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EDITORIAL

The safety and Long-term Health Effects of Using e-cigarettes

[Chest Heart J. 2019; 43(1) : 1-4]
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Electronic cigarettes are battery-operated devices used for a type of smoking called vaping. They produce a mist that is inhaled deep into the lungs, mimicking the feeling of smoking regular cigarettes. Like traditional cigarettes, most e-cigarettes contain nicotine. The exact amount varies by brand. Some have as much or more than paper cigarettes. They may also have added flavors and contain a variety of other chemicals.

Electronic cigarettes or e-cigarette or vape started growing popularity about a decade ago as a smokeless alternative to cigarette. E-cigarette works by using an electronic current to vaporize a fluid containing in most cases nicotine and flavorings. The general term vaping is commonly used to refer to the practice of inhaling such vaporized liquids through a wide range of electronic devices. E-cigarette was unregulated until 2016, when the FDA issued regulations that covered all tobacco products, including e-cigarettes. There is now over 800 vaping flavors on the market, most of which have not been evaluated for safety[1].

E-cigarette was first discovered by a Chinese pharmacist Hon Lik in Beijing 2003 and quickly become popular healthier alternative for those who wanted the feelings of tobacco smoking. The first E-cigarette model is named "Ruyan". There are three parts of E-cigarette – "Rechargeable battery" contain lithonium polymer that can be charge by USB. Battery has processor and micro switch. "Atomizer" – this is ultrasonic atomizer high frequency piezoelectric ultrasound emits heating element. A plastic "Cartridge" containing a solution. The whole device is called E-pen having different design and brand and the liquid in the cartridge contains nicotine solution and flavoring agents called E-juice. These flavoring agents are refillable and having, strawberry, orange, lemon, mint etc. flavor[2].

Activation of device has several steps, during inhalation airflow started and micro switch in the battery become On, by this switch, Atomizer become activated and there is connection between Atomizer and Cartridge. Atomizer heats up the liquid in the Cartridge until it turns into a mist. The mist may contain: nicotine, chemical flavorings, microscopic particles, volatile organic compounds (VOCs), heavy metals, such as lead, tin, and nickel. E-cigarettes can look like regular cigarettes, pipes, or cigars. E-cigarettes can also be used to inhale other drugs, such as marijuana.

The general consensus from the researcher that, those who wants to quit smoking they can be advice for using E cigarette or vaping[3]. According to medical science the different approved way of quit smoking is the primary means for targeted people, but if these fails then E cigarette is the useful option.

The approved way for quitting smoking is nicotine replacement therapy that means nicotine patch, chewing gum, lozenge or oral tablets. These can be try primarily as their efficacy have already proven but if these fails then vaping can be the option. About 12.2 % people worldwide smoke daily, they are mostly poor and chain smoker, it is impossible for them to buy nicotine replacement therapy because of cost[4]. They can be advised for vaping. The vaping can fulfill the requirement of nicotine and also the harmful effect of cigarette can be avoided. Some people are in favor of banning E-cigarette because they have minimum idea about

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e-cigarette which also will hamper the effort of stop smoking campaign. What is the long term effect of vaping it is not yet certain but it is safer than formal burning cigarette no doubt because burning of paper cigarette produces 4000 harmful elements most of them are carcinogens[5]. Drawback of E-cigarette is that most of the consumers at present are young, they are using vape because of curiosity and also for giving up conventional cigarette

The risks of using e-cigarettes include

E-cigarette or vaping product use–associated lung injury (EVALI): Worldwide 82% of individuals hospitalized with EVALI due to using tetrahydrocannabinol (THC)-containing products, and the additive vitamin E acetate has also been strongly linked to this outbreak, according to a study published in the Centers for Disease Control and Prevention (CDC) *Morbidity and Mortality Weekly Report*. Although other chemicals including flavoring agents may be responsible for injuries in some cases, the CDC recommends refraining from use of THC-containing vaping or e-cigarette products.[6,7]

Of the 2668 hospitalized EVALI cases as of January 2020, 66% were men, the median age was 24 years (range, 13-85 years), and 76% were younger than 35 years . Of the 2022 patients with available information on substance use, 82% (n=1650) reported using any THC-containing e-cigarette or vaping product, including 33% (n=669) who exclusively used THC-containing products. A total of 57% (n=1162) reported using any nicotine-containing product, including 14% (n=274) who exclusively used nicotine-containing product. Vitamin E acetate is used as an additive, most notably in THC-containing e-cigarette, or vaping. Vitamin E acetate usually does not cause harm when ingested as a vitamin supplement or applied to the skin. However, previous research suggests that when vitamin E acetate is inhaled, it may interfere with normal lung functioning. Additionally, a strong link has been found between vitamin E acetate and the EVALI outbreak, as the additive being detected in patient lung fluid sample

Nicotine addiction

Nicotine is highly addictive, and most e-cigarettes include it as a main ingredient. Some e-cigarette labels have claimed that their product had no nicotine when, in fact, it was in the vapor. For this reason, it's important to use only trusted brands if you vape. Originally, it was thought that vaping might be helpful for people trying to quit smoking. But, this early theory has not been proven. Some people who vape also continue to smoke regular cigarettes, despite a strong desire to quit.

Drug and alcohol addiction

There are some reports that nicotine in e-cigarettes might prime the brain for addiction to other things, such as alcohol and cocaine. This is especially true for teens.[8]

Lung disease- E-cigarettes contain added flavors that young people enjoy. Some of these additives have health risks, such as diacetyl which has a buttery taste. Diacetyl has been found to cause a severe lung disease similar to bronchiolitis. Cinnemaldehyde, which tastes like cinnamon, is another popular vaping flavor that may be harmful to lung tissue.

Cancer- E-cigarettes contain many of the same cancer-causing chemicals that regular cigarettes do. Research published in 2017 found that the high temperatures needed to form the mist for vaping can create dozens of toxic chemicals, such as formaldehyde, which is thought to cause cancer.[9] Explosions-E-cigarettes have been known to spontaneously explode. This has caused injury. Vape explosions have been linked to faulty batteries in vaping devices. Though rare, vape explosions can be very dangerous and can cause severe injury. Commonly asked question that whether water can be used inspite of e juice the answer is no because of explosion by producing excessive heat.

Regardless of the ongoing investigation E-cigarette, or vaping, products should never be used by youths, young adults, or women who are pregnant. Adults who do not currently use tobacco products should not start using e-cigarette, or vaping, products. There is no safe tobacco product. All tobacco products, including e-cigarettes, carry a risk. THC use has been associated with a wide range of health effects, particularly with prolonged and frequent use. The best way to avoid potentially harmful effects is to not use THC-containing e-

cigarette or vaping products[10]. People with ongoing problematic marijuana use that causes significant impairment or distress should seek evidence-based treatment by a healthcare provider.

Carbon monoxide & nicotine: A dangerous duo

Carbon monoxide is a harmful gas inhaled when some one smoke. Once in the lungs, it's transferred to bloodstream. Carbon monoxide decreases the amount of oxygen that is carried in the red blood cells. It also increases the amount of cholesterol that is deposited into the inner lining of the arteries which, over time, can cause the arteries to harden. This leads to heart disease, artery disease and possibly heart attack.

Nicotine is a dangerous and highly addictive chemical. It can cause an increase in blood pressure, heart rate, flow of blood to the heart and a narrowing of the arteries. Nicotine may also contribute to the hardening of the arterial walls, which in turn, may lead to a heart attack. This chemical can stay in the body for six to eight hours depending on how often some one smoke. Also, as with most addictive substances, there are some side effects of withdrawal. Some e-cigarettes and newer tobacco products deliver even more nicotine than traditional cigarettes.

The bottom line

Cigarettes, e-cigarettes and tobacco products contain many dangerous toxins. The best thing should be is to quit tobacco entirely and not to spend the rest of life chained to a nicotine addiction. Thousands of people kick the habit every year, and you can be one of them. It may not be easy, but can do it.

E-cigarettes are still relatively new, so their long-term effects are not yet known. They may, however, pose multiple risks. In general, e-cigarettes are not safe for young people or for pregnant women. Vaping is not safer for developing fetuses than smoking traditional cigarettes. Vaping may have some benefit for smokers who switch it as a complete substitute for using other tobacco products.

Smoking is the most preventable cause of death worldwide. Almost one third of deaths from coronary heart disease are due to smoking and secondhand smoke. Smoking is linked to about 90%

of lung cancer cases. Smoking rates overall are down, but too many adults still smoke, vape and use other forms of tobacco especially between the ages of 21 and 34. About half of children ages 3-11 are exposed to secondhand smoke. On average, smokers die more than 10 years earlier than nonsmokers. You can be one of the millions of people who successfully quit every year.

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Chest Heart Journal
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ORIGINAL ARTICLE

Bone Mineral Density among Chronic Obstructive Pulmonary Disease Patients Admitted in a Tertiary Level Hospital

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Abstract:

Background: *Chronic obstructive pulmonary disease (COPD) is a major cause of chronic morbidity and mortality throughout the world. It is a preventable and treatable disease with significant extrapulmonary manifestations that may contribute to the severity in individual patients. Osteoporosis is an important systemic feature of COPD and causes significant morbidity. Osteoporosis gradually worsens as the COPD progresses. This study was undertaken to investigate the relationship between BMD and disease severity of COPD patients.*

Objective: *To evaluate the status of BMD among patients with COPD.*

Methods: This was an observational descriptive cross-sectional study carried out in Departments of Medicine of Sir Salimullah Medical College & Mitford Hospital, from July 2017 to December 2017. According to inclusion and exclusion criteria, a total of 50 COPD patients were selected and their BMD was done.

Results: *Of the 50 patients, on the basis of BMD femoral neck t- score, 100% of very severe & severe COPD patient had osteoporosis, 15% of moderate COPD patients had osteoporosis, while mild COPD patients had no osteoporosis. And also, on the basis of lumber spine t-score, osteoporotic changes were highest among very severe COPD patients (100.0%) which reduced with the reduction of severity of COPD while osteopenia was highest among mild and moderate COPD patients. Mean of BMD femoral neck t-test was lowest among very sever COPD patients (-3.21± 0.16) and highest among mild COPD patients (-1.37± 0.83). ANOVA test revealed that this mean difference was significantly associated (p=<0.001, F= 29.07).*

Mean of BMD lumber neck t-test was lowest among very sever COPD patients (-3.53± 0.69) and highest among mild COPD patients (-1.16± 0.51). ANOVA test revealed that this mean difference was significantly associated (p=0.012, F= 4.04).

Conclusion: *BMD alterations are common in COPD patients. A high proportion of patients with COPD experience a significant bone loss which is associated with increased morbidity and mortality. Such patients should be provided with adequate preventive & curative therapy of osteoporosis for better survival.*

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Introduction:

Chronic obstructive pulmonary disease (COPD) is a disease characterized by nonreversible airflow obstruction. Although the main symptoms originate from the respiratory system, COPD is considered a systemic disease.[1] Chronic obstructive pulmonary disease (COPD) is a major cause of mortality worldwide.[2] In the care of patients with COPD, the primary focus of the physician is respiratory function. However, as COPD progresses and the patient becomes more debilitated, osteoporosis is a common finding.[3] COPD not only involves the lungs but also causes extra-pulmonary abnormalities with systemic features, such as, for example, cachexia, fluid water retention and skeletal muscle wasting. Osteoporosis is also an important systemic feature of COPD.[4]

Osteoporosis is a systemic skeletal disease characterized by a low bone mineral density (BMD) and micro architectural changes in bones, leading to increased bone fragility and, increased fracture risk.[5] Osteoporotic fractures cause many symptoms and complications, including the impairment of ventilation, and create a heavy economic burden.[5] To predict the risk of osteoporotic fractures, measurements of bone mineral density (BMD) have been widely used[6] and it has been reported[7] that BMD is lower in COPD patients than in healthy subjects. Thus, it is important to evaluate BMD in the management of COPD.[4]

A bone mineral density test uses X-rays to measure the amount of minerals - namely calcium - in bones. This test is important for people who are at risk for osteoporosis, especially women and older adults.[8] Decreased Bone Mineral Density (BMD), which occurs with age, is an important health problem among elderly persons, contributing to disability and premature mortality. Decreased BMD has also become an important socio-economic issue. Decreased BMD may result in osteopenia and osteoporosis, of which the latter is more serious. An Osteoporosis Risk Assessment study has confirmed that the risk of fracture increases with decreasing BMD.[9] Previous studies reporting osteoporosis in 24-44% of patients with COPD. The aetiology of this loss is likely to be due to multiple factors including female sex, corticosteroid (CS) therapy, smoking, physical de-conditioning, vitamin D deficiency, hypogonadism and chronic systemic inflammation.[10] Although a low BMD is often asymptomatic, subsequent vertebral fractures may further compromise lung function,[11] while hip fractures decrease mobility and increase the mortality risk.[2] Traditionally, loss of BMD, and osteoporosis in particular, have been considered "late manifestations" related to cumulative oral CS treatment of airways disease.[12] However, significant loss of BMD occurs in mild airways obstruction[9] and vertebral fractures have been reported in a high proportion of CS naive men with COPD. That said, BMD is only one, albeit important, contributory cause of vertebral fractures, and other factors for e.g. heavy lifting, may play important roles.[2]

Those patients requiring oral glucocorticoid therapy have lower T scores and more fractures than those treated with bronchodilators only. Patients receiving oral glucocorticoid therapy (average [±SD] cumulative dose, 19.5 ± 24.8 g) have been found to have a 1.8-fold (95% confidence interval [CI], 1.08 to 3.07) increased incidence of one or more vertebral fractures. However, glucocorticoid use does not fully account for the low BMD in these patients.[3]

Smoking has been shown to be an independent risk factor for osteoporosis in both men and women.[13] Reported that lumbar spine BMD was 12% lower in smokers who have smoked 20 pack-years compared to nonsmokers.[14] Several groups have confirmed the finding of a significantly greater rate of bone loss in smokers. The combination of tobacco and alcohol use markedly increases the risk for osteoporosis. Alcohol use has been shown to be independently related to bone loss in a dose-dependent manner.[3]

The gold standard of measuring bone density is dual energy X-ray absorptiometry (DXA). Currently, the method is the examination of choice for diagnosis and follow-up of patients with osteoporosis, as proposed by the International Society for Clinical Densitometry, because of its worldwide availability, low radiation dose, and results' reproducibility.1 However, the technical drawbacks of this method are well acknowledged[15] as DXA is a two-dimensional method assessing bone mineral density (BMD), superimposed tissue may cause artifacts and inaccurate measurements.[1]

We planned to assess the BMD status among COPD patients in a tertiary level hospital

Materials and Methods:

The research has been undertaken with the objective to estimate status of Bone mineral density among Chronic Obstructive Pulmonary

Disease patients admitted in a tertiary level hospital. For achieving the objectives this study have been conducted systematically methodically.

Inclusion criteria:

1. Patient diagnosed as COPD according to clinical and spirometric findings
2. Age more than 18 years
3. Both sexes
4. Agreed to give informed written consent.

Exclusion criteria:

(1) History of pulmonary tuberculosis;
(2) History of chest surgery
(3) COPD with bronchial carcinoma
(4) Disease or durg that may interfere BMD, such as- diabetes mellitus, chronic kidney disease, systemic lupus erythematosus, rheumatoid arthritis, steroid.
(5) Unwilling to give written consent

Operational definition:

COPD:

COPD was confirmed on spirometric examination, when post bronchodilator FEV1 /FVC< 0.70

Severity of COPD:

COPD is divided into five stages according to the severity by GOLD (Global Initiative For Chronic Obstructive Pulmonary Disease) criteria.

GOLD stages of COPD:

Stage	Severity	FEV1
I	Mild	FEV1 /FVC< 0.70 FEV1 ≥80% predicted
II	Moderate	FEV1 /FVC< 0.70 FEV1 50-79% predicted
III	Severe	FEV1 /FVC< 0.70 FEV1 30-49% predicted
IV	Very Severe	FEV1 /FVC< 0.70 FEV1 <30% predicted or FEV1 <50% predicted if respiratory failure present

BMD:
The BMD will be expressed as an absolute value and as a T score (standard deviations from a young).
Osteoporosis will be defined as a T score less than -2.5
Osteopenia as T score less than -1 but greater than -2.5.

Results and Observation:

This study was intended to investigate the relationship between COPD and osteoporosis. To achieve this goal, 50 COPD patients attended in Sir Salimullah Medical College Mitford Hospital were selected as per inclusion and exclusion criteria. Complete history was taken, physical examination and spirometric examination was done for confirmation & staging of COPD and then BMD was done.

Table-I

Age distribution of COPD patients (n=50)

Age groups (years)	Numbers of patients	Percentage
<40	None	0%
40-49	11	22%
50-59	18	36%
60-69	15	30%
≥70	6	12%
Total=	50	Total=100%

All the patients were above 40 years of age, mean age was 56 years, maximum 66% patients were in 50-69 years of age, 22% patients were below 50 years & only 12% were above 70 years of age.

Table-II

Sex distribution of COPD patients (n=50)

Sex groups	Number of patients	Percentage
Male	47	94%
Female	3	6%
	Total=50	Total=100%

Maximum of the respondents were male (94.0%) and 6.0% of the respondents were female.

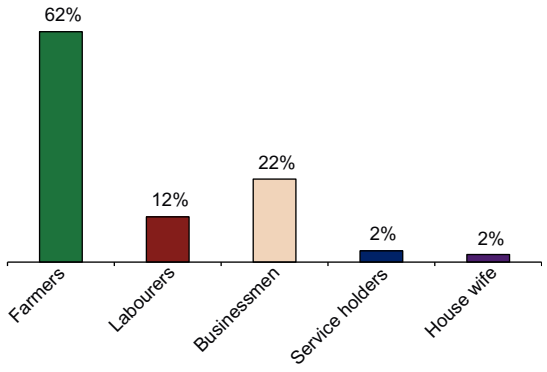

Fig.-1: *Distribution of COPD patients according to occupation (n=50)*

Among COPD patients 62%(31) were farmers, 12%(6) were labourers, 22%(11) were businessman, 2%(1) were service holder and 2%(1) were housewife

More than half of the respondents were illiterate and 32.0% of the respondents completed primary education and only 8.0% of the respondents completed secondary education.

So, COPD found to be more prevalent among less educated persons.

About half of the respondents had income below of 15000 tk per month while 22% of the respondents had income between 15000 - 29999tk and 24% of the respondents had income between 30000 - 49999.

Table-III

Distribution of the respondents by smoking (n=50)

Smoking	Number	Percentage
Present smoker	45	90.0%
Nonsmoker (exposed to biomass fuel)	2	4.0%
Ex-smoker	3	6.0%
Total	50	100.0%

Maximum of the respondents were smoker (90.0%) while only 6.0% of the respondents had past history of smoking and 4.0% had no history of smoking but they were exposed to biomass fuel.

Table-IV

Distribution of COPD patients according to amount of smoking (n=50)

Pack year	Number of patients	Percentage
<10	0	0%
10-20	16	32%
>20	34	68%
	Total =50	Total =100%

68% (34) patients had smoked more than 20 pack year and 32% (16) had smoked 10-20 pack year. Mean amount of smoking was 20 pack year.

Table-V

Common presenting symptoms of COPD patients (n=50)

Symptoms	Number of patients	Percentage
Breathlessness	48	96%
Chronic cough	43	86%
Sputum product	35	70%

96% (48) COPD patients presented with breathlessness, 86% (43) patients presented with breathlessness and 70% (35) patients presented with chronic sputum production.

Table-VI

Common physical signs COPD of patients (n=50)

Signs	Number of patients	Percentage
Barrel shaped chest	17	34%
Edema	10	20%
Cyanosis	05	10%
Wheeze	43	86%
	Total=50	Total=100%

On clinical examination, 34%(17) patients had barrel shaped chest, 20%(10) patients had edema, 10%(05) patients had cyanosis and 86%(43) patients had wheeze.

Table-VII

Distribution of the respondents by severity of COPD (n=50)

Stages of COPD	Number	Percentage
Very Severe FEV1 <30%	6	12%
Severe FEV1 ≥30%,<50%	16	32%
Moderate FEV1 ≥50%, <80%	20	40%
Mild FEV1 ≥80%	8	16%
Total	50	100%

Table-VIII

Relation between severity of COPD and amount of smoking (n=50)

Pack year	Number of patients	Very severe COPD	Severe COPD	Moderate COPD	Mild COPD
<10	0	0	0	0	0
10-20	16(100%)	0	1 (6%)	5 (31%)	10 (63%)
>20	34(100%)	23 (67%)	9 (27%)	2 (6%)	0
	Total =50				

Among our respondents 40.0% of them were in moderate stage, 16.0% of them were in mild stage, 32.0% of them were in severe stage and only 12.0% of them were in very severe stage.

Patients who smoked >20 pack year, 67% of them was suffering from very severe COPD, 27% severe COPD & 6% had moderate COPD. Patients who smoked 10-20 pack year 63% had mild COPD, 31% had moderate COPD & 6% had severe COPD. There was no patient of <10 pack year.

Table-IX

Relationship between severity of COPD & mean amount of smoke pack year (n=50)

Stages of COPD	Number of patients	Mean amount of smoke pack year
Very Severe FEV1 <30%	6	28
SevereFEV1 ≥30%,<50%	16	22
Moderate FEV1 ≥50%, <80%	20	16
Mild FEV1 ≥80%	8	14
Total	50	

Among our respondents mean amount of smoking was highest (28 pack year) in very severe COPD patients and lowest (14 pack year) in mild COPD patients.

Table-X

Distribution of the respondents by BMD Femoral neck t-score (n=50)

BMD Femoral neck t-score	Number	Percentage
Osteoporotic t-score < -2.5	25	50%
Osteopenia -2.5 < t-score < -1	20	40%
Normal t-score > -1	05	10%
Total	50	100%

Among our respondents 42.0% of them had Osteoporotic while 38.0% of them were osteopenia of femoral neck and rest of them (20.0%) was normal.

Table –XI

Distribution of the respondents by BMD Lumber Spine t-score (n=50)

BMD Lumber Spine t-score	Number	Percentage
Osteoporotic t-score < -2.5	26	52%
Osteopenia -2.5 < t-score < -1	17	34%
Normal t-score > -1	07	14%
Total	50	100%

Among our respondents, on the basis of BMD lumber spine t- score, 52%(26) were Osteoporotic, 34%(17) were osteopenic and 14%(7) were normal.

Very severe COPD & severe COPD had osteoporosis 100%. Patient with moderate COPD- 15% had osteoporosis, 17% had osteopenia & 15% had normal BMD. Patient with mild COPD- 75% had osteopenia, 25% had normal BMD. Chi-square test revealed that this difference were statistically significant (p=<0.001).

Table-XII

Relationship between BMD (BMD Femoral neck t-score) and Stages of COPD (n=50)

Stages of COPD	BMD			Mean t-score	P value
	Osteoporotic	Osteopenia	Normal		
Very Severe (6)	6 (100%)	0 (0%)	0 (0%)	-3.21 (±0.16)	<0.001
Severe (16)	16 (100%)	0 (0%)	0 (0%)	-2.90 (±0.32)	
Moderate(20)	3 (15%)	14 (70%)	3 (15%)	-1.80 (±0.66)	
Mild (8)	0 (0%)	6 (75%)	2 (25%)	-1.37 (±0.83)	
TOTAL (50)	25 (52%)	20 (34%)	5 (10%)		
			$\chi^2 = 23.403$		

Table-XIII

Relationship between BMD (BMD Lumber Spine t-score) and Stages of COPD (n=50)

Stages of COPD	BMD			Mean t-score	P value
	Osteoporotic	Osteopenia	Normal		
Very Severe (6)	6 (100%)	0 (0%)	0 (0%)	-3.53 (±0.69)	
0.012					
Severe (16)	12 (75%)	3 (18.8%)	1 (6.3%)	-2.56 (±2.03)	
Moderate (20)	8 (40%)	10 (50%)	2 (10%)	-2.19 (±0.83)	
Mild (8)	0 (0%)	4 (50%)	4 (50%)	-1.16 (±0.51)	
TOTAL (50)	26 (52%)	17 (34%)	7 (14%)		
			$\chi^2 = 23.403$		

Very severe COPD had osteoporosis 100%. Patient with severe COPD- 75% had osteoporosis, 18.8% had osteopenia, 6.3% had normal BMD. Patient with moderate COPD- 40% had osteoporosis, 50% had osteopenia & 10% had normal BMD. Patient with mild COPD- 50% had osteopenia, 50% had normal BMD. Chi-square test revealed that this difference were statistically significant (p=<0.001).

Table-XIV

Statistical relationship between BMD of femoral neck & Lumber spine (t-score) with stages of COPD (n=50)

	Stages of COPD	Mean t-score	SD	F value	P value
BMD Femoral neck t-score	Very severe	-3.21	0.16	29.07	< 0.001
	Severe	-2.90	0.32		
	Moderate	-1.80	0.66		
	Mild	-1.37	0.83		
BMD Lumber Spine t-score	Very severe	-3.53	0.69	4.04	0.012
	Severe	-2.56	2.03		
	Moderate	-2.19	0.83		
	Mild	-1.16	0.51		

Mean of BMD femoral neck t-test was lowest among very sever COPD patients (-3.21± 0.16) and highest among mild COPD patients (-1.37± 0.83). ANOVA test revealed that this mean difference was significantly associated (p=<0.001, F= 29.07).

Mean of BMD lumber neck t-test was lowest among very sever COPD patients (-3.53± 0.69) and highest among mild COPD patients (-1.16± 0.51). ANOVA test revealed that this mean difference was significantly associated (p=0.012, F= 4.04).

Discussion:

Chronic Obstructive Pulmonary Disease (COPD) is a leading cause of morbidity and mortality world-wide and leads to an economic and social burden that is both substantial and increasing. Prevalence and morbidity data greatly underestimate the total burden of COPD because the disease is usually not diagnosed until the patients already have had symptoms for some time and the disease is then often already quite advanced.

Osteoporosis is a systemic skeletal disease characterized by a low bone mineral density (BMD) and micro architectural changes in bones, leading to increased bone fragility and increased fracture risk.[5] Osteoporotic fractures cause many symptoms and complications, including the impairment of ventilation, and create a heavy economic burden.[5] To predict the risk of osteoporotic fractures, measurements of bone mineral density (BMD) have been widely used[6] and it has been reported[7] that BMD is lower in COPD patients than in healthy subjects. Thus, it is important to evaluate BMD in the management of COPD.[4]

A bone mineral density test uses X-rays to measure the amount of minerals — namely

calcium — in bones. This test is important for people who are at risk for osteoporosis, especially women and older adults.[8] Decreased Bone Mineral Density (BMD), which occurs with age, is an important health problem among elderly persons, contributing to disability and premature mortality. Decreased BMD has also become an important socio-economic issue. Decreased BMD may result in osteopenia and osteoporosis, of which the latter is more serious. An Osteoporosis Risk Assessment study has confirmed that the risk of fracture increases with decreasing BMD.[9] In 2015,Liu et al in a study in Turkey found, osteoporosis in 24-44% of patients with COPD.[2]

In our study, there is no patient below 40 years. Mean age was 56 years. Maximum 66% patients were in 50-69 years of age, 22% patients were 40-49 years of age and only 12% were above 70 years old. According to a study conducted in Bangladesh on burden of obstructive lung diseases in Bangladeshi, the main age group involved by COPD is 50-59 years (36%). In NICE study conducted by Fukuchi Y et al[16], in Japan, COPD is significantly more prevalent in older people. 3.5% in 40-49 years old Vs. 24.4% in those >70 years of age and this increasing prevalence with increasing age is consistent with our study upto age of 60 years after which there was a decline in our study.

In our study, we found 94% (47) of the COPD patient were male and only 6% (3) were female, this reflects that more males are habituated to smoking. This finding is consistent with other national studies. Hallin R et al[17] shown their study in South Korea, found 8% COPD patients were female. This is also similar to our study.

According to GOLD (Global Initiative for chronic obstructive lung disease) in its Global strategy for diagnosis, management and prevention-executive summary, updated 2014, the risk of developing COPD is inversely related to socioeconomic status i.e. COPD occurs more in less educated and lower income groups of people. Our study result is consistent with this because our study showed that COPD had occurred more in illiterate (60%), farmers (62%) and low income group population <15000 taka/month (54%).

In our study, 90% COPD patients are present smoker and 6% are ex-smoker, that means 96% COPD cases are due to smoking, 4% COPD patients were exposed to biomass fuel.[18] This result is consistent with other national and international studies. BOLD-BD study showed 88% COPD patients were smoker, 10% COPD patients were ex-smoker and 2% were exposed to biomass fuel.

In our study, 68% COPD patients smoked more than 20 pack year and 32% COPD patients smoke (10-20) pack year. Mean amount of smoking was 20 pack year. In BOLD-BD study, it has been shown that about 80% smokers need to smoke only around 10 pack year to catch the disease and the study has considered this finding as more alarming than the international findings, where 20 pack-year are set as a bench mark in developing COPD.[18] Here, our finding is consistent with international finding.

The mean amount of smoking is respectively 28, 22, 16, 14 pack year among very severe, severe, moderate and mild COPD patients. So it is obvious that severity of COPD depends upon the amount and duration of smoking.

In our study, breathlessness (96%), chronic cough (86%), sputum production (70%) are the most common presenting complaints. GOLD has mentioned any of chronic cough, sputum production and dyspnoea as a key indicator of COPD. In our study, all of these symptoms were present singly or in combination among smokers having COPD.

In our study, we found wheeze (86%), barrel shaped chest (34%) as the commonest signs. Other signs were, edema (20%) and cyanosis (10%). Harikmitra et al[19] showed in their study, in Chennai India, 37% had barrel shaped chest, 26% had edema, 15% had cyanosis and 90% had wheeze. This difference is not very significant.

In our study, according to BMD femoral neck t-score, we found that 50% of COPD patients have osteoporosis, 40% have osteopenia and only 10% have normal bone. According to BMD lumber spine t-score, we found that 52% of COPD patients have osteoporosis, 34% have osteopenia and only 14% have normal bone.

Among our respondents, on the basis of BMD lumber spine t-score, 52% (26) were Osteoporotic, 34% (17) were osteopenic and 14% (7) were normal. The prevalence of low BMD by QCT in patients was high; 37.8% of our patients were osteopenic

and 43.2% were osteoporotic.[1] These results are in accordance with a published meta-analysis, which has shown that, in COPD patients, there is a prevalence of osteoporosis of 35.1% and a prevalence of

osteopenia of 38.4%.[20] The TORCH study[21] demonstrated a higher prevalence of osteoporosis and osteopenia at baseline, in those patients with spirometrically confirmed COPD.

Mean of BMD femoral neck t-test was lowest among very sever COPD patients (-3.21± 0.16) and highest among mild COPD patients (-1.37± 0.83). This mean difference was significantly associated. Other studies, however, support that there is a positive correlation between stage of COPD and osteoporosis which is statistically significant.[22]

In our study, on the basis of BMD lumber spine t-score, very severe COPD had osteoporosis 100%. Patient with severe COPD- 75% had osteoporosis, 18.8% had osteopenia. This difference were statistically significant (p=<0.001).

In another study, majority of patients who had osteoporosis, had very severe COPD (81.81%) and severe COPD (73.91%). Incidence of osteoporosis increased with severity of COPD from 14% (mild) to 80% (very severe) among males. Among females, osteoporosis is also increased with severity of COPD.[23] Study is on par with Jørgensen and Schwarz study.[24] In a study by Stevenson *et al*.[25] it was observed that there was increased incidence of osteopenia and osteoporosis with advancing COPD stage. They observed that 68% had either low bone mass (osteopenia or osteoporosis) or a previously undiagnosed vertebral fracture, with 25% of the included patients having a vertebral fracture. Consistent with the above studies, another study by de Vries *et al*.,[26] observed that the risk of osteoporotic fracture increased in patients with COPD. It was also observed that patients with more severe airway obstruction in COPD had increased risks of osteoporosis and bone fractures as compared with patients without a history of obstructive airway disease.

In 2015, Liu et al in a study in Turkey found that, after adjustment age, sex and FEV1 (%) matched COPD patients with and without osteoporosis, determined that BMDs at the lumbar spine, total hip, and femoral neck sites were lower in COPD patients with osteoporosis. These results are consistent with our study.[2]

In summary, we have found that osteoporosis has a close association with COPD. And BMD value decreases as the disease progresses.

Conclusion:

COPD is a systemic disease. Along with respiratory system it involves other systems of the body. Skeletal involvement is a major effect of COPD. This study showed positive relation between severity of COPD and bone loss. The more severe the COPD is the more severe the bone loss. So, early detection of bone loss by BMD and appropriate preventive and therapeutic measures should be taken to reduce the mortality and morbidity of COPD patients.

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ORIGINAL ARTICLE

Surgical Intervention of Extrapulmonary Tuberculosis Patients Admitted in Department of Surgery in 250 Bedded TB Hospital, Shyamoli, Dhaka

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Abstract:

Objective: *The objective of the present study is to ascertain the role of surgical intervention in managing various types of extra pulmonary tuberculosis.*

Methods: *This was a prospective, cross-sectional, observational study conducted among the patients who were admitted in department of surgery in 250 Bedded TB Hospital, Shyamoli, Dhaka. The study period was July 2017 to June 2018.*

Results: *Maximum number of extra-pulmonary tuberculosis belong to cervical tubercular abscess which was about 68% .This was followed by axillary tubercular abscess (7%). Incision and drainage of abscess constitute highest number of surgical operation. It was about 85.22%. The second highest (7%) surgical intervention was Tube thoracostomy. 68.47% patients were female suffer from extra pulmonary tuberculossis. About 25.7% patients were in between 21-25 years age group. Next most affected group was 16-20 years*

Conclusions: *Improvement of diagnostic facilities and effective medical management along with surgical intervention are essential for early recognition and better treatment of EPTB cases.*

Keywords: *Surgical intervention, Extra-pulmonary, Tuberculosis*

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Introduction:

Tuberculosis is a specific infectious disease caused by Mycobacterium tuberculosis. This disease primarily affects lungs parenchyma known as pulmonary tuberculosis- which is world-wide public health issue.Extra-Pulmonary Tuberculosis (EPTB)- refers to Any Bacteriologically Confirmed Or Clinically diagnosed case of TB. involving organs other than lungs e.g. pleura (26%), lymph nodes (17%), genitourinary(15%), bones (14%), military (8%), peritoneum (4%) and gastrointestinal TB (1%) rarely breast, vascular and penile TB[1]. EPTB constitutes about 15 to 20 percent of all cases of tuberculosis in immunocompetent patients and accounts for more than 50 percent of the cases in HIV positive individuals[2-4]. Lymph node

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tuberculosis constitutes 20 40% of extrapulmonary tuberculosis. It is more common in children and women than other forms of extrapulmonary tuberculosis and is more common in Asians and Pacific islanders. In developing and under developed countries, it continues to be caused by Mycobacterium tuberculosis and atypical mycobacteria are seldomly isolated. Commonly involved superficial lymph nodes (Scrofula or king's evil) include those in posterior and anterior cervical chains or the suprascapular fossae but others like submandibular, periauricular, inguinal and axillary groups may also be involved. Often, the lymphadenopathy is bilateral and noncontiguous1. Intrathoracic (hilar, paratracheal and mediastinal in decreasing order) and abdominal lymph nodes are also involved in tuberculosis[5]. Among EPTB cases the lymphnode most commonly involved are the cervical nodes[6-8]. The disease usually responds to standard antituberculosis drug treatment. Biopsy and surgery is required to obtain tissue samples for diagnosis and for managing complication[4]. The objective of the present study is to ascertain the role of surgical intervention in managing various types of extra pulmonary tuberculosis.

Materials and Methods:

This was a prospective, cross-sectional, observational study conducted among the patients who were admitted in department of surgery in 250 Bedded TB Hospital, Shyamoli, Dhaka. The study period was July 2017 to June 2018. A detailed history, complete physical examination, various laboratory work and radiological studies were carried out. Histological confirmation was tried in every case. Diagnosis of TB was made by histological or cytological examination or demonstration of Acid Fast Bacillus. Informed consent was taken from the Patient or legal guardian. The cases were treated with anti tuberculosis chemotherapy (WHO Schedule) and the patients were followed up weekly, foreweekly and monthly after surgery during the period of chemotherapy. All findings were noted in case record form. The results were calculated and interpreted through appropriate statistical analysis with the help of a statistician and presented in tables.

Result:

Table 1 shows that maximum number of extra-pulmonary tuberculosis belong to cervical tubercular abscess which was about 68% .This was followed by axillary tubercular abscess (7%).

Table-I

Distribution of extra-pulmonary tuberculosis.

Site	Number (%)
Cervical tubercular abscess	138 (68%)
Axillary tubercular abscess	14 (7%)
Tubercular plural effusion	11 (5.4%)
Tubercular hydro pneumothorax	3(1.47%)
Midline neck tubercular abscess	7(3.44%)
Skin tuberculosis	3(1.47%)
Submandibular tubercular abscess	1(0.49%)
Chest wall tubercular abscess	3(1.4%)
Breast TB	2(1%)
Potts TB back	1(0.49%)
Inguinal tubercular abscess	6(3%)
Cervical Lymphadenitis	5(2.46%)
Tubercular abscess in left elbow	1(0.49%)
Tubercular abscess in Right palmer surface	3(1.47%)
Wound debridement of post C-section	5(2.46%)
Total	203 (100%)

Table 2 reveals that Incision and drainage of abscess constitute highest number of surgical operation. It was about 85.22%. The second highest (7%) surgical intervention was Tube thoracostomy.

Table-II

Name of surgical intervention of extra pulmonary tubercular diseases.

Name	Number (%)
Incision and drainage of abscess	173 (85.22%)
Tube thoracostomy	14(7%)
Excisional biopsy of lymphnode	5(2.46%)
Excision of skin TB	3(1.47%)
Excisional biopsy of breast TB mass	2(1%)
Incision and drainage of potts diseases	1(0.49%)
Wound debridement	5(2.46%)
Total	203 (100%)

Table 3 show that 68.47% patients were female suffer from extra pulmonary tuberculossis.

Table-III

Distribution of patients according to sex

Sex	Number
Female	139 (68.47%)
male	64(31.52)
Total	203 (100%)

According to table 4, about 25.7% patients were in between 21-25 years age group. Next most affected group was 16-20 years.

Table-IV

Distribution of patients according to age

Age (years)	Number
0-5	1(0.49%)
6-10	1(0.49%)
11-15	14(7%)
16-20	50(24.63%)
21-25	52(25.7%)
26-30	34(16.8%)
31-35	23(11.33%)
36-40	5(2.46%)
41-45	2(1%)
46-50	6(3%)
51-55	3(1.47%)
56-60	2(1%)
61-65	3(1.47%)
66-70	5(2.46%)
71-75	2(1%)
Total	N= 203(%)

Discussion:

Extra pulmonary tuberculosis (EPTB) is a significant public health problem that represents a diagnostic challenge in Bangladesh. In this study The most frequent form of EPTB was tubercular abscess followed by tubercular pleural effusion. Among the tubercular abscess, cervical tubercular abscess was most frequent (68%). in our study 85.29% tubercular abscess was found in different parts of the body while in karim et al, 2006 it was 11.2 %. The number was significantly increased in this study. In kamal et al, 2016, about 21.5% were cervical tubercular abcess among cervical tubercular lymphadenitis patients. This study demonstrated that 5.4% was tubercular pleural effusion. While it was 8.47% in mohan et al, 2015 which was similar to this study.

In mohan et al, 2015 breast TB was constituted 13.55%. in comparison to this study which was 1%.

In present study 2.46% was cervical lymphadenitis. In Abdallah et al, 2015 it was 35.3%.[9]

In present study, highest surgical intervention was incision and drainage of abscess in different parts of the body that was 85.22% . In mohan et al,2015 it was 20.51% in psoas abscess.

Tube thoracostomy was done in 7% cases while it was 2.56% in mohan et al, 2015 .

In this study 68.47% EPTB patients were female which was 52.4% was in mohan et al, 2015 and 63.4% was in Mohammadien et al, 2017. About 58% were female and 45% were male in Karim et al in 2015. In most of the patients (56.29%) were in age group 21-40 years where it was 67.8% in mohan et al,2015.

Conclusion:

EPTB is major health problem though it is not communicable disease.EPTB should be taken serious as pulmonary tuberculosis. Improvement of diagnostic facilities and effective medical management along with surgical intervention are essential for early recognition and better treatment of EPTB cases.

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ORIGINAL ARTICLE

Mediastinal Mass: Review of 48 Cases Admitted in Thoracic Surgery Dept. of a Tertiary Hospital in Bangladesh

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Abstract:

Introduction: *Mediastinal mass is relatively uncommon chest tumor with only 3% prevalence worldwide but the incidence is rising in last 4 decades. As there is very little published data in our country we tried to release a report of mediastinal mass in a tertiary hospital of Bangladesh.* ***Patients and Methods:*** *48 patients with mediastinal mass were considered in this retrospective descriptive study. All these patients were admitted in our institute in a 3 years period from January 2016 to December 2018.* ***Result:*** *Most of the patients presented in 3rd decade (33.3%), 5th (18.75%) and 4th decade (14.58%) being the next in frequency. Most of them were present in anterior mediastinum (68.75%), the rest were almost equally distributed in middle (16.7%) and posterior (14.58%) mediastinum. Total 12 histological types were found of which mature cystic teratoma (27.08%) and lymphoma (27.08%) were prevalent. Most of them were benign (54.17%) and presenting symptoms were chest pain (68.58%), dyspnea (52.08%) and cough (45.63%) in most of the patients.* ***Conclusion:*** *This was a small effort to sort out the variety of this fascinating entity and a multicenter large scale study is needed to ascertain the true nature and outcome of this group of disease.*

Key Words: *Mediastinal mass, Mediastinal tumor.*

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Introduction:

Mediastinal masses are relatively uncommon tumors, that varies in histologic distribution, location, symptomatology, and prevalence of malignancy between different age groups.[1,2] Tumors of anterior mediastinum include thymoma, germ cell tumors, thyroid enlargement and lympfoma. Middle mediastinal masses include pericardial cysts, bronchogenic cysts, lymphoma and mediastinal granuloma. Posterior mediastinal

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masses are predominantly tumors of neurogenic origins.[3] After suspicion from symptoms and signs radiograph (Figure 1) and CT scan (Figure 2, Figure 3) remains the mainstay for diagnosis. Approaches for tissue assessment include percutaeneous needle aspiration, mediastinoscopy, video assisted thoracoscopy and anterior mediastinotomy.[3] Recent advances in radiographic techniques and immunohistochemistry have led to more accurate preoperative delineation and histologic diagnoses.[4] The treatment of choice is surgery and/or chemo/ radiotherapy. We reviewed all cases of mediastinal masses diagnosed and treated over a 3-year period between 2016-2018 in Dhaka medical college hospital (DMCH) in Bangladesh to determine the presentingfeatures- location- histology-relationshipof age to the type of lesion and benignityversus malignancy in these unusual tumors.

Patients and methods:

This study was a retrospective, descriptive study performed on 48 patients with mediastinal masses who were admitted in DMCH over a 3 year period from 2016 to 2018.

Age and sex distribution, location, histologic types of tumors, symptoms and signs, associated diseases and complications were recorded from patients' files. All resected masses had a definitive pathologic diagnosis. Data analysis was performed by SPSS Software (v.24), using descriptive statistics indices such as frequency, mean, median, standard deviation and standard error.

Results:

A total of 48 patients with mediastinal masses including 31 males (64.58%) and 17 females (35.42%) with a mean age of 31.08 years (range 1-68 years) who were admitted in department of Thoracic surgery, DMCH entered the study.

Most mediastinal tumors (53.05%) were identified in the third and fifth decades of life. (Table I) The incidence of malignancy was 45.83%, the heist being in 6th and 7thdecades (Table I) and the most common malignancy was malignant lymphoma (27.08%). The most common benign tumour was mature cystic teratoma (27.08%). Inflammatory pseudotumors were found which looked like a mediastinal mass but actually found to be lung mass later on during surgery. (Table II)

Considering the location of mediastinal masses, the anterior mediastinum was the most common site (68.75%)followed by middle mediastinum (16.7%) and posterior mediastinum(14.58%) (Table IV). The commonest tumor of anterior mediastinum was mature cystic teratoma. Malignant lymphoma was found both in anterior and middle mediastinum.54.17% were solid and 45.83% were cystic in nature.

Symptoms such as pain (64.58%), dyspnea (52.08%) and cough (45.83%%) constituted the most commonly presentingcomplaints followed by fever (35.42%) and weight loss (27.08%). Pleural effusion found in one patient only and one patient was asymptomatic. Encapsulated Thymoma was the asymptomatic case. (Table III)

The most common complication observed in this seriesof mediastinal tumors was Superior Vena Cava (SVC)syndrome. Other complications were brachial plexus involvement, horner's syndrome and pleural effusion. There was no post operative complications. No in hospital mortality were recorded.

Table-I

Age distribution and type

Age group	Frequency	Malignancy	Benign
1st decade	5 (10.42%)	1 (20%)	4 (80%)
2nd decade	8 (16.7%)	2 (25%)	6 (75%)
3rd decade	16 (33.3%)	7 (43.75%)	9 (56.25%)
4th decade	7 (14.58%)	3 (42.86%)	4 (57.14%)
5th decade	9 (18.75%)	6 (66.67%)	3 (33.33%)
6th decade	2 (4.2%)	2 (100%)	0 (00%)
7th decade	1 (2.1%)	1 (100%)	0 (00%)

Table-II

Distribution of patients according to histological type

Histological type	Frequency
Lymphoma	13 (27.08%)
Mature cystic teratoma	13 (27.08%)
Thymic cyst	5 (10.42%)
Thymoma	2 (4.17%)
Cystic lymphangioma	2 (4.17%)
Immature teratoma	2 (4.17%)
Bronchogenic cyst	1 (2.08%)
Pericardial cyst	1 (2.08%)
Inflammatory pseudotumor	2 (4.17%)
Undifferentiated carcinoma	3 (6.25%)
Neurogenic sarcoma	1 (2.08%)
Undifferentiated pleomorphic sarcoma	1 (2.08%)

Table -III

Distribution of patients according to symptoms

Symptoms	Frequency
Pain	31 (64.58%)
Dyspnoea	25 (52.08%)
Cough	22 (45.83%)
Fever	17 (35.42%)
Weight loss	13 (27.08%)
Pleural effusion	1 (2.08%)
Asymptomatic	1 (2.08%)

Table-IV

Distribution of patients according to location

Mediastinum	Frequency
Anterior	33 (68.75%)
Middle	8 (16.7%)
Posterior	7 (14.58%)

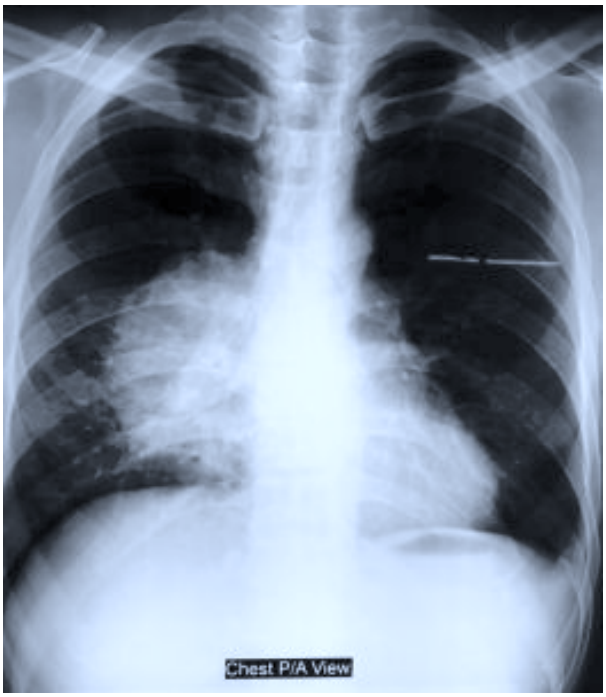

Fig.-1: *X-ray chest P/A view showing a mediastinal mass.*

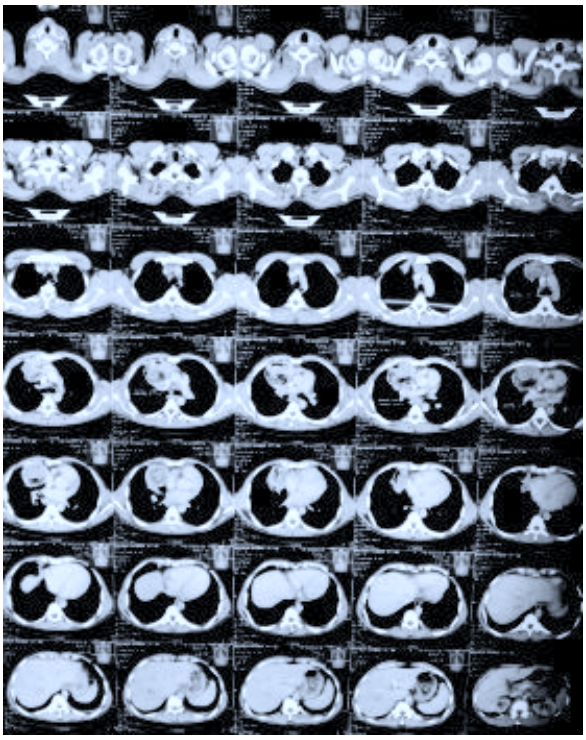

Fig.-2: *CT scan of chest multi-axial view showing mediastinal mass*

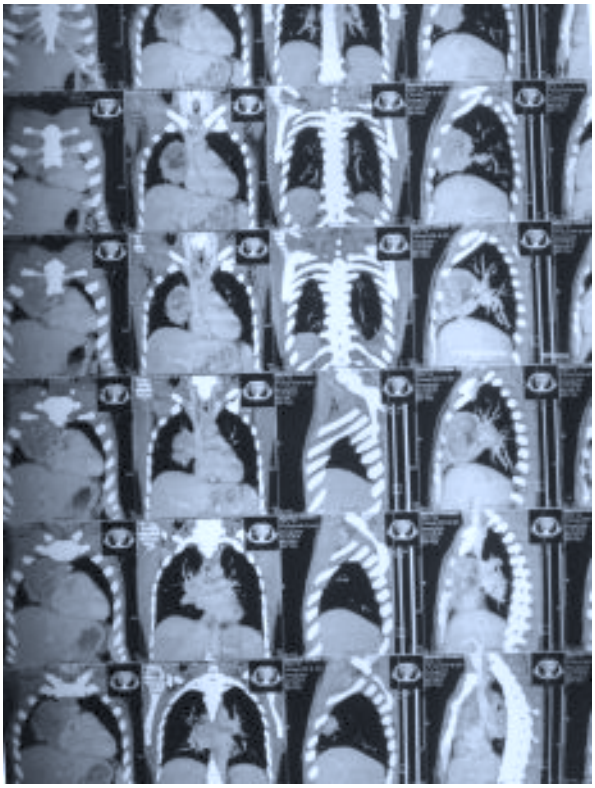

Fig.-3: *CT scan of chest coronal and saggital view showing mediastinal mass .*

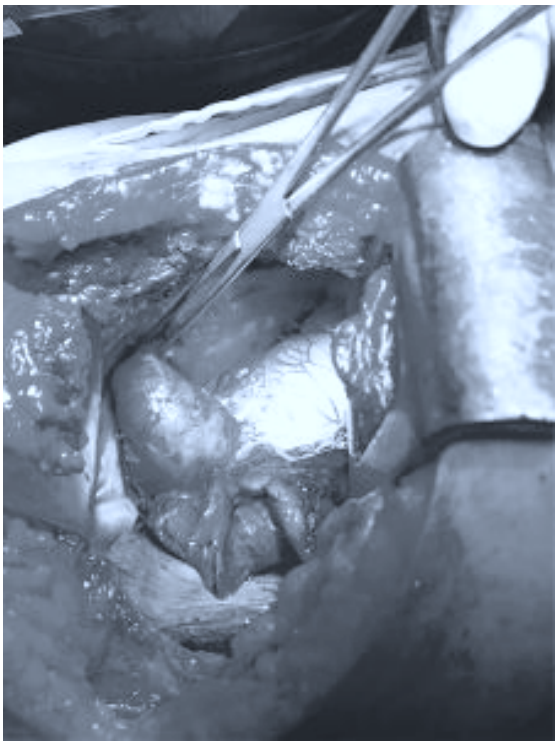

Fig.-4: *Per-operative picture of mediastinal mass*

Discussion:

Different types of tumors and cysts occur in the mediastinum and affect people of all ages. They are not that much common as only about 8 cases are found per year and accounts of 3% of total tumors of chest.[5] In this study we encountered important differences inhistologic distribution, malignancy rate, age range, site and type of mediastinal tumors between ourpatients and other reported series.

Diagnoses were made on the basis of clinical features which led us to do radiograph, CT scan of chest, MRI of chest. Histopathological type were sort out from biopsy taken by needle aspiration guided by CT scan and ultrasonography, biopsy by VATS, excisional biopsy through thoracotomy.

Most of the tumors were found in anterior mediastinum (68.75%) as most of our cases were mature cystic teratoma (27.08%) and lymphoma (27.08%). Other studies have reported that anterior mediastinalneoplasms account for 50% of all mediastinal masseswith thymomas being the most common.[6] There was no significant difference in the incidence of solid (54.17%) and cystic (45.83%) masses.

In our study most of the patient presented in 3rd decade (33.3%), 5th and 4th decade being the next higher in frequency. This probably due to higher prevalence of teratoma in the 3rd decade. Patients with lymphoma presented mostly in 4th and 5th decade of life. In most of the series the frequency was highest in 3rd decade as us and next frequent age group were 5th and 2nd decade.[1,7,8]

Most of the patient presented with pain, dyspnea and cough. Fever and weight loss were also common. Only one patient was asymptomatic and he was found to have encapsulated thymic tumor.

Most of the cases in our study were benign (54.17%) although with the increase of age malignancy increased and all the patients of 6th and 7th decade were found to have malignant tumor. There were 12 histological types of tumors among bthe most common malignat tumor was lymphoma and most common benign tumor was mature cystic teratoma. In collected series of mediastinal masses, 25% to49% of these lesions are malignant[1,8,9] which matched ur study. They also foundthe lowest incidence of malignancy in children with 10years of age and younger (50%) and the highest incidencein patients in the eighth and second decades of life(80%).[7] there is an interesting fact that we found 2 cases of inflammatory pseudotumor which by all means mimicking mediastinal mass but on operation turned out to be lung mass.

Some patient presented with thoracic outlet obstruction, brachial plexus compression, horner's syndromeand pleural effusion. No significant post operative complications were seen. We couldn't report any mortality probably because it was a retrospective study and there were no in hospital mortality.

In conclusion findings in our study almost matched previously encountered reports although higher incidence of mature cystic teratoma was a new finding and surprisingly all of the teratomas we found were primary and none of them had testicular disease sort out by ultrasonography. Whether in later life they developed any testicular tumor or not in unknown to us as we didn't follow up them yet.

Conclusion:

Mediastinal tumors have always fascinated thoracic surgeons because of their variety and

unpredictability of diagnosis which recently have been conquered due to advances in radiology and histopathology. The majority is amenable to permanent surgical excition, excluding some malignantcases that need to obtain a diagnosis for neoadjuvantchemotherapy before surgery. In our study we demonstrated differences in histologic distribution, location,and symptomatology in mediastinal tumors. These differences shouldbe considered carefully to evaluate and plan a therapeutic modality with mediastinaltumors. A multicenter study can accurately predict its nature in our country.

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ORIGINAL ARTICLE

A Prospective Study of Pleurodesis by Autologous 'Blood Patch' Mixed with Tranexemic Acid in the Management of Persistent Air Leak

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Abstract:

Objective: *To evaluate the efficacy and risks of autologous 'blood patch' pleurodesis in patients with persistent air leak.* ***Method:*** *All patients with persistent air leak following recurrent pneumothorax, secondary spontaneous pneumothorax and pulmonary surgery, admitted In our institute between January 2018 to December 2018 were treated with 20 mL of autologus blood through chest drain tube mixed with 10 ml Tranexemic acid, starting from 6th day of persistent air leak and followed up closely. Sample size was 25.* ***Results:*** *This procedure showed 96% success rate with 84% patients recovered from persistent air leak within 12 hours and another 12% within 24 hours. No significant adverse effects were seen except 8% transient fever and 4% pleural effusion which recovered conservatively. Early discharge and early restoration of working life was achieved in all patients at a very low cost.* ***Conclusion:*** *In our experience a single injection of 20 ml of blood mixed with tranexemic acid is sufficient to seal persistent air leaks in less than 24 hours. As it is a cost effective procedure, it is very much suitable for our country and should be practiced more widely.*

Key Words: *Persistent air leak, Autologus blood patch, Pleurodesis.*

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Introduction:

Pneumothorax is a common problem for thoracic surgeons which may occur spontaeneously or after thoracic surgery. Spontaeneous pneumothorax can occur primarily or may be due to a secondary cause. Primary spontaeneous pneumothorax (PSP) occurs in persons without coexisting pulmonary disease, usually from rupture of a pulmonary bleb, while secondary spontaneous pneumothorax (SSP) is associated with underlying pathology,such as chronic obstructive pulmonary disease (COPD), bullous emphysema, pulmonary tuberculosis (PTB), interstitial lung disease (ILD), bronchogenic carcinoma etc. Spontaneous pneumothorax following clinical cure of a previous episode is referred to as recurrent.[1,2]

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Persistent air leakage is defined as air leakage more than5 to 7 days after intercostal drainage, which are more common with secondary pneumothorax than with primary pneumothorax.[3-5] They are also seen after lung surgery or trauma. Video assisted thoracoscopy (VATS) has been advocated in the management of patients with PSP and SSP who suffer from persistent air leakage. For those in whom operation is not feasible chemical pleurodesis is a fair option.[6]

Pleurodesis is a procedure to achieve symphysis between the two layers of pleura to prevent recurrent pleuraleffusion or recurrent pneumothorax.[7-9] This can be done by both chemical and surgical means. The principal is to induce inflammation and fibrosis causing the symphysis betweenthe two layers of pleura.[10] Chemical pleurodesis has been widely applied for stopping air-leak or for preventing pneumothorax recurrence. It can beapplied through the intercostal drainage tube, medical thoracoscopy, or during the operation. A variety of sclerosant agents are used clinically including tetracycline and derivatives (doxycycline or minocycline), talc,

bleomycin, autologous blood patch, iodopovidone, picibanil,silver nitrate, and quinacrine, of which most commonly used agent was talc followed by tetracycline derivatives and bleomycin.[11]

In this study we are aiming to see the efficacy of autologus blood patch, applied through intercostal drain tube, as a agent of pleurodesis in patients with persistent air leak for several reasons. We added tranexemic acid with autologus blood due to its antifibrinolytic action.

Material and Methods:

Patient Selection:

The study was done in Dept. of Thoracic Surgery, Dhaka Medical College Hospital (DMCH), Dhaka, Bangladesh between January 2018 and June 2019. Total 25 patients with persistent air leak after 6 days of introducing intercostals chest drain tube who were already admitted in DMCH were taken. These patients developed persistent air leak either after recurrent pneumothorax, SPS and post operative. Pleurodesis was done in radiologically expanded lungs but persistent air leak for at least 6 days, despitea properly placed chest tube. Written informed consent of each patient was taken. Patients were examined prospectively in terms of timing and success rate of pleurodesis, cessation of air leak, timing of tube removal, recurrence of pneumothorax, hospital length of stay (LOS), procedure related complications, and additional interventions required. After discharge follow up was done at 1 month, 3 months and 6 months.

Study Type:

It is an interventional study.

Pleurodesis Technique:

20 cc of blood is drawn from the patient's median cubital or cephalic vein,and injected directly into the chest drain aseptically, without applying any analgesics or sedation. 10cc tranexemic acid was injecded into the tube afterwards and the tube was flushed with 10cc normal saline in order to inhibit clotting inside the drain and ensuring all the blood is kept in the thoracic cavity.[12] Tranexemic acid was used so that clotted blood can seal the air leakage site and it remain sealed. It may also cause the fibrin in tissue to retain its original structure by antifibrinolytic effect so that healing is fastened. In order to achieve continuous air drainage but keepthe injected blood in the thorax, the chest tube line is elevated 40-50 cm above the patient and kept unclamped for 2 hours. During this period, the patient was asked to change his position in bed every 15 minutes, to attain homogenous distribution of blood within the pleural cavity. Neither antibiotic prophylaxis nor negative suction was applied to any patient.[13,14]

Results:

Total 25 patients were taken out of which 72%were male and 28% were female. The mean age was 59.2 years (Table I). 24% patients presented with recurrent pneumothorax, 44% had SSP out of which 28% had COPD, 8% had H/O PTB and 8% was suffering from ILD. Remaining 28% patients developed persistent air leak after lung surgery, 20% lobectomy and 8% decortication (Table II).

In 68% patients involved side was right and rest developed it in left side (Table III). Most of the bronco-pleural fistulas 64% were of medium size. 28% were small and rest were of large size (Table

IV). Pleurodesis was done after certainity that air leak was present for at least 6 days (44%). We waited a few more days in patients with small fistula with a hope that it will cease eventually but when it persisted for 8 days we went for pleurodesis. In 12% patients pleurodesis was done at 11th day (Table V).

Table-I
Age and sex distribution

Total Patients (n)		25
Sex	Male	18 (72%)
	Female	7 (28%)
Age (years)	Range	32-76
	Mean	59.2 ± 9.7 SD

Table-II
Aetiology

Recurrent Pneumothorax		6 (24%)
Secondary Spontaeneous Pneumothorax (SSP)		11 (44%)
	COPD	7 (28%)
	H/O PTB	2 (8%)
	ILD	2 (8%)
After Thoracic Surgery		7 (28%)
	Lobectomy	5 (20%)
	Decortication	2 (8%)
Previous H/O Pleurodesis		1 (4%)

Table-III
Side involved

Rt Side	17 (68%)
Left Side	8 (32%)

Table-IV
Size of Fistula

Severity of air leak	
Large (continuous air leak)	2 (8%)
Medium (air leak during talking)	16 (64%)
Small (air leak during coughing)	7 (28%)

Table-V
Duration of air leak before pleurodesis

Duration of air leak before Pleurodesis (days)	
6	11 (44%)
7	7 (28%)
8	4 (16%)
11	3 (12%)

After pleurodesis patients were followed up closely and it was seen that in 84% patients air leak ceased within 12 hours. In 12% patients it ceased between 12-24 hours and persistence of air leak remained in 4% of patients even after 72 hours, so repeat pleurodesis needed for them and it was done after 72 hours of first one. After repeatation air leak stopped within 12 hours (Table VI). Tubes were removed the following day of stoppage of air leak in all patients (Table VII). Follow up was done closely in all patients during and after pleurodesis, in the period of hospital stay and at 1, 3 and 6 months after discharge. Complications were very less as only 8% patients developed transient fever and 4 % developed pleural effusion which was treated conservatively. No pain, irritation, empyema chest tube obstruction or recurrence was found (Table VIII)

Table-VI
Timing of cessation of air leak after pleurodesis
Efficacy of Blood Patch Pleurodesis

Air leak cessation in <12 hours	21 (84%) [p value <0.001]
Air leak cessation in <24 hours	3 (12%)
Persistent air leak after 72 hours	1 (4%) Repeat pleurodesis was done and leak stopped within 12 hours of repeatation.

Table-VII
Timing of tube removal after pleurodesis

Tube removal	
After 24 hours	21 (84%)
After 48 hours	3 (12%)
Couldn't be removed after 1st pleurodesis	1 (4%) removed after 24 hours of repeat pleurodesis

Table-VIII
Complications

Complications	
Pain, Irritation	0 (0%)
Fever	2 (8%)
Pleural effusion	1 (4%)
Empyema	0 (0%)
Chest tube obstruction	0 (0%)

Discussion:

Persistent air leak (PAL) reamin one of the most common complication in modern thoracic surgery.[15] PAL is a complication which can occur after PSP, SSP and also lung surgery. These There are numerous diseases in the etiology of SSP.The most frequent factor seen is COPD, and it is responsibleapproximately in 70% of all patients.[16,17] Other diseases contributing to it includes PTB, ILD, malignancy etc. Trauma is also an important cause in our country. In our study most patients presented with SSP were COPD cases (63.6%). Another important entity is PSP which usually occur in tall, slender, young, male, smoker. Recurrence is also quite common among them. Rice and Kirby have reported a 15.2% rate of air leak persisting more than 7 days after pulmonary lobectomy in a series of197 consecutive patients,[18] and others and we have reported a14.8% rate in 182 patients treated by VATS wedge resection for spontaneous pneumothorax.[19] In our study we found SSP (44%), recurrent primary pneumothorax (24%) and post surgical cases (28%). 4% of patients had previous history of chemical pleurodesis.

Many techniques have been tried for the treatment of persistent air leaks but non proved to be superior than the others. Some of the procedures applied by surgeons are; a drain *in situ* and a Heimlich valve, more aggressive approaches such as intra-pleural chemical agents (pleurodesis) or even primaryrepair by re-operation and injection of fibrin glue.[20] Every procedures have some merits and demerits. Spontaeneous recovery following drain tube placement usually requires a lot of time and increases patient morbidity and mortality by increasing the chance of empyema, prolonged pain and immobility. Most of the sclerosing agents used for pleurodesisare not well accepted, since they can cause systemic reactions and severe pain. Moreover, in the presence of a large air leak or bronchopleural fistula, chemical pleurodesis involves

a risk of reflux of the agent into bronchial segments.[2] Surgical repair or re-thoracotomy is also problematic specially in patients with poor condition. So we prefferd to go for autologus blood patch pleurodesis (ABPP) as it has been shown as a cheap, painless method with good success rate.

In 1987, Robinson[13] first reported using patch pleurodesis with autologous blood to treat SSP with PAL, and he obtained an 85% success rate in a series of 25 patients receiving 1 to 3 instillations of 20 mL of blood mixed with 10ml tranexemic acid into thepleural cavity. ABPP has since been used to treat persistent postoperative air leak after pneumonectomy.[21] As summarized by Chambers and associates,[22] the overall success rates from 43 studies were 92.7% from patients having undergone pulmonary procedures and 91.7% of patients with pneumothorax. Several prospective studies (including 2 randomized controlled trials) showed unanimously that ABPP had superior outcomes, such as shorter sealing time, higher success rate, and fewer complications for PAL, when compared with conservative treatment.[22-24] Furthermore this bedside surgical procedure is easy to perform, inexpensive, and painless.[22,25] Our success rate was 96% as air leak ceased in 84% patients within 12 hours and another 12% patients within 24 hours. Drain was removed the next day and patients were discharged. Only in 1 patient air leak didn't stop within 72 hours, so we had to re-inject blood after 72 hours and this time air leak stopped within 24 hours. Only 2 patients developed transient fever and one patient developed pleural effusion which resolved with conservative treatment. Obstruction of the catheter is an important problem which occurs during autologous blood pleurodesis which may even cause tension pneumothorax.[12] But that didn't happen in our study probably due to flashing the tube with 10mL normal saline after installation of blood.

Autologous blood pleurodesis is believed to work by multiplemechanisms. Immediate cessation of air leak after instillation takes place because of direct mechanical action of the fibrindue to a blood patch effect or direct sealing of the leak with hematomaor coagulated blood. The presence of

blood in the cavity induces adhesions between the visceral and parietal pleural layers, due to inflammation of pleural surfaces.[26] Cessation of air leakage within 24 hours in most of the cases in our study supports the first mechanism. In our experience 20 ml of blood have been sufficient in all patients, whereas in most series 50–250 ml have been necessary to seal the air leak.[27,28] We didn't use more than 20 mL as we thought it may act as a medium for colonization which may cause empyema thoracis.[2] No empyema occurred to any of the patients of our study. We added 10 ml of tranexemic acid with blood to keep the blood in clotted condition so that it can remain as a patch and seal the fistula with the clot. As tranexemic acid is anti-fibrinolytic fibrin in tissue may remain in its original state with the use of it and it may enhance healing. This was our view to use tranexemic acid and our results were excellent and more research in the use of tranexemic acid should be carried out to see its role in healing. The timing of pleurodesis is still controversial.[23,28] Some authorspropose the use of autologous blood pleurodesis on the 9th day of continuing air leak while other reports recommend initiating treatment on the 5th day.[23,27] In our study patients with continuingair leak for six days were selected for autologous blood patch pleurodesis as per definition. We belived that early intervention can prevent the chance of empyema and reduce the pain and immobility which in turn reduce the morbidity and mortality to give the patient a chance of early discharge and better quality of life as recovery will be quick.

For a country like us where cost is a major issue in the treatment of the patient, it is an excellent method in the treatment of persistent air leak as the cost is almost zero. Moreover early recovery means less hospital stay and less chance of infection which is also contributing in reducing the expenditure of the patient.

Small sample size and only 6 month follow-up are the main limitations of our study. So Large prospective trials are further needed to signify the importance and efficacy of this procedure.

Conclusion:

ABPP is a simple bedside procedure for the treatment of PAL in PSP, SSP and post surgical patients. It is highly efficacious as success rate is 96% in 24 hour, cost effective and side effects and complications are almost negligible. It is a blessing for a country like ours where cost is a important factor in treatment of the patients as by using only 50 mL of patients own blood we can treat and discharge the patient at earliest possible time.

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ORIGINAL ARTICLE

Comparison between Bronchoscopic Morphological Finding and Histopathological Report in Endobronchial Lesion

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Abstract:

Background: *Bronchoscopy and guided techniques have a definite role in diagnosis of endobronchially visible tumors. It allows the sampling of cytological specimens as well as biopsies for histological diagnosis.*

Objective: *This study aims to assess the comparison between bronchoscopic finding and histopathological report in endobronchial lesion.*

Methods: *This cross sectional study was conducted in the Department of Respiratory Medicine in collaboration with the Department of Pathology, National Institute of Diseases of the Chest & Hospital, Mohakhali, Dhaka, from January 2018 to December 2018. 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 90 patients with endobronchial lesions were included in the study. Uncooperative patients, patients with recent myocardial infarction and blood dyscrasias were excluded from the study. 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 90 patients with endobronchial lesions, majority (55.6%) patients belonged to age 41 to 60 years, male: female ratio was 3.3:1. In FOB morphological findings, 59(65.6%) had endobronchial mass followed by 54(60.0%) mucosal edema, 35(38.9%) mucosal infiltration, 22(24.4%) hemorrhagic secretion and 21(23.3%) had mucosal hypertrophy. In histopathology biopsy, majority (36.0%) patients were found squamous cell carcinoma followed by 17(18.9%) adenocarcinoma, 12(13.3%) small cell carcinoma, 3(3.3%) adenocystic carcinoma and 6(6.7%) carcinoid tumour. In squamous carcinoma, 31 patients had endoscopic findings of endobronchial mass followed by 22 had mucosal edema, 13 had mucosal infiltration, 10 had widening of the main carina and 9 had hemorrhagic secretion. In adenocarcinoma, 12 patients had endoscopic findings of mucosal edema, 9 had endobronchial mass, 5 had hemorrhagic secretion and purulent secretion respectively.*

Conclusion: *Our results show that an endobronchial mass is the most common bronchoscopic finding that is suggestive of malignancy. Proportionally, mucosal infiltration is the most common finding in small cell carcinoma. The diagnostic yield and tumour detection rate of flexible bronchoscopy in endoscopically visible lung malignancies is considerably high. For endoscopically visible lung malignancies, forceps biopsy alone has a high diagnostic yield.*

Key words: *Bronchoscopy, endobronchial lesion.*

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Introduction:

Lung cancer is the malignancy with the highest mortality worldwide, being the only one whose incidence of death has progressively increased despite improved and more aggressive therapy in recent years. The mean five-year survival ranges from 13% to 21% and from 7% to 10% in developed and in developing countries, respectively.[1] The prognosis of lung cancer is unfavorable, early diagnosis plays an important role in increasing survival in lung cancer patients. 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.[2] Flexible bronchoscopy plays a central role in the diagnosis of lung malignancy, especially in endobronchial tumours. It allows the sampling of cytological specimens as well as biopsies for histological diagnosis.[3] Prior to the introduction of the fiberoptic bronchoscope, the collection of cytologic specimens directly from the lesion was difficult in many cases. With the advent of the fiberoptic bronchoscope, a biopsy of the lesion by forceps or brushing under direct vision or by fluoroscopic control is possible in the majority of suspected bronchogenic carcinomas.[4] Pulmonologist come across significant number of intrabronchial mass lesions on bronchoscopy.[5] For endoscopically visible tumours, biopsies are the most common method of specimen collection with high diagnostic yield. 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.[6]

Materials and Methods:

This cross sectional study was conducted in the Department of Respiratory Medicine in collaboration with the Department of Pathology, National Institute of Diseases of the Chest & Hospital, Mohakhali, Dhaka, from January 2018 to December 2018. 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 90 patients with endobronchial lesions were included in the study. Uncooperative patients, patients with recent myocardial infarction and blood dyscrasias were excluded from the study. All flexible bronchoscopies were carried out or supervised by the same bronchoscopist using the Olympus BF-1T150 fiberoptic bronchoscope. The patients were made to stay nil per orally for at least 6 hours before the procedure. Written informed consent was obtained from each patient. Topical anaesthesia was achieved with 10% lignocaine spray to the oropharynx and 2% lignocaine solution infused through the scope during the procedure. Once the endobronchial lesion was localized, biopsy was taken using the reusable round cup biopsy forceps FB-20C-1. Whenever possible, at least four biopsies were obtained from the centre of the most abnormal area and the specimens were immediately fixed in formalin and sent for histopathological examination. In each patient, biopsy was followed by bronchial washing. For bronchial washing, 10 to 20 ml aliquots of 0.9% normal saline at room temperature was instilled repeatedly and the aspirate was collected in a plastic trap bottle. The washing and biopsy specimens were sent to the laboratory for cytological and histopathological study respectively. All patients received supplemental oxygen and were monitored throughout the procedure. When the cytological or biopsy specimens showed atypical or suspicious cells, they were considered non diagnostic. 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:

Out of total 90 patients with endobronchial lesions, majority (55.6%) patients belonged to age 41 to 60 years, 69(76.7%) patients were male, 76(84.4%)

were unmarried and 49(54.4%) were farmer (Table-I). All (100.0%) patients were found in fever followed by 90(100.0%) in cough, 71(78.9%) in haemopytysis, 70(77.8%) in weight loss and 66(73.3%) in chest pain. Twenty seven (30.0%) cases, the tumor was located in the upper lobe bronchi, 23.3% being located in the right upper lobe bronchi and 6.7% being located in the left upper lobe bronchi. In the right and left lower lobe bronchi, respectively, tumors were visualized in 6.7% and 15.6% of the cases (Table-II). In FOB morphological findings, 59(65.6%) had endobronchial mass followed by 54(60.0%) had mucosal edema, 35(38.9%) had mucosal infiltration, 22(24.4%) had hemorrhagic secretion and 21(23.3%) had mucosal hypertrophy (Table-III). In BAL cytology, 5(5.6%) patients were found positive for malignant cell (Table-IV). In brush cytology, 47(52.2%) patients were found positive malignancy (Table-V). In histopathology biopsy, majority (36.0%) patients were found squamous cell carcinoma followed by 17(18.9%) adenocarcinoma, 12(13.3%) small cell carcinoma, 3(3.3%) adenocystic carcinoma and 6(6.7%) carcinoid tumour (Table-VI). In squamous carcinoma, 31 patients had endoscopic findings of endobronchial mass followed by 22 had mucosal edema, 13 had mucosal infiltration, 10 had widening of the main carina and 9 had hemorrhagic secretion. In adenocarcinoma, 12 patients had endoscopic findings of mucosal edema, 9 had endobronchial mass, 5 had hemorrhagic secretion and purulent secretion respectively (Table-VII).

Table-I

Demographic characteristics of the study patients (n=90)

	Number of patients	Percentage
Age (years)		
15-40	12	13.3
41-60	50	55.6
>60	28	31.1
Sex		
Male	69	76.7
Female	21	23.3
Marital status		
Married	76	84.4
Unmarried	10	11.1
Widow	4	4.4
Occupational status		
Farmer	49	54.4
Business	10	11.1
Housewife	13	14.4
Service	12	13.3
Driver	2	2.2
Others	4	4.4

Table-II

Complaints of the study patients (n=90)

Complaints	Number of patients	Percentage
Fever	90	100.0
Cough	90	100.0
Haemopytysis	71	78.9
Weight loss	70	77.8
Chest pain	66	73.3
Smoker	60	66.7
Breathlessness	52	57.8
COPD	36	40.0
Co-morbidity		
Tuberculosis	12	13.3
Diabetes mellitus	7	7.8
SOL in liver	4	4.4

Table-III

FOB morphology findings of the study patients (n=90)

FOB finding	Number of patients	Percentage
Endobronchial mass	59	65.6
Mucosal infiltration	35	38.9
Widening of the main carina	19	21.1
Luminal widening	11	12.2
Mucosal hyperemia	13	14.4
Mucosal edema	54	60.0
Mucosal hypertrophy	21	23.3
Serous secretion	2	2.2
Hemorrhagic secretion	22	24.4
Purulent secretion	16	17.8

FOB= Fiber-optic bronchoscope

Table-IV

BAL cytology of the study patients (n=90)

BAL cytology	Number of patients	Percentage
Negative for malignant cell	85	94.4
Positive for malignant cell	5	5.6

BAL= Bronchoalveolar lavage

Table-V

Brush cytology of the study patients (n=90)

Brush cytology	Number of patients	Percentage
Negative	43	47.8
Squamous cell carcinoma	25	27.8
Adenocarcinoma	22	24.4

Table-VI

Histopathology type of the study patients (n=90)

Histopathology type (Biopsy)	Number of patients	Percentage
Squamous cell carcinoma	36	40.0
Adenocarcinoma	17	18.9
Small cell carcinoma	12	13.3
Adenocystic carcinoma	3	3.3
Carcinoid tumour	6	6.7
Normal	16	17.8

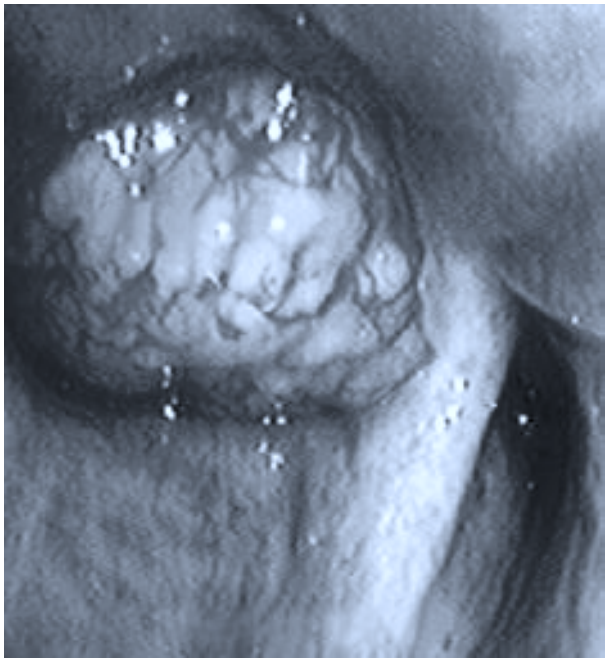

Fig.-1: *Fiberoptic bronchoscopy findings in hypervascular vegetative lesion in the right upper lobe bronchus (squamous carcinoma).*

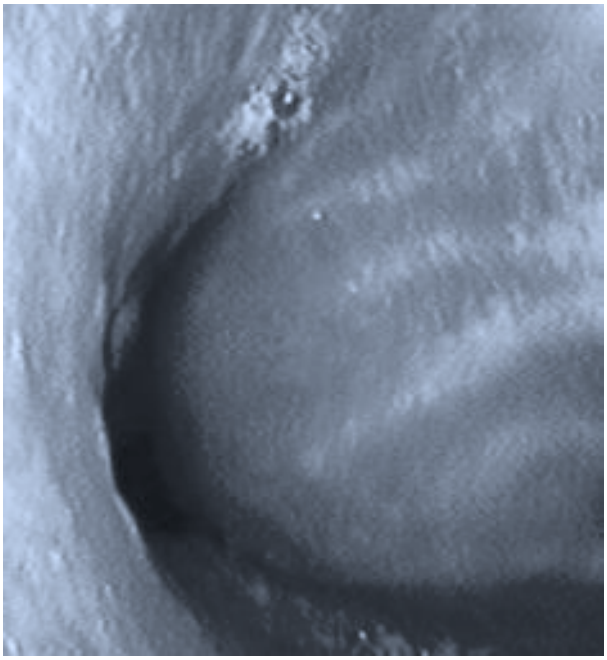

Fig.-2: *Fiberoptic bronchoscopy findings in external compression (adenocarcinoma).*

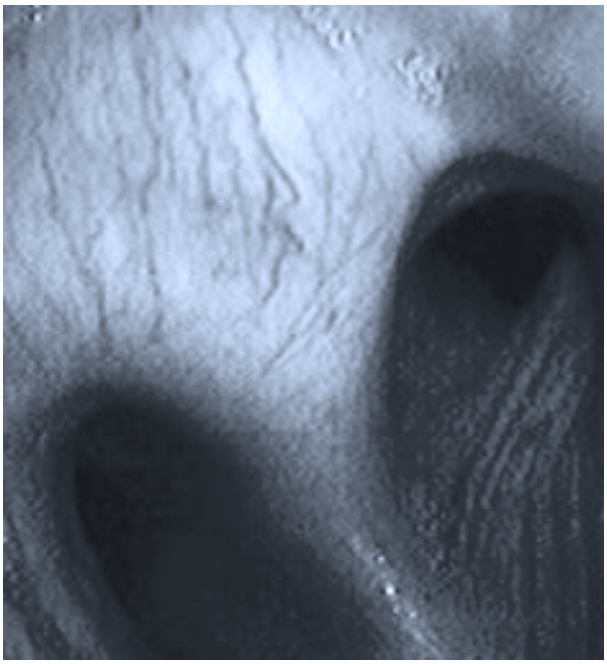

Fig.-3: *Fiberoptic bronchoscopy findings in widening of the main carina*

FOB findings evaluation for malignancy, true positive 73 cases, false positive 12 cases, false negative 1 case and true negative 4 cases in identification by histopathological findings (Table-VIII). The validity of histopathological findings evaluation for malignancy was correlated by

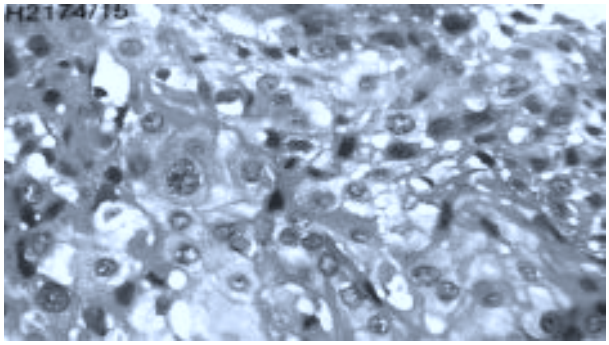

Fig.-4: *Histopathological of biopsy specimen showing features of squamous cell carcinoma.*

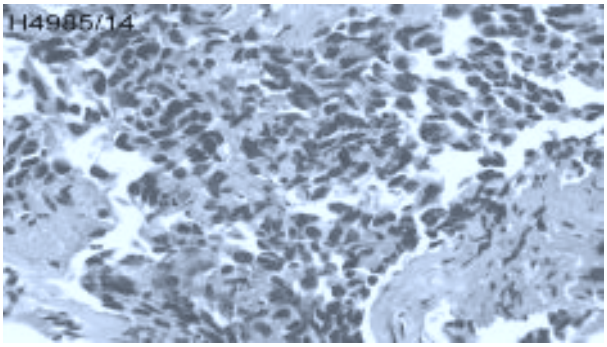

Fig.-5: *Histopathological of biopsy specimen showing features of adenocarcinoma.*

Table-VII

Association between bronchoscopic morphology findings with histopathological findings

FOB findings (morphology)	Histopathological findings				
	Squamous cell carcinoma	Adenocarcinoma	Small cell carcinoma	Adenocystic carcinoma	Carcinoid tumour
Endobronchial mass (n=59)	31	9	7	1	4
Mucosal infiltration (n=35)	13	2	8	1	5
Widening of the main carina (n=19)	10	4	3	0	2
Luminal widening (n=11)	4	3	0	0	3
Mucosal hyperemia (n=13)	2	4	2	0	4
Mucosal edema (n=54)	22	12	9	2	6
Mucosal hypertrophy (n=21)	8	5	3	1	2
Serous secretion (n=2)	1	1	0	0	0
Hemorrhagic secretion (n=22)	9	5	3	2	3
Purulent secretion (n=16)	8	5	1	0	2

Table-VIII

Comparison between histopathological findings and FOB findings evaluation for malignancy

FOB findings (morphology)	Histopathological findings	
	Positive(n=74)	Negative (n=16)
Positive (n=85)	73 (True positive)	12 (False positive)
Negative (n=5)	1 (False negative)	4 (True negative)

calculating sensitivity 98.6%, specificity 25.0%, accuracy 85.6%, positive predictive value 85.9% and negative predictive value 80.0%.

Discussion:

Flexible bronchoscopic examination remains an indispensable minimally invasive tool for diagnosis of lung cancer. However, there remains a

controversy regarding the ideal combination of different bronchoscopic techniques to give the best results.

In this study it was observed that majority (55.6%) patients belonged to age 41 to 60 years, 69(76.7%) patients were male, 76(84.4%) were married and 49(54.4%) were farmer. Ibungo et al.[7] reported that most of the patients (32.9%) belonged to the age group of 71 to 80 years. Majority of the cases of lung malignancies were found in males (70%) when compared to females (30%). Rabahi et al.[8] consisted that 59% patients were male and the mean age was 65 years (range, 14-89 years). Another relevant finding is the age bracket in which the incidence of lung cancer is highest, i.e., the 50-70 year age bracket. In patients younger than 40 years of age, the incidence is lower than 5%.[9,10]

In our study it was observed that all (100.0%) patients were found in fever followed by 90(100.0%) in cough, 71(78.9%) in haemopytysis, 70(77.8%) in weight loss and 66(73.3%) in chest pain. Sareen et al.[11] showed that cough was the most common presenting complaint (62%) followed by dyspnea (55.3%), chest pain (45%) and weight loss (31.67%).

In this study 27(30.0%) cases, the tumor was located in the upper lobe bronchi, 23.3% being located in the right upper lobe bronchi and 6.7% being located in the left upper lobe bronchi. In the right and left lower lobe bronchi, respectively, tumors were visualized in 6.7% and 15.6% of the cases. The most commonly affected sites are the upper lobes and the central sites of the right lung, in 28% of the cases analyzed.[12]

Regarding FOB morphological findings in this study it was observed that 59(65.6%) had endobronchial mass followed by 54(60.0%) had mucosal edema, 35(38.9%) had mucosal infiltration, 22(24.4%) had hemorrhagic secretion and 21(23.3%) had mucosal hypertrophy. Ibungo et al.[7] reported that when all the 95 endobronchial lesions are taken into account, including benign lesions, overall diagnostic yield of bronchoscopy was 90.5%. 7 cases gave inconclusive results (4 cases were lost to follow up while the other 3 did not give consent for repeat bronchoscopy).

In BAL cytology, 5(5.6%) patients were found positive for malignant cell. Rabahi et al.[8] showed that of the 212 patients, 3 did not undergo biopsy and 6 did not undergo BAL. Therefore, 203 patients underwent both procedures. Several studies in the literature have shown that the combination of the two tests results in a higher positivity rate, which ranges from 48% to 95%, depending on whether or not the lesion is endoscopically visible; therefore, we routinely perform lavage and biopsy.[2, 13]

In Brush cytology, 47(52.2%) patients were found positive malignancy. Ibungo et al.[7] documented that of the 73 patients with lung malignancy, a positive diagnosis was established by forceps biopsy in 71 of them giving a diagnostic yield of 97.3%. A positive cytology by bronchial washing was established in 2 cases giving a diagnostic yield of only 2.7%. Both bronchoscopic biopsy and washing were unable to provide diagnosis in 2 cases, in which a definite diagnosis of lung carcinoma was made by other investigations. However the diagnostic yield was reported to be much lower (76.92%) in the study done by Fuladi et al.[14] who recommends adopting all the diagnostic procedures including brushing and washing, in addition to biopsy, in order to increase the overall diagnostic yield.

In histopathology biopsy, majority (36.0%) patients were found squamous cell carcinoma followed by 17(18.9%) adenocarcinoma, 12(13.3%) small cell carcinoma, 3(3.3%) adenocystic carcinoma and 6(6.7%) carcinoid tumour. Ibungo et al.[7] consisted that out of the total 73 confirmed cases of lung malignancies, squamous cell carcinoma was found to be the most common histological type accounting for 76.7% (n=56) followed by small cell carcinoma and adenocarcinoma which were found in 10.9% (n=8) each. 1.4% (n=1) turned out to be adenosquamous type. Similar to the findings of Zavala[15] who reported a diagnostic yield of 97% for forceps biopsy of endoscopically visible lung malignancies. This results are contrary to the findings of the more recently published studies which suggest that adenocarcinoma is the most prevalent lung cancer in India.[16,17] Rabahi et al.[8] reported that of the 212 patients, 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%. The least common

histological type was large cell carcinoma, a finding that is consistent with the literature.[2,10, 18]

In squamous carcinoma, 31 patients had endoscopic findings of endobronchial mass followed by 22 had mucosal edema, 13 had mucosal infiltration, 10 had widening of the main carina and 9 had hemorrhagic secretion. In adenocarcinoma, 12 patients had endoscopic findings of mucosal edema, 9 had endobronchial mass, 5 had hemorrhagic secretion and purulent secretion respectively. Rabahi et al.[8] reported that of the patients with squamous carcinoma, 58 (74%) had endoscopic findings of an endobronchial mass, 28 (36%) had mucosal infiltration, 8 (10%) had lumen narrowing, and 5 (6%) had external compression. Of the 41 patients diagnosed with adenocarcinoma, 20 (49%) had an endobronchial mass, 13 (32%) had mucosal infiltration, 9 (22%) had lumen narrowing, and 10 (24%) had external compression. Of the 25 patients diagnosed with small cell carcinoma, 16 (64%) had an endobronchial mass, 15 (60%) had mucosal infiltration, none (0%) had lumen narrowing, and 6 (24%) had external compression. Adenocarcinoma was most commonly located in peripheral areas and showed indirect findings, such as bronchial obstruction and external compression, which are endoscopically invisible, or no findings at all.[12] The reason for this could be due to the central location of these tumours which are easier to assess by bronchoscopy when compared to adenocarcinomas which have a predominantly peripheral location which makes them nonvisible endoscopically. However, similar findings of squamous cell carcinoma as the predominant type were reported in certain other studies[19,20] of the total 73 confirmed lung malignancies, both bronchoscopic procedures i.e, biopsy and bronchial washing, failed to give a definite diagnosis in 2 cases.

In this study, FOB findings evaluation for malignancy, true positive 73 cases, false positive 12 cases, false negative 1 case and true negative 4 cases in identification by histopathological findings. The validity of histopathological findings evaluation for malignancy was correlated by calculating sensitivity 98.6%, specificity 25.0%, accuracy 85.6%, positive predictive value 85.9% and negative predictive value 80.0%. Chowdhury[18] reported that 175 cases subjected to bronchoscopy, lung cancer was confirmed in 146 (83.4%) cases by histopathology of bronchial biopsy. Similar study Ibungo et al.[7] reported that 73 patients with lung malignancy, a positive diagnosis was established by forceps biopsy in 71 of them giving a diagnostic yield of 97.3%.

Conclusion:

Our results show that an endobronchial mass is the most common bronchoscopic finding that is suggestive of malignancy. Proportionally, mucosal infiltration is the most common finding in small cell carcinoma. The diagnostic yield and tumour detection rate of flexible bronchoscopy in endoscopically visible lung malignancies is considerably high. For endoscopically visible lung malignancies, forceps biopsy alone has a high diagnostic yield.

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ORIGINAL ARTICLE

Association of CA-125 with Pulmonary Tuberculosis

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Abstract

***Background**: Ca-125, a biochemical marker may be increased in malignant diseases, like ovarian cancer but also in other medical conditions, such as pulmonary and extrapulmonary tuberculosis. This cross sectional observational study was aimed to find out any association of CA 125 with pulmonary tuberculosis.*

***Methods**: A total of 75 new cases of both smear positive & smear negative pulmonary tuberculosis were enrolled in this study, which was conducted at the Department of Respiratory Medicine in National Institute of Diseases of the Chest and Hospital from June 2018 - June 2019. **Results**: Out of 75 pulmonary tuberculosis patients, half (45.3%) patients belonged to age 21-40 years. The mean age was found 43.5±17.2 years. Almost three fourth (74.7%) patients were male and 19 (25.3%) patients were female. Male female ratio was 2.9:1. Majority 30(40.0%) patients completed primary education level. More than one third (36.0%) patients were service holder. Majority (90.7%) patients were married. More than half (56.0%) of the patients came from rural area. Average monthly income was 25680.0±38050.2 taka. Almost two third (62.7%) patients were smoker. The mean Hb was found 11.2±1.3 gm/dl, mean total count of WBC was 10837.7±4132.8 /mm^3, mean ESR was 69.5±27.2 mm in 1st hour, mean MT was 13.9±4.4. Almost two third (64.0%) patients were found patchy opacity followed by 17(22.7%) consolidation, 3(4.0%) cavitary lesion, 2(2.7%) pneumothorax and 2(2.7%) patchy opacity with cavitary lesion. Majority (93.3%) patients were found in abnormal (e"36 U/ml) CA-125. The CA-125 was found 68.3±31.2 U/ml with range from 8.8 to 197.0 U/ml. Only 3(4.0%) patients had diabetes mellitus. Almost three fourth (73.3%) patients was found positive sputum for AFB and 20(26.7%) was negative sputum for AFB. In positive sputum for AFB, 23(41.8%) patients were found two number of zone involved followed by 13(23.6%) were one, 11(20.0%) were three and 8(14.5%) were more than three number of zone involved. Mean CA-125 was found 44.5±13.1 U/ml in negative sputum for AFB and 77.0±31.4 U/ml in positive sputum for AFB. The difference was statistically significant (p <0.05) between two groups. Significant association was found between CA-125 level with number of zone involved and sputum for AFB respectively. Positive significant correlation was found between number of zone involved (r=0.590; p=0.001) and sputum for AFB (r=0.852; p=0.001) with CA-125 level respectively.*

***Conclusion:** In conclusion the present study shows that CA-125 level was significantly higher in positive sputum for AFB patients than negative patients. CA-125 level was significantly associated with number of zone involved. Positive significant correlation was between number of zone involved and sputum for AFB with CA-125 level respectively. Serum CA-125 may be used as a marker for diagnosis of active pulmonary tuberculosis especially when tuberculosis is suspected clinically and radiologically in patients without sputum production or sputum negative for AFB. Serum CA-125 may be used as a marker in assessment of severity of active pulmonary tuberculosis.*

***Keywords:** Cancer antigen 125 (CA-125), Pulmonary tuberculosis*

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Introduction

Tuberculosis represents an important health problem worldwide that was declared by World Health Organization (WHO) to be global emergency.[1] The World Health Organization estimates that each year more than 8 million new cases of tuberculosis occur and approximately 3 million persons die from the disease. Ninety-five percent of tuberculosis cases occur in developing countries.[2] TB currently holds the seventh place in the global ranking of causes of death. Unless intensive efforts are made, it is likely to maintain that position through to 2020.[3] Pulmonary TB, the most important type of TB from the public health point of view, can be diagnosed by its symptoms, chest radiography, CRP, TST, MT, ESR, sputum smear microscopy, and by cultivation of M. tuberculosis.[4] However, in some cases of pulmonary TB, acid-fast bacilli stains in sputum samples may be negative or respiratory specimens may not be available, and other methods have to be used to establish the diagnosis of TB. Recent advances in the field of molecular biology have provided new tools for the rapid diagnosis of TB by molecular methods. However, the high cost of most of these techniques, and their requirement for sophisticated equipment or highly skilled personnel have precluded their implementation on a routine basis, especially in low-income countries.[5] Apart from microbiological molecular diagnostic tests, different biochemical parameters have been proposed as helpful tools for this purpose, including various markers of cellular activity, acute phase reactants and enzymes.[6-10] The tumor marker Cancer antigen 125 has been proposed as a useful diagnostic tool for tuberculosis.[11]

Ca 125 is most consistently elevated in epithelial ovarian cancer, but can be expressed in a number of gynecologic (endometrial, fallopian tube) and non-gynecologic (pancreatic, breast, colon and lung) cancers.[12] High levels of Ca-125 have been reported in patients with pulmonary disease.[13-17] In pulmonary TB, it was claimed that raised levels of Ca 125 can greatly increase the likelihood of tuberculosis activity. The diagnostic value of Ca-125 to help differentiate pulmonary tuberculosis from other pulmonary infections has been poorly studied.[13-15] Serum CA-125 may be used as a marker in assessment of severity of active pulmonary tuberculosis.

Materials and methods

Study subjects

With approval of protocol by Institutional Review Board of National Institute of Diseases of the Chest and Hospital (NIDCH), this cross sectional observational study was carried out in the Department of Respiratory Medicine in NIDCH, Mohakhali, Dhaka during the period from January 2018 to December 2018, to find out any association of CA 125 with pulmonary tuberculosis.

For this purpose, a total of 75 new pulmonary tuberculosis (both smear positive and smear negative) patients were attending in the above hospital were included this study. Active malignancy, patient with benign gynaecological lesions (eg: PID, endometriosis), malignant gynaecologicaltumours, pregnancy, menstruating women, liver cirrhosis, renal failure and heart failure patients were excluded from the study.

Data analysis

All data were analyzed by using computer based SPSS 23 (statistical package for social sciences). Data were presented in frequency, percentage and mean and standard deviation as applicable. Mann Whitney U test and ANOVA test was used for continuous variables as shown cross tabulation. Spearman's rank correlation coefficient was used for number of zone involved and sputum for AFB with CA-125 level. P value of less than 0.05 was considered as significant.

Results:

Table-I

Baseline characteristics of the study subjects (n=75)

Variables	
Male/female (n)	56/19
Age (years)	43.5±17.2
Smoker (%)	62.7
Diabetes mellitus (%)	96
Monthly income (taka)	25680.0±38050.2
Hb (gm/dl)	11.2±.3
Total count of WBC (/mm^3)	10837.7±4132.8
ESR (mm in 1^{st} hour)	69.5±27.2
MT	13.9± 4.4
CA-125 (U/ml)	68.3±31.2

Continuous variables reported as mean±SD & categorical variables as absolute or relative frequencies.

Table-II

Distribution of the study patients according to sputum for AFB (n=75)

Sputum for AFB	Number of patients	Percentage
Negative	20	26.7
Positive	55	73.3
+	18	24.0
++	19	25.3
+++	18	24.0

Table 2 shows that 55(73.3%) patients was found positive sputum for AFB and 20(26.7%) was negative sputum for AFB.

Table-III

Distribution of the study patients according to CA-125 (n=75)

CA-125 (U/ml)	Number of patients	Percentage
0-35 U/ml (Normal)	5	6.7
≥36 U/ml (Abnormal)	70	93.3
Mean ±SD	68.3±31.2	
Range (min-max)	8.8-197.0	

Table 3 shows that majority (93.3%) patients were found in abnormal (≥36 U/ml) CA-125. The CA-125 was found 68.3±31.2U/ml with range from 8.8 to 197.0 U/ml.

Table-IV

Distribution of the study patients according to number of zone involved in chest X-ray (n=55)

Number of zone involved	Number of patients	Percentage
1	13	23.6
2	23	41.8
3	11	20.0
>3	8	14.5

In positive sputum for AFB, 23(41.8%) patients were found two number of zone involved followed by 13(23.6%) were one, 11(20.0%) were three and 8(14.5%) were more than three number of zone involved.

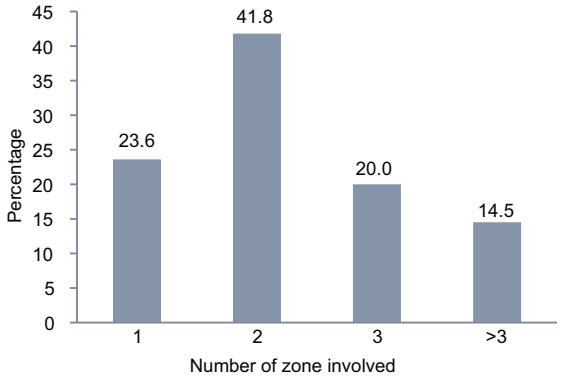

Fig.-1: *Bar diagram showing number of zone involved of the study patients.*

Table-V

Association between CA-125 with sputum for AFB (n=75)

	Sputum for AFB		P value
	Negative (n=20) Mean±SD	Positive (n=55) Mean±SD	
CA-125 (U/ml)	44.5±13.1	77.0±31.4	0.001[s]
Range (min-max)	8.8-56.0	20.0-197.0	
Mean rank	15.58	46.15	

s= significant

P value reached from Mann-Whitney U test

Table 5 shows that mean CA-125 was found 44.5±13.1 U/ml in negative sputum for AFB and 77.0±31.4 U/ml in positive sputum for AFB. The difference was statistically significant (p<0.05) between two groups.

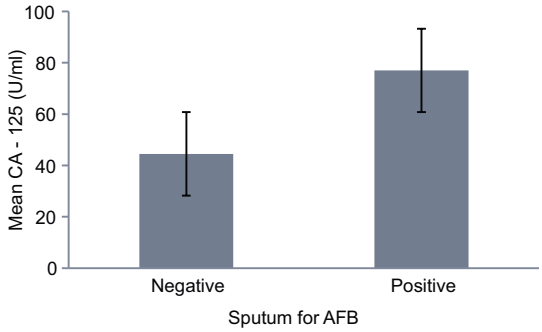

Fig.-2: *Bar diagram showing association between CA-125 with sputum for AFB.*

Table -VI

Association between CA-125 with number of zone involved in chest X-ray (n=55)

Number of zone involved	n	Mean±SD	Min-max	P value
1	13	52.6±18.7	20.0-78.0	
2	23	73.3±10.6	55.0-100.0	0.001[s]
3	11	94.4±42.8	46.9-177.0	
>3	8	103.6±39.9	70.0-197.0	

s= significant
P value reached from ANOVA test

Thirteen patients were found one number of zone involved and their mean CA-125 was found 52.6±18.7 U/ml. Twenty three patients were found two number of zone involved and their mean CA-125 was found 73.3±10.6 U/ml. Eleven patients were found three number of zone involved and their mean CA-125 was found 94.4±42.8 U/ml. Eight patients were found more than three number of zone involved and their mean CA-125 was found 103.6±39.9 U/ml. The difference was statistically significant (p<0.05) among four groups.

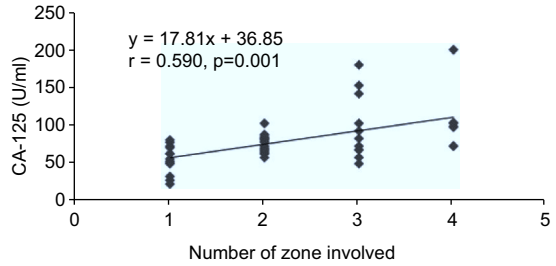

Fig.-3: *Scatter diagram showing positive significant correlation (r=0.590; p=0.001) between number of zone involved and CA-125.*

Table-VII

Association between CA-125 with level of sputum for AFB (n=55)

Sputum for AFB	n	Mean±SD	Min-max	P value
Negative	20	44.5±13.1	8.8-56.0	
+	18	55.6±18.8	20.-100.0	0.001[s]
++	19	69.8±7.9	46.9-80.0	
+++	18	106.0±35.7	70.0-197.0	

s= significant
P value reached from ANOVA test

Twenty patients were found negative sputum for AFB and their mean CA-125 was found 44.5±13.1 U/ml. Eighteen patients were found one plus for AFB and their mean CA-125 was found 55.6±18.8 U/ml. Nineteen patients were found two plus for AFB and their mean CA-125 was found 69.8±7.9 U/ml. Eighteen patients were found three plus for AFB and their mean CA-125 was found 106.0±35.7 U/ml. The difference was statistically significant (p<0.05) among four groups.

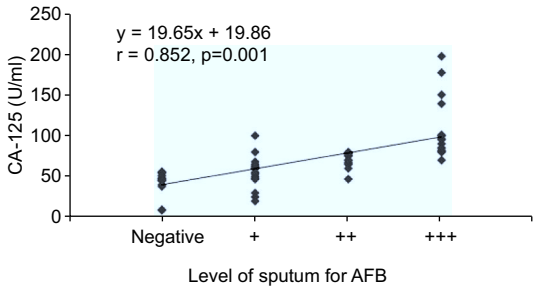

Fig.-4: *Scatter diagram showing positive significant correlation (r=0.852; p=0.001) between sputum for AFB and CA-125.*

Discussion

Pulmonary TB, the most important type of TB from the public health point of view, can be diagnosed by its symptoms, chest radiography, sputum smear microscopy, and cultivation of M. tuberculosis.[4] However, in some cases of pulmonary TB, Acid Fast Bacilli stains in sputum samples may be negative or respiratory specimens may not be available, and other methods have to be used to establish the diagnosis of TB.[5] The tumor marker Cancer antigen 125 has been proposed as a useful diagnostic tool for tuberculosis.[11] High levels of Ca-125 have been reported in patients with pulmonary and extra-pulmonary tuberculosis, including pleural, peritoneal, pelvic, miliary, and intraabdominal disease.[16-17]

This cross sectional, observational study was carried out with an aim to observe any positive association of serum CA 125 level with pulmonary tuberculosis.

A total of 75 pulmonary tuberculosis patients were attending in the Department of Respiratory Medicine in National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka during the period from June 2018 - July 2019 were included in this study. PTB cases (both smear positive and smear negative) were enrolled in this

study. Active malignancy, patient with benign gynaecological lesions (eg: PID, endometriosis), malignant gynaecologicaltumours, pregnancy, menstruating women, liver cirrhosis, renal failure and heart failure patients were excluded from the study. The present study findings were discussed and compared with previously published relevant studies.

In this present study it was observed that almost half (45.3%) patients belonged to age 21-40 years. The mean age was found 43.5±17.2 years with range from 18 to 83 years. El Hoshy et al.[18] found their study the age of the studied patients ranged from 26 to 60 years with a mean of 44.87± 13.557 years. In a study conducted by Said et al.[19] where they showed mean age was 36.5 years with range of 15–70. Mohammad et al.[20] reported that mean age was 34.2±15.15 years with range of 19–75. Another study conducted by Sahin and Yildiz where they consisted mean age was 35.62±9.48 years.[21]

In this study it was observed that almost three fourth (74.7%) patients were male and 19(25.3%) patients were female. Male female ratio was 2.9:1. Similarly, Sahin and Yildiz suggested males were 26(61.9%) and females were 16(38.1%).[21] Said et al.[19] demonstrated their study males were 14(51.9%) and females were 13(48.1%). Another study conducted by El Hoshy et al.[18] where they documented 12 patients (60%) were males whereas 8 patients (40%) were females.

In this current study it was observed that 30(40.0%) patients completed primaryeducation, 18(24.0%) completed SSC, 16(21.3%) completed HSC, 6(8.0%) completed secondary and 5(6.7%) completed graduate. Zuberi et al.[22] found 38.55% below Matric, 61.45% Matric and above level.

In this series it was observed that more than one third (36.0%) patients were service holder followed by 15(20.0%) were businessman, 15(20.0%) were farmer, 11(14.7%) were housewives, 5(6.7%) were student, 1(1.3%) was worker abroad and 1(1.3%) was rickshaw puller. Majority (90.7%) patients were married, 6(8.0%) were unmarried and 1(1.3%) was divorce. More than half 42(56.0%) of the patients come from rural area and 33(44.0%) from urban area. Average monthly income was found 25680.0±38050.2 taka with range from 10000 to 300000 taka. Smoker was found 47(62.7%) and non smoker was 28(37.3%).

In this present study it was observed that mean Hb was found 11.2±1.3gm/dl with range from 8.0 to 14.0 gm/dl. The mean total count of WBC was found 10837.7±4132.8 /mm^3 with range from 3380.0 to 29700.0 /mm^3. Mean MT was found 13.9±4.4with range from 5.0 to 22.0.

In this current study it was observed that mean ESR was found 69.5±27.2mm in 1^{st} hour with range from 20.0 to 142.0 mm in 1^{st} hour. Mohammad et al.[20] found their study mean ESR was 51.13±19.99 mm in 1^{st} hour with range from 22 to 100.

In this study it was observed that almost two third (64.0%) patients were found patchy opacity followed by 17(22.7%) consolidation, 3(4.0%) cavitary lesion, 2(2.7%) pneumothorax and 2(2.7%) patchy opacity with cavitary lesion. Mohammad et al.[20] observed their study serum CA 125 levels in group I was significantly higher in far advanced and moderate advanced disease than minimal lesion one. These results were in agreement with those reported by Kanagarajan et al.[23] who studied CA-125 as a reliable serum marker for diagnosis of tuberculosis, and found that levels of CA-125 were the highest in cavitary pulmonary TB and in military TB, so they concluded that we can take CA 125 as one of the parameters in the assessment of severity of TB. Also these results were in agreement with those reported by Kim et al.[24] who found that CA-125 levels appeared to be the highest in patients with cavitary rather than nodular type and this may reflect the level or extent of the infection. Said et al.[19] also consisted their study 20 patients (74%) of active pulmonary tuberculosis had a moderate advanced lesion on chest X-ray and 7 patients (26%) had a far advanced lesion. No patients had a minimal lesion on chest X-ray.

In this series it was observed that majority (93.3%) patients were found in abnormal (e"36 U/ml) CA-125. The CA-125 was found 68.3±31.2U/ml with range from 8.8 to 197.0 U/ml. Similar study documented by Mohammad et al.[20] where reported that mean Ca 125 levels was 65.58 ±69.77 U/ml with range from 4.5 to 285.5. El Hoshy et al.[18] demonstrated their study mean ± SD level of CA125 in pleural fluid was 41.732 ±20.744 U/ml. In Yilmaz et al.[25] study, the mean Ca-125 level in patients

with active pulmonary tuberculosis was (109.7 ±86.9 U/ml), while it was (118.46± 248.41 U/ml) in Ozsahin et al.[26] study which are to some extent close to the value in the present study (93.5± 138.9 U/ml). On the other hand, Kim et al.[24] study showed a lower mean value of Ca 125 in patients with active pulmonary TB (54.5± 22.4) than in our study. This may be due to the difference in ways of the diagnosis of tuberculous patients. They depend on sputum culture while in this research; we depended on sputum smear-probably with a higher bacillary load than culture. Another study conducted by Fortun et al.[11] where suggested that mean Ca 125 value was 59.5 (± 88.5) IU/ml and the median was 31 (range: 13 to 63)

In this study it was observed that 55(73.3%) patients was found positive sputum for AFB and 20(26.7%) was negative sputum for AFB. Sputum for AFB +, ++ and +++ was found 24.0%, 25.3% and 24.0% respectively. Mohammad et al.[20] observed their study 28 cases (70%) of group I were sputum positive while 12 cases (30%) were sputum negative for AFB. sputum for AFB +, ++ and +++ was 25.0%, 30.0% and 15.0% respectively. Kim et al.[24] studied the clinical significance of CA-125 in pulmonary tuberculosis, his study included 100 patients with active pulmonary tuberculosis that were divided into 47 (47%) patients with positive sputum and 53 (53%) patients with negative sputum. Another study documented by Tasc1 et al.[25-27] where they showed sputum smear results of the 54 patients with pulmonary TB were as follows: four positive acid-fast bacilli in five patients (9.2%), three positive in 16 patients (33.7%), two positive in seven patients (7.7%), and one positive in seven patients (7.7%).

In positive sputum for AFB, 23(41.8%) patients were found two number of zone involved followed by 13(23.6%) were one, 11(20.0%) were three and 8(14.5%) were more than three number of zone involved.

In this present study it was observed that mean CA-125 was found 44.5±13.1 U/ml in negative sputum for AFB and 77.0±31.4 U/ml in positive sputum for AFB. The difference was statistically significant (p<0.05) between two groups. Mohammad et al.[20] found their study there was a statistically significant difference in serum CA 125 levels in group I regarding the results of sputum analysis for AFB. Kim et al.[24] found that CA-125 was higher in patients with positive sputum for AFB than those with sputum negative pulmonary tuberculosis. In the study, there was a statistically significant difference between sputum negative pulmonary tuberculosis in group I and group II regarding CA 125.

In this current study it was observed that 13 patients were found one number of zone involved and their mean CA-125 was found 52.6±18.7 U/ml. Twenty three patients were found two number of zone involved and their mean CA-125 was found 73.3±10.6 U/ml. Eleven patients were found three number of zone involved and their mean CA-125 was found 94.4±42.8 U/ml. Eight patients were found more than three number of zone involved and their mean CA-125 was found 103.6±39.9 U/ml. The difference was statistically significant (p<0.05) among four groups. Positive correlation (r=0.590; p=0.001) between number of zone involved and CA-125.

In this series it was observed that 20 patients were found negative sputum for AFB and their mean CA-125 was found 44.5±13.1 U/ml. Eighteen patients were found one plus for AFB and their mean CA-125 was found 55.6±18.8 U/ml. Nineteen patients were found two plus for AFB and their mean CA-125 was found 69.8±7.9 U/ml. Eighteen patients were found three plus for AFB and their mean CA-125 was found 106.0±35.7 U/ml. The difference was statistically significant (p<0.05) among four groups. Tasc1 et al.[27] Therefore, the present authors claim that CA 125 can be used in the monitoring of treatment response in pulmonary TB patients. Fortun et al.[11] reported that CA 125 values increase in patients with pul-monary TB and decrease to normal values during treatment. According to reported articles, the CA 125 level evaluated in patients with a negative sputum acid-fast bacillus stain. Huang et al.[28] suggested that CA 125 serum levels – in combination with clinical responses, chest radiography, and sputum examinations – can offer improved monitoring of therapeutic responses in anti-TB treatment.

In this study it was observed that positive correlation (r=0.852; p=0.001) was found between

sputum for AFB and CA-125. Similarly, Tasc1 et al.[27] consisted their study higher serum CA 125 levels were obtained from the patients with a higher degree of sputum smear positivity ($r = 0.341$, $P = 0.012$).

Conclusion

In conclusion the present study shows that CA-125 level was significantly higher in smear positive patients as well as negative one.CA-125 level was significantly associated with number of zone involved. Positive significant correlation was found between number of zone involved in chest X-ray and sputum for AFB with CA-125 level respectively. Like pleural fluid ADA, Ca-125 may augment diagnosis of pulmonary tuberculosis, specially the smear negative cases where other radiological and clinical evidence suggests the diagnosis. Serum CA-125 may be used in assessment of severity of active pulmonary tuberculosis.

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Author Contribution:

Conflict Of Interest: The authors of this paper have declared that there is no conflict of interest to any of the authors.

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Chest Heart Journal
Vol. 43, No. 1, January 2019

REVIEW ARTICLE

ACO (Asthma COPD Overlap)

Shamim Ahmed[1], Md. Atiqur Rahman[2], Shah Ashiqur Rahman Ashiq Choudhury[3], Subrata Kumar Gain[4]

Abstract:

Asthma-COPD overlap (ACO), which was previously called asthma-COPD overlap syndrome, happens when the patient has symptoms of both asthma and chronic obstructive pulmonary disease (COPD). The worldwide prevalence of ACO has been markedly increased over last few decades and it is associated with increased morbidity and mortality than Asthma or COPD alone. There have been several criteria and hypotheses proposed regarding diagnosis of ACO. Among them "Spanish Criteria" is most notable. Till now the treatment strategy remains same for ACO as for Asthma and COPD. As this is quite an up to the minute concept so further research and experiments are gravely needed to build a formidable management guideline to fight against ACO.

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Introduction:

ACO is a new term and new scientific concept in the practice of Respiratory medicine. It means Asthma-COPD overlap. In our day to day practice we find some patients who have the features of asthma as well as the features of COPD. Asthma is often confused with COPD when present in individuals with significant smoking history over the age of 40(GINA, 2019).So those patients who have features of both asthma and COPD are called ACO (Asthma COPD overlap). Previously it was called "ACOS" or Asthma COPD overlap syndrome.

The syndrome was first described in 2014, when the Global Initiative for Asthma (GINA) and Global Initiative for Chronic Obstructive Lung Disease (GOLD) committee released a common document on the Asthma-COPD Overlap (ACO)[1]. But since 2017, it has been called "ACO."

The" Global Initiative for Asthma (GINA)" has recommended use of the term "ACO" rather than "ACOS", to avoid giving the impression that this is a single disease and the term "syndrome" suggests a condition of unknown origin in which the clinical symptoms and/or laboratory findings indicate a common patho-physiologic mechanism.

Definition:

If we want to study a disease we must define it. Unfortunately there is no formal definition of ACO. This is simply a description because there has no consensus been made among various groups and authors so far. So it is not properly defined yet. But as a whole, when a patient has both the features of asthma and COPD it can be defined as ACO. This is none but a working definition. Both GINA and GOLD (Global Initiative for Obstructive Lung disease) are trying to formulate a definition but till now no subjective or quantitative definition has been proposed. Also the approach previously stated by the GINA and GOLD which was a stepwise approach; it is not advised or followed now. So, various respiratory societies all over the world are following their own practical experience to tackle this disease.

Why ACO?

It is very important to have a sound knowledge about ACO as because:

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1. ACO is associated with increased morbidity and mortality than Asthma or COPD alone.
2. Increased number of exacerbation and hospitalization.
3. Very few randomized control trials (RCT) are available as in asthma trials, smokers are excluded and in COPD trials, asthmatics are excluded.

Every medical personnel should know about this condition to deliver better healthcare. Hence, it is essential to diagnose and treat ACO at an early stage.[2]

Worldwide prevalence:

Most estimates prevalence of ACO among asthma patients appears to be slightly higher, with estimates ranging 27.1%–38%, whereas estimates of ACO among COPD patients appear to be slightly lower, ranging mostly from 13%–28.6%.[3]

Bangladesh Perspective:

A study conducted by DG health and Biostatistics department showed that 22% adult people aged more than 40 years are suffering from obstructive lung disease who fill the category of ACO.The prevalence of ACO was found 7.8% in rural areas of Matlab, Bangladesh. Exposure to biomass fuel smoke may be a contributing risk factor for this high prevalence).[4]

Dutch Hypothesis and British Hypothesis:

If we talk about ACO, interestingly we should consider two hypotheses; Dutch hypothesis and British hypothesis. In 1961 "Orie" reported that there are patients who have manifestations of bronchial asthma and chronic obstructive pulmonary disease and that common pathogenetic mechanisms may underlie disease pathogenesis in selected patients with those disease.[5] But the British hypothesis denied it mentioning "asthma and COPD are different in clinical aspect and also in aetiology" Now the enchanting fact following those two hypotheses, ACO finally brings asthma and COPD to the same point.

How to Diagnose?

Patients with ACO are characterized by increased reversibility of airflow obstruction, eosinophilic bronchial and systemic inflammation, and increased response to inhaled corticosteroids, compared with the patients with COPD alone.[6] It is pretty much difficult as well as intricate to diagnose ACO as there is no clear cut criteria; specially when this diagnosis is done much more on experience basis. In the year 2012, The Spanish Respiratory Society first tried to formulate a guideline defining some major and some minor criteria which later became familiar as "Spanish criteria." These criteria include:

Major criteria:

- Documented history of asthma before 40 years of age
- Sputum Eosinophilia
- Post bronchodialator reversibility of FEV_1 is more than 15% from baseline values and 400 mL

Minor criteria:

- Documented history of Atopy
- Post bronchodialator reversibility of FEV1 ≥200 mL and 12% from baseline values on 2 or more visits
- Elevated total IgE level

However, these criteria are neither sensitive nor specific. Recently all the respiratory societies of the world have recommended diagnosing of ACO on the basis of history, clinical features and a few investigations. These history and clinical features include patient's age>40 years, asthma patients with longstanding history of smoking or smoking equivalents like indoor or outdoor air pollution, clinical features of asthma or COPD like shortness of breath, cough with sputum production, wheeze or chest tightness, COPD patients with history of allergic manifestations or atopy like rhinitis or eczema etc. Also we can perform some investigations in these patients before labeling it as ACO, such as: Chest x-ray to see any hyperinflation, CT scan of chest will provide further detailed information regarding lung parenchymal changes, Diffusing capacity of the lungs for carbon monoxide (DLCO) to see how much oxygen travels from the alveoli of the lungs to the blood stream in COPD. Spirometry is a must to do investigation. Post bronchodialator FEV_1 and FVC ratio less than 70% and increase of FEV_1 more than 15% and 400 mL will go more in favour of ACO. We can also perform other investigations like sputum and

peripheral blood Eosinophil, Fractional exhaled Nitric Oxide test (FENO)in sputum and some bronchoprovocation and bronchial reversibility tests. So meticulous history taking, clinical features and some relevant investigations are the pre-requisite to diagnose ACO accurately. In a country like Bangladesh there are many patients who cannot afford those costly investigations. For them we should put our focus more on clinical features and some preliminary investigations. In a nutshell; if a patient visits us whose age is more than 40 years, smoker for a long time, have features of COPD and also have features of atopy or allergy should be diagnosed as ACO rather than asthma or COPD alone.

Treatment:

Basically ACO should be treated promptly because it causes more morbidity and exacerbation that asthma or COPD alone. The treatment is same as for asthma or COPD. That means for asthma the choice of treatment is corticosteroids and for COPD the choice of treatment is bronchodialators. In ACO we should give both corticosteroids and bronchodilators. Long acting bronchial agonists (LABA) and inhaled corticosteroids (ICS) combination is the key in treating ACO in addition to antihistamines. Adjunctive treatments such as leukotriene receptor antagonists, 5-lipoxygenase inhibitors, methylxanthines, or omalizumab deserve further study and should be administered by pulmonary or allergy subspecialists.[8] Other management options include smoking cessations, regular exercise, vaccination, pulmonary rehabilitation. These are also important as a part of treatment as well as reducing the number of exacerbations in ACO patients. Sound knowledge of the disease, detailed information regarding the drugs used in ACO, early diagnosis and prompt treatment are the mainstay of ACO management. The major disadvantage is that it groups patients with very different characteristics under the ACO's umbrella. In view of this heterogeneity, we recommend a strategy of defining specific and measurable therapeutic objectives for every single patient and identifying the traits that can be treated to achieve those objectives.[9]

Prognosis:

Prognosis of ACO is relatively better than COPD or persistent asthma if we treat this condition effectively and also according to the consensus. In our country we do have good support system and also we have available drugs to treat this condition properly.

Future Development:

As this a new terminology, we need more research to unveil further patho-physiology, genetic and host factors, specific investigations and drugs related to ACO. The ideal study would be a longitudinal prospective population study that follows anyone with respiratory symptoms, involving the whole spectrum of future disease. Such a study would then involve robust measurements like spirometry with reversibility, body box, small airway function, AHR, blood cells and constituents, DNA and nasal epithelial cells for (epi)genetic assessments as easy accessible tools separately from bronchoscopies that are more invasive, and computed tomography, to dissect the different subsets of airway and parenchymal diseases.[10] Especially our new generation can initiate it but our pharmaceutical companies should come forward to provide logistical and financial support to aid this research to find out more information, remedies and also for the better management of this condition.

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CASE REPORT

Endobronchial Intracavitary Fluconazole Irrigation for the Treatment of Pulmonary Mycetoma Complicating Fibrocystic Old Pulmonary Tuberculosis –A Case Report

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Abstract:

Pulmonary mycetomas often occur in fibrocystic old pulmonary tuberculosis. When this condition is complicated by hemoptysis or other overt symptoms definitive surgery is usually precluded because of poor lung function. Intracavitary antifungal therapy has been described for the treatment of symptomatic pulmonary mycetomas. We report the first use of intracavitary fluconazole in the management of a Aspergillus fumigatus *pulmonary mycetoma complicated by paroxysmal cough in a patient with fibrocystic old tuberculosis.*

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Introduction:

Pulmonary mycetoma formation in fibrocystic pulmonary tuberculosis is common[1] and may cause significant hemoptysis[2]. In addition to the more commonly reported *Aspergillus* species, *Pseudallescheria boydii* complex, of which *Pseudallescheria angusta* is a part[3], has been described as an etiologic agent of pulmonary mycetomas in these patients[4,5]. Treatment of this condition is problematic as surgery, the definitive therapy, is often precluded because of poor pulmonary function[6] Although previous reports have described intracavitary antifungal therapy in symptomatic pulmonary mycetoma[6], the use of intracavitary fluconazole, to our knowledge, has not been reported in the literature in Bangladesh We discuss a case with fibrocystic old tuberculosis complicated by pulmonary mycetomas presented with hemoptysis and intractable cough and dyspnea that was successfully treated with intracavitary fluconazole.

Case Report:

A 45 year-old Bangladeshi man with proven fibrocystic post pulmonary tuberculosis presented with blood tinged sputum with persistent cough, and dyspnea. He had no chest pain, fever, chills, or night sweats. He had a history smear positive *pulmonary tuberculosis* infection treated with anti TB drug CAT-I four years back

The patient was admitted to NIDCH in medical ward. His physical examination at admission was unremarkable. His hemoglobin 12.1 g/dl, a normal WBC, and normal coagulation parameters (INR 1.05, PTT 23.3 sec). Pulmonary function testing revealed moderate restriction with an FVC of 2.45 l (66% of predicted), FEV1 2.01 l (69% of predicted), and FEV1/FVC ratio 0.82. Chest CT demonstrated enlargement of the LUL cavities. Fibre optic Bronchoscopy was done, it shows a large irregular cavity containing a fairly large lobulated whitish movable ball which moved with suction and BAL was taken and send for fungal cultures which

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yielded an organism morphologically similar to aspergillus fumigatus. Microscopic morphology showed septate hyphae with simple, long conidiophores bearing single, unicellular, oval conidia that also darkened as the mold aged. *Aspergillus* serum precipitins and antigen were negative. Sixty milligrams of fluconazole diluted in 40 ml 0.9% NaCl was instilled via the working channel of Fibre optic Bronchoscope for every alternate day 3 sessions and a total of 200 mg fluconazole was installed for irrigation, after which hemoptysis and other symptoms significantly decreased. Mild cough occurred with instillation; however, he experienced no hallucinations during therapy.

At one month follow-up, he had only frequent episode of cough. He was followed up in OPD; CXR PA view shows marked improvement of cavity and shrinkage of the size of fungal ball.

Discussion: Aspergillus fumigatus species are fungal pathogens which can cause localized infection in immunocompetent patients, overwhelming sinopulmonary and disseminated disease among the immunocompromised[7]. Invasive pneumonia from *aspergillus* species can occur without structural lung disease in the immunosuppressed or with massive inoculation[7]. Pulmonary disease caused by aspergillus species include airway colonization, allergic bronchopulmonary hypersensitivity, and pulmonary mycetoma; the latter of which is thought to occur by colonization of devitalized lung resulting in a saprophytic state. We report the first case of pulmonary mycetoma

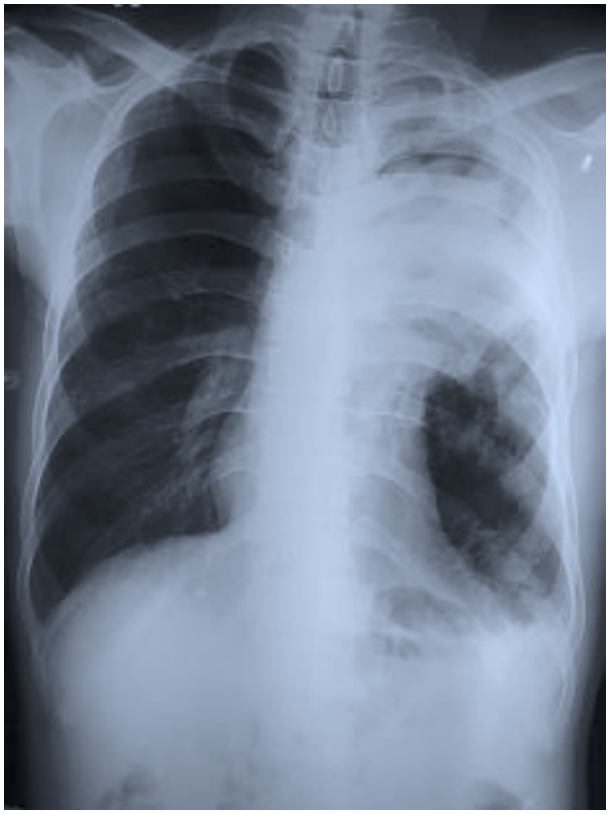

Fig.-1: *X-ray chest of patient.*

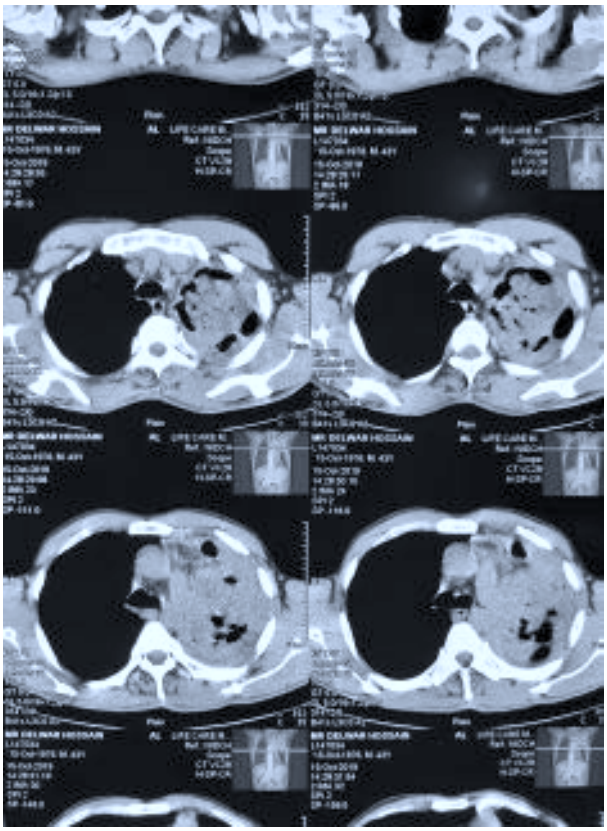

Fig.-2: *CT scan chest of patients*

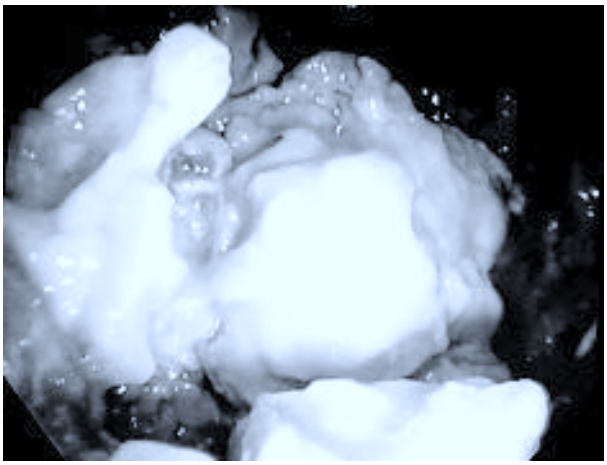

Fig.-3: *Bronchoscopic view of the lesion*

treated with intracavitary irrigation by antifungal drug, which responded well showing marked reduction of fungal ball size and improvement of symptoms.

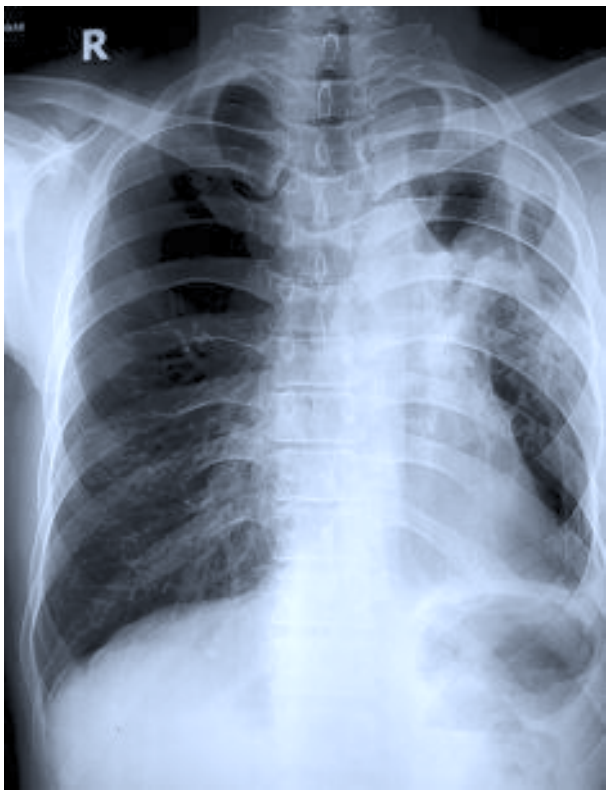

Fig.-4: *Chest x-ray PA view after treatment.*

Surgical excision is the accepted treatment of a symptomatic pulmonary mycetoma in patients with adequate pulmonary function and localized disease[8]. However, in many patients with fibrocystic tuberculosis, surgery is contraindicated as they frequently have poor pulmonary function[6]. Moreover, as compared to other populations with mycetomas and cavitary lung disease, the mortality of mycetomas in fibrocystic tuberculosis is worse. One review of 28 cases of pulmonary aspergilloma[9] demonstrated a substantially decreased one year survival in those with fibrocystic tuberculosis as compared to patients with cavitary lung disease from other cause.

Hemoptysis frequently complicates pulmonary mycetomas in fibrocystic tuberculosis[10]. When such hemoptysis is life-threatening, bronchial artery embolization (BAE) is recommended as a temporary procedure[11]. The sustained effects of BAE, however, are limited due to collateral vascularization, making future repeated embolization less efficacious. While systemic antifungal therapy has shown little or no benefit in the management of chronic symptoms[12], it is not effective in controlling acute hemorrhage. A number of case reports and series have shown success in using intracavitary fluconazole for the acute management of hemoptysis complicating pulmonary aspergilloma in patients for whom surgery was contraindicated or the patient refuses surgery[13-16].

Surgical resection could not be performed in our patient because of his poor pulmonary reserve and patient also refuses surgery. After identification of the fungus by seeing through FOB and from cultures of the mycetoma, intracavitary fluconazole was instilled following an adaptation of the protocol by Shapiro *et al.*[16]. We chose fluconazole as it, in comparison to other triazoles, has the highest reported *in vitro* activity against clinical aspergillosis[17] and has shown promise in treating clinical infection[18]. The concentration of fluconazole solution of approximately 1 mg/ml was similar to previously reported tolerable concentrations of fluconazole instilled via the intracavitary approach to treat pulmonary aspergillomas[16]. Although we never measured serum levels of Fluconazole after treatment, we postulated that local installation of fluconazole into the mycetoma cavity would be effective without raising serum concentrations to the level that would cause side-effects the patient experienced with prior systemic therapy.

At subsequent follow-up, his clinical improvement persisted with only infrequent episodes of cough which we speculate was secondary to a decreased fungal burden within the cavity. The lack of complete resolution of the mycetoma on repeated chest imaging was also not unexpected as these are comprised mostly of cellular debris rather than viable fungal organisms. One series showed persistence of aspergilloma following intracavitary amphotericin B in 28% patients[14]. Furthermore, other reports demonstrating mycetoma resolution following such therapy involved daily cavity irrigation[15] or low-pressure suction via the catheter[16], both of which were not performed in our patient.

In summary, we report the first case of mycetoma treated with the use of intracavitary fluconazole

in the treatment of symptomatic pulmonary mycetoma. In our experience, intracavitary antifungal therapy is useful for controlling and preventing the recurrence of hemoptysis and symptomatic improvement of patient. It is important to determine the specific fungal species involved in the pulmonary mycetoma formation, and its antifungal susceptibility, to provide appropriate intracavitary therapy for those patients who cannot undergo definitive surgery.

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CASE REPORT

Atypical Presentation of Carcinoma Lung- Experiences of 5 Cases Series in NIDCH

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Abstract:

Lung carcinoma often manifests with some atypical symptoms which delay the diagnosis of malignancy. Primary Lung cancer is one of the most common cancers in Bangladesh with relatively poor prognosis compared to other types of cancers. In early stages of lung cancer there are usually no signs or symptoms. Many of the symptoms are nonspecific and their onset is gradual. Therefore, early detection and timely curative treatment remains a challenge. We present five cases of lung cancer patients with atypical presentations to a secondary care centre in Bangladesh followed by discussion on the importance of awareness of these symptoms among healthcare professionals and need for high index of suspicion for lung cancer in high-risk groups.

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Introduction:

Lung cancer, the most common cause of cancer related death in men and women, is responsible for 1.3 million deaths worldwide annually.[1] The vast majority of primary lung cancers are carcinomas of the lung, derived from epithelial cells. The main types of lung cancer are small cell lung carcinoma (SCLC) and non-small cell lung carcinoma (NSCLC). Beside these epithelial cancers primary mesenchymal tumors of the lung account for less than 1 % of all primary lung cancers. Early diagnosis of any cancer improves prognosis. That's why being aware of atypical presentation and undergoing age- and risk-appropriate screenings where available can improve outcomes for many cancer patients. However, lung cancer typically has few symptoms early in the disease. By the time individuals notice something is wrong, their cancer is usually at an advanced stage. Many tumors in the lung never cause symptoms.So without screening, three-quarters of patients presented in advanced stage for surgery.There are no nerve endings in the lungs, so patient can have a large tumor in the lungs without noticing.Most lung cancer patients are diagnosed from symptoms that result from the spread (metastasis) of the cancer to another site, such as the spine or liver. The most typical

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symptoms are shortness of breath, coughing, hemoptysis and weight loss.Only 30% of these carcinomas are diagnosed in surgically treatable stage, usually presenting with long lasting cough and hemoptysis.[2] There is an overlap between these symptoms and those of chronic respiratory conditions that can delay diagnosis and early treatment, which may contribute to the poor prognosis .Also, there is considerable delay in investigating patients with atypical symptoms like joint pain, back pain, shoulder pain, visual disturbance, fatigue or even asymptomatic than with typical symptoms.We will present four cases of lung cancer patients with atypical presentations to NIDCH in Bangladesh.Our aim is to create awareness about these symptoms among health professionals.

Case 1:

A 65 years aged gentleman with history of accidental fall from height 1 months back. He went to local doctor and CXR (fig:1) done. On admission he gave no history of any respiratory complaints and examination revealed no significant abnormality. So we did CT Scan(Fig:2) of Chest and Fiber optic bronchoscope(FOB).

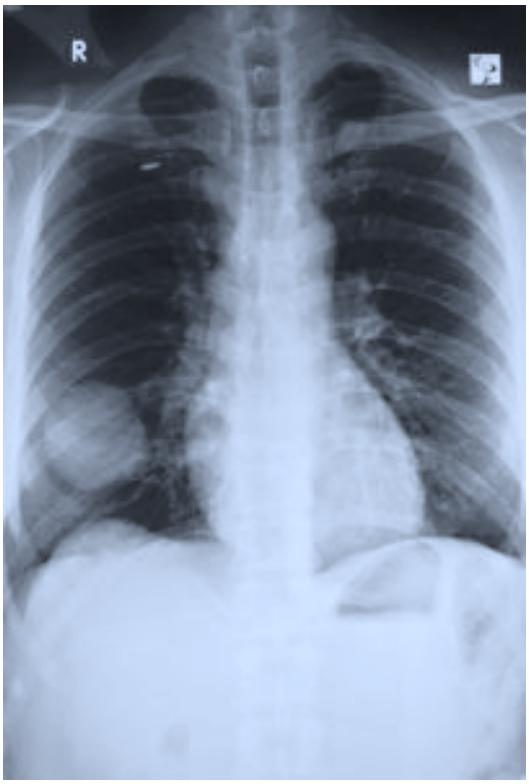

Fig.-1: *CXR P/A View*

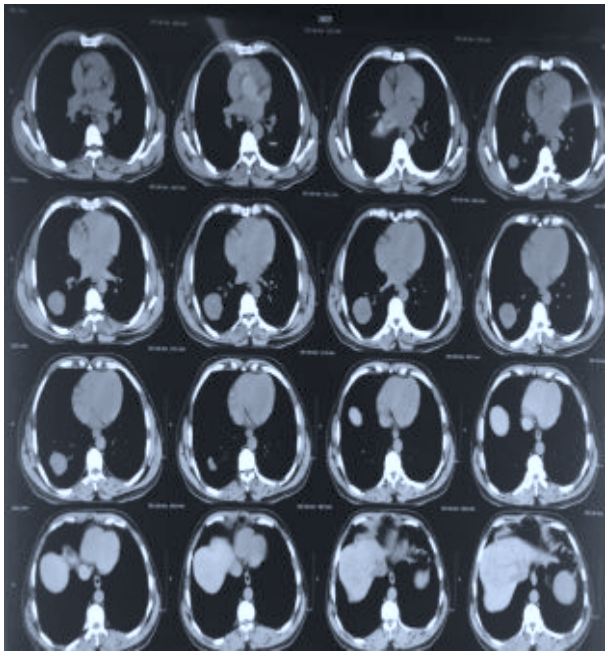

Fig.-2: *CT Scan Mediastinal view*

FOB reveals external compression of right lower lobe bronchus with no mucosal abnormality. And CT Scan guided FNAC revealed no malignancy or granuloma. After giving conservative treatment with antibiotics lung mass did not resolve.With the suspicion of malignancy we decided to do thoracotomy and right lower lobectomy with mediastinal lymphnodes dissection was done.Final histopathology report, lung mass: Chondro sarcoma low grade. Lymph nodes : Reactive change.

Case 2: A 45-years aged male smoker of 20 pack year with history of moderate chronic obstructive pulmonary disease and hypertension presented with bilateral knee pain for 4 months. No current respiratory symptoms however had history of weight loss of about 5 kg in 3 months. His examination revealed finger clubbing but was otherwise unremarkable.

Knee x-ray (Fig:4) revealed bilateral periosteal reactions affecting the distal femur and proximal tibia suggestive of hypertrophic pulmonary osteoarthropathy. Chest x-ray (Fig:5) demonstrated a left lung lesion. CT chest (Fig:6) revealed a 3.3cm spiculated left lung mass associated with left hilar lymph nodes. CT guided lung biopsy confirmed primary lung adenocarcinoma.

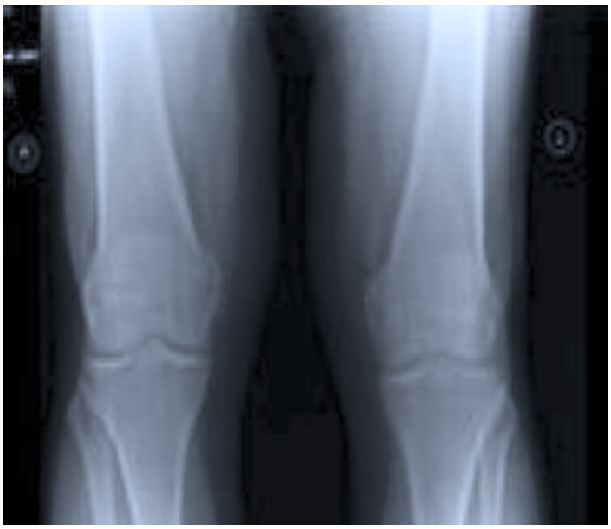

Fig.-3: *X-Ray Knee jointFig*

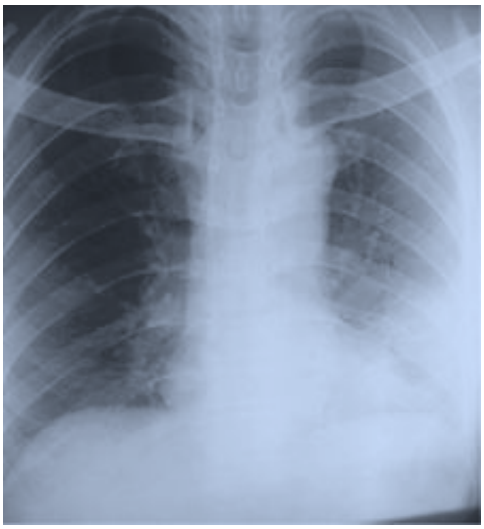

Fig.-4: *CXR P/A*

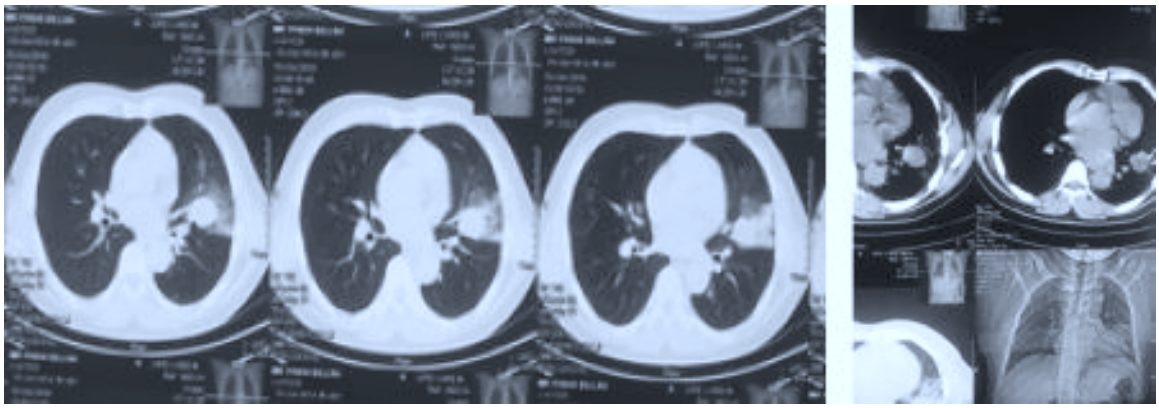

Fig.-5: *CT Scan of chest.*

Case 3: 52 years old smoking male presented to emergency department with complains of extreme right sided shoulder joint pain progressively worsening over 3 weeks, radiating to his right arm and neck. His vital signs were normal. He had no digital clubbing or palpable cervical lymphadenopathy on examination. Shoulder and systemic examination were normal. Shoulder x-ray (Fig:7) revealed no fractures or dislocation. however a lung mass was noted.

Subsequent chest x-ray (Fig:8) demonstrated lung mass in the right upper zone.CT scan (Fig:9) demonstrated a large irregular solid mass in the right upper lobe. CT guided biopsy confirmed undifferentiated adenocarcinoma, most likely of lung origin.

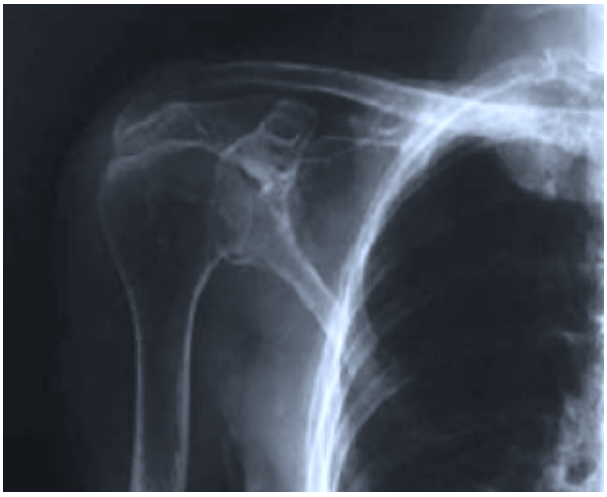

Fig.-6: *X-ray of shoulder joint*

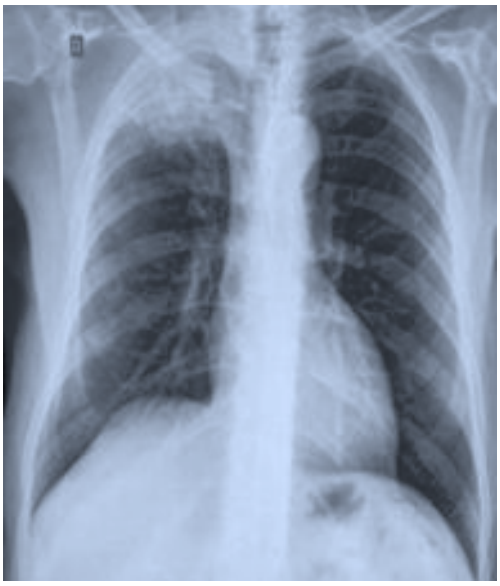

Fig.-7: *CXR P/A View*

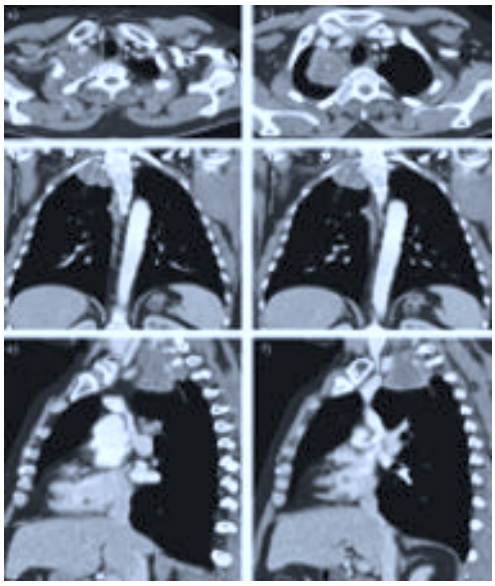

Fig.-8: *CT Scan of the chest.*

Case 4 :A 60 years old housewife, non -smoker presented with blurring of vision. She also complained of headache over the previous few weeks. She had no significant past medical history and systemic enquiry was unremarkable. Her examination revealed a left homonymous hemianopia with a normal systemic examination. Blood results were normal.CT scan of brain (Fig: 10) showed a right parieto-occipital mass with surrounding white matter oedema and mass effect that was confirmed on MRI Brain (Fig:11). Subsequent investigation with chest x-ray (Fig:12) revealed left upper lobe lung mass and was confirmed on CT chest (Fig:13). FNAC confirmed primary lung adenocarcinoma.

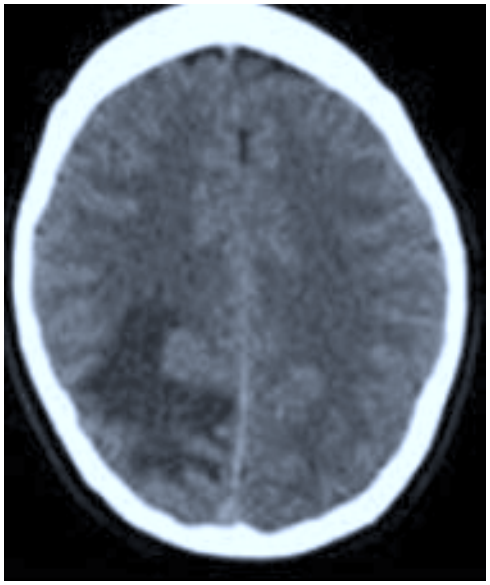

Fig.-9: *CT Scan of Brain*

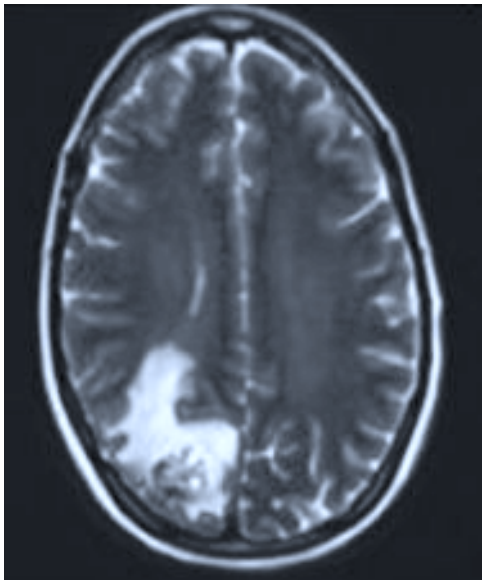

Fig.-10: *MRI of Brain*

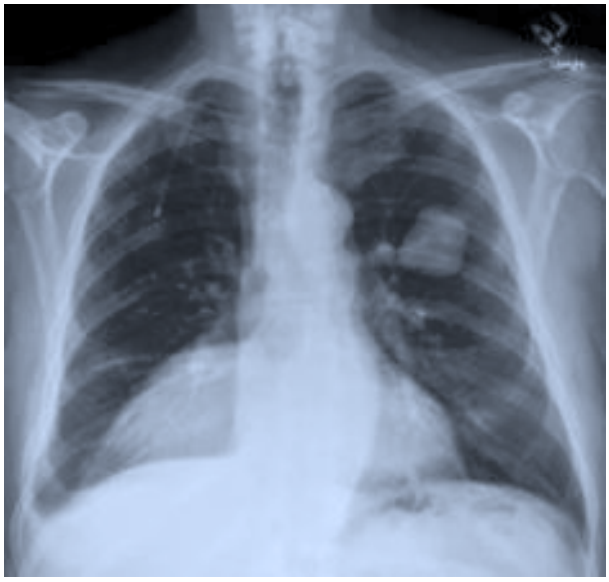

Fig.-11: *Chest X-Ray*

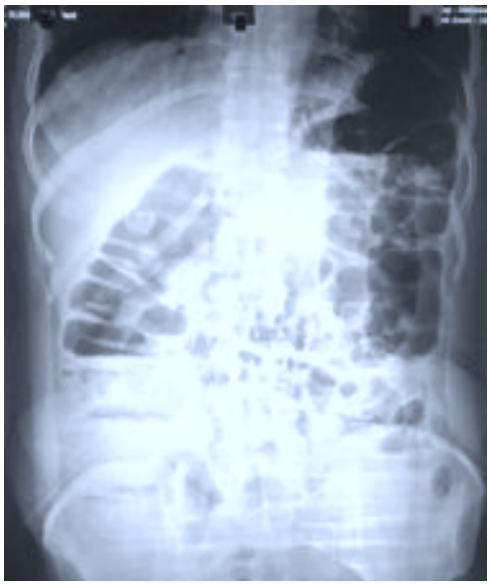

Fig.-13: *Abdominal x-ray*

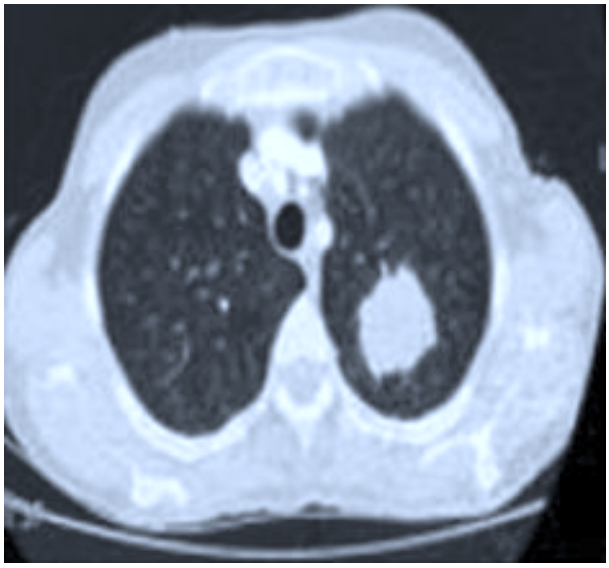

Fig.-12: *CT Scan of chest.*

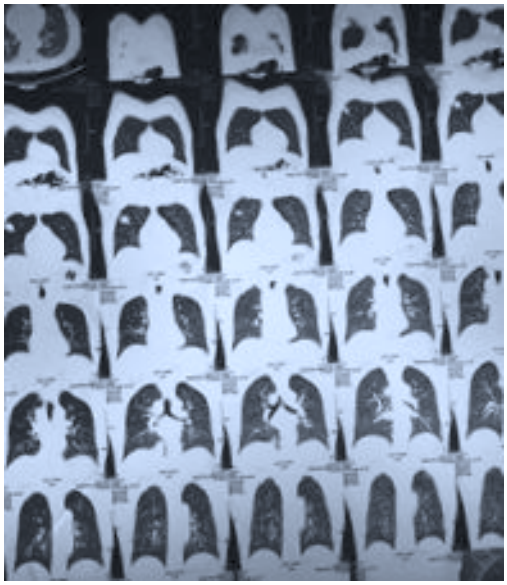

Fig.-14: *CT Scan of Chest*

Case 5: A 55 years gentleman smoker presented with abdominal pain and distension with occasional vomiting for 7-10 days. He had no significant past medical history and systemic enquiry was unremarkable.Abdominal distension subsided with conservative treatments. Blood results were normal. Subsequent investigation with abdominal and chest x-ray (Fig: 14) revealed right upper lobe lung mass and was confirmed on CT chest (Fig: 15). FNAC confirmed primary lung adenocarcinoma.

Discussion:

lung cancer commonly presented with persistent cough, haemoptysis, dyspnoea, chest pain, and weight loss. Haemoptysis is the most important symptom associated with lung cancer, but this is reported as the first symptom in less than 5% of cases[3]. Some less common un important symptoms include fatigue, anorexia and hoarseness of voice. There are some atypical symptoms that can delay diagnosis and early treatment. which may contribute to the poor prognosis.In most cases,

lung cancer was detected with subjective symptoms, but 6.5% of cases had no symptoms indicative of lung cancer at the time of diagnosis.[4-6] Asymptomatic patients received surgery in 60.0% of cases, and they showed significantly longer survival times than symptomatic patients. In our case 1, patient was asymptomatic at the time of admission but through investigation reveals only mass lesion in the right lower lobe. Our final diagnosis was chondro sarcoma which showed better outcome after surgery though asymptomatic.In case 2 patient presented with bilateral knee pain and X-Ray revealed hypertrophic pulmonary osteoarthropathy. And subsequent investigation showed left lower lobe adenocarcinoma. Hypertrophic pulmonary osteoarthropathy (HPO) is a rare paraneoplastic syndrome that is frequently associated with lung cancer. The incidence of clinically apparent HPO is not well known. The recent few studies have shown that the incidence is around 1.8%-4.5%[7-9]. About 10% cases of lung cancer may presented with para neoplastic syndrome. In case 3 a smoking male presented with excruciating shoulder joint pain with no digital clubbing but X-ray and CT Scan showed Right upper lobe mass. FNAC suggested adenocarcinoma of lung origin. Shoulder joint pain is one of the common symptoms in general practice but can be a clue for underlying lung cancer.

The incidence of shoulder joint pain associated with lung cancer is 16%.[10] Pancoasttumour can present with such type of shoulder joint pain and other associated features. In case 4 patient complaints of blurring of vision with headache over the previous few weeks without any history of smoking. CT scan of brain & MRI Brain showed mass effect. Subsequent investigation with chest x-ray revealed left upper lobe lung mass and was confirmed on FNAC primary lung adenocarcinoma. The visual disturbance was due to brain metastasis secondary to lung cancer.The exact incidence of lung cancer with brain metastasis in initial presentation is unknown. Around 10% patients presented with brain metastasis with lung cancer in initial period. In case 5 the patient had presented with abdominal pain and distensions raising the possibility of abdominal metastases of lung cancer. Following further investigations, he was found to have lung cancer. Abdominal metastases of lung cancer are rare and are commonly clinically silent. The largest reported series have evaluated gastrointestinal (GI) metastases from lung cancer by autopsies: only 12% of patients with lung cancer present with GI metastases.[10,11]

Conclusion:

Different literatures review suggested that about 25% cases of lung cancer presented with atypical presentation. Atypical presentation is an important factor for delay in diagnosis with poor prognosis. To overcome this, every physician related to respiratory diseases should evaluate the patient properly for early diagnosis of lung cancer.

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Figure should be professionally designed symbols, lettering, and numbering should be clear and large. The back of each figure should include the sequence number and the proper orientation (e.g. “top”). Photographs and photomicrographs should be supplied as glossy black and white prints unmounted. Legend for each illustration should be submitted in separate sheets. All photographs, graphs and diagrams should be referred to as figures numbered consecutively in the text in Roman numerals.

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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.

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Kaplan SJ. Post-hospital home health care: the elderly's access and utilization (dissertation). St. Louis (MO). Washington Univ; 1995.

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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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a) In press

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

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

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