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## INSTRUCTION TO AUTHORS ABOUT UNIFORM MANUSCRIPT WRITING

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

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Emphasize the new and important aspects of the study and the conclusions that follow from them. The detail data or other material given in the Introduction or the Results section should not be repeated. The implications of the findings and their limitations, including implication for future research should be included in the Discussion section. The observations should be compared and related to other relevant studies, new hypothesis is appreciated, and however they should be clearly labeled as such. Recommendations may be included only when appropriate.

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Karalus NC, Cursons RT, Leng RA, et al. Community acquired pneumonia: aetiology and prognostic Index evaluation. *Thorax* 1991; 46 : 413-12.
- c) No author given;  
Cancer in South Africa (editorial). *S Afr Med J* 1994; 84-15.
- d) Organization as author  
The Cardiac Society of Australia and New Zealand. Clinical exercise stress training. Safety and performance guideline. *Med J Aust* 1996; 164 : 282-4.

### 2. Books and Other Manuscripts

- a) Personal author  
Tierney LM, -McPhee SJ, Papakadis MA. *Current Medical Diagnosis and Treatment*. Lange Medical books/McGraw Hill 2000.
- b) Editor(s), compiler(s) as author  
Baum GL, Wolinsky E, editor. *Text Book of Pulmonary diseases*. 5th ed. New York: Little Brown Co. 1994.
- c) Organization as author and publisher  
World Health Organization, *Ethical Criteria for Medical Drug Promotion*. Geneva: World Health Organization; 1988.
- d) Chapter in a book  
Macnee W. Chronic bronchitis and emphysema. Seaton A, Seaton D, editors. *Crofton and Douglas's Respiratory Diseases*. 5th ed. UK. The Blackwell Science; 2000; p.616-95.
- e) Dissertation  
Kaplan SJ. *Post-hospital home health care: the elderly's access and utilization (dissertation)*. St. Louis (MO). Washington Univ; 1995.

### 3. Other published material

- a) Newspaper article  
Lee G. Hospitalizations tied to ozone pollution: study estimates 50,000 admissions annually. *The Washington Post* 1996, June 21; Sect. A : 3(col. 5).
- b) Dictionary and similar references  
*Student's medical dictionary*. 26th ed. Baltimore: Williams & Wilkins; 1995. Apraxia; p.119-20.

#### **4. Unpublished Material**

a) In press

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a) Journal articles in electronic format

Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis Serial online I 1995 Jan-Mar I cited 1996 June 5 I; 1(1): 24 screens I

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## ORIGINAL ARTICLE

# A Comparative Study to Evaluate the Performance of APACHE II, SAPS II & SOFA Scoring Systems for Assessment of Severity and Outcome of Critically Ill Respiratory Patients in NIDCH, Dhaka

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Md. Khairul Anam<sup>4</sup>, Md. Meer Mahbulul Alam<sup>5</sup>, Rezaul Haque<sup>1</sup>, Bijoy Pada Gope<sup>6</sup>,  
Mir Iftekhar Mostafiz<sup>7</sup>, Sharif Ahmed<sup>8</sup>, Rezaul Hoque<sup>9</sup>

### Abstract

**Background:** Scoring systems are increasingly used in the ICUs in an attempt to accurately predict the mortality outcome in critically ill patients. The aim of this study was to assess the prognostic accuracy of Acute Physiology and Chronic Health Evaluation II (APACHE II), Simplified Acute Physiology Score II (SAPS II) and Sequential Organ Failure Assessment (SOFA) scoring systems to predict in-hospital mortality of critically ill patients with respiratory diseases.

**Method:** The performance of APACHE II, SOFA, and SAPS II was compared in terms of calibration and discrimination in critically ill patients admitted to the ICU. This prospective observational comparative study was conducted in National Institute of Diseases of the Chest and Hospital (NIDCH), Dhaka, Bangladesh from January 2013 to December 2014. Mean admission APACHE II, SAPS II, and SOFA scores as well as SOFA(max) score were compared in 106 patients. The outcome measure was in-hospital mortality. The discriminatory ability of the scores was evaluated using the area under the receiver operating characteristic curve. Calibration was tested using the Hosmer–Lemeshow goodness-of-fit test.

**Results:** Mean APACHE II and SAPS II scores were almost double in non-survivors than survivors and the difference was three fold in case of SOFA scores. These differences were statistically highly significant. The cutoffs obtained by the receiver operating characteristic curve were 22.5 for APACHE II, 5.5 for SOFA, 7.5 for SOFA (max) and 39.5 for SAPS II score. All the tests had good discrimination power with AUC more than 0.9; among them APACHE II (AUC=0.97) and SOFA (max) (AUC=0.96) performed better than SAPS II or SOFA (AUC=0.91 each). In terms of calibration, it was found that SAPS II ( $\chi^2 = 3.04$ ) with  $p=0.88$ , had the best calibration and SOFA (max) ( $\chi^2 = 4.564$ ) with  $p=0.80$  had the worst calibration. From the point of accuracy, APACHE II showed highest accuracy (90.57%) followed by SAPS II (89.62%) and SOFA(max) found least accurate (84.91%).

**Conclusion:** APACHE II and SOFA (max) scores have better discriminatory power, whereas SAPS II score has better calibration. But in terms of accuracy, APACHE II shows the highest accuracy followed by SAPS II. Yet, more studies are needed on a larger number of patients to support our findings.

[Chest & Heart Journal 2015; 39(1) : 1-6]

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**Introduction:**

Critical illness is any disease process which causes physiological instability leading to disability or death within minutes or hours. The outcome of critically ill patients can now be predicted and evaluated using well planned severity of illness scoring systems.<sup>1</sup> Scoring systems allow an assessment of the severity of disease and provide an estimate of in-hospital mortality.

In APACHE II, there are 12 physiological variables. The model uses the worst value from the first 24 hours in the ICU. A main reason for ICU admission has to be chosen from a list of 50 operative and non-operative diagnoses, in order to transform the APACHE II score into a probability of death (in the hospital). The APACHE II score varies from 0 to 71 points: up to 60 for physiological variables, up to 6 for age and up to 5 for previous health status.<sup>2</sup>

SAPS II includes 17 variables: 12 physiologic variables, age, type of admission (non-operative and emergency/elective surgery) and three chronic diagnoses (AIDS, metastatic cancer and hematological cancer). The SAPS II model uses, the most deranged physiologic values registered during the first 24 hours in the ICU. The SAPS II score can vary between 0 and 163 points (up to 116 points for physiological variables, up to 17 points for age and up to 30 points for previous diagnosis).<sup>3</sup>

SOFA score was developed to quantify the severity of patient's illness, based on the degree of organ dysfunction. Six organ systems (respiratory, cardiovascular, renal, hepatic, central nervous, coagulation) were selected, and the function of each is scored from 0 (normal function) to 4 (most abnormal), giving a possible score of 0 to 24. The SOFA scoring system takes into account the time course of a patient's condition during the entire ICU stay. For the SOFA score, the worst value on each day is recorded. From the daily calculated SOFA scores, SOFA(max) can be calculated from the worst values during the entire hospital stay. A maximum total SOFA score (SOFA(max)) greater than 15 correlated with a mortality rate of 90%.<sup>4</sup>

**Materials and Methods:**

This prospective observational comparative study was conducted in NIDCH, Dhaka, Bangladesh from January 2013 to December 2014. Mean admission APACHE II, SAPS II, and SOFA as well as

SOFA(max) scores were compared in 106 critically ill patients with respiratory diseases admitted in ICU. The performance of APACHE II score, SOFA score, and SAPS II score was compared in terms of calibration and discrimination. The outcome measure was in-hospital mortality. The discriminatory ability of the scores was evaluated using the area under the receiver operating characteristic curve. Calibration was tested using the Hosmer–Lemeshow goodness-of-fit test.

Discrimination refers to how well the model discriminates between individuals who will live and those who will die. It is measured by calculating the area under the receiver operating characteristic curve (AUC). An AUC of 0.50 is no better than mere chance, whereas values > 0.90, >0.80 and >0.70 are considered excellent, good and satisfactory, respectively.<sup>5</sup>

Calibration assesses the degree of correspondence between the estimated probability of mortality and that actually observed. This can be tested using the Hosmer-Lemeshow's goodness-of-fit test. Over the range of probabilities, the expected and observed mortality are compared and a *P*-value derived. The H-L is similar to the  $\chi^2$  test. Low  $\chi^2$  value with a high *P*-value (>0.05) indicates good-fit. A *P*-value >0.05 indicates no significant difference between the predicted and observed outcome and the model is considered well calibrated. Calibration is considered to be good if the predicted mortality is close to the observed mortality.

If a scoring model predicts that a patient has a probability of in-hospital mortality of 0.25, it means that, in a sample population of 100 patients, 25 would be expected to die and 75 patients would survive. When the number of deaths in the actual population is near to that predicted by the scoring system, the model is considered well calibrated.<sup>6</sup>

**Study Procedure:**

A total of 106 cases were enrolled in the study. Informed written consent was taken from each and every patient/ patient's guardian after elaborative explanation regarding the study. Patient's name and particulars were recorded in the case record file as well as data collection sheet.

Physical examination including GCS, pulse, BP, respiratory rate, temperature was done and recorded in data collection sheet. Arterial oxygen saturation (SpO<sub>2</sub>) was detected using pulse oxymeter. 24 hours urinary output was recorded.

Arterial blood gas analysis, serum electrolytes, blood urea, serum creatinine, CBC, serum bilirubin were done as soon as possible. Investigations were repeated as a required basis and at least once daily. Results were recorded in data collection sheet containing APACHE II, SAPS II & SOFA scoring table.

APACHE II and SAPS II scoring systems were calculated within first 24 hours of hospital admission. SOFA score was calculated daily including first 24 hours of hospital admission. SOFA(max) was calculated from the worst value of each component from daily SOFA score. All three scoring systems were calculated by automated free online calculators, i.e. APACHE II calculator, SAPS II calculator and SOFA calculator.

### Statistical Analysis:

Result of the study was calculated and analyzed by standard statistical method and was presented in forms of tables and graphs. Data were expressed as mean  $\pm$  SD. A value of  $P < 0.05$  was considered statistically significant. For analysis of data SPSS for Windows (IBM SPSS Statistics for Windows, version 19.0, Armonk, NY:IBM Corp.) software was used. Performance of each scoring system was assessed by detecting sensitivity, specificity, accuracy and receiver operating characteristic (ROC) curve. The discriminatory ability of the scores was evaluated using the area under the ROC curve. Calibration was tested using the Hosmer–Lemeshow goodness-of-fit test.

### Results and Observations:

A total of 106 critically ill patients were included in the study. Of them 80 (75%) were male and rest 26 (25%) were female. The mean age of the patients was 61.11 ( $\pm$  12.56) years with a range of 22-90 years.

Table I shows the patient profile. Exactly half of the patients were suffering from COPD exacerbation. The other notable condition were ILD, Bronchial

asthma & Bronchiectasis (7.5% each); Pleural disease & Post TB fibrosis (6.6% each); Bronchial carcinoma & Pneumonia (4.7% each).

**Table-I**  
*Diagnosis of all patients (n=106)*

Diagnosis	Frequency	Percentage
COPD exacerbation	53	50.00
ILD	8	7.55
Bronchial asthma	8	7.55
Bronchiectasis	8	7.55
Pleural disease	7	6.60
Post TB fibrosis	7	6.60
Bronchial carcinoma	5	4.72
Pneumonia	5	4.72
OSAS	2	1.89
Post-pneumonectomy complications	2	1.89
ARDS	1	0.94

Table II shows outcome at hospital discharge. Out of 106 patients 41 (38.7%) expired in the hospital while getting treatment but 65 patients (61.3%) did survive and were discharged from hospital after improvement.

**Table-II**  
*Outcome of all patients at hospital discharge (n=106)*

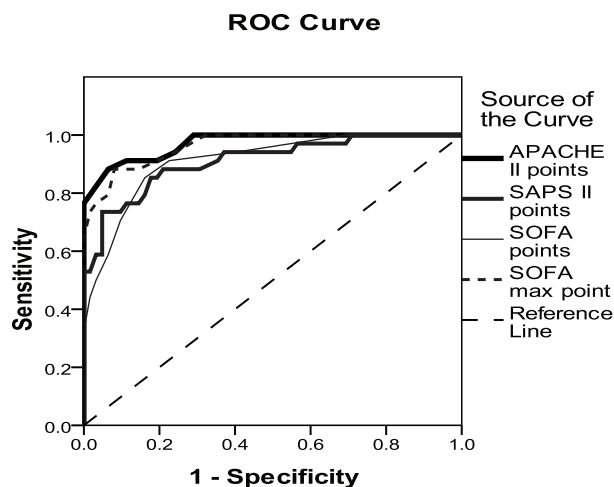
Patient Outcome	Frequency	Percentage
Survived	65	61.32
Expired	41	38.68

APACHE II, SAPS II, SOFA and SOFA(max) scores were compared between survivors and non-survivors groups. Mean APACHE II and SAPS II scores were almost double in non-survivors than survivors and the difference was three fold in case of SOFA scores. These differences were statistically highly significant (Table III).

**Table-III**  
*Comparison between the admission scores and SOFA(max) in survivors and non-survivors (n=106)*

Scoring system	Survivors (n = 65)	Non-survivors (n = 41)	p value
	Mean $\pm$ SD	Mean $\pm$ SD	
APACHE II score	15.69 $\pm$ 4.799	30.85 $\pm$ 7.22	<.001
SAPS II score	33.446 $\pm$ 9.2382	61.244 $\pm$ 16.774	<.001
SOFA score	3.6462 $\pm$ 1.891	9.804 $\pm$ 4.007	<.001
SOFA(max) score	4.95 $\pm$ 2.343	13.32 $\pm$ 3.827	<.001

By using ROC curve with respect to outcome, cutoff points for each scoring systems were measured. Sensitivity, specificity, accuracy and measure of AUC were calculated. Figure 1 depicts the ROC curves of different scores. APACHE II blue line, SAPS II green line, SOFA red line and SOFA (max) violet colour.



**Fig.-1:** ROC curve of APACHE II, SAPS II, SOFA and SOFA (max) scores

It was observed that APACHE II had highest accuracy (90.57%) followed by SAPS II (89.62%) and SOFA (85.85%). All the tests had good discrimination power with AUC more than 0.9; of them APACHE II (AUC=0.97) and SOFA (max) (AUC=0.96) performed better than SAPS II or SOFA (AUC=0.91 each) (Table IV).

**Table- IV**  
Predictive probability of APACHE II, SAPS II, SOFA & SOFA (max) scores

Parameters	APACHE II	SAPS II	SOFA	SOFA (max)
Cutoff	22.5	39.5	5.5	7.5
Sensitivity (%)	89.23	80.0	91.6	81.54
Specificity (%)	92.68	90.24	87.8	90.24
Accuracy (%)	90.57	89.62	85.85	84.91
AUC	0.972	0.911	0.912	0.963
p-value	<0.001	<0.001	<0.001	<0.001

By using Hosmer-Lemeshow goodness of fit tests for evaluating the calibration of the scoring systems it was found that SAPS II ( $\chi^2 = 3.04$ ) with  $p=0.88$ ,

had the best calibration and SOFA (max) ( $\chi^2 = 4.564$ ) with  $p=0.80$  had the worst calibration (Table V).

**Table-V**  
Hosmer-Lemeshow goodness of fit tests for evaluating the calibration of the scoring systems

Scoring system	$\chi^2$	p-value
SAPS II	3.04	0.88
SOFA	3.38	0.64
APACHE II	4.111	0.77
SOFA (max)	4.564	0.80

**Discussion:**

To find out the most appropriate severity scoring system for critically ill patients among commonly used scoring systems to predict in-hospital mortality this prospective observational comparative study was conducted in National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka.

Out of 106 patients, 41 patients (38.7%) expired in the hospital while getting treatment and 65 patients (61.3%) survived.

In this study, we determined the initial scores of APACHE II, SAPS II and SOFA during the first 24 hour of admission in the ICU. Only for SOFA repetitive scoring system for five days was employed and SOFA(max) was calculated from the worst values of the daily SOFA scores. We further compared the performance of these scores with respect to their calibration and discrimination. The outcome measure was in-hospital mortality.

In this study, mean APACHE II and SAPS II scores were almost double in non-survivors than survivors and the difference was three fold in case of SOFA scores. These differences were statistically highly significant. However, several studies reported that admission APACHE II score and SAPS II score did not differ significantly between survivors and non-survivors and did not have an influence on the risk for mortality in ICU patients.<sup>7-9</sup> The cause for such discrepancy is not clear but age, ethnicity and different health delivery system prevailing in our country could contribute in this regard. Some studies were in agreement with my study findings with respect to admission SOFA score that differed

significantly between survivors and non-survivors.<sup>10-12</sup> Yet, owing to the difference in the study population with respect to the type of ICU under study and the diagnosis on admission besides the knowledge that in some studies the repetitive daily scores were used instead of the admission scores, some studies reported that APACHE II and SAPS II scores differed significantly between survivors and non-survivors.<sup>13-15</sup>

The cutoffs obtained by the receiver operating characteristic curve were 22.5 for APACHE II, 39.5 for SAPS II, 5.5 for SOFA and 7.5 for SOFA (max). It was observed that APACHE II had highest accuracy (90.57%) followed by SAPS II (89.62%) and SOFA (85.85%). All the tests had good discrimination power with AUC more than 0.9; of them APACHE II (AUC=0.97) and SOFA (max) (AUC=0.96) performed better than SAPS II or SOFA (AUC=0.91 each). In a study, the discrimination power of SOFA score was better than that of APACHE II score.<sup>16</sup> In a recent study, calibration was worst for APACHE II score compared with SAPS II score, which showed good calibration.<sup>17</sup>

### Conclusion:

It can be concluded that APACHE II and SOFA (max) scores have better discriminatory power, whereas SAPS II score has better calibration. But in terms of accuracy, APACHE II shows the highest accuracy followed by SAPS II. These findings were not surprising on the basis of the understanding that, it is not possible for any model to have perfect calibration and discrimination at the same time.<sup>18</sup> So, from the findings of my study, it can be concluded that APACHE II score is better than other scores in terms of prediction of in-hospital mortality. Yet, more studies are needed on a larger number of patients to support these findings.

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## ORIGINAL ARTICLE

# Bacterial Isolates and Their Antimicrobial Sensitivity Pattern of Different Clinical Specimens From the COPD And Non-COPD Patients Admitted In ICU of National Institute of Diseases of The Chest & Hospital (NIDCH)

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### Abstract

**Background:** Intensive care unit is one of the potential sources of infection even in countries where extensive infection control measures are routinely implemented. Both Gram negative bacilli (GNB) and Gram positive bacilli (GPB) are reported as important causes of hospital-acquired infections. The antibiotic sensitivity pattern of organism is changing very rapidly over a short period. Periodic evaluation of sensitivity pattern is essential for rational and appropriate use of antibiotics in ICU.

**Methods:** This observational comparative study was conducted in the ICU of NIDCH, Dhaka over a period of July 2012 to June 2014. Patients of any age & of either sexes admitted at Intensive Care Unit, NIDCH with COPD and Non-COPD over two years period were the study population. Thus a total of 116 patients were included in study group. The sampling technique was purposive sampling.

**Result:** Growth of microorganisms from the COPD (n=51) and Non-COPD (n=65) patients were 56.9% and 72.3% respectively. Thus, a total of 76 (65.5%) out of 116 patients showed growth of microorganisms with gram negative bacilli infection was predominant in both groups. In terms of total bacterial isolates Pseudomonas was the commonest organisms followed by Acinetobacter, Klebsiella, E.coli in both groups. Non-COPD patients were more prone to acquire Pseudomonas infection than their COPD counterparts (p=0.009). There was significant difference in antibiotic sensitivity to microorganisms between two groups and highest sensitivity was obtained with Colistin.

**Conclusion:** The result of this study concluded that Gram negative bacilli infection was predominant in both COPD and Non-COPD patients. Among them Pseudomonas was the significantly common organism in Non-COPD than COPD patients. There was significant difference in antibiotic sensitivity to microorganisms between groups.

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## Introduction:

Worldwide, ICUs are faced with increasingly rapid emergence and spread of antimicrobial resistant bacteria because of frequent use of broad spectrum antimicrobials, crowding of patients with high levels of disease acuity in relatively small, specialized areas of the hospital, and the presence of more chronically and acutely ill patients who require prolonged hospitalization<sup>1</sup>. The international study of infection in ICU which was conducted in 2007, and involved with 1265 ICUs from 75 countries, demonstrated that patients who had longer ICU stays had higher rates of infection, especially infections due to resistant *Staphylococci*, *Acinetobacter*, *Pseudomonas* and *Candida* species. Moreover, the ICU mortality of infected patients was more than twice than that of non-infected patients<sup>2</sup>. In a recent report, Infectious Disease Society of America, specifically addressed three categories of Gram negative bacilli (GNB), namely extended spectrum beta lactamase (ESBL) producing *Escherichia coli* and *Klebsiella* spp., multidrug resistant (MDR) *Pseudomonas* and carbapenem resistant *Acinetobacter* spp., as high priority bacterial pathogens<sup>3</sup>. The antibiotic sensitivity pattern of organism is changing very rapidly over a short period<sup>4</sup>. It is particularly true for developing countries like Bangladesh where in almost all cases, antimicrobials are prescribed prophylactically and empirically without carrying out sensitivity studies. This type of scenario is also reported by Palikhe in Nepal<sup>5</sup>. Development of antimicrobial resistance is directly proportional to the volume of antimicrobial consumed. Therefore, to reduce the development of antimicrobial resistance, the antibiotic usage should be rational and be guided by research data<sup>6</sup>. In the hospitals of Bangladesh there are very few studies of antibiotic use and their outcome for patients especially in ICU. Therefore the aim of this study was to determine the pattern of bacterial isolates and their antimicrobial sensitivity pattern in different clinical specimens obtained from the COPD and Non-COPD patients admitted in Intensive Care Unit (ICU) of NIDCH.

**Materials and Methods:** This observational comparative study was conducted in the Intensive care unit at National institute of Diseases of the Chest & Hospital (NIDCH), Dhaka over a period of 02 years between July 2012 to June 2014. Patients of any age & of either sexes admitted at Intensive

Care Unit, NIDCH with COPD and Non-COPD over two years period were the study population. Patient with active tuberculosis, pregnant women & transferred from another ICU staying for more than 48 hours were excluded from the study. Thus a total of 116 patients were included in study group. The sampling technique was purposive sampling. Specimens were collected from the patients as early as possible after being admitted in ICU. All the patients were on different types of locally available antibiotics. The different specimens like sputum, tracheal aspirate, blood and urine were sent to the laboratory for Gram staining and culture sensitivity test. Collected data were processed and analyzed using SPSS (Statistical Package for Social Sciences), version 20. Test statistics used to analyzed data were Chi-square (for comparison of data presented on categorical scale) and Unpaired t-Test (for data presented on continuous scale). Level of significance was set at 0.05 and  $p < 0.05$  was considered as significant.

## Results and observations:

Growth of micro organisms of the COPD (n=51) and Non-COPD (n=65) patients showed 29(56.9%) and 47(72.3%) respectively. Thus, a total of 76 (65.5%) out of 116 patients showed growth of microorganisms with gram negative bacilli being the predominant in both COPD and Non-COPD patients (**Table I**).

**Table I**

*Types of isolated microbes from ICU patients between groups:*

Types of organisms	Diagnosis		P-value
	COPD (n=51)	Non-COPD (n=65)	
Only Gram positive #	1(2.0)	0(0.0)	0.199
Only Gram negative*	25(49.0)	41(63.1)	0.170
Both (+ve and -ve)#	3(5.9)	6(9.2)	0.149

(Figures in the parentheses denote corresponding percentage, \*Data were analysed using Chi-square Test, # Fisher's Exact Test was employed to analyse the data).

Of the total 316 samples was taken from 116 patients, 93 were sputum, 27 tracheal aspirates (TA), 80 blood and 116 urine samples. Majority (81.5%) of the tracheal aspirate culture sensitivity



yielded growth of organisms followed by sputum (57%), urine (8.6%) and blood (6.2%). Sputum culture (Table II) from Non-COPD patients exhibited significant growth of bacteria ( $p = 0.006$ ). Growth of bacteria in tracheal aspirate, blood and urine was no significant difference between groups ( $p > 0.05$ ).

**Table II**

*Microorganisms were isolated from Sputum of COPD and Non-COPD patients:*

Sputum*	Group		P-value
	COPD (n = 43)	Non-COPD (n = 50)	
Growth present	18(41.9)	35(70.0)	
No growth	25(58.1)	15(30.0)	0.006

(Figures in the parentheses denote corresponding %; \*data were analysed using Chi-square Test.)

Association of microorganisms with lung diseases (**Table III**) showed that Non-COPD patients in the ICU were more prone to acquire *Pseudomonas* infection than the COPD patients ( $p=0.009$ ). Other microorganisms shown in Table II are almost identically distributed between the groups ( $p > 0.05$ ).

**Table III**

*Comparison of organisms between COPD and Non-COPD patients*

Organisms	Diagnosis		P - value
	COPD (n=51)	Non-COPD (n=65)	
Gram Negative			
<i>Pseudomonas</i> *	9(17.6)	26(40.0)	0.009
<i>Acinetobacter</i> *	7(13.7)	15(23.1)	0.202
<i>Klebsiella</i> *	5(9.8)	11(16.9)	0.270
<i>E coli</i> *	5(9.8)	7(10.8)	0.865
<i>Haemophilus influenzae</i> #	1(2.0)	1(1.5)	0.862
<i>Proteus</i> #	1(2.0)	1(1.5)	0.862
<i>Enterobacter</i> #	1(2.0)	0(0.0)	0.257
<i>Citrobacter</i> #	1(2.0)	0(0.0)	0.257
Gram Positive			
<i>Staphylococcus</i> #	2(3.9)	1(1.5)	0.422
<i>Streptococcus</i> #	0(0.0)	2(3.1)	0.206
<i>Enterococcus</i> #	2(3.9)	3(4.6)	0.855

(Figures in the parentheses denote corresponding percentage, \*Data were analysed using Chi-square Test, # Fisher's Exact Test was employed to analyse the data).

There was significant difference (**Table IV**) in antibiotic sensitivity to microorganisms among COPD and Non-COPD patients in case of ampicillin, amikacin, carbenicillin, ciprofloxacin, colistin, gentamicin, imipenem, meropenem, (piperacillin + tazobactam) and tobramycin ( $p < 0.05$ ). The highest sensitivity was obtained with colistin; moderate with amikacin, azithromycin, ceftazidime, imipenem, levofloxacin, meropenem, netilmycin, polymixin-B, tobramycin and lowest sensitivity with ampicillin, amoxiclavulanic acid, aztreonam, cephalexin, cefotaxim, ceftriaxone, nalidixic acid, nitrofurantoin, tetracycline etc.

**Table IV**

*Comparison of sensitivity pattern of microorganisms to antibiotics between groups*

Antibiotics	Diagnosis		P-value
	COPD (n=51)	Non-COPD (n=65)	
Ampicillin#	3(5.9)	0(0.0)	0.048
Amoxyclavulanic acid#	1(2.0)	0(0.0)	0.257
Amikacin*	9(17.6)	25(38.5)	0.015
Azithromycin#	4(7.8)	10(15.4)	0.216
Aztreonam#	1(2.0)	1(1.5)	0.862
Cephalexin#	0(0.0)	1(1.5)	0.374
Cefuroxim#	1(2.0)	0(0.0)	0.257
Cefotaxim#	0(0.0)	1(1.5)	0.374
Ceftriaxone#	1(2.0)	2(3.1)	0.707
Ceftazidime#	4(7.8)	12(18.5)	0.100
Cotrimoxazole#	3(5.9)	3(4.6)	0.760
Chloramphenicol#	1(2.0)	1(1.5)	0.862
Ciprofloxacin#	2(3.9)	10(15.4)	0.044
Colistin*	23(45.1)	42(64.6)	0.036
Carbenicillin#	3(5.9)	2(3.1)	0.048
Gatifloxacin#	1(2.0)	2(3.1)	0.707
Gentamicin#	3(5.9)	13(20.0)	0.029
Imipenem#	2(3.9)	11(16.9)	0.028
Linezolid#	5(9.8)	3(4.6)	0.274
Levofloxacin*	5(9.8)	12(18.5)	0.191
Meropenem*	5(9.8)	17(26.2)	0.026
Nalidixic acid#	1(2.0)	0(0.0)	0.257
Nitrofurantoin#	1(2.0)	0(0.0)	0.257
Netilmycin#	4(7.8)	11(16.9)	0.148
Pefloxacin#	3(5.9)	6(9.2)	0.503
Piperacillin+ Tazobactam#	2(3.9)	15(23.1)	0.004
Polymixin-B*	8(15.7)	18(27.7)	0.124
Tobramycin*	5(9.8)	20(30.8)	0.006
Tetracyclin#	2(3.9)	5(4.6)	0.397
Vancomycin#	4(7.8)	3(4.6)	0.469

### Discussion:

In the present study a total of 316 samples were obtained from 116 patients. Of them 93 were sputum, 27 tracheal aspirates (TA), 80 blood and 116 urine samples. Majority (81.5%) of the tracheal aspirates exhibited growth of organisms followed by sputum (57%), urine (8.6%) and blood (6.2%). Growth of microorganisms of the COPD (n=51) and Non-COPD (n=65) patients showed 56.9% and 72.3% respectively. Thus, a total of 76(65.5%) out of 116 patients showed growth of microorganisms with gram negative bacilli infection was predominant in both COPD and Non-COPD patients. In terms of total bacterial isolates *Pseudomonas* was the commonest organisms followed by *Acinetobacter*, *Klebsiella*, *E.coli* in both COPD and Non-COPD patient. However, Non-COPD patients were more prone to acquire *Pseudomonas* infection than their COPD counterparts ( $p = 0.009$ ). Sputum culture from Non-COPD patients exhibited significant growth of bacteria ( $p=0.006$ ) and predominantly showed growth of *Pseudomonas* infection whereas tracheal aspirate, blood and urine cultures exhibited least growth of the same organism. Growth of bacteria in tracheal aspirate, blood and urine samples was no significant differences between groups ( $p>0.05$ ).

Several studies have shown that most common bacterial agents of LRTI in the ICU are *Pseudomonas*, *Acinetobacter*, *Klebsiella*, *Citrobacter*, *Escherichia coli*.<sup>7,8,9</sup> However a recent study conducted in Ahmadabad by Zaveri et al (2012)<sup>10</sup>, showed that the commonest organism isolated from all samples was *E.coli* (25%) followed by *Acinetobacter* spp. and *Pseudomonas* spp. (21.3%). So the pattern of bacterial involvement may vary from region to region and with respect to types of ICU. The isolation pattern of organisms may vary over time and hospital settings as well and, in general, gram-negative are more common than Gram positive ones.<sup>11,12</sup>

In the present study there was significant difference in antibiotic sensitivity to microorganisms among COPD and Non-COPD patients. The highest sensitivity was obtained with colistin; moderate with amikacin, azithromycin, ceftazidime, imipenem, levofloxacin, meropenem, netilmycin, polymixin-B and tobramycin. *Pseudomonas* was significantly ( $P<0.05$ ) sensitive to amikacin, azithromycin and meropenem; *Acinetobacter* to colistin and

polymixin-B; *Klebsiella* sp. to amikacin, aztreonam and carbenicillin; *E.coli* to colistin and aztreonam.

Zaveri and colleagues (2012)<sup>10</sup> in their study demonstrated that *E.coli* was most commonly sensitive to amikacin (87.5%), CONS to cefotaxime (95%), *Klebsiella* sp. to combined Cefoperazone + salbactam (78%), *Pseudomonas* to piperacillin + tazobactam (65%), and *Acinetobacter* sp. to cefoperazone & sulbactam (55%). The most common multidrug resistant organisms were *Citrobacter* spp. (66.7%) followed by *Proteus* spp. (33.3%) and *Enterococcus* (33.3%). The extreme antibiotic use results in the emergence of multi-resistant microorganisms in the ICU environment. Infection with resistant strains in the ICUs leads to increased mortality and cost.<sup>13</sup> The present study revealed high prevalence of antibiotic resistant organisms in our ICU.

### Conclusion:

The result of this study concluded that Gram negative bacilli infection was predominant in both COPD and Non-COPD patients that required ICU admission. *Pseudomonas* was the significantly common organism and Non-COPD patients were more prone to acquire this type of infection than their COPD counterparts. There was significant difference in antibiotic sensitivity to microorganisms between groups. On the basis of infecting microorganisms and their sensitivity pattern if we want to start empirical antimicrobial therapy in ICU setting, it would be to cover Gram negative infection and wise to choose any of the moderately sensitive antibiotics. Although colistin demonstrated highest sensitivity, it should not be chosen for empirical therapy, for its indiscriminate use may soon cause the bacteria to develop resistance against it. Colistin should therefore, be employed when any one the moderately sensitive drugs fail to control infection.

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## ORIGINAL ARTICLE

# Comparison of Physiological Responses Between Six Minute Walk Test and Incremental Shuttle Walk Test in Moderate to Severe Copd Patients in A Tertiary Hospital

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### Abstract

**Background:** COPD leads to a reduction in exercise capacity. Exercise tests such as six minute walk test (6MWT) and Incremental Shuttle Walk Test (ISWT) can be used for the objective evaluation of functional exercise capacity as well as to measure outcome of interventions like pulmonary rehabilitation. The aim of this study was to compare the physiological responses between the 6MWT and ISWT in moderate to severe COPD patients.

**Materials and Methods:** This prospective cross-over study was done in the National Institute of Diseases of the Chest & Hospital, Mohakhali, Dhaka from July 2013 to June 2015, to compare the physiological responses between the 6MWT and ISWT. Ninety six patents were included in the final analysis. Paired t-test and Coefficient of variation (CV) were calculated for the comparisons of variables. Data were expressed as mean + SD. A value of  $P < 0.05$  was considered statistically significant.

**Results:** Out of 96 patients 88 (92%) were male. The mean age of the patients was  $58.54 \pm 9.937$  years with a range of 40-80 years. Analyzed data showed significant differences regarding heart rate, oxygen saturation and dyspnoea score between 6MWT and ISWT ( $p < 0.05$ ) although the changes of blood pressure (BP) and respiratory rates were similar between the two tests ( $p > 0.05$ ). After each minute observation, the changes of HR,  $SpO_2$  and dyspnoea score from baseline were found less but gradual in case of ISWT than 6MWT. The mean value for the distance walked in 6MWT was  $292.47 \pm 28.18$  meter and that of the ISWT was  $314.84 \pm 19.067$  meter which were significantly different. ( $p < 0.001$ ).

**Conclusion:** Incremental Shuttle Walk Test (ISWT) can be considered as a better tool than six minute walk test (6MWT) in terms of physiological responses in moderate to severe COPD patients.

**Key words:** 6MWT, ISWT, COPD

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**Introduction:**

Chronic obstructive pulmonary disease (COPD), a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles and gases. Exacerbations and comorbidities contribute to the overall severity in individual patients<sup>1</sup>.

COPD leads to a reduction in exercise capacity that affects the quality of life and increases mortality of these patients. Limited exercise tolerance is one of the main complaints in patients with chronic obstructive pulmonary disease (COPD). Exercise capacity has become an important outcome measure in COPD, as many patients complain of exercise intolerance and exertional dyspnoea, and because it is a major determinant of an impaired health status<sup>2</sup>. So, exercise tests are considered as an essential component of the clinical evaluation of the patients with COPD<sup>3</sup>. There are several modalities of exercise tests available for the objective evaluation of functional exercise capacity. The most popular clinical exercise tests in order of increasing complexity are stair climbing, a six minute walk test (6MWT), a incremental shuttle walk test (ISWT), detection of exercise-induced asthma, a cardiac stress test (e.g. Bruce protocol), and a cardiopulmonary exercise test<sup>4,5</sup>.

Although the laboratory-based tests are the gold standard for the exercise testing, they are not widely available, require advanced technical equipment and may be difficult to access. However, the field walking tests such as 6MWT and ISWT are usually used in pulmonary rehabilitation as both assessment tools as well as outcome measures in pulmonary rehabilitation program<sup>6,7</sup>.

The 6MWT is a self-paced, simple walking test that requires a 100-ft hallway. This test measures the distance that a patient can quickly walk on a flat, hard surface in a period of 6 minutes (6MWD). Although attractive, these protocols are difficult to standardize and may be influenced by motivation and encouragement<sup>8</sup>. The self-paced 6MWT assesses the submaximal level of functional capacity. In addition, their very simplicity limits the information that can be obtained from them about the physiological and symptomatic changes that occur during exercise<sup>9</sup>. However, because most activities of daily living are performed at submaximal levels

of exertion, the 6MWD may better reflect the functional exercise level for daily physical activities but the six minute walking test appears to overestimate the extent of disability in some patient<sup>8</sup>. The fact that investigators have used the 6MWT in moderate to severe COPD does not prove that the test is clinically useful (or the best test) for determining functional capacity or changes in functional capacity due to an intervention in patients with these diseases. Further studies are necessary to determine the utility of the 6MWT in various clinical situations<sup>10</sup>.

More recently, an ISWT has been developed. The subjects are required to walk up and down a 10 m course marked by cones placed 9 m apart, allowing 0.5 m for turning at each ends. The speed is regulated by an audio signal played on a tape cassette. It is an externally paced, standardized, incremental field walking test where by subjects are to increase their walking speed each minute progressively to a point at which the test is terminated due to breathlessness or unable to maintain the required walking speed<sup>8</sup>. It provokes a symptom limited maximal performance. It provides an objective measurement of disability and allows direct comparison of patients' performance, less influenced by the therapist encouragement, and it has been proposed as a more reproducible test to evaluate exercise tolerance. The gradual increase in exercise intensity increases the safety of the test. The shuttle walk test provokes a graded cardiovascular response not evident in the six minute test. The defined speeds of walking in the shuttle test ensure that the work load increases in a manner which provides an incremental and quantitatively similar cardiorespiratory stress for all the patients<sup>11</sup>.

A study done by Turner et al. showed that similar peak exercise responses were achieved in the 6MWT, ISWT and CET, with greater oxygen desaturation observed during the field walking tests<sup>12</sup>. Studies comparing the 6MWT and ISWT suggested that the peak exercise responses are similar between each test in subjects with moderate-to-severe COPD<sup>13,14</sup> while other study indicated that they are lower in the 6MWT in population with mild COPD<sup>8</sup>.

Previous study suggested there are no significant differences in the changes of systolic blood pressure, heart rate, respiratory rate, oxygen saturation and dyspnea score among 6MWT and ISWT, with significant correlation between the distances walked

in both tests<sup>11</sup>. Recent study found that there are wide variations in oxygen saturation between the two walking tests<sup>15</sup>. So, the aim of this study was to assess and compare the physiological responses between the 6MWT and ISWT in moderate to severe COPD patients to find out a better test for assessment of functional capacity of COPD patients.

### Materials and Methods

The study was conducted in the department of Respiratory medicine in National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka. It is a prospective cross over study. The study was conducted from July 2013 to June 2015 for a period of two years. A total of 101 consecutive hospitalized patients were enrolled in this study. Informed written consent was taken from all the subjects after full explanation of the nature, purpose and potential risks of all procedures used for the study. Inclusion Criteria were all COPD patients of 40-80 years of both sexes with stage-II and stage-III COPD (GOLD criteria). Exclusion Criteria were acute exacerbation of COPD; COPD associated with asthma, restrictive lung disease, respiratory failure, severe bronchiectasis, lung cancer, recent thoracic or abdominal surgery; Uncontrolled comorbidities such as severe cardiac, neurologic, musculoskeletal or vascular disease in the lower extremities and unable to perform spirometry, the 6MWT and the ISWT; Patients who refused to give consent to take part in this study.

A standard questionnaire was designed with a view to collect data. Initial evaluation of the patient by history and clinical examination was performed and recorded in the preformed data sheet. Pulse, blood pressure, respiratory rate, base line laboratory investigations like CBC, CXR, ECG, blood sugar, liver and renal function test were done. Spirometry was performed by spirometry G (product of MEDICAL INTERNATIONAL RESEARCH (MIR), ROMA, ITALY) and severity was defined according to the GOLD guidelines. Then both 6MWT & ISWT was done in the respiratory laboratory of NIDCH in each

patient on the same day at a particular point of time after a rest of at least 30 minutes in between the two tests. A standardized instruction was given to each patient about the both tests. The baseline measurements of Blood Pressure (BP), Heart Rate (HR), Respiratory Rate (RR), Oxygen Saturation (SpO<sub>2</sub>) and dyspnea score were done. Then BP and RR was also measured at the end and five minutes after the test. The HR, SpO<sub>2</sub> and dyspnea score was taken after each minute, at the end and five minutes after the test. The HR and SpO<sub>2</sub> were taken from a portable pulse oximeter (ChoiceMMed, Baijing Choice Electronic Technology Co., Ltd.) placed on the finger of the patient during the procedure. Dyspnea score was taken from the patient by the perceived dyspnea according to the Borg breathlessness scale. Distance walked in each test was recorded. The 6MWT was done according to the American Thoracic Society guideline (2002). The ISWT was done according to protocol developed by the Singh et al (1992).

All the data were recorded systematically. Results of the study were calculated and analyzed by standard statistical method and presented in the forms of tables and graphs. Data were expressed as mean + SD. The t-test was calculated for paired comparisons. Coefficient of variations (CVs) were calculated for the comparison of variables. A value of  $P < 0.05$  was considered statistically significant.

### Results and Observations

On the basis of the inclusion and exclusion criteria a total of 101 cases were enrolled in the study. Of them 96 cases successfully performed the ISWT and 6MWT and included in the final analysis. The findings derived from the data analysis are presented below: Figure 1 showed the age and sex distribution of the patients (n=96). The mean age of the patients was 58.54 ( $\pm 9.937$ ) years with a range of 40-80 years. The leading age group was 51-60 years (39.6%). Of the 96 patients, 88 (92%) were male and rest 8 (8%) were female.

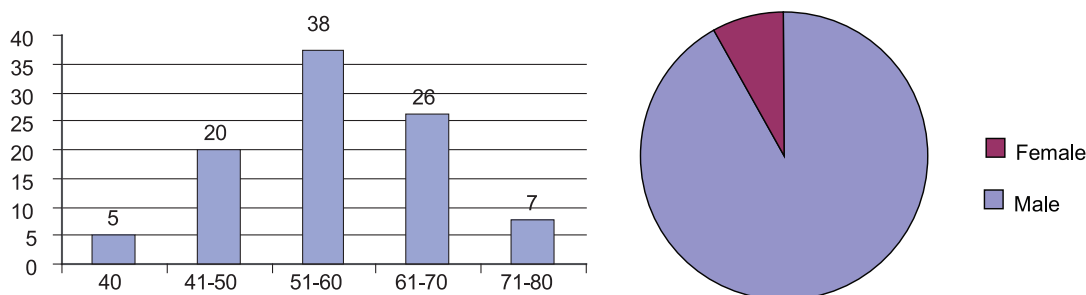


Fig.1: Age and sex distribution of the patients (n=96)

### Blood pressure change in both 6MWT and ISWT

Blood pressure in different points of time in both tests is presented in the figure 2. However, no significant difference was observed in blood pressure between these two test.

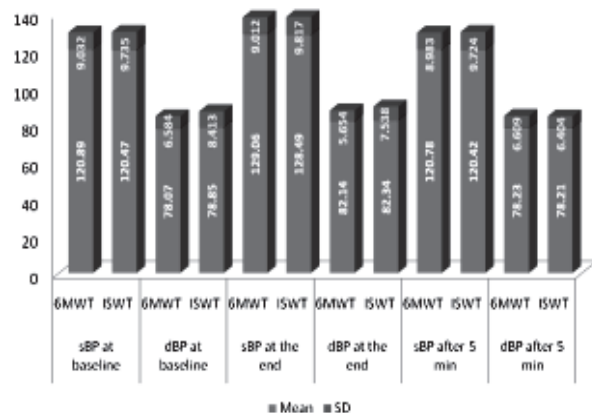


Fig.-2: Blood pressure in different point of time in both tests.

### Heart Rate (HR) change in both 6MWT and ISWT

Heart rates in different points of time in both tests are presented in the figure 3. A significant difference in HR was observed in between the two tests.

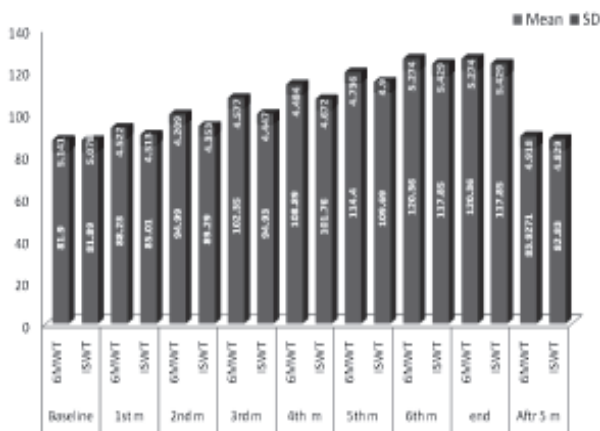


Fig.- 3: Heart rate in different point of time in both tests.

### Oxygen saturation (SpO<sub>2</sub>) change in 6MWT and ISWT

Oxygen saturation in different points of time in both tests is presented in the figure 4. Except baseline, at the end and 5 minutes after test results, all other observations were significantly different between the two test .

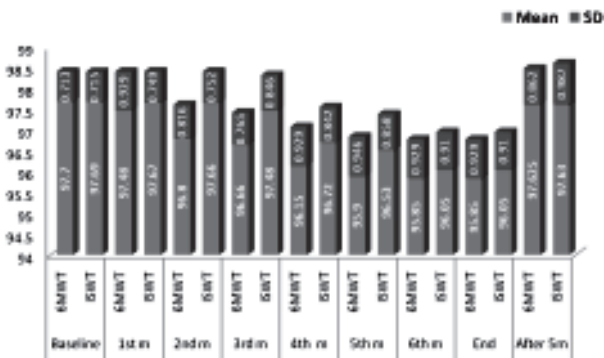


Fig.-4: Oxygen saturation in different point of time in 6MWT and ISWT

### Respiratory Rate (RR) change in 6MWT and ISWT

Respiratory rate (RR) in different points of time in both tests is presented in the figure 5. However, a significant difference was observed after five minutes of the tests.

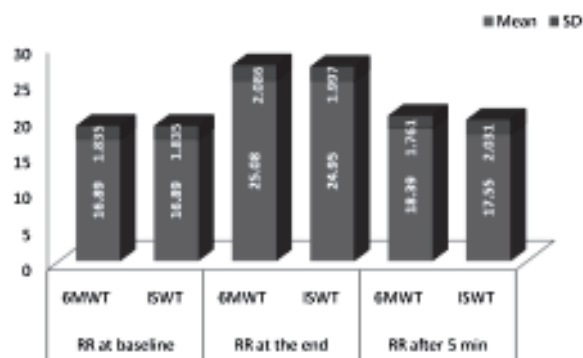


Fig.-5: RR in different point of time in 6MWT and ISWT

### Dyspnoea score change in 6MWT and ISWT

Dyspnoea score in different points of time in both tests is presented in the figure 6. Significant differences were found after each minute of observation except baseline, at 6min and at the end.

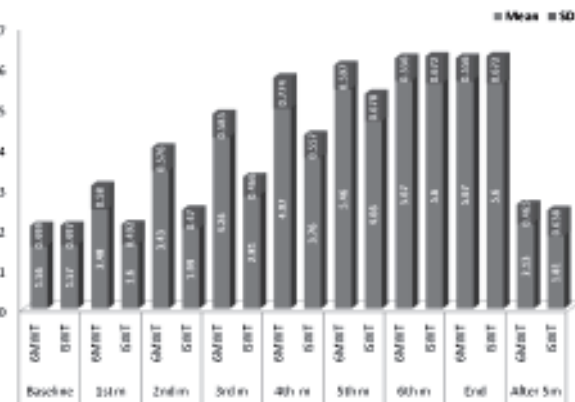
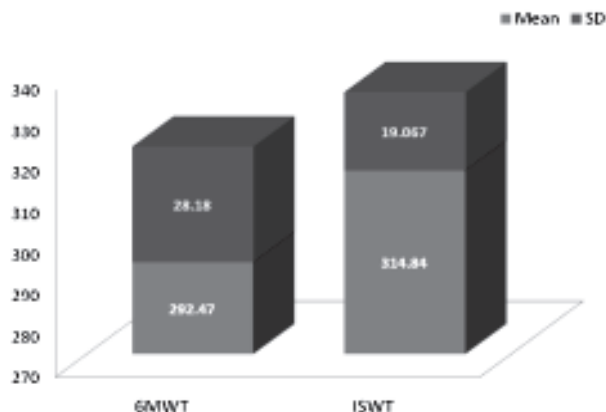


Fig.-6: Dyspnoea score in different point of time in 6MWT and ISWT

### Distance walked in 6MWT and ISWT

Distance walked in both tests is presented in the figure 7. The mean value for the distance walked in 6MWT was  $292.47 \pm 28.18$  meter and that of the ISWT was  $314.84 \pm 19.067$  meter which was statistically significantly different.



**Fig. 7:** Distance walked in 6MWT and ISWT

### CVs of response variables

Coefficient of variation of different physiological response variables i.e. HR, SpO<sub>2</sub> and DS are given in the following table. For first two variables CVs appeared to be almost similar in two tests. In case of dyspnoea score, CVs were different in two tests.

**Table-I**

*Coefficient of variation of different physiological response variables*

Time	Test	CV of HR	CV of SpO <sub>2</sub>	CV of DS
At baseline	6MWT	6.28	0.73	31.99
	ISWT	6.20	0.73	31.66
At 1 <sup>st</sup> minute	6MWT	5.13	0.95	23.39
	ISWT	5.31	0.77	30.75
At 2 <sup>nd</sup> minute	6MWT	4.43	0.84	16.79
	ISWT	4.88	0.77	23.62
At 3 <sup>rd</sup> minute	6MWT	4.47	0.79	13.73
	ISWT	4.68	0.87	16.58
At 4 <sup>th</sup> minute	6MWT	4.12	0.97	15.57
	ISWT	4.59	0.87	14.81
At 5 <sup>th</sup> minute	6MWT	4.14	0.99	10.93
	ISWT	4.47	0.89	14.55
At 6 <sup>th</sup> minute	6MWT	4.38	0.97	9.81
	ISWT	4.61	0.95	12.00
At the end	6MWT	4.38	0.97	9.81
	ISWT	4.61	0.95	12.00
After 5 minutes	6MWT	5.86	0.88	21.83
	ISWT	5.83	1.01	35.25

CV= Coefficient of variation= SD/MeanX100; HR= Heart rate; SpO<sub>2</sub>= Oxygen saturation; DS=Dyspnoea score

### Discussion

To compare the physiological responses between the 6MWT and ISWT in moderate to severe COPD patients this prospective cross over study was done in the National Institute of Diseases of the Chest & Hospital from July 2013 to June 2015. A total of 96 cases were enrolled in the study of them 88 (92%) were male. The mean age of the patients was 58.54 ( $\pm 9.937$ ) years with a range of 40-80 years. Just more than half of the (52.1%) patients had normal BMI and the rest had either low (40.6%) or high BMI (7.3%). Most of the patients were smokers (55/96) and 39 patients (40.6%) were ex-smokers.

In the current study cardiac performance was compared between 6MWT and ISWT among COPD patients. However, no significant difference was observed in blood pressure between these two tests ( $p > .05$ ) which was consistent with the finding of the study done by Vagaggini et al. 2003<sup>11</sup>. But significant differences were observed regarding heart rate (HR) between the two tests ( $p < 0.05$ ). After each minute observation HR was found significantly less in Incremental Shuttle Walk Test than 6 Minute Walking Test. This finding contradicts other study finding (Casas et al. 2002<sup>14</sup>, Turner et al. 2004<sup>12</sup>, Vagaggini et al. 2003<sup>11</sup>) who reported no difference regarding HR in the two tests. This difference might be due to the adoption of different protocols of 6MWT and use of different devices for recording of heart rate. The HR increment at the end of each minute in both test showed a graded cardiovascular response to the ISWT which was not observed in the 6MWT. Similar finding was reported by Singh et al. 1992<sup>8</sup>. The present study showed that HR had a fast increase in the first few minutes of 6MWT and maintained a lower increment after that which was consistent with the study finding of Turner et al. 2004<sup>12</sup>. Regarding HR recovery after 5 minutes of tests significant difference was also observed between the two tests.

Oxygen saturations in different points of time in both tests were measured. Except baseline, at the end and 5 minutes after test results, all other observations were significantly different between the two tests ( $p < 0.05$ ) which was also reported by Lewko et al. 2007<sup>15</sup>. The changes of SpO<sub>2</sub> from baseline were less but more gradual in ISWT than 6MWT. The recovery of SpO<sub>2</sub> after 5 minutes of the two tests was grossly identical ( $p > 0.05$ ).



Regarding respiratory rate (RR), no significant difference was observed during the two tests ( $p>0.05$ ) but only significant difference was noted after 5 minutes of the tests where RR was found to be less in ISWT test than 6MWT which was also reported by Vagaggini et al. 2003<sup>11</sup>.

Regarding dyspnoea score significant differences were observed between 6MWT and ISWT ( $p<0.05$ ) except at baseline and at 6 minute. This finding was consistent with the study by Singh et al. 1992<sup>8</sup>. The changes dyspnoea score from baseline were less but more gradual increment in ISWT than 6MWT. A significant difference was also noted in despnouea recovery after 5 minutes of the two tests.

In this study, the mean value for the distance walked in 6MWT was  $292.47 \pm 28.18$  meter and that of the ISWT was  $314.84 \pm 19.067$  meter which was significantly different but with significant correlation between the two tests ( $R=0.55$ ;  $p<0.001$ ). It means that the distances walked were consistent and inter-related in both tests, as suggested in previous study (Vagaggini et al. 2003<sup>11</sup>, Turner et al. 2004<sup>12</sup>, Ayiesah & Chang 2010<sup>16</sup>).

Finally Coefficient of Variations (CV) of different physiological response variables were examined. For HR and SpO<sub>2</sub> no considerable differences were noted in CV scores. In case of dyspnoea score, CVs were different in two tests.

### Conclusion:

Comparison of physiological responses between 6MWT and ISWT showed that significant differences were observed regarding heart rate, oxygen saturation and dyspnoea score although the changes of blood pressure and respiratory rates were similar between the two tests. After each minute observation, the changes of HR, SpO<sub>2</sub> and dyspnoea score from baseline were found less but gradual in case of ISWT than 6MWT. Walked distance was significantly more in ISWT than 6MWT. So, the ISWT can be considered as a better tool than 6MWT in terms of physiological responses in patients with moderate to severe COPD.

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## ORIGINAL ARTICLE

# Profiles of Tuberculosis Affected Workers in the Selected Tea Garden Areas of Bangladesh

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### Abstract:

**Background:** In 1993 WHO declared TB as a global emergency and recommended DOTS strategy for TB control worldwide. The National Tuberculosis Control Program (NTP) of Bangladesh adopted this strategy to achieve the dual targets of 70 % case detection and 85 % treatment completion as set by the World Health Organization. But TB prevention and control in the Tea Garden areas still remained a big challenge for NTP. There is a gap and lack of information regarding Tea garden workers where stigma, knowledge, attitude and practice (KAP) are the most important aspect to implement which is essential for designing an effective TB control program. This study determined the profiles of Tuberculosis affected Workers of selected Tea garden areas.

**Objective:** a) To determine the socio-demographic factors of Tuberculosis affected Tea garden workers. b) To see the stigma and knowledge about TB among the patients. c) To determine the time lag between appearance of symptoms and treatment

**Methods:** This descriptive cross sectional study was conducted at Shamshernagar, Bharaura & Deanstone Tea Garden Health Centers jointly organized by HEED Bangladesh and the garden authority of Kamalganj and Srimongal upazila. All the registered pulmonary TB patients of 15 years old and above of the three gardens were selected for data collection. A pre-tested structured questionnaire and observational check list were used for data collection through face to face interview. Socio-demographic factors and stigma, knowledge and time lag between symptoms and treatment were statistically evaluated by using uni-variate analysis of chi-square and 95% confidence intervals.

**Results:** A total of 113 Pulmonary TB patients were interviewed. Among them the age of the respondent were between 15 to 64 years, Mean and SD were 40.3 & 11.9 years respectively; 59.3% was male and the rest 40.7% were female, 59.3% illiterate, 37.2% primary and the rest 3.5% were S.S.C; 79.6% were married and 17.7% were unmarried and the rest 2.7% were widow. Mean monthly family income of the respondent was Tk.1505.3 and SD Tk. 604.4, 91.2% lived in kacha house and the rest in semi-pucca house. Based on BMI 53.1% had normal nutritional status, 2.7% were over nourished, BMI>24.99 kg/m<sup>2</sup> while the rest 44.2% were under nourished, BMI<18.5 kg/m<sup>2</sup>. Mean BMI=19.04 kg/m<sup>2</sup> and SD = ± 3.55 kg/m<sup>2</sup>, none of them had BMI<sup>2</sup>>30. Among them 58.4% were alcoholic and 46.9% smoker, 17.7% had previous family history of TB, 54.9% told treatment

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*was available at govt. hospital, 1.8% at Fakir/Darbesh. and 16.8% at non govt. & tea garden hospital, 75.8% had one year time lag between the symptoms appear and seeking treatment, and the rest 24.2% had >1 year time lag.*

**Conclusion:** *Results reveal that the Tuberculosis affected garden workers lead a very low profile life, had various misconceptions and stigma towards TB and poor knowledge regarding its cause, transmission and prevention. This would interfere the targeted goals and objectives of NTP. Thus NTP needs strengthening of Health Education Activity to overcome these challenges.*

**Key Words:** *Tea garden workers, Pulmonary Tuberculosis, Stigma & Knowledge.*

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### **Introduction:**

In 2003, the World Health Organization (WHO) and the International Labor Organization (ILO) highlighted workplace as an appropriate setting for initiating Tuberculosis (TB) prevention and control activities [1]. They emphasized the importance for the vulnerable group of people especially garments/tea garden area for implementing TB DOTS (Directly Observed Treatment, Short course) program because “the workplace represents an opportunity to infect workers and employers very easily”.

The consequences of TB for workers are missed work, work disruptions, and reduced productivity<sup>1,2</sup>. In 2006, Global Fund estimated that in the developing world, TB causes a loss in productivity amounting to US\$12 billion per year as 75% of TB deaths occur in persons in the economically productive age of 15 to 54 years<sup>3</sup>. In many instances, workers do not have access to the community-based TB DOTS program during working hours and TB DOTS program often provides no alternative for such workers<sup>4</sup>. Thus, manufacturing workplaces are of particular interest to national TB control program (NTP), especially in high burden countries like Bangladesh which has a TB prevalence of 402 (all forms, PTB and non-PTB) and incidence of 224 per 100,000 per year in 2006<sup>6</sup>.

Bangladesh adopted community-based DOTS strategy for prevention and control of TB in 1993 and the NTP, through public-private partnership (PPP), succeeded in achieving the target of 70 % case detection and 85 % treatment success by 2003 as set by the WHO<sup>7</sup>. To expand TB prevention and control activities in areas not covered before, the NTP in its 5-year strategic plan (2006–2010) emphasized the involvement of business organizations in providing TB services in workplaces in line with WHO recommendations<sup>2,3</sup>.

In 2006 under a PPP (Public-Private Partnership) model, NTP signed a MOU with the Labor Ministry to implement TB DOTS program in 157 Tea gardens in association with the partner NGOs. The program included advocacy and orientation activities among the workers of the Tea garden, and TB management training for the medical officers of the health centers. Besides, sputum test for chronic cough patients and supervised DOTS therapy for sputum positive cases were provided<sup>8,9</sup>.

Workers engaged in Tea factories (02 % of all manufacturing establishments) constitute only 15 % of the total workforce (6,50000) engaged in manufacturing industries in Bangladesh in 2005 [10,13]. TB in other types of workplaces in other parts of the country especially hard to reach area remained largely an uncharted area for NTP in Bangladesh. However, designing more study in those areas for TB prevention and control program, information is needed from different Tea Garden factories and this study aimed to fill-in this knowledge gap.

### **Methods and Materials:**

This was a descriptive cross sectional study done in the Shamshernagar, Bharaura & Deanstone Tea Garden Health Centers following DOTS strategy jointly organized by HEED Bangladesh and garden authority of Kamalganj and Srimongal upazila, Moulvibazar. All registered Pulmonary TB patients of 15 years old and above of the three gardens which were total 113 in numbers were selected. A pre-tested structured questionnaire and observational check list were used for data collection. Number of patients detected was very low. So sampling was done purposively according to the researcher's convenience. The study was conducted from 1<sup>st</sup> January to 31<sup>st</sup> December 2006.

**Inclusion criteria:**

Newly Tuberculosis affected tea garden workers both positive and negative, aged 15 years and above.

**Exclusion criteria:**

Patients <15 years old, Extra pulmonary, Relapse and Re-treatment case.

**Ethical Implication:**

As the study was conducted in the garden areas, first of all a written permission was taken from the garden authority. Then both verbal and written consent was taken from the respondents for taking interview.

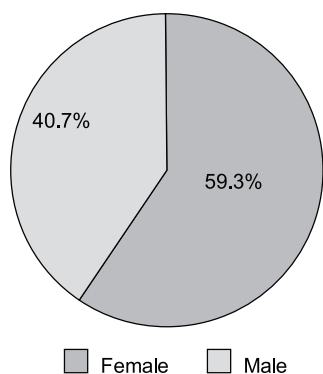
**Results:**

**Table-I**

*Distribution of the respondents by age n=113*

Age group(completed years)	Frequency	Percentage
15-24	13	11.5
25-34	21	18.6
35-44	38	33.6
45-54	26	23.0
55-64	15	13.3
Total	113	100.0

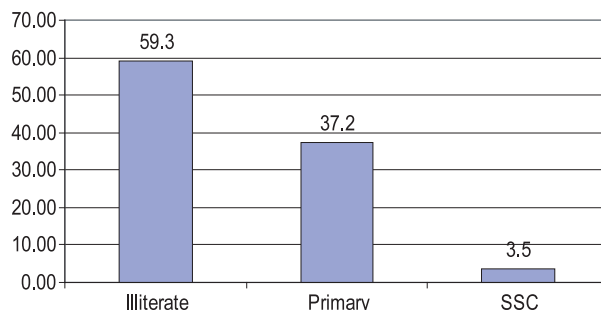
Age of the respondents ranged from 15 to 64 years. The highest number of the respondents (33.6%) lies in the age group of 35-44 years while the lowest number of the respondents was in the 14 to 24 years age group. The mean age of the respondents was 40.3 years and SD 11.9 years.



**Fig -1:** *Distribution of the respondents by sex*

Among 113 respondents, 59.3% (67) respondents were male and rests 40.7% (46) of the were female.

Most of the respondents 59.3% (67) were illiterate. While 37.2% and 3.5% had received primary and S.S.C level education respectively



**Fig.-2:** *Distribution of the respondents by their education*

**Table-II**

*Distribution of the respondents by number of family member, monthly income, housing condition, nutritional status, family history of TB, knowledge about TB & cause of delay of taking treatment and knowledge about treatment available and Chronic Cough*

Characteristics	Frequency	Percentage
<b>Number of Family member</b>		
< 5	45	39.8
>5	68	60.2
<b>Monthly income</b>		
<1000	20	17.7
1000-2000	72	63.7
>2000	21	18.6
<b>Housing Condition</b>		
Kacha	103	91.2
Semi-Kacha	10	8.8
<b>Nutritional status</b>		
Under-nutrition (<18.50 kg/m <sup>2</sup> )	50	44.2
Normal (18.50-24.99 kg/m <sup>2</sup> )	60	53.1
Over nutrition (>24.99 kg/m <sup>2</sup> )	3	2.7
<b>Family history of TB</b>		
Yes	20	17.7
No	93	82.3
<b>Knowledge about TB &amp; Cause of delay of taking treatment</b>		
Ignorance	60	53.2
Poverty	23	20.3
Stigma	30	26.5
<b>Knowledge of treatment available</b>		
Govt. hospital	62	54.9
Non govt. hospital	30	26.5
Fakir/Darbesh	2	1.8
Others (Tea garden hospital)	19	16.8
<b>Chronic Cough&gt;3weeks</b>	80	33

The number of family member of the respondents ranged from 1 to 10. Among 113 respondents highest number 60.2 % (68) were from families having >5 members. While rest of the respondents 39.8 % (45) were from families having 5 or less than 5 members.

Monthly income of the respondents ranged from Tk.600-3000. The mean monthly income was Tk.1508.3 and SD=Tk. ±604.4; 63.7% (72) had a monthly family income of Tk.1000-2000, 18.6% (21) had monthly family income of Tk. >2000 while rest of the respondents 17.7% (20) had less than Tk.1000.

Among the respondents, 91.2% (103) lived in a Kacha house and the rest (8.8%) lived in Semi-pucca house. Based on BMI, 53.1% (60) had a normal nutritional status, 2.7% (3) were found to be over nourished (BMI>24.99 kg/m<sup>2</sup>) while the remaining 44.2% (50) were found to be under nourished (BMI<18.5 kg/m<sup>2</sup>). Mean BMI=19.04 kg/m<sup>2</sup> and SD =± 3.55 kg/m<sup>2</sup>, none of the respondents had BMIe”30.

Majority of the respondents 82.3% (93) were from families in which there was no history of TB among its members while the remaining 17.7% (20) had a previous family history of TB.

Most of the respondents 53.2% (60) made delay to take treatment due to ignorance while lowest number of respondents 20.3% (23) made delay due to poverty. 26.5% (30) respondents made delay due to stigma.

Among the respondents 54.9% (62) told that treatment was available at govt. hospital where as the lowest number of respondents 1.8% (2) thought that treatment was available at fakir/darbesh, 26.5% (30) and 16.8% (19) respondents stated that treatment was available at non govt. & tea garden hospital, 71% workers did not intend to go for sputum test, may be due to the fact that the workers were not allowed to go outside or lack of knowledge [8] and the complexities of attending DOTS diagnostic services<sup>22</sup>.

**Table-III**

*Distribution of the respondents by personal habit*

Personal Habit		Number	Total
Smoking	Yes	53 (46.9%)	113
	No	60 (53.1%)	
Alcohol consumption	Yes	66 (58.4%)	113
	No	47 (41.6%)	

Among the 113 respondents, 46.9% (53) were smoker & the remaining 53.1% (60) were non-smoker. As regards to alcohol consumption 58.4% were alcoholic and the remaining 41.6% were non alcoholic.

**Table-IV**

*Distribution of the respondents by time lag between appearance of symptoms and time of seeking treatment*

	Time lag (year)		Total
	<1 year	>1 year	
No of respondent	82 (72.57%)	31 (27.43%)	113

Among 113 respondents, 82(75.8%) had 1 or less than 1 year time lag between the appearance of symptoms and the time of seeking treatment, and the rest 31(27.43%) had >1 year time lag.

#### **Discussion:**

It was a descriptive cross sectional study which was conducted in three tea gardens i.e. Shamsheernagar, Bharaura and Deanstone tea garden of Kamalgonj and Srimongal upazila. All the registered New Pulmonary TB affected tea garden workers were selected as sample size purposively from the above three tea gardens which was 113 in numbers. The Study was done to know the profiles of TB affected tea garden workers. But unfortunately the study findings could not be compared with other study as because so far the knowledge of the author concerned no such study on profile of TB affected tea garden workers was made in Bangladesh.

This study was done to fill-in current gaps regarding TB affected tea garden workers' stigma, knowledge, attitude and practice about TB and their time lag for seeking treatment. The information is expected to help NTP in designing a TB prevention and control program for workplaces in Bangladesh. Findings reveal poor knowledge on different aspects of TB among a substantial proportion of the workers. A high level of misperception exists regarding TB and its prevention and management, including a stigmatized attitude towards TB and TB patients.

The age of the respondents ranged from 15 to 64 years and the mean age of the respondents were 40.3 years with the SD 11.9 years. Highest number 38 (33.6%) of the respondents were in the age group of 35-44 years and the lowest 13(11.5%) was in the age group of 15-24 years<sup>8,14</sup>.

In this study the mean age of the respondents was 40.3 years and most of the TB cases were in the age group of 35-44 years<sup>1,2</sup>. The reason of high frequency of TB in adult age group might be due to the fact that frequent exposure to external environment. More over people are afraid of disclosure of the disease and the disease itself remains stationary and symptoms less for a long period. That is why seeking medical treatment by patient is often greatly late which account for delayed diagnosis at adult or even oldest. Hiding tendency also play a great role on this connection.

Among 113 respondents 67 (59.3%) were male and the rest 46(40.7%) were female i.e. ratio of male & female about 3:2<sup>10,12</sup>. It was seen that the male respondents were 1.46 times higher than the female. Higher number 85.8% (97) of the respondents was founds to be belonging to Hindu religion and Muslim constitutes 12.4% (14) while Christians were only 1.8% (2). Most of the respondents 59.3% (67) were illiterate, 37.2% (42) Primary & the rest 3.5% (4) had received S.S.C education.

Majority of the respondents were male and from Hindu religion because this community had been traditionally engaged in the tea gardens. The workers were Hindu because they are non-Bengali and bought from south & north India. Male probably more affected due to the fact that they are more exposed to the risk than female as they go out more frequently. The comparatively low rate of TB among the female may be attributed to biological or environmental factors. Male are more exposed to outside which also attributes to increase number of male respondents to a some extent.

About the marital status, among 113 respondents, 90 (79.6%) were married, 20 (17.7%) were unmarried & rest 3 (2.7%) were widow. Among 113 respondents 39.8% (45) have family numbers d"5 and rest 60.2% (68) had family members >5. The mean of the monthly family income was Tk.1508.3 with the SD Tk.604.9. Among 113 respondents, 72 (63.7%) belong to the group having monthly income Taka 1000-2000, 20 (17.7%) less than taka 1000 & the rest 21 (18.6%) had monthly income more than taka 2000<sup>6,7</sup>.

In this study 63.7% cases belong to the lower socio-economic group having monthly income Tk. 1000-2000 and 59.3% cases were illiterate which attributes low socio-economic group<sup>2,3</sup>. Among 113,

most 103 (91.2%) of them had kacha house, while the rest 10 (8.8%) had semi-pucca house. Regarding personal habit, among 113 respondents, 53 (46.9%) were smoker & 60 (53.1%) were non-smoker. On the other hand 66 (58.4%) were alcoholic while 47 (41.6%) non-alcoholic.

Regarding nutritional status the current study revealed that the significant number of the respondents 42.2% (50) had BMI <18.5 kg/m<sup>2</sup> and SD 3.55 kg/m<sup>2</sup>. There was no study available regarding nutritional status by BMI. But it was reported that nutrition plays an important role in the occurrence of TB.

The study showed that maximum 93 (82.3%) portion of the respondents had no previous family history of TB whereas the rest 20 (17.7%) of the respondents had previous positive family history<sup>1,2</sup>.

Among 113 respondents, 82(75.8%) had 1 or less than 1 year time lag between the appearance of symptoms and the time of seeking treatment, and the rest 31(27.43%) had >1 year time lag.

Among 113 respondents, most of the respondents (54.9%) told that treatment was available at govt. hospital while lowest number of the respondents (1.8%) said that treatment was available at fakir/darbesh<sup>3,4</sup>.

It was observed that despite having symptoms suggestive of TB (e.g., chronic cough of more than 3 weeks), 71% workers did not intend to go for sputum test, may be due to the fact that the workers were not allowed to go outside or lack of knowledge<sup>8</sup> and the complexities of attending DOTS diagnostic services<sup>22</sup>. Low paid workers often go to informal providers, which is common with the poor population in this country<sup>23</sup>.

Workers' fear of social isolation due to contraction of the disease and associated stigma observed in this study is a common phenomenon worldwide<sup>19,21</sup>. Stigma combined with poor knowledge of TB, delays its diagnosis and causes treatment non-adherence, and may act as an important barrier to service utilization. Social support can help patients overcome these barriers along with multiple IEC (information, education and communication) intervention.

This study used sampling from some selected tea gardens and as such, may not be representative of the whole garden Ares. However, used samples

drawn from the major tea garden belts in the country and thus, the findings gave a fair idea about the current state of the workers' knowledge, attitudes and practices related to TB.

### Conclusion:

Findings reveal that the workers studied had various misperceptions and stigma towards TB, and poor knowledge regarding its cause, transmission and prevention. This would interfere with TB case detection in the tea gardens including sputum test for chronic cough and appropriate treatment-seeking from DOTS centers. Thus, NTP needs to address these challenges and design appropriate IEC and motivation campaigns to overcome these barriers while expanding DOTS facilities in the tea gardens.

### Recommendation:

On the basis of findings of the study following recommendations were proposed.

1. Organize rapid survey for early detection of TB among the tea garden workers
2. Organize health education activity in the tea garden areas.
3. Strengthening of diagnosis and treatment facilities in the tea gardens
4. Well-designed studies should be conducted in different gardens to validate the findings of the present study.

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## ORIGINAL ARTICLE

# Airway Foreign Body in Children

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Syed Rezaul Huq<sup>4</sup>, AKM Razzaque<sup>5</sup>

### Abstract

**Objective:** To determine the clinical characteristics and the results of bronchoscopic treatment of children due to foreign body aspiration in NIDCH.

**Method:** Children who underwent bronchoscopies for foreign bodies aspirated into the airway between January 2013 to December 2013. Each patient was analyzed for age, sex, initial clinical diagnosis, nature and location of the foreign body, duration of symptoms between aspiration and bronchoscopy, radiological findings, results of bronchoscopic removal, complications of bronchoscopy and presence of foreign bodies in the airways.

**Results:** Hundred two children, 60 (59%) boys, ages ranging from nine months to eleven years (median = 42 months). In 99 (94%) children the foreign body was removed by rigid bronchoscope, and three resulted in thoracotomy. Foreign bodies were more frequent in children under three years of age (66%). A clinical history of foreign body inhalation was obtained in 80 (80%) cases. Most of the foreign bodies removed were inorganic (70%) and more frequently found in the right bronchial tree (59%). Foreign bodies were removed within 24 hours in 54 (53%) cases. The most frequent radiographic findings were: unilateral air trapping, atelectasis and radiopac foreign body. Major bronchoscopy complications occurred in Twenty two children (22%), and there were no deaths.

**Conclusions:** More attention is necessary to the respiratory symptoms of aspirations, mainly in boys at early ages, with clinical history and compatible radiological findings. Most foreign bodies removed were of inorganic nature. In this case series, therapeutic rigid bronchoscopy was effective with few complications.

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### Introduction

Foreign body aspiration (FBA) in the airway is a universal problem, being still an important cause of childhood morbidity and mortality. Socioeconomic-cultural and educational factors are determinants for the frequency and particularities of the foreign body (FB) aspirated<sup>1</sup>.

According to statistics of the *National Safety Council* of the United States, of 1995, mechanical

suffocation was responsible for 5% (167) of accidental deaths in children under the age of four<sup>(1)</sup>. Aspiration is the most important cause of accidental death of children younger than six years of age in American homes<sup>2</sup>.

The clinical feature of children with foreign body in the airways depends on the size and location of the material aspirated, and varies from asymptomatic to severe respiratory failure<sup>4,5</sup>.

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FBA history is present in 72 to 85% of the cases confirmed by endoscopy; however, the aspiration episode is often not the main family complaint, being it necessary to get a guided history<sup>6</sup>.

Rigid bronchoscopy is the procedure of choice for removal of aspirated foreign bodies, and other methods are not encouraged<sup>7</sup>. Fortunately, most of the aspirated foreign bodies are visualized by endoscopy and removed by one of the several types of capture forceps. This procedure must be accomplished by expert bronchoscopists and anesthesiologists, due to the risks of bronchospasm, pneumomediastinum, and heart arrhythmias<sup>6</sup>. Several reports mention the need to perform an open thoracotomy, resection of a pulmonary segment or several endoscopic procedures to remove the FB peripherally impacted<sup>8</sup>.

The purpose of this study was to determine the clinical characteristics and the result of the bronchoscopy approach for foreign body aspiration in children's airways, referred to NIDCH.

## Method

In this study, we evaluated children who underwent respiratory bronchoscopy for BFA in the period between January 2013 and December 2013 in the Department of Thoracic surgery NIDCH, Bangladesh.

The present study is a time series of cases, with data obtained from specific FBA protocols, with all bronchoscopy exams performed by the same examiner.

Suspected FBA included clinical evaluation and thoracic radiological exams and, if an emergency endoscopy is needed, it is referred to a surgical procedure. In clinically stable cases, the necessary exams are performed, such as, intravenous hydration, antibiotics when necessary, and pre-anesthetic evaluation. All patients undergo rigid bronchoscopy (Lutz) in FBA cases, under general anesthesia with spontaneous respiration maintained whenever possible, and continuous monitoring of electrocardiogram, blood pressure, oxygen saturation by pulse oxymetry and precordial stethoscope auscultation. The foreign bodies were removed with adequate forceps for each case, including reintroducing the bronchoscope for removal of any

remaining fragments, aspiration of secretion, and evaluation of tissue reaction, edema, and other lesions. During the post-operative period, the children were observed in the recovery room or, if necessary, in the intensive care unit.

The following information was obtained from the revised protocols: age, gender, time between aspiration and bronchoscopy finding, previous clinical diagnosis, type of foreign body found, location of the foreign body, radiological finding, complications from the foreign body and bronchoscopic procedure. Bronchoscopy-related complications were divided in major (laryngospasm or larynx bronchospasm with bradycardia; laryngospasm or larynx bronchospasm, with desaturation; desaturation with bradycardia and bilateral pneumothorax) and minor (desaturation).

Data were analyzed by the Epi-Info software version 6.04. The statistical test was the chi-square and the level of significance was set at 5%.

## Results

Hundred- two children who underwent rigid bronchoscopy for removal of foreign body in the airways were evaluated.

### Clinical characteristics of the patients

Their age varied from nine months to eleven years. Most cases (66%) occurred within the first four years and, in 74% (80) of the cases, in children younger than five years old. Foreign body impairing the airways occurred in 59% of the cases in boys.

Clinical diagnosis other than FBA were initially determined in 59% of the patients in this study, where the most frequent were: asthma (18%); pneumonia (26%); bronchiolitis (6%) and laryngitis (6%), although in most of the cases (80%) the parents or guardians reported positive history for FBA.

Regarding the time elapsed between the aspiration and the bronchoscopic finding, removal of FB occurred within the first 24 h in 53% of the cases.

Table-I shows the distribution of patients by age, gender, clinical manifestations, and the time between aspiration and bronchoscopic finding.

**Table-I**  
*Clinical characteristics of patients*

Charectaretics	n	%
Gender	88/42	59/41
M/F		
Age		
Median	1 year and 11months	
Minimum	9 months	
Maximum	11 years	
Distributions(years)		
=1	15	15
1-3	51	50
3-5	09	09
=5	27	26
Time of evolution between onset of symptoms and bronchoscopic findings		
Median	2days	
Minimum	1days	
Maximum	1 year	
Initial diagnosis		
Pulmonary diseases	48	47
FBA suspicions	42	41
Others	12	

### Type of aspirated foreign body

In most cases, the foreign bodies were inorganic in nature (74%), with alpin, small toys and pen tip predominating (Table-II). Foreign bodies are most frequently aspirated by children in their first five years of life (Table III).

**Table-II**  
*Nature of the foreign body*

Nature of foreign body	n	%
Metal parts(Board pin, alpin Screws etc)	48	47
Small toys	12	12
Pen tip	16	16
Peanut, seeds	08	08
Others	18	17

**Table-III**  
*Age range and nature of the foreign body*

Age	Inorganic (n=73)	Organic (n=29)
=5years	42(70%)	18(30%)
>5years	31(74%)	11(26%)

### Radiological study

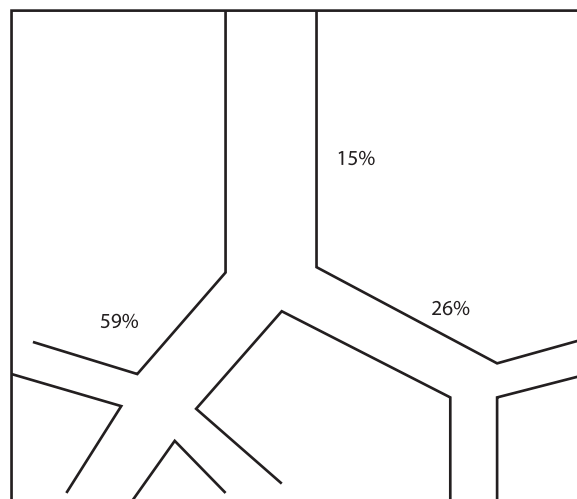
All children in this study underwent thoracic X-ray, withins technique and forced expiration in doubtful cases. The most frequent alterations were hyperinsufflation, atelectasis and radioopac foreign body. Only four exams were considered normal (Table-IV).

**Table-IV**  
*Radiological findings*

Findings	n	%
Hyperinsufflation	33	32
Atelectasis	21	21
Radiopac FB	21	21
Infiltration/consolidation	15	15
Normal	12	11

### Location of foreign body

The predominant location of foreign bodies were the bronchia (85%), with 59% of the cases in the right main bronchus. Foreign body impairing the upper airway occurred in only five cases (Figure 1).



**Fig.-1:** Location of the FB affecting the airway

### Successful bronchoscopic removal

In 99 cases it was possible to remove the foreign body. In three cases of peripheral foreign body, thoracotomy with bronchotomy were decided after several unsuccessful attempts.

### Bronchoscopy complications

Bronchoscopy-related complications in our sample were observed in 53% of the cases, being most of

them (32%) minor complications, such as desaturation; and only twenty three (21%) cases were major ones, such as laryngospasm with desaturation, laryngospasm with bradycardia; laryngo- bronchospasm with bradycardia and bilateral pneumothorax, all of which were successfully treated.

### FBA-related complications

Two children were submitted to tracheostomy before being admitted to our care; 60 (59%) were being treated for other pathologies, such as asthma, pneumonia, laryngitis and bronchiolitis; three children required thoracotomy with bronchotomy to remove FB peripherally located.

The foreign body complications observed during bronchoscopy were: bronchial stenosis and formation of granulation tissue (one patient); one case of pulmonary sequela in the right lower lobe verified by perfusion scintigraphy; and one case of stenosis in the right main bronchus.

### Discussion

Children present a higher risk of foreign body aspiration, which is attributed to several factors: a) tendency to put objects in their mouth; b) absence of molars to chew some types of food; c) to cry, walk and run with objects inside their mouth; d) lack of coordinating mechanism of swallowing, associated to the elevation of the larynx and to the protective reflex, which is immature in small children. Boys are usually more involved in foreign body aspiration, with a ratio boys/girls of two to one, which might be explained by their more adventurous personality and sharper curiosity, compared to girls<sup>1,7,9,10</sup>.

In our sample, the findings of FB predominated in boys (59%), especially in the first five years of their lives (66%), which is in agreement with literature data<sup>3,4,6,7,9,11,12</sup>.

The positive history of FBA is present in 72 to 85% of the cases confirmed by endoscopy, with reports of up to 89.2%<sup>11,13</sup>. Fraga et al.<sup>4</sup> referred to FBA clinical history in 77% of the cases. In our sample we obtained 80% of positive history for aspiration, confirmed by bronchoscopic finding, which is in accordance with the above mentioned authors.

The clinical features associated to the permanence of foreign bodies in the airways are the consequence of bronchial reaction and secondary infections. The

low level of medical suspicion associated to the absence of FBA clinical history often leads to a mistaken initial diagnosis<sup>9,11,13-15</sup>. In our sample, 59% of the children submitted to bronchoscopy were given an initial clinical diagnosis other than FBA, being the most frequent: asthma, asthma associated to pneumonia, pneumonia, laryngitis and bronchiolitis. These diagnostics are in agreement with those obtained by Piva et al.<sup>7</sup>, in which the most frequent were asthma, bronchopneumonia and laryngitis, where only 31.5% were FBA.

The foreign material aspirated into the airway must be removed as soon as the diagnosis is suspected or confirmed, and when the children's clinical conditions allow airway manipulation under anesthesia<sup>4</sup>. The consequence of a delayed diagnosis is the delay in performing the endoscopy procedure<sup>7</sup>. In our sample, FB was removed within 24 h in 53% of the cases, 20% in seven days, 6% within the first month, and 22% beyond 30 days. These results are similar to those found by Wiseman<sup>5</sup>, Cotton et al.<sup>(19)</sup> and Hugles et al.,<sup>20</sup> who obtained an early diagnosis in 46 to 48% of the cases. Regarding the late findings (over 30 days), we obtained a percentage similar to the 16% reported by Wiseman<sup>5</sup> and lower than the 26% reported by Lima et al.<sup>3</sup>.

The distribution of FB location in our sample showed the predominance on right main bronchus (59%) in relation to other areas, which is in agreement with the literature<sup>3,5,17,21-23</sup>. However, studies by Piva et al.<sup>7</sup> and Fraga et al.<sup>(4)</sup> show the predominance of FB in the left main bronchus (LMB). This finding is explained by Fraga et al.<sup>4</sup> as probably occasional because of the small number of patients analyzed, whereas for Piva et al.<sup>7</sup> and Campbell et al.<sup>12</sup> the explanation would be in the fact that FB in the LBO is hardly expelled spontaneously<sup>4,7,12</sup>.

The predominance of aspiration of radiotransparent foreign bodies recommends special attention to indirect radiological alterations, among which the most frequent are hyperinsufflation, atelectasis, infiltration and consolidation. These alterations are usually restricted and depend on time elapsed, on the nature of the foreign body, and on the degree of the airway obstruction<sup>21</sup>. In our sample, all patients with foreign body aspiration underwent a simple thoracic X-ray.

In our study, 97% of the foreign bodies were removed with rigid bronchoscope. In three cases,

thoracotomy with bronchotomy was necessary to remove the FB. The review of 50 published papers, involving 6,393 patients with FBA, made by Bittencourt and Camargos<sup>21</sup> revealed the need of thoracotomy in 2.5% of the cases. In 74 FBA patients, Cataneo et al.<sup>16</sup> performed thoracotomy to remove FB in 10.8% of the cases. Fraga et al.<sup>4</sup> referred that it was not necessary to perform surgical exploration by thoracotomy in any of their 26 children treated for FBA. In both our patients submitted to bronchotomy, the foreign body was peripherally located, causing mucosa edema, making its removal difficult.

Despite the development of bronchoscopic equipment, the report of complications related to foreign body removal in children still occurs<sup>21</sup>. To Ahmed<sup>23</sup>, bronchoscopy is a delicate procedure and must be performed by an experienced team, due to the risk of bronchospasm and arrhythmias. The removal of foreign bodies in our service is performed by means of rigid bronchoscopy, allowing adequate ventilation for the patient, while the flexible bronchoscopy is a recommended approach to be only used for diagnosis in some cases<sup>2,3,6,7,16,21,23,24</sup>. We emphasize the difficulty of comparing our results with those of the literature, due to the absence of standardization and the lack of reference to complications by most authors. To Mélon et al.<sup>25</sup>, among the complications of the endoscopic procedures that deserve special attention are larynx edema, subglottic epithelial erosion, bronchial edema due to excessive local manipulation, which may lead to atelectasis, pneumothorax, pneumomediastinum and subcutaneous emphysema evolving to cardiac buffering, hemorrhages and septic complications – which were almost non-existent in our sample, except for one case of pneumothorax.

Um et al.<sup>26</sup>, consider that the delayed diagnosis has a remarkable effect on the frequency of complications, probably higher than any other factor. In our series of cases, the complications of the FB staying in the airway were: one patient with bronchial stenosis, another patient with granuloma and partial stenosis of the right main bronchus, and a third patient with lung sequela in the right lower lobe verified by perfusion scintigraphy.

In this series of cases, we noticed a higher risk of inorganic material aspiration, predominantly in

boys during their first five years of life, often with clinical diagnoses other than FBA. A well-conducted anamnesis and more careful observation of indirect FBA radiological signs are surely main factors to increase the rate of correct diagnosis. Clinical manifestations can vary, easily mimicking other diseases and resulting in a diagnosis delay and consequent increase of childhood morbidity. The present study allows us to conclude that rigid bronchoscopy is an efficient and safe therapy.

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## ORIGINAL ARTICLE

# Role of Bronchoalveolar Lavage in the Diagnosis of Central Lesion in Bronchial Carcinoma

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### Abstract:

**Introduction:** *Bronchoalveolar lavage (BAL) can provide diagnostic information in bronchial carcinoma. It is non-invasive, easily performed and well tolerated procedure that is useful in routine assessment of patients for carcinoma lung. The accuracy of BAL is comparable with endobronchial biopsy in central lesions in bronchial carcinoma. It was designed to compare the diagnostic efficacy of BAL cytology in diagnosis of primary lung carcinoma using histopathological examination of endobronchial biopsy as the gold standard.*

**Methods:** *This cross-sectional study was conducted in the Department of Medicine Sylhet MAG Osmani Medical College Hospital, Sylhet during the period from July 2011 to June 2013. For this purpose 36 patients with bronchial carcinoma were enrolled in this study after inclusion and exclusion criteria.*

**Results:** *The mean age of the patients with bronchial carcinoma was 59.4 (SD ± 11.1) years; and 88.9% patients were male and 11.1% patients were female with a ratio of male to female of 8:1. The sensitivity and specificity of bronchoalveolar lavage in the diagnosis of central lesion in bronchial carcinoma was 59.4% and 100.0% respectively; the positive predictive value and negative predictive value was 100.0% and 23.5% respectively; and the accuracy of was 63.9%. Three (8.3%) patients developed respiratory distress as a minor complication of bronchoscopy procedure while no one developed major complication.*

**Conclusion:** *Bronchoalveolar lavage is a useful diagnostic tool in the diagnosis of central lesion in bronchial carcinoma.*

[*Chest & Heart Journal 2015; 39(1) : 32-38*]

### Introduction

Bronchial carcinoma is currently the most frequently diagnosed and the commonest cause of cancer mortality worldwide.<sup>1</sup> It constitutes 12.8% of cancer patients and is responsible for 17.8% of cancer deaths worldwide.<sup>2</sup> It is the leading cause of cancer death in industrialized countries and also rising at alarming rates in developing countries.<sup>3-5</sup>

Exact incidence of bronchial carcinoma in Bangladesh is not known due to lack of nation based survey or cancer registry. However, several regional studies showed that bronchial carcinoma ranked top in the case of male and 3<sup>rd</sup> or 4<sup>th</sup> position in case of female. Tobacco consumption is the leading risk factors of bronchial carcinoma in Bangladesh.<sup>5</sup>

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The increasing incidence could be due to increase in smoking habit, change in life styles of the people, increased environmental pollution and also the availability of different modern diagnostic modalities to detect bronchial carcinoma.<sup>7</sup>

The only hope of combating the disease successfully remains in diagnosing the disease at the earliest possible stage, preferably before the lesion has reached the stage of a visible and palpable tumor.<sup>8</sup> A long-standing goal of cancer researchers has been to develop techniques that would facilitate earlier diagnosis and treatment of bronchial carcinoma and thereby decrease its mortality.

Before start of treatment a clear distinction between small cell and non small cell carcinoma must be made, for that histopathology remains the mainstay of treatment. Bronchial biopsies cannot be performed in adjacent to carina and more peripheral site or in patients at risk of hemorrhage. So, alternative methods for obtaining a diagnosis are sometimes required. Bronchoscopic washing, brushing and fine needle aspirations may complement tissue biopsies in the diagnosis of bronchial carcinoma.<sup>9</sup>

Cytologic techniques are safer, economical and provide quick results. The diagnostic yield for cytologic examination is comparable to that of other widely used endoscopic techniques such as transbronchial biopsy. Pulmonary cytology and histopathology are valuable tools in the diagnosis of bronchial carcinomas.<sup>10</sup>

Bronchoalveolar lavage (BAL) is a diagnostic and therapeutic procedure conducted by placing a fiberoptic scope into the lung of a patient, then wedging the tip of a bronchoscope into a bronchus (subsegmental), and instilling a known volume of saline (sterile water) solution into the distal airway, then aspirating up this volume. The sterile water removed contains secretions, cells, and protein from the lower respiratory tract. BAL can provide diagnostic information in cases of primary and metastatic bronchial carcinoma. It is a valuable diagnostic tool in detecting peripheral, primary pulmonary malignant neoplasm.<sup>11</sup> The efficacy of BAL is comparable with transbronchial biopsy both in central and peripheral lesions. The sensitivity of BAL for the diagnosis of bronchial carcinoma is similar to that of transbronchial biopsy. The diagnostic yield of BAL for cytological examination is comparable to that of other widely used

endoscopic techniques such as transbronchial biopsy (TBB). It is an easily performed and well tolerated procedure that is useful in routine assessment of patients for bronchial carcinoma. It is a procedure that is non-invasive, easily performed, cost effective and less hazardous.<sup>10</sup>

As there is no study on the role of bronchoalveolar lavage in the diagnosis of central bronchial carcinoma in Sylhet M.A.G. Osmani Medical College Hospital, Sylhet; so, this study is designed to compare the diagnostic utility of bronchoalveolar lavage in the diagnosis of central bronchial carcinoma in our setting.

## Aims and Objectives

### General Objective:

- To determine the role of bronchoalveolar lavage cytology in the diagnosis of central lesion in bronchial carcinoma.

### Specific Objective:

- To perform bronchoalveolar lavage cytology and bronchial biopsy in all cases of central lesion in bronchial carcinoma.
- To determine the sensitivity, specificity and accuracy of bronchoalveolar lavage in the diagnosis of central lesion in bronchial carcinoma.

## Methodology

**Study design:** This was a cross sectional and comparative study.

**Place of Study:** This study was carried out in the Department of Medicine in collaboration with the Department of Respiratory Medicine, Sylhet M.A.G. Osmani Medical College Hospital, Sylhet.

**Period of Study:** This study was conducted from 1<sup>st</sup> July 2011 to 30<sup>th</sup> June 2013.

**Study Population:** The patient with clinically and radiologically suspected central bronchial carcinoma, admitted in the different unit of Medicine and Respiratory Medicine, Sylhet M.A.G. Osmani Medical College Hospital, Sylhet during the study period from 1<sup>st</sup> July 2011 to 30<sup>th</sup> June 2013 were the target population and those fulfilled the inclusion and exclusion criteria were considered the study population in this study.

## Selection Criteria

### Inclusion Criteria

- The clinical features suggestive of bronchial carcinoma:
  - i. Cough
  - ii. Haemoptysis
- Chest radiography suggestive of neoplasm:
  - i. Prominence of a hilar shadow with whiskering appearance.
  - ii. Complete or partial collapse of lung.
  - iii. Consolidation which touches the hilum or within 1 cm of the hilum.
  - iv. Lateral view showing central and peripheral lesion.
- A suspected mitotic lesion in the chest x-ray that failed to resolve after a variable period of broad spectrum antibiotic treatment or observation or both with or without the following symptoms and signs:
  - i. Chest pain
  - ii. Cough
  - iii. Hemoptysis
  - iv. Weight loss
  - v. Clubbing
- Central bronchial carcinoma endoscopic findings visible by fiberoptic bronchoscopy
- Adult patients of both sex.

### Exclusion Criteria

- Bronchial carcinoma approaching carina.
- All peripheral lung lesion endoscopic findings not visible by fiberoptic bronchoscopy
- Significantly disabled patients due to poor general condition.
- Associated systemic or pulmonary diseases;
- Recent MI.
- Vascular lesions.
- Haemorrhagic diathesis, anti-coagulant therapy.
- Sputum specimens positive for AFB.
- Patient who are not agreed to do fiberoptic bronchoscopy.
- Patients where EBB could not be done.

**Sample size:** calculated sample size was 32. But we took 36 patients with suspected central bronchial carcinoma visible by fiberoptic bronchoscopy and fulfilling the inclusion and exclusion criteria.

**Sampling technique:** Consecutive sampling technique was employed as sampling technique in this study.

**Data Collection:** Data were collected in a pre-designed data collection sheet.

### Study Procedures:

**Preparation of questionnaire:** Standard questionnaire was designed with a view to collecting patient's medical records (Appendix-I).

**Consent taking of the patient:** Informed written consent was obtained from the patients or attendants after full explanation of the details of the disease process (Appendix-II).

**Recording of patient's information:** Demographic information like age, sex, occupation, socio-economic status, smoking status, etc were obtained.

Each patient was assessed by taking complete history and meticulous clinical examination both general and systemic examination.

All relevant information was recorded in a predesigned and pretested questionnaire.

**Laboratory investigation:** Necessary investigations were done for selection of cases included the following:

- X-ray chest P/A and Lateral view
- Blood for CBC and ESR
- Sputum for malignant cell and AFB
- BT and CT
- ECG

**Identification of patients clinically suitable for inclusion as cases:** The accumulated questionnaires were analyzed to find out the patients who met inclusion and exclusion criteria.

### Study proper:

#### Procedure of Bronchoscopy:

One or more of forceps biopsy and bronchoalveolar lavage was performed in all patients. Bronchoalveolar lavage was performed following general inspection of tracheobronchial tree, by wedging the bronchoscope into a segmental

bronchus leading to the abnormal area on the chest radiogram. After wedging the bronchoscope into the related bronchial subsegment and when the tumour was visible bronchoscopically, three 20 ml aliquots of sterile isotonic 0.9% saline solution at room temperature was injected rapidly over the tumour by hand held syringe and then immediate and gently aspirated until no further fluid was obtained for BAL (60 ml for BAL). The aspirate was collected in a plastic specimen trap in circuit.

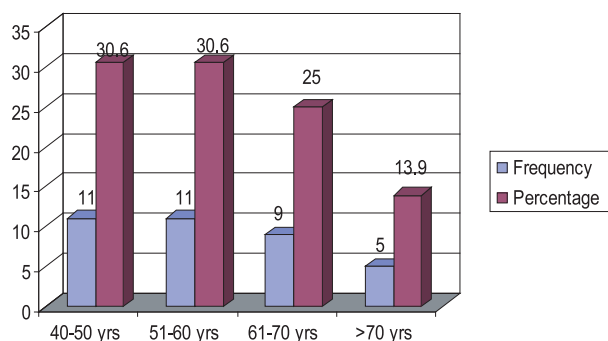
Following BAL endobronchial biopsy was performed with FB-15C alligator forceps with serrated jaws (Olympus, Tokyo, Japan). Whenever possible, at least three biopsies were obtained from the centre of the most abnormal area and the specimens were immediately fixed in 10% buffered formalin.

Cytologic examination was carried out to BAL. The fluid was not filtered, only centrifuged. The specimen for cytologic study was centrifugated at 1500rpm for 10 minutes. The sediment of BAL was smeared into albuminized slides and placed in 95% alchol for routine hematoxilin-eosin staining.

Tissue specimens for histopathologic study was fixed in formalin, embedded in parafin, and stained with hematoxilin-eosin stain.

**Results**

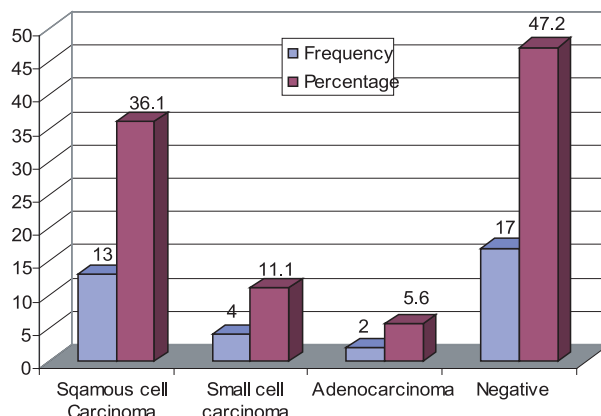
This cross-sectional study was conducted in the Department of Medicine Sylhet MAG Osmani Medical College Hospital, Sylhet, Bangladesh during the period from July 2011 to June 2013 with a view to find out the role of bronchoalveolar lavage cytology in the diagnosis of central lesion in bronchial carcinoma. For this purpose 36 patients with bronchial carcinoma were enrolled in this study. The outcome of the study was as follows:



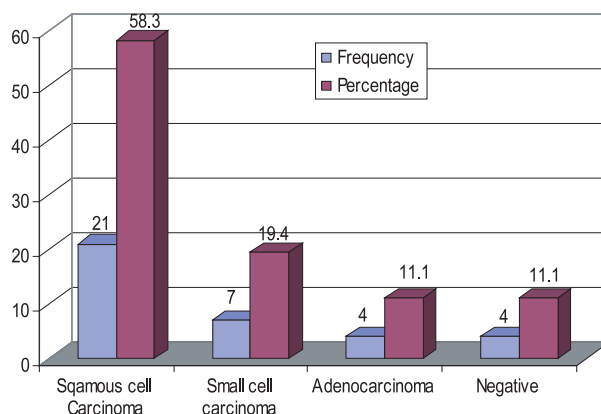
**Fig.-1:** Distribution of the respondents on age (n=36)

**Table-I**  
*Distribution of Patients according to sex (n=36)*

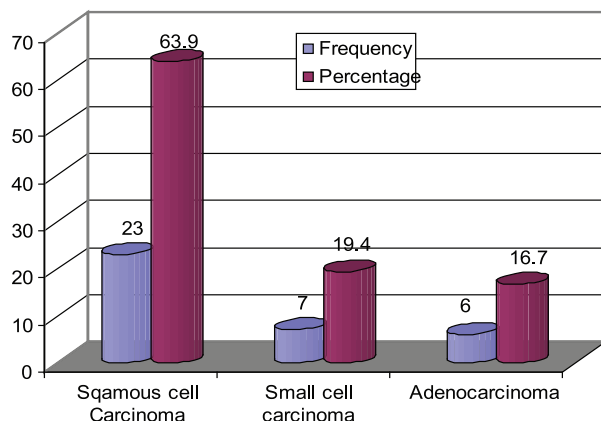
Sex	Frequency	Percentage
Male	32	88.9
Female	4	11.1
Total	36	100.0



**Fig.-2:** Diagnosis of bronchial carcinoma by bronchoalveolar lavage cytology (n=36)



**Fig.-3:** Diagnosis of bronchial carcinoma by endobronchial biopsy and histopathology (n=36)



**Fig.-4:** Distribution of patients by final diagnosis (n=36).

**Table-II**

*Distribution of respondents according to smoking status and histopathological types of bronchial carcinoma*

Histopathological types of bronchial carcinoma	Smoking status	
	Smoker (n=32)	Non-smoker (n=4)
Squamous cell carcinoma	22 (68.8%)	1 (25.0)
Small cell carcinoma	7 (21.9)	0 (00.0)
Adenocarcinoma	3 (9.4)	3 (75.0)
Total	32 (100.0)	4 (100.0)

**Table-III**

*Cross tabulation of bronchoalveolar lavage and endobronchial biopsy in the diagnosis of central lesion in bronchial carcinoma (n=36)*

Test	Endobronchial biopsy			*p-value
	Positive	Negative	Total	
Bronchoalveolar lavage				
Positive	19(TP)	0(FP)	19	p=0.04
Negative	13(FN)	4(TN)	17	
Total	32	4	36	

\*Fisher's Exact test was applied to find out level of significance.

#### **Sensitivity of Bronchoalveolar lavage in the diagnosis of central lesion in bronchial carcinoma:**

In this study sensitivity of Bronchoalveolar lavage in detecting central lesion in bronchial carcinoma was 59.4%.

**Specificity of Bronchoalveolar lavage in the diagnosis of central lesion in bronchial carcinoma :**In this study specificity of Bronchoalveolar lavage in the diagnosis of central lesion in bronchial carcinoma was 100.0%.

**Positive predictive value of Bronchoalveolar lavage in the diagnosis of central lesion in bronchial carcinoma:** In this study positive predictive value of Bronchoalveolar lavage in the diagnosis of central lesion in bronchial carcinoma was 100.0%.

**Negative predictive value of Bronchoalveolar lavage in the diagnosis of central lesion in bronchial carcinoma:** In this study negative predictive value of Bronchoalveolar lavage in the diagnosis of central lesion in bronchial carcinoma was 23.5%.

**Accuracy of Bronchoalveolar lavage in the diagnosis of central lesion in bronchial carcinoma:** In this study accuracy of Bronchoalveolar lavage in the diagnosis of central lesion in bronchial carcinoma was 63.9%.

#### **Discussion:**

This cross-sectional study was conducted in the Department of Medicine Sylhet MAG Osmani Medical College Hospital, Sylhet, Bangladesh during the period from July 2011 to June 2013 with a view to find out the role of bronchoalveolar lavage cytology in the diagnosis of central lesion in bronchial carcinoma. For this purpose 36 patients with bronchial carcinoma were enrolled in this study. The outcome of the study was discussed below:

In this study the age of the patients with bronchial carcinoma ranged from 40 to 80 years with the mean age of 59.4 (SD  $\pm$  11.1) years. Hassan et al.<sup>5</sup> supported the result that age of the patients ranged from 35 to 85 years with the mean age of 60.14 years. This result was also in agreement with other studies.<sup>12,13</sup> But Shah et al.<sup>14</sup> reported the mean age of their lung cancer patients was 45.6 years which was lower mean age than the present study.

This study also showed that 30.6% of patients with bronchial carcinoma were in the age group of 40 to 50 years, another 30.6% of patients were in the age group of 51 to 60 years, 25.0% of patients were in the age group of 61 to 70 years and 13.9% of patients were in the age group of above 70 years. This result was almost correlated with the study of Hassan et al.<sup>5</sup> that 23.7% of patients were in the age group of 51 to 60 years, 25.4% of patients were in the age group of 41 to 50 years, 30.5% of patients were in the age group of 61 to 70 years, 13.6% of patients were in the age group of above 70 years and 6.8% of patients were in the age group of 31 to 40 years.

This study showed that 88.9% of patients were smoker and 11.1% of patients were non-smoker. This result was correlated with the study of Hassan et al.<sup>5</sup> that 93.2% of their bronchial carcinoma patients were smoker. This finding was almost similar to the findings of Shah et al.<sup>14</sup> that 80.3% of the patients were smoker, 19.7% were non-smoker.

In the present study the right lung lesion was found in 61.1% of patients with bronchial carcinoma; while left lung lesion was found in 38.9% of patients. Hassan et al.<sup>5</sup> found lung lesion was found more in the right side (54.2%) than those of left lung (45.8%).

In this study squamous cell carcinoma was found in 63.9% of patients, small cell carcinoma in 19.4% of patients and adenocarcinoma in 16.7% of patients. Among the bronchial carcinoma Hassan et al.<sup>5</sup> found squamous cell carcinoma in 66.1% of patients, adenocarcinoma in 25.4% of patients, small cell carcinoma in 3.4% of patients, large cell carcinoma in 3.4% of patients and poorly differentiated carcinoma in 1.7% of patient.

This may be due to higher number of smoker in this study.

In the present study there were true positive (TP) in 19, false negative (FN) in 13, true negative (TN) in 4 and no false positive (FP) in relation to bronchoalveolar lavage and endobronchial biopsy in the diagnosis of central lesion in bronchial carcinoma. Thus the sensitivity and the specificity of bronchoalveolar lavage in the diagnosis of central lesion in bronchial carcinoma was 59.4% and 100.0% respectively. The positive predictive value and negative predictive value of bronchoalveolar lavage in the diagnosis of central lesion in bronchial carcinoma was 100.0% and 23.5%. The accuracy of Bronchoalveolar lavage in the diagnosis of central lesion in bronchial carcinoma was 63.9%. This result was correlated with that study of Khan and Uddin,<sup>15</sup> that bronchial wash cytology had sensitivity of 77.3% and a specificity of 100.0% with a positive predictive value of 100.0% and a negative predictive value of 59.5% in compared with the results of transbronchial biopsies taken as gold standard in the diagnosis of bronchial carcinoma. In this regards Ahmed and Ahmed,<sup>10</sup> found sensitivity of bronchoalveolar lavage cytology in the diagnosis of bronchial carcinoma was 93.44%, specificity 100%, positive predictive value 100%, negative predictive value 75% and diagnostic efficacy 94.52% which was much higher diagnostic efficacy than the present study. Rangdaeng et al.<sup>16</sup> found a diagnostic sensitivity of bronchoalveolar lavage was 36.1%. Khan and Uddin,<sup>15</sup> reported that bronchial wash cytology had sensitivity of 77.3% and a specificity of 100.0% with a positive predictive value of 100.0% and a negative predictive value of 59.5% in compared with the results of transbronchial biopsies taken as gold standard in the diagnosis of bronchial carcinoma. Garg et al.<sup>7</sup> found that bronchoalveolar lavage had a sensitivity of 37.5% and specificity of 100.0% in various samples in neoplastic lung

diseases. Sensitivity has been reported to vary between 57.3% and 75.9% in earlier studies.<sup>55,56</sup> Gaur et al.<sup>17</sup> reported that sensitivity of cytodiagnostic results of BAL was 39.4%, specificity was 89.6% and accuracy was 71.4%. This reported wide range of sensitivity may be due to difference in case selection. Some investigators discard the first aliquot which is relatively enriched in bronchial material. For malignancies originating in bronchial tree, this may represent the material with the highest diagnostic yield.

Although flexible fiberoptic bronchoscopy is generally safe, potentially life threatening complications can occur. In this study respiratory distress was developed in 3 (8.3%) patients as a minor complication of bronchoscopy procedure. All were controlled with bed rest and oxygen inhalation. No major complication occurred in any patients. Careful screening and proper preparation of the patient and by skillful bronchoscopy techniques eliminated major complication in the present study.

### Conclusion

This study revealed that the sensitivity and the specificity of bronchoalveolar lavage was 59.4% and 100.0% respectively; the positive predictive value and negative predictive value was 100.0% and 23.5% respectively; and the overall accuracy was 63.9% in the diagnosis of central lesion in bronchial carcinoma.

So, bronchoalveolar lavage is a useful diagnostic tool in the diagnosis of central lesion in bronchial carcinoma.

### Limitations of the Study

- Open biopsy and histopathology is the gold standard in the diagnosis of any cancer which was not done in this study.

### Recommendation

Based on results of this study followings could be recommended:

- i. Bronchoalveolar lavage is a useful diagnostic tool in the diagnosis of central lesion in bronchial carcinoma
- ii. It is useful in debilitating person because of less invasive procedure than that of endobronchial biopsy.

- iii. Bronchoalveolar lavage may be an alternative to endobronchial biopsy in patients with bleeding diathesis.
- iv. Further study should be conducted to see bronchoalveolar lavage in the diagnosis of central lesion in bronchial carcinoma to improve the diagnostic efficiency in a multi-centres and large scale study to confirm this result and to draw a better conclusion and recommendation.

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## ORIGINAL ARTICLE

# Effects of Ramadan Fasting on Spirometric Values and Clinical Symptoms in Asthmatic Patients

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### Abstract:

**Objective:** To investigate the effect of Ramadan fasting on the Spirometric variables and clinical symptoms on well-controlled Asthmatic Patients during Ramadan.

**Design:** A cohort study

**Setting:** Out Patient Department of National Institute of Disease of Chest & Hospital, Mohakhali, Dhaka, Bangladesh.

**Methods:** A cohort study was conducted in National Institute of Disease of Chest & Hospital, Dhaka, Bangladesh. Fifty Eight (38 males and 20 females) well controlled asthmatic patients aged 40 years completed the study. The average duration of fasting was 26.5 days. Assessment of spirometric variables (daily peak expiratory flow, peak expiratory flow variability, peak expiratory flow home monitoring) as well as asthma clinical symptoms including dyspnea, cough, wheezing, and chest tightness were carried out.

**Results:** No significant changes in clinical symptoms were reported in asthmatic patients at the end of Ramadan fasting. Among spirometric variables, only peak expiratory flow improved after Ramadan ( $p < 0.05$ ). There was a reduction in the mean peak expiratory flow variability from 13% at the first week of fasting to 10% at the fourth week ( $p < 0.05$ ).

**Conclusion:** In well controlled asthmatic patients, Ramadan fasting resulted in improvement in peak expiratory flow and peak expiratory flow variability.

**Keywords:** Asthma, Spirometric values, Clinical Symptoms, Ramadan Fasting.

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## Introduction

Ramadan, the 9th month of the lunar Islamic year lasting for 29-30 days, is the holiest month in Islamic calendar during which Muslims all over the world abstain from eating, drinking, conjugal relationships, and smoking from sunrise till sunset as a sign of restraint and introspection. Depending on season and geographical location of a country, the length of fasting day varies from 11 to 18 hours; being longer in the summer and in temperate regions. (1) All healthy Muslims are allowed to fast, except children, frail elderly, those who are traveling, (2) women during menstruation, pregnancy, and breast feeding. (2, 3) In Bangladesh, prevalence of asthma has increased during the recent years. Asthma Prevalence study has announced that the prevalence of asthma has stood at around 7% for the whole country (4). Although many studies were carried out on the effects of Ramadan intermittent fasting on chronic diseases such as Dyslipidaemia (8,9) diabetes, (7) congestive heart failure, and chronic fatigue syndrome, the number of studies on the effects of Ramadan fasting on asthma were very limited. (14,,16). Moreover, most of the studies focused on spirometric changes during Ramadan were performed on healthy subjects. (16,18).

The aim of present study was to investigate the changes in clinical and spirometric variables before and after Ramadan as well as peak expiratory flow (PEF) home monitoring as an accurate method in well controlled asthmatic patients. (16).

## Material and Methods

### *Study Design*

The study was conducted in the Islamic month of Ramadan 1434 A.H (Hijri Muslim calendar) (July-August) 2014). The average length of fasting day was 14 hours. An informed written consent was obtained from the subjects prior to participation. Patients were enrolled from outpatient department of National Institute of Disease of Chest & Hospital (NIDCH)

A prospective cohort study was performed in a group of well controlled asthmatic patients who fasted more than 16 days. Subjects were asked to complete the questionnaire whether or not they have fasted, and the number of fasted days.

## Patients

Sixty Five well controlled asthmatic patients whose symptoms and pharmacotherapy were stable during 3 months prior to the study were recruited. Their asthma were diagnosed by a physician based on Global Initiative on Asthma (GINA) criteria. (16).

Patients with exacerbation of asthma within last three months, those with concomitant cardiopulmonary disease, pregnant and lactating women, and those who fasted fewer than 16 days were excluded from the study.

Subjects' weight and height were measured with light clothing and without shoes. A brief medical assessment including past medical history, duration of asthma, use of medication, and smoking was carried out.

## Asthma Clinical Symptoms

Severity of asthma was assessed by a validated Asthma Control Test (ACT) questionnaire. (16,20) Frequency of respiratory symptoms during day and night such as dyspnea, cough, wheezing, and chest tightness were recorded pre and post Ramadan.

## Lung Function Tests

A Spirometric test was performed in all subjects. Spirometry was carried out twice (one week before, and at the end of Ramadan) using an electronic spirometer (Spirolab II, MIR, Italy) in the sitting position using a nose clip. Pre and post Ramadan measures of five lung function parameters (FVC, FEV1, FEV1/FVC, PEF, and MMFR) were performed. Standardization of bronchodilators was performed prior to lung function measurements. The patients were instructed to avoid using short acting bronchodilators [including Short Acting Beta Agonist (SABA) and short acting anticholinergics] 6-8 hours prior to the test.

## Peak Expiratory Flow (PEF)

All subjects were provided with a PEF device (Micro Peak, Micromedical, UK), and appropriate training for doing PEF home monitoring was performed. Patients were asked to measure their PEF three times a day at 6:00 a.m., 12:00 p.m., and 6:00 p.m. throughout Ramadan fasting period. Patients were advised to take a deep breath and then blow as fast and forcefully as they could do into the device. The highest value of the three attempts was recorded. PEF variability was defined using the following equation" (Maximum PEF - Minimum PEF)/Maximum PEF" and calculated daily for each patient during the Ramadan<sup>6</sup>.



**Table-I**  
*Medications Used By the Study Subject*

Medication	Percentage using
SABA	4.3%
LABA+ICs	82.6%
ICs	8.3%
Theophylline	12.5%

SABA: Short Acting Beta Agonist, LABA: Long Acting Beta Agonist, ICs: inhaled corticosteroid.

### Statistical Analysis

Statistical analyses were performed using SPSS statistical software (version 11.5, SPSS Inc. Chicago, IL, USA). Results were expressed as mean and standard deviation (Mean (SD)). Paired t tests were performed to compare spirometric variables before and after Ramadan. Repeated Measures of ANOVA was done to compare mean values of PEF variability

in four weeks of Ramadan. The level of statistical significance was considered as  $p$  value  $<0.05$ .

### Results

Fifty Eight patients (38 males and 20 Females) aged 47 (12) years (range: 23 to 70 years) with mean FEV1 of 82.3 (26.1) and 86.9 (28.2) pre and post Ramadan, respectively, completed the study. Seven patients were excluded; Two patient exhibited asthma exacerbation during the study and Five patients withdrew their consent for personal reasons. Fasting time was on average 14 hours (range: 13.3 to 14.4 hours) a day, and subjects fasted for 26.5 days out of 29 Ramadan days. There was not outlying data.

### Asthma Clinical Symptoms

The changes in all daily and nocturnal symptoms such as dyspnea, cough, wheezing, and chest tightness were not statistically significant.

**Table-II**  
*Comparison of ACT Before and After Ramadan in Well Controlled Asthmatic Patients*

		ACT.A			Total
		a	b	c	
ACT.B	Count	16	2	0	18
	% of Total	27.6%	3.4%	.0%	31.0%
b	Count	0	26	0	26
	% of Total	0%	44.8%	.0%	44.8%
c	Count	2	4	8	14
	% of Total	3.4%	6.9%	13.8%	24.1%
Total	Count	18	32	8	58
	% of Total	31.0%	55.2%	13.8%	100.0%

ACT.A: Asthma control test after Ramadan. ACT.B: Asthma control test before Ramadan.

a: asthma seems to be well controlled (score=25). b: asthma seems to be controlled (score=20-24). c: asthma may not be controlled as well as it could be. (score<20)

### Spirometry

Table-III shows five spirometric variables before and after Ramadan. PEF was the only parameter with significant increase at the end of Ramadan. ( $p<0.05$ )

**Table-III**  
*Subjects' Spirometric Variables Pre and Post*

Variable	Pre-Ramadan Mean (SD)	Post-Ramadan Mean (SD)
FVC (% predicted)	81.2 (19.8)	84.7 (21.5)
FEV1 (% predicted)	82.3 (26.1)	86.9 (28.2)
FEV1/FVC (%)	78.1 (11.7)	80.7 (8.9)
PEF* (L/s)	70.04 (24.6)	87.7 (32.4)
MMFR (L/s)	75.2 (38.5)	83.2 (44.3)

\* $p<0.001$ .

Mean values of PEF variability is presented in Table 4. Mean peak expiratory flow variability decreased from 13% in the first week to 10% in the fourth week of fasting. ( $p<0.05$ )

**Table-IV**  
*Comparison of Peak Expiratory Flow Variability during 4 Weeks of Ramadan (n=58).*

	1ST WEEK	2ND WEEK	3RD WEEK	4TH WEEK
	MEAN (SD)	MEAN (SD)	MEAN (SD)	MEAN (SD)
PEF VARIABILITY*	0.131 (0.07)	0.107 (0.06)	0.092 (0.06)	0.107 (0.09)

\* p <0.05

## Discussion

In this study PEF variability home monitoring, spirometry, and clinical symptoms were collectively measured in a group of patients with stable asthma. It is important to note that the measured PEF home monitoring is an index for severity of asthma.

It was shown that among the spirometric values assessed, PEF was the only parameter with a significant improvement after Ramadan. Bener and colleagues showed no significant changes in all measured spirometric variables (FVC, FEV1, FEF 25 75, FEV1/FVC, and PEF), while studies evaluating lung function measures of healthy subjects during Ramadan showed variable results. (17 19) Subhan *et al* mentioned significant increase in the amounts of FEF 75% and FEF 75 85% after Ramadan in healthy persons. (19) Mirmiran *et al.* showed an increase in lung volumes in healthy subjects after fasting (FEV1%, PEF, FEF 50%, FEF 75%). (14) On the other hand, Siddiqui showed that FVC decreased significantly post Ramadan with no significant changes in lung function in healthy persons. (17). Results of our study showed no significant changes in dyspnea, cough, wheezing, and chest tightness. This is consistent with previous studies.

Azizi F and colleagues showed that many Muslim asthmatic patients did not consider asthma as a drawback to fasting, and thus they continued fasting. (14) Indeed, study of Pirani *et al.* did not show any major effect of Ramadan fasting on the control of asthma. (15) Hospitalization rate in asthmatic subjects also did not change compared to other months. (15) Finding of this study might be relevant weight changing during Ramadan. Various cytokines and mediators such as Interleukin 6, TNF alpha, eotaxin, leptin, and reduction of anti inflammatory adipokines in obese subjects may possibly contribute to the development or increased clinical expression of asthma in promoting airway inflammation. Therefore, weight loss may improve

asthma. (17) However, after Ramadan, the weight loss was quickly regained. (17) It appears that fasting does not worsen clinical symptoms. Although sufficient water drinking is needed for remodeling of endothelial airways cells, there might be a redistribution of extracellular water to the bronchial airways to prevent dehydration.

Our study had many limitations; the sample size was not large, however we observed significant changes in PEF home monitoring and its variability. PEF home monitoring was only performed during Ramadan, although spirometric variables were measured before and after Ramadan. It would be better to study our findings in a larger sample with a comparison of PEF home monitoring for at least a complete month prior and after Ramadan. Another important limitation of study was the lack of a control group, as it was difficult to find people not on fasting during this month.

Future research with a larger sample size, recording weight changes, and evaluating food intake and patterns is warranted.

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## REVIEW ARTICLE

# Tuberculosis in Pregnancy

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### Abstract

*Tuberculosis (TB) was declared a public health emergency by WHO in 2005. The disease is a significant contributor to maternal mortality and is among the three leading causes of death among women aged 15–45 years in high burden areas. The exact incidence of tuberculosis in pregnancy, though not readily available, is expected to be as high as in the general population. Diagnosis of tuberculosis in pregnancy may be challenging, as the symptoms may initially be ascribed to the pregnancy, and the normal weight gain in pregnancy may temporarily mask the associated weight loss. Obstetric complications of TB include spontaneous abortion, small for date uterus, preterm labour, low birth weight, and increased neonatal mortality. Congenital TB though rare, is associated with high perinatal mortality. Rifampicin, INH and Ethambutol are the first line drugs while Pyrazinamide use in pregnancy is gaining popularity. Isoniazid preventive therapy is a WHO innovation aimed at reducing the infection in HIV positive pregnant women. Babies born to this mother should be commenced on INH prophylaxis for six months, after which they are vaccinated with BCG if they test negative.*

*Successful control of TB demands improved living conditions, public enlightenment, primary prevention of HIV/AIDS and BCG vaccination.*

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### Introduction

Tuberculosis (TB) is believed to be nearly as old as human history. Traces of it in Egyptian mummies date back to about 7000 years ago, when it was described as phthisis by Hippocrates<sup>1</sup>. It was declared a public health emergency in the African Region in 2005 [1] and has since continued to be a major cause of disability and death. About 9.4 million new cases of tuberculosis were diagnosed in 2009 alone and 1.7 million people reportedly died from the disease in the same year, translating to about 4700 deaths per day<sup>2</sup>. About one-third of the world's population (estimated to be about 1.75 billion) is infected with the tubercule bacillus<sup>3</sup>. As much as 75% of individuals with TB are within the economically productive age group of 15 to 54 years. This significantly impairs socioeconomic

development, thereby perpetuating the poverty cycle<sup>4</sup>. Tuberculosis has been on the rise in tandem with HIV/AIDS. This is because people with HIV/AIDS, whose immune systems are weakened have with a 20–37 times the risk of developing a progressive disease compared with HIV-negative individuals<sup>4</sup>.

### Tuberculosis in Pregnancy

The wide array of opinion of Medical practitioners on tuberculosis in pregnancy simply reflects the Public Health significance of the condition. It is best described as a doubled-edged sword, one blade being the effect of tuberculosis on pregnancy and the pattern of growth of the newborn, while the other is the effect of pregnancy on the progression of tuberculosis. Tuberculosis not only accounts for a

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significant proportion of the global burden of disease, it is also a significant contributor to maternal mortality, with the disease being among the three leading causes of death among women aged 15–45 years<sup>2</sup>. The exact incidence of tuberculosis in pregnancy is not readily available in many countries due to a lot of confounding factors. It is, however, expected that the incidence of tuberculosis among pregnant women would be as high as in the general population, with possibly higher incidence in developing countries. Earlier study by Schaefer reported a new case rate of 18–29/100,000 in pregnancy, which was similar to the 19–39/100,000 reported for the city of New York [7]. A recent United Kingdom study, however, quoted an incidence of 4.2 per 100,000 maternities [8], which may be a reflection the current global fall in the incidence of the disease<sup>2</sup>.

### Effects of Pregnancy on Tuberculosis

Researchers from the days of Hippocrates have expressed their worries about the untoward effects that pregnancy may have on preexisting tuberculosis. Pulmonary cavities resulting from tuberculosis were believed to collapse as a result of the increased intra-abdominal pressure associated with pregnancy. This belief was widely held till the beginning of the fourteenth century! Indeed, a German physician recommended that young women with TB should get married and become pregnant to slow the progression of the disease. This was practiced in many areas till the 19th century [9], while in the early 20th century, induced abortion was recommended for these women<sup>10,11</sup>. Researchers like Hedvall<sup>12</sup> and Schaefer<sup>7</sup>, however, demonstrated no net benefit or adverse effect of pregnancy on the progression of TB. Frequent, consecutive pregnancies may, however, have a negative effect, as they may promote recrudescence or reactivation of latent tuberculosis. It is, however, important to note that the diagnosis of tuberculosis in pregnancy may be more challenging, as the symptoms may initially be ascribed to the pregnancy. The weight loss associated with the disease may also be temporarily masked by the normal weight gain in pregnancy.

### Effects of Tuberculosis on Pregnancy

The effects of TB on pregnancy may be influenced by many factors, including the severity of the disease, how advanced the pregnancy has gone at

the time of diagnosis, the presence of extrapulmonary spread, and HIV coinfection and the treatment instituted. The worst prognosis is recorded in women in whom a diagnosis of advanced disease is made in the puerperium as well as those with HIV coinfection. Failure to comply with treatment also worsens the prognosis<sup>13</sup>. Other obstetric complications that have been reported in these women include a higher rate of spontaneous abortion, small for date uterus, and suboptimal weight gain in pregnancy<sup>14,15</sup>. Others include preterm labour, low birth weight and increased neonatal mortality<sup>13</sup>. Late diagnosis is an independent factor, which may increase obstetric morbidity about fourfolds, while the risk of preterm labour may be increased ninefolds<sup>15-18</sup>.

### Tuberculosis and the Newborn

Congenital tuberculosis is a rare complication of in utero tuberculosis infection<sup>19</sup> while the risk of postnatal transmission is significantly higher<sup>20</sup>. Congenital tuberculosis may be difficult to distinguish from other neonatal or congenital infections from which similar symptoms may arise in the second to the third week of life. These symptoms include hepato-splenomegaly, respiratory distress, fever, and lymphadenopathy. Radiographic abnormalities may also be present but these generally appear later<sup>13</sup>. The diagnosis of neonatal tuberculosis may, however, be facilitated by employing a set of diagnostic criteria developed by Cantwell et al.<sup>22</sup>, including the demonstration of primary hepatic complex/caseating granuloma on percutaneous liver biopsy at birth, tuberculous infection of the placenta, or maternal genital tract tuberculosis, and the demonstration of lesions during the first week of life.

### Diagnosis of Tuberculosis in Pregnancy

To diagnose this condition, history of exposure to individuals with chronic cough or recent visit to areas endemic with tuberculosis should be obtained. History of symptoms, which is likely to be the same as in nonpregnant women, is also essential. Caution must, however, be exercised, as these symptoms may be nonspecific in pregnancy<sup>27,28</sup>. These symptoms include night sweat, evening pyrexia, haemoptysis, progressive weight loss, and chronic cough of over 3 weeks duration. There may also be a history of ineffective attempts at antibiotics therapy<sup>27,29</sup>. In pregnant women with suggestive symptoms and signs of TB, a tuberculin skin test

should be carried out. This has since been accepted to be safe in pregnancy<sup>21, 30</sup>. The debate, however, is about the sensitivity of tuberculin test during pregnancy. Earlier reports suggested diminished tuberculin sensitivity in pregnancy<sup>31</sup>, while recent studies revealed no significant differences in the pregnant and nonpregnant populations<sup>27, 32-35</sup>. The two types of tuberculin skin tests are discussed below.

### **Tine Test**

This test utilises an instrument with multiple needles that are dipped in a purified form of the TB bacteria called old tuberculin (OT). The skin is pricked with these needles and the reaction is analysed 48–72 hours later. It is, however, no longer popular except in large population screening.

### **Mantoux Test**

A single-needle intradermal injection of 0.10mL of purified protein derivative (5 Tuberculin units) is administered, and the skin reaction is analysed 48–72 hours later, based on the largest diameter of the indurations developed. It is a more accurate and reproducible test than the Tines test. False-positive results may be obtained in individuals who had previously been vaccinated with the BCG vaccine, those with previously treated tuberculosis, as well as in people with infection from other Mycobacterium species. False negatives on the other hand are commonly due to a compromised immune system and technical errors<sup>36</sup>. A chest radiograph with abdominal lead shield may be done after the tuberculin skin testing, though pregnant women are more likely to experience a delay in obtaining a chest X-ray due to concerns about fetal health<sup>27</sup>. Microscopic examination of sputum or other specimen for Acid-fast bacilli (AFB) remains the cornerstone of laboratory diagnosis of TB in pregnancy. Three samples of sputum should be submitted for smear, culture, and drug-susceptibility testing.

### **Culture**

The traditional culture on Lowenstein-Jensen's medium may take 4–6 weeks to obtain a result. This may, however, still be useful in cases of diagnostic doubts and management of suspected drug-resistant tuberculosis<sup>38</sup>. Newer diagnostic tools are now available to facilitate diagnosis, including the liquid Bactec culture medium, which has been endorsed by WHO. Other culture media

that could be used include the modified Lowenstein's medium, Petraghani medium, Trudeau Committee medium, Peizer's medium, Dubos Middlebrook media, Tarshis blood agar, Middlebrook's 7-H3, Middlebrook's 7-H9, and Middlebrook's 7H-10 media<sup>38</sup>. Liquidisation and decontamination with N-Acetyl-L-Cysteine in 1% Sodium Hydroxide solution before inoculation may enhance sensitivity [38]. M. tuberculosis produces niacin and heat-sensitive catalase and it lacks pigment. It may, therefore, be differentiated from other mycobacterium species using these features. Others include reduction of nitrates and its isoniazide sensitivity, which may, however, not be reliable in cases of INH resistance. Molecular Line Probe Assay (LPA) as well as the use of polymerase chain reaction (PCR) are presently facilitating the specific identification of the tubercle bacilli<sup>37</sup>.

### **Treatment of Tuberculosis**

“Untreated tuberculosis represents a far greater hazard to a pregnant woman and her fetus than does treatment of the disease”<sup>39</sup>. The management of tuberculosis in pregnancy is a multidisciplinary approach, with the team comprising the obstetrician, communicable disease specialty personnel, neonatologists, counselling unit, and public health officials. Treatment is achieved through the use of Directly Observed Therapy, Short Course (DOTS). This therapy entails the use of combination therapy for at least 6 months, depending on the combination of antituberculous agents that are available. This combination includes isoniazide and rifampicin compulsorily, supported by ethambutol and pyrazinamide<sup>40</sup>. For patients with drug-susceptible TB and good drug adherence, these regimens will cure around 90% of TB cases. Treatment is done on out-patient basis, unless otherwise indicated<sup>37</sup>. The use of these first-line antituberculous drugs in pregnancy are considered safe for the mother and the baby by The British Thoracic Society, International Union Against Tuberculosis and Lung Disease, and the World Health Organisation<sup>16</sup>.

### **Isoniazide**

INH is safe during pregnancy even in the first trimester, though it can cross the placenta<sup>11</sup>. The women must, however, be followed up because of the possibility of INH-induced hepatotoxicity. Pyridoxine supplementation is recommended for all pregnant women taking INH at a dose of 50 mg daily<sup>39</sup>.

### **Rifampicin**

This is also believed to be safe in pregnancy, though in an unknown proportion of cases, there may be an increased risk of haemorrhagic disorders in the newborn (some authorities prescribe supplemental vitamin K (10µmg/day) for the last four to eight weeks of pregnancy.) while some other researchers reported the possibility of limb deformity but none of these are in excess of what is obtained in the normal population.

### **Ethambutol**

The retrobulbar neuritis that may complicate the use of this drug in adults generated the fear that it may interfere with ophthalmological development when used in pregnancy but this has not been demonstrated when the standard dose is used.

### **Pyrazinamide**

The use of pyrazinamide in pregnancy was avoided by many physicians for a long time due to unavailability of adequate data on its teratogenicity. Presently, many international organizations now recommend its use, including the International Union Against Tuberculosis And Lung diseases (IUATLD), British Thoracic Society, American Thoracic Society, the World Health Organisation as well as the Revised National Tuberculosis Control Programme of India. There are no reports of significant adverse events from the use of this drug in the treatment of TB in pregnant women.

### **Streptomycin**

The drug has been proven to be potentially teratogenic throughout pregnancy. It causes fetal malformations and eighth-nerve paralysis, with deficits ranging from mild hearing loss to bilateral deafness.

### **Multidrug-Resistant Tuberculosis in Pregnancy (MDR-TB)**

Pregnant women with MDR-TB have a less favourable prognosis. They may sometimes require treatment with second-line drugs, including cycloserine, ofloxacin, amikacin, kanamycin, capreomycin, and ethionamide. The safety of these drugs is unfortunately not well-established in pregnancy<sup>49</sup>. Para-amino salicylic acid had been used as combination therapy with INH in pregnancy in the past without any significant teratogenic side effects, though maternal gastrointestinal side effects may be pronounced.

Ethionamide is associated with growth retardation, central nervous system and skeletal abnormalities in animal studies involving rats and rabbits. Human studies also demonstrated increased central nervous system defects following its use in early pregnancy. Its use is, therefore, not recommended in pregnancy. Therapeutic abortion has been proposed as an option of management for these women, as MDR-TB poses more risk to the woman and the society at large. Another option is to delay initiating treatment to the second trimester where possible<sup>10</sup>. Individualised Treatment Regimen (ITR) using various combinations of the 2nd line antituberculous agents based on their susceptibility profile had, however, been tried in some pregnant women with no adverse obstetric outcome. The outlook for those patients is expected to improve as experience and knowledge in the management of the condition increases.

### **Treatment of TB in Lactating Women**

Breastfeeding is simply the cheapest and healthiest way to feed a baby. The final decision on breastfeed must, therefore, be taken with necessary input from the neonatologists, obstetricians, and pharmacologists. The American Academy of Pediatrics recommends that women with tuberculosis who have been treated appropriately for two weeks or more and who are not considered contagious may breastfeed, while the RNTCP recommends breast-feeding of neonates regardless of the mother's TB status. Antituberculous drugs are excreted into breast milk, though the dose is less compared with the therapeutic dose for infants. Breastfed infants may receive as much as 20% of the therapeutic dose of INH for infants, while other antituberculous drugs are less excreted. No toxicity has been reported from this small concentration in breast milk<sup>49</sup>. Caution must, however, be exercised as the breast milk dose may contribute to the development of abnormally high plasma levels in newborns who are on antituberculous medications. To minimise this possibility, the mother may take her medications immediately after a feed and substitute a bottle for the next feed. She may then return to her usual pattern of feeding<sup>49</sup>. Pyridoxine deficiency may cause seizures in the newborn. Supplemental pyridoxine should, therefore, be administered to infants on INH or whose mother is taking the drug. Breastfeeding may be discouraged

in women who are yet to commence treatment at the time of delivery and those who are still actively excreting the bacillus while coughing.

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## CASE REPORT

# Reexpansion Pulmonary Oedema: An Uncommon Complication of Common Procedure

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### Abstract

*When a rapidly re-expanding lung has been in a state of collapse for several days, pulmonary oedema sometimes occurs in it. This is called re-expansion pulmonary oedema (RPE). In our case, a young man without having any previous illness presented with right sided pneumothorax. Few hours after insertion of intercostal tube, he felt discomfort and increased breathlessness with profuse pink colour frothy sputum. Chest examination revealed right sided coarse crepitation. Chest radiograph showed heterogenous opacity of right hemithorax consistent with pulmonary oedema. He was managed conservatively and improved completely with radiographic resolution of oedema. Re-expansion pulmonary oedema is an uncommon but fatal complication of treatment of pneumothorax, massive pleural effusion, haemothorax and diagnostic procedures like medical thoracoscopy. The exact pathophysiology is still unknown. Prompt diagnosis and immediate measure is needed to save life.*

**Key words:** Re-expansion pulmonary oedema (RPE), Pneumothorax

*[Chest & Heart Journal 2015; 39(1) : 51-55]*

### Introduction:

Re-expansion pulmonary oedema is an uncommon but fatal complication following re-expansion of lung as treatment of certain conditions such as pneumothorax, massive pleural effusion, haemothorax, after lobectomy, during medical thoracoscopy, or even during single-lung ventilation. Among these, majority of cases of RPE were observed with treatment of pneumothorax.<sup>1</sup> RPE is unlikely if the period of lung collapse is less than 3 days.<sup>2</sup> There is still controversy regarding mechanism though there are several hypothesis and experimental studies. Surfactant depletion,

hypoxic capillary damage leading to increased capillary permeability and free radical injury are important among them.<sup>3</sup> Onset is sudden and dramatic.<sup>4</sup> Mortality rate is as high as 20%.<sup>5</sup>

### Case Report:

A twenty six year old young man presented to us with the complaints of right sided chest pain and breathlessness for 20 days. Pain was localized, dull in nature and there was no aggravating or relieving factor. He did not give any history of trauma. There was no cough, fever, hemoptysis and wheeze. For the same duration he developed breathlessness

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which he overlooked at earlier stage and took some analgesic. But as pain was increasing and breathlessness was progressive, he consulted a physician at district hospital 18 days after onset of symptom. A chest X-ray was done and he was referred to consult a chest specialist.

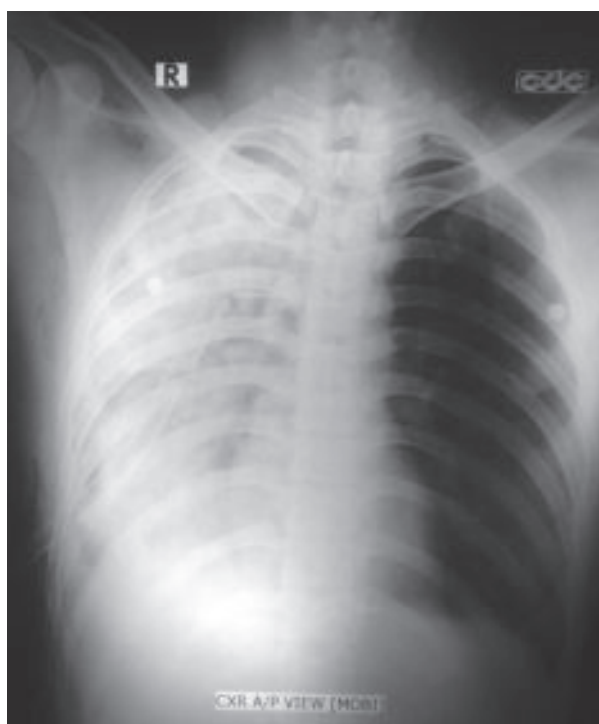
He is a businessman with no definable physical problems. He is a smoker with history of 4 pack years. He also gave history of intravenous drug abuse (morphine, heroine) occasionally. He is unmarried and there was no history of exposure. There was no previous history of tuberculosis.

On examination, he was anxious and dyspnoeic with average body built. His pulse rate was 96/minute, blood pressure 110/82 mmHg, and respiratory rate 24/minute. Chest examination revealed movement restricted on right side, breath sound absent, vocal fremitus and vocal resonance diminished and percussion note hyper resonant on the same side. Examination of other systems revealed no abnormality. A diagnosis of right sided primary spontaneous pneumothorax was made. CXR confirmed pneumothorax (right side) without midline shifting.

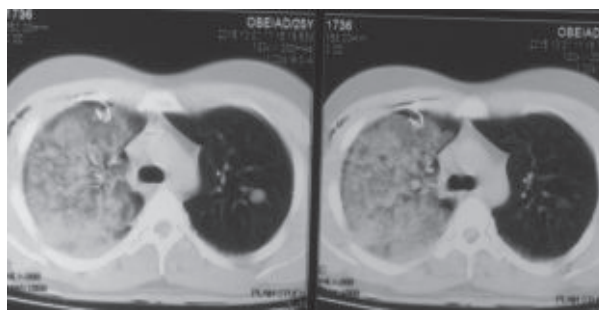


**Fig.-1:** Chest X-ray showing right- sided pneumothorax.

Tube thoracostomy was done on right side in 5<sup>th</sup> intercostal space mid axillary line under local anaesthesia. Gushes of air came out and patient's breathlessness reduced. Few hours later, he complained chest discomfort, breathlessness and cough. There was frothy, pink colour sputum and profuse sweating. His pulse was non-recordable, blood pressure 60/40 mmHg and was cyanosed. Chest auscultation revealed coarse crepitation over right hemithorax. SpO<sub>2</sub> was 80%. Re-expansion pulmonary oedema was suspected and an urgent CXR was done. Chest X-ray P/A view showed dense heterogenous opacity occupying right hemithorax and the clinical diagnosis was established.

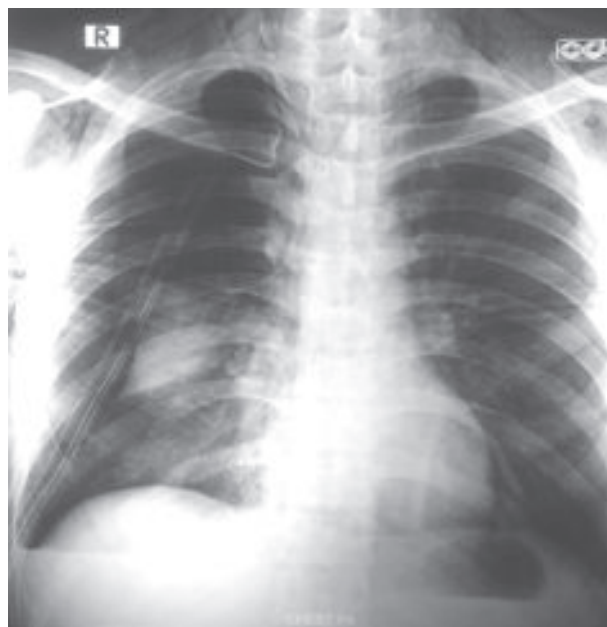


**Fig.-2:** Chest radiograph showing heterogenous opacity occupying right hemithorax.

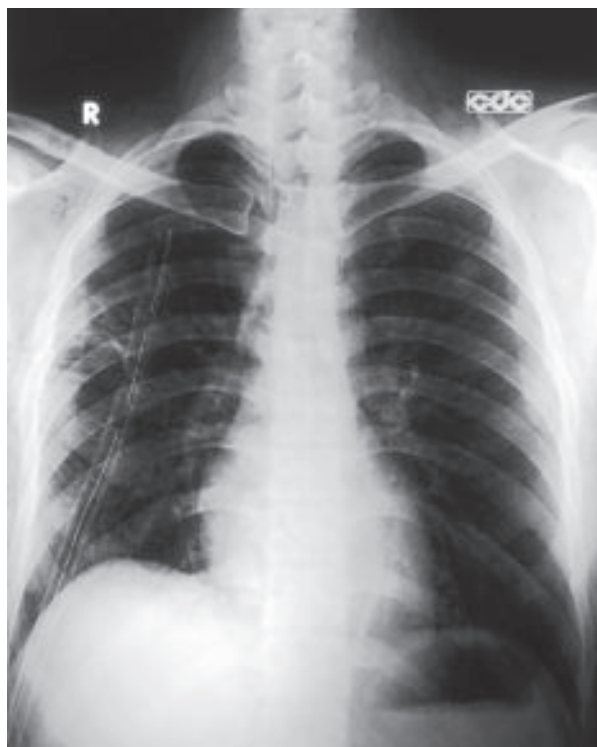


**Fig.-3:** CT scan of chest showing right-sided pulmonary oedema.

As there was cardiovascular deterioration, intensive care support was summoned. Patient was started on intravenous fluid (5% dextrose in normal saline), inotropic agent (Dopamine), high flow oxygen supplementation with  $\text{FiO}_2$  0.5, nebulization (salbutamol and ipratropium bromide), injectable antibiotic (Ceftriaxone) and the patient was on close observation. Complete blood count showed haemoglobin 20.3 gm%, total count 29000/cmm with neutrophil 90%. HIV screening, HBsAg and Anti HCV was negative. After 24 hour of treatment, his condition was stable with pulse rate 78/min, BP 110/70 mmHg and  $\text{SpO}_2$  95%. Arterial blood gas report was  $\text{pH}$  7.62,  $\text{PCO}_2$  20.9,  $\text{PO}_2$  67.2,  $\text{HCO}_3$  17.4. Chest auscultation revealed crepitation on right chest but reduced in intensity. Dopamine was tapered off gradually. Oxygen supplementation was maintained at  $\text{FiO}_2$  0.3. Follow up CXR on day 7 revealed right- sided encysted pleural effusion and blunted right costophrenic angle. Supplemental oxygen was stopped and  $\text{SpO}_2$  was 97%. Subsequent radiograph taken on day 10 and day 15 revealed complete expansion of right lung. Chest tube was removed on 15<sup>th</sup> day without any further complication. He was discharged on 16<sup>th</sup> day with advice to come for follow-up after one week. On follow-up evaluation, he was fine without having any further complaints.



**Fig.-4:** Chest radiograph on 7<sup>th</sup> day showing small encysted right-sided pleural effusion and blunting of right costophrenic angle.



**Fig.-5:** Chest radiograph on 14<sup>th</sup> day showing complete expansion of right lung.

### Discussion

In day to day clinical practice pulmonologists and thoracic surgeons encounter many cases of pleural pathology like pleural effusion, pneumothorax, haemothorax etc. Pleurocentesis is a common procedure, either bedside or by using intercostal tube. In some cases pulmonary oedema develop after drainage of air or fluid which is called re-expansion pulmonary oedema. Though uncommon, the condition is often fatal.

The first reference of pulmonary oedema after pleurocentesis with emptying of large volume of pleural fluid was made by Pinault, in 1853.<sup>6</sup> In 1959, Carlson and colleagues described the first re-expansion pulmonary oedema case following pneumothorax drainage.<sup>7</sup> Between 1958 and 1999 only 60 cases of RPE were published, confirming the rare occurrence of this clinical condition.<sup>4,8</sup>

Miller et al showed that in the experimental animal, RPE occurs only if the lung has been collapsed for more than 3 days and if negative pressure is applied to the pleural space.<sup>3</sup> However re-expansion pulmonary oedema in human have been encountered even when no negative pressure used while managing the pleural effusion.<sup>5, 9-11</sup>

Pathogenesis is multifactorial. Several factors may be involved in the process, especially pulmonary collapse with more than 72 hours of evolution.<sup>3</sup> This component generates permeability alteration and alteration of lung capillary pressure, as well as surfactant loss.<sup>5, 12</sup> Therefore, we can define re-expansion oedema as being caused by two main entities: alteration of capillary permeability and increase of hydrostatic pressure.<sup>5, 13</sup>

The alteration of capillary permeability has two basic causes. The first one is vascular predominance. The voluminous and prolonged collapse (longer than 72 h and larger than 1500 ml) causes local hypoxemia, damages the capillary wall and reduces the production of surfactant. Hypoxemia and capillary lesion causes release of inflammatory mediators (IL-8, MCP-1, nitric oxide, and free radicals), which perpetuate the microvascular lesion, also altering the capillary permeability.<sup>14-20</sup>

The role of the mediators of local inflammation on the genesis and maintenance of RPE is not clear. The presence of neutrophils in the alveolar space seen by Nakamura and colleagues in the bronchial-alveolar lavage suggest an active role of this cell component, either by direct oxidative lesion or by production of local inflammatory mediators, such as IL-8 and leukotrienes.<sup>21</sup>

The second cause - alveolar predominance. Here capillary permeability is increased by the alteration of the alveolar-capillary barrier produced by mechanical lesion of the alveolus, induced either by surfactant reduction (due to hypoxemia) or by pulmonary re-expansion-induced abrupt alveolar distension.<sup>5</sup> Pulmonary re-expansion results not only in alveolar alteration, but it also makes fast bloodflow to increase the lung capillary pressure leading to increased hydrostatic pressure.<sup>13</sup> Vascular permeability, altered by the capillary and alveolar lesion and associated to the increased hydrostatic pressure, leads to liquid and protein overflow into the interstitium and alveoli, thus characterizing re-expansion pulmonary edema.<sup>22</sup>

The clinical picture varies from asymptomatic radiological findings to dramatic respiratory failure with circulatory shock. The commonest presentation is cough or chest tightness during or immediately following thoracentesis or chest tube placement. The cough can be productive with copious amounts of frothy pink sputum. Other signs and symptoms

include dyspnea, tachypnea, tachycardia, fever, hypotension, nausea, vomiting, and cyanosis. The symptoms progress for 24 to 48 hours and chest radiograph reveals pulmonary oedema in the ipsilateral lung. Rarely pulmonary oedema can be bilateral or in contra-lateral lung. If the patient does not die within the first 48 hours, recovery is usually complete.<sup>23</sup>

The duration of collapse seems to be a risk factor for RPE in patients with effusion or pneumothorax who are undergoing tube thoracostomy or thoracentesis.<sup>19</sup> In such cases underwater-seal drainage should be preferred rather than to a negative pressure apparatus and the amount of pleural fluid withdrawn during thoracentesis should not exceed to 1000 ml unless pleural pressures are monitored.<sup>23</sup> Matsura et al revealed young age and extent of lung collapse as independent risk factors for re-expansion pulmonary oedema.<sup>19</sup>

The best treatment of RPE remains supportive with intravenous fluids, oxygen, and morphine. Diuresis is detrimental due to hypovolemic status and should be avoided.<sup>23</sup> In severe conditions mechanical ventilation is required; however there are a few literature case reports of the treatment of re-expansion pulmonary oedema with non-invasive continuous positive airway pressure.<sup>9</sup>

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## CASE REPORT

# Lymphangioma in an Adult Patient : A Case Report

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### Abstract:

*Lymphangioma is a rare congenital malformation of the lymphatic system. It is most frequently detected in the head and neck region. Other rare sites include axilla, mediastinum, groin and retroperitoneum. It is usually evident at birth. Occasionally diagnosis is also happened in adults. The medical treatment of lymphangioma consists of the administration of sclerosing agents. Definitive treatment includes complete surgical excision.*

*In this paper, a case is reported of cervical lymphangioma with mediastinal extension in an adult male which was evident at 31 years of age. He was taken to various hospitals but treatment delayed due to diagnostic dilemma. At last definitive treatment was done at the age of 44 years.*

*Surgical excision of the neck mass and its thoracic extension was done. He attended hospital after 1 month of surgery for follow up presenting himself free of symptoms.*

*Any adult presenting with a mass in the neck since long period, the diagnosis should be kept under consideration of lymphangioma. Though it is sometimes medically treated with sclerosing agents, surgery is the definitive treatment. Prognosis of lymphangioma is excellent if complete surgical removal is possible.*

**Key Words:** Lymphangioma, adult.

[Chest & Heart Journal 2015; 39(1) : 56-60]

### Introduction:

Lymphangiomas are rare congenital benign lesions which occur mainly in the head, neck and oral cavity and usually diagnosed during childhood, mostly (90%) before the age of two years. The lesions constitute 6% of all benign tumors of childhood<sup>1</sup>. Pathogenetically, they are considered as congenital anomalies, hamartomas, acquired lesions or true tumors<sup>2,3,4</sup>. They consist in localized centres of

abnormal development of the lymphatic system. Three theories have been proposed to explain the origin of this abnormality. The first suggests that a blockage or arrest of normal growth of the primitive lymph channels occurs during embryogenesis, the second that the primitive lymphatic sac does not reach the venous system, while the third advances the hypothesis that, during embryogenesis,

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lymphatic tissue lays in the wrong area<sup>5</sup>. Lymphangiomas occur exceedingly rarely in adults and few cases are described in the literature<sup>1-4</sup>.

Although they can occur anypart of the body, the most common sites are in the posterior triangle of the neck (75%), axilla (20%), mediastinum (5%), groin, retroperitoneal space and pelvis<sup>6</sup>. Lymphangiomas are classified as microcystic (capillary lymphangiomas), macrocystic (cavernous lymphangiomas) and cystic hygromas according to the size of the lymphatic cavities incorporated<sup>7</sup>. Capillary lymphangiomas usually consist of small superficial lesions that are generally asymptomatic. Cavernous and cystic lymphangiomas are almost identical histopathologically and are distinguished by the larger size of the latter at clinical presentation. These three types are frequently found together in a same patient, depending on the severity of the disease. Diagnosis is based on previous medical history and clinical examination, followed by cervical ultrasonography. The treatment of choice is complete surgical removal; however, the tumor tends to spread along vital structures and sometimes make it impossible to resect completely, and in consequence recurrence rate is 21–88%<sup>2,8</sup>. Other treatment options, such as sclerotherapy have been proposed as an alternative to reduce the impact and complications of surgery.

Here, we report a case of successful management of cystic lymphangioma in an adult patient.

### Case Report:

A 44 year old male had been suffering from hoarseness of voice & swelling in right side of neck in supraclavicular region for last 13 years. After having noticed the swelling over the right side of neck, his local physician did a chest X - Ray, which showed solid or cystic mass in right upper zone of lung. Afterwards the physician got him to do FNAC of right cervical mass which revealed lymphangioma. Then he was referred to tertiary hospital for better management.

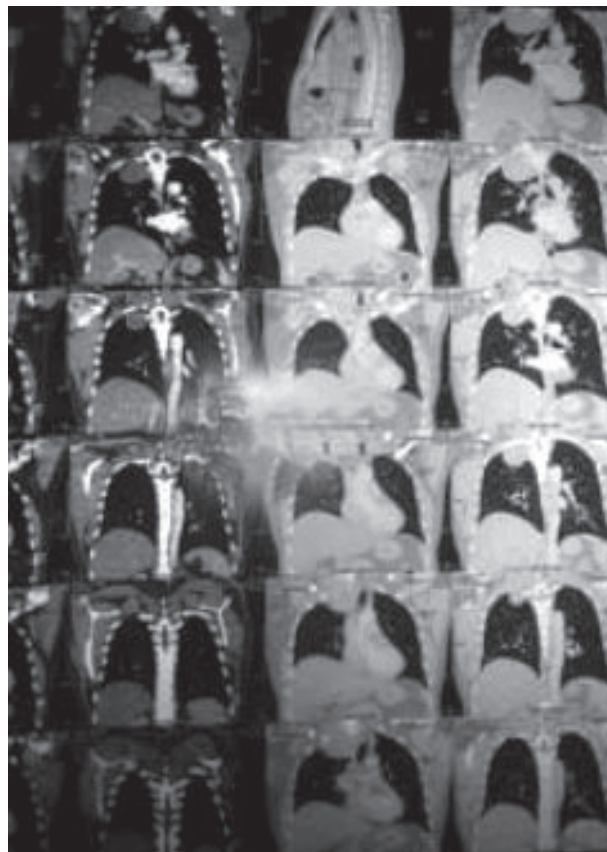
On general examination, patient was healthy, and respiratory rate is 20 breaths/min. On palpation, trachea was slightly shifted to left from midline. Restricted chest expansion was found on right side. Percussion note was dull on right side of upper chest and breath sound was diminished on right side on auscultation. On routine investigation, Chest X-ray

P/A view showed a mass lesion in right upper zone or in mediastinum. [figure1]. CT scan showed a large lobulated heterogenous soft tissue mass (10 x5 cm) centered at the root of neck extending down to right hemithorax and displacing the trachea to the left. Both lung fields appeared clear[figure2]. FNAC of neck swelling was done which revealed mature occasional lymphocytes, and that was compatible with Lymphangioma . Then a core biopsy was recommended. Later on after admission in our hospital, an excision biopsy of cervical swelling was done & its histopathology report revealed that benign lesion was made of dilated empty channels lined by endothelial cells and no malignant cell was seen. Final diagnosis was made as lymphangioma.

So, we then planned for operative treatment. After having proper evaluation of general condition, patient was operated on 29-01-15. Under general anaesthesia with one lung(right) ventilation , chest was opened with standared postero-lateral thoracotomy incision through right fourth intercostal space. A cystic mass filled with fluid was found



**Fig.-1:** Chest Xray P/A view shows a mass lesion in right hemithorax (Arrow pointing the mass)



**Fig.-2:** CT scan showing soft tissue mass in right hemithorax (Arrow pointing the mass)

occupying the right upper chest cavity. The cystic mass was carefully dissected out and part of neck root of the mass was excised. The stalk was ligated properly. After removal of mass, right lung was expanded properly. After having secured proper haemostasis, chest wall was closed in layers keeping two drain tube in right chest cavity.

The whole resected lesion was sent for histopathology. The microscopic examination shows: fibro-collagenous tissue containing many vascular channels filled with lymphocyte. Diagnosis has been made Lymphangioma.

On first post-operative day, breath sound was present on both side of chest in all area and chest radiograph showed broncho-vascular marking present in right side of the chest, suggestive of proper expansion of right lung. Drain tube collection was minimum. Apical chest tube was removed on 3rd POD and basal chest tube was removed on 8th POD. All stitches were removed on 10th POD with advice to follow up visit after one month with Chest X-ray P/A view.

### Discussion:

Lymphangiomas are extremely rare benign tumors occurring in adults. They occur frequently in infants or children younger than two years of age<sup>6</sup>. The etiology in the adult population has long been controversial. Some authors attribute adult lymphangioma to delayed proliferation of the congenital or acquired lymphoid rests following trauma or preceding respiratory infection<sup>9</sup>, though our patient didn't give any such type of history of trauma. The most common documented site is the neck<sup>10</sup>. In children cervical lesions can cause dysphagia and airway obstruction, however, this is rare in adults. Adults usually present with an asymptomatic, soft fluctuant, well defined mass with a capsule, but it is less defined in children<sup>11</sup>. Our patient came with the complaints of hoarseness of voice for 13 years. The anatomic location of the lymphatic malformation plays an important role in determining the histologic type of lymphangioma. The various sites reported are intraabdominal, mediastinal, axillary, thigh and neck. Among them neck is the most common<sup>1,2,4</sup>. Diagnosis is not difficult in most cases. The lymphangiomas are usually characterized by the presence of a soft, compressible, loculated and ill-defined mass, which is usually located in the posterior cervical triangle. The lesions are not attached to the skin or movable across deeper tissues, and readily transilluminate<sup>12</sup>. In our patient mild swelling was found in right posterior triangle of neck, which was cystic in nature, measuring about 3X5 cm.

A radiological diagnosis can be difficult. Extension into the oropharynx is present in 20% cases, and extension to the mediastinum is found in about 10% cases. Ultrasound, computed tomography, and magnetic resonance imaging are useful in confirming the diagnosis of lymphatic malformation<sup>13-16</sup>. They are also helpful in delineating the extent of the mass and revealing its relationship to the surrounding structures. Furthermore, imaging will suggest the presence of any hemangiomatous component or large blood vessels. In our patient, Chest X-ray P/A view showed solid or cystic mass in right upper zone or mediastinal mass. CT scan showed a large lobulated heterogeneous soft tissue mass (10x 5 cm) centered at the root of neck extending down to right hemithorax and displacing the trachea to the left. Lung field appeared clear. No sign of infiltration, consolidation, fibrosis,

emphysema, bronchiectasis, cavitory or soft tissue lesion was noticed. Histologically, lymphangiomas are thin walled, cystic unilocular or multilocular cystic tumors lined by endothelial cells containing clear yellow fluid<sup>3,5,9</sup>. In our patient FNAC and excisional biopsy was done and mature lymphocytes are seen which favours the diagnosis of lymphangioma.

Complete surgical excision is the preferred treatment of cervical lymphangioma<sup>11</sup>. However, complete resection may be considered impossible because of spread of the lesion along adjacent vital structures (e.g. the jugular vein and carotid artery). In such instances, partial resection is still recommended, as disease control could be achieved when all macroscopically detectable cystic structures are removed<sup>8</sup>. This is especially true for adult patients. Surgical removal is usually easier in adults than in children, and adult lesions have lower chance of recurrence after complete excision<sup>17</sup>. So, we then planned for operative treatment. A cystic mass filled with fluid was found occupying the right upper chest cavity. The cystic mass was carefully dissected out and part of neck root of the mass was excised. The stalk was ligated properly. Other therapeutic options include intralesion injection of various substances, either with curative intent (e.g. sclerosing agents) or to facilitate subsequent surgical removal, temperature mapping of magnetic resonance-guided laser interstitial thermal therapy, and radiofrequency-induced thermotherapy<sup>(18,19,20)</sup>. As surgical excision remains the preferred treatment, we have chosen for surgical excision of the lymphangioma in our patient.

Despite all the advanced imaging techniques, the diagnosis of adult lymphangiomas remains a challenge<sup>21</sup>. We report this case to further emphasize the need to consider cystic lymphangioma in the differential diagnosis of neck masses in adults.

### Conclusion:

Lymphangioma of the head and neck are benign neoplasms which are often difficult to diagnose. Surgical intervention represents the treatment of choice.

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## CASE REPORT

# Monostotic Fibrous Dysplasia of the Ribs

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Md. Aftabuddin<sup>4</sup>, Asit Baran Adhikary<sup>5</sup>

### Abstract:

*Fibrous dysplasia (FD) is a non-neoplastic tumour-like congenital process, manifested as a localised defect in osteoblastic differentiation and maturation, with replacement of normal bone with large fibrous stroma and islands of immature woven bone. Monostotic fibrous dysplasia accounts for 28% in the ribs. It is often asymptomatic and incidentally detected on radiographs. We report a case of a 35 year-old male who presented with swelling on left side of the chest wall for 6 years duration and sudden increase in size and pain for 10 months. Radiologically, X-ray and CT scan showed an large bone forming mass measuring about 18.9×10×6.5cm arising from shaft of the left 7<sup>th</sup> -8<sup>th</sup> ribs, gives sun ray speculation and mass compress the mid & lower portion of left lung and have sharp interface. The resected lesion was a variable in consistency, well-defined solid, grey-white mass replacing the medullary cavity. Histopathologically, well circumscribed intra-medullary lesion has destroyed the bone. The lesion composed of curvilinear trabeculae of woven bone mimic Chinese letters, cystic degeneration, hemorrhage and foamy macrophage are found. No evidence of granuloma or malignancy is seen.*

**Key Words:** *Fibrous dysplasia, benign, monostotic, chest wall reconstruction.*

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### Introduction

Fibrous dysplasia (FD) is a cystic, noninherited developmental bone disorder in which abnormal differentiation of osteoblasts lead to replacement of normal marrow and cancellous bone by immature woven bone with fibrous stroma<sup>1</sup>. Fibrous dysplasia can affect any bone and can be monostotic (single bone) or polyostotic (multiple bones). Any bone may be affected, the long bone, skull, and ribs most often. Fibrous dysplasia is found predominantly in children and young adults, with ~75% of patients presenting before the age of 30 years (highest incidence between 3 and 15 years). In polyostotic form, patients usually present by 10 years

old. There is no recognised gender predilection. FD of the ribs accounts up to 28% of all benign chest wall tumors and monostotic forms are about four-six times more common than polyostotic forms<sup>3</sup>. It is usually an incidental imaging finding. However, it may be complicated by pathologic fracture and rarely by malignant change. It can also be associated with aneurysmal bone cysts (ABCs)<sup>5,6</sup>. The development of ABC in FD may hasten the course of presentation and may lead to rapid growth, suggesting a malignant change<sup>7</sup>. We report a case of monostotic FD in a 35 years old male who presented with sudden increase in size and pain in the swelling of 6 year duration on the chest wall since 10 months. The aim of the report is to describe

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the implications of fibrous dysplasia and to discuss diagnostic and treatment strategies.

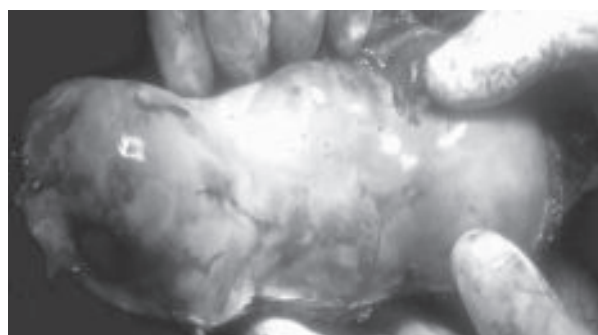
### Case Presentation:

A 35 years old male came with sudden increase in size and pain in the swelling of 6 year duration on the left side of chest since 10 months. On clinical examination he was diagnosed as a case of chest wall tumor. Then patient referred to thoracic surgery department, NIDCH for further evaluation and management. On clinical examination patient was well looking, cooperative, body built was below average, mildly anemic, pulse-78b/min, BP-110/70mmHg. On chest examination, chest wall movement restricted on left side. A large swelling was present on left side of the chest over the 6<sup>th</sup>, 7<sup>th</sup> & 8<sup>th</sup> ribs, overlying skin condition was normal and no impulse on coughing. Trachea centrally placed, apex beat situated in the left 5<sup>th</sup> ICS just medial to mid clavicular line, chest expansion was reduced (2cm). Vocal fremitus was decreased on the left side of the chest in mid axillary line. Dull on percussion over the mass area and rest of the lung field were resonant. Breath sound was decreased over left side of the chest in mid axillary line and normal over the rest of the lung field. Added sound-absent. Vocal resonance was decreased over left side of the chest in mid axillary line. Examination of the mass reveals- A large swelling on left side of the chest over the 6<sup>th</sup>-8<sup>th</sup> ribs about 30cm×10cm in size, overlying skin was normal and cough impulse absent. Local temperature mildly increased. Lump was tender, smooth surface, margin was regular, hard in consistency, not reducible, fixed to the underlying structure but free from overlying skin, Slipping sign - absent, Pulsatility and Expansibility - absent, Trans-illumination test - negative. Bruit absent on auscultation. On investigations, blood reports were essentially normal. Radiologically, X-ray and computed tomography(CT) scan showed an large bone forming mass measuring about 18.9×10×6.5cm arising from shaft of the left 7<sup>th</sup> - 8<sup>th</sup> ribs, gives sun ray speculation and mass compress the mid & lower portion of left lung and have sharp interface (Figures 1). Surgical treatment was scheduled based on radiographical findings. On surgical procedure, with all aseptic precaution elliptical incision over the mass was made under GA with one lung ventilation (OLV). A hard mass arising from the 6<sup>th</sup>, 7<sup>th</sup>, 8<sup>th</sup> ribs that compress the left lung but doesn't invade it. Mass was excised



**Fig-1:** A large bone forming mass measuring about 18.9×10×6.5cm arising from shaft of the left 7<sup>th</sup> - 8<sup>th</sup> ribs, gives sun ray speculation. Mass compress the mid & lower portion of left lung and have sharp interface.

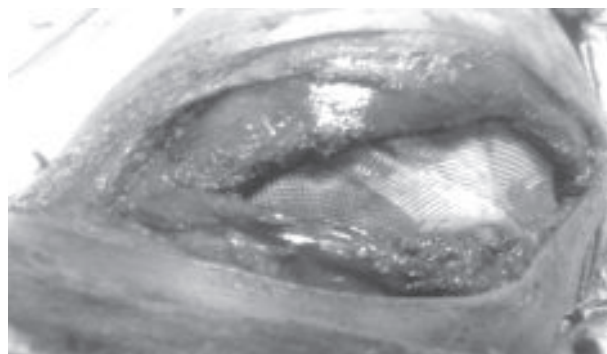
with 6<sup>th</sup> - 8<sup>th</sup> ribs (anteriorly upto costochondral junction and posteriorly upto the angle of rib) (Figure-2). Proper hemostasis was done. Chest drain tube was given. Then chest wall reconstruction done



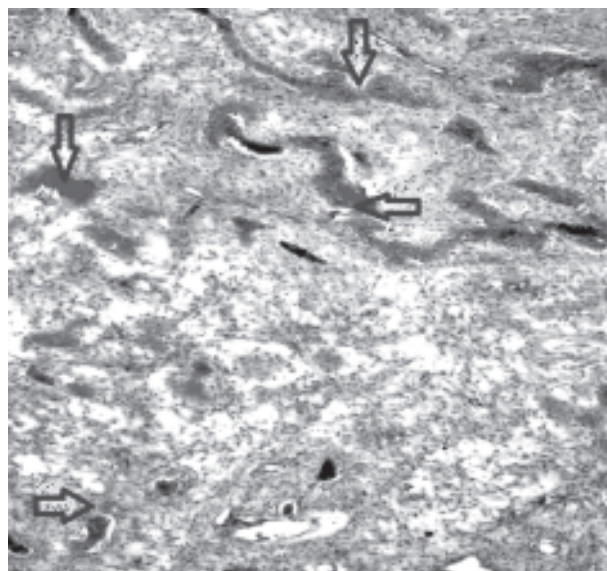
**Figure-2:** Resected mass from chest wall with whole ribs (6<sup>th</sup> – 8<sup>th</sup> ribs).

with prolene mesh fixed with prolene 3/0 (Figure-3). Reinforcement done with fixation of overlapping muscle. Then skin was closed in layers. The resected lesion was a variable in consistency, well-defined solid, grey-white mass measuring about 20×7×5 cm, and replacing the medullary cavity. The mass was surrounded by thin bony cortex that has not invaded the surrounding structures. Histopathologically, well circumscribed intramedullary lesion has destroyed the bone. The lesion composed of curvilinear trabeculae of woven bone mimic Chinese letters, cystic degeneration,

hemorrhage and foamy macrophage are found (Figure-4). No evidence of granuloma or malignancy was seen. The final diagnosis was fibrous dysplasia. Patient was discharged on 18<sup>th</sup> Post operative day with an advice to attend thoracic surgery OPD after 1(one) month. Postoperative period was uneventful with successful anatomical correction.



**Fig.-3:** Chest wall reconstruction with prolene mesh



**Fig.-4:** Photomicrograph (hematoxylin-eosin [H-E] stain) shows “Chinese letters” spicules of woven bone (arrows) separated by abundant fibrous stroma

#### Discussion:

First described by Lichtenstein in 1938<sup>1</sup> and Lichtenstein and Jaffe in 1942, that fibrous dysplasia (FD) is a non-inherited, skeletal developmental abnormality, where normal bone is replaced by fibrous tissue and poorly formed area of immature bone. It accounts for 0.8% of primary and 7% of benign bone tumors. FD is monostotic (involving a single bone) in 70–80% of cases and

polyostotic ( involving two or more bones ) in 20–30% of cases. Any bone may be affected, the long bone, skull and ribs most often. Albright’s syndrome( multiple bone cysts, skin pigmentation and precocious sex maturity in girls ) should be suspected if multiple lesions occurs<sup>1</sup>. FD of ribs accounts for up to 28% of all benign chest wall tumours, and monostotic forms are about four times more common than polyostotic forms. It is typically present in the third or fourth decade of life as an asymptomatic mass. Age of our patient was 35 years, which supports the previous findings. Wide age range presentation between 10 and 70 years, with 75% of patients presenting before the age of 30 years<sup>1,5-7,10,11,12</sup>. In polyostotic form, FD may associated with McCune-Albright syndrome (in 2-3% of cases with the polyostotic form, café-au-lait spots, and endocrine dysfunction) and Mazabraud’s syndrome (polyostotic FD with soft-tissue myxomas)<sup>7,9</sup>. The more extensive and aggressive lesions are commonly found in polyostotic FD, which can affect as few as two bones to as much as 75% of the skeleton, predominantly involving the femur, tibia, pelvis, and foot. Polyostotic lesions progress in number and size until skeletal maturity and then usually become quiescent<sup>5</sup>. Uncomplicated monostotic FD are generally asymptomatic. As a rule, monostotic does not transform to the polyostotic form. Lesions do not increase in size over the time and the disease becomes inactive at puberty<sup>9</sup>. The most common sites of involvement include the ribs (28%), proximal femur (23%), and craniofacial bones (20%). Solitary involvement of other bone is unusual<sup>11</sup>. Monostotic FD in the long bones occurs most frequently in adolescence. In the jaws it is found mainly in early adult life. It presents later in the ribs, probably because it is often asymptomatic in this site<sup>1</sup>.

Fibrous dysplasia develops due to developmental dysplasia and focal arrest in normal osteoblastic activity secondary to non-hereditary mutation which result in the presence of all of the components of normal bone with lack of normal differentiation into their mature structures. It was recognized that both monostotic and polyostotic FD are non-neoplastic processes associated with postzygotic-activating mutations of signal-transducing G proteins encoded by GNAS1 on chromosome 20. Osteoblasts carrying this mutation show increased proliferation and inappropriate differentiation which resulted in fibrotic bone matrix<sup>3,6,8,11</sup>. The gross appearance

of FD is a intramedullary well circumscribed firm solid grey-white mass replacing the medullary cavity and surrounded by cortical bone. Histopathologically, the lesion appears as large fibrous matrix with scattered curvilinear trabeculae of woven bone without surrounding osteoblastic rim. Fibrocellular matrix of immature collagen contains small irregularly shaped trabeculae of immature, inadequately mineralized bone. Trabeculae are not rimmed by osteoblasts (differentiating feature from cemento-ossifying fibroma). Cartilaginous islands present in 10% case (differentiating feature from chondrosarcoma). There is some morphological variation in the woven bone spicules. The classic, most commonly seen pattern is that of curvilinear, "Chinese letters" spicules of woven bone separated by abundant fibrous stroma. Less commonly, the woven bone may be deposited either in sclerotic, interconnected lamellae, cementoid bodies, or in orderly and parallel spicules<sup>5,6,9,11</sup>.

Radiographically (X-ray and CT scan), the lesions are classically described by their ground-glass appearance characterized by a variable degree of mineralization with a faint homogeneous increase in density. Although non-specific, bone scintigraphy is sensitive in the identification of the extent of skeletal FD, particularly in polyostotic form<sup>3,4,5</sup>. Amorphous or irregular calcification is often seen in the lesion on CT scans. Magnetic resonance (MR) imaging is useful in accurately defining the full extent of the lesion. The signal intensity varies from low to high on T2-weighted images but typically is low in areas of lesion involvement on T1-weighted images<sup>9</sup>. Sudden increase in development of already existing FD will be either due to superimposed ABC or malignant transformation<sup>9</sup>. ABC is an unusual benign mass that has the potential for rapid growth, bone destruction, and extension into adjacent soft tissue. The masses contain a network of multiple blood-filled cysts lined by fibroblasts and multinucleated giant cells of the osteoclast type. Malignant transformation with rapid expansion of the bone has been reported in about 0.5% of patients with monostotic FD but in nearly 4% of those with McCune-Albright syndrome. It may develop after irradiation of the involved bones. Malignant transformation is most common to osteosarcoma, although fibrosarcoma, chondrosarcoma, or malignant fibrous histiocytoma noted<sup>6,7</sup>. Malignant transformation of FD suggested by radiologically lytic regions in previously

mineralized zones, intralesional calcification, periosteal reaction, cortical disruption, and a soft-tissue mass<sup>6-9</sup>. Histologically, low-grade osteosarcoma is more cellular; cytologically, it is more atypical; and mitotically, it is more active than FD. Moreover, the regularly spaced spicules of woven bone seen in FD are not present in osteosarcoma, where malignant osteoid is often deposited in broader and irregular trabeculae<sup>6</sup>. Treatment for asymptomatic FD should be conservative, they do not require surgery; simply monitored. Resection (surgery) is indicated for pain and enlarging lesions, confirmatory biopsy, correction of the deformity, prevention of pathologic changes, and/ or eradication of symptomatic lesions<sup>12</sup>. Our treatment plan was based on the above principle. When surgery is not possible and in the polyostotic form, bisphosphonate therapy is indicated with positive effects exerted on bony density and the reduction of pain. Some authors prefer a surgical management than simple surveillance, especially in ribs location of FD, because it can raise the difficult problem of differential diagnosis with malignant tumours<sup>2,3,8,11</sup>.

We believe that symptomatic monostotic FD in ribs, excised involved bone must be indicated for both curative and diagnosis intention, to rule out malignancy and provide relief from symptoms. In this report, clinical, diagnosis problems and treatment are discussed.

### Conclusion:

Chest wall tumors are an interesting diagnostic and therapeutic challenge for thoracic surgeons. Careful preoperative evaluation of the patient, radiographic imaging, and histopathology is required. In symptomatic monostotic FD of ribs, the involved segment of bone should be excised to rule out malignancy and for relief from symptoms. Excellent outcomes for patients with benign, primary malignant and metastatic lesions of the chest wall can be obtained with complete surgical resection and appropriate reconstruction.

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