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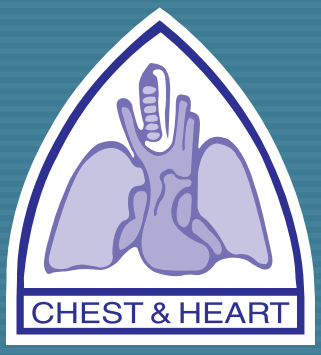

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Chest Heart Journal
Vol. 44, No. 1, January 2020

EDITORIAL

Covid-19 Vaccine. Time for Waiting is Over !

[Chest Heart J. 2020; 44(1) : 1-4]

COVID 19 pandemic is the defining global health crisis of this time and greatest challenge we have faced since World war II. Since its emergence in Asia in 2019, the virus has spread to every content except Antarctica. Cases were raising daily in America, Europe and Africa. Countries are racing to slow the spread of the disease by testing, treating patients, carrying out contact tracing, limiting travel, quarantining citizens and cancelling large gathering such as sporting events, concerts and schools.

But COVID 19 is much more than a health crisis. By stressing every people of the countries, it has the potential to create devastating social, economic and political crisis that will leave deep scars. Every people are losing jobs and income with no way of knowing when normality will return. The International Organization estimates that 24 million jobs could be lost.

After coronavirus was isolated in December 2019 its genetic sequence was published on 11 January 2020 triggering an urgent international response to prepare for an outbreak and hasten development of a preventive COVID 19 vaccine. Since early 2020, vaccine development has been expedited via unprecedented collaboration in the multinational pharmaceuticals industry and between government. The urgency to create a vaccine for COVID 19, led to compressed schedules that shortened the standard vaccine development timeline.

Three vaccine front runners are those developed by Pfizer/BioNTech, Moderna and Oxford/ AstraZeneca. Pfizer and Moderna have both developed mRNA vaccine- a new approach that is incredibly quick to design where they inject tiny fragments of viral genetic code into the body, this has been approved by UK, Europe and US.

Oxford vaccine is subtly different as it uses a harmless virus to carry the same genetic material into the body. This has been approved in the UK and Europe. It is the easiest of the three to use as it can be stored in a fridge, rather than needing very cold temperature.

New approach to vaccines

mRNA vaccines are a new type of vaccine to protect against infectious diseases. As in January 2021, nine different technology platforms are under research to create an effective vaccine against COVID 19. Platforms being developed in 2020 involves- Nucleic acid technology, non replicating viral Vectors, Peptides, Recombinant proteins, Live attenuated viruses, and Inactivated viruses. Currently, four main types of COVID 19 vaccine that are being used. Below is a description of how each type of vaccine prompts our bodies to recognize and protect us from the virus that causes COVID 19. Non of these vaccines can give rise to COVID 19.

mRNA vaccines contains genetic code from the virus that causing COVID- 19 and gives body cells instructions to make a harmless protein which is unique to the virus. After body cells make copies of the protein, they destroy the genetic material from the vaccine as body recognize that the protein should not be there. They build T-lymphocyte and B-lymphocytes that will remember how to fight against the virus that causes COVID-19 if infected in future.

Protein subunit Vaccines include harmless pieces of the virus that cause COVID-19 instead of the entire germ. After vaccination immune system recognizes that this proteins do not belongs to the

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body, so they begins to build T- lymphocytes and antibodies. If we are ever infected in future memory cell will recognize and fight against the virus.

Vector vaccines contain a weakened version of a live virus other than the virus causes COVID- 19. That different virus has genetic material from the virus causes COVID-19 which is inserted by genetic engineering (this is called vector virus).Once the vector virus is inside our body cell, the genetic material gives cells instructions to make a protein that is unique to the virus that causes COVID 19. Using these instructions our cells make copies of the protein. This prompts our bodies to build T lymphocytes and B lymphocyte that will remember how to fight COVID- 19 virus if we are infected in the future.

Inactivated virus Vaccine consist of virus particles that have been grown in culture and then are killed using a method such as heat or formaldehyde to lose disease producing capacity while still stimulating an immune response.

After vaccination it typically takes a few weeks for the body to produce T lymphocyte and B lymphocyte. Therefore it is possible that a person could be infected with the virus that causes COVID- 19 just before or after vaccination and the get sick because the vaccine did not have enough time to provide protection.

Vaccines are safe except minor symptoms after vaccination such as fever which are thought to be associated with the process of building immunity. But very rarely there is evidence of blood clotting specially in cerebral sinus venous thrombosis(CSVT) may occur in vector based vaccination,

Some expert continue to work of this very rare side effect associated with AstraZeneca vaccine. The vector vaccine COVID-19 appears to be associated with autoimmune thrombosis that mimics heparin-induced thrombocytopenia (HIT). The United Kingdom, European Union, and Scandinavian countries have reported rare cases of cerebral sinus vein thrombosis (CSVT) and thrombocytopenia in patients who received the vector based COVID-19 vaccine. The majority of affected patients are women under the age of 55 years, and CSVT seems to occur 4 to 20 days after vaccination. The likely mechanism is antibodies that induce massive platelet activation, reducing the platelet count and causing thrombosis.[1,2] This phenomenon mimics heparin-induced thrombocytopenia (HIT) yet it does not require heparin as a trigger. It has been named vaccine-induced prothrombotic immune thrombocytopenia (VIPIT). The incidence of VIPIT appears to be between 1 in 125,000 and 1 in 1 million.[3]

Clinically Patients with VIPIT may present with CSVT, or with other arterial or venous clots. Some symptoms make it more likely that a patient has VIPIT: persistent and severe headache, focal neurological symptoms, seizures, or blurred or double vision; shortness of breath or chest pain suggesting pulmonary embolism or acute coronary syndrome; abdominal pain suggesting portal vein thrombosis; or limb swelling, redness, pallor, or coldness suggesting deep vein thrombosis or acute limb ischemia. VIPIT seems to occur between 4 to 20 days post-vaccination. Symptoms in this time frame should raise the clinical suspicion of VIPIT.

For diagnosis clinicians should ask patients about their COVID-19 vaccine history and should draw a complete blood count (CBC). VIPIT is more likely if symptoms of blood clotting fall in the 4-to-20-day time frame AND the platelet count is < 150 x 109/ L.[3] Patients with suspected VIPIT should go on to have a D-dimer level and a blood film drawn. They should also have diagnostic imaging to investigate for blood clots based on clinical suspicion. Other than clinical suspicion and blood count the confirmatory diagnosis of VIPIT is made by testing for heparin-induced thrombocytopenia (HIT). This testing should be done even if the patient has had no previous exposure to heparin. HIT testing involves two steps: identification of antibodies against the complex of platelet factor4 and heparin; and confirmatory functional testing of the antibodies' ability to activate platelets.[4]

The Presumptive and confirmed VIPIT should be treated similarly to HIT. Until VIPIT has been ruled out, anticoagulation with heparin (both unfractionated heparin and low molecular weight heparins) and Platelet transfusions should not be given.[4]

Alternative anticoagulants that are safe to use in HIT are likely safe to use in VIPIT include direct thrombin inhibitors and anti-Xa inhibitors (e.g., rivaroxaban, apixaban, edoxaban). If the patient

has severe renal impairment that makes direct oral anticoagulants unsafe, advice from a hematologist should be sought to guide the use of parenteral anticoagulants that are safe to use in HIT.

In patients with confirmed VIPIT and severe or life-threatening blood clots (e.g., CSVT, splanchnic vein thrombosis), it is important to dampen the prothrombotic response with intravenous immunoglobulin (IVIG). Administration of high dose IVIG (1 g/kg of body weight daily for two days) is appropriate and can be guided by the consulting hematologist.[5]

Controversy /Confusion

Commonly asked questions:

-*Whether the existing vaccine will be effective against the new variant of covid-19 virus?*

-Can some body receive different type of vaccine in two doses of Covid-19 vaccine ?

-After Covid-19 infection how long should wait to receive the first dose or second dose?

The COVID-19 vaccines are expected to provide at least some protection against new virus variants and are effective at preventing serious illness and death. That's because these vaccines create a broad immune response, and any virus changes or mutations should not make vaccines completely ineffective. Thus vaccines protect us from these new variants and this is something that is kept in mind when vaccines are being manufactured. If any of these vaccines become less effective against one or more variants, it will be possible to change the composition of the vaccines to protect against these variants. Data continues to be collected and analysed on new variants of the COVID-19 virus.[6]

Till the time it is very confused that a single person can take two different type of vaccine in first and second dose and is not recommended. Some scientists says that there is no reason to believe that giving two dose of different production will boost a persons' immune response beyond what can be achieved by giving same. They also said there may be some adverse effect and truly they do not favor to mismatch with previously received vector vaccine specially Astra Zeneca vaccine. NACI(National advisory committee on immunization) do not preferred AstraZeneca as they are associated with VIPIT.

In this regard COVID-19 Heterologous Prime boost study or ComCOV study is going on in UK. The early massage from the senior officer of the study, they do not see any safety problem or additional danger in mismatched vaccine. This is because different vaccine administration as a part of two dose regimen do not directly interact with each other because the vaccine particles are swiftly cleared by the immune system within days of immunization. There is no remaining vaccine mRNA or viral vector around when given a second dose.

Canadian health officials are now reviewing the research on mismatched vaccine for COVID-19, though their current guideline is AstraZeneca to AstraZeneca for two shots. Very recently Christine Elliott, Ontarios' Health Minister declared that person who received the AstraZeneca vaccine may receive a different vaccine for their second dose.

Fritz, microbiologist and immunologist, professor at McGill university said it better to take mismatched vaccine than to wait too long time for second dose. He also urgue that we give immunization to infant with several different types of vaccine over a period of one month and year without safety concern. He also mention that mismatched vaccine regimen was approved for Ebola last year

Time between two shots was initially 4 months thinking about availability of vaccine and lack of study. Now Pfizer vaccine scheduled 21 day between two dose and Moderna scheduled 28 days between two dose. If some body suffered from COVID-19 he or she should wait 4 weeks to receive the covid-19 vaccination. If someone get infected after 1st dose he can take the second dose after 10 days of recovery from symptoms. Patients suffering from severe disease of COVID- 19 treated by Convalacent plasma or monoclonal antibody, they should wait for 90 days to receive the vaccination.

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ORIGINAL ARTICLE

Spirometric Assessment of Lung Function in Garment Workers in Bangladesh: A Cross Sectional Study

Shamim Ahmed[1], Anita Rubaiya Husain[2], Shah Ashiqur Rahman Ashiq Choudhury[2], Mohammed Atiqur Rahman[3]

Abstract:

Background: *Exports of textiles and garments are the principal source of foreign exchange earnings in Bangladesh. Exports of textiles, clothing, and ready-made garments (RMG) account for 85% of Bangladesh's total merchandise exports and provide employment to around 5 million workers. Workers of garment factories are susceptible to various respiratory morbid conditions, by virtue of workplace and working conditions and are at risk of suffering from various chronic respiratory illnesses. Early studies in textile workers throughout the world have focused on the relationship between hemp or cotton dust exposure and the development of a syndrome termed Byssinosis. Even though quite a few studies have been conducted in among garment workers in Bangladesh enough emphasis has not been given on the epidemiological aspects of chronic respiratory illnesses affecting pulmonary functions among the workers in these mills.*

Objective: *The purpose of the study is to observe pulmonary function among garment workers in Bangladesh and compare it with unexposed population.*

Methods: *This cross sectional observational study was conducted at cotton mill in Gazipur, Dhaka,Bangladesh. A control group was taken from BSMMU for the purpose of comparison. A modified questionnaire was used to inquire about socio demographic characteristics, socioeconomic history, complete occupational history, potential confounding factors, physical parameters and spirometry was done among workers.*

Results: *There was significant association of pulmonary function FEV1, FVC, PEF with cotton dust exposure and a significant reduction of both FEV1 predicted 2.92±0.38 and observed 2.47±0.67 p<0.001 (paired t test) and PEF predicted 7.3%±1.10, observed 5.34±1.67, p<.001 (paired t test) was found among garment workers in comparison to non-exposed population group. Also female workers are more affected than male workers. No significant association of pulmonary function was found with the duration of exposure and distribution.*

Conclusion: *We conclude that there is a significant association of pulmonary function in both long term and short term cotton exposed workers in comparison to non-exposed control group. There is a significant association of pulmonary function parameters (FEV1 and PEF) among female workers. It is justified to tell that cotton dust exposure has an effect on pulmonary function impairment.*

Keywords: *Cotton dust, Garment workers, Pulmonary Function*

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Introduction:

Since the dawn of civilization, occupation related respiratory diseases have always been a matter of grave concern for respiratory health. Its prominence reached the peak during the timeframe of industrial revolution. There is growing interest in the contribution of workplace exposures to obstructive lung disease, given that 25-45% of patients with chronic obstructive pulmonary disease (COPD) worldwide have never smoked[1]. While a number of non-tobacco related environmental exposures may cause COPD, including biomass fuel, early childhood infections, and pulmonary tuberculosis, occupational exposure to dusts are a major contributor, with one U.S. based study citing a population attributable risk of 9%[2].

Early stage byssinosis in many respects fulfills the criteria for the diagnosis of asthma: reversible airflow obstruction and airway hyper-responsiveness. (National Heart, Lung, and Blood Institute, 2007) Large changes in FEV1 before and after a work-shift (cross-shift drop in FEV1) has been noted in a number of different studies.[3]

Most studies in cotton and hemp workers report an increased incidence of chronic and progressive dyspnea, cough, and sputum production characteristic of symptoms seen in COPD[4]

Pathologic studies in garment workers have been conflicting, reporting variable associations between cotton dust and emphysema but confirming the presence of airways disease[5]; all of these studies have been limited by lack of quantitative exposure assessment to cotton dust and tobacco.

The pulmonary function test (PFT) become an important modality in this new era in diagnosis, prognosis and management of pulmonary disorders[6].

Parameters seen in spirometry:

a) FVC: FVC is the maximum volume of gas that can be expired when the patient exhales as forcefully and rapidly as possible after a maximal inspiration. It is the primary indicator of the presence of possible restrictive impairment.[7] The FVC is reduced or restrictive when the compliance of the lung is decreased or when the chest wall expansion or neuromuscular function are limited.

b) FEV1: FEV1 measures the volume expired over the first second of an FVC maneuver. FEV1 is reported as a volume, although it measured flow over a specific interval.[8] It is the most widely used spirometric parameter, particularly for the assessment of airway obstruction.[9]

c) FEV1/ FVC ratio: Disproportionate reduction in the FEV1 as compared to the FVC is reflected in the FEV1/FVC ratio and is the hallmark of obstructive lung disease.[10]

Forced expiratory volume over 1 second (FEV1) is a dynamic measure of flow used in formal spirometry. It represents a truer indication of airway obstruction than does PEFR.[11] Although PEFR usually correlates well with FEV1, this correlation decreases in patients with asthma as airflow diminishes. Interpretation of spirometry results should begin with an assessment of test quality.[12] Failure to meet performance standards can result in unreliable test results.

As in Bangladesh there is scarcity of research, so this study would be beneficial for the health of the workers.

To assess the effect of exposure to cotton dust on the health of garment workers, this study was initiated and conducted in a Bangladeshi garment industry company. The purpose of this review was to observe the pulmonary function among garment workers and to compare it with a matched non-exposed control group.

Methodology

Place of study

Our study has two parts. 100 male and female workers from a garment factory in Konabari, Gazipur were interviewed and spirometry was done. Same number of people that belong to the control group were interviewed and spirometry was done at BSMMU.

Study period

One Year after clearance from IRB.

Type of study

Cross sectional, Observational study.

Data collection procedure

100 exposed persons with at least 2 years employment at the factory as a study subject and

100 matched persons from BSMMU as a control group were selected. All subjects were first interviewed by a modified standardized questionnaire[13]. Personal information including name, age, and history of smoking and tobacco chewing were covered. Work history including questions covering all the details of present and past employment, history of job-related occupational exposure, job responsibilities, working time, working area, duration of employment, and the use of protective equipment during work were taken meticulously. Physical measurements including weight, Height and BMI of each subject were noted. Clinical examination of chest was done. Spirometric pulmonary function test was aimed at calculating forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), FEV1/FVC ratio using the spirometry system according to the guidelines of American Thoracic Society. For spirometry, MIR spirolab 4 (made in Italy) was used.

Estimation of air quality in working sections

Ai quality was measured by respiratory dust sampler (temptop air quality detector) in blow section, ring and packaging section. It measured suspended particulate matter PM 2.5 and PM 10 (microgram/cubic meter). The highest recorded value was taken among all the readings displayed in the monitor.

Criteria for selection of workers

Inclusion criteria:

1) All workers of 18 years and above (male and female) willing to participate having at least 2 years of experience in the production chain were included in the exposed population.
2) The population exposed to cotton dusts having at least 2 years of job activities.
3) Willing to participate

Exclusion criteria:

1) Previous exposure to other occupational dust such as Silica, Coal dust, silk.
2) Those with history of smoking.
3) Those diagnosed with tuberculosis, asthma or COPD.
4) Subjects with neuromuscular disease, with gross clinical abnormalities in thoracic cage and vertebral column.
5) Unable to perform spirometric procedure

Data collection

All data were checked after collection. Then the data were entered in to computer and statistical analysis of the results were obtained by using windows based computer software devised with Statistical Packages for Social Science (SPSS-23), (SPSS Inc, Chicago, IL, USA).The variables were expressed as mean, frequency and standard deviation. The qualitative data were analyzed by chi--square test and quantitative data were analyzed by paired t-test, unpaired t test and Bonferroni test. Multiple comparison test were analyzed by one way ANOVA test. P value of less than 0.05 was considered statistically significant. p-value less than .001 was considered highly significant.

Observations and Results:

This study included 100 (one hundred) subjects who were working in the cotton spinning mill in Gazipur, Dhaka. These workers were working in different sections of the spinning mill like blow room, ring room, and packaging. Air quality was measured Both PM2.5 and PM 10. The main objective of the study was the observation of pulmonary function among cotton mill workers.

Frequency of demographic variables

Table-I

Demographic profile (age) of the study subjects (n=100)

Age (years)	Frequency (n)	Percentage (%)
18-20	46	46.0
21-25	20	20.0
26-30	17	17.0
>30	17	17.0

Among 100 workers the age of workers were 18 years and above. All workers came under almost the same economic category since all of them were interviewed of their actual assets. This table] showing range of age was 18-50 years. The mean + SD of age (in years) was found as 25.0 + 8.2. The age group with the largest number of exposed workers was less than 20 years and the frequency was 46%.

Table-II

Demographic profile (age) of the control group (n=100)

Age (years)	Frequency (n)	Percentage (%)
18-20	46	46.0
21-25	20	20.0
26-30	17	17.0
>30	17	17.0

Among 100 people of the control group, the age of people were 18 years and above. This table showing range of age was 18-50 years. The mean + SD of age (in years) was found as 25.0 + 8.2.

Table-III

Demographic profile (gender) of the study subjects (n=100)

Gender	Frequency (n)	Percentage (%)
Male	44	44.0
Female	56	56.0

Regarding gender, the male frequency was 44% and female was 56%. So the proportion of female workers were high.

Table-IV

Demographic profile (gender) of the control group (n=100)

Gender	Frequency (n)	Percentage (%)
Male	44	44.0
Female	56	56.0

Regarding gender of the control group, the male frequency was 44% and female was 56%. So the proportion of female subjects were high in here also.

Table-V

Distribution of the study subjects according to the working section (n=100)

Section	Frequency (n)	Percentage (%)
Blow	30	30.0
Ring	40	40.0
Packaging	30	30.0

In this present study, pulmonary function was assessed by spirometry. Pulmonary functions of cotton mill workers in different sections of the factory were recorded. Spirometric parameters that were used FEV1, FVC, FEV1/FVC, and PEFR.

Table-VI

PM level at working area (n=100)

Section	PM 2.5
Blow	125.0
Ring	19.0
Packaging	25.5

Here in this table it is showing PM 2.5 level was the highest in blow room that is 125.0 which is regarded as unhealthy among other sections. PM 2.5 is the microdust which causes damage to the gas exchange part of lung. So, this particle was measured considering as important independent variable to cause pulmonary function impairment.

Table-VII

Distribution of confounding factors among the study subjects (n=100)

	Frequency (n)	Percentage (%)
Use of Biomass fuel	5	5.0
Passive smoker	25	25.0

Passive smoking and biomass fuel using were confounding factors which were found 25% and 5% respectively.

Table-VIII

Distribution of confounding factors among the control group (n=100)

	Frequency (n)	Percentage (%)
Use of Biomass fuel	0	0.0
Passive smoker	30	25.0

Passive smoking and biomass fuel using were confounding factors which were found 30% and 0% respectively.

Table-IX

Distribution of work-related variables among the study subjects (n=100)

	Frequency (n)	Percentage (%)
Use mask during work	47	47.0
Duration of work (years)	5.2±3.1 (2-14)	

Several other variables were selected in this study which included mask use, duration of work in years. Among 100 workers the mean SD of duration of work exposure (in year) was found as 5.33.1. The range of work exposure was 2 to 14 years. During work, mask users were 47%. So it implies the rest of the workers were not using respiratory masks as protective devices during work shift.

Table-X

Distribution of work-related variables among the control group (n=100)

	Frequency (n)	Percentage (%)
Use mask during work	51	51.0
Duration of work (years)	6.24.1 (2-14)	

Several other variables were selected in this study which included mask use, duration of work in years. Among 100 people, the mean SD of duration of work exposure (in year) was found as 6.24.1. The range of work exposure was 2 to 14 years. During work, mask users were 51%. So it implies that mask usage among control group was higher than garment factory workers.

Table-XI

Spirometry findings of the study subjects (n=100)

	Predicted	Observed	p-value
FEV1	2.92 0.38	2.47 0.67	<0.001*
FVC	3.34 0.43	2.86 1.19	<0.001*
FEV1/FVC	87.43 4.78	86.36 14.62	0.027
PEF	7.03 1.10	5.34 1.67	<0.001*

Paired t-test was done to measure the level significance

In table VIII showing there was a high significant decrease in the observed value of FEV1, FVC and PEF among 100 workers in comparison with respective predicated value.

Table-XII

Spirometry findings of the control group (n=100)

	Predicted	Observed	p-value
FEV1	2.96 0.38	2.93 0.67	>0.05
FVC	3.34 0.43	3.32 1.19	>0.05
FEV1/FVC	88.62 4.78	88.25 14.62	>0.05
PEF	8.15 1.01	8.14 1.27	>0.05

Paired t-test was done to measure the level significance

In table XIII showing there was no significant decrease in the observed value of FEV1, FVC and PEF among the control group in comparison with respective study subjects.

Here mean value of FEV1, FVC, FEV1/FVC and PEF were compared among three different sections of spinning mill and high significant reduction of FEV1 was found in blow room. (p value <0.001) and PEF was also significantly reduced.

Table XII is showing there was statistical significance of pulmonary function among genders. FEVI and PEF showed statistical significant that is high is high significant reduction of FEVI and PEF among female exposed Workers.

Table XVIII is showing there was no statistical significance of pulmonary function among genders of the control group.

Table-XIII

Spirometry findings of the study subjects working at different section (n=100)

	Blow	Ring	Packaging	p-value
FEV1	2.08 0.68	2.42 0.57	2.92 0.53	<0.001*
FVC	2.76 1.10	2.83 1.13	2.98 1.37	0.766
FEV1/FVC	86.19 20.85	92.94 7.28	89.17 14.01	0.156
PEF	4.99 1.84	5.11 1.50	6.02 1.56	0.028*

ANOVA test was done among the groups.
*p <0.001 is highly significant
*P <0.05 is significant
*p >0.05 is non-significant

Table-XIV

Pulmonary function in male and female of the study subjects (n=100)

	Male	Female	P-Value
FEV 1	2.95	2.09 0.49	<0.001*
FVC	2.96 1.09	2.77 1.27	0.429
FEV1/FVC	89.93 16.41	89.66 13.19	0.927
PEF	6.511.52	4.43 1.12	<0.001*

An unpaired t-test was done to measure the level of significance.

Table-XV

Pulmonary function in male and female of the control group (n=100)

	Male	Female	P-Value
FEV 1	2.99	2.92 0.49	>0.05
FVC	3.36 1.09	3.32 1.27	>0.05
FEV1/FVC	88.98 16.41	87.95 13.19	>0.05
PEF	6.511.52	6.43 1.12	>0.05

An unpaired t-test was done to measure the level of significance.

Discussion:

Sociodemographic data of the study population were evaluated in this study. Among 100 workers pulmonary functions were observed by using spirometry. Among them 44 were male and 56 were female with the age of 18 years and above. The mean + SD of age (in years) was found as 25.08.2. The age group with the largest number of exposed workers was less than 20 years and the frequency was 46%. Among 100 workers the mean+ SD of work exposure (in years). was 5.343.1. During work, mask users were 47%. So it implies the rest of the workers were not using respiratory masks as protective devices during work shift. Passive smoking was another confounding factor that was found at 25%.

Garment workers group showed significant (P<0.001) decrease in forced expiratory volume in 1 s (FEV1), ratio of FEV1 and forced vital capacity (FVC) and peak expiratory flow rate, and no significant difference of FVC between groups. Garment workers showed a significant decrease in spirometric parameters as the duration of exposure and symptoms increased, spirometric abnormality increased[14]. This study also showed a statistically significant decrease in the observed value of FEV1, FVC, and PEF among 100 workers in comparison with the respective predicted value in comparison to the control group. A study[15] shows that respiratory morbidity was higher in cotton textile mill workers compared to unexposed comparison group. They found that age >30 years, dust exposure, duration of exposure >10 years, and smoking were significant risk factors for respiratory morbidity. In this study, the mean age frequency was 25 years (SD=8.2). The age group with the largest number of exposed workers was less than 20 years and the frequency was 46%. Among 100 workers work exposure was 5.3years (SD=3.1). During work, mask users were 47%. So it implies the rest of the workers were not using respiratory masks as protective devices during work shift. Passive smoking was another confounding factor that was found at 25%. So it implies that in this study workers had a low duration of exposure, smokers were not included in the study only passive smokers[16]. Hence this study did not show the changes in pulmonary function parameters as other studies. Another study was conducted in flour mills and it also showed the duration of employment more than 10 years causes a significant reduction of pulmonary function parameters.[17]

The differences in PEFR mean were highly significantly reduced in symptomatic workers than asymptomatic. There is a study which was done in Bangladesh mentioning about non-significance of duration of exposure and symptoms and lung function[18] .The lower lung function indices in cigarette smokers and occupational substance exposure have been supported by various studies.[19] In our study particulate matter was measured in different sections. In the blow room, FEV1 was significantly reduced than FVC, PEF, and FEVI/ FVC. A significant difference between the mean percentages in the predicted value of PEFR, FVC, and FEV1 of nonsmokers and smokers in the exposed and control groups were found. But our study excluded smokers. So the significant change of pulmonary function is solely due to dust exposure. Considering other biomass (5%) or passive smoking (25%) which were included in our study the percentage was so low that it was not considered as a culprit agent for such reduction.

Also, the results of this study were in agreement with the results of another study which revealed that the FEV1% was significantly lower among exposed workers than control[20]. Also, the same results were found in another study where 198 textile workers and 50 subjects were taken as control and found that FEV1 was significantly lower in the exposed group as compared to control[21]. In this study, about 47% of the workers used a protective mask during their work. It was a reusable cotton cloth mask. Statistical analysis showed no statistical significance of pulmonary function parameters. It somehow correlates with the study[22] which showed that in spite of using face mask lung function changes were there. Hence at the end of the discussion, it has been revealed that there was a significant reduction of FEV1, FVC and PEF in cotton mill workers with a wide range of exposure was observed. As there were different study which showed both short term and long term exposure can cause pulmonary function change. Cotton dust exposure was solely the culprit agent as nonsmoker was included in this study. Our limitation of the study was no endotoxin level was measured and the control group was not included. In most of the studies, smokers were included and lung function impairment was found in association with cotton dust exposure. Some studies showed the changes in pulmonary function with endotoxin levels. Few percentage of workers were exposed to biogas and passive smoking which were not being considered as culprit for pulmonary function changes in our study. Regarding gender female workers showed a significant reduction of pulmonary function FEV1 and PEF which also agreed with some studies.

Conclusion:

It was found that there was a significant reduction of FEV1, FVC and PEF among garment factory workers in comparison to the control group. Female workers were predominantly affected as there were significant reduction of FEV1 and PEF. No significant relation was found with duration of exposure. As there was high concentration of PM 2.5 in blow room and significant reduction of FEV1 was found in this section. So it could be told that there may be presence of possible association between cotton dust exposure and impaired lung function. Hence the most important finding of this study is the higher the exposure of cotton dust the more significant association of pulmonary function (significant reduction of FEV1).

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ORIGINAL ARTICLE

Prevalence of Respiratory Symptoms among Cotton Mill Workers

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Abstract:

Introduction: *Cotton textile mill is one of the largest sectors providing a prominent source of growth in the rapidly developing economy of Bangladesh. This sector employs about 5 million workers of whom the majority (80%) are the women. During the processing from fiber to fabric, the workers are constantly at risk of suffering from various respiratory problems. The study was carried out to evaluate the association of long term exposure to organic cotton dust with different respiratory symptoms in the workers. Based on the results, the study may provide information on respiratory health risks and finally, the data can be used to help the policymakers in executing appropriate strategy regarding the work environment.*

Materials and Methods: *This cross sectional study was conducted in a cotton mill at Gazipur, Dhaka, Bangladesh for 1 year. Three hundred and eighty- four workers had participated in this study. Inquiry was made regarding respiratory symptoms with the help of a pretested questionnaire. An air quality monitor was used to measure the amount of dust (PM 2.5) in the workplace.*

Results: *73.18% of workers had one or more respiratory symptoms, 54.2% had cough, 31.8% had phlegm production. Breathlessness was complained by 27.9%, chest tightness by 24.2% and wheezing by 14.3%. Only one upper respiratory tract symptom was considered which was runny nose; 47.1% of workers reported about it.*

The blow room workers were more affected (47%) in comparison to ring and packaging room workers. Working section had significant association with respiratory symptoms. Using biomass fuel came out as a potential confounding factor. Most importantly, it was demonstrated that the level of PM 2.5 varied in the different working sections based on activities of the processing of cotton, and it significantly had a greater impact on respiratory symptoms.

Conclusion: *The prevalence of respiratory symptoms was higher among the workers exposed to cotton dust. Working section, level of PM 2.5 and use of biomass fuel in some respondents are some of the significant risk factors for the presence of symptoms.*

Keywords: *Textile mill, cotton dust, respiratory symptoms, PM 2.5.*

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Introduction:

We take for granted that we breathe, but respiratory diseases impose an enormous global health burden. Before the pre-covid period, more than 1 billion people altogether used to suffer from either acute or chronic respiratory conditions. Only

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cardiovascular diseases are second to respiratory diseases.[1] According to a report of the Forum of International Respiratory Societies (FIRS) 2017, over 50 million people are struggling with occupational lung diseases. Bangladesh being also under this trap as a promising middle-income country, faced 11% death due to respiratory diseases among all non- communicable diseases (NCDs).

Occupational lung diseases are a group of diseases due to long-term and repeated exposure to certain job-related irritants that may persist even after exposure ceases. The textile industry is one such occupational group. This sector provides yarn which is the primary raw material to produce fabrics. During carding, blowing, spinning and weaving of cotton fibers, workers are exposed to cotton dust. Particles with aerodynamic diameter between 0.1- 2.5 μm are labeled as fine particulates because they are lodged in the gas-exchange area of the lung.

Several types of lung disease have been reported which can be linked with cotton dust exposure.[2] Several centuries ago a syndrome was described which was observed due to the adverse effects of exposure to cotton dust on the lung which was later called as byssinosis.[3] Respiratory symptoms are the earliest response to cotton dust exposure, followed by changes in lung function.[4] Cough, phlegm, shortness of breath, nasal and eye irritation, and work exacerbated asthma had been associated with occupational exposure to the raw materials, cotton dust, and products of several chemicals.[5]

Several different other studies showed large changes in FEV1 before and after a work-shift (cross-shift drop in FEV1).[6,7] It has been studied that 25-45% of patients with chronic obstructive pulmonary disease (COPD) worldwide have never smoked, hence a there is a growing interest in the contribution of workplace exposure to obstructive airway disease.[8]

Information is scarce concerning the health effects of cotton dust exposure in our country. We conducted an epidemiological study aiming to find out the prevalence of respiratory symptoms among an occupational group working in a cotton spinning mill located at Gazipur, Dhaka, Bangladesh and also to observe the associated factors with the prevalence of these symptoms as well as to measure cotton dust level in the workplace by an air quality monitor.

Materials and Methods:

Study population: The frame of this study is a cotton textile mill located at Gazipur, Dhaka, Bangladesh. The total workforce in the factory numbers 3000.

Selection of participants:

Inclusion and exclusion criteria: Study subjects were workers of 18 years and above of either sex having at least 2 years of experience in the production chain willing to take part in the study. Participants were excluded on the basis of:

1) Smoking status (Who has smoked 100 cigarettes in his or her lifetime and who currently smokes cigarettes);
2) Previous exposure to other occupational dust such as silk textile mill, coal dust, silica;
3) Those with pre-existing lung disease diagnosed by a registered physician.

Sample size: Sample size was being adjusted to three hundred and eighty- four using the formula $n=z^2\ pq/d^2$. The prevalence of respiratory symptoms was taken as 51% according to previous work.[9] The minimal size of the sample with a margin of error of 5% was 384 subjects.

Sampling method: Non-probability purposive sampling.

Study design: It was a cross-sectional study which was carried out from July 2018 to June 2019.

Data collection: Before performing the study prior permission of the main authorities (Managing Director) of the mill was taken and also the detail of the study was explained to each participant and informed consent from the respondents was obtained. Then data were collected through face-to-face interviews with the workers.

Data was collected using a preformed standardized questionnaire that was developed and modified.[10,11] Personal information, respiratory symptoms (cough, phlegm, breathlessness, chest tightness, wheezing, runny nose), detailed work history, history of cooking fuel type at home and passive smoking at home were also documented.

Cough without sputum was defined in this study occurring on most of the days in a month for three consecutive months or more in a year. Phlegm as production on most days in a month, for three consecutive months or more in a year. Chest tightness was defined as feeling ever at any time in the last 12 months. Dyspnea 2+, any attack of wheezing in the last 12 months and runny nose was documented.

Physical measurements including weight, height, and BMI of each subject were noted.

PM 2.5: The dust level of the working environment was measured by an air quality monitor. Air quality was checked in each section for two days on different occasions. The highest recorded value among all the readings displayed in the monitor was taken.

PM2.5 standard:

Good: PM2.5 < 12 ug/m^3

Moderate: 12 ≤PM2.5 < 35.5 ug/m^3

Unhealthy for Sensitive Groups: 35.5 ≤PM2.5 < 55.5 ug/m^3

Unhealthy: 55.5 ≤PM2.5 < 150.5 ug/m^3

Very Unhealthy: 150.5 ≤PM2.5 < 250.5 ug/m^3

Hazardous: PM2.5 ≥250.5 ug/m^3

The data processing and analysis was done by SPSS-23 version. Chi square test, unpaired student's t test, and fisher's exact test were used to find out the differences of different variables. P value of less than 0.05 was considered statistically significant.

Results:

Socio-demographic characteristics of the study participants:

Total 384 participants were selected by purposive sampling. The mean ± SD of age (in years) was found as 25.1 ± 7.8. Both males and females participated in the study and among them 167 (43.5%) were males and 217 (56.5%) were females.

Working area of the study participants:

Workers were divided into 3 groups according to their area of work- the blow, ring and packaging section. The maximum number of workers being found from the ring room (144) and the percentage was 45.8% (Fig 1), then were the blow room participants (37.5%) followed by packaging section (16.7%)

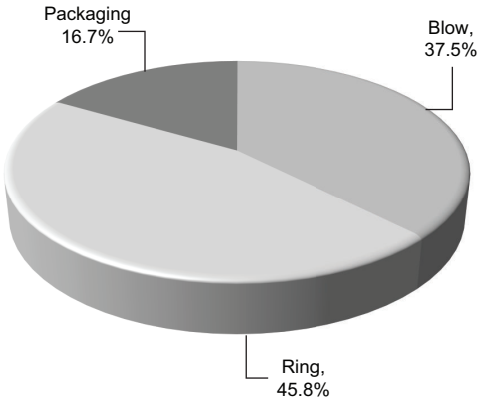

Fig.-1: *Distribution of study subjects in different working sections*

PM 2.5 level was monitored in three working sections with the help of an air quality monitor (Table I).

Table-I

PM 2.5 level at different sections of mill

Section	PM 2.5
Blow	125.0
Ring	19.0
Packaging	25.5

Unit = μg/m^3

Prevalence of respiratory symptoms among the study participants:

About 73.18% of workers reported one or more respiratory symptoms and were considered symptomatic in this study. Out of all, 208 workers complained of cough which was the biggest percentage found among all symptoms (54.2%). Distribution of other symptoms are shown in table II.

Table-II

Distribution of respiratory symptoms of the study subjects (n=384)

	Frequency (n)	Percentage (%)
Runny nose	181	47.1
Cough	208	54.2
Phlegm	122	31.8
Breathlessness (grade 1+)	107	27.9
Chest tightness	93	24.2
Wheezing	55	14.3

Distribution of respiratory symptoms among demographic variables:

During the subgroup analysis, age had no significant association with respiratory symptoms, neither any gender-based difference as well.

Comparison between different working sections with regard to the presence of respiratory symptoms:

Significant association was observed between different working sections and respiratory symptoms. P value was found <0.001 which is statistically very significant (Table III). Among all the respondents, blow room workers had more respiratory symptoms (47%) compared to the ring and packaging section. Chi-square test was done to measure the level of significance

Table-III

Distribution of respiratory symptoms in different working sections (n=384)

Section	Respiratory symptoms		p-value
	Yes (n=281) (%)	No (n=103) (%)	
Blow	132 (47.0)	31 (30.1)	
Ring	104 (37.0)	58 (56.3)	<0.001
Packaging	45 (16.0)	14 (13.6)	

Confounding factors among the workers:

In our study, certain confounding factors became the part. 6.5% of workers found out to be using biomass fuel for cooking purpose. Another confounding variable was passive smoking, the percentage of which was quite large (22.4%). About half of the workers (55.7%) used personal protective mask during their work. Analysis of the use of personal protective mask had no significant association.

During the analysis of whether there is any significant association of use of biomass fuels and passive smoking with respiratory symptoms, fisher's exact test was done. Significant association was found among the biomass users ($p < 0.05$) and no significant association found among the passive smokers (Table IV, V). Fisher's exact test was done to measure the level of significance.

Table-IV

Distribution of respiratory symptoms according to biomass fuel use (n=384)

Biomass fuel	Respiratory symptoms		p-value
	Yes (n=281) (%)	No (n=103) (%)	
Use	23 (8.2)	2 (1.9)	0.033
Not use	258 (91.8)	101 (98.1)	

Table-V

Distribution of respiratory symptoms according to passive smoking (n=384)

Passive smoker	Respiratory symptoms		p-value
	Yes (n=281) (%)	No (n=103) (%)	
Yes	68 (24.2)	18 (17.5)	0.161
No	213 (75.8)	85 (82.5)	

Discussions:

The effect of cotton dust on lung can be wider; ranging from non-specific respiratory symptoms such as cough, phlegm, dyspnea to Byssinosis, occupational asthma and chronic bronchitis.[12,13]

The high prevalence of respiratory symptoms in cotton workers (73.18%) is similar to that reported by other studies carried out in India, Pakistan and China,[14,15] but varied from a study done in Nigeria (11.5%). The variation in different studies can be explained partly by genetic predisposition, atopy and different levels of sensitization to the organic substances. The use of personal protective measures and environmental dust control measures of the workplace may also explain this.

In our study, cough was found in 54.2% of workers, and production of phlegm in 31.8% of all exposed workers. These two were the most prevalent among the lower respiratory tract symptoms. The results were in agreement with the study done by Mansouri et al. where cough was found in 47% and that of sputum in 41% of workers.[9] Ahasan et al. also reported that 42.9% had cough with or without sputum in a Bangladeshi based study.[16]

Overall, runny nose was commoner than lower respiratory symptoms (47.1%) except cough. This observation is in line with the study by Nagoda et

al. where cough and rhinitis were the most prevalent ones. [17]

There is an increased risk of asthma in the textile workers- previous reports say that. The prevalence ranges from 32% to 57% .[18,19,20] Though we didn't search for asthma particularly in our study, rather focused on non-specific symptoms; but who knows these chest tightness, wheezing and breathlessness might be just the asthmatic manifestation of the workers! As lung function test and further follow up is needed to comment on that.

In our study, out of 384 workers, the mean (±SD) of the duration of workers was observed as (4.8±3.1) years, and duration of exposure had no significant association with the prevalence of respiratory symptoms though the association was quite higher. This report is matched with a survey done on 210 Bangladeshi textile workers where no significant association was noticed with the length of work.[16] But this finding contradicts with the study done in Misr spinning and weaving company on 100 exposed workers.[21] Another study done in Maharashtra, India reported that duration of exposure more than 10 years was one of the significant risk factors for developing respiratory morbidity. In our study, there was not a single worker who had such duration in the workplace. Moreover, as this was a cross-sectional study, so we couldn't follow-up with the workers with increasing duration. That's one of the limitations of our study.

Of total 384 workers working in the spinning mill, they were divided into 3 groups according to their area of work- the blow, ring and packaging section. The blow room participants had more symptoms (47%) compared to others. Working section had significant association with respiratory symptoms. As the PM 2.5 level of the blow room was higher (in an unhealthy range) and blow room workers had more symptoms, a probable association can be made. This association has been shown in several studies done in Bangladesh, Pakistan, Egypt and Ethiopia.[16,21,22,23] It can be explained by the fact that workers working in high level of dust concentration like blow room or carding are more likely to develop symptoms. This explanation exactly matched with our finding of dust level (PM 2.5) in different sections. PM 2.5 in blow room was found 125 ug/m^3 which lies in the "unhealthy" range, which means everyone may begin to experience health effects; members of sensitive groups may experience more serious health effects. Studies are controversial in this regard. There has been increasing evidence that cotton dust itself is not the only agent and that endotoxin is regarded as a bioactive agent. Alternatively, it has been explained that there have been some other interactive factors that can alter the dose-response relationship.[24]

In our study, about half of the workers (55.7%) used personal protective mask during their work. It was reusable cotton cloth mask. Analysis of the use of personal protective mask had no significant association. It somehow correlates with the study by Dangi and Bhise who showed that, in spite of using face mask, lung function changes were there.[25] The opposite observation was made by Memon et al. who disclosed that nonuse of face mask in a Pakistani cotton mill was one of the contributory factors of developing respiratory symptoms.[26]

In summary, we found a high prevalence of different respiratory symptoms among the workers of a cotton mill. The blow room workers were more significantly affected. Most importantly, we demonstrated that the level of PM 2.5 varied in different working sections based on activities of the processing of cotton. And it significantly had a greater impact on respiratory symptoms.

Conclusion:

This cross-sectional study was done in a cotton mill (spinning section) located at Gazipur, Dhaka, Bangladesh from July 2018 to June 2019 to observe the prevalence of respiratory symptoms. Results showed a high prevalence of various respiratory symptoms among the workers. Working at blow room and use of biomass fuel for cooking purposes by some respondents were some of the significant risk factors. The level of PM 2.5 significantly had a greater impact on respiratory symptoms.

Recommendations

1. An appropriate ventilation system and ample measures to reduce dust exposure are badly needed to lessen the effect.
2. To ensure that work-related problems are kept to a minimum, regular health and safety surveillance is needed.

3. Alternative methods of cooking instead of using biomass fuel should be considered, and workers should be educated regarding respiratory health hazards from biomass combustion.
4. Further works are needed to strengthen and to figure out the actual picture by doing the lung function test, and other appropriate investigations of the affected workers. Hopefully, this will come up with any future researcher!
5. This study may be repeated with a larger sample size.

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ORIGINAL ARTICLE

Association of CT Scan Finding of Bronchial Carcinoma with Fiber Optic Bronchoscopy

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Abstract:

Background: *Bronchoscopy is highly sensitive investigation for patients with suspected lung malignancy. Beside histology, a cytological diagnosis is also possible with the help of bronchoscopy.*

Objective: *The main objective of the present study was to evaluate the effectiveness of fiber optic bronchoscopy and CT in the diagnosis of bronchial carcinoma.*

Methods: *This cross sectional study was conducted in the Department of Pathology and Department of Respiratory Medicine, National Institute of Diseases of the Chest & Hospital, Mohakhali, Dhaka, between January 2019 and December 2019. Patients in whom an endoscopically visible lung mass and who had a definite cytological or histological diagnosis of lung cancer were included in the study. The diagnosis of pulmonary malignancy could have been established by bronchoscopy. Out of total 50 patients with suspected bronchial carcinoma were included in the study. A detailed clinical history, physical examinations was done before hand and necessary investigations were also done. Selected patients with chest x-ray and CT scan and clinical findings consisting with lung cancer were subjected for flexible fiberoptic video bronchoscopy after obtaining well informed written consent.*

All flexible bronchoscopies were carried out or supervised by the same bronchoscopist using the Olympus BF-1T150 fiberoptic bronchoscope. Collected data were compiled and appropriate analyses were done by using computer based software, Statistical Package for Social Sciences (SPSS) version 23.0.

Results: *In this study 50 patients with bronchial carcinoma, majority 25 (50.0%) patients belonged to age 41 to 60 years, male: female ratio was 3.5:1. All 50(100.0%) patients were presented with cough followed by 43(86.0%) with fever, 39(78.0%) with haemopytysis, 38(76.0%) with weight loss and 36(72.0%) patients presented with chest pain. Regarding pathologic findings, 18(36.0%) patients was found were squamous cell carcinoma followed by 11(22.0%) were small cell carcinoma, 10(20.0%) were adenocarcinoma and 5(10.0%) were large cell carcinoma. In radiographic findings, 18(36.0%) patients was found in lobar collapse followed by 13(26.0%) were pulmonary masses, 11(22.0%) were pulmonary consolidation, 6(12.0%) were unilateral hilar disease and 2(4.0%) in mediastinal/subcarinal*

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disease. The validity of CT findings evaluation for malignancy was correlated by calculating sensitivity 82.2%, specificity 60.0%, accuracy 80.0%, positive predictive value 94.9% and negative predictive value 27.3%.

Conclusion: *Our results show that lung cancer diagnosis is essentially achieved by CT and bronchoscopic techniques. The association of bronchoscopy and CT is useful in the accurate diagnosis of lung cancer, since the occurrence of false-positive results of CT is minimized, improving the specificity of the method. On the other hand, the utilization of CT to detect the presence of peripheral lesions, which increase the incidence of false-negative results of bronchoscopy, allows a better descission for the OT predictive diagnosis of lung cancer which occasionally gives false positive result is minimized & improved by combination with FOB, increasing the diagnostic accuracy.*

Key words: *Fiber Optic Bronchoscopy, Bronchial Carcinoma, CT.*

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Introduction:

Bronchogenic carcinoma is a primary tumor of lung. Lung cancer is one of the leading fatal malignancies worldwide both in male and female subjects. Primary lung cancer is a leading cause of carcinoma related deaths for both men and women in the developed and developing countries. They are subdivided into four main cell types: squamous cell carcinoma, small-cell carcinoma, adenocarcinoma, and large-cell carcinoma.[1] The incidence and mortality of primary lung cancer began its inexorable rise in the late ninetieth decade. It has been estimated that approximately 87% of lung cancers in male and 85% in female subjects can be attributed to cigarette smoking. The risk increased with both the duration and quantity of all smoking products.[2] The other causative factors are some industrial materials, particularly asbestos and rising air pollution. Chest computed tomography (CT) plays a relevant role in the determination of presence and extent of lung cancer, demonstrating the size and site of the tumor. However, this method presents some limitations such as high cost, utilization of ionizing radiation, contrast agent nephrotoxicity, besides the necessity of further procedures to confirm the diagnosis.[3] The CT indispensability in the study of lung cancer is associated with the obligatoriness of endoscopy of the respiratory tract with flexible endoscope. Endoscopic signs of cancer are quite variable, from a simple bright loss in a small region of the bronchial mucosa to a typical vegetative mass. Classically, three types of typical lesions or direct signs of tumor are taken into consideration: mass, infiltration and obstruction. The techniques associated with bronchofibroscopy include bronchial wash and brush cytology and bronchial biopsy.[4-6] Fiberoptic bronchoscopy is a procedure that allows a clinician to examine the breathing passages (airways) of the lungs. Fiberoptic bronchoscopy can be either a diagnostic procedure (to find out more about a possible problem) or a therapeutic procedure (to try to treat an existing problem or condition). The bronchoscope is now being used with lasers to help remove and destroy tumor in the lungs. Sometimes, probes can be passed through the scope to freeze bleeding sites or to shrink the tumors.[7] The prognosis of lung cancer is unfavorable, early diagnosis plays an important role in increasing survival in lung cancer patients.[8] The use of various methods can contribute to early diagnosis. Among the most commonly used methods are imaging tests (chest X-ray and CT), sputum cytology, and fiberoptic bronchoscopy. Fiberoptic bronchoscopy is currently considered the primary method for evaluating the tracheobronchial tree in patients with suspected lung cancer.[9] In addition to allowing visualization of the lesion, the method allows the collection of cytological specimens (by bronchial lavage and bronchial brushing) and histological specimens (by endobronchial biopsy and transbronchial biopsy). However, bronchoscopists can face difficulties in describing endobronchial lesions. Such lesions range from a devitalized area showing loss of natural luster to gross presentations of large

exophytic masses obstructing the bronchial lumen. The description of images as seen under the cold light of the endoscope is subjective, reflecting the variability to which any scientific observation is subject. Fiberoptic bronchoscopy reports show a bias in description: the same lesion can be described with different words, and the cold light of the endoscope can cause artifacts (as it often does). In addition, at best, examiners recognize endoscopic signs of malignancy, but no histopathological diagnosis can be presumed from the results of the test.[10] The main objective of the present study was to evaluate the effectiveness of fiber optic bronchoscopy and CT in the diagnosis of bronchial carcinoma.

Materials and methods:

This cross sectional study was conducted in the Department of Pathology and Department of Respiratory Medicine of National Institute of Diseases of the Chest & Hospital, Mohakhali, Dhaka, between January 2019 and December 2019. The diagnosis of pulmonary malignancy could have been established by fiber optic bronchoscopy. Out of total 50 patients with bronchial carcinoma were included in the study. In this study all patients with suspected lung cancer and subjected to fiber optic bronchoscopy were recruited in the study after taking informed consent. A detailed clinical history, physical examinations was done before hand and necessary investigations were carried out for example chest radiography, CT scan of chest, haematological examination, sputum for AFB, etc. Patients with HIV AIDS were excluded from the study. Children less than 18 years of age, patients who did not give consent for the study and patients who had absolute contraindications for performing fibreoptic bronchoscopy were excluded from the study. Fiber optic bronchoscopy and CT studies were considered as either negative or positive according to the data included in the respective reports. Fiber optic bronchoscopy studies and the subsequent reports preparation were performed by a pulmonologist. On average, a two-day time interval was observed between the performance of CT studies and fiber optic bronchoscopy. It is important to mention that chest, upper abdomen and skull CT and fiber optic bronchoscopy were performed for the disease staging. FOB was done in all of these patients through transnasal route. Bronchoscope used was Pentax adult bronchoscope, model no FB-15P. After proper visualization of the tracheobronchial tree to exclude endobronchial growth, mucosal irregularities, ulceration or external compression, BAL fluid was taken from every patient. Bronchitis was diagnosed by bronchoscopic evidence of inflammation in the wall that is redness and edema involving multiple segments with mucosal biopsy report suggesting non specific bronchitis. Collected data were compiled and appropriate analyses were done by using computer based software, Statistical Package for Social Sciences (SPSS) version 23.0. Qualitative variables were expressed as percentage.

Results:

In this study 50 patients with bronchial carcinoma, majority (50.0%) patients belonged to age 41 to 60 years, 39(78.0%) patients were male with male: female ratio was 3.5:1, 39(78.0%) were married and 28(56.0%) were cultivator (Table-1). All (100.0%) patients were found in cough followed by 43(86.0%) in fever, 39(78.0%) in haemopytysis, 38(76.0%) in weight loss and 36(72.0%) in chest pain (Table-2). Twenty (40.0%) patients had COPD, 6(12.0%) had hypertension, 4(8.0%) had diabetes mellitus and 2(4.0%) had SOL in liver (Table-3). In pathologic findings, 18(36.0%) patients was found in squamous cell carcinoma followed by 11(22.0%) in small cell carcinoma, 10(20.0%) in adenocarcinoma and 5(10.0%) in large cell carcinoma (Table-4). In radiographic findings, 18(36.0%) patients was found in lobar collapse followed by 13(26.0%) in pulmonary masses, 11(22.0%) in pulmonary consolidation, 6(12.0%) in unilateral hilar disease and 2(4.0%) in mediastinal/subcarinal disease (Table-5). CT findings evaluation for malignancy, true positive 37 cases, false positive 2 cases, false negative 8 cases and true negative 3 cases in identification by FOB findings (Table-7). The validity of CT findings evaluation for malignancy was correlated by calculating sensitivity 82.2%, specificity 60.0%, accuracy 80.0%, positive predictive value 94.9% and negative predictive value 27.3% (Figure-1).

Table-I

Demographic characteristics of the study patients (n=50)

	Frequency	Percentage
Age (years)		
≤40	18	36.0
41-60	25	50.0
>60	7	14.0
Sex		
Male	39	78.0
Female	11	22.0
Marital status		
Married	39	78.0
Unmarried	9	18.0
Widow	2	4.0
Occupational status		
Cultivator	28	56.0
Housewife	8	16.0
Service	7	14.0
Business	5	10.0
Driver	1	2.0
Others	1	2.0

Table-II

Complaints of the study patients (n=50)

Complaints	Frequency	Percentage
Cough	50	100.0
Fever	43	86.0
Haemopytysis	39	78.0
Weight loss	38	76.0
Chest pain	36	72.0
Smoker	33	66.0
Breathlessness	28	56.0

Table-III

Co-morbidity of the study patients (n=50)

Co-morbidity	Frequency	Percentage
COPD	20	40.0
Hypertension	6	12.0
Diabetes mellitus	4	8.0
SOL in liver	2	4.0

Table-IV

Pathologic diagnoses of the study patients (n=50)

	Frequency	Percentage
Malignant diseases		
Lung cancer (n=44)		
Adenocarcinoma	10	20.0
Large cell carcinoma	5	10.0
Squamous cell carcinoma	18	36.0
Small cell carcinoma	11	22.0
Metastatic cancer (n=1)		
Colon	1	2.0
Inflammatory diseases (n=5)		
Tuberculosis	3	6.0
Mucous plug	1	2.0
Pneumonia	1	2.0

Table-V

Radiographic findings of the study patients (n=50)

	Frequency	Percentage
Parenchymal disease (n=42)		
Pulmonary masses	13	26.0
Pulmonary consolidation (segmental/subsegmental)	11	22.0
Lobar collapse	18	36.0
Mediastinal and hilar disease (n=8)		
Unilateral hilar disease	6	12.0
Mediastinal/subcarinal disease	2	4.0

Table-VI

Relation of pathologic diagnoses with radiographic findings (n=50)

Pathologic diagnoses	**Radiographic findings**				
	Pulmonary masses	Lobar collapse	Unilateral hilar disease	Mediastinal/ subcarinal disease	Pulmonary consolidation
Adenocarcinoma	5	2	1	0	2
Large cell carcinoma	2	1	1	0	1
Squamous cell carcinoma	4	9	2	1	2
Small cell carcinoma	1	5	2	0	3
Colon	0	0	0	1	0
Tuberculosis	0	1	0	0	2
Mucous plug	0	0	0	0	1
Pneumonia	1	0	0	0	0

Table-VII

Comparison between CT findings and FOB findings evaluation for malignancy

CT findings	FOB findings	
	Positive(n=45)	Negative(n=5)
Positive (n=39)(suggestive)	37(True positive)	2(False positive)
Negative (n=11)(Not suggestive)	8(False negative)	3(True negative)

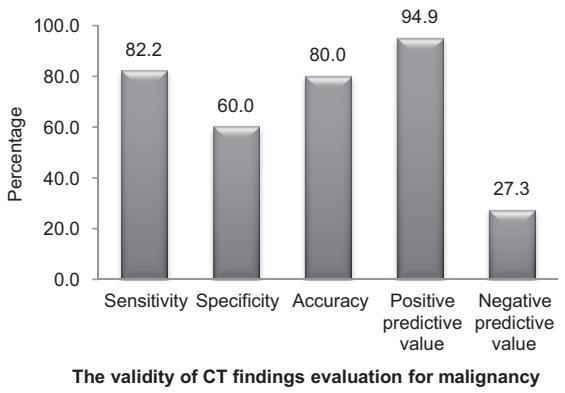

Fig.-1: *Bar diagram showing the validity of CT findings evaluation for malignancy*

Discussion:

A common problem in clinical practice is high-risk patients presenting with symptoms compatible with lung cancer. The first step in the diagnosis of a suspected lesion is the imaging of the chest. Chest CT scan is a valuable tool which has demonstrated high sensitivity and specificity rates. Over the years, various advanced techniques have been developed aiming to a more detailed assessment of the lungs and chest, using 2-D and 3-D reconstruction algorithms.[11] With these techniques, a clinician can interpret more accurately the information obtained by the axial CT.[12] Although chest CT can offer valuable information for suspected endobronchial lesions, fiberoptic bronchoscopy (FOB) usually represents the first choice diagnostic modality for the accurate diagnosis.[13,14]

In this study out of total 50 patients with bronchial carcinoma, half (50.0%) of the patients belonged to age 41 to 60 years. Hathila and Goswami[1] reported that the maximum prevalence of bronchogenic carcinoma was seen between 60–69 years of age (50.76%). Oliveira and Saraiva[15] observed that the mean age was found 66.24 years. Rabahi et al.[10] also documented that the mean age was 66 years (range, 34-88 years) for the male patients and 64 years (range, 14-89 years) for the female patients.

In the present study 39(78.0%) patients were male with male: female ratio was 3.5:1. Oliveira and Saraiva[15] consisted that 23(62.2%) patients were male and 14(37.8%) were female, male-female ratio was 1.6:1. Studies in the literature report that male individuals are most affected by lung cancer, despite the increase observed in the number of cases among women in the last decades.[16,17] Hathila and Goswami[1] also found that male patients were predominance, that was (90.76%).

Regarding complaints in this study, all (100.0%) patients were found in cough followed by 43(86.0%) in fever, 39(78.0%) in haemopytysis, 38(76.0%) in weight loss and 36(72.0%) in chest pain. Oliveira and Saraiva[15] consisted that most of the patients smoked or had ever smoked, corresponding to 55.7% (n = 39), while the number of the non-smoking ones corresponded to 44.3% of the whole study sample. Another study conducted by Hathila and Goswami[1] where they observed of the total 65 patients, 60 (92.31%) patients showed positive smoking history. The most common complaint was cough with expectoration (93.84%). The other common complaints were weight loss (81.53%), anorexia (67.69%) and chest pain (56.92%).

Regarding pathologic findings in this study, 18(36.0%) patients was found in squamous cell carcinoma followed by 11(22.0%) in small cell carcinoma, 10(20.0%) in adenocarcinoma and 5(10.0%) in large cell carcinoma. In a study done by Oliveira and Saraiva[15] where they found histologically 40.54% were adenocarcinoma, followed by squamous carcinoma (32.43% cases) and small-cell lung cancer (18.92%). Rabahi et al.[10] also reported that 199 were evaluated for tumor histological type and the results were as follows: squamous carcinoma in 39%, adenocarcinoma in

21%, small cell carcinoma in 12% and large cell carcinoma in 1%.

In this study radiographic findings, 18(36.0%) patients was found in lobar collapse followed by 13(26.0%) in pulmonary masses, 11(22.0%) in pulmonary consolidation, 6(12.0%) in unilateral hilar disease and 2(4.0%) in mediastinal/subcarinal disease. Naidich et al.[18] had observed that only limited conclusions can be drawn concerning the potential of CT as a screening procedure. As discussed previously, in this series all cases with positive FOB had correspondingly abnormal chest radiographs. From this select population it can be concluded that CT may be of value as a screening technique. The airways were interpreted as normal in only five of 64 cases in which focal disease was identified at FOB. This suggests that CT may provide adequate screening in patients for whom bronchoscopy is either contraindicated or refused. In their opinion these results also support selective use of CT in screening patients for whom there is a low clinical suspicion of endobronchial disease, especially in young patients presenting with either infection or hemoptysis.[19,20] Another study conducted by Hathila and Goswami[1] where they found other common findings by CT scan were loss of patency of bronchus (41.53%), hilar enlargement (38.46%), enlarged mediastinal lymph nodes (35.38%), mediastinal invasion (24.61%), rib, chest wall, and plural invasion (20%), pleural effusion (15.38%), calcification (13.84%), necrosis (10.76%), cavitation (12.3%), and superior vena cava compression (10.76%).

In this study CT findings evaluation for malignancy, true positive 37 cases, false positive 2 cases, false negative 8 cases and true negative 3 cases in identification by FOB findings. Naidich et al.[18] studied observed that CT detected 59 of 64 cases confirmed to be abnormal by FOB. For individual airways, CT identified 88 (90%) of 98 lesions visualized bronchoscopically. CT incorrectly predicted the presence of focal airway disease in only three of 38 cases subsequently confirmed as normal at FOB. Among 24 patients who had FOB, a total of 40 abnormalities were detected either by CT or bronchoscopy. In 25 of 40 cases there was general agreement between CT and FOB.[21] In three, CT failed to detect lesions identified at FOB, including one case in which tumor involved the middle lobe bronchus in a patient with distal atelectasis. In 12 cases, CT detected abnormalities not seen at FOB. This included three cases in which the lesion was distal to a proximally abnormal bronchus verified by FOB and two cases in which the CT abnormality was confirmed by bronchial washings obtained at the site of the specified airway. Unfortunately, in seven cases there was no pathologic confirmation, making an accurate determination of sensitivity difficult. Colice et al.[22] studied the potential role of CT by retrospectively comparing scans with bronchoscopic findings in 53 patients with known or suspected lung cancer. The authors reported considerable interobserver variation with sensitivities ranging from 63% to 85% and negative predictive values ranging from 67% to 80%. Oliveira and Saraiva[15] reported that among the 42 CT studies interpreted as positive, 30 (71.4%) corresponded to a positive diagnosis of lung cancer, and 12 (28.6%) corresponded to a negative diagnosis of the disease. As regards the 28 tomographic studies interpreted as negative, 21 (75%) really corresponded to absence of lung cancer, while 7 (25%) ended up demonstrating the presence of disease. In these 7 cases, the final diagnosis was achieved by means of bronchial biopsy in 6 cases, and by means of transthoracic biopsy in 1 case.

The validity of CT findings evaluation for malignancy in this study was correlated by calculating sensitivity 82.2%, specificity 60.0%, accuracy 80.0%, positive predictive value 94.9% and negative predictive value 27.3%. Oliveira and Saraiva[15] reported that the CT sensitivity was of 81.1%, specificity, 63.6%, and accuracy, 72.8%. False-positive results corresponded to 36.4% and false-negative results, to 18.9%. Another study conducted by Choe et al.[23] where they found the diagnosis compatibility was 95.8% and 59.7% by CT and FOB respectively. The diagnosis compatibility in cases with central airway disease was 96.3% and 100.0% by CT and FOB respectively. CT has higher sensitivity and diagnostic compatibility than FOB for identifying the causes of hemoptysis and is more helpful for patients with hemoptysis from parenchymal or airway disease.

Conclusion:

Lung cancer diagnosis is essentially achieved by CT and bronchoscopic techniques. The association of bronchoscopy and CT is useful in the accurate diagnosis of lung cancer, since the occurrence of false-positive results of CT is minimized, improving the specificity of the method. On the other hand, the utilization of CT to detect the presence of peripheral lesions, which increase the incidence of false-negative results of bronchoscopy, allows a better management of patients, increasing the diagnostic accuracy. Bronchoscopic technologies are the safest and most precise apparatus to assess both central and distal airway mucosa. The association of these two methods, besides the discussion between pulmonologists and radiologists constitute the best approach for lung cancer patients. Proper screening and early diagnostic methods should be applied on a large scale to find out suspected patients who are at risk of developing lung cancer.

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ORIGINAL ARTICLE

Histological Pattern of Neoplasm Resulting Malignant Pleural Effusion among the Patients Admitted in NIDCH, Bangladesh

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Abstract:

Background: *Malignant pleural effusion is a common findings in chest hospital like NIDCH. It may be due to pleural malignancy but mostly due to metastasis. Metastasis mostly occur from bronchial carcinoma but it may occur from any other organs. Sometimes primary site of malignancy is not known. Findings of specific type of malignant cells in pleural effusion or pleural biopsy examination may give information regarding histological type of malignancy. There is no available statistics regarding etiologies and histological type resulting malignant pleural effusion in NIDCH as well as Bangladesh.* ***Aim:*** *To detect the most common type of histological pattern of neoplasm resulting malignant pleural effusion. Which may be an important information for diagnosis and management of malignant pleural effusion.* ***Methods:*** *This was a crass sectional retrospective study, was carried out in the department of respiratory medicine of National Institute of Diseases of Chest and Hospital (NIDCH), Dhaka, during the period of July 2010 to June 2011. Total 69 patients were enrolled consecutively. The information's regarding malignant pleural effusion was collected from each patient in whom the diagnosis was confirmed by pleural biopsy (done by Abram's punch biopsy needle) and presence of malignant cells in pleural fluid.* ***Results:*** *Figure II shows that among 69 patients 51(73.91%) patients diagnosed as Adeno-carcinoma and 7(10.15%) patients diagnosed as Squmous cell carcinoma. Lymphoma 4(5.8%) and small cell carcinoma 4 (5.8 %). So malignant pleural effusion is mostly due to adenocarcinoma.* ***Conclusions:*** *So, most common cause of Malignat Pleural effusion is adeno-carcinoma, it may be due to metastasis from bronchial carcinoma or any other part of the body.*

Key words: *Malignant pleural effusion, Adeno-carcinoma.*

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Introduction:

Malignant pleural effusions (MPEs) are a troublesome and debilitating complication of advanced malignancies. MPEs are one of the commonest causes of pleural effusion in our neighbouring country like Myanmar. According to the hospital statistics, approximately 500 patients with various causes of exudative pleural effusion were admitted to Chest Medical Ward, Yangon General Hospital in every year. The commonest causes are tuberculosis and malignant pleural effusions. Malignant pleural effusions are most commonly associated with cancer of the breast, lung, gastrointestinal tract, ovary, and with lymphomas. Malignant effusions also occur with pleural metastases, direct extension of lung cancer

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to the pleura, impaired lymphatic drainage from mediastinal tumors without direct pleural invasion (particularly in lymphoma). The mechanisms that cause the effusions include increased capillary permeability that allows fluid leakage into the pleural space, decreased oncotic pressure that normally holds fluid in the intravascular space due to hypoalbuminemia, increased negative pressure in the pleural space as a result of atelectasis [1]. A pleural effusion is a condition where abnormal fluid builds up in the pleural space. The accumulation of pleural fluid can usually be explained by increased pleural fluid formation or decreased pleural fluid absorption, or both. Increased pleural fluid formation can result from elevation of hydrostatic pressure, decreased colloid osmotic, increased capillary permeability, passage of fluid through openings in the diaphragm, or reduction of pleural space pressures. Decreased pleural fluid absorption can result from lymphatic obstruction or from elevation of systemic venous pressures resulting in impaired lymphatic drainage (e.g., superior vena cava obstruction syndrome). In patients with MPE, metastasis to pleural spaces may causes significant shifts or fluid imbalance from derangements in the Sterling forces that regulate the reabsorption of pleural fluid [2] . That derangement may cause MPE. MPE is caused by cancer that grows in the pleural space. It can be a complication of virtually any malignancy. The pleura is involved in neoplastic disease more commonly through metastasis than through primary tumours. Lung and breast cancers are the leading causes of metastatic disease to the pleura. Other less common causes are hematologic (e.g., lymphoma, leukemia), ovarian, mesothelioma and gastrointestinal tumours. Cytological examination of the pleural fluid is positive in more than 50% of cases with pleural involvement. Primary and metastatic pleural neoplasms, and non-neoplastic pleural diseases, can have similar clinical, radiographic and gross features. However, treatments and prognoses of these diverse pleural conditions vary greatly. Accurate diagnosis of pleural disease is therefore extremely important, and histological interpretation of pleural biopsies is vital to rendering an accurate diagnosis. Smaller biopsies contribute to the difficulties in accurately characterizing pleural lesions, and immunostains are frequently employed in their assessment[3].

Malignant pleural effusion is a common and debilitating complication of advanced malignant diseases. This problem seems to affect particularly those with lung and breast cancer, contributing to the poor quality of life. Approximately half of all patients with metastatic cancer develop a malignant pleural effusion at some point, which is likely to cause significant symptoms such as dyspnea and cough. Evacuation of the pleural fluid and prevention of its reaccumulation are the main goals of management[4]. Tumor markers (e.g., carcinoembryonic antigen) are not specific enough to be recommended routinely in establishing the diagnosis. Immunocytometry has been used to establish the diagnosis of lymphoma and has been helpful in cases of idiopathic effusions when conventional techniques were non-diagnostic[5]. Quality of life with MPE is often compromised due to debilitating symptoms like shortness of breath, dry cough, pain, feeling of chest heaviness, inability to exercise and malaise (feeling unwell). The diagnosis of malignant pleural effusion as well as finding of the exact location of the pleural effusion, or plan treatment will be based on physical examination, chest x-ray, Computed tomography scan, ultrasound and thoracentesis. The presence of fluid in the normally negative-pressure environment of the pleural space has a number of consequences for respiratory physiology. Pleural effusions produce a restrictive ventilatory defect and also decrease the total lung capacity, functional residual capacity, and forced vital capacity [6]. They can cause ventilation-perfusion mismatches and, when large enough, compromise cardiac output. Evaluation of exudative pleural effusion usually includes thorough history taking, complete clinical examination, appropriate blood tests, radiographs, studies of pleural fluid and needle biopsy of pleura using Abram's pleural biopsy needle. However following these procedures some patients still have undiagnosed condition and the clinical management of these cases is controversial. The initial step of the investigation is the distinction between transudates and exudates, as this gives an indication of the pathophysiologic mechanisms, the differential diagnosis and the need for further investigations. Various tests can be done on pleural fluid to determine the cause of a pleural effusion. If a malignant effusion is suspected, the fluid will be sent for cytology analysis. About 50% to 60% of

cytology tests on pleural fluid are positive for malignancy in patients already known to have cancer. At least 250 mL of pleural fluid is needed for a proper cytologic examination. Other tests done on pleural fluid include protein, LDH, glucose, pH, and cell counts. If a patient has cancer, but the pleural cytology is negative and there is no other obvious cause of the effusion (as will occur in about 25% of cases), thoracoscopy can be performed to confirm the diagnosis through a pleural biopsy of abnormal areas of the pleurae under direct visualization. Thoracoscopy is diagnostic in at least 90% of patients with malignant pleural effusion.[1] In a randomized controlled trial, Abrams' biopsy correctly diagnosed malignancy in eight of [7] patients (sensitivity 47%, specificity 100%, negative predictive value 44%, positive predictive value 100%).[8] Because of their high sensitivity in identifying exudates, the criteria proposed by Light et al8 have become the standard method for making the distinction. The classic work of Light and colleagues demonstrated that 99% of pleural effusions could be classified into two general categories: transudative or exudative .A basic difference is that transudates, in general, reflect a systemic perturbation, whereas exudates usually signify underlying local (pleuropulmonary) disease. The 'Light' criteria include a pleural fluid to serum protein ratio greater than 0.5, a pleural fluid to serum LDH ratio greater than 0.6 and a pleural LDH concentration more than two thirds normal upper limit for serum. If any one of these critical values is exceeded, the effusion is exudates. The original study of Light and colleagues had a diagnostic sensitivity of 99% and specificity of 98% for an exudates. In a study by Alemán C et al, 1014 consecutive pleural effusion patients were treated over a 12- year period, of whom 346 were diagnosed as having an idiopathic or malignant aetiology. Eighty-three patients with idiopathic effusions and 263 with malignant effusions were included. Idiopathic pleural effusion resolved in 47 patients, improved in 20 and persisted in 16. Biochemical pleural fluid analysis did not predict these outcomes. A history of neoplasm, chest X-ray and CT features, as well as additional examinations according to clinical findings, established a diagnosis or suspicion of malignancy in 256 (97.7%) of the 263 patients who received a diagnosis of malignant effusion. Diagnostic thoracoscopy was helpful in seven patients in whom malignant disease was strongly suspected, despite the absence of other pathological findings.[9] In this study they report their experience with 73 patients with confirmed diagnosis of MPE and discuss the clinical features, radiological findings, biochemical, cytological and microbiological analysis of pleural fluid, hematological and biochemical profiles of serum and positivity rates of blind pleural biopsy in these patients. We also analyzed the likelihood ratios of some of the important presenting features in this study. The objective of the study was to review the natural history of patients with a malignant pleural effusion but without obvious evidence of a primary lesion and to assess the value of investigations to confirm the diagnosis of malignant pleural effusion. They also like to report other findings such as age, gender, clinical features, nature and microscopic examination of pleural fluid, positivity rate of blind pleural biopsy results in patients diagnosed with bronchogenic carcinoma in the Chest Medical Department in Yangon General Hospital, Myanmar.

Material and Method:

This was a crass sectional retrospective study, was carried out in the department of respiratory medicine of National Institute of Diseases of Chest and Hospital (NIDCH), Dhaka, during the period of July 2010 to June 2011. Total 69 patients were enrolled consecutively who was confirmed as a case of malignant pleural effusion. The information regarding malignant pleural effusion was collected from each patient in whom the diagnosis was confirmed by pleural biopsy (done by Abram's punch biopsy needle) and presence of malignant cells in pleural fluid. Exclusion criteria were 1) Multiple pathology of pleural effusion.2) Patients with more than one etiology of pleural effusion were excluded. 3) Patient's refusal Written informed consent was obtained from patient. Before requesting consent, the individual was explained in an understandable language about the aims of the study, the methods of conduct, expected duration of subject participation, benefits, foreseeable rights or discomfort, the extent of confidentiality, extent of investigators responsibility, provision of medical services, the right to refuse to participate and withdraw from

the study without affecting further medical care. Detailed history, thorough physical examination, radiological findings, haematological and biochemical findings were recorded in the proforma. Pleural aspiration and biopsy was performed on all patients after obtaining the written consent. Macroscopic examination, cytological, microbiological and biochemical analysis of pleural fluid were performed in all patients.

Results:

Among 69 patients 51(73.91%) patients were diagnosed as Adeno-carcinoma and 7(10.15%) patients were diagnosed as Squmous cell carcinoma. Cases of Lymphoma were 4(5.8%) and small cell carcinoma 4 (5.8 %). So malignant pleural effusion is mostly due to adenocarcinoma. Pleural effusion due to lymphoma were within the younger age group.

Table-I

Age group (years)	n=69	%
11 years to 25 years	3	4.35
26 years to 40 years	4	4.71
> 40 years	62	89.86
Total	69	100.0

Table-I: Age of the respondents in malignant pleural effusion. Most of the cases of malignant pleural effusion in more than 40 (forty) age group of patients as most of the malignancy including bronchial carcinoma occurs in this age group. All three cases of malignant pleural effusion in 11 years to 25 years were due to lymphoma. In the same way most of the malignant pleural effusion due to small cell carcinoma in earlier age group (26 years to 40 years age group). Malignant pleural effusion due to metastasis from extra pulmonary sites

Fig.-1: Sex distribution among the respondents suffering from malignant pleural effusion. Malignant pleural effusion was more common in male than female as bronchial carcinoma was more common in male respondent.

Fig.-2: Type of malignancy among the respondents suffering from malignant pleural effusion (n = 69). Malignant pleural effusion due to metastatic adenocarcinoma was significantly higher than any

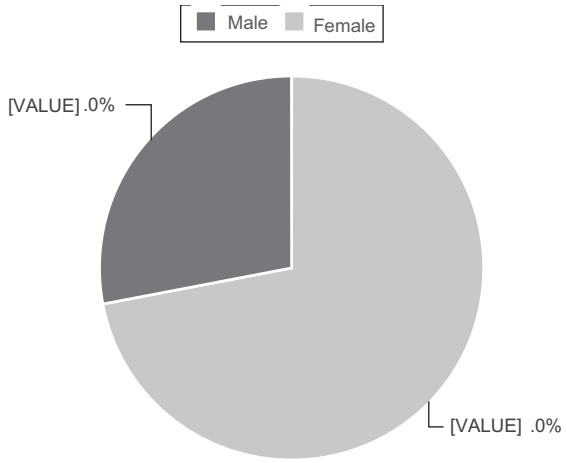

Fig.-1:

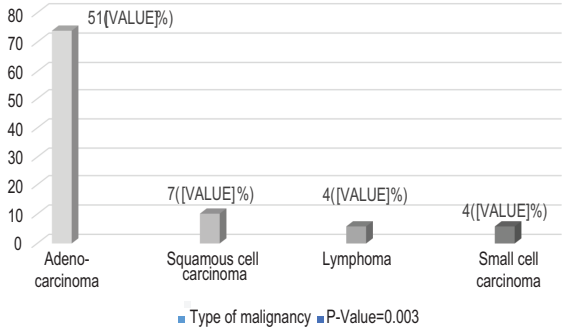

Fig.-2:

other histological type. As p-value less than 0.05 (typically ≤0.05) is statistically significant. Among the histological type of bronchial carcinoma, adeno-carcinoma are peripherally situated and they have tendency to metastasis in distant sites including pleura.

Table-II

Primary site	Total number	%	P value
Bronchial carcinoma	42	82.35	
GIT	2	3.92	
Breast	3	5.88	0.003
Primary site, not known	4	7.84	

Table-II: Primary sites of metastatic adenocarcinoma. Most common primary sites are bronchial carcinoma. As p-value less than 0.05 (typically ≤ 0.05) is statistically significant. Among the adenocarcinoma few have metastasis from extra-pulmonary sites like GIT, breast etc.

Discussion:

MPEs were more common in male than female. It may be related to chronic smoking history in male patient. It is obvious that incidence of MPEs is significantly higher in patients with age above 40 and those with history of heavy smoking. 82.2% of malignant pleural effusions are heavy smokers or ex heavy smokers. Heavy smoking is the primary cause of the high prevalence of this disease. Dyspnea and cough were significant symptoms in one study, which is consistent with our finding. In our study, breathlessness, cough, chest pain, weight loss, loss of appetite, and sputum production are common symptoms of malignant pleural effusion. Less than 50% of patient developed fever. Haemoptysis is an uncommon symptom of MPE (20.5%). According to the likelihood ratio calculation, chest pain and pulmonary consolidation are the important features for haemoptysis. These signs should guide in clinical teaching. Other features are not positively associated to each other in likelihood ratio calculation. MPEs were more common on left side and the reason of side predilection is unknown. Half of the pleural aspirates of MPEs were blood stained in their morphologic appearances. Mean ADA activity (SD) in malignant pleural effusion was general low. In our previous report, mean ADA activity of TB pleural effusion was significantly higher than malignant group (73.91 Vs 23.83)[10,11]. There was a linear correlation among biochemical parameters of pleural fluid such as protein and LDH. This can be concluded that production of all biochemical parameters in abnormal pleural fluid are related to single aetiology probably by inflammatory process. It is also suggested that pleural fluid levels of protein and LDH are partially depends on their plasma values and need measuring the plasma levels at the same time to get more accurate result. M Keshmir stated that pleural fluid cholesterol can be used to differentiate tuberculous from malignant pleural effusion[11]. There was no association between MPEs and any WBC subsets of peripheral blood. Although a number of tests have been proposed to differentiate pleural fluid transudates from exudates, the tests first proposed by Light et al have become the criterion standards [8] . The fluid is considered exudates if any of the following apply: Ratio of pleural fluid to serum protein greater than 0.5 and ratio of pleural fluid to serum lactate dehydrogenase (LDH) greater than 0.6 or pleural fluid LDH greater than two thirds of the upper limits of normal serum value. In our study, the nature of MPE was that of an exudates which is easily demonstrable by applying the Light criteria. Light RW et al also found that pleural fluid glucose level below 60 mg/dl (3.3 mmol/l) suggests MPE, TPE or lupus pleuritis. In our study mean pleural fluid glucose concentration was 4.8 mmol/l which is not consistent with the finding of Light et al. Most of the patients with MPE were anaemic (Mean haemoglobin concentration was 10.8 ± 1.65 g/dl) which are considered as multiple aetiology such as anaemia of chronic disease, depression, lack of nutrition and dietary deficiency. No leukocytosis is noted. Mean ESR was high at 62.23 which reflects inflammatory state in general. It has no diagnostic value for any specific disease. International Journal of Collaborative Research on Internal Medicine & Public Health Vol. 4 No. 5 (2012) 769 Diagnostic pleural aspiration and pleural biopsy could be performed by a single session of procedure. Since it is a blind procedure and in patients with non-informative pleural fluid and pleural biopsy examinations, the procedure needed to be repeated. Cagle PT, Allen TC pointed out that smaller biopsies contribute to the difficulties in accurately characterizing pleural lesions, and immunostains are frequently employed in their assessment. But in our study, we could not perform special staining procedures of the histology slides because of limited facilities. The positivity rate of first session of pleural biopsy was 65.7 % of MPE in this study. The second and third biopsy sessions were needed for the rest of patients. Repeat performance of pleural biopsy is obviously an inconvenience to the patients and also consumes a certain amount of medical resources. Closed pleural biopsy is a fairly blind procedure rendering it into a diagnostic procedure with less than desired positivity rate. Pleuroscopy resolves the diagnostic problem but the procedure requires more material resources and expertise . 8 patients (11.1%) were diagnosed only by identification of malignant cells in the pleural fluid cytology because subsequent biopsies revealed chronic nonspecific pleuritis. They were diagnosed by pleural fluid cytology and exact histological type of malignancy may not be

identified in the cytology report. However, 64.4% of overall MPEs revealed positive pleural fluid cytology for malignant cells which is a substantial number to diagnosed MPEs even though exact histology cell type is difficult to identify. This finding supports that statement about 50% to 60% of cytology tests on pleural fluid are positive for malignancy in patients already known to have cancer[1] . In a randomized controlled trial, Abrams' biopsy correctly diagnosed malignancy in eight of 17 patients (sensitivity 47%, specificity 100%, negative predictive value 44%, positive predictive value 100%).[7] In our study, 88.9% of patients were correctly diagnosed malignancy but needed to be repeated in 23.2%. In our study, metastatic adenocarcinoma carcinoma was the commonest histologically identified cell type. The origin is considered mainly from bronchogenic carcinoma.

Conclusion:

Pleural fluid analysis have an important contribution for investigation of patients with pleural effusion. Repeated pleural biopsy procedures will be necessary if first session failed to fetch the definitive tissue diagnosis. Pleuroscopy is recommended procedure for tissue diagnosis in MPEs. Most common cause of malignant pleural effusion is due to metastatic adeno-carcinoma. Most of the metastatic adenocarcinoma are due to bronchial carcinoma. Male are commonly affected by malignant pleural effusion. In few cases of adenocarcinoma primary sites might not be known, in those cases PET/CT could be done for further evaluation.

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ORIGINAL ARTICLE

Diagnostic Value of Serum ADA in Smear-Negative Pulmonary Tuberculosis

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Abstract:

Background & Objective: *Diagnosis of tuberculosis (TB) is not always easy, particularly if it is a case of smear-negative pulmonary tuberculosis (SNPTB). Patients with respiratory symptoms resembling SNPTB is difficult to differentiate on the basis of clinical features, X-ray chest and Xpert MTB/RIF negativity. So additional diagnostic tests with high sensitivity and specificity is needed to increase the yield of the ongoing diagnostic strategy for SNPTB. That purpose the present study tested the value of serum adenosine deaminase (ADA) as an adjunct to the existing diagnostic aids.*

Patients & Methods: *The present cross-sectional analytical study was carried out in the Department of Respiratory Medicine, National Institute of Diseases of the Chest & Hospital (NIDCH), Mohakhali, Dhaka over a period of one year from April 2018 to March 2019. Patients attending in the above-mentioned hospital with respiratory ailments and were suspected of having pulmonary tuberculosis from their clinical presentation, chest radiography, sputum smear and Xpert MTB/RIF negativity were the study population. A total of 60 such patients (suspected SNPTB), 30 smear-positive pulmonary tuberculosis (SPPTB) cases and 30 healthy controls were included in the study. According to National Guidelines for Management of Tuberculosis, if a patient with symptoms suggestive of TB with two consecutive sputum specimens being negative for AFB, Xpert MTB/RIF negative, chest X-ray abnormalities consistent with active TB and the diagnosis was made by a qualified physician, the case was considered as having SNPTB.*

Result: *The SNPTB patients had a moderate rise of serum ADA (35.4 U/L) compared to the SPPTB patients who had the highest serum ADA and the healthy controls who had the lowest serum ADA (41.1 ± 11.8 vs. 22.7 ± 5.5 U/L respectively). In order to find a cut-off value for serum ADA at which it is fairly sensitive and specific to diagnose SNPTB, a receiver-operating characteristic (ROC) curve was constructed with an area under the curve being 0.851(95% CI = 0.745-0.957, p < 0.001). The ROC curve gave a cut-off value 27.5 U/L at which the serum ADA had a sensitivity, specificity, PPV, NPV and the diagnostic accuracy of 80, 80, 88.9, 66.7 and 80% respectively. The LR+ and LR- were 4.0 and 0.25 respectively.*

Conclusion: *From the findings of the study, it can be concluded that the serum ADA has a modest sensitivity and specificity in the diagnosis of SNPTB. However, the results of ADA assays should be interpreted in conjunction with clinical presentations and other laboratory test findings. As the LR+ is only 4, the test is of little clinically useful in the diagnosis of SNPTB. Therefore, estimating ADA levels should not be a valuable additional test, in the rapid diagnosis of SNPTB patients provided a large-scale study on a cross-section of diverse SNPTB population to confirm its limited usefulness.*

Key words: *Serum ADA, Smear-negative Pulmonary Tuberculosis (SNPTB), sensitivity and specificity etc.*

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Introduction:

Tuberculosis (TB) is one of the leading causes of morbidity and mortality, amongst infectious diseases.[1] It has been estimated that about one-third of world's population was affected with TB and more than 95% patients died in developing countries.[2] According to European Centre for Disease Prevention and Control, TB remains responsible for the deaths of nearly 1.7 million people each year and representing the ninth leading cause of death globally.[3] Bangladesh ranks sixth among the world's 22 high-burden TB countries with estimated 350,000 new cases and 70,000 deaths each year.[4]

Although TB is a known infectious disease with a definite epidemiological pattern and known principles of treatment since last 60 years, there are still a considerable number of TB cases in many parts of the world who are not timely diagnosed and properly treated.[5] Tuberculosis, can present as pulmonary tuberculosis (PTB) or extra-pulmonary tuberculosis (EPTB). Sputum smear microscopy is routinely used for diagnosis of PTB. The diagnosis of smear-positive pulmonary tuberculosis (SPPTB) does not pose any problem. However, definitive laboratory diagnosis and confirmation of sputum smear-negative pulmonary tuberculosis (SNPTB) still remains elusive and poses a major challenge in the management and control of active pulmonary tuberculosis. Cliniciansoften have to face difficulties in smear negative patients, and sometimes, it becomes almost impossible to diagnose this entity.[6]

The symptoms of active pulmonary TB are coughing, sometimes with sputum or blood, chest pain, weakness, weight loss, fever, and night sweats and it is treatable with a 6-months course of antetubercular chemotherapy.[7] Chest radiograph provides only a probable diagnosis of tuberculosis; they are sometimes difficult to differentiate from other causes of lung shadows, such as, pneumonia and malignancies.[8]In resource-poor settings, SNPTB is difficult to diagnose and also difficult to exclude, especially in HIV infected patients.[9] Although the standard method for TB diagnosis is direct observation of acid-fast bacilli (AFB) in sputum smear or *M. tuberculosis* isolation in specific culture media,[5] this method is not always easy to perform. The sensitivity of acid-fast bacilli (AFB) staining result is known to be poor varying between 30-70% depending on a number of factors relating to how the test is implemented.[10] Thus, nearly half of all cases of pulmonary TB are smear-negative, meaning that the overall disease burden is substantial and is associated with treatment delay and hospitalization.[11]Moreover, the presence of comorbidities like diabetes mellitus, HIV and other immune- compromised conditions further complicate the picture as they lead to atypical clinical and radiological presentations.[12] This delay in diagnosis and subsequent treatment leads to increased disease transmission and chances of drug resistance.[13]Therefore, finding a laboratory test for SNPTB cases, that is simple, easy-to-perform, rapid, reliable and inexpensive is an urgency and efforts to improve the quality of existing diagnostic methods are necessary.[14]

Adenosine deaminase (ADA) is one such biomarker which is now a days being studied as a diagnostic tool in tuberculosis.[15] Studies are available on its role in effusion fluids.[16] However, limited literature is available regarding the use of serum ADA in active disease, and whether the levels fall with the recovery of the patients from infection.[17-19] Human adenosine deaminase (an enzyme of purine catabolism) activity has been found to increase in various diseases such as tuberculosis,[20] HIV, typhoid, infectious mononucleosis and certain malignancies especially those of hemopoietic origin.[21] ADA assay in various body fluids had established its usefulness in the laboratory diagnosis of extrapulmonary TB,[22] smear-positive TB and SNPTB.[23]Now there is sufficient data suggestingthat ADA assays can be performed in many health care centres with limited diagnostic facilities other than mycobacterial culture, PCR etc. In addition, it is cheap and has good sensitivity. ADA may be used for early diagnosis of TB, especially in case of negative AFB smear from the body specimens.[24] Considering the issues and constraints in the diagnosis of TB, this study was designed to determine the diagnostic accuracy of serum ADA in the diagnosis of SNPTB.

Materials and Methods:

This cross-sectional study was carried out in the Department of Respiratory Medicine, National

Institute of Diseases of the Chest & Hospital (NIDCH), Mohakhali, Dhakaover a period of one year between April 2018 to March 2019.Patients (whose age ranged from 18-65) attending in the study hospital with respiratory ailments and were suspected of having pulmonary tuberculosis from their clinical presentation, chest radiography, sputum smear and Xpert MTB/RIF negativity were the study population.Patients with characteristics of extra pulmonary tuberculosis, old treated cases of pulmonary tuberculosis and patients diagnosed with other respiratory diseaseswere excluded from the study. A total of 60 SNPTB cases, 30 SPPTB cases and 30 healthy controls were taken in the study.

Having obtained ethical clearance from the Ethical Committee and verbal consent from the patients, the data collection was commenced. Statistical analyses were carried out using Statistical Package for Social Sciences, version 25.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Categorical data were presented as frequency and percentage and continuous data were expressed as mean ± SD (standard deviation). While categorical data were compared between groups using Chi-square ($Ç^2$) Test, continuous data were compared between groups using Independent sample t-Test. The cut-off value of serum ADA at which it had optimum sensitivity and specificity was found out using receiver-operating characteristic (ROC) curve with 95% confidence interval. The area under the curve (AUC) with 95% confidence interval (CI) was statistically determined to find the accuracy of serum ADA in diagnosing smear negative pulmonary tuberculosis (SNPTB). For all analytical tests, the level of significance was set 5% and p-value < 0.05 was considered significant. The findings obtained from data analyses are presented below:

Results:

Age distribution shows that the subjects of SPPTB were older compared those of SNPTB, who were again older than healthy control subjects. ANOVA test revealed that the groups were significantly heterogeneous in terms of age ($p < 0.001$). Sex distribution among the three study groups was also significantly different with a male predominance in SPPTB and in healthy controls ($p < 0.001$) (Table I). The SPPTB, SNPTB patients were predominantly rural residents, while the healthy subjects were invariably urban residents ($p < 0.001$). Around two-thirds of the study subjects in the SPPTB and SNPTB were married, whereas 96.7% of the healthy subjects were married ($p = 0.004$). In terms of occupation, farmers, labor and business together comprised 63% of the SPPTB cases, while 66.6% of the SNPTB cases were students and other occupants. Healthy controls were all service-holder ($p < 0.001$). Around three-quarters of the SPPTB and SNPTB cases belonged to poor and lower middle class. SPPTB cases had the lowest monthly income compared to other two groups ($p < 0.001$). Average weights of SPPTB and SNPTB patients were also lower than that of healthy controls ($p < 0.001$) (Table II).

The symptoms like chest pain, dyspnoea, weight loss, haemoptysis and fever were considerably higher in the SPPTB subjects than those in the SNPTB subjects(Fig.1). There was no significant difference between the groups with respect to haematological parameters, except the percentage of neutrophil, which was significantly higher in SNPTB than that in the SPPTB ($p = 0.004$). The lymphocyte waspredominentin the SPPTB subjects than that in the SNPTB subjects, although the difference was not statistically significant ($p= 0.064$). Cavitation and patchy opacity were more readily found in SPPTB cases, whereas consolidation was more frequent in SNPTB cases ($p = 0.023$) (Table IV). Analysis of the distribution of serum ADA level among the three study groups revealed that SPPTB group had the highest mean serum ADA (41.1 ± 11.8 U/L) followed by SNPTB (35.4 ± 11.7 U/L) and healthy controls (22.7 ± 5.5 U/L) ($p < 0.001$) (Table V). Before determining the accuracy of serum ADA in diagnosing SNPTB, an optimum cut-off value for serum ADA was determined using Receiver Operating Characteristic (ROC) curve (Fig.2):

The sensitivity of serum ADA, at a cut-off value of 27.5 U/L, in diagnosing SNPTB was, therefore, 48/60 ´ 100 = 80.0% (95% CI = 0.682 – 0.882) and the specificity of the test in correctly excluding those who did not have PTB was 24/30 ´ 100 = 80.0% (95% CI = 0.627 – 0.905). The positive and negative predictive values of the test were 48/54 ´ 100 = 88.9% (95% CI = 0.778 – 0.948) and 24/36 × 100 = 66.7% (95% CI = 0.503 – 0.798) respectively. The

percentages of false positive and false negatives are 6/54 ´ 100 = 11.1 and 12/36 ´ 100 = 33.3% respectively. The positive likelihood ratio (LR+) = sensitivity/(1-specificity) = 4.0 (95% CI = 1.93 – 8.27) and negative likelihood ratio (LR-) = 1- sensitivity / specificity = 0.25 (95% CI = 0.15 - 0.43) The overall diagnostic accuracy of the test was (48 + 24)/ (48 + 6 + 12 + 24) × 100 = 80.0% (table VII, Table III).

The best cut-off value for optimum sensitivity without much compromise with specificity obtained from the table below was 27.5 with an area under the curve being 0.851(95% CI = 0.745-0.957), p < 0.001 (Table VI & VII). The area under the curve indicates that 85.1% of the SNPTB could be correctly diagnosed with serum ADA level 27.5 and more in patients with SNPTB.

Table-I

Comparison of patients' demographic characteristics between groups

Demographic characteristics	Group			P-value
	SPPTB (n = 30)	SNPTB (n = 60)	Healthy control (n = 30)	
Age (years)#	43.8 ± 18.8	35.9 ± 19.1	31.6 ± 3.9	< 0.001
Sex*				
Male	22(73.3)	28(46.7)	29(96.7)	< 0.001
Female	8(26.7)	32(53.3)	1(3.3)	

Figures in the parentheses indicate corresponding %;
*Chi-squared Test (c^2) was done to analyze the data.
#Data were analyzed using ANOVA statistics and were presented as mean ± SD.

Table-II

Patients' demographic characteristics among groups (Contd.)

Demographic characteristics	Group			P-value
	SPPTB (n = 30)	SNPTB (n = 60)	Healthy control (n = 30)	
Residence*				
Urban	12(40.0)	23(38.3)	30(100.0)	< 0.001
Rural	18(60.0)	37(61.7)	0(0.0)	
Marital status*				
Married	20(66.7)	39(65.0)	29(96.7)	0.004
Unmarried	10(33.3)	21(35.0)	1(3.3)	
Occupation*				
Farming	6(20.0)	4(6.7)	0(0.0)	
Labor	7(23.3)	12(20.0)	0(0.0)	
Business	6(20.0)	4(6.7)	0(0.0)	< 0.001
Service	4(13.3)	0(0.0)	30(100.0)	
Student	2(6.7)	24(40.0)	0(0.0)	
Others	5(16.7)	16(26.6)	0(0.0)	
Socioeconomic status*				
Poor	17(56.7)	24(40.0)	2(6.7)	
Lower middle class	5(16.7)	22(36.7)	8(26.7)	
Middle class	7(23.3)	14(23.3)	8(26.7)	< 0.001
Upper middle class	1(3.3)	0(0.0)	8(26.7)	
Rich	0(0.0)	0(0.0)	4(13.3)	
Income#	19866 ± 12340	23733 ± 12423	28216 ± 21640	< 0.001
Weight#	50.6 ± 5.1	47.4 ± 5.8	64.9 ± 6.0	< 0.001

Figures in the parentheses indicate corresponding %;
*Chi-squared Test (c^2) was done to analyze the data.
#Data were analyzed using ANOVA and were presented as mean ± SD.

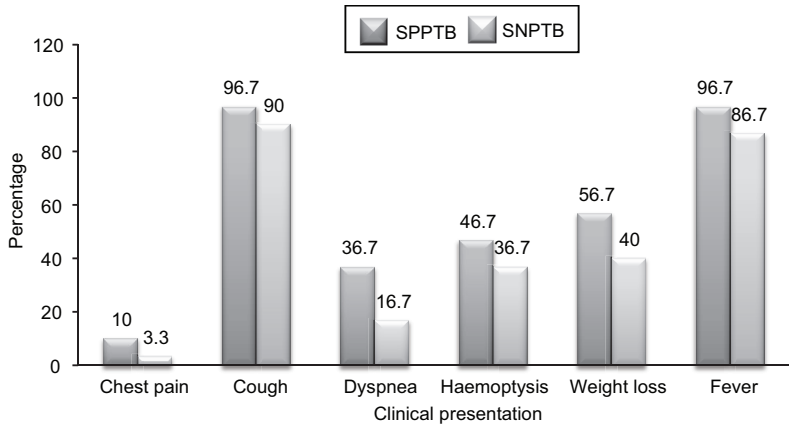

Fig. 1: Comparative clinical presentations of SPPTB and SNPTB

Table-IV

Comparison of patient's Investigation between groups

Investigations	Group		P-value
	SPPTB(n = 30)	SNPTB(n = 60)	
Total count of WBC (cu-mm of blood)#	10094 ± 2602	13712 ± 3440	0.146
Neutrophil (%)#	61.8 ± 11.1	68.4 ± 6.1	0.004
Lymphocyte (%)#	32.4 ± 11.5	28.2 ± 5.9	0.064
Level of Hb (gm/dl)#	12.1 ± 0.8	11.7 ± 0.9	0.134
ESR (mm at the 1st hr)#	83.3 ± 12.3	81.1 ± 11.4	0.420
X-ray chest findings*			
Consolidation	5(16.7)	14(23.3)	
Cavitation	3(10.0)	2(3.3)	0.023
Patchy opacity	20(66.7)	32(53.4)	
Fibrosis	2(6.6)	4(6.7)	
Others	0(0.0)	8(13.3)	

Figures in the parentheses indicate corresponding %;
*Chi-squared Test (c^2) was done to analyze the data.
#Data were analyzed using Unpaired t-Test and were presented as mean ± SD.

Table-V

Comparison of patient's Investigation between groups

Investigations	Group			P-value
	SPPTB (n = 60)	SNPTB (n = 30)	Healthy control (n = 30)	
Serum ADA level (U/L)#	41.1 ± 11.8	35.4 ± 11.7	22.7 ± 5.5	< 0.001

Figures in the parentheses indicate corresponding %;
#Data were analyzed using ANOVA and were presented as mean ± SD.

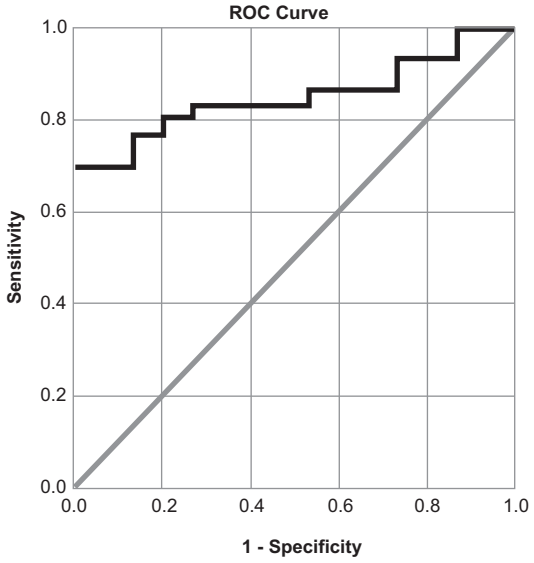

Fig. 2 *showing area under the ROC curve*

Table-VI

Area Under the Curve

Test Result Variable(s): Serum ADA

Area	Std. Error[a]	p-value[b]	95% Confidence Interval of Area Under the Curve	
			Lower Bound	Upper Bound
0.851	0.054	< 0.001	0.745	0.957

a. Under the nonparametric assumption
b. Null hypothesis: true area = 0.5

Table-VII

Accuracy of serum ADA in predicting SNPTB with clinical pictures and X-ray chest suggestive of PTB

Serum ADA (U/L)	SNPTB		Total
	Present	Absent	
≥27.5	48	06	54
< 27.5	12	24	36
Total	60	30	90

Discussion:

The present study intended to evaluate the usefulness of serum ADA in the diagnosis of SNPTB demonstrated that SNPTB patients had a mean serum ADA of 35.4 U/L, while the SPPTB patients had the highest and the healthy controls had the lowest serum ADA (41.1 ± 11.8 vs. 22.7 ± 5.5 U/L respectively). The study indicates that there is moderate rise of ADA in the SNPTB – lower than the SPPTB but higher than the normal individuals. Previous studies had also shown elevated levels of serum ADA in SNPTB patients.[23,25] Chander and associates[17] showed significantly increased serum ADA levels in SNPTB patients compared to that in healthy controls (42.26 ± 21.22 U/L vs. 18.88±6.67 U/L, $p < 0.001$), which is fairly comparable to the findings of the presents study. They, however, did not include SPPTB cases rather they included the non-tubercular chest disease – COPD cases which exhibited a moderate rise of ADA (23.35±8.22 U/L, $p < 0.001$). Gupta and associates[26] also demonstrated mean serum ADA level of their

smear negative pulmonary tuberculosis patients to be clearly elevated (43.5±6.10 U/L).

In order to find a cut-off value for serum ADA at which it is fairly sensitive and specific to diagnose SNPTB, we constructed receiver-operating characteristic (ROC) curve. The ROC curve gave a cut-off value 27.5 U/L at which the serum ADA was 80% sensitive and 80% specific. From ROC curve it appears that increasing the cut-off value, increases the specificity of the of serum ADA to exclude SNPTB but at the cost of sensitivity, while decreasing the cut-of value increases its sensitivity but with compromise of specificity. So for the present study the serum ADA 27.5 U/L seems to be an optimum cut-off value. At this cut-off value, the sensitivity, specificity, PPV, NPV and the diagnostic accuracy of serum ADA were 80, 80, 88.9, 66.7 and 80% respectively. The LR+ and LR- were 4.0 and 0.25 respectively. As the LR+ is 4 (much greater than 1), the test is of greater value in the diagnosis of SNPTB, because the odds of having the condition have changed significantly after the test.Chander and associates[17]using a cut-value of 30 U/L, demonstrated a high sensitivity (91.2%) and specificity (83.1%) of serum ADA in the diagnosis of SNPTB. Their reason for choosing the cut-off value at 30 U/L was that a previous study, at this cut-off value, had shown the specificity and sensitivity of ADA to be nearly 100%. A high positive predictive value (88.9%) in the present study as well as in Chandler's study (94%) indicate that ADA activity measurements could be a promising diagnostic marker in the differentiation of SNPTB from COPDs.

Increased serum ADA levels in pulmonary TB may be due to a stimulation of cell mediated immunity. A fully functioning cell mediated immune response is dependent on normal lymphocyte metabolism which is, in part regulated by the purine salvage enzyme, adenosine deaminase. ADA catalyzes the deamination reaction from adenosine to inosine that increases in TB because of the stimulation of T-cell lymphocytes by mycobacterial antigens[27]Increased serum ADA activity is also found in other diseases involving stimulation of cell-mediated immunity such as typhoid fever, infectious mononucleosis and bronchogenic carcinoma.[25]These non-tubercular infections can be ruled out on the basis of clinical presentations and other laboratory investigations. But patients with respiratory symptoms mimicking SNPTB is difficult to diagnose on the basis of clinical signs and symptoms, X-ray chest and Xpert MTB/RIF negativity. So additional diagnostic tests with high sensitivity and specificity may act as an adjunct to the existing diagnostic aids for SNPTB. Considered in this context, the serum ADA as a screening test for differentiating SNPTB from other cases of COPD has immense value and may add an impetus to the diagnostic yield of SNPTB.

Despite availability of culture facilities for the tubercle bacilli at our hospital, culture confirmation of the SNPTB cases was not done, for our diagnosis of SNPTB was based on National Tuberculosis Management Guidelines. Patients with active TB are also capable of transmitting the infection. Existing diagnostic approaches have largely failed to interrupt TB transmission in populations with a high prevalence of HIV and drug-resistant TB.[28]Although, persons with SNPTB are less infectious than the smear-positive patients, their overall contribution to disease transmission is considerable because half of all patients with TB can present with negative sputum smear findings. Thus, accurate diagnosis of SNPTB patients is of utmost significance. Though newer rapid diagnostic tests for TB are being developed, but these are either not available in developing countries or are technology-intensive and expensive, have poor sensitivity and specificity for smear-negative sputum samples and are not yet considered as diagnostic of the cases. In the developing countries where TB is endemic, an ideal test for tuberculosis should be economic, minimally invasive, of high accuracy,easy and quick to perform.[15]

The present study revealed that measuring ADA level is a rapid, sensitive, inexpensive diagnostic marker for diagnosing SNPTB patients, in whom otherwise the diagnosis is missed by sputum smear findings. However, the results of ADA assays should be interpreted with clinical presentations and with other laboratory examination findings. Now before drawing conclusion from the findings of the study, it would be worthwhile to discuss the strengths and limitations of the study. The following strengths and limitations deserve mention.

Strengths and limitations of the study:

The strength of the study lies in its sample size, which in the present study was more than the required size. Another strength of the study was that we constructed a ROC curve to find a cut-off value of serum ADA which is optimally sensitive and specific. The limitations of the study were that there was no 'Gold standard' for the diagnosis of SNPTB and the diagnosis was not confirmed by culture of tubercle bacilli. Another limitation is that we included SPPTB patients. Had we included chronic lung disease (like bronchial asthma or COPD) cases instead of SPPTB, the findings could have better explained the role of ADA in the diagnosis of SNPTB.

Conclusion:

From the findings of the study, it can be concluded that the serum ADA has a modest sensitivity and specificity in the diagnosis of SNPTB. However, the results of ADA assays should be interpreted in conjunction with clinical presentations and other laboratory test findings. As the LR+ is only 4, the test is of little clinically useful in the diagnosis of SNPTB. Therefore, estimating ADA levels should not be a valuable additional test, in the rapid diagnosis of SNPTB patients provided a large-scale study on a cross-section of diverse SNPTB population to confirm its limited usefulness.

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REVIEW ARTICLE

Diffusing Capacity of Lung for Carbon Monoxide (DLCO) in evaluation of lung function.

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Abstract:

Diffusing capacity of lung for carbon monoxide (DLCO), also known as transfer factor of the lung for carbon monoxide (TLCO)[1], is a measurement to assess the ability of the lungs to transfer gas from inspired air to the bloodstream [2]. In the United States, the test is known as the DLCO and the units of measure are mL/min/mm Hg. DLCO is indicated in the evaluation of parenchymal and non-parenchymal lung diseases in conjunction with spirometry. A D_{LCO} of less than 60% predicted portends a poor prognosis for lung cancer resection. Inability to follow instructions is a contraindication to a DLCO test (CPT code 94729). In the single breath method, the patients are asked to take normal resting breaths initially; this is followed by full exhalation up to residual volume (RV), after which the patient is asked to rapidly inhale the test gas up to vital capacity (VC). Anemia can reduce DLCO. Hence DLCO is adjusted for hemoglobin values. ***KCO*** *is CO transfer coefficient, usually written as DLCO/Va, which indicates the efficiency of CO transfer by alveoli. High KCO occur in extra-parenchymal restriction and in "Extra-Hb". Low DLCO and Low KCO is seen in COPD with emphysema due to alveolar destruction. Decreased DLCO seen in obstructive lung diseases, cardiovascular diseases also in systemic disease involving lungs. Causes of increased DLCO includes polycythemia , obesity, asthma, which are characterized by large lung volumes.[11] High DLCO also seen in pulmonary hemorrhage. A normal DLCO with a restrictive pattern on PFT suggests neuromuscular or chest wall disorder.*

Key words: *DLCO, hemoglobin, KCO, PFT.*

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Diffusing capacity of lung for carbon monoxide (DLCO), also known as transfer factor of the lung for carbon monoxide (TLCO)[1], is a measurement to assess the ability of the lungs to transfer gas from inspired air to the bloodstream [2]. Carbon monoxide (CO) has high affinity for hemoglobin (200-250 times that of oxygen) and follows the same pathway as that of oxygen to finally bind with hemoglobin. It should be noted that different units of measure exist worldwide. In the United States, the test is known as the DLCO and the units of measure are mL/min/mm Hg (traditional unit of measure). In contrast, the test is also known as the TLCO and the units of measure are mmol/min/kPa (International System of Units or SI units). The conversion from SI units (mmol/min/kPa) to traditional (mL/min/mm Hg) can be done by multiplying the SI value by 2.987. The test was introduced in 1909[3]. The respiratory membrane forms the diffusing barrier. It separates air within the alveoli from blood flowing in the pulmonary capillaries. It consists of the following layers:

alveolar epithelium , interstitium ,capillary endothelium.

According to the Fick's equation for the diffusion of gas[4]:

Vg=[k*(A)("P)] / T

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V = volume of gas transferred per unit time ,K = diffusion coefficient of the gas ,A = surface area for gas exchange ,"P = partial pressure difference of gas ,T = membrane thickness from this law, factors that influence the movement of gas molecules across the capillary membrane are the surface area of the membrane (A), the thickness of the membrane (T), driving pressure/pressure gradient across the capillary membrane ("P)[5].

As a consequence, the diffusion of gas across the alveolar membrane increases with:

Increased surface area of the membrane (A) , increased alveolar pressure gradient("P) ,increased solubility of the gas ,decreased membrane thickness (T)

Indications

DLCO is indicated in the evaluation of parenchymal and non-parenchymal lung diseases in conjunction with spirometry. The severity of obstructive and restrictive lung diseases, pulmonary vascular disease, and preoperative risk can be assessed using DLCO[8]. A D_{LCO} of less than 60% predicted portends a poor prognosis for lung cancer resection. FEV_1 is of lesser prognostic value for lung resection survival[14].

Contraindications

Inability to follow instructions is a contraindication to a DLCO test (CPT code 94729). Patients should be alert, oriented, able to exhale completely and inhale to total lung capacity, able to maintain an airtight seal on a mouthpiece, and able to hold a large breath for 10 seconds. DLCO also contraindicated in case of the chest and abdominal pain, oral or facial pain, dementia, or stress incontinence[10]. It is usually recommended to postpone pulmonary function testing by a month in case of acute coronary syndrome or myocardial infarction. PFT is also contraindicated in case of pneumothorax, ascending aortic aneurysm, pulmonary embolism, severe hypertension, hemoptysis, and major surgeries like thoracic/ abdominal /brain/eye/ear/otolaryngological surgery[9].

DLCO is measured using the following techniques[1]:

Single breath method ,intra-breath method ,re-breathing technique.

Procedures

In the single breath method, the patients are asked to take normal resting breaths initially; this is followed by full exhalation up to residual volume (RV), after which the patient is asked to rapidly inhale the test gas up to vital capacity (VC). The test gas contains: 0.3% CO ,0.3% tracer gas (helium, methane or neon), 21% oxygen ,balance nitrogen. Recommendations for a standard technique for the test were first published by the American Thoracic Society (ATS) in 1995. A joint task force from the ATS and the European Respiratory Society (ERS) published updated standards in 2017[8].The updated standards include some important changes in the criteria used to determine the technical acceptability and expected repeatability of

Technical Mistake	Consequences	Recommendation
Failure to reach residual volume before inhalation of the gas mixture Failure to inhale completely from residual volume to total lung capacity	↓D_{LCO} ↓↓V_A ↑Kco	• The inspired volume should be within 85 % of the largest vital capacity • VA within 200 mL or 5 % (whichever is greater) of the highest VA among acceptable maneuvers
Slow inspiration	"!D_{LCO} Slower lung filling decreases the amount of time the lung is at full inspiration	Inspiration of test gas should be sufficiently rapid such that 85 % of the air must be inspired in < 4.0 s
Valsalva maneuver during breath hold	"! D_{LCO} Lower pulmonary blood volume	Avoid the maneuver
Muller maneuver during breath hold	'! D_{LCO} Higher pulmonary blood volume	Avoid the maneuver

measurements, as well as recommendations on the increased utility of the procedure when rapid-responding gas analyzer (RGA) technology is used. RGA technology has been available for over a decade and most commercial equipment currently sold uses the RGA technology. It is likely that most of the slower-responding analyzer technology will phased out by equipment replacement over the coming decade.

The patient is asked to hold his breath for 10 seconds at total lung capacity (TLC). Subsequently, the patient exhales out completely, and exhaled gas is collected for analysis after excluding the initial amount of gas from dead space. The collected gas is analyzed for CO and tracer concentrations. Total lung volume, initial and final CO concentration, and breath-holding time are used to calculate DLCO. The recommended timing method used is the Jones and Meade method, which measures breath holding time at thirty percent of inspiratory time up to half of the sampling time. Usually, an average of two or more attempts is considered for DLCO calculation in the single breath-holding technique.

Another method to calculate DLCO is the intrabreath method, which is calculated during exhalation. The gas that exits during the initial phase of exhalation has less time to diffuse from alveoli to capillaries and will have a higher concentration of CO as compared to the gas during later stages of exhalation. The difference between various exhaled gas samples can be used to calculate DLCO.

Key problems in respiratory maneuvers

- Role of Registered Respiratory Therapist

  An optimal test performance requires optimal patient performance. It is important to coach patients to adapt instructions in different ways, including exaggerated body language. Registered respiratory therapists and other laboratory personnel play an important role in achieving acceptable and repeatable trails. [9]

  The 2017 ATS/ERS criteria for acceptability of DLCO efforts are as follows[2]:

- VI (inspired volume of test gas) greater than 90% of the largest VC measured by same-day slow or forced spirometry (2005 standard was >85%) or
- VI greater than 85% of largest VC and alveolar volume (VA) within 0.2 L or 5% (whichever is greater) of the largest VA from other acceptable maneuvers
- 85% of test gas VI inhaled in less than 4 seconds (unchanged from 2005 standards)
- Breathe hold time of 10 + 2 seconds without evidence of significant leaks, Valsalva maneuver, or Mueller maneuver (unchanged from 2005 standards)
- Sample collection completed within 4 seconds of the start of exhalation (was 3 seconds in 2005 standards); for RGA systems, virtual sample collection should be initiated after dead-space washout is complete

  The 2017 criterion for DLCO repeatability is as follows:

- At least two acceptable DLCO measurements within 2 mL/min/mm Hg (0.67 mmol/min/kPa) of each other (2005 standard was 3 mL/min/mm Hg or 1 mmol/min/kPa)

Quality grading for DLCO measurements is as follows:

- Score of A: (1) VI/VC 90% or VI/VC greater than 85% and VA within 0.2 L or 5% of largest VA from another acceptable maneuver; (2) breath hold time of 8-12 seconds; and (3) sample collection less than 4 seconds
- Score of B: (1) VI/VC greater than 85%; (2) breath hold time of 8-12 seconds; and (3) sample collection less than 4 seconds
- Score of C: (1) VI/VC greater than 80%; (2) breath hold time of 8-12 seconds; and (3) sample collection less than 5 seconds
- Score of D: (1) VI/VC greater than 80%; (2) breath hold time of less than 8 seconds or greater than 12 seconds; and (3) sample collection less than 5 seconds
- Score of F: (1) VI/VC less than 80%; (2) breath hold time of less than 8 seconds or greater than 12 seconds; and (3) sample collection greater than 5 seconds

Only grade A maneuvers meet all acceptability criteria. The average DLCO values from two or more grade A maneuvers that meet repeatability criterion should be reported. If only one grade A maneuver is obtained, the DLCO value from that maneuver should be reported. If no grade A maneuver is obtained, maneuvers of grades B to D might still have clinical utility, and the average of such maneuvers should be reported. However, these deviations from the acceptability criteria must be noted to caution the interpreter of the test. Maneuvers of grade F are not useable.

Severity and classification of DLCO reduction[9]:

- Normal DLCO: >75% of predicted, up to 140%
- Mild: 60% to LLN (lower limit of normal)
- Moderate: 40% to 60%
- Severe: <40%

Interfering Factors

DLCO adjustment:

- Effect of hemoglobin on DLCO: Anemia can reduce DLCO. Hence DLCO is adjusted for hemoglobin values. Various calculators are available to calculate DLCO adjusted for hemoglobin but following is applied usually.
- For men normal value is 14.6 g/dl and
- For women and children under 15 years - 13.4 g/dl

So, Hb adjusted for men:

$$\text{Observed DLCO} \times \frac{(10.22 + \text{Hb})}{1.7 \times \text{Hb}}$$

and for Women :

$$\text{observed DL CO} \times \frac{(9.38 + \text{Hb})}{1.7 \times \text{Hb}}$$

4 % DLCO decrease for each g/dl below normal Hb
2 % increase for each g/dl above normal Hb

- DLCO may need to be adjusted for several other factors like carboxyhemoglobin

Interpretation of DLCO

- DLCO= Va X KCO

Va: number of contributing alveolar units measured by tracer gas (helium)

- KCO: CO transfer coefficient, usually written as DLCO/Va, which indicates the efficiency of CO transfer by alveoli.
- KCO occurs in
- *Parenchymal* lung diseases like IPF ,Sarcoidosis ,Asbestosis,Other ILDs
- *Pulmonary vascular abnormality:*Pulmonary Hypertension,Pulmonary Embolism, Vasculitis , Chronic Heart Failure.
- *Intrapulmonary right to left shunt:* PAM, Hepato pulmonary syndrome
- *Obstructions:* Emphysema, Cystic Fibrosis, Bronchiectasis, Bronchiolitis

*'!*KCO occur in

Extra-parenchymal restriction

Incomplete expansion like: Pleural diseaseses , NMD ,Chest wall diseases.

Discrete loss of units: Pneumonectomy ,Local destruction/,Infiltrates, atelctasis.

"Extra-Hb"

Extra vascular: PulmonaryHemorrhage,Wegener's Capillaritis

Intra-vascular: Asthma, Obesity, Polycythemia ,L-to-R shunting

A decrease in DLCO will be due to a decrease in Va, Kco, or both.

Low DLCO and Low KCO: seen in COPD with emphysema due to alveolar destruction (usually normal in chronic bronchitis) with an obstructive pattern on PFT.

Smoking can also cause a decrease in DLCO[10]

Causes of decreased DLCO

- Obstructive Lung Diseases
  - Emphysema
  - Cystic Fibrosis
    Parenchymal Lung Disease
  - Interstitial Lung Disease
    Idiopathic
    Asbestosis,
    Allergic alveolitis
    Drug induced
- Pulmonary involvement in systemic disease
  - SLE
  - Progressive systemic sclerosis
  - Mixed connective tissue disease
  - Rheumatoid arthritis
  - Dermatomyositis
  - Polymyositis
  - Wegeners granulomyositis
  - Inflammatory bowel disease
- Cardiovascular disease
  - Pulmonary edema
  - Chronic heart failure[12]
  - Pulmonary thrombo-embolism
  - Primary pulmonary hypertension
  - Acute myocardial infarction
  - Fat embolization
- Others
  - Anemia
  - Chronic renal failure
  - Marijuana smoking
  - Acute and chronic ethanol ingestion
  - Cigarette smoking
  - Bronchiolitis obliterans with organizing pneumonia

Causes of increased DLCO

- Polycythemia
- obesity, asthma, which are characterized by large lung volumes.[11]
- Pulmonary hemorrhage
- Increased pulmonary blood flow
- *Left to right intracardiac shunts*
- Exercise
- Mueller maneuver

Abnormal pattern of DLCO,KCO and VA in various disease states:

Conditions	VA	KCO	DLCO
Incomplete lung expansion (Diaphragm palsy, collapse)	↓↓↓	↑↑	↓
Loss of lung units (lobectomy, fibrosis)	↓↓↓	↑	↓↓
Diffuse alveolar damage(ILD)	↓↓	↓	↓↓↓
Emphysema	↓	↓↓	↓↓↓
Pulmonay vascular disease	Normal	↓↓	↓↓
High pulmonary blood volume (Shunt, cardiac failure)	Normal	↑	↑
Alveolar hemorrhage	↓	↑↑↑	↑↑

Both DLCO and KCO are also reduced in interstitial lung diseases, pulmonary fibrosis due to the thickening of the alveolar-capillary membrane with a restrictive pattern on PFT.[8]

A normal DLCO with a restrictive pattern on PFT suggests neuromuscular or chest wall disorder.

In cases of dyspnea of unknown etiology, the pattern of normal spirometry with low DLCO increases the likelihood of pulmonary vascular disease. However, this pattern may also be seen in other disorders, e.g., mild ILD.[1]

High DLCO and high KCO may also be observed in conditions involving profuse pulmonary hemorrhage (e.g. Goodpasture's syndrome, systemic lupus erythematosus, granulomatosis with polyangiitis). This is due to increased uptake of CO.

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REVIEW ARTICLE

Glimpses of Pitfalls of Asthma Management

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Abstract:

Asthma needs continuous attention. Main problem in asthma lies in airway of the lung. Symptoms depend on degree of airway inflammation.But the tragedy is that, despite the high quality of available medications and treatment regimens that are being simplified on a regular basis, asthma is still not sufficiently controlled in many cases.World-wide, it is estimated that 300 million people are affected with bronchial asthma and of all asthma patients, 50% have symptoms on a daily basis and almost all patients report limitations to daily activities[1].So it is very important to search for any pitfall meticulously and try to solve it out. Here we will discuss some aspect of pitfall of asthma management.

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Introduction:

In managing asthma, health-care providers and the patients are often face lot of challenges and these challenges of asthma management include:

- Challenges in diagnoses
- Challenges in the treatment
- Follow-up challenges and
- Other general challenges

I. Challenges in diagnoses

1 The major clinical challenge facing asthma diagnoses is that there is no single satisfactory diagnostic test for all asthmatic patients. As a result, physicians often use different criteria in making a bronchial asthma diagnosis.

2 Simple prompt diagnoses are not achieved

3 A study also showed most hospitals lacked the services of respiratory physicians, internists, and pediatricians that are needed to provide the standard of care required for asthma management. A study found an average of 0.8 respiratory physicians per hospital in a survey of 68 tertiary hospitals in Nigeria[2]

The proper diagnosis might be another disease entity rather than bronchial asthma. In children it might be congenital heart disease, valvular heart disease, cystic fibrosis, bronchiolitis. In the adult is might be heart failure or COPD. So proper history taking, passionate physical examination relevant investigations is the key. Family history of bronchial asthma, atopy and history of smoking should be noted. Lack of standard diagnostic equipment such as peak flow meters, and spirometers are obviously evident. Skin allergy tests test/allergen specific IgE estimation, equipment for exhaled nitric oxide, histamine/ methacholine challenge tests are also lacking too.In a review of 68 tertiary hospitals in Nigeria,

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26 (38.2%) had peak expiratory flow rate meter in the emergency rooms, 20 hospitals (29.4%) had spirometer, only 10 of the 68 hospitals reviewed (14.7%) had skin allergy test facilities.[3]

Even when the equipment are available, physicians often are not conversant with their use owing to lack of proper training on their use.The overall effect of these diagnostic challenges will lead to:

*under diagnoses*over diagnoses*misdiagnosis and

*sometimes undiagnosed/unreported cases of asthma.[4]

This will ultimately lead to increased morbidity and mortality.

2. Challenges in the treatment:

Treatment challenges include:

I. high-cost

II. unavailability of essential asthma medications.

III. The unaffordability of inhaled corticosteroids as a potential barrier to treatment of asthma in developing countries.

IV. The Lack of essential devices like nebulizers, spacer devices that are used for effective medication administration constitute a strong challenge affecting correct management of asthma.

V. Poor technique of use of medication devices especially the inhalational drugs contribute to poor delivery of medications tothe required site of action resulting in poor asthma control and the increase in the health resource utilization.[5]

Steroid is the key drug for asthma.[6]It reduces inflammation of the airway to the extent that the symptoms goes away for the time being. The treatment should be long term. Unfortunately many patients do not know the difference between reliever and controller. The think salbutamol is the ultimate drug. So, we must inform our patient about the basis of airway inflammation right kind of drug. Fire is on the pipe line. We should teach our patient that it is better no to have fire in the pipeline than to put water on it. The steroid should be given as low dose or high dose. It depends on the asthma severity scale. Step case management should be followed. We can go for asthma scoring prescribe the drug accordingly. Higher doses of steroids have some side effects on its own. Even inhaled steroids have its toll. So we should be cautious about dose. Excessive dosing and its side effects are not acceptable. Inhaled drugs are always preferable. Inhaled drug goes directly to airway, less drug is needed quick response is noted. Oral drugs are associated with many unwanted side effects. Controlling asthma at the cost of Cushing syndrome or diabetes mellitus is not desirable. Oral drugs may be given in the emergency set up but inhaled medication is always desirable.Another problem of asthma management is that people get smart over time. After enduring few acute exacerbation some patients feel confident. They do not take medication properly. This erratic behavior in drug intake ultimately take its toll. To speak harshly, asthma is not a disease of cure rather this is a disease of control. So long term treatment plan, May be lifelong should be kept in mind from the first day of diagnosis.

Inhaler technique is very important but we often ignore this crucial aspect. In a study conducted in BSMMU, 70% study Population cannot use inhaler properly. So drugs do not reach the final destination, the airway. Rather, it is deposited on the oropharynx. So inhaler technique is the key.[7]We should be cautious whether to prescribe metered dose inhaler or dry powder inhaler. If a person cannot take the MDI properly, then spacer or respochamber should be employed.[8]We must demonstrate the patient how to use the inhaler. In a busy practitioner's life, this is not always that much easy. But we must make it a habit to demonstrate and check the inhaler technique. An attractive alternative to metered-dose aerosols, either with or without spacers, are dry-powder inhalers (DPIs) which eliminate the problem of coordination for patients as they are breath activated.[9] Dry-powder systems use the force of a patient's inspiration to break up the released active-ingredient conglomerate into respirable particles. The amount of force required to do this varies from device to device.[10]

Another challenge of asthma treatment is that the very newer asthma medications are of limited benefit,[11]For a small percentage of patients and

often more expensive, e.g., leukotrienes antagonist, omalizumab (monoclonal IgE antibody), thermoplasty etc., thereby making it impossible for patients with poor resources to benefit from them.

Thus, treatment challenges highlighted could lead to

- under-treatment
- unnecessary treatments
- poor control.
- Increased adverse drug reactions,
- increased morbidity and mortality and
- Poor quality of life.

In a survey of asthma patients in Ife, 40% of respondents reported the presence of depressive symptoms, 48.1% of them reported low scores on the Mini-Asthma Quality of Life questionnaire.[12]

Trigger: Asthma need education, medication and caution. We should inform our patient about various trigger factors, weather, even role of psychological factors. Patient should always be cautious. Avoiding the practical approach. Wearing mask, influenced vaccination yearly, regular physical exercise may help.

Triggers may be in the patient's own household, From Cockroach to feather or the ordinary food. Patient must keep a personal asthma diary to role which trigger factor hurt him much. Triggers must be identified and checked before it becomes perilous.

3. Follow-up challenges:

The main aspects of follow up challenges are:

- Communication gap between the health-care providers and the patients
- Lack of patients self-monitoring equipment
- lack of educational materials
- Lack of adequate public health nurses
- Lack of proper GP referral

A survey of level of asthma control among bronchial asthma patients attending follow-up in two tertiary hospitals in north-central and southwestern Nigeria showed that: 69.3% of them had uncontrolled asthma, 22.6% had partly controlled asthma, and only 8.1% had controlled asthma.[13]Asthma patient should not be lost. A good rapport with the patient is a must. Patient should visit the doctor at least in every three months. Doctor will review the treatment plan, peak flow, level of control, inhaler technique and suggest necessary adjustment. Proper management of asthma is like coordinated human endeavor. Sooner the understanding, empathy mutual trust, better the outcome.

4. Other general challenges:

- Lack of will by the government/hospital administrative staff in the provision of basic infrastructure such as asthma clinics, asthma clinic registers, appointment and recall systems in the clinics[14]
- Lack of adequate asthma care training courses for doctors and nurses.
- There is poor medication purchase regulations as people are able to buy medications to wrongly treat asthma or even to trigger attacks. Purchase of over the counter medications such as NSAIDs and beta blockers are known to trigger attacks of asthma.[15]

5. How to overcome the challenges?

Several challenges affect asthma management in a developing countries which borders on poverty, inadequate resources, weak health systems, and poor infrastructure. Efforts should be made to address these challenges by the government through the provision asthma diagnostic facilities at all levels of care, training of health-care workers, coverage of asthma care in the National Health Insurance Scheme in order to ensure affordability of asthma care.[16]In addition, pharmaceutical companies could help address these challenges by partnering with government to reduce/subsidize the price of asthma medications as this will in the long run ensure good asthma control as asthma patients will not lose control due to inability to purchase asthma drugs.[17] Furthermore, there is a need to commence training and re-training of health care providers through sustained continuing professional development CPD/CME activities on current management of asthma.[18]

Asthma management is a long journey. Like Hypertension or diabetes mellitus asthma needs longer version of treatment. There are so many pit fills of asthma management but we should be vigilant and try our best to control this time old disease. Control is our goal rather than to cure it.

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CASE REPORT

A 40 Years Old Man with Esophageal Leiomyoma - A Case Report Of Uncommon Tumor

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Absract :

Leiomyoma is the most prevalent benign tumor of esophagus. It is very rare, and the incidence in autopsy series is 0.006 to 0.1%. It is mostly observed in the mid 1/3 or lower parts of esophagus. Its characteristic feature is the proliferation of the smooth muscle layer, causing circumferential thickening localized on the esophagus wall. Frequently, it is observed as a single lesion. It can be hereditary or sporadic. Half of the patients are asymptomatic. Our case was 40 years old man presented with giant esophageal leiomyoma has been presented first time in Bangladesh very few case report was been published worldwide through rare diagnosis should be keep in mind as it is benign & curable by resection.

Keywords : *esophagus, leiomyoma, Thoracotomy, enucleation.*

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Introduction :

Benign esophageal tumors are relatively rare; they constitute 1% to 10% of all esophageal neoplasms[1]. Esophageal leiomyoma is the commonest benign esophageal tumor which arise from smooth muscle[2]. It usually affects patients between 20 and 50 years of age, with male to female ratio of 2 : 1. Giant esophageal leiomyoma is defined as tumor of more than 10 cm in diameter; its incidence has been reported in 17% of cases.[3,4] It can involve any part of esophagus but reportedly it affects distal third in 60%, middle third in 30%, and upper third of esophagus in 10% of the cases. This distribution parallels the relative amount of smooth muscle cells' presence along the esophagus. It is a slow growing intramural tumor which has got very limited malignant potential. Size of esophageal leiomyoma varies from 1 to 30 cm.[5] Histologically, leiomyomas comprise of bundles of interlacing smooth muscle cells, well-demarcated by adjacent tissue or by a definitive connective tissue capsule.

We describe this case report , a 40 years old man with giant oesophageal leiomyoma underwent total excision of tumor by right postero-lateral thoracotomy.

Case Report:

Mr. Amzad 40 years old man doptori of a government school came from Jamalgonj, Shonamgonj with H/O difficulty in swallowing and occational chest pain. His symptoms started from about 7 years back and initially he felt only a mild discomfort during swallowing solid and bullous of food,nothing else. Gradually that problem was more and felt always difficulty during swallowing specially solid and semi solid food. He could take liquid food only without difficulty. He also noticed occational central chest pain which was dull aching in nature, no radiation , persist for 2/3 days and relieved by some medications. He had no history of weight loss. Gave no h/o resp. distress, cough, heamoptysis, jaundice, heamatemesis, meleana, bone pain. His bowel and bladder habit was normal. For that he consulted with many specialist and also went to in Medical College Hospital few years back. Lastly, few days ago he admitted to a Gastro

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Liver Specialists of Hospital. For better treatment he was reffered to thoracic surgery dept. of NIDCH and admitted here on 15/12/20 (reg.— 5649/7). He had no co-morbidities. He had no past medical or surgical history. No significant family history. No allery to any specific food or medicine. He was non-smocker and non-alcoholic but betel-nut chewer. He was married and father of three sons. He came from low class family and was immunized according to EPI schedule.

On physical examination, we found, patient looked good health but only mildly anxious. All vitals were normal limit, had no any peripheral lymphadenopathy including neck gland. Chest and other systemic examination revealed normal findings. Chest X-ray P/A view revealed, a homogenous opacity in near the hium of rt. Lung field which marge with mediastinum like mediastinal mass.

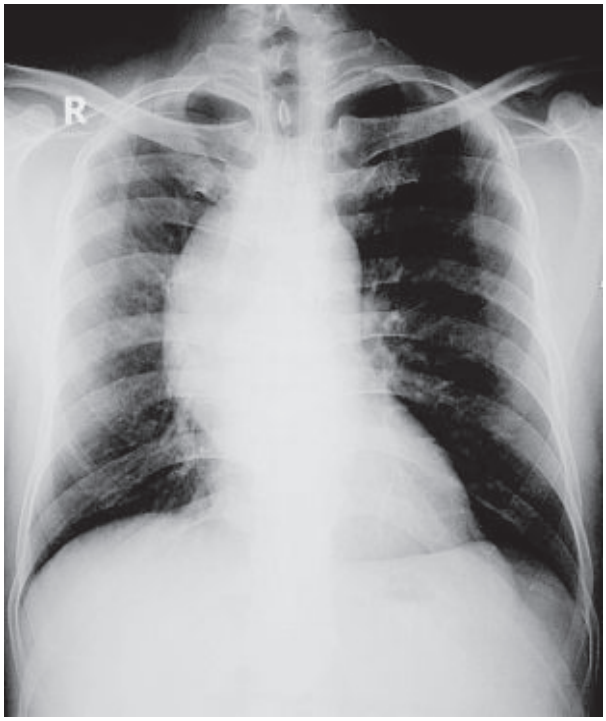

Fig.-1: *CXR P/A view of patient before operation*

Upper G.I endoscopy done on 2 times (30/11/20 & 06/12/20) found, there is an eccentric luminal narrowing of oesophagus from 20 cm to 25 cm from upper incisor teeth and no mucosal ulceration or growth. This narrowing probably due to external compression.

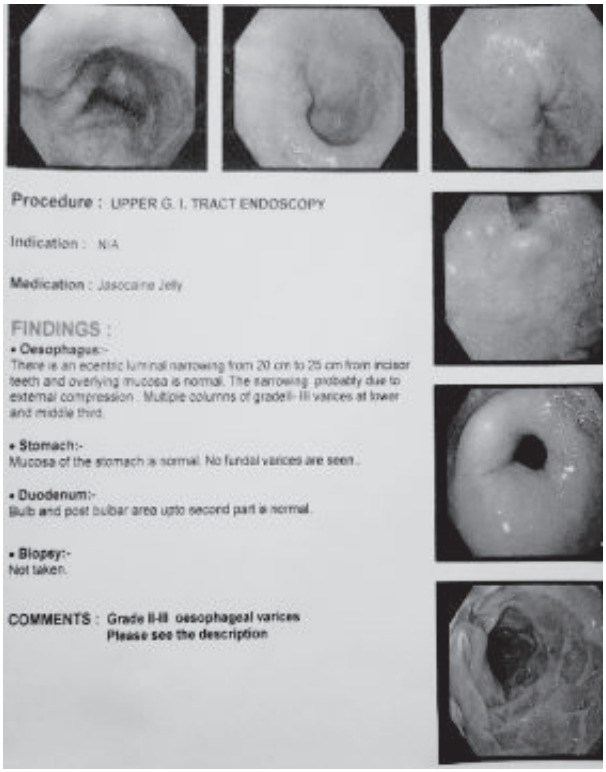

Fig.-2: *Endoscopic view of patient showing grade II OV.*

CT scan revealed a large oesophageal mass in mid part causing irregular narrowing of oesophagus.

All other routine investigations found within normal limit.

So we planned for total excision of tumor through Rt. Postero-lateral thoracotomy incision Under G/A with one lung ventilation. Patient underwent thorough pre anesthetic check up and surgery was performed. During procedure,there was no collection within thoracic cavity, adhesions were visualized between tumor with lung and chest wall . All adhesion were freed meticulously and then inspected all around . A large tumor found all around the thoracic part of oesophagus. At first arch of azygos vein ligated and cut. Tumor dissected intracapsulerly & extramucosal started from anterior part and gradually from all around of oesophagus. Then checked any injury/ leak of oesophagus and a NG tube kept upto stomach. Also saw lung expansion properly. After sequired haemostsis,a chest drain kept in situ and wound closed in layers.

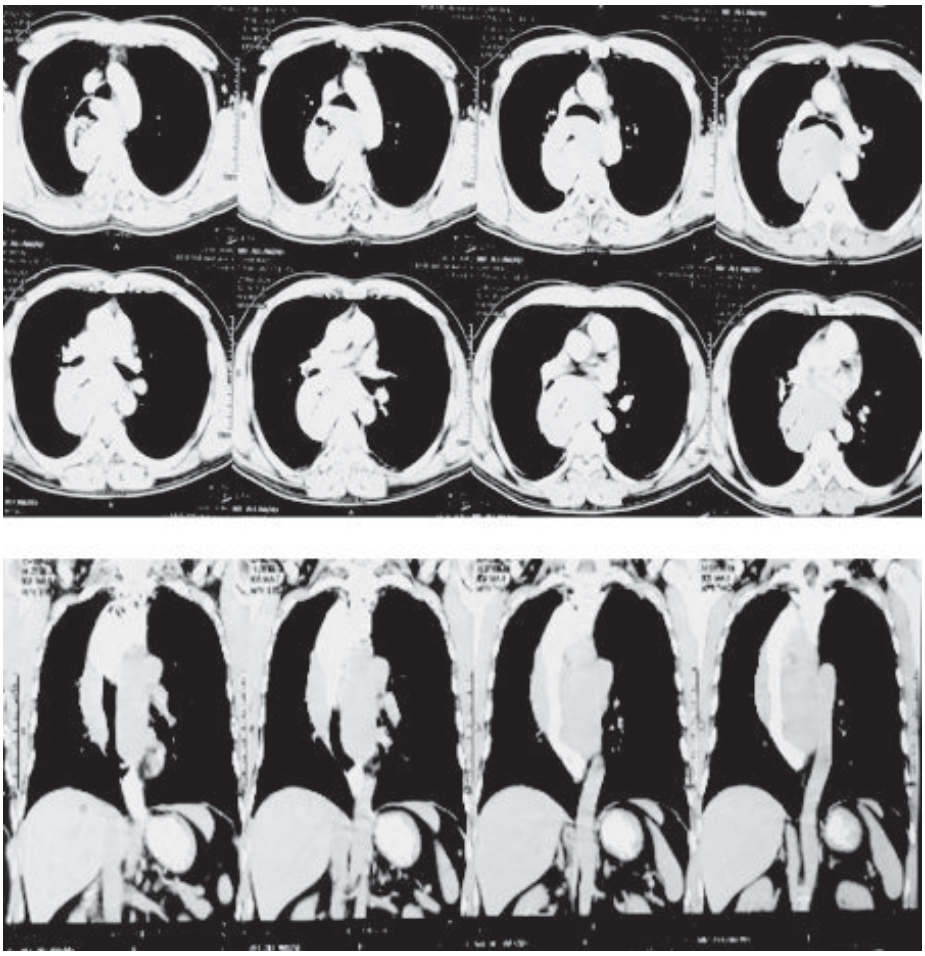

Fig.-3: CT scan of chest with contrast of the patient.

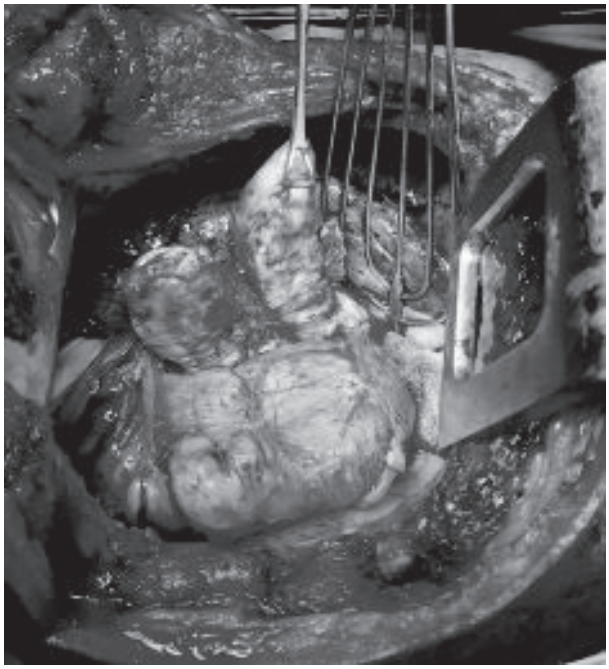

Fig.-4: Per-operative tumor

Fig.-5: *Esophagus after excision tumor*

Obtaining materials were send for histological analysis. Leiomyoma was confirmed histopathologically in our case. Post operative recovery was uneventful. On 7th POD contrast X-ray of oesophagus done which revealed no leak. Also gave orally Xension violet mixed water to checked any leak. On 8th POD NG tube removed and gave liquid diet. On 9th POD chest drain removed and then discharged later.

Fig.-6: *Tumor specimen after operation.*

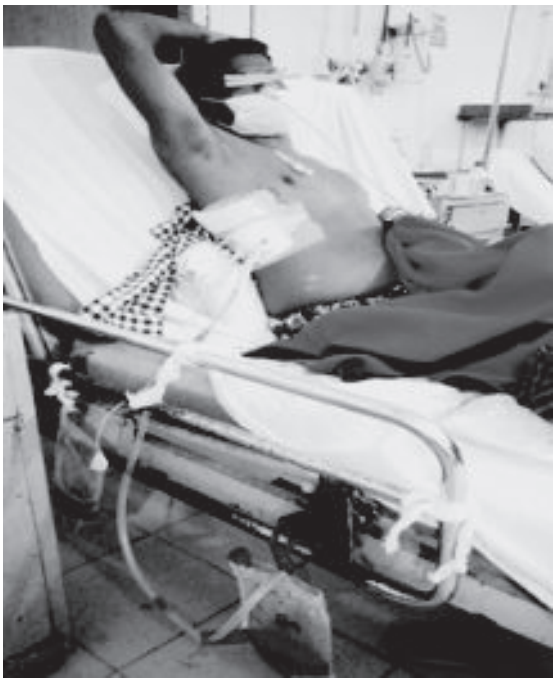

Fig.-7: *Patient post-operative period.*

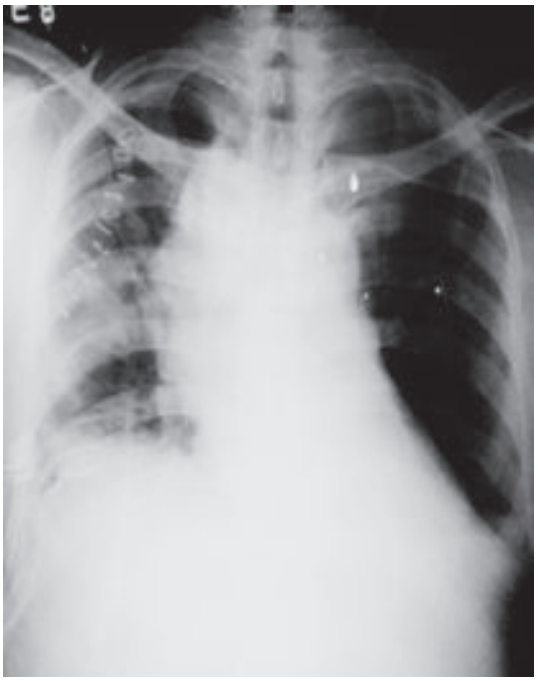

Fig.-8: *Post-operative CXR P/A view.*

Discussion :

Esophageal leiomyomas are multiple in approximately 5% of patients.[6] They rarely cause symptoms when they are smaller than 5 cm in diameter. Large tumors can cause dysphagia, vague retrosternal discomfort, chest pain, esophageal obstruction, and regurgitation. Rarely, they can cause gastrointestinal bleeding, with erosion through the mucosa. Other than the nonspecific symptoms associated with esophageal leiomyomas, very few physical findings are usually noted. In extremely rare cases where severe esophageal obstruction is caused by a leiomyoma, weight loss and muscle wasting may be observed.[7]

Preoperative diagnosis of esophageal leiomyoma is often a challenge. Incidentally, radiologically (CXR) found as a mediastinal mass like feature. Esophagoscopy will show normal mucosa and submucosal lesion. Barium swallow is the most common imaging study advised for esophageal lesions; it will show smooth filling defect in esophageal lumen without mucosal abnormality. Computed tomography (CT) and endoscopic ultrasound (EUS) are very valuable in making diagnosis, they will delineate the intramural nature of tumor without any mediastinal lymphadenopathy. Preoperative biopsy of tumor

is a controversial issue. In our case, we have avoided preoperative biopsy as imaging studies were diagnostic. Disadvantages in doing preoperative biopsy as it would cause scarring at the biopsy site, which would hamper definitive extramucosal resection at surgery and inconclusive biopsy are often due to inadequate material.[8]

Surgical excision is recommended for symptomatic leiomyomas and those greater than 5 cm. Although a formal esophageal resection is not mandatory for leiomyomas. Tumors of the middle third of the esophagus may be approached using a right thoracotomy. Tumors in the distal third of the esophagus may be resected through a left thoracoabdominal approach, transhiatally or by a left thoracotomy. For extramucosal excision or enucleation, the outer esophageal muscle is incised longitudinally. Careful dissection is done to separate and remove the leiomyoma from the underlying submucosa. Segmental esophageal resection (esophagogastrectomy) may be indicated for giant leiomyomas of the cardia. Intraoperative esophagoscopy combined with video-assisted thoracoscopic approach is the method used for easing the process and shortening the length of hospitalization.[9,10]

Our patient had giant leiomyoma at the mid part of oesophagus and done extramucosal excision or enucleation of tumor by right postero-lateral thoracotomy successfully with symptomatic improvement of the patient.

Conclusion :

When esophageal leiomyoma is identified, lesion has to be removed even if the patient is asymptomatic. If the treatment is delayed or failed, the symptoms would probably develop and it will be hard to differentiate it from malignancy though usually can undergo cystic degeneration; however, progression to malignancy is rare. Surgery provides relief in all symptomatic patients.

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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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Provide on a separate page an abstract of not more than 250 words. This abstract should consist of four paragraphs, labeled Background, Methods, Results and Conclusions. They should briefly describe the problem being addressed in the study, how the study was performed, the salient results, and what the authors conclude from the results.

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

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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.

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Tierney LM, -McPhee SJ, Papakadis MA. Current Medical Diagnosis and Treatment. Lange Medical books/Mcgrow Hill 2000.

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

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Student's medical dictionary. 26th ed. Baltimore: Williams & Wilkins; 1995. Apraxia; p.119-20.

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Leshner AI. Molecular mechanisms of cocaine addition. N Engl J Med In Press 1997.

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