prescribed form, inadequate dose or duration, frequent exacerbation or de novo infection with drug resistant organism. Epidemiological studies have clearly demonstrated direct relationship between antibiotic consumption and the emergence and dissemination of resistant strains.[9]

Exacerbation of bronchiectasis has detrimental effect on one's quality of life, most of them require hospitalization and parenteral antibiotics. The current treatment option focused on the use of directed antibiotic treatment aimed at pathogen reduction as well as pathogen eradication. Empirical antibiotics should be started while awaiting sputum microbiology.[10] Infection caused by resistant organism is associated with high morbidity, prolonged hospital stay and reduced quality of life. Moreover, it accounts for a large proportion of the clinical workload, health burden to the individual and the economic impact on health care systems internationally, which is far more immense in developing countries like Bangladesh.

Use of optimal antibiotic is crucial, especially in an era of rising antibiotic resistance and lack of new antimicrobial development.[11] Infections caused by MDR gram-negative organisms are associated with high morbidity and mortality.[12] Moreover, the financial burden of antimicrobial resistance can be significant as a result of prolonged hospitalizations due to antibiotic treatment failures. The economic impact of antibiotic resistance can be measured not only through direct health care expenses but also through health burden to the individuals affected and to the society.[13]

The impact of antibiotic resistant bacteria is suggested to be far more serious in low and middle income countries (LMICs) than in well-resourced countries, where unregulated antimicrobial use, and poor infection control practices may result in increased numbers of infections related to resistant bacteria.[8] Routine screening is vital due to the circulation of resistant organisms in the community resulting high mortality rate of patients of bronchiectasis in Intensive Care Unit (ICU).[14] In the emergence of drug resistance, antibiotic susceptibility pattern should be monitored regularly.

Materials and Methods

This was a cross-sectional study and was conducted at the Intensive Care Unit of National Institute of Diseases of the Chest and Hospital (NIDCH) for 1 years of period from July 2019 to June 2020. Total 50 patients in ICU with bronchiectasis were included after screening in according to the

inclusion criteria with patients of bronchiectasis in ICU of NIDCH whose sputum or endotracheal specimen showed bacterial growth were included in this study & Radiological evidence considered for diagnosis of bronchiectasis and exclusion criteria with patients transferred from another ICU where stayed for more than 48 hours. Study samples were selected by purposive sampling who fulfilled the criteria. Data were presented in frequency, percentage and mean and standard deviation as applicable. Chi square test was used for categorical variables. Univariate and Multivariate logistic analysis were used for risk factors. P value of less than 0.05 was considered as significant.

Results:

Total 50 patients with bronchiectasis in the ICU of NIDCH were included in this study with the main aim to explore the spectrum of bacteria isolated from sputum or endotracheal specimen cultures and their susceptibility to antibiotics and to evaluate the possible factors responsible for antibiotic resistance among pathogenic organism.

Average age of all patients was 51.04±16.43 years. Maximum age was 75 years and minimum age 17 years. Major part (58%) of the patients was aged 50 years or above. Greater part of the patients was male (80%) and rest 20% were female. Maximum patients were from rural (64%) and rest 36% were from the urban residence. Of all, 52% of patients were from lower class followed by middle class (44% and only 4% were belonged to higher socio-economic status.

Table-I

Demographic characteristics of the study patients (n=50)

Demographic characteristics	Number of patients	Percentage
Sex		
Male	40	80%
Female	10	20%
Mean age (years)	51.04	±16.43
Range (min-max)	17.0	-75.0

Table represent percentage (%);
Chi-squared Test was done to analyze the data.

We found patients with bronchiectasis were infected by Pseudomonas species (40%) , Acinetobacter species (28%), Klebsiella species (20%), Staphylococcus aureus (16%), Enterobacter species (12%) and Candida species (8%).

Table-II

Identification of the isolated organisms from sputum culture of patients with bronchiectasis in ICU of NIDCH. (n=50)

	Frequency	Percent
Pseudomonas species	20	40
Acinetobacter species	14	28
Klebsiella species	10	20
Staphylococcus aureus	8	16
Enterobacter species	6	12
Candida species	4	8

Table represent percentage (%);
Chi-squared Test was done to analyze the data

Table II shows that maximum patients were infected by *Pseudomonas species* (40%) followed by *Acinetobacter species* (28%), *Klebsiella species* (20%), *Staphylococcus aureus* (16%), *Enterobacter species* (12%) and *Candida species* (8%).

Out of 20 Pseudomonas species, all were sensitive(100%) to Colistin whereas all were resistant(100%) to Ampicillin, Cefuroxime and Cefepime.

Out of 14 Acinetobacter species, all were sensitive(100%) to Collistin whereas resistance showed to Amoxicilin+clavulanic acid(85.71%) and Ceftriaxone(78.57%).

Out of 10 Klebsiella species, all 10 Klebsiella species were sensitive(100%) to Collistin whereas all were resistant(100%) to Ampicillin, Amoxicilin+ clavulonic acid, Ceftriaxone, Cefixim, Cefuroxim, Cefepime.

Out of 8 Staphylococcus aureus, all 8 Staphylococcus aureus were sensitive to Ceftazidim, cotrimoxazole, Collistin and Tigecycline whereas all showed resistance(100%) to Ampicillin, Ceftriaxone, Cefepime and Imipenem.

Out of 6 Enterobacter species, all were sensitive(100%) to colistin, Tigecycline and also sensitive(50%) to Clotrimoxazol and showed resistance(100%) to rest all antibiotics.

For identification of risk factors for antibiotic resistance, we found most of the patients had h/o taking antibiotic without doctor's prescription (62%), h/o taking various type of antibiotic (56%) and h/o taking antibiotic on increased interval (52%). Half (50%) of the total patients had h/o taking inadequate dose of antibiotic. 40% patients were in old age (e"60 years) and 16% suffered from malnutrition

Tablie-III

Antibiotics sensitivity pattern of Pseudomonas species among patients (n=20)

Antibiotic	Sensitive	Resistant
Ampicillin	0 (0%)	20 (100%)
Amoxicilin+clavulonic acid	1 (5%)	19 (95%)
Ceftriaxone	8 (40%)	12 (60%)
Cefixim	7 (35%)	13 (65%)
Cefuroxim	0 (0%)	20 (100%)
Cefepime	0 (0%)	20 (100%)
Ceftazidim	7 (35%)	13 (65%)
Levofloxacin	4 (20%)	16 (80%)
Ciprofloxacin	6 (30%)	14 (70%)
Cotrimoxazol	2 (10%)	18 (90%)
Cefoperazone+sulbactum	10 (50%)	10 (50%)
Gentamycin	13 (65%)	7 (35%)
Amikacin	16 (80%)	4 (20%)
Meropenem	10 (50%)	10 (50%)
Imipenem	8 (40%)	12 (60%)
Pipericillin+Tazobactam	11 (55%)	9 (45%)
Aztreonam	12 (60%)	8 (40%)
Collistin	20 (100%)	0 (0%)
Tigecycline	14 (70%)	6 (30%)

Table represent percentage (%);
Chi-squared Test was done to analyze the data

Table III shows that out of 20 *Pseudomonas species* were sensitive to Colistin (100%), Amikacin (80%), Meropenem (50%), whereas were resistant(100%) to Ampicillin, Cefuroxime and Cefepime.

Table-IV

Antibiotics sensitivity pattern of Acinetobacter species among patients (n=14)

Antibiotic	Sensitive	Resistant
Ampicillin	2 (14.28%)	12 (85.71%)
Amoxicilin+clavulonic acid	2 (14.28%)	12 (85.71%)
Ceftriaxone	3 (21.42%)	11 (78.57%)
Cefixim	5 (35.71%)	9 (64.29%)
Cefuroxim	2 (14.28%)	12 (85.71%)
Cefepime	2 (14.28%)	12 (85.71%)
Ceftazidim	8 (57.14%)	6 (42.85%)
Levofloxacin	1 (7.14%)	13 (92.86%)
Ciprofloxacin	4 (28.57%)	10 (71.43%)
Cotrimoxazol	4 (28.57%)	10 (71.43%)
Cefoperazone+sulbactum	5 (35.71%)	9 (64.29%)
Gentamycin	4 (28.57%)	10 (71.43%)
Amikacin	4 (28.57%)	10 (71.43%)
Meropenem	3 (21.42%)	11 (78.57%)
Imipenem	3 (21.42%)	11 (78.57%)
Pipericillin+Tazobactam	3 (21.42%)	11 (78.57%)
Aztreonam	4 (28.57%)	10 (71.43%)
Collistin	14 (100%)	0 (0%)
Tigecycline	11 (78.57%)	3 (21.42%)

Table represent percentage (%);
Chi-squared Test was done to analyze the data

Table IV shows that out of 14 *Acinetobacter species* were sensitive to Collistin(100%), Tigecycline(80%), whereas resistance showed to Amoxicilin+ clavulonic acid(85.71%), Ceftriaxone(78.57%).

Table-V

Antibiotics sensitivity pattern of Klebsiella species among patients (n=10)

Antibiotic	Sensitive	Resistant
Ampicillin	0 (0%)	10 (100%)
Amoxicilin+clavulonic acid	0 (0%)	10 (100%)
Ceftriaxone	0 (0%)	10 (100%)
Cefixim	0 (0%)	10 (100%)
Cefuroxim	0 (0%)	10 (100%)
Cefepime	0 (0%)	10 (100%)
Ceftazidim	2 (20%)	8 (80%)
Levofloxacin	7 (70%)	3 (30%)
Ciprofloxacin	2 (20%)	8 (80%)
Cotrimoxazol	2 (20%)	8 (80%)
Cefoperazone+sulbactum	2 (20%)	8 (80%)
Gentamycin	3 (30%)	7 (70%)
Amikacin	3 (30%)	7 (70%)
Meropenem	4 (40%)	6 (60%)
Imipenem	2 (20%)	8 (80%)
Pipericillin+Tazobactam	1 (10%)	9 (90%)
Aztreonam	2 (20%)	8 (80%)
Collistin	10 (100%)	0 (0%)
Tigecycline	8 (80%)	2 (20%)

Table represent percentage (%);
Chi-squared Test was done to analyze the data

Table V shows that out of 10 *Klebsiella species* were sensitive to Collistin (100%), Tigecycline (80%), Levofloxacin (70%) whereas were resistant(100%) to Ampicillin, Amoxicilin+clavulonic acid, Ceftriaxone, Cefixim, Cefuroxim, Cefepime.

Table-VI

Antibiotics sensitivity pattern of Staphylococcus aureus among patients (n=8)

Antibiotic	Sensitive	Resistant
Ampicillin	0 (0%)	8 (100%)
Amoxicilin+clavulonic acid	4 (50%)	4 (50%)
Ceftriaxone	0 (0%)	8 (100%)
Cefixim	3 (37.5%)	5 (62.5%)
Cefuroxim	3 (37.5%)	5 (62.5%)
Cefepime	0 (0%)	8 (100%)
Ceftazidim	8 (100%)	0 (0%)
Levofloxacin	3 (37.5%)	5 (62.5%)
Ciprofloxacin	3 (37.5%)	5 (62.5%)
Cotrimoxazol	8 (100%)	0 (0%)
Cefoperazone+sulbactum	3 (37.5%)	5 (62.5%)
Gentamycin	6 (75%)	1 (12.5%)
Amikacin	1 (12.5%)	7 (87.5%)
Meropenem	2 (25%)	6 (75%)
Imipenem	0 (0%)	8 (100%)
Pipericillin+Tazobactam	3 (37.5%)	5 (62.5%)
Aztreonam	6 (75%)	2 (25%)
Collistin	8 (100%)	0 (0%)
Tigecycline	8 (100%)	0 (0%)

Table represent percentage (%);
Chi-squared Test was done to analyze the data

Table VI shows that out of 8 *Staphylococcus aureus* were sensitive to cotrimoxazole(100%), Tigecycline (100%), whereas showed resistance(100%) to Ceftriaxone.

Table-VII

Antibiotics sensitivity pattern of Enterobacter species among patients (n=6)

	Sensitive	Resistant
Ampicillin	0 (0%)	6 (100%)
Amoxicilin+clavulonic acid	0 (0%)	6 (100%)
Ceftriaxone	0 (0%)	6 (100%)
Cefixim	0 (0%)	6 (100%)
Cefuroxim	0 (0%)	6 (100%)
Cefepime	0 (0%)	6 (100%)
Ceftazidim	0 (0%)	6 (100%)
Levofloxacin	0 (0%)	6 (100%)
Ciprofloxacin	0 (0%)	6 (100%)
Cotrimoxazol	3 (50%)	3 (50%)
Cefoperazone+sulbactum	0 (0%)	6 (100%)
Gentamycin	0 (0%)	6 (100%)
Amikacin	0 (0%)	6 (100%)
Meropenem	0 (0%)	6 (100%)
Imipenem	0 (0%)	6 (100%)
Pipericillin+Tazobactam	0 (0%)	6 (100%)
Aztreonam	0 (0%)	6 (100%)
Collistin	6 (100%)	0 (0%)
Tigecycline	6 (100%)	0 (0%)

Table represent percentage (%);

Chi-squared Test was done to analyze the data

Table VII shows that out of 6 *Enterobacter species* were sensitive to colistin (100%), Tigecycline(100%), Cotrimoxazol(50%) and rest all antibiotics showed 100% resistance.

Table-VIII

Identified risk factors of developing antibiotic resistance among patients (n=50)

	Frequency	Percent
H/o taking inadequate dose of antibiotic	25	50%
H/o taking short duration of antibiotic	20	40%
H/o taking antibiotic on increased interval	26	52%
H/o taking antibiotic without doctor's prescription	31	62%
H/o taking various type of antibiotic	28	56%
Old age	20	40%
Malnutrition	8	16%

Table represent percentage (%);
Chi-squared Test was done to analyze the data

Table VIII shows that most of the patients had h/o taking antibiotic without doctor's prescription (62%), h/o taking various type of antibiotic (56%) and h/o taking antibiotic on increased interval (52%). Half (50%) of the total patients had h/o taking inadequate dose of antibiotic. 40% patients were in old age (≥60 years) and 16% suffered from malnutrition.

Discussion:

This cross-sectional observational study was performed in the Intensive care unit(ICU) of NIDCH, Dhaka, to explore the spectrum of bacteria isolated from sputum culture and their susceptibility to antibiotics in patients of bronchiectasis. Total 50 patients with bronchiectasis in ICU were included in this study.

In this study it was observed that mean age of all patients was 51.04±16.43 years (17-75 years) with male predominance (80%). Majority (58%) of the patients were aged 50 years or more. This findings correlate with others study[15-17]. A study[18] found ninety five percent (142 cases), and 5 % (8cases) of patients were male and female respectively. However, unlike age distribution, sex distribution was not compatible with several studies. In a study[19] only 30.2% were males and in another study[5] found 31.3% were males.

Most (68%) of the patients had cylindrical type of bronchiectasis whereas rest 32% had cystic-varicose type of bronchiectasis. Like us, a study[18] found the majority of patients had cylindrical type and minor percent have varicose type BE. Another study[6] found 73% patients with cylindrical type and 27% with cystic-varicose type of bronchiectasis

We found majority of the patients were infected by single organism (80%) and rest by dual organism (20%). Most of the patients were infected by *Pseudomonas species* (40%) followed by *Acinetobacter species* (28%), *Klebsiella species* (20%), *Staphylococcus aureus* (16%), *Enterobacter species* (12%) and *Candida species* (8%). In a study,[5] in 32 exacerbations of Bronchiectasis sputum bacteriology showed *P. aeruginosa* in 19 Patients (59.3%). In another study,[12] among 33 patients with exacerbation of bronchiectasis, normal flora in sputum was found in 24% with most frequent isolates were: *P. aeruginosa* (30%), *H. influenzae* (6%), *Streptococcus spp.* (3%), MSSA (15%), MRSA

(6%) of patients. In another study[16] conducted prospectively at King Khalid University Hospital (KKUH) and Sahary Chest Hospital in Riyadh, *Pseudomonas aeruginosa (PA)* was the most common organism (43%). In a study[21] commonest organism isolated from sputum was *Pseudomonas aeruginosa* (34%) and *Haemophilus influenzae* (19%), respectively. In the study[19] commonest organisms were *Pseudomonas aeruginosa*. Furthermore, in our study there was no growth of *Haemophilus influenzae*, which was conflicting with other previous studies. This may be due to the fastidious nature of *Haemophilus influenza* which requires supplemented media to isolate. Also, *Haemophilus influenza* may be overgrown by other bacteria.

We found isolated organisms were sensitive to few antibiotics whereas resistant to multiple antibiotics. All 20 Pseudomonas species were sensitive(100%) to Colistin whereas all were resistant(100%) to Ampicillin, Cefuroxime and Cefepime. Out of 14 Acinetobacter species, all were sensitive(100%) to Collistin whereas resistance showed to Amoxicilin+clavulanic acid(85.71%) and Ceftriaxone(78.57%). All 10 Klebsiella species were sensitive(100%) to Collistin whereas all were resistant(100%) to Ampicillin, Amoxicilin+ clavulonic acid, Ceftriaxone, Cefixim, Cefuroxim, Cefepime. All 8 Staphylococcus aureus were sensitive to Ceftazidim, cotrimoxazole, Collistin and Tigecycline whereas all showed resistance(100%) to Ampicillin, Ceftriaxone, Cefepime and Imipenem Out of 6 Enterobacter species, all were sensitive(100%) to colistin, Tigecycline and also sensitive(50%) to Clotrimoxazol and showed resistance(100%) to rest all antibiotics.

We also found various risk factors for antibiotic resistance present in studied patients with bronchiectasis. Identified risk factors were taking previous antibiotics without doctor's prescription (62%), taking different types of antibiotic (56%) and history of taking antibiotic on increased interval (52%). Half (50%) of the total patients had history of taking inadequate dose of antibiotic. Old age,e"60 years(40%) and malnutrition(16%) were also found risk factors for antibiotic resistance. In a study[14] risk factors for antibiotic resistance found were co-exist illness, chronic disease and immune deficiency conditions.

These microbial profiles of pathogens causing infective exacerbation of bronchiectasis may differ between hospitals and ICU settings, even within the same institution. Therefore, surveillance of bacterial susceptibility should be conducted and local epidemiological data should be provided for every ICU. Because of increasing rate of lungs colonization with resistant strains, it is recommended that in lower respiratory tract infections screening programs for resistant organisms being implemented routinely in hospital settings.[18] This information can help in guiding the initial empiric antibiotic therapy, which would be helpful in decreasing mortality and preventing development of MDR bacteria. Antibiotic choices based on published guidelines may be ineffective if local microbial flora shows different susceptibility patterns. Therefore, this study might help to find out most common pathogen associated with bronchiectasis in ICUs and its antibiotic sensitivity pattern which is useful to modify antibiotic policy of bronchiectasis in our hospital ICUs to reduce emergence of multidrug-resistant organisms and morbidity, mortality associated with bronchiectasis. Furthermore, in order to achieve higher levels of evidence, further studies with larger sample size and different study design would be desirable to find out the risk factors for developing antibiotic resistance.

Limitation of the study

The study population was selected from a single tertiary care specialized center. Therefore, it might not be reflective to the scenario of the country. Conventional microbiological culture sensitivity test was used, so extended antibiogram was not possible to conduct.

Conclusion:

The common identified organisms were Pseudomonas species, Acinetobacter species, klebsiella species. Isolated organisms were sensitive to colistin, tigecycline, meropenem, piperacillin-tazobactam, amikacin and resistant to ampicillin, amoxicilin+clavulanic, cefuroxime, cefepime, ceftriaxone and cefixime. We should consider antimicrobial agent that covers Gram negative infection. Empirical antibiotic should be combination of Piperacillin-tazobactam with Levofloxacin or Meropenam with amikacin or ceftazidim with amikacin. Taking various types of

antibiotics without doctor prescription is the most common factor for developing antibiotic resistance among pathogenic organisms and should be considered during use of antibiotics.

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ORIGINAL ARTICLE

Association Of Serum Adenosine Deaminase with Sputum Conversion at the End of Second Month and at the End of The Anti-Tuberculous Drug Treatment among New Smear Positive Pulmonary Tuberculosis Patients

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Abstract:

Background: *Tuberculosis (TB) is global public health problem. Sputum microscopy for AFB is a well-known method for treatment monitoring in case of smear positive PTB patients. But it is not always easy to obtain sputum samples at the end of treatment. Many studies have proved the role of ADA in diagnosis of tuberculosis in effusion fluids and a decrease in ADA activity at the end of treatment. But association between serum ADA level with treatment monitoring in sputum smear positive PTB cases is not widely studied.*

Objective: *To determine the association of serum adenosine deaminase with sputum conversion at the end of second month and at the end of the treatment among new smear positive pulmonary tuberculosis patients.*

Materials & Methods: *This prospective observational study was conducted in the department of respiratory medicine of National Institute of Diseases of the Chest and Hospital (NIDCH) from June 2020 to September 2021. Ninety-eight new smear positive pulmonary tuberculosis patients were enrolled in this study according to inclusion and exclusion criteria of the study. Sputum sample was collected from each subject for microscopic examination at initial, at the end of the 2nd month and at the end of 6th month. Blood was collected from each subject for measurement of serum ADA level at initial, at the end of 2nd month and at the end of 6th month. Serum ADA was measured by enzymatic photometric method using MICROEXPRESS ADA-MTB reagent and result was expressed as U/L. Data analysis was done through Statistical Package for Social Science (SPSS) version 23.*

Results: *Mean age of the study subject was 39.7±13.0 years with male (82.8%) predominance. Ultimately 10 patients were lost to follow-up and 1 died during the study period. Rest of the study subjects (87 out of 98) showed that their sputum were converted at the end of 2nd month and remained negative at the end of 6th month. Mean serum ADA level was significantly decreased at the end of 6^{th} month (21.8±5.7 U/L) than 2nd month (25.1±8.3 U/L) and baseline (29.8±11.5 U/L) (P value = 0.001). To see the association between serum ADA level and sputum smear for AFB, Analysis of Variance test was done and it revealed that at the*

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end of 2nd month and 6th month mean serum ADA level was significantly higher among patients with higher bacillary load (P value =0.001). Multivariate regression analysis was done which found independent relationship between serum ADA and sputum for AFB 3+.

Conclusion: *This study showed there is significant association between serum ADA level and sputum smear conversion among the new smear positive pulmonary tuberculosis patients.*

Keywords: *Smear positive pulmonary tuberculosis, Serum ADA, Sputum smear conversion*

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Introduction:

Tuberculosis (TB) is one of the most ancient diseases of mankind, with molecular evidence going back to over 17,000 years. Inspite of newer modalities for diagnosis and treatment of TB, unfortunately, people are still suffering, and worldwide it is among the top 10 killer infectious diseases, second only to HIV[1].

TB is an airborne bacterial infection caused by M. Tuberculosis which affects any part of the body and most commonly the lungs[2].

Globally, an estimated 10.0 million (range, 8.9–11.0 million) people fell ill with TB in 2019, a number that has been declining very slowly in recent years. There were an estimated 1.2 million (range, 1.1– 1.3 million) TB deaths among HIV-negative people in 2019 (a reduction from 1.7 million in 2000), and an additional 208000 deaths (range, 177 000–242 000) among HIV-positive people (a reduction from 678000 in 2000)[3].

Epidemiological studies have shown that tuberculosis is a disease that endangers the health of a community with increasing incidence rate. In diagnosis of tuberculosis microbiologic, genetic, immunologic and biochemical methods are used[4].

When sputum smear positive patients are initiated on multidrug anti-tuberculosis treatment, there is a multifold reduction in bacillary load expelled in sputum. Patients, who respond are likely to become smear and culture negative during the course of treatment. It is expected that 80 to 90% of patients will undergo smear conversion within two to three months of treatment[5].

The World Health Organization (WHO) recommends sputum smear follow-up tests at two or three, five, and six or eight months[6].

Adenosine deaminase (ADA) is an enzyme of purine and is needed for the breakdown of adenosine from food and for the turnover of nucleic acids in tissues. Moreover, it regulates lymphocyte metabolism and is important for lymphocytic differentiation and growth. It is present in lymphocytes in high concentration[7].

Its activity appears to be necessary for an effective immune response as shown by many studies, such as in combined immunodeficiency disease[8].

Increased serum ADA activity can be seen in diseases associated with cellular system stimulation, such as typhoid fever, infectious mononucleosis, liver disease, sarcoidosis, leukemia, brucellosis, acute pneumonia, rheumatoid arthritis, malignancies and tuberculosis[9].

The significance of ADA level in diagnosis of Tuberculosis is known in effusion due to pleural, pericardial, meningeal and peritoneal tuberculosis specially in countries with high tuberculosis prevalence[4].

This study was conducted to find out the association of serum ADA levels with sputum conversion in new smear positive PTB cases, so as to assess its role as a possible treatment monitoring method in PTB.

Materials and methods:

This prospective analytical study was conducted in the department of respiratory medicine of National Institute of Diseases of the Chest and Hospital, Mohakhali, Dhaka during the period from July 2020 to September 2021.

Inclusion criteria were:

Newly diagnosed sputum smear positive pulmonary tuberculosis patients and age e”18 years.

Exclusion criteria were:

1. Extra-pulmonary tuberculosis, previous history of PTB, DR-TB patient
2. HIV infected/AIDS patient
3. Any malignancy
4. DM, CLD, CKD, rheumatological diseases, typhoid fever

5. Pregnant and lactating women.
6. Patient who refused to be part of study

Ninety eight (98) patients were included in the study using purposive sampling method. All newly smear positive pulmonary tuberculosis patients with inclusion & exclusion criteria were selected for the study, full information regarding nature of study, possible outcome, and importance of follow up, written consent was obtained from the patient. Enrolled patients were supplied with a predesigned questionnaire in locally understandable language. Blood sample was collected from each participant for measurement of serum adenosine deaminase level and treatment was started. Serum adenosine deaminase level and sputum smear examination were done at the end of second month and at the end of treatment. All the data was recorded systematically in a preformed data collection sheet and analyzed using appropriate statistical formula

Results:

Total 98 patients were preliminary enrolled in the study, among them 11 (10 patients were lost to follow up and 1 died) were excluded. Finally 87 patients were included for analysis. The majority (26.4%) patients belonged to the age group 21-30 years with mean age was 39.7±13.0 years. Male patients were predominant 72(82.8%) with male female ratio was 4.8:1. Most of the patients 48(55.2%) from urban background. (Table I).

Table-I

Demographic characteristics of the study patients (n=87)

Demographic characteristics	Number of patients	Percentage
Age (years)		33
≤20	4	4.6
21-30	23	26.4
31-40	18	20.7
41-50	22	25.3
51-60	19	21.8
>60	1	1.1
Mean±SD	39.7	±13.0
Range (min-max)	18.0	-70.0
Sex		
Male	72	82.8
Female	15	17.2
Geographical location		
Urban	48	55.2
Rural	39	44.8

Initially majority 51(58.6%) patients had BMI 18.5-24.9 kg/m^2, at the end of 2nd month more than three fourth (75.9%) patients had BMI 18.5-24.9 kg/m^2 and at the end of 6th month 80(92.0%) patients had BMI 18.5-24.9 kg/m^2.(Table II).

Table-II

BMI in different follow up (n=87)

BMI (kg/m^2)	Number of patients	Percentage
Initial		
<18.5	35	40.2
18.5-24.9	51	58.6
>25.0	1	1.1
At the end of 2nd month		
<18.5	19	21.8
18.5-24.9	66	75.9
>25.0	2	2.3
At the end of 6th month		
<18.5	5	2.3
18.5-24.9	80	92.0
>25.0	5	5.7

At the time of diagnosis, 40.2% patients had 3+ sputum AFB. At the end of the 2nd month and 6th month there was complete sputum conversion. (Table III).

Table-III

Sputum for AFB in different follow up (n=87)

Sputum for AFB	Number of patients	Percentage
Initial		
1+	22	25.3
2+	30	34.5
3+	35	40.2
At the end of 2nd month		
Negative	87	100.0
At the end of 6th month		
Negative	87	100.0

Mean serum ADA at the start of treatment was 29.0±11.5 U/L, at the end of 2nd month 25.1±8.3 U/L, at the end of 6th month 21.8±5.7 U/L. Mean serum ADA level was significantly decreased at the end of 6th month than initial. (Table IV)

Twenty two patients had 1+ AFB initially and their mean serum ADA level was significantly decreased at the end of 2nd month (19.1±3.4 U/L) and 6th month (17.7±3.2 U/L) than initial (21.1±4.0 U/L). (Table V)

Thirty patients had 2+ AFB initially and their mean serum ADA level was decreased at the end of 2nd

month (23.7±5.6 U/L) and 6th month (21.7±4.6 U/L) than initial (26.3±7.2 U/L) which was statistically significant (P value 0.001%). (Table V)

Thirty five patients had 3+ AFB initially and their mean serum ADA level was significantly decreased at the end of 2nd month (30.2±9.4 U/L) and 6th month (24.6±6.1 U/L) than initial (36.4±13.2 U/L). (Table V)

A significant relationship was found between sputum conversion with serum ADA level initially, at the end of 2nd month and 6th month. Mean serum ADA level was higher in patients with higher bacillary load in sputum. (Table V)

In multivariate analysis, baseline low BMI and serum ADA were found to be independent predictors for bacillary load in sputum. It was evident that patients who had high serum ADA had 18.02 times risk of having smear positive PTB. Again, 2.50 times risk prevailed among the patient who had low BMI. However, no association was found between sputum result and patient demographics (e.g. age, sex, geographical location). (Table VI)

Table-IV

Serum ADA in different follow up (n=87)

Serum ADA (U/L)	Mean±SD	*P value (Initial vs at the end of 6th month)*
Initial	29.0±11.5	0.001s
Range (min-max)	16.0-67.1	
At the end of 2nd month	25.1±8.3	
Range (min-max)	14.3-54.0	
At the end of 6th month	21.8±5.7	
Range (min-max)	11.9-38.5	

s= significant

P value reached from paired t-test

Table-V

Association between initial sputum for AFB with serum ADA level (n=87)

Serum ADA (U/L)	Initial sputum for AFB			F value	df	P value
	1+ (n=22) Mean±SD	2+(n=30) Mean±SD	3+(n=35) Mean±SD			
Initial	21.1±4.0	26.3±7.2	36.4±13.2	18.84	2	0.001s
Range (min-max)	16.0-32.0	17.7-55.0	19.3	-67.1		
At the end of 2nd month	19.1±3.4	23.7±5.6	30.2±9.4	17.73	2	0.001s
Range (min-max)	14.3-28.6	16.4-46.6	16.6-54.0			
At the end of 6th month	17.7±3.2	21.7±4.6	24.6±6.1	12.95	2	0.001s
Range (min-max)	11.9-25.0	15.18-37.1	15.7-38.5			

s= significant

P value reached from ANOVA test

Table-VI

Multivariate regression analysis for sputum for AFB 3+ (n=87)

	Adjusted OR	95% CI		P value
		Lower	Upper	
Age	0.454	0.141	1.456	0.184ns
Sex	0.293	0.061	1.416	0.127ns
Geographical location	1.557	0.504	4.812	0.442ns
Low BMI	2.509	1.067	4.869	0.039s
Serum ADA	18.022	5.321	61.041	0.001s

s= significant, ns= not significant

p-value reached from multivariate analysis by binary logistic regression analysis

OR=Odd's Ratio

Discussion:

This prospective observational study was carried out in the department of respiratory medicine, NIDCH, Dhaka from June 2020 to September 2021. 98 patients were included for the study among them 11 (10 patients were lost to follow-up and 1 died) patients were excluded in this study. Finally 87 patients were analyzed.

We observed that the majority 23(26.4%) patients belonged to the age group 21-30 years with mean age was 39.7±13.0 years. Almost similar study conducted by Lende et al.[10] where they found the mean age of the participants was 40 years. Soedarsono et al.[11] consisted of 42.85 years.These findings are consistent with the present study.

In this present study it was observed that male patients were predominant 72(82.8%) and female was 15(17.2%) with male female ratio was 4.8:1. Similarly, Soedarsono et al.[11] had observed that men were 21(80.8%) and females were 5(19.2%).These findings are consistent with my study.

Regarding body mass index (BMI) our observation showed that initially significant proportion of study population (40.2%) were underweight (BMI <18.5). On successful treatment there was improvement of nutritional status i.e. BMI >18.5 in 75.9% and 92% patients on 2nd and 6th month of therapy respectively. In a study done by Phan et al.[12] showed that BMI increased significantly after 2 months of treatment.

In this study it was observed that initial serum ADA was 29.0±11.5 U/L, at the end of 2nd month mean serum ADA 25.1±8.3 U/L, at the end of 6th month mean serum ADA was 21.8±5.7 U/L. Mean serum ADA level was significantly decreased at the end of 6th month than initial. In a study of Kartaloglu et al.[13] reported that the mean serum ADA levels at one month was 45.1±10.6 U/l, two months 34.6±10.1 U/l, and six months 24.6±4.7 U/l in the patients. The differences in serum ADA levels between the first measurement and that at one month, one month and two months, and one month and six months were statistically significant (p=0.005, p=0.016, and p<0.001, respectively). Soedarsono et al.[11] had observed that all patients experienced sputum conversion at the end of 2nd month of TB treatment. Examination of serum ADA levels showed that the mean value of serum ADA levels before treatment was higher than after receiving anti-tuberculous drug with (26.40 IU/L vs. 19.67 IU/L). A significant difference in serum ADA levels before and after the intensive phase of TB treatment with $P < 0.001$. Serum ADA levels in PTB patients decreased with TB treatment and suggest that serum ADA levels can be used as a prognostic marker. Higher AFB sputum smear shows the severity of the disease based on the number of bacterial loads. Saini et al.[14] stated that the average level of serum ADA levels increased significantly in PTB patients. A study by Pandey et al.[15] reported that the increase in serum ADA levels along with the increase of the sputum AFB grading, and the increase in serum ADA level was caused by stimulation of cell mediated immunity.

All participants in their study experienced sputum conversion. The results of the examination of serum ADA levels after the end of the intensive phase of TB treatment have decreased. This indicates that examination of serum ADA levels can be used in monitoring TB therapy response. Serum ADA levels were expected to increase twice in PTB patients at the time of diagnosis and subsequently experienced a significant decrease in the mean value of serum ADA levels after treatment in PTB patients[4]. Serum ADA levels decreased to normal levels after 1 month of effective treatment in patients with PTB. A decrease in serum ADA levels can be caused by changes in the number of lymphocytes induced by *M. tuberculosis*[16]. Significant differences were obtained in ADA serum activity before and after treatment and also from older TB patients and healthy control patients, indicating that serum ADA activity was increased in PTB patients[17].

Rao *et al.*[18] reported the decrease in serum ADA levels during PTB treatment. They found significant difference of serum ADA level before and after the 2nd month of TB treatment and concluded that measurement of serum ADA could help the evaluation of therapy response. Other study reported the same results that serum ADA levels decreased during TB treatment[19,20].

In this study, twenty-two patients had 1+ AFB, thirty patients had 2+ AFB and initially and thirty-five patients had 3+ AFB initially with baseline ADA their mean serum ADA level (17.7±3.2 U/L),

(26.3±7.2 U/L) and (36.4±13.2 U/L) respectively. At the end of 2nd month was (19.1±3.4 U/L), (23.7±5.6 U/L), (30.2±9.4 U/L) and at the end of 6th month it was (17.7±3.2 U/L), (21.7±4.6 U/L), (24.6±6.1 U/L) respectively. In every aspect mean serum ADA level was significantly decreased after the end of intensive phase and at the end of 6th month. The results were consistent with the study done by Soedarsono et al.[11] Patients with 3+ AFB have a higher mean value of serum ADA level before and after the end of the intensive phase of TB treatment. Previous study reported the same results that the mean value of serum ADA level was higher among 3+graded sputum-positive patients. This is due to the stimulation of cell-mediated immunity[15].

In this study it was observed that initially, at the end of 2nd month and 6th month mean serum ADA level was significantly higher in 3+sputum for AFB than 2+AFB and 1+ AFB. Saini et al.[14] showed that that irrespective of the sputum smear status ADA can help determine the patients who can be suffering from PTB, but difficult to diagnose on the basis of sputum smear examinations. Levels of serum ADA in sputum positive TB patients were correlated with severity of disease. Severity of disease was determined on the basis of acid fast bacilli (AFB) grading on sputum microscopy and was categorized as scanty, 1+, 2+ and 3+.

Multivariate regression analysis was done to evaluate the relationship among the different variables. Here we found that low BMI and high serum ADA level were independent predictors of sputum bacillary load. It was evident that patients who had high serum ADA had 18.02 times risk of having smear positive PTB. Again, 2.50 times risk prevailed among the patients who had low BMI. However, age, sex, geographical location were not found to be independent predictor for sputum smear positive PTB.

Conclusion:

Mean serum ADA level was independently associated with sputum smear conversion at the end of the second month and at the end of anti-tuberculous drug treatment from baseline in sputum smear positive PTB patients. Monitoring of Serum ADA level have a potential utility to evaluate the therapeutic response of anti TB treatment in sputum smear positive PTB patients. Further studies may be done to validate our findings by measuring the cut-off value, sensitivity, specificity, PPV and NPV of serum ADA level through further studies.

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REVIEW ARTICLE

The Implication of Fiberoptic Bronchoscopy in diagnosing Smear Negative or Sputum-scarce Pulmonary Tuberculosis: A Review

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Abstract:

Objective: *The diagnosis of smear-negative pulmonary tuberculosis is both challenging and time-consuming. Fiberoptic Bronchoscopy (FOB) may provide a confirmative and early diagnosis in such patients. Our objective is to assess the role of fiberoptic bronchoscopy in diagnosing smear-negative Pulmonary Tuberculosis (PTB) along with clinical and radiological correlations.*

Method: *We searched the literature in PubMed and Google Scholar using a search strategy PICO model on 'smear-negative pulmonary tuberculosis' and 'Fiberoptic bronchoscopy' and related sampling techniques. Studies that provided sufficient data regarding the sensitivity and specificity of bronchoalveolar lavage for acid-fast bacilli, GeneXpert, and Culture were included.*

Results: *The search yields thousands of papers, of which 12 publications are included for the full review.*

Conclusion: *Fiberoptic bronchoscopy was found to be a useful tool for early recognition of PTB in patients with smear-negative patients. Its sensitivity, specificity, PPV & NPV were found more significant when a High-Resolution CT (HRCT) scan of the chest revealed tree-in-bud appearances.*

Keywords: *Fiberoptic bronchoscopy, Smear negative pulmonary Tuberculosis, Sputum scarce Pulmonary Tuberculosis, Bronchoalveolar lavage*

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Introduction:

One of the top 10 killer diseases in the world is tuberculosis (TB). Every year, it has an impact on millions of people [1]. It is one of the most significant global public health issues. An essential part of tuberculosis control strategies is identifying patients with active pulmonary tuberculosis (PTB), as early treatment renders these patients non-infectious and breaks the tuberculosis transmission chain [2].

In order to start treatment early, getting a quick and correct diagnosis is one of the biggest hurdles in the fight against the burden of TB. The sample most frequently utilized to diagnose PTB is

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sputum. However, some PTB patients may be unable to expectorate sputum, in which case the condition is sputum-scarce pulmonary tuberculosis. In 30%–60% of instances, or smear-negative PTB, microscopy may not detect acid-fast bacilli (AFB) in individuals who can cough up phlegm[3–5]. This poses a diagnostic dilemma[6].

In situations of smear-negative and sputum-scarce PTB, fiberoptic bronchoscopy (FOB) with bronchoalveolar lavage (BAL) may be helpful in making the diagnosis. Mycobacterial culture is regarded as the gold standard for diagnosing tuberculosis, yet it has considerable disadvantages. The technique is labor-intensive, requires skilled personnel, and takes 2–6 weeks to confirm the diagnosis. Contrarily, tests using the amplification of nucleic acids can provide results in a matter of hours, and cartridge-based improvements like Xpert MTB/RIF significantly simplify test execution[6].

There are a number of research papers however, very few review articles on FOB in regard to diagnosing smear-negative PTB cases. Hence, we set out to conduct a systematic review to identify the usefulness of fiberoptic bronchoscopy in detecting smear-negative pulmonary tuberculosis.

Method:

We performed a comprehensive search of databases named PubMed and Google Scholar from the year 2000-2022 without language restriction. We searched by the keyword "fiberoptic bronchoscopy", "smear-negative pulmonary tuberculosis", and "sputum scarce pulmonary tuberculosis". Among thousands of searched papers, we kept 12 papers for review by some selection criteria. Case reports, a study conducted ADA level in BAL, small sample sized articles were excluded.

Selection criteria

Studies on diagnostic precision utilizing respiratory specimens from adults with PTB suspicion were also included. The reference standards for pulmonary TB detection were culture.

Result:

For the diagnosis of pulmonary TB, where sputum smear microscopy is challenging, FOB has been demonstrated to be a reliable and safe approach. The literature that is currently available on this subject demonstrates variable bronchoscopy diagnostic yields that range from 30 to 90%[7]. Higher diagnostic yields were reported in the majority of studies. However, few studies have demonstrated that bronchoscopy has no significant advantages over sputum induction[7]. The sensitivity, specificity, PPV & NPV for PTB of FOB were found more significant when there were tree-in-bud appearances on HRCT of chest[2].

Discussion:

One of the biggest global burdens on public health is tuberculosis. Early detection of PTB halts disease progression, morbidity, disease dissemination, and lung damage[8].

The organ most frequently impacted is the lung. Chest X-rays and sputum microscopy are the traditional diagnostic procedures for pulmonary tuberculosis[9].

Regarding clinical manifestations, there were no discernible variations between patients with positive and negative smears. There were no differences between the AFB positive and AFB negative patients' X-ray and CT results when the results of the two patient groups were compared[10].

Some clinicians start early empirical anti-TB treatment based on clinical features and chest radiography, which is frequently wrong and cannot substitute or support etiological confirmation. A sputum culture may boost the diagnostic yield, but it takes time. Hence, in order to promote the early identification of PTB and exclude other disease processes, doctors must turn to alternative procedures like FOB[2].

The lower respiratory tract can be sampled for study using FOB [11]. It enables low-risk direct observation of the lesion as well as the collection of clean specimens for bronchoalveolar lavage, washings, brush cytology, and biopsy[9].

Moreover, the best way to diagnose endobronchial TB early is through bronchoscopy. To make a diagnosis, one can employ direct bronchoscopic visualization, as well as bronchoscopic techniques like a biopsy, brushings, needle aspiration, bronchoalveolar lavage (BAL), and endobronchial ultrasonography[12].

Conclusion:

When a smear is either negative or scanty, fiberoptic bronchoscopy is regarded as a safe and

extremely reliable method to identify patients with pulmonary tuberculosis. The main issue is that strict protocols and thorough cleaning processes should be put in place to prevent the nosocomial spread of TB and other infectious pathogens via contaminated bronchoscopes. The bulk of TB cases occurs in underdeveloped nations with low resources. Because of accessibility issues, high costs, and logistical difficulties, bronchoscopy's function in the diagnosis of tuberculosis is probably limited. In order to improve early TB detection and prevent more invasive surgical operations, additional research is required to clearly characterize the function of the more recent diagnostic and therapeutic bronchoscopic methods.

Conflict of Interest

This study has no conflicts of interest.

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CASE REPORT

Erasmus Syndrome in a 35-Year-Old Male: A Rare Case Report

Mohammad Shahjahan Siddike Shakil[1], S.M. Abdur Razzaque[2] , Golam Sarwar Mohammad Liaquat Hossain[3], Abdullah Al Masud[4], Mirza Mohammad Asif Adnan[4],

Abstract:

Silicosis is an inflammatory disease of the lung that develops from prolonged pulmonary inhalation and retention of crystalline silica and an immune reaction characterized by irreversible lung fibrosis. It mainly occurs in people involved in stone-quarrying, mining, and sand blasting. Erasmus syndrome is a rare condition where systemic sclerosis develops following exposure to silica with or without silicosis. Only a few case reports are available in the literature. We report here a case of Erasmus syndrome in a 35-year-old manual laborer who presented with arthralgia, Raynaud's phenomenon, skin tightening and microstomia along with features of Interstitial Lung Disease (ILD) and pulmonary arterial hypertension. Serological markers of systemic sclerosis were strongly positive. After a diagnosis of Erasmus syndrome was made, a combination of drugs including Prednisone, Cyclophosphamide, and Nifedipine was instituted. This led to improvement in his symptoms over 6 months.

Keywords: *Interstitial lung disease, Pulmonary arterial hypertension, Silicosis, Systemic sclerosis]*

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Case Report:

A 42-year-old non-diabetic and non-hypertensive male patient presented to our facility with a history of progressively worsening shortness of breath and persistent dry cough for 2 years. For this he was given CAT 1 anti tubercular therapy 5 months after his initial symptoms without significant improvement. After 2-3 months he noticed both hypo ad hyper pigmentation on different part of the body including over the scalp, upper part of the neck, chest and leg [figure 1]. Subsequently he also noticed gradual thickening and tightening of the skin of hand [fig 2], face, feet and trunk. As it was progressive, he felt difficulty in gripping as well as difficulty in opening of mouth. There was also typical color change on exposure to cold. He also gave history of multiple joint swelling and pain involving small joints of hand and feet, both wrist and knee joints without stiffness and was improved with rest but required analgesic at times. He had repeated episodes of heart burn without any difficulty in deglutition. Occupational history revealed that he worked as a stone crusher for nearly 10 years in a stone quarry but left his job 2 years ago. No family history of similar complaints was noted.

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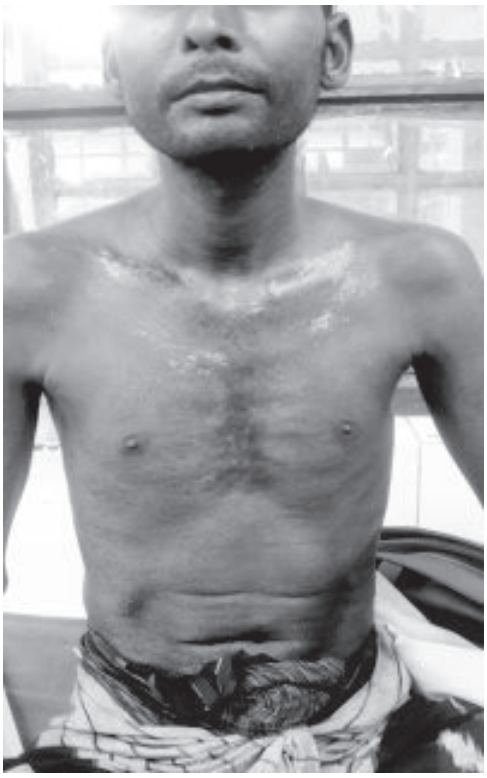

Fig.-1: skin pigmentation over body.

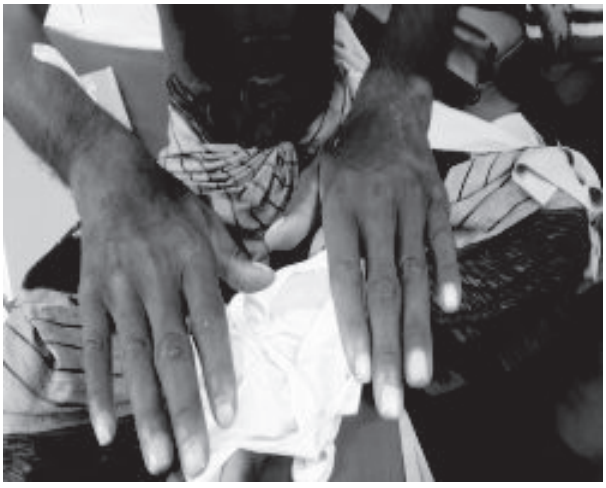

Fig.-2: Sclerodactyly and pseudoclubbing

On examination he was anxious and ill-looking. Face is smooth, shiny, tight, immobile with hypo and hyper pigmented area. There was loss of wrinkling of forehead. Nose was pinched up and tapered. There was puckering of skin around the lip with difficulty in opening the mouth. The skin of the both hands is smooth, shiny, tight, thick, edematous, with pigmented and hypo pigmented area. Skin of the other parts of the body was also tight and thick. Respiratory system examination revealed bilateral end-inspiratory crepitations in upper and mid-chest. Cardiological evaluation showed normal heart rate and rhythm, S1- normal and P2- loud with no added sounds. CBC, urinalysis, LFT and electrolytes were within normal limit. HIV, HBV and HCV serology was negative. Interestingly chest x-ray was unremarkable [fig 3]. High resolution Computed Tomography (HRCT) of the chest revealed diffuse fibrosis, nodular lesions, occasional ground glass changes involving mainly the upper and middle lobes suggestive of Interstitial Lung Disease (ILD) [fig 4]. In Pulmonary function test spirometry revealed moderate restrictive defect, 6MWT revealed desaturation with moderate limitation of walking distance and DLCO consistent with restrictive ventilatory defect. Anti nuclear antibody by indirect fluorescent (IF) was positive and Anti Scl-70 antibody was also strongly positive. Echocardiogram showed left ventricular ejection fraction of 66% and raised pulmonary artery systolic pressure (PASP=55 and PAMP=40 mm Hg).

Considering the presence of telltale clinical manifestations like arthralgia, Raynaud's phenomenon, skin tightening over the face and extremities, microstomia, and Interstitial Lung Disease (ILD), along with supporting laboratory evidence including significant pulmonary arterial hypertension and strongly positive anti-Scl 70, a serological marker, clinic-pathological diagnosis of systemic sclerosis was safely made.

Again, in light of the significant occupational exposure to silica and the absence of any chronic drugs that induce lung fibrosis, such as bleomycin, methysergide, cyclophosphamide, and others, as well as any significant family history, a final etiological diagnosis of Erasmus syndrome (diffuse cutaneous systemic sclerosis associated with silica exposure) was made in the absence of any other possibility. Treatment was started with prednisone and cyclophosphamide for ILD and nifedipine for pulmonary hypertension and Raynaud's with avoidance of cold exposure. There was improvement in skin tightening, arthralgia, Raynaud's phenomenon, and cough, although marginal improvement in dyspnoea on follow up over the phone as the patient could not attend

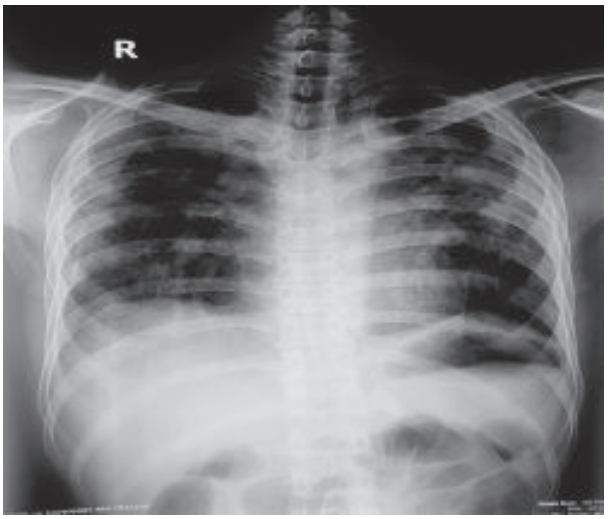

Fig.-3: chest x-ray

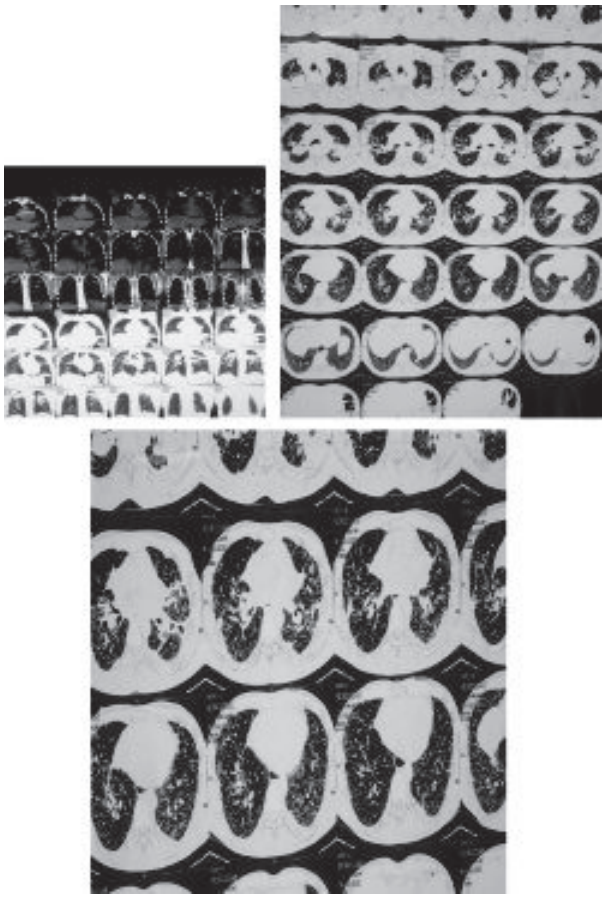

Fig.-4 (a,b,c): HRCT of chest.

physically due to the COVID pandemic situation. As his condition was static, he refused to come in our institute due to economic constraint.

Discussion:

Systemic sclerosis is an autoimmune inflammatory disease that causes vascular changes and degeneration with diffuse tissue fibrosis affecting the skin, lung, kidney, heart, gastrointestinal tract, and synovium[1]. Numerous occupational and other exposures, including vinyl chloride, epoxy benzene, organic solvents, silica environmental and occupational exposures have been implicated as potential causes of SSc[2].

Continuous inhalation of mineral dust containing silica leads to silicosis, probably the most common form of pneumoconiosis. Silicosis is an inflammatory disease of the lung that develops from prolonged pulmonary inhalation and retention of crystalline silica that causes an immune reaction mounted by the body to this extraneous chemical characterized by irreversible lung fibrosis. It mainly affects people involved in stone-quarrying, mining, and sand blasting as an occupational hazard[3]. Silicosis is often associated with other diseases of the lung, such as pulmonary tuberculosis, lung carcinoma, and less commonly, autoimmune diseases like systemic sclerosis (SSc), rheumatoid arthritis (RA), and systemic lupus erythematosus (SLE)[4]. Continuous exposure to silica is associated with abnormalities of humoral and cellular immunity as well as alterations in T-helper and T-suppressor lymphocytes, hypergammaglobulinemia, and antinuclear antibody and rheumatoid factor often become positive[5]. Based on these immunological aberrances, silica exposure has been incriminated as a cause of progressive systemic sclerosis.

Erasmus in 1957 first described the association [6] of exposure to silica and the development of systemic sclerosis, although credit for the first observation of this association goes to Bramwel in 1914. Patients with silica-associated systemic sclerosis (SA-SSc) are clinically, serologically, and immunologically indistinguishable from those with idiopathic systemic sclerosis (SSc), but SA-SSc patients have a higher prevalence and severe pulmonary involvement (bibasilar fibrosis)[7,8]. Although spontaneous remission in idiopathic SSc was reported, no such event was found in silica-induced SSc[8]. Anti-SCL-70, which is the predominant autoantibody present in SA-SSc, is usually associated with severe interstitial lung

disease. Perhaps there is increased production of the anti-Scl-70 antibody in genetically susceptible people who are exposed to silica[9]. Survival in SA-SSc patients was found to be less than in the control "idiopathic" SSc group[10].

So, it is clear that silicosis should be ruled out in every patient with SSc, especially in males, because lung involvement is an important aspect in the prognostic outcome and avoidance of exposure to toxic agents can stabilize the disease progression and even lead to improvement in some cases.

Conclusion:

An underlying systemic sclerosis, which contributes to dyspnoea by multiple mechanisms-pulmonary fibrosis, pulmonary artery hypertension, and localized thoracic skin disease, must be kept in mind whenever the degree of dyspnoea cannot be explained by the extent of silicosis induced lung fibrosis alone and especially if additional clinical pointers are present.

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