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

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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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World Health Organization, Ethical Criteria for Medical Drug Promotion. Geneva: World Health Organization; 1988.

d) Chapter in a book
Macnee W. Chronic bronchitis and emphysema. Seaton A, Seaton D, editors. Crofton and Douglas's Respiratory Diseases. 5th ed. UK. The Blackwell Science; 2000; p.616-95.

e) Dissertation
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3. Other published material

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

b) Dictionary and similar references
Student's medical dictionary. 26th ed. Baltimore: Williams & Wilkins; 1995. Apraxia; p.119-20.

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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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EDITORIAL

Endovascular Intervention – An Innovative Procedure for the Management of Hemoptysis

[Chest Heart Journal 2018; 42(1) : 1-3]
DOI: http://dx.doi.org/10.33316/chab.j.v42i1.2019570

Hemoptysis is a common clinical problem. It is a symptom, not a disease entity. It is a challenging problem for the pulmonologist. Other than respiratory disease, different systemic disease may present with hemoptysis like mitral stenosis, hepatopulmonary syndrome, Wegener's Granulomatosis, heart failure, pulmonary edema etc. but interventional pulmonologis is the focal person for management of massive hemoptysis.

Massive hemoptysis is a frightening and potentially life threatening clinical event. Patient with chronic inflammatory lung disease such as bronchiectasis, sarcoidosis, tuberculosis and cystic fibrosis develop markedly hypertrophied and fragile bronchial artery that may lead to clinically significant hemoptysis. Surgery had been the definitive therapy historically. Unfortunately surgical intervention carries a mortality about 20-40% and conservative management carries mortality >50% and embolization have mortality less than 5%. Furthermore Surgical intervention is hazardous and often impossible in the patient with diffuse parenchymal lung disease. Super selective catheterization of the bronchial arteries feeding the affected areas followed by particulate embolization has proven to be an effective treatment for controlof bleeding.

Massive hemoptysis is carries a 50-85% mortality rate when treated conservatively[1]. Death most often due to asphyxiation from the aspirated blood leading to airway obstruction, less commonly death occurs due to exsanguation and acute hypotension[2]. Because of poor outcome associated with conservative therapy alone, many center have institute more aggressive therapeutic maneuvers

The source of bleeding must be defined clearly and hemoptysis must be differentiated from bleeding from the upper airway or alimentary tract. Once hemoptysis has been established, a multidisciplinary approach involving interventional pulmonology, thoracic surgery and interventional radiology should be optimal. All the drug that might contribute to bleeding should be stopped. A coagulation profile should be obtained and a sputum sample sent for culture and sensitivity including bacteria, mycobacteria and fungus.

Chest X-ray is required to identify any acute radiologrphic changes in the lung fields to localize the site of bleeding and discover other potential cause of bleeding, such as foreign body or cavity with Mycetoma. If no localizing features are present, a review of the recent CT chest might identify area of severe bronchiectasis or new infiltrate, which will help to determine the site. Bronchoscopy might help to identify the site of bleeding but may be non diagnostic in the setting of severe hemoptysis[3].

Bronchial artery anatomy

The bronchial artery typically arises from the thoracic aorta at the T3 to T8 level and also supply the bronchi, vagus nerve, mediastinum and esophagus. 80% of the artery arises from the T5 to T6 level there are many bronchial artery anatomic variations[4]. The more common combination include a single right intercostobronchial artery with single left bronchial artery, single. Two bronchial arteries can be seen either on the right or in the left. As many as 20% of the bronchial artery have anomalous origin other than aorta. Aberrant origin includes subclavian,thyrocervical, internal mamary, innominate, superior intercostal and inferior

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phrenic arteries. Pulmonary parenchyma may receive arterial blood supply from transpleural systemic collateral to the bronchial circulation via intercostals, mamary, phrenic and thyrocervical arteries[5].

Endovascular management of hemoptysis can be done in acute massive hemoptysis to stop bleeding as well as recurrent hemoptysis. These are safe procedure with minimal complication; the endovascular procedures are –

Bronchial Artery Embolization:

I) This can be done temporarily or permanent which can be done by different agents like gel foam, glue, and recently developed agents like thombosphere, polyvinyl alcohol. Particulate agent is more preferable than liquid agents because liquid agents are prone to develop tissue ischemia. Larger particulate size like(350-550μm) are preferable.

II) Bronchial artery embolization by platinum coil.

Angiographic and embolization technique:

Prior to the procedure a brief systemic and general examination should be performed to establish the baseline. A preliminary descending thoracic aortogram can be performed as a roadmap to the bronchial arteries but selective catheterization can be done if the patient does not have the history of prior embolization procedure. Five or six French sheath are commonly used, through which selective catheter is placed, reverse curve catheters (Mikael son, Simons, SOS, Omni) are initially used. Forward looking catheters can also be effective. Typically 4, 5 or 5.5 Fry catheters are used routinely[6].

The left main stem bronchus serves as a convenient fluoroscopic land mark for the general location of the bronchial arteries. the catheter is directed laterally or anterolaterally for the right bronchus and more anterior for the left. A selective bronchial arteriogram must be performed prior to any embolization. One must be sure not to occlude the artery during the selective injection, especially on the right, because this may result in spinal cord ischemia if spinal artery branch is present. Bronchial artery will have branch that follow the course of the main stem bronchus,where as the intercostal artery will travel laterally along the under surface of the rib. Abnormal angiographic appearances that support a site of bleeding include – tortuosity, hypertrophy, hyper vascularity, aneurism, extravasation and bronchial artery to pulmonary artery or vein shunting[7]. The bronchial artery injection may elicit a cough response although this is far less common with the use of newer nonoinic and isoosmolar contrast agent. If the site of hemorrhage is known, all abnormal bronchial arteries to that region should be embolized. However if the site of bleeding cannot be localized, any abnormal bronchial artery should be treated. If the abnormal bronchial artery cannot be identified, a continued search for additional bronchial artery and nonbronchial system must be performed.The presence of hypertrophied nonbronchial systemic collateral is particularly common in patients having undergone prior embolization procedures.

A stable catheter position is required for any embolization. There are many new available micro catheters that will easily exit a 0.038-in taper diagnostic catheter.

Ideally, distal embolization should be performed. Particulate greater than 200 to 250μm should be used to avoid tissue ischemia and neurologic damage. Currently polyvinyl alcohol (PVA) particulate size ranges 300 to 500μm are commonly used with good result. Other embolic agent s used includes gel foam, pledgets (1-2mm), gel foam slurry, thrombin and Glue[8]. Proximal occlusion with large particles or coil should be avoided if possible. Proximal occlusion Provides very temporary relief because collateral pathways readily develop. Very small particles less than 200μm or liquid embolic agent should always be avoided because these causes tissue infarction. Care should be taken for initial diagnostic arteriogram for the presence of bronchial artery to pulmonary artery or vein shunt. Particulates which traverse shunt into the pulmonary artery circulation will cause small pulmonary emboli and those that enter the pulmonary venous circulation can result in catastrophic systemic emboli. In those cases larger particles should be chosen, and in the case of very large shunt coil may be indicated.

Complication

Major complication is rare and immediate clinical success defined as cessation of hemorrhage ranges from 85-100% with recurrence rate about 10%. Spinal cord ischemia and transverse myelitis are the most feared and recognized complication. They are fortunately very rare. The use of nonionic contrast agents has significantly reduced the risk of transverse myelitis. With the current use of nonionic contrast media, particulate agent greater than 200μm and modern micro catheter or micro guide wire, nontarget embolization is quite rare. Chest pain and dysphagia commonly occur with selective embolization within the first week following procedure. These symptoms are secondary to the interruption of the blood supply to the posterior mediastinum and mid portion of the esophagus. This is less common when distal super selective catheterization is used[9].

Conclusion;

Major hemoptysis is life threatening complication of variety of chronic inflammation of the lung. The development of bronchial artery embolization technique has revolutionized the approach to these patients. Recurrent hemoptysis is due to continued presence of acute on chronic inflammation and the recanalization of an embolized bronchial artery or bleeding from a site supplied by non-embolized systemic collaterals. Recurrent hemoptysis also can be successfully controlled with embolization. Therefore, despite a prior history of bleeding and prior embolization procedures, no patient should be denied the opportunity for additional trans catheter therapy.

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Reference:

1. Wholey M H, Chamorro H A, Rao G, et al. Bronchial artery embolization for massive hemoptysis. JAMA. 1976;236:2501-2504
2. Guo J X. Arteriography and bronchial artery embolization for massive hemoptysis in 100 cases of tuberculous. Zhonghua Jie He He Hu Xi Za Zhi. 1992;15:77-78.
3. Saumench J, Excarrabill J, Padro L, et al. Value of fiberoptic bronchoscopy and angiography for diagnosis of the bleeding site in hemoptysis. Ann Thorac Surg. 1989;48:272-274.
4. McPherson S, Routh W D, Nath H, et al. Anomalous origin of bronchial arteries: potential pitfall of embolotherapy for hemoptysis. J Vase Interv Radiol. 1990; 1:86-88.
5. Keller F S, Rosch J, Loflin T G, et al. Nonbronchial systemic collateral arteries: significance in percutaneous embolotherapy for hemoptysis. Radiology. 1987;164:687-692.
6. Uflacker R, Kaemmerer A, Picon P D, et al. Bronchial artery embolization in management of hemoptysis: technical aspects and long-term results. Radiology. 1985;157:637-644.
7. Osada H, Kawada T, Ashida H, et al. Bronchial artery aneurysm. Ann Thorac Surg. 1986;41:440-442.
8. Mauro M A, Jaques P F. Transcatheter embolization with a Gelfoam slurry. J Interv Radiol. 1987;2:157-159.
9. Munk P L, Morris D C, Nelems B. Left main bronchial-esophageal fistula: a complication of bronchial artery embolization. Cardiovasc Intervent Radiol. 1990;13:95-97.

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Vol. 42, No. 1, January 2018

ORIGINAL ARTICLE

Prevalence of Multidrug Resistance Tuberculosis Among Presumptive MDR-TB Patients Attending at 250 Bedded Tuberculosis Hospital

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Abstract:

The emergence of resistance to drugs used to treat tuberculosis (TB), and particularly multidrug resistant TB (MDR TB) has become a significant problem in number of countries and obstacle to effective TB control. In Bangladesh, the National Tuberculosis Control Programme (NTP) carried out its 1st national wide drug resistance survey (DRS) in tuberculosis patient in collaboration with WHO and SNRL, Antwerp, Belgium in 2010-2011. The result shows the overall number of MDR TB cases is low, 1.4% among new cases and 28.5% among re-treatment cases.

In this study, from January 2013 to September 2018 at 250 Bedded TB Hospital, Shyamoli, total presumptive MDR-TB cases were 10021. Among them MTB detected in 2188 (21.83%) patients. About 92.75% are RIF sensitive and 7.3% are RIF resistance (MDR-TB). Among the MDR-TB cases 53.4% were male and 46.58% were female. Among 161 MDR-TB cases 31.7% are Relapse ,13.04% are new cases, 6.8% are lost to Follow up cases and 48.4% are others (Non convertor of CAT I and II, CAT I and CAT II failure, close contact of MDR patients).

Our study shows that the prevalence of MDR-TB is more in retreatment cases (Relapse, Lost to follow up, Non convertor of CAT I and II, CAT I and CAT II failure, close contact of MDR patients) when compare to new cases. It should be emphasized that the prevalence of MDR-TB in new cases is higher in compare to the values stated under PMDT 2012 and WHO annual TB report 2015. This is a threat to TB control programme in Bangladesh. We have done this study on the basis of GeneXpert of sputum. Culture was not available in our institute. So MDR-TB diagnostic facility and surveillance activity should be expanded. Our study emphasize the need of first line drug sensitivity testing in all the new cases of Tuberculosis should be implanted to control, reduce the prevalence and improve the outcome of MDR –TB treatment.

Key words: *Tuberculosis (TB), Multidrug Reasistant Tuberculosis (MDR-TB), Rifampicin Resistant (RIF- resistant), Gene-Xpert, Sputum.*

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Introduction:

The emergence of resistance to drugs used to treat tuberculosis (TB), and particularly multidrug resistant TB (MDR TB) has become a significant problem in number of countries and obstacle to effective TB control[1]. According to the Global TB Report 2012 (WHO) there were an estimated incidence of 31000 MDR TB cases among notified TB patients with pulmonary TB. Among them, 3.7% (2.1-5.2%) of new cases and and 20% (13-26%) of previously treated cases are estimated to have MDR TB[2].

In Bangladesh, the National Tuberculosis Control Programme (NTP) carried out its 1st national wide drug resistance survey (DRS) in tuberculosis patient in collaboration with WHO and SNRL, Antwerp, Belgium in 2010-2011(2). The result shows the overall number of MDR TB cases is low, 1.4% among new cases and 28.5% among re-treatment cases. Although the rates of MDR TB in Bangladesh do not appear to be high, the absolute number of MDR TB cases in higher considering the overall high TB burden[2].

In present study, we have estimated the prevalence of MDR-TB (defined as resistance to Rifampicin in Gene-Xpert of sputum) in MDR-suspect patients attending at 250 Bedded TB Hospital from January 2013 to September 2018. These MDR-suspect patients (according to Guidelines on Programmatic Management of Drug Resistant TB (PMDT) in Bangladesh April, 2013) include any TB patient who fails category I and II, non converters of Category I and II, Relapses (Category I / Category II), Treatment after loss to follow up (Category I/ Category II), close contacts of MDR TB, HIV infected patients.

Materials & Methods:

This retrospective observational study was conducted at 250 Bedded TB Hospital that involved all MDR-suspects attending from January, 2013 to September, 2018. All data were collected from hospital records.

After identifying potential MDR-TB suspect cases, early morning sputum samples were collected from each patient and Gene-Xpert(Cepheid, 16 module) was done.

Genotyping drug susceptibility testing: For each of the samples, unscrew lid of sputum collection container, add Sample Reagent 2:1 (v/v) to the sample, replace the lid, and shake vigorously 10-20 times. Incubate for 15 minutes at room temperature. At one point between 5 and 10 minutes of the incubation again shake the specimen vigorously 10-20 times. Samples should be liquefied with no visible clumps of sputum. Particulate matter may exist that is not part of the sample. At least 2 ml, of processed sample was taken with the plastic transfer pipette from the collection container to the single-use, disposable, self contained GeneXpert cartridge. Then it was subjected to GeneXpert MTB/RIF to creat a test result were noted after 2 hours[3].

Result:

In this study, from January 2013 to September 2018 at 250 Bedded TB Hospital, Shyamoli, total presumptive MDR-TB cases were 10021. Figure 1 shows that among 10021 cases, MTB detected in 2188 (21.83%) patients. About 92.75% are RIF sensitive and 7.3% are RIF resistance (MDR-TB). Table 1 shows that among the MDR-TB cases 53.4% were male and 46.58% were female. According to Table 2 among 161 MDR-TB cases 31.7% are Relapse, 13.04% are new cases, 6.8% are lost to Follow up cases and 48.4% are others(Non convertor of CAT I and II, CAT I and CAT II failure, close contact of MDR patients).

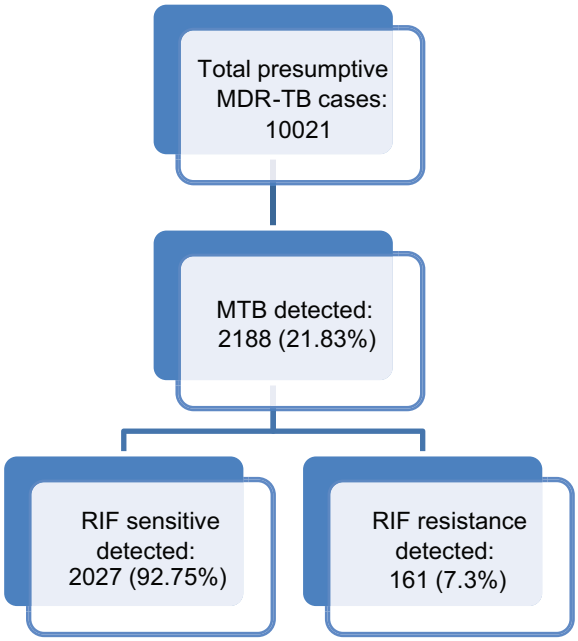

Figure 1: p*revalence of multidrug resistant tuberculosis (MDR-TB)*

Table-I

Sex distribution of MTB detected cases

Sex	MDR-TB cases	NonMDR-TB cases	Total
Male	86 (53.4%)	1546 (76.27%)	1632
Female	75 (46.58%)	481(23.72%)	556
Total	161	2027	2188

Table-II

Distribution of Rifampicin resistance cases according to patient´s category.

Groups	Relapse	New cases	Lost to Follow up	Others	Total
MDR-TB	51(31.7%)	21(13.04%)	11(6.8%)	78(48.4%)	161
Non MDR-TB	926(45.68%)	765(37.74%)	144(7.1%)	192(9.47%)	2027
Total	977	786	155	270	2188

Table-III

Distribution of MTB cases according to patient's category (N=2188)

Groups	Relapse	New cases	Lost to Followup	Others	Total
	977	786	155	270	2188
	(44.65%)	(35.92%)	(7.08%)	(12.34%)	(21.83%)

Table-IV

Distribution of MTB cases according to patient's category

Characteristics	MDR TB		Non MDR TB		OR	95% Cl	P value
Reoapse case versus new case	51	21	926	765	2.0	1.2-3.4	p=0.01*
Lost to follow up vs new case	11	21	144	765	2.78	1.3-5.9	p=0.01*
Relapse case vs lost to follow up	51	11	926	144	0.72	0.4-1.4	p=0.44

*significant

Discussion:

Pulmonary Tuberculosis (TB) is a contagious bacterial infection that involves the lungs but may spread to others organs. Pulmonary tuberculosis is caused by Mycobacterium tuberculosis. One gets TB by breathing in air droplets from a cough or sneeze of an infected person[4]. According to WHO, TB patients resistant to at least two drugs (Rifampicin and Isoniazid) are called multidrug resistant tuberculosis (MDR-TB)[5]. Now a days this is a serious threat in developing countries[6]. MDR-TB most commonly develops due to inappropriate treatment, patient missing doses, failing to complete their treatment[7].

According to the Global TB Report 2012 (WHO) there were an estimated incidence of 31000 MDR TB cases among notified TB patients with pulmonary TB. Among them, 3.7% (2.1-5.2%) of new cases and and 20% (13-26%) of previously treated cases are estimated to have MDR TB. According to PMDT May 2012, the prevalence of MDR-TB in India to be about 3% in new cases and 12-17% in re treatment cases[8]. In this study also shows, Among the 161 MDR-TB cases 31.7% are Relapse, 13.04% are new cases, 6.8% are lost to Follow up cases and 48.4% are others (Non convertor CAT I and II, CAT I and CAT II failure, close contact of MDR patients). That proves that relapse cases are more prone to develop MDR-TB.

In India among the MDR-TB cases, 14.89% were male and 12.5% were female. In this study, we observe 53.4% were male and 46.58% were female, which are more or less same proportion. These two studies reveal that sex distribution is not an important indicator to develop MDR-TB.

Conclusion and Recommandation:

Our study shows that the prevalence of MDR-TB is more in retreatment cases (Relapse, Lost to follow up, Non convertor CAT I and II, CAT I and CAT II failure, close contact of MDR patients) when compare to new cases. It should be emphasized that the prevalence of MDR-TB in new cases is higher in compare to the values stated under PMDT 2012 and WHO annual TB report 2015.(TB1) This is a threat to TB control programme in B angladesh. We have done this study on the basis of GeneXpert of sputum . culture was not available in our institute. So MDR-TB diagnostic facility and surveillance activity should be expanded. Our study emphasize the need of first line drug sensitivity testing in all the new cases of Tuberculosis should be implanted to control, reduce the prevalence and improve the outcome of MDR –TB treatment.

Referrence:

1. Prevalence of Multidrug Resistance Tuberculosis in Presumptive Multidrug Resistant Tuberculosis Cases Attending Tertiary Care Center. *Ijmsci* 2016, 3(9):2120-2125.
2. National Guidelines and Operational Manual for Programmatic Management of Drug Resistant TB (PMDT) in Bangladesh-April 2013.
3. Use of GeneXpert *Mycobacterium tuberculosis*/ rifampicin for rapid detection of rifampicin resistant *Mycobacterium tuberculosis* strains of clinically suspected multidrug resistance tuberculosis cases. *Ann Transsl Med* 2016,4(9):168.
4. Prevalence of MDR TB in Suspected Pulmonary Tuberculosis Patients in A Tertiary Care Hospital Kanchipuram, Chennai, Tamilnadu, India. *IOSR-JDMS* 2016,15(4):106-108.
5. National Guidelines and Operational Manual for Programmatic Management of Drug Resistant TB (PMDT) in Bangladesh-April 2013, p-9.
6. Surveillance of resistance to anti tuberculosis drugs in developing countries. *Tuberc Lung Dis* 1994; 75:163-167.
7. Treatment of multi-resistant tuberculosis, *N Engl J Med* 1993; 329 (11):784-791.
8. Revised National Tuberculosis Control Program Guidelines on Programmatic Management of Drug Resistant TB (PMDT) in I ndia – May 2012.

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ORIGINAL ARTICLE

Study of plasma C - Reactive Protein Level in Bacteriological Sputum Culture Positive & Culture Negative Patients of COPD with Exacerbation

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Abstract

Objective: *To determine whether levels of Plasma C-reactive protein (CRP) could be a useful biomarker in addition to bacteriological sputum culture for early decision of antibiotic treatment in COPD patients with exacerbation*

Material and Methods: *This cross sectional observational study was done in the Department of Respiratory Medicine, NIDCH, Mohakhali, Dhaka during July, 2015 to June, 2016. A total of 100 patients with COPD exacerbations admitted in NIDCH were included in this study. C-reactive protein (CRP) and sputum culture were done in all of the patients. Patients having sputum culture positive and culture negative were considered as group I and group II respectively. Age 40 or over, both sexes, acute exacerbation of COPD according to the GOLD guideline, criteria for hospital admission according to the GOLD guideline, former or current smoker with a minimum smoking history of 20 pack years and/or exposure to biomass fuel were enrolled.*

Results: *Fourty two (42.0%) patients had sputum culture positive and 58(58.0%) patients had culture negative. Majority (40.5%) patients age belong to 50-59 years in group I. Male were predominant 40(95.2%) and 48(82.8%) in both group I and group II. 22(52.4%) patients had raised plasma CRP level >10(mg/dl) in culture positive group and that was only 3(5.2%) in culture negative group. In addition, more than 90% culture positive patients had CRP level >5 (mg/dl) as a whole whereas it was only 19% in culture negative group. ROC curve for prediction of sputum culture positive according to CRP level with a cutoff value 5.0mg/dl having area under curve (AUC) 0.893, with 76.2% sensitivity and 86.2% specificity for prediction of culture positive result.*

Conclusion: *Elevated C-reactive protein (CRP) could be a useful biomarker in addition to bacteriological sputum culture for early decision of antibiotic treatment in COPD patients with exacerbation*

Key words: *AECOPD, sputum culture, C-reactive protein.*

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Introduction:

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality throughout the world. It is the fourth leading cause of death worldwide. [1] A clinical diagnosis of COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease.[2]

COPD may be punctuated by periods of acute worsening of respiratory symptoms, called exacerbations.[3] Exacerbations can be precipitated, among other causes, by bacterial and viral infections, and by common pollutants, such as tobacco and air pollution. But in up to 30% of cases, an etiological diagnosis cannot be achieved.[4] In addition to this, 25-50% of COPD patients are colonized with potential respiratory pathogens, especially Haemophilus influenza, Streptococcus pneumonia and Moraxella catarrhalis.[4] In fact, in some COPD patients it is possible to isolate potential pathogenic bacteria in sputum, not only during an exacerbation but also during at stable state, so the presence of pathogenic bacteria does not prove its direct implication in the episode.

For these reasons, new strategies for the management of COPD patients are required, not only for identifying the origin of the exacerbation episodes, but also to assess individual risk for each patient. Culture of sputum is time consuming and frequently do not give reliable result. Even though the presence of mucopurulent sputum expectoration is associated with isolation of pathogenic bacteria, it is difficult, or even impossible, to differentiate colonization from infection. Color of sputum reported by patients is not always reliable and inspection of sputum is not always possible. Thus, a negative result or a normal flora does not exclude the presence of a microorganism responsible for the exacerbation. The criteria published by Anthonisen et al and the presence of other clinical symptoms are likelihood criteria for infective exacerbation. But they are subjective and prone to interobserver variation. In contrast, the measurement of biological markers offers objective data, although it has to be considered in combination with the clinical criteria.[5]

Several serum biomarkers such as C-reactive protein (CRP) and procalcitonin (PCT) are now available. Procalcitonin test is expensive. In some recent trials, it has been found that plasma CRP is significantly high in sputum positive bacterial exacerbation of COPD and can guide for antibiotic therapy and can reduce overall treatment cost & also contributes to the spread of resistant microorganisms.[8]

Materials & Methods:

This cross sectional observational study was carried out - Consecutive 100 patients of both sexes with the age of 40 years or above admitted to Inpatient Department of NIDCH, Mohakhali, Dhaka during July 2015-June 2016 due to acute exacerbation of COPD. Criteria for the diagnosis of COPD, acute exacerbation of COPD and hospital admission were based on GOLD guideline.[9] CBC , ECG, Chest X-Ray P/A View , Spirometry, ABG, Sputum for AFB, Plasma CRP level & Sputum for culture were done for all patients . Total 42 patients having positive sputum culture for bacterial organisms were considered as group I and 58patients having negative sputum culture were considered as group II. Recent antibiotic treatment, pneumonia, bronchiectasis, malignancy, pneumothorax, Tuberculosis & IHD were excluded from the study.

Results:

Total 100 COPD patients with acute exacerbations were included in the study and among them 42(42.0%) patients were found to have positive sputum culture for bacteriological organisms (Group I). On the other hand, 58 (58.0%) patients were found to have negative sputum culture for bacteriological organisms (Group II). (Figure-1)

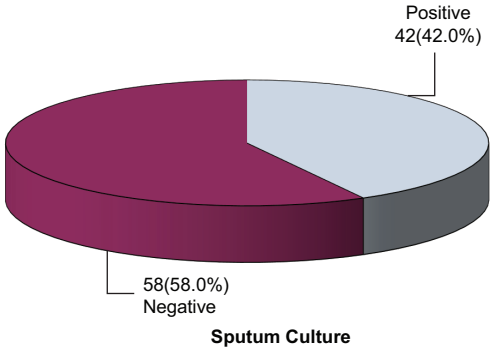

Fig.-1: *Pie chart showing distribution of the study population by Sputum culture*

It was observed, in the demographic variables, that majority (40.5%) patients belonged to 50-59 years age group in group I. On the other hand, majority (34.5 %) patients belonged to 60-69 years age group in group II. Majority patients were male in both group I and group II (95.2% & 82.8% respectively).Regarding occupation, farmers predominated in both the groups (50.0%& 27.6% respectively). More than three forth (78.6%) patients were current smoker in group I and 37(63.8%) in group II. Based on age, sex, occupational status and smoking habit, there was no statistically significant difference ($p<0.5$) between the two groups. (Table- I)

It was observed that, almost three fourth (71.4%) patients expectorated 15-30 ml sputum per day in group I who were positive for bacteriological organism in sputum culture and only 8(13.8%) patients expectorated this volume in group II who were negative for bacteriological organism in sputum culture. In addition 12(28.6%) patients expectorated >30ml/day in group I where as none in group II. The difference was statistically significant ($p<0.05$) between two groups. (Table-II)

It was found in this study that, almost three fourth (71.4%) patients had mucopurulent sputum in group I and 54(93.1%) had mucoid sputum in group II. Purulent sputum was found in 11(26.2%)patients in group I and none in group II. Number of patients having mucopurulent and purulent sputum were significantly higher in group I and the difference was statistically significant ($p<0.05$) between the groups.(Table-III)

It was observed that 4(9.5%) patients in culture positive & 39(67.2%) patients in culture negative group belonged to 0.5-5 (mg/dl) CRP level and more than half (52.4%) patients belonged to >10 (mg/dl) CRP level in culture positive patients and only 3(5.2%) patients in culture negative group belonged to this range of CRP. More than 90% culture positive patients had CRP level >5 (mg/dl) as a whole, in comparison to only 19% in culture negative group. (Table-V)

Table-I

Distribution of the study population by demographic variable (n=100)

	Group-I (n=42)		Group-II (n=58)		P value
	N	%	N	%	
Age group (years)					
40-49	5	11.9	7	12.1	
50-59	17	40.5	19	32.8	
60-69	10	23.8	20	34.5	0.843^{ns}
70-80	9	21.4	11	19	
>80	5	11.9	7	12.1	
Sex					
Male	40	95.2	48	82.8	0.058^{ns}
Female	2	4.8	10	17.2	
Occupational status					
Farmer	21	50	16	27.6	
Service holder	3	7.1	9	15.5	
Businessman	3	7.1	6	10.3	0.188^{ns}
Laborer	7	16.7	7	12.1	
House wife	3	7.1	8	13.8	
Rickshaw-puller	5	11.9	12	20.7	
Smoking Status					
Smoker	33	78.6	37	63.8	
Ex-smoker	5	11.9	10	17.2	0.263^{ns}
Non-smoker	4	9.5	11	19.0	

s=significant, ns= not significant, p value reached from chi square test

Table-II

Presentation of the study population by sputum production (n=100)

Sputum Production (ml/day)	Group-I (n=42)		Group-II (n=58)		P value
	N	%	N	%	
<15	0	0	50	86.2	
15-30	30	71.4	8	13.8	0.001[s]
>30	12	28.6	0	0	

s=significant ,p value reached from chi square test

Table-III

Presentation of the study population by sputum Character (n=100)

Sputum Character	Group-I (n=42)		Group-II (n=58)		P value
	N	%	N	%	
Mucoid	1	2.4	54	93.1	
Mucopurulent	30	71.4	4	6.9	0.001[s]
Purulent	11	26.2	0	0	

s=significant , p value reached from chi square test

Table-V

Association between plasma CRP level with sputum culture of the population (n=100)

Plasma CRP status (mg/dl) Positive(n=42)	Plasma CRP on the basis of sputum culture Negative(n=58)			
	n	%	n	%
0.5-5.0	4	9.5	39	67.2
5.1-10.0	16	38.1	8	13.8
>10 22	52.4	3	5.2	
Mean±SD	6.7	±5.7	5.1	±4.8
Reange (min, max)	0.5	,44.6	0.5	,29.9

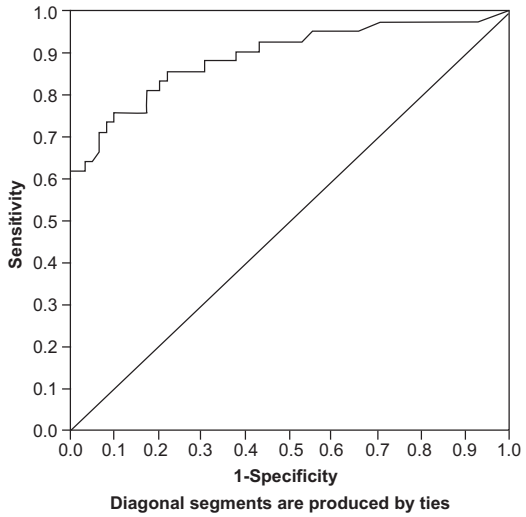

Fig.-4*: Receiver-operator characteristic curves of plasma CRP by culture positive population*

A receiver-operator characteristic (ROC) curve was formulated to find out the ideal cutoff point of Plasma CRP for distinguishing patients of AECOPD with positive sputum culture from AECOPD patients with negative sputum culture. The area under the curve (AUC) for prediction of Plasma CRP was 0.893, which gave a cut off value 5.0 mg/dl with 76.2% sensitivity and 86.2% specificity for prediction of culture positivity. (Figure- 4)

Discussion

In this present study, it was observed that 42 cases were sputum culture positive and 58 cases were culture negative. Bari and colleagues found the similar result.[10]

Sputum purulence may be a marker of bacterial infection during an exacerbation of COPD.

Stoller and colleagues showed that sputum purulence is an important indicator of bacterial infection in patients with an exacerbation of COPD.[11] In this study it was observed that almost three forth (71.4%) patients expectorated 15-30 (ml/day) in group I and 8(13.8%) in group II. There was also 12(28.6%) patients expectorate >30 (ml/day) in group I whereas none in group II. The difference was statistically significant ($p<0.05$) between two group.

It was observed that almost three fourth (71.4%) patients had mucopurulent sputum in group I and 93.1% had mucoid sputum in group II. Purulent sputum was found 26.2% in group I and not found in group II. Mucopurulent and Purulent sputum were significantly higher in group I. Weis and Almdal reported in 2006 that mucopurulent expectoration had higher levels of CRP than patients with mucoid expectoration.[12] Bircan and colleagues also reported similar findings.[13]

It was observed that 4(9.5%) patients in culture positive & 39(67.2%) patients in culture negative group belonged to 0.5-5 (mg/dl) CRP level and. More than half (52.4%) patients belonged to >10 (mg/dl) CRP level in culture positive patients and only 3(5.2%) patients in culture negative group belonged to this range of CRP. More than 90% culture positive patients had CRP level >5 (mg/dl) as a whole, in comparison to only 19% in culture negative group. A study by Stolz and colleagues demonstrated at the time of acute exacerbation, the mean CRP level in patients whose sputum was sterile on culture was 4.5+1.9 mg/dl while in patients whose sputum yielded any of the organisms, it was 7.9+1.6 mg/L which is significantly higher ($p<0.05$).[16] The above findings was concordant with the previous study done by Arora and colleagues in which, they found that CRP level was elevated (>10mg/dl) in all COPD patients where recognized bacterial pathogens were isolated in 62.0% patients.[15]

Chunhong et al reported that high median CRP levels were observed in AECOPD with bacterial aetiology compared with nonbacterial AECOPD.[17] The ideal cutoff point for distinguishing patients with bacterial AECOPD from those with nonbacterial AECOPD was 3.9 mg/dl with sensitivity 78.18%; specificity 84.61%; AUC, 0.832. Purulent sputum had a significantly higher CRP level than mucoid sputum, but with an AUC of only 0.617 (95% confidence interval, 0.49-0.74) to diagnose bacterial AECOPD. The cutoff value differs with the current study, which may be due to genetic causes, geographical variations, racial and ethnic differences with our population.

Conclusion

It can be concluded that the elevated Plasma C-reactive protein (CRP) could be a useful biomarker in addition to bacteriological sputum culture for early decision of antibiotic treatment in COPD patients with acute exacerbation as it is an early maker of the exacerbation.

This study did not search for viral etiology of AECOPD though it is one of the important causes of AECOPD & also raise serum CRP level. Detection of virus in sputum is expensive & often not available in our setting. The study was also missing the mixed infectious etiology (ie, viral with bacterial cause in a same individual) due to resource limitation & unavailable tools.

References

1. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Medicine. 2006; 3:2011-2030.
2. Gunen H, Haecievliyagil SS, Kosar F, Muthlu LC. Factors affecting survival of hospitalized patients with COPD. Eur Respir J. 2005; 26 : 234-41.
3. Bartolome R. 2004, Celli Clinical Aspects of Chronic Obstructive Pulmonary Disease. eds Baum GL, Crapo M, Glassroth JL, Karlinsky J editors. Lippincott Williams & Wilkins, Philadelphia, USA, pp. 827-829.
4. Sethi S, Murphy TF. Bacterial infection in chronic obstructive pulmonary disease in 2000: a state-of-the-art review. Clin Microbiol Rev. 2001;14(2):336-63.
5. Anthonisen NR, Manfreda J, Warren CP, Hershfield ES, Harding GK, Nelson NA. Antibiotic therapy in exacerbations of chronic obstructive pulmonary disease. Ann Intern Med. 1987; 106(2):196-204.

6. Wouters EF, Groenewegen KH, Dentener MA, Vernooy JH. Systemic inflammation in chronic obstructive pulmonary disease: the role of exacerbations. Proc Am Thorac Soc. 2007 Dec;4(8):626-34.

7. Puhan MA, Siebeling L, Frei A, Zoller M, Bischoff-Ferrari H, TerRiet G. No association of 25-hydroxyvitamin D with exacerbations in primary care patients with COPD. Chest. 2014; 145(1):37-43.

8. Nseir S, Ader F. Prevalence and outcome of severe chronic obstructive pulmonary disease exacerbations caused by multidrug-resistant bacteria. Curr Opin Pulm Med. 2008;14(2):95-100.

9. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management and prevention of Chronic Obstructive Pulmonary Disease. (Revised 2017). [accessed on September, 2017]. Available from: http://goldcopd. org/gold-2017-global-strategy-diagnosis-management-prevention-copd/pdf.

10. Bari MR, Hiron MM, Zaman SM, Rahman MM, Ganguly KC. Microbes responsible for acute exacerbation of COPD. Mymensingh Med J. 2010; 19(4):576-85.

11. Stoller JK. Management of acute exacerbations of chronic obstructive pulmonary disease. Infect Dis Clin N Am. 2004; 18: 861.

12. Weis N, Almdal T. C-reactive protein—can it be used as a marker of infection in patients with exacerbation of chronic obstructive pulmonary disease? Eur J Intern Med. 2006;17(2):88-91.

13. Bircan A, Gokirmak M, Kilic O, Ozturk O, Akkaya A. C-reactive protein levels in patients with chronic obstructive pulmonary disease: role of infection. Med Princ Pract. 2008;17(3):202-8.

14. Gupta R, Kaur R, Singh V, Goyal V, Dahiya K, Gupta A et al. Serial estimation of serum CRP levels in patients of COPD with acute exacerbation. GJMEDPH. 2012; 1 : 212-4.

15. Arora N, Daga MK, Mahajan R, Prakash SK, Gupta N. Microbial pattern of acute infective exacerbation of chronic obstructive pulmonary disease in a hospital based study. Indian J Chest Dis Allied Sci. 2001; 43: 157-62.

16. Stolz D, Crain MC, Bingisser R. Antibiotic treatment of exacerbations of COPD. Chest. 2007; 131: 9-19.

17. Chunhong P, Chan T, Yonggang Z, Xiaodong Y, Yulin F, Hong F. C-Reactive Protein Levels Predict Bacterial Exacerbation in Patients With Chronic Obstructive Pulmonary Disease. American Journal of the Medical Sciences. 2013; 345: 190-194.

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ORIGINAL ARTICLE

Central venous line (CVL): Importance of its use in the Cardiac ICU and its complications

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Abstract:

A key concept of management of the patients in the intensive care unit (ICU) during immediate postoperative period is optimization of cardiovascular function including provision of an adequate circulating volume and titration of cardiac preload to improve cardiac function. Monitoring circulatory filling as well as cardiac preload is done by measuring the central venous pressure (CVP) with the use of a central venous line (CVL). So, all patients undergoing open heart surgery cannot go without CVP monitoring.

In the department of Cardiac Surgery CVL serves many other purposes in the management of peri-operative patients, particularly those in the ICU, in addition to CVP monitoring. These may include massive blood or fluid transfusion, administering multiple drugs simultaneously for prolonged period, giving medicines that affect heart, especially if quick response is required, taking frequent blood samples etc.

But placement of CVL is a highly technical job that is usually performed by anesthetists and is associated with some complications. These complications are not common but may cause significant morbidity and possibly even mortality even when CVL access is obtained by experienced staff.

Our study period was from January 2010 to January 2015 and our study sample was randomly selected 3000 patients. All patients underwent open heart surgery and all patients underwent CVL insertion. To manage ICU patients, we monitored CVP of all patients. Measured CVP helped management of ICU patients, determined outcome and prognosis. Patients with CVP remaining equal to or less than preoperative CVP with no or single inotropic support required minimum ICU stay (1-2 days) 1583(52.77%). Patients with CVP remaining equal to or less than preoperative CVP with multiple inotrope required 2-4 days ICU stay 1144(38.13%). But those whose CVP remained greater than preoperative CVP or CVP greater than 15 cm of water had ICU stay greater than 4 days 273(9.1%) and mortality was greatest in this group of patients.

Key Words: *Central Venous Line, Central venous pressure, Internal jugular vein, Subclavian Vein, External Jugular Vein, Right Atrium*

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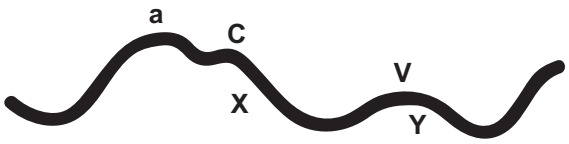
Introduction:

Inspite of the appearences of several newer monitoring technologies, central venous pressure monitoring remains in common use as an index of circulatory filling . [1] Central venous access is achieved through various routes such as internal jugular vein (IJV), sub clavian vein (SCV), external jugular vein (EJV) etc. But in NICVD and all other cardiac centers of Bangladesh, IJV is used commonly via anterior approach. Less frequently and when access through IJV is failed, SCV and EJV route is used. Through these routes central venous catheter tip reaches into superior vena cava (SVC) or into Right Atrium (RA)[2]. Central veins are those great veins that open into RA without any intervening valves. [3] Monitoring circulatory filling as well as cardiac preload is done by measuring the central venous pressure with the use of a central venous line keeping the patient in supine position in a point over the right atrium at the intersection of 4th intercostals space with the mid axillary line.[4]

Normal value of CVP ranges from 0 to 6 cm of water. CVP is the index of circulatory filling and cardiac preload. It actually measures right atrial pressure. CVP is commonly measured by means of fluid filled cannula (CVP catheter) with its tip into SVC or RA, connected to either a fluid filled manometer or more commonly to an electronic pressure transducer linked to a monitor which will display a continuous pressure wave.[3]

Central venous waveform has three ascending waves (a, c & v) and two descending waves (x & y). a wave is due to atrial systole. a wave is followed by x descent which corresponds to atrial relaxation. x descent is punctuated by c (+ve) wave. c wave is caused by closure and bulging back into RA of the tricuspid valve leaflet during ventricular systole. v wave is caused by build up of pressure into atria due to continued venous return into atria when tricuspid valve (TV) is closed as a result of ongoing ventricular systole and early diastole. y descent is due to opening of tricuspid valve and rapid passive flow of atrial blood into ventricle. But in the department of Cardiac Surgery, we use only average baseline CVP.[5]



Central Venous Trace

CVP is influenced by volume of blood in the central venous compartment and compliance of that compartment. There is definite relationship between venous return and CVP, and, CVP and cardiac output.[1,6] Increasing CVP (i.e. preload) by infusing fluid or blood increases cardiac output proportionately.[6] But this occurs up to a point beyond which further increase in CVP will not increase cardiac output. Moreover it will carry the risk of fluid overload. This is the minimum CVP for maximum cardiac output. [7]

There are some factors that affect measured CVP.[4] They are as follows;

1. Central venous blood volume:
   - Venous return
   - Total blood volume
   - Regional vascular tone
2. Compliance of central compartment:
   - Vascular tone
   - Right ventricular compliance
     - Myocardial disease
     - Pericardial disease
     - Tamponade
3. TV disease :
   - Stenosis
   - Regurgitation
4. Cardiac rhythm:
   - Junctional rhythm
   - Atrial fibrillation (AF)
   - Atrioventricular rhythm
5. Reference level of transducer
6. Intra-thoracic pressure:
   - Respiration
   - Intermittent positive pressure ventilation (IPPV)
   - Positive end expiratory pressure (PEEP)
   - Tension pneumothorax

But the CVP of the patients in the ICU who underwent open heart surgery is little affected

by vasomotor reflexes which have been blocked pharmacologically by the anesthetic agents. Other cardiac organic factors that might affect measured CVP are absent in our patients because they have been surgically corrected. Moreover intra-thoracic pressure [eg respiration, Intermittent positive pressure ventilation(IPPV), Peak end expiratory pressure(PEEP) etc] will not affect CVP because we measure CVP at the end of expiration in the absence of PEEP.

Potential uses of CVL:

Measurement of CVP:

Measurement of CVP is extremely important for management of patients in the ICU during immediate post operative period following open heart surgery. CVP which is an index of preload is a common essential invasive monitoring system of these patients for proper fluid management. For optimum fluid therapy, we record preoperative CVP in the operation theater just before starting operation. This preoperative CVP acts as a guide for fluid therapy.[8] After completion of surgery, we maintain CVP equal to or below preoperative CVP which is associated with good outcome.

Higher CVP or very low CVP is associated with cardiac dysfunction which may culminate to death of the patient if not intervened in time. There is a special relationship between measured CVP and outcome of the patients. After initial optimization and fluid restriction (zero balance) patients whose CVP does not cross preoperative CVP and who maintain satisfactory cardiac output with minimum inotropic support show better outcome in terms of shorter period of ICU stay. CVP higher than 15 mm Hg with multiple inotropes in higher doses is associated with poor outcome.[9]

Sometimes we utilize CVP measurement to predict fluid responsiveness of the patient. Despite CVP around preoperative CVP when we see cardiac output is not satisfactory, we give a bolus of fluid, usually 200 ml, very rapidly to raise CVP. If the rise of CVP is associated with increase in cardiac output and rise of BP, then we maintain the higher CVP. Dynamic change in CVP with respiration i.e. fall in CVP e" 1 mm Hg during inspiration is highly predictive of fluid responsive cardiac index (CI).[10,11]

Other uses of CVL (Besides CVP measurement) :

Besides CVP measurement CVL has many other important uses in the department of Cardiac Surgery[12]:

- To give multiple inotrope and vasoactive drugs simultaneously for prolonged period.
- To give medicine that affect heart specially if quick response of the medicine is required.
- To give medicine which is very irritant for the vein and tissue if given through a peripheral line, eg K^+
- To give large amount of blood or fluid quickly.
- To take frequent blood samples.
- To give parenteral nutrition occasionally when required (eg. during prolonged ventilation).

Despite its important use in the department of Cardiac surgery, the CVL is associated with some hazards or complications, a few of which may be life threatening.[13,14] A list of complications is given below:

1. Arterial puncture
2. Blood stream infection
3. Hemothorax
4. Pneumothorax
5. Hemopneumothorax
6. Vessel occlusion
7. Catheter malposition
8. Catheter induced thrombosis
9. Arrythmia
10. Venous air embolism
11. Hematoma
12. Endocarditis
13. Multiple punctures & change of route of access
14. Thrombosis

But the benefits of the use of CVL in the department of Cardiac Surgery is indispensible and life saving and it greatly outweighs the danger of the complications associated with its placement.

Materials and methods:

This study was conducted at the department of Cardiac Surgery, NICVD, Dhaka, Bangladesh.

The period of study was from January, 2007 to January, 2016. A retrospective observational study was performed. In this study all adult patients (18^+ years) who underwent open heart surgery were included. The patients were randomly selected. We enrolled 3,000 patients in our study.

After the patient has been shifted from operation theater (OT) to ICU, we connect the patient with monitor and ventilator. We revise fluid, blood, inotrope to optimize hemodynamic condition. Then we send blood sample for arterial blood gas (ABG), electrolytes and random blood sugar (RBS) and urgent requisition for chest X-ray. We analyze the reports and correct accordingly if any derangement was noted and reset ventilator if required. This optimized state is the study point of CVP monitoring. We record CVP every one hour and half hourly in some patients if deemed appropriate. We restrict fluid and try to keep in a state of zero balance. We classify our patients in three categories:

1. Whose CVP remain equal to or below preoperative CVP and requires no or minimum inotropic support (eg. single inotrope) to maintain satisfactory hemodynamic condition.
2. Whose CVP tends to rise above preoperative CVP but be kept equal to or below preoperative CVP with moderate dose of single or multiple inotrope to maintain satisfactory cardiac output.
3. Whose CVP remains above preoperative CVP or above 15 mm Hg despite high doses of multiple inotropes.

We assessed their outcomes in terms of period of ICU stay. We also analyzed the CVP of patients who died in ICU during early post operative period. Other uses of CVL & its complications were also recoded and analyzed.

But placement of CVL is a highly technical job that is usually performed by anesthetists and is associated with some complications. These complications are not common but may cause significant morbidity and possibly even mortality even when CVL access is obtained by experienced staff.

Results:

Demographic data analysis shows that male: female is about 3:2.Distribution of number of patients in different age groups shows small variations with maximum concentration in 56-65 years and minimum in >65 years age. (Table l)

The patients (52.77%) whose CVP remains equal or less than preoperative CVP with no inotrope or single inotrope are associated with excellent outcome of surgery in terms ICU stay (1-2 days).But those (91% of patients) whose CVP tends to remain higher than preoperative CVP or higher than 15 mm of Hg. despite the support of higher doses of multiple inotropes are associated with worst outcome (> 4 days).An intermediate group of patients (38.13%)whose CVP was kept equal or

Table-I

Age and sex distribution of patients.(n=3000)

SL	Age(yrs)	male	female	total	Percentage (%)
1	18-25	210	302	512	17
2	26-35	252	238	490	16
3	36-45	356	242	598	20
4	46-55	218	187	405	13.5
5	56-65	432	183	615	20.5
6	>65	258	122	380	13
total				3000	100

Table-Il

Relationship between CVP with inotropes and length of ICU stay (n=3000)

Category	CVP with inotrope	No. of patients	ICU stay	Percentage
1	CVP ≤ preoperative CVP with single or no inotrope	1583	1-2 days	52.77%
2	CVP ≤ preoperative CVP with multiple inotropes	1144	2-4 days	38.13%
3	CVP Ã preoperative CVP or > 15 mm Hg with high dose of multiple inotropes	273	> 4 days	9.1%

less than pre operative CVP with moderate dose of multiple inotropes have also satisfactory outcome (2-4 days).(Table ll)

There is strong relation between CVP and mortality following cardiac surgery.90.67% mortality is associated with very high CVP (>15 mm of Hg).Mortality is very low (9.33%) seen in patients with CVP equal or less than preoperative CVP. (Table lll)

CVL has multiple essential uses in cardiac ICU and used to take frequent blood sample from all patients (100%).But its most important common uses are to monitor CVP (100%) and to give multiple inotropes, other vasoactive medications and antibiotics for prolong period (99%).Other common and important uses of CVL are rapid infusion of large volume of blood and fluid (93.13%) and rapid optimization of serum potassium through CVL (60.43%).Parental nutrition (1.73%) and medication other than inotrope (5.03%) are less frequent uses of CVL.(Table IV)

Complications due to CVL insertion and in situ position are uncommon and most are amenable

Table-Ill

Relationship between CVP and mortality (total mortality n=150)

SL	CVP	No. of death	Percentage
1	CVP ≥ 15 mm Hg	136	90,67%
2	CVP ≤ preoperative CVP	14	9.33%

Table-IV

Uses of CVL in cardiac ICU (n=3000)

SL	Use	No. of patients	Percentage
1	Monitoring of CVP	3000	100%
2	To give multiple inotropes and vasoactive medications and antibiotics for prolonged period	2970	99%
3	To give K^+(irritant, if given peripherally)	1813	60.43%
4	Rapid infusion of large amount of blood and fluid	2794	93.13%
5	To take frequent blood samples	3000	100%
6	To give parenteral nutrition	52	1.73%
7	To give medicines (other than inotropes) whose quick response is essential (eg. amiodarone, sodi-bi-carb, lignocaine, dessication therapy etc.)	151	5.03%

Table-V

Complications of CVL (insertion and in situ position): n=3000

SL	Complications	No. of patients who sustained the complication	Percentage
1	Arterial puncture	63	2.1%
2	Blood stream infection	46	1.53%
3	Hemothorax	12	0.4%
5	Pneumothorax	18	0.6%
4	Catheter malposition	14	0.47%
5	Arrythmia	7	0.23%
6	Hematoma	87	2.9%
7	Endocarditis	1	0.03%
8	Haemopneumothorax	4	0.13%
9	Multiple puncture & change of route of access	122	4.07%

to minor intervention. Hemothorax (0.4%), blood stream infections (1.53%) and endocarditis (0.03%) are also seen and these may be very dangerous and life threatening. (Table V)

Discussion:

In the department of cardiac surgery, CVL is inserted in all patients undergoing open heart surgery. CVL insertion is mandatory because of its indispensable uses in peri-operative patients. CVL is inserted in OT before starting operation and preoperative CVP is recorded.

CVL is used to measure CVP in ICU. It is a common essential monitoring system to manage postoperative patients in ICU. It is useful for judicious use of fluid management and determination of appropriate inotropic support. After initial stabilization measured CVP reflects outcome and prognosis of the patients. It is obvious from this study (Table ll) that if patients' CVP remains d" preoperative CVP with minimal or no inotropic support, patients' recovery is good and associated with shorter period of ICU stay. If the patients need multiple support and higher doses, ICU stay period is seen to increase parallely. If the patients' CVP remains higher despite high doses of multiple inotropes, the prognosis is poor and mortality is higher in this group. This observation correlates well with the work of Rady MY, Ryan T et al in 1998.[9]

We analyzed CVP of the patients who died in immediate and late postoperative period and could establish a clear cut relationship between measured CVP and mortality. Most death cases had high CVP (> preoperative) and high doses of multiple inotropes.[9]

We studied other uses of CVL. In most patients (100%) CVL is used to give multiple medications simultaneously (inotropes, vasoactive and cardioselective medications). In 93.13% patients CVL is used to give large amount of blood and fluid transfusion. All patients required frequent blood sampling through CVL. Frequent electrolyte monitoring and correction is a common procedure in immediate postoperative cardiac patients and many patients require K^+ infusion which is irritant if infused through peripheral lines. In our study, 60.43% patient required K^+ infusion through CVL. 52 (1.73%) patients required parenteral nutrition through CVL for prolonged ICU stay due to complications. CVL is also used to give medicines (other than inotropes) where quick response was essential such as amiodarone, sodibicarb etc. in about 5.03% of patients. Almost similar uses have been shown in the study of Boon, J.M., Van Schoor et al. 2008.[12]

CVL related complications were not common (6%).[5] Arterial (carotid>subclavian>femoral artery) puncture occurred in 63 (2.1%) patients. Blood stream infection noted most commonly in those patients whose CVL remained in situ for longer period and occurred in 1.53% cases. Haemothorax occurred in 12 (0.4%) cases, two of which developed instability before opening chest due to gross concealed hemorrhage into right pleural cavity. Although no other studies found hemothorax while doing CVL insertion through internal jugular vein. Local hematoma was the commonest complication and occurred in 87 (2.9%) patients. Catheter related arrhythmia and endocarditis were two less frequent complications. One (0.03%) patient developed CVL related prosthetic valve endocarditis. Same organism was isolated from blood C/S and CVL tip C/S. This patient died due to failure to control infection. Although this was a very very rare CVL related complication, it was life threatening. The complication rate of our study is closely related to the work of Sznajder Ji et al. 1986.[15]

Conclusion:

To manage ICU patients following open heart surgery, CVP measuring is essential for judicial fluid management and selection of inotropes and vasoactive drugs. Measured CVP can reflect outcome and prognosis of these patients. CVL has many other valuable uses in ICU patients, which cannot be replaced by peripheral lines. But there are some CVL related complications, a few of them, if occur, are very dangerous. In spite of this, use of CVL in cardiac ICU is so indispensable and life saving for each patient that it greatly outweighs its potential risks of complications. All doctors and nurses managing postoperative cardiac patients should have adequate knowledge regarding the use and importance of CVL.

Reference:

1. Patterson SW, Piper H and Starling EH. The regulation of the heart beat. *The Journal of physiology*. 1914;*48*(6):465-513.
2. Bannon MP, Heller SF, Rivera M. Anatomic considerations for central venous cannulation. *Risk management and healthcare policy*. 2011; *4*:27.
3. Reems MM, Aumann M. Central venous pressure: principles, measurement, and interpretation. *Compend Contin Educ Vet. 2012;34*(1):E1.
4. Godje O, Peyerl M, Seebauer T. Central venous pressure, Pulmonary capillary wedge pressure and intrathoracic blood volume as preload indicators in cardiac surgery patients. *European Journal of Cardio-Thoracic Surgery. 1998;* 13: 533-540.
5. Vincent JL ED. Updates in Intensive Care & Emergency Medicine. Functional hemodynamic monitoring. Brussels. Springer. 2017; Vol 42: 99.
6. Patterson SW, Starling EH. On the mechanical factors which determine the output of the ventricles. *The Journal of physiology*. 1914;*48*(5):357-379.
7. Kuhtz-Buschbeck JP, Lie RK, Schaefer J, Wilder N. Reassessing diagrams of cardiac mechanics: from Otto Frank and Ernest Starling to Hiroyuki Suga. *Perspectives in biology and medicine*.2016;*59*(4):471-490.
8. Venn, R., Steele, A., Richardson, P., Poloniecki, J., Grounds, M. and Newman, P., 2002. Randomized controlled trial to investigate influence of the fluid challenge on duration of hospital stay and perioperative morbidity in patients with hip fractures. *British journal of anaesthesia*, *88*(1), pp.65-71.
9. Rady MY, Ryan T, Starr NJ. Perioperative determinants of morbidity and mortality in elderly patients undergoing cardiac surgery. *Critical care medicine*. 1998;*26*(2):225-235.
10. Magder S, Georgiadis G, Cheong T. Respiratory variations in right atrial pressure predict the response to fluid challenge. *Journal of Critical Care*. 1992;*7*(2):76-85.
11. Magder S, Lagonidis D. Effectiveness of albumin versus normal saline as a test of volume responsiveness in post-cardiac surgery patients. *Journal of critical care*. 1999;*14*(4):164-171.
12. Boon JM, Van Schoor AN, Abrahams PH, Meiring JH, Welch T. Central venous catheterization—An anatomical review of a clinical skill, Part 2: Internal jugular vein via the supraclavicular approach. *Clinical Anatomy*. 2008;*21*(1):15-22.
13. Smith RN, Nolan JP. Central venous catheters. *Bmj*,2013;347:f6570.
14. McGee DC, Gould MK. Preventing complications of central venous catheterization. *New England journal of medicine*. 2003;*348*(12):1123-1133.
15. Sznajder JI, Zveibil FR, Bitterman H, Weiner P, Bursztein S. Central vein catheterization: failure and complication rates by three percutaneous approaches. *Archives of internal medicine*. 1986;*146*(2):259-261.

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ORIGINAL ARTICLE

Depressive Disorders Among Patients In Chronic Obstructive Pulmonary Diseases

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Abstract:

Background: *This study was done to see the prevalence of depressive disorders in COPD patients and that will be able to draw attention of the relevant personnel's in effective treatment of COPD.*

Materials and Methods: *This was a cross sectional comparative study. The study was carried out in the Department of Psychiatry in collaboration with the Department of Respiratory Medicine, Sylhet M.A.G. Osmani Medical College Hospital, Sylhet, during the study period from 1st July 2014 to 30th June 2015 were the study population. All COPD patients those got admitted in the different unit of Medicine and Respiratory Medicine fulfilling inclusion and exclusion criteria were taken as case. Control subjects were age and sex matched accompanying person of the patients or other patients attending them. After fulfilling the inclusion and exclusion criteria 96 patients of COPD (based on clinical history, examination and lung function test spirometry) were selected as study subjects (Group-A). Age and sex matched 96 healthy subjects who were fulfilling the inclusion and exclusion criteria selected as control subjects (group-B).The clinical parameters and results were analyzed by Un-paired t test, Chi-square test and Fishers Exact test.*

Results: *In this study, there was significant increase in major depressive disorder (MDD) in COPD patients than in control group (27.1% vs 8.3%) (χ^2=11.58, p=<.05) and persistent depressive disorder (PDD) was present in 15 COPD patients and in1respondent of control group which was also statically significant (χ^2=13.35, p=<.001) .*

Conclusion: *This study showed that the proportion of depressive disorders is significantly higher in patients suffering from COPD than that of control subjects. Major depressive disorder and persistent depressive disorder are also significantly more frequent in patients of COPD.*

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Introduction:

Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable disease characterized by persistent airflow limitation that is usually progressive. It is commonly associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. The prevalence of COPD directly related to the prevalence of tobacco smoking and the use of biomass fuels, more common in low and middle income countries. Current estimate suggest that 80 million people worldwide suffer from moderate to severe stage of COPD [1].

Chronic obstructive pulmonary disease (COPD) is a chronic illness and is a major cause of morbidity and mortality worldwide [2] . By 2030

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COPD has been predicted 3rd leading cause of death and 5th leading cause of disability in the world. The overall prevalence of COPD is 4.32% in general population in Bangladesh [3].

COPD patients suffer from limitations of activities, loss of independence, decreased social functioning and quality of life .Commonly associated co-morbid conditions include cardiovascular disease, the metabolic syndrome, osteoporosis, depression, lung and other cancer [4].

Among psychiatric morbidities depression is the most common complication in COPD patient. The prevalence of depressive symptoms among COPD patients has been estimated to be 40 to 50% [5]. Depression is the 1st leading cause of disability worldwide [6]. Most often depression is unexplored in a patient due to variations of clinical presentation [7].

The Medical Outcomes Study suggested that patients with chronic respiratory disease (next only to patients with chronic gastro-intestinal disease) appeared worst off on their mental health status than patients with all other chronic diseases [7, 8].

Mortality is significantly high in patients with depressive disorders, largely due to suicide. Rates of suicide in patients with mood disorder are at least 15 times higher than those in the general population and tend to be higher in unipolar depression than in bipolar disorder [9]

Unrecognized and untreated depressions is associated with poor treatment compliance, increased frequency of consultation, hospital admission, hospital stay, treatment cost and increased overall health care burden to the health care services [8]. Risk of dropout from pulmonary rehabilitation is significantly greater in depressed COPD patients, irrespective of severity of breathlessness [10, 11] .

Due to the irreversible nature of chronic obstructive pulmonary disease (COPD), the aim of treatment in patients with COPD is not to cure but to reduce symptoms, increase functioning and improve the patient's quality of life. Along with the disease process itself, attention should given to co-morbid depression in CODP patient [12].

Material and Methodology

This was a cross sectional comparative study was carried out in the Department of Psychiatry in collaboration with the Department of Respiratory Medicine, Sylhet M.A.G. Osmani Medical College Hospital, Sylhet from 1st July 2014 to 30th June 2015. A total of 96 COPD patients those got admitted in the different units of Medicine and Respiratory Medicine fulfilling inclusion and exclusion criteria were taken as case. Control subjects were age and sex matched accompanying person of the patients or other patients attending Sylhet M.A.G. Osmani Medical College Hospital, Sylhet during the study period from 1st July 2014 to 30th June 2015 were the study population. Informed written consent was obtained from the patients after full explanation of purpose of the study. After fulfilling the inclusion and exclusion criteria 96 patients of COPD (based on clinical history, examination and lung function test spirometry and confirmed by chest specialist) were selected in this study as study subjects (Group-A). Age and sex matched 96 healthy subjects examined by chest specialist who were fulfilling the inclusion and exclusion criteria selected as control subjects (group-B). By spirometry the following values were obtained from the test: Forced Expiratory Volume 1 sec [FEV1], Forced Vital Capacity [FVC], and FEV1/FVC ratio for the staging of COPD patients according to GOLD guidelines .· Post bronchodilator spirometry (Salbutamol 2.5mg by nebulization) was performed in all the patients to exclude the diagnosis of bronchial asthma. All data were recorded systematically in a preformed check list. Quantitative data were summarized as mean and standard deviation; and comparison was performed between the two groups by unpaired t- test. Qualitative data were summarized as frequency and percentages. Comparison between two groups was done by chi-square ($Ç^2$) test and Fisher's exact test. A probability (p) value of, <0.05 was considered statistically significant and $p>0.05$ was taken as non-significant. Statistical analysis was performed by using SPSS (Statistical package for social science) for windows version 21.

Results:

Table-I

Distribution of the respondents on the basis of age

Age in years	Study group		p-value
	Group-A (n=96) Frequency (%)	Group-B (n=96 Frequency (%)	
41-50 years	6 (6.2)	5 (5.2)	*p=0.935
51-60 years	32 (33.3)	36 (37.5)	
61-70 years	49 (51.0)	47 (49.0)	
71-80 years	9 (9.4)	8 (8.3)	
Mean (years)	63.35 (SD ± 6.68)	61.90 (SD ± 6.37)	†p=0.123

The table shows that most of responder in both case group and control group where within 61 to 70 years age range and lowest responders were from 41 to 50 years age range.

Table-II

Distribution of the respondents according to sex

Sex	Study group		*p-value
	Group-A (n=96) Frequency (%)	Group-B (n=96 Frequency (%)	
Male	85 (88.5)	85 (88.5)	-
Female	11 (11.5)	11 (11.5)	
Total	96 (100.0)	96 (100.0)	

The table shows that both case and control group had 85 male and 11 female responders. Male were more than females in both case and control group.

Table-III

Distribution of respondents according to their social background

Social background	Study group		*p-value
	Group-A (n=96) Frequency (%)	Group-B (n=96 Frequency (%)	
Rural	78 (81.2)	84 (87.5)	*p=0.233
Urban	18 (18.8)	12 (12.5)	
Total	96 (100.0)	96 (100.0)	

*χ^2 (Chi- square) test was employed to analyze the data ($Ç^2$=1.422; p=0.233).

In COPD group, 78 (81.2%) respondents were rural dweller whereas in control group, 84 (87.5%) were rural and 12 (12.5%) respondents were urban inhabitant. The difference between the two groups was statistically non-significant

Table IV

Distribution of respondents according to smoking status

Smoking status	Study group		p-value
	Group-A (n=96) Frequency (%)	Group-B (n=96 Frequency (%)	
Smoker	91 (94.8)	57 (59.4)	*p<001
Non-smoker	5 (5.2)	39 (40.6)	
Total	96 (100.0)	96 (100.0)	

*χ^2 (Chi- square) test was employed to analyze the data. . ($Ç^2$=34.084; p<0.001).

Here, 91 (94.8%) respondents were smoker in COPD group and 57 (59.4%) were smoker in control group. Smoker were significantly more in COPD group than that of control group

Fig.-1 shows 34 (35.4%) patients were steroid user and 62 (64.6%) patients did not use any steroid.

Fig.-2 shows the distribution of respondents according to duration of COPD. Duration of COPD was 1 to 5 years in 27 (28.1%) cases, 6 to 10 years in 40 (41.7%) cases and above 10 years in 29 (30.2%) cases.

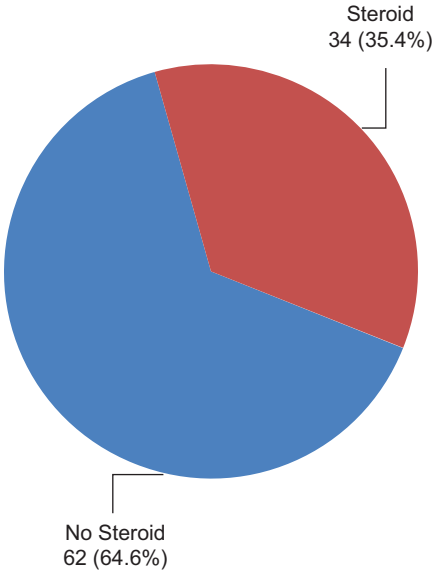

Fig.-1: *Distribution of the patients of COPD according to steroid use (n=96)*

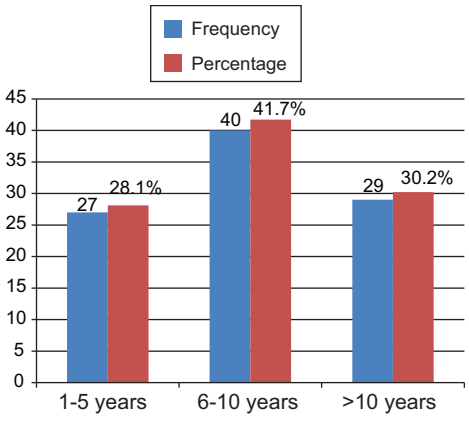

Fig.-2: *Distribution of respondents according to duration of COPD (n=96)*

Fig.3 shows the distribution of the patients by severity of COPD according to GOLD criteria. GOLD stage-III was the most frequent and was present in 47.9% of cases, followed by stage-IV (45.8%) and stage –II (6.2%).

Fig.-4 shows CES-D score was positive for depressive disorders in 47 (49.0%) COPD patients and 11 (11.5%) respondents of control group. The difference was statistically significant ($Ç^2$=32.016; p<0.001).

Depressive disorders were present in 41 (42.7%) COPD group which was significantly higher than that in control group, n=9 (9.4%). (χ^2=27.691; p<0.001).

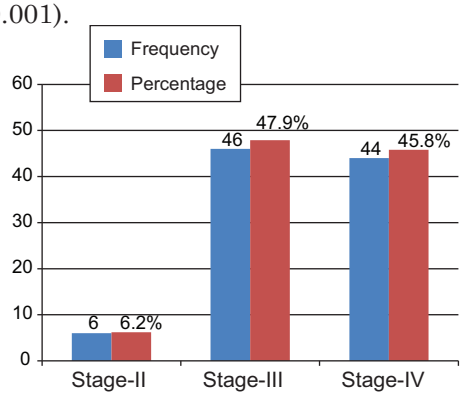

Fig.-3: *Distribution of the patients by severity of COPD according to GOLD criteria (n=96)*

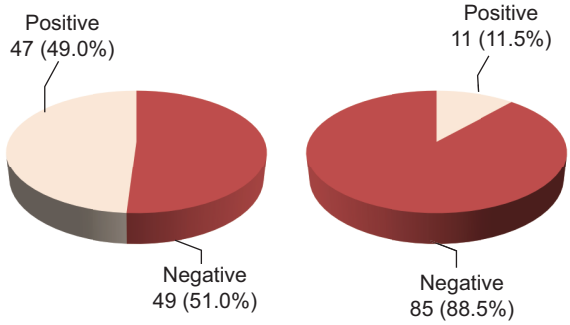

Fig.-4: *Distribution of respondents by CES-D score*

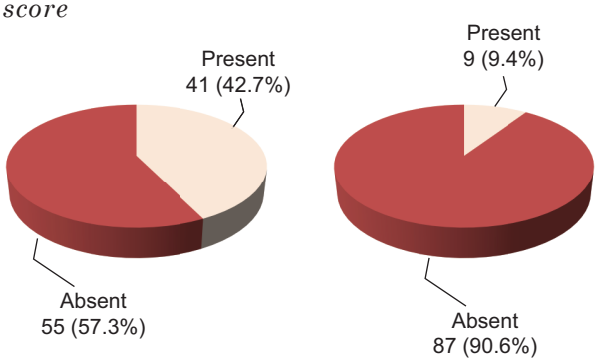

Fig.-5: *Distribution of respondents by depressive disorders according to DSM-5 criteria.*

Table-V

Association of smoking and depressive disorders in COPD

Smoking status	Depressive disorders		p-value
	Present Frequency (%)	Absent Frequency (%)	
Smoker (n=91)	39 (42.9)	52 (57.1)	*p=1.000
Non-smoker (n=5)	2 (40.0)	3 (60.0)	

*Fisher's Exact test was employed to analyze the data. (p=1.000).

Depressive disorders were present in 39 (42.9%) smoker patients and 2 (40.0%) non-smoker. Smoking status did not affect the depressive disorders in COPD,

Table-VI

Association of steroid intake and depressive disorders

Steroid intake	Depressive disorders		p-value
	Present Frequency (%)	Absent Frequency (%)	
Yes (n=34)	17 (50.0)	17 (50.0)	*p=0.285
No (n=62)	24 (38.7)	38 (61.3)	

*Chi-Square ($Ç^2$) test was employed to analyze the data. Figure in the parenthesis indicates corresponding percentage.

Table VIII shows Depressive disorders were present in 17 (50.0%) steroid users. Although steroid intake increased the rate of depressive disorders in COPD but did not reach the level of significance. ($Ç^2$=1.144; p=0.285). Association of steroid intake and depressive disorders in COPD was shown in table- VI.

Table-VII

Association of duration of COPD and depressive disorders

Duration of COPD	Depressive disorders		p-value
	Present Frequency (%)	Absent Frequency (%)	
1-5 years (n=27)	9 (33.3)	18 (66.7)	*p=0.231
6-10 years (n=16)	16 (40.0)	24 (60.0)	
11-15 years (n=44)	16 (55.2)	13 (44.8)	

*Chi-Square ($Ç^2$) test was employed to analyze the data. ($Ç^2$=2.931; p=0.231).

Table VII shows depressive disorders were present in 9 (33.3%) patients of COPD for 1 to 5 years range duration , 16 (40.0%) patients of 6 to 10 years group and 23 (52.3%) patients in 11 to 15 years of disease duration . Though the rate of depressive disorders increased with duration of COPD but did not reach the level of significance .

Table-VIII

Association of COPD stage and depressive disorders

COPD stage	Depressive disorders		p-value
	Present Frequency (%)	Absent Frequency (%)	
Stage-II (n=6)	1 (16.7)	5 (83.3)	*p=0.176
Stage-III (n=46)	17 (37.0)	29 (63.0)	
Stage-IV (n=44)	23 (52.3)	21 (47.7)	

*Fisher's Exact test was employed to analyze the data (p=0.176).

Depressive disorders were present in 16.7% patients in stage-II, 37.0% in stage-III, and 52.3% patients in stage-IV COPD. Though the rate of depressive disorders increased with stage of COPD but did not reach the level of significance,

Table- IX

Distribution of respondents by type of depressive disorders

Depressive disorders	Study group		*p-value
	Group-A (n=96) Frequency (%)	Group-B (n=96) Frequency (%)	
MDD	26 (27.1)	8 (8.3)	p=0.001
PDD	15 (15.6)	1 (1.0)	p<0.001

*$Ç^2$ (Chi- square) test was employed to analyze the data. ($Ç^2$=11.580; p=0.001) ,($Ç^2$=13.354; p<0.001).

Table-IX shows the distribution of respondents by types of depressive disorders. Major depressive disorder (MDD) was present in 26 COPD patients. Presence of MDD was statistically significant in COPD patients Persistent depressive disorder (PDD) was present in 15 cases. There was also significant difference of presence of PDD in COPD patients than that of control subjects

Discussion

This cross sectional and comparative study was conducted to evaluate depressive disorders among COPD patients. 96 COPD patients were selected according to inclusion and exclusion criteria and categorized as COPD group (group-A) and age, sex matched 96 persons were studied as control group (group-B).

In this study, the mean age was 63.35 (SD ± 6.68) years in COPD group; whereas in control group it was 61.90 (SD ± 6.37) years which is almost similar (p=0.123). This result correlated with the study of Jorgensen[11] where mean age of male patients with COPD was 62.8 ±5.8 years. In some other studies like, Graat-Verboom [12] mean age was 65.6 (SE 0.4) years, Naghshin [13.],Van Menon[14] found 69.34 ± 9.47 years, Julian [15.], found 66.4 ± 5.9 years which also support our result.

In this study male predominance was observed as both case and control group had 85 (88.5%) males. Male preponderance of COPD was reported in some other studies such as Dursun [16] , .91.3%, and Balcells [17] 94%. But female preponderance of COPD was also reported in Ng[7] 64.6%, Julian[15] 60.1%.. Katz [18] 57.6%;

In this study, 91 (94.8%) respondents were smoker in COPD group and 57 (59.4%) in control group. Smoker were significantly more in COPD group than that of control group (p<0.001). Sijapati [19] supports this result that 93 (93%) patients with COPD were smokers. Balcells [17] found that 99.4% of COPD patients were smoker (current or ex-smoker) and only 0.06% patients were never smoker. Julian[15] found that 19.1% of COPD patients were current smoker and 79.3% of patients were ever smoker.

In this study, among 91 smoker patients, depressive disorders were present in only 39 (42.9%) responders. Smoking did not affect the depressive disorders in COPD (p>0.05). Prospective cohort studies show that depression predicts smoking initiation [20] and increases in smoking behavior [21], and decreases in physical activity [22]. We did not find the association of smoking and the depressive disorders in COPD patients (p value). This may be due to inclusion of both current and ex-smoker in smoker group; as there are complex associations between nicotine dependence, depression and anxiety disorders, and smoking cessation [22] .

In the present study 34 (35.4%) patients were steroid user. Depressive disorders were present in 17 (50.0%) patients on steroid and 24 (38.7%) patients without steroid. Though steroid intake increased the rate of depressive disorders in COPD but did not reach the significant level (p>0.05).

In the current study depressive disorders were present in 9 (33.3%) patients with 1 to 5 years duration of COPD , 16 (40.0%) patients with 6 to 10 years duration of COPD and 23 (52.3%)

patients 11 to 15 years duration group. Though the rate of depressive disorders increased with duration of COPD but did not reach the level of significance (p>0.05). Depressive disorders increased with the duration of diseases may be due to with the progression of diseases process as patients become physicaly inactive, weak and breathing become more laborious with increased of diseases sevierity with time. Schneider [23] reported a longer lag time between the first COPD diagnosis. We also found increase rate of depression increased with COPD duration but difference was not significant may be due to small sample and method of screening and diagnosis of depression by DSM-5 criteria.

Depressive disorders were present in 1 (16.7%) patient of stage-II COPD, 17 (37.0%) patients of stage-III, and 23 (52.3%) patients of stage-IV COPD. Though the rate of depressive disorders increased with severity of COPD but was non-significant (p>0.05) . There are reports indicating no relationship between lung function and depression [24]; [25]. Conversely, Van Mannen[14] found the prevalence of depression to be 19.6% in patients with mild to moderate COPD, and 25.0% among patients with severe COPD suggesting an association between the severity of lung function and depression. Gudmandsson [25] reviewed the prevalence of depression and anxiety, using the HADS, in 79 in-patients with COPD, and found that those with more severe impairment in lung function had higher scores of depression and anxiety. Atlantis [22] , in a systematic review and meta-analysis showed that the increased burden of co-morbid depression in COPD likely rises with the degree of disease severity. Iguchi[19] found that the prevalence of depression increased with BODE stage, being 12.5% (1/8) in stage I, 45.5% (5/11) in stage II, 38.2% (13/34) in stage III, and 75% (12/16) in stage IV (P=.02). In this study the rate of depressive disorders increased with severity of COPD but not significant may be due to small sample size, diagnosis of depression by CES-D scoring and followed by DSM-5.

This study showed that CES-D score was positive for depressive disorders in 47 (49.0%) patients in COPD group and in 11 (11.5%) respondents of control group. The difference between these two groups was significant (p<0.001). This result is supported by Van Manen[14]. He also reported that among COPD patients attending the GP practitioner, depressive disorders were present in 25.0% based on CES-D scale and it reached 50% in moderate to severe stages of COPD.

In this study major depressive disorder (MDD) was present in 26 (27.1%) COPD patients and 8 (8.3%) respondents in control group. There was a significant difference of presence of major depressive disorder in COPD patients than that of control subjects (p=0.001). Persistent depressive disorder (PDD) was present in 15 (15.6%) COPD patients and was in 1 (1.0%) respondents of control group. There was a significant difference of presence of persistent depressive disorder in COPD patients than that of control subjects (p<0.001). Julian[15] found that major depressive disorder (11.2%), minor depression (12.2%) and dysthymia (1.6%) among their COPD patients. Patten [3,] found major depressive disorder in 31 (24.8%) COPD patients and 914 (16.4%) control subjects, major depressive disorder was significantly higher in COPD patients than that of control subjects (p=0.01). Patients with COPD may have a spectrum of symptom severity ranging from short-term depressive symptoms to dysthymia to clinical depression. A few studies (Yohannes[6]; Kim [26.),], have reported that approximately two thirds of COPD patients with depression have from moderate-to-severe depression. In one study [8], it was reported that approximately one fourth of COPD patients had unrecognized subclinical depression. Such patients commonly have a high burden of physical disability and are at risk for a major depression.

Conclusion

The results of this study showed that the proportion of depressive disorders is significantly higher in patients suffering from COPD than that of control subjects. Major depressive disorder and persistent depressive disorder are also significantly more frequent in patients of COPD. Thus the null hypothesis is rejected and alternate hypothesis (hypothesis of this study) is established. A liaison between medicine and psychiatry practice is essential for early detection and treatment of depression in patients suffering from COPD.

References:

1. Reid PT, Innes JA.. Respiratory disease. *In*: Walker BR, Colledge NR, Ralston SH, Penman ID, editors. *Davidson's Principles and Practice of Medicine*. 22nd ed. Edinburgh: Churchill Livingstone, Elsevier; 2014, p. 643-732.
2. Lehouck A, Boonen S, Decramer M, Janssens W.. COPD, Bone Metabolism, and Osteoporosis. *Chest,* 2011, 139(3), 648-57.
3. Patten SB, Williams JV, Lavorato DH, Eliasziw M.. A longitudinal community study of major depression and physical activity. *Gen Hosp Psychiatry*, 2009, 31(6), 571-5.
4. Habib GMM, Hassan MR, Rahman MM, Hossain MA, Mahmud AM, Bennoor KS, et al.. Burden of Obstructive Lung Diseases in Bangladesh (BOLD-BD). 5th IPCRG World Conference, June 2-5, 2010, Toronto, Canada. Abstracts accepted for publication in the PCRJ. *Primary Care Respir J*, 19(2),
5. Ng T-P, Niti M, Fones C, Yap KB, Tan W-C.. Co-morbid association of depression and COPD: A population-based study. *Respiratory Medicine*, 2009,103, 895-901.
6. Jordan N, Lee TA, Valenstein M, Pirraglia PA, Weiss KB.. Effect of Depression Care on Outcomes in COPD Patients with Depression. *Chest*, 2009, 135, 626–32.A1-A25.
7. Ng TP, Niti M, Tan WC, Cao Z, Ong KC, Eng P.. Depressive symptoms and chronic obstructive pulmonary disease: effect on mortality, hospital readmission, symptom burden, functional status, and quality of life. *Arch Intern Med*, 2007, 167, 60-7.
8. Yohannes AM, Alexopoulos GS.. Depression and anxiety in patients with COPD.*Eur Respir Rev*, 2014,23, 345–9.
9. Cowen P, Harrison P, Burns T.. *Shorter Oxford Textbook of Psychiatry*. 6th ed. United Kingdom: Oxford University Press; 2012. p. 234. *COPD*, 6(6), 452–458.
10. Alexopoulos GS, Morimoto SS.. The inflammation hypothesis in geriatric depression. *Int J Geriatr Psychiatry*, 2011, 26, 1109–18.
11. Jorgensen NR, Schwarz P, Holme I, Henriksen BM, Petersen LJ, Backer V.. The prevalence of osteoporosis in patients with chronic obstructive pulmonary disease: a cross sectional study. *Respir Med*, 2007, 101(1), 177-85.
12. Graat-Verboom L, Wouters EFM, Smeenk FWJM, van den Borne BE, Lunde R, Spruit MA.. Current status of research on osteoporosis in COPD: A systematic review. *Eur Respir J*, 2009. 34(1), 209-18
13. Naghshin R, Javadzadeh A, Mousavi SAJ, Adeli SH, Heydari A. Comparison of the Osteoporosis between Male Smokers with and without Chronic Obstructive Pulmonary Disease. *Tanaffos*, 2004., 3(9), 13-8.
14. Van Manen JG, Bindels PJ, Dekker FW, IJzermans CJ, van der Zee JS, Schadé E.. Risk of depression in patients with chronic obstructive pulmonary disease and its determinants. *Thorax*, 2002, 57(5), 412 - 6.
15. Julian LJ, Gregorich SE, Earnest G, Eisner MD, Chen H, Blanc PD, et al.. Screening for Depression in Chronic Obstructive Pulmonary Disease. *COPD*, 2009,6(6), 452–458.
16. Dursun AB, Ay_enaz Özcan, Çiçek T.. The Comparison of Anxiety and Depression Levels in Asthma and COPD Patients. *J Lung Pulm Respir Res*, 2015, 2(2), 00038.17..
17. Balcells E, Antó JM, Gea J, Gómez FP, Rodríguez E, Marin A, et al.. Characteristics of patients admitted for the first time for COPD exacerbation. *Respir Med*, 2009, 103(9), 1293-302.
18. Katz PP, Julian LJ, Omachi TA, Gregorich SE, Eisner MD, Yelin EH, et al.. The impact of disability on depression among individuals with COPD. *Chest*, 2010. 137(4), 838-45.
19. Sijapati MJ, Bhatta N, Khanal B, Lamsal M, Chaudhary S.. Study of factors determining outcomes in the hospitalized patients with acute exacerbation of chronic obstructive pulmonary disease (COPD). *J Univ Coll Med Sci*, 2014, 2 (2), 28-34.
20. Iguchi A, Senjyu H, Hayashi Y, Kanada R, Iwai S, Honda S, et al.. Relationship Between Depression in Patients With COPD

and the Percent of Predicted FEV_1, BODE Index, and Health-Related Quality of Life. *Respir Care,* 2013,58(2), 334–9.

21. Patton GC, Carlin JB, Coffey C, Wolfe R, Hibbert M, Bowes G.. Depression, anxiety, and smoking initiation: a prospective study over 3 years. *Am J Public Health*, 1998. 88(10), 1518-22.
22. Atlantis E, Fahey P, Cochrane B, Smith S.. Bidirectional Associations between Clinically Relevant Depression or Anxiety and COPD: A Systematic Review and Meta-analysis. *Chest*, 2013. 144(3), 766–77.
23. Schneider C, Jick SS, Bothner U, Meier CR.. COPD and the Risk of Depression. *Chest*, 2010.137(2), 341–7.
24. Hajiro T, Nishimura K, Tsukino M, Ikeda A, Oga T. 2000. Stages of disease severity and factors that affect the health status of patients with chronic obstructive pulmonary disease. *Respir Med*, 94(9), 841-6.
25. Gudmundsson G, Gislason T, Janson C, Lindberg E, Suppli Ulrik C, Brøndum E, et al.. Depression, anxiety and health status after hospitalisation for COPD: a multicentre study in the Nordic countries. *Respir Med*, 2006. 100(1), 87-93
26. Kim HF, Kunik ME, Molinari VA, Hillman SL, Lalani S, Orengo CA, et al. Functional impairment in COPD patients: the impact of anxiety and depression. *Psychosomatics*, . 2000, 41, 465–71.

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ORIGINAL ARTICLE

Prevalence and Socio Demographic Factors of Tuberculosis Patients in Selected Slum Areas of Dhaka City

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Abstract:

Background: *In Bangladesh WHO recommended DOTS has been provided free of charge since 1993, yet information on access to TB services by different population groups is not well documented and challenging especially in Urban Slum and hard to reach areas There is a gap and lack of information about TB services among the urban slum areas due to frequent migration of a large number of population.*

Objectives: *The objective of this study was to detect prevalence and assess the socio demographic factors of actively detected cases from selected slum areas of Dhaka City.*

Method: *This was a cross-sectional study which was conducted in several urban slum areas of Dhaka city. The household members were actively screened to assess the presence of TB-related signs and symptoms; cough e"3 weeks and body mass index (BMI) <17 kg/ m^2. Sputum specimens from suspects were collected for acid fast bacilli (AFB) microscopy.*

Result: *Total 9,000 screened for pulmonary TB (PTB), Total 26 cases were detected of which 19 were positive for AFB on microscopy 06 were negative and 01 was child and the prevalence of new PTB cases was estimated to be 250/100,000. Out of 25 cases, 20(80%) had cough for several duration and 6(18%) did not present with cough at the time of screening. No multidrug resistant case was found. 50% percent of all TB cases had BMI <17 kg/m2 (p = <0.001). Out of 26 cases, 16 (62%) were male and 10 (38%) were female, with a ratio of 1.46"1; 20 (76%) were smear positive and the remaining 6 (24%) cases were smear negative.*

Conclusion: *The study revealed high prevalence of TB in urban slums. Screening using low BMI can be beneficial among risk group population. It is important to conduct larger study to validate clinical variables like cough <3 weeks and low BMI to define TB suspect and also to investigate the transmission of TB in slum settings.*

Key Words: *DOTS, Prevalence, Socio Demographic Factors.*

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Introduction:

The global burden of Tuberculosis (TB) in 2010 is estimated to be 8.8 million in the form of incident cases, 12 million in the form of prevalent cases[1]. The incidence is estimated indirectly through notification of passively detected patients. The real burden of TB could be markedly higher if active case finding would be employed on larger scale than is now often done.

In many countries, differences in TB incidence between urban and rural areas have been described[2]. TB in urban areas often results specifically among certain urban risk groups, such as slum dwellers who are exposed to poor environmental conditions (overcrowding, poor living conditions)[3]. TB is still believed to be a disease that disproportionately affects the poor and marginalized[4].

The National Tuberculosis Control Program (NTP) of Bangladesh first adopted the directly observed treatment short course (DOTS) strategy in 1993. The program rapidly expanded in the following years to almost all areas of the country reaching 100% coverage in 2006[5]. There are still some gaps in the DOTS services provided for the urban slum dwellers. DOTS strategy is entirely based on passive case finding which is often influenced to a great extent by the treatment seeking behavior of the patients suffering from active TB, social stigmatization, access to health service and even diagnostic delay at health facility[6]. This in turn results in decreased TB case detection with underestimated number of actual TB cases prevailing in the community. Bangladesh had comparatively higher percentage (81%) of notified cases of pulmonary TB (PTB) that were sputum smear-positive (SS+) among the 22 high burden countries with TB [1]. Delay in the diagnosis of these open TB cases can result in transmission of TB among the contacts of the active TB cases and more likely to fuel its transmission in the community apart from increased morbidity and mortality[7].

The prevalence of SS+ TB was found to be higher in the rural population (86.0/100 000) compared to urban (51.1/100 000) in the recently completed (2007–2009) nationwide TB prevalence survey of Bangladesh[8]. A lesser number of cases in urban areas were also notified in the NTP in 2010 [9]. In 2010, the NTP notified a total of 158,709 of all forms of TB cases (103/100 000 population) nationwide of these 13% were reported from urban areas. However, there are still some pockets in urban area where TB notification rate believed to be higher. One of these is high burden settings like urban slums.

There are still major gaps in our epidemiological knowledge regarding the transmission dynamic of TB despite the fact that TB is endemic and highly prevalent in Bangladesh. Results from one of our previous studies performed in a rural community of Matlab showed that TB in rural Bangladesh is caused primarily by reactivation of latent infections, with the recent emergence of Beijing strain clusters[9]. Urban areas in Bangladesh are densely populated and about one third of the populations are slum dwellers, creating conditions where a high transmission can occur.

The aims of this study were to investigate the burden of active TB in an urban slum of Dhaka city with increased number of case detection based on active symptom screening. We also aimed to test the feasibility of a larger study to investigate TB transmission in this setting.

Methods:

Study Setting:

The study was conducted at a densely populated low income urban slum (Mohammadpur Slum) in Dhaka, Bangladesh Mohammadpur is one of the 40 thanas of Dhaka City with a population of about one million in an area of 55 square kilometers. We conducted the activities of this project in several slums including Geneva Camp Slum. The population of these slums is approximately 45,000. These slums are inhabited by poor and lower class families, residential and sanitary conditions are typical of any congested urban settlement.

Study Procedure:

This cross-sectional house-to-house survey was conducted from July 2009 to June 2010. Individuals not present at the household during the first house visit were attempted to be included on at least one subsequent visit. The team consisting of two trained field workers and

one research assistant visited the study area on a daily basis and screened them for TB symptoms using simple standardized questionnaires. The socio-demographic characteristics, history regarding TB symptoms and other relevant information were collected from the consenting participants. Individuals having productive cough for three or more weeks with or without other clinical presentation were identified as suspects for PTB. We also considered a body mass index (BMI) <17 kg/m^2 as a single inclusion criteria for the study as one of our previous study showed more likelihood of developing TB among individuals with BMI<17[10]. Three sputum specimens from each PTB suspect were collected by the field worker after further clinical evaluation of the suspects by the research assistant. The first sputum specimen was obtained immediately after identifying the subject as suspect. The second specimen was overnight sputum collected on the next morning and the third was spot during collection of the second sputum specimen. PTB suspects who did not provide consent to provide sputum specimens in the study were re-invited at least once. The specimens were immediately brought to Shyamoli Tuberculosis Laboratory in a cool box for acid-fast bacilli (AFB) microscopy.

Laboratory Investigations:

Concentrated sputum smears were examined for AFB using the Ziehl-Neelsen staining under light microscope. Sputum specimens were decontaminated following the Petroffs' NaOH method.

Case definitions for TB disease:

The diagnosis of TB was made according to the case definition given by the NTP depending on the site and bacteriological status.SS+ PTB was defined as a positive sputum smear confirmed with a second positive or chest radiological X-ray abnormalities consistent with active TB; and smear negative PTB was defined by two positive cultures of *M. tuberculosis* while three sputum specimens negative for AFB.

Epidemiological investigation:

Clustered patients were investigated to further establish or strengthen potential epidemiological connections in place, time, and person among cluster members. Participants were being considered to share a strong epidemiological link if they would have had been in the same workplace, household, village or area at overlapping times (even a known single exposure to patients).

Statistical analysis:

Data were entered and analyzed using the Statistical Package for Social Sciences (SPSS) version 17.0. Univariate analyses were performed to examine the association between demographic and clinical variables of TB cases. $P<0.05$ was considered as evidence of significant difference[11] To identify the independent risk factors for TB and non TB, adjusted odds ratio (AOR) and 95% CI were calculated by logistic regression analysis.

Results:

A total of 3700 households were visited and 16,500 eligible participants belonged to those households; of them 15,000 (90%) consented subjects were screened during 12 month period. Of these 9,800 (66%) were aged 15 years or more (adults) and 5,200 (34%) were aged below 15 years (children) (Table 1). Out of 1431(14% of 9,000) adult PTB suspects, sputum specimens were collected from 618 (43%) suspects. Majority (87%) of these suspects who were unable to provide sputum specimen were initially identified as a suspect because of their low BMI even in the absence of cough for any duration. Among the child population, 36 child suspects were identified and sputum smear microscopy and relevant tests were performed in 29 child suspects (Figure 2). We have detected 26 (4% of 647 suspects) TB cases during this time period. Out of 26 cases, 16 (62%) were male and 10 (38%) were female, with a ratio of 1.66"1. Only one child TB case was diagnosed. Out of the 25 adult TB cases identified in our study, 19 (76%) were smear positive; and the remaining 6 (24%) cases were smear negative but showed growth in culture. The estimated number of new pulmonary TB cases (AFB and/or culture) was 253/100,000 population and the estimated number of new SS+ TB cases was 192/100,000 populations; among the subjects aged ≥15 years, who participated in the study. All 26 identified PTB cases were brought under treatment by DOTS program.

Table-I
Characteristics of study population

Variables		Study population			
		All screened (n = 15024)	TB (n = 26)	Non-TB (n = 14998)	
Category	Sub categories	Number (%)	Number (%)	Number (%)	p Value
Demographics					
Sex	Male	6757 (45.0)	16 (61.5)	6741 (44.9)	0.09
	Female	8267 (55.0)	10 (38.5)	8257 (55.1)	
Age	0–14 yrs	5151 (34.3)	1 (3.8)	5150 (34.3)	<0.001
	15–24 yrs	3739 (24.9)	7 (26.9)	3732 (24.9)	
	25–34 yrs	2601 (17.3)	4 (15.4)	2597 (17.3)	
	35–44 yrs	1665 (11.1)	4 (15.4)	1661 (11.1)	
	45–54 yrs	926 (6.2)	6 (23.1)	920 (6.1)	
	55–64 yrs	553 (3.7)	2 (7.7)	551 (3.7)	
	65+ yrs	389 (2.6)	2 (7.7)	387 (2.6)	
Occupation*	Self-employed	1681(17.0)	10 (40.0)	1671 (17.0)	0.02
	Business	481(4.9)	2 (8.0)	479 (4.9)	
	Service	2490 (25.2)	5 (20.0)	2485 (25.2)	
	Unemployed	1982 (20.1)	5 (20.0)	1977 (20.1)	
	Housewife	3236 (32.8)	3 (12.0)	3233 (32.8)	
Smoking	No	14346 (95.5)	19 (73.1)	14327 (95.5)	<0.001
	Yes	678 (4.5)	7 (26.9)	671 (4.5)	
Symptoms					
Cough	No	14488 (96.4)	5 (19.2)	14483 (96.6)	<0.001
	Yes	537 (3.6)	21 (80.8)	516 (3.4)	
	<2 weeks	157 (29.2)	1(4.8)	156 (30.2)	0.02
	≥2 weeks <3	47 (8.8)	3 (14.3)	44 (8.5)	
	≥3 weeks	333 (62.0)	17 (81.0)	316 (61.2)	
Haemoptysis	No	14989 (99.8)	24 (92.3)	14965 (99.8)	<0.001
	Yes	35 (0.2)	2 (7.7)	33 (0.2)	
Evening rise of temperature	No	14898 (99.2)	14 (53.8)	14884 (99.2)	<0.001
	Yes	126 (0.8)	12 (46.2)	114 (0.8)	
Chest pain	No	14847 (98.8)	19 (73.1)	14828 (98.9)	<0.001
	Yes	177 (1.2)	7 (26.9)	170 (1.1)	
Shortness of breathe	No	14884 (99.1)	11 (42.3)	14873 (99.2)	<0.001
	Yes	140 (0.9)	15 (57.7)	125 (0.8)	
Risk factors					
Previously diagnosed as TB	No	14784 (98.4)	17 (65.4)	14767 (98.5)	<0.001
	Yes	240 (1.6)	9 (34.6)	231(1.5)	
Exposure to TB patient	No	13991 (93.1)	25 (96.2)	13966 (93.1)	>0.1
	Yes	1033 (6.9)	01 (3.8)	1032 (6.9)	
BMI*	BMI (e”17.0)	8676 (87.8)	12 (48.0)	8664 (87.9)	<0.001
	BMI (<17.0)	1201 (12.2)	13 (52.0)	1188 (12.1)	

All value are n (%). p values are comparing TB patients (n = 26) against no. no-TB (n = 14998).
*Occupation and BMI were calculated among the adult group only;
Fisher exact test are shown in boldface font.

A number of clinical variables were assessed for an association with TB in this study. Out of 26 diagnosed cases; 21(81%) had cough and 5(19%) did not present with any cough at the time of active screening, they were suspected on the basis of their poor nutritional status (Table 1). Malnutrition, as defined by low BMI (<17 kg/m^2), was also associated with TB; this can either be a risk factor or result of TB. Fifty two percent of all TB cases had BMI <17 kg/m^2 (p=<0.001) (Table 1). Thirty five percent of the identified TB cases had a previous history of TB (p = <0.001). Other clinical variables which were associated with TB were fever, haemoptysis, chest pain and shortness of breath (not statistically significant). No significant association was observed between TB and diabetes mellitus, exposure to TB patients, and alcohol consumption. After adjusting for confounding factors, a risk factor analysis showed that a higher likelihood of developing active TB was associated with smoking, previous history of anti-TB treatment & low BMI (Table II)

Table-II

Odds ratios (ORs) for TB by Socio Demographic characteristics and Potential risk factors.

Variables Category	Sub categories	Unadjusted OR (95% CI)	Adjusted *P* Value	AOR (95% CI)	*P* Value
Socio demographic					
Sex	Female	1.00			
	Male	1.960 (0.9 – 4.3)	0.09		
Age	0–14 yrs	1.00			
	15–24 yrs	9.7 (1.2–78.5)	0.03		
	25–34 yrs	7.9 (0.9 –71.0)	0.06		
	35–44 yrs	12.4 (1.4–111.0)	0.02		
	45–54 yrs	33.6 (4.0–279.3)	0.001		
	55–64 yrs	18.7 (1.7–206.5)	0.01		
	65+ yrs	26.6 (2.4–294.2)	0.007		
Occupation*	Self-employed	1.0			
	Business	6.4 (1.8 – 23.4)	0.005		
	Service	4.5 (0.8 – 26.9)	0.10		
	Unemployed	2.2 (0.5 – 9.1)	0.29		
	Housewife	2.7 (0.7 – 11.4)	0.17		
Smoking	No	1.0		1.0	
	Yes	7.9 (3.3 – 18.8)	<0.001	3.7 (1.5– 9.3)	0.005
Risk factors					
Previously diagnosed as TB	No	1.0		1.0	
	Yes	33.8 (14.9 –76.7)	<0.001	15.7(6.6–37.3)	<0.001
BMI*	BMI (e”17.0)	1.0		1.0	
	BMI (<17.0)	7.9 (3.6–17.4)	<0.001	5.3 (2.3–12.0)	<0.001

OR = odds ratio; AOR = adjusted odds ratio; CI = confidence interval; adjusted odds ratio are not presented for variables with *P* values more than 0.1; * Occupation and BMI were calculated among the adult group only.

Out of 26 cases, DST was done on 20 strains of *M. tuberculosis* available. Five cases were not available (one was unable to produce valid culture result, two started anti-TB treatment before collection of specimens for culture, one specimen was missing for culture and the child TB case was negative on culture) for DST and another one was excluded from the analysis as it was non tuberculosis mycobacterium (NTM) strain. One (5%) strain was resistant to streptomycin alone and 1 (5%) was resistant to all four drugs. The remaining 18 (90%) strains were susceptible to first line drugs. The DR-TB case was notified to the NTP for subsequent management.

Discussion:

There is lack of data on the prevalence of TB in urban slums of Bangladesh. According to the recently completed national TB prevalence survey in Bangladesh, the prevalence of new SS+ TB was estimated to be 79.4 per 100,000 and the prevalence rate for urban area was 51.1 per 100,000[12]. Whereas our study, conducted in an urban slum area, revealed high prevalence of TB which is more than two times higher than overall prevalence and nearly four times higher than the prevalence in urban settings[13-15].This study has provided insight into the prevalence of TB, increased the case detection and identified some of the contributing factors for increased rate of SS+ PTB in a densely populated urban slum in Bangladesh.

This study also showed that active case finding for TB in urban slum setting is effective, given the high rate of participation, the feasibility of timely transportation of collected specimens to the central laboratory (no contamination), as well as laboratory testing which were used to investigate the TB burden along with molecular epidemiology of TB in settings like an urban slums[16-20].

The study results of our study indicate that clinical variables like cough <3 weeks and low BMI should be considered for suspecting TB cases and these issues should be addressed in the current NTP guidelines and awareness campaign which usually addresses only those with cough for at least three weeks[21]. This could eventually detect those masked TB cases without cough or cough for less than three weeks duration[22-24]. According to existing NTP

guidelines in Bangladesh a patient is not suspected to have TB unless the patient has been coughing for three or more weeks[25]. The gap of this current criteria poses the risk that we might be missing quite a large number of TB cases. Our study indicates that pulmonary TB with a history of cough is not significantly less frequent, when duration of cough is shorter than three weeks[26-28]. This observation was also done in the prevalence study where the majority of TB cases identified did not have a history of cough[29-30]. One of the recent studies also presents the data with relevance of duration of cough and TB in line with our findings[31-32]. Several studies in the past showed an association between malnutrition and TB[33,34,35] and in one of our previous studies in prison we confirmed that in the prison population in Bangladesh[36]. The presence of low BMI in such a population is an important screening indicator of the disease in this population. However, more research with larger population should be performed to support these findings among different population group of Bangladesh[37].

In our study, among the detected cases the male-female ratio was 1.66"1. In recently completed prevalence survey, TB in males was three times higher than females. Among the adult population a higher male: female ratio has also been found in data from the NTP report . However, we cannot comment whether TB is more common in men or we have missed the women with TB due to their perceptions of TB, denial about the suspicion of having TB related with social stigma or their ability to produce quality sputum specimen. It is evident that, women experienced longer delays in help seeking for TB at different stages of the disease ccompared with men[38]. There is definite need of study addressing gender differences in TB diagnosis and treatment to see the gender variations in treatment seeking behaviour in the community.

One of the objectives of our study was to characterize those strains that caused TB in an urban slum of Bangladesh and to investigate the extent of transmission. However, it is difficult to draw a conclusion from our study results as we have smaller numbers of detected cases and the study period was short to observe the transmission pattern . A relatively higher proportion (20%) of our *M. tuberculosis* isolates were clustered during this short study period compared to 11% cluster in our previous study in the rural community[38]. There was no apparent epidemiological link among the clustered cases. However, there is every possibility of recent transmission of TB among the infected persons considering the fact that this study was performed in an urban slum which was overcrowded and congested[39]. Interestingly, the clustering was found among the younger age group (mean age 29; range: 19–40 yrs) which also favours recent transmission . It might not be possible to find the index case but considering the TB incubation period ranging from few months to few years there is possibility of recent transmission. It is important to determine whether TB disease has resulted from recent exogenous infection/reinfection or endogenous reactivation of a long-term latent infection to have an effective TB control measure strategy [40]. The results showed that it is feasible to conduct this transmission study in urban slum settings and being a high burden country, Bangladesh warrants these transmission dynamic studies in larger scale.

One of the limitations of our study was the purposive selection of Mirpur urban slum. This was selected as the area had been used as field sites for different studies conducted by icddr,b and we have a harmonious relationship with the population of the study area. We have not taken the HIV status into consideration as the prevalence of HIV in Bangladesh is low (less than 1%). Another reason for not taking the HIV status into consideration was the requirement of voluntary counseling prior asking the patient about the HIV status, which was difficult in active screening based field study. However, we believe that the interpretation of results in our study has not been influenced by the HIV status. It is important to conduct a prospective study with a larger sample size in the urban slum settings to estimate the prevalence of TB and its transmission in this high risk group . The current study identified areas in which design and data collection can be strengthened. It will be interesting to understand and know how the programmatic factors like screening only for

chronic cough (less sensitivity), diagnosis by sputum smear microscopy (<70% sensitivity), others (services, human resource, quality etc.) and non-programmatic factors like care seeking, private sector, socioeconomic status etc.affecting detection of SS+ TB cases in urban improvised areas[40]. This system bypass or non use of or non-detection by DOTS is important and should be addressed particularly with the growing threat of HIV infection and drug resistant TB in the country.

References:

1. WHO (2011) Global tuberculosis control: WHO report 2011: World Health Organization.
2. Hayward A, Darton T, Van-Tam J, Watson J, Coker R, et al. Epidemiology and control of tuberculosis in Western European cities. The International Journal of Tuberculosis and Lung Disease 2003; 7: 751–757.
3. Braden CR, Templeton GL, Cave MD, Valway S, Onorato IM, et al. Interpretation of restriction fragment length polymorphism analysis of Mycobacterium tuberculosis isolates from a state with a large rural population. Journal of Infectious Diseases 1997; 175: 1446.
4. Hossain S, Quaiyum MA, Zaman K, Banu S, Husain MA, et al. Socio Economic Position in TB Prevalence and Access to Services: Results from a Population Prevalence Survey and a Facility-Based Survey in Bangladesh 2012; PloS one7: e44980.
5. Hossain S, Quaiyum MA, Zaman K, Banu S, Husain MA, et al. Socio Economic Position in TB Prevalence and Access to Services: Results from a Population Prevalence Survey and a Facility-Based Survey in Bangladesh 2012; PLoS One7: e44980.
6. Ford CM, Bayer AM, Gilman RH, Onifade D, Acosta C, et al. Factors associated with delayed tuberculosis test-seeking behavior in the Peruvian Amazon. The American journal of tropical medicine and hygiene 2009; 81: 1097–1102.
7. Asch S, Leake B, Anderson R, Gelberg L Why do symptomatic patients delay obtaining care for tuberculosis?American journal of respiratory and critical care medicine 1998;157: 1244–1248.
8. Zaman K, Hossain S, Banu S, Quaiyum M, Barua P, et al. Prevalence of smear-positive tuberculosis in persons aged 15 years in Bangladesh: results from a national survey, 2007-2009. Epidemiology and Infection 2012; 140: 1018–1027.
9. (DGHS) DGoHS 'Tuberculosis Control in Bangladesh' Annual Report National Tuberculosis Control Program (NTP), 2011.
10. Banu S, Uddin M, Islam M, Zaman K, Ahmed T, et al. Molecular epidemiology of tuberculosis in rural Matlab, Bangladesh. The International Journal of Tuberculosis and Lung Disease 2012; 16: 319–326.
11. Van Embden J, Cave M, Crawford J, Dale J, Eisenach K, et al. Strain identification of Mycobacterium tuberculosis by DNA fingerprinting: recommendations for a standardized methodology. Journal of Clinical Microbiology 1993; 31: 406–409.
12. Supply P, Magdalena J, Himpens S, Locht C Identification of novel intergenic repetitive units in a mycobacterial two-component system operon. Molecular microbiology 1997; 26: 991–1003.
13. Supply P, Mazars E, Lesjean S, Vincent V, Gicquel B, et al.Variable human minisatellite-like regions in the Mycobacterium tuberculosis genome. Molecular microbiology 2000; 36: 762–771.
14. Hawkey PM, Smith EG, Evans JT, Monk P, Bryan G, et al. Mycobacterial interspersed repetitive unit typing of Mycobacterium tuberculosis compared to IS6110-based restriction fragment length polymorphism analysis for investigation of apparently clustered cases of tuberculosis. Journal of Clinical Microbiology 2003; 41: 3514–3520.
15. Mazars E, Lesjean S, Banuls A-L, Gilbert M, Vincent V, et al. High-resolution minisatellite-based typing as a portable approach to global analysis of

Mycobacterium tuberculosis molecular epidemiology. Proceedings of the National Academy of Sciences 2000; 98: 1901–1906.

16. Tessema B, Beer J, Merker M, Emmrich F, Sack U, et al. Molecular epidemiology and transmission dynamics of Mycobacterium tuberculosis in Northwest Ethiopia: new phylogenetic lineages found in Northwest Ethiopia. BMC infectious diseases 2013; 13: 1–11.
17. Banu S, Hossain A, Uddin MKM, Uddin MR, Ahmed T, et al.Pulmonary tuberculosis and drug resistance in Dhaka central jail, the largest prison in Bangladesh 2010; PloS one5: e10759
18. Graham SM, Ahmed T, Amanullah F, Browning R, Cardenas V, et al. Evaluation of tuberculosis diagnostics in children: 1. Proposed clinical case definitions for classification of intrathoracic tuberculosis disease. Consensus from an expert panel. Journal of Infectious Diseases 2012; 205: S199–S208.
19. Stegen G, Jones K, Kaplan P Criteria for guidance in the diagnosis of tuberculosis. Pediatrics 1969; 43: 260–263.
20. Mehnaz A, Arif F Applicability of scoring chart in the early detection of tuberculosis in children. Journal of the College of Physicians and Surgeons—Pakistan 2005; JCPSP15: 543.
21. Petroff S A new and rapid method for the isolation and culture of tubercle bacilli directly from the sputum and faeces. J Exp Med 1915; 21: 38–42.
22. Banu S, Mahmud AM, Rahman MT, Hossain A, Uddin MKM, et al.Multidrug-Resistant Tuberculosis in Admitted Patients at a Tertiary Referral Hospital of Bangladesh PloS one 2012; 7: e40545.
23. Canetti G, Fox W, Khomenko Aa, Mahler H, Menon N, et al. Advances in techniques of testing mycobacterial drug sensitivity, and the use of sensitivity tests in tuberculosis control programmes. Bulletin of the World Health Organization 1969; 41: 21.
24. Kamerbeek J, Schouls L, Kolk A, van Agterveld M, van Soolingen D, et al. Simultaneous detection and strain differentiation of Mycobacterium tuberculosis for diagnosis and epidemiology. J Clin Microbio 1997; l35: 907–914.
25. Kox LF, Rhienthong D, Miranda AM, Udomsantisuk N, Ellis K, et al. A more reliable PCR for detection of Mycobacterium tuberculosis in clinical samples. J Clin Microbio 1994; l32: 672–678.
26. Van Soolingen D, De Haas P, Hermans P, Groenen P, Van Embden J Comparison of various repetitive DNA elements as genetic markers for strain differentiation and epidemiology of Mycobacterium tuberculosis. Journal of clinical microbiology 1993; 31: 1987.
27. Brosch R, Gordon SV, Marmiesse M, Brodin P, Buchrieser C, et al. A new evolutionary scenario for the Mycobacterium tuberculosis complex. Proc Natl Acad Sci U S A 2002; 99: 3684–3689.
28. Mazars E, Lesjean S, Banuls AL, Gilbert M, Vincent V, et al. High-resolution minisatellite-based typing as a portable approach to global analysis of Mycobacterium tuberculosis molecular epidemiology. Proceedings of the national academy of Sciences 2001; 98: 1901.
29. Banu S, Gordon SV, Palmer S, Islam R, Ahmed S, et al. Genotypic analysis of Mycobacterium tuberculosis in Bangladesh and prevalence of the Beijing strain. Journal of clinical microbiology 2004; 42: 674–682.
30. National Guidelines and Operational Manual for Tuberculosis Control: National Tuberculosis Control Programme, Bangladesh 2009.
31. Sola C, Filliol I, Legrand E, Mokrousov I, Rastogi N Mycobacterium tuberculosis phylogeny reconstruction based on combined numerical analysis with IS 1081, IS 6110, VNTR, and DR-based spoligotyping suggests the existence of two new phylogeographical clades. Journal of molecular evolution 2001; 53: 680–689.

32. Brosch R, Gordon SV, Marmiesse M, Brodin P, Buchrieser C, et al. A new evolutionary scenario for the Mycobacterium tuberculosis complex. Proceedings of the national academy of Sciences 2002; 99: 3684.

33. Gagneux S, Small PM Global phylogeography of Mycobacterium tuberculosis and implications for tuberculosis product development. The Lancet infectious diseases 2007; 7: 328–337.

34. Zaman K, Hossain S, Banu S, Quaiyum M, Barua P, et al. Prevalence of smear-positive tuberculosis in person's aged~* 15 years in Bangladesh: results from a national survey, 2007–2009. Epidemiology and Infection 2011; 1: 1–10.

35. Ngadaya ES, Mfinanga GS, Wandwalo ER, Morkve O Detection of pulmonary tuberculosis among patients with cough attending outpatient departments in Dar Es Salaam, Tanzania: does duration of cough matter?BMC health services research 2009; 9: 112.

36. Karyadi E, Schultink W, Nelwan RHH, Gross R, Amin Z, et al. Poor micronutrient status of active pulmonary tuberculosis patients in Indonesia. The Journal of nutrition 2000; 130: 2953–2958.

37. Onwubalili J Malnutrition among tuberculosis patients in Harrow, England. European journal of clinical nutrition 1998; 42: 363.

38. Saha K, Rao K Undernutrition in lepromatous leprosy. V. Severe nutritional deficit in lepromatous patients co-infected with pulmonary tuberculosis. European journal of clinical nutrition 1989; 43: 117.

39. Karim F, Islam MA, Chowdhury A, Johansson E, Diwan VK Gender differences in delays in diagnosis and treatment of tuberculosis. Health policy and planning 2007; 22: 329–334.

40. Cohen T, Colijn C, Finklea B, Murray M Exogenous re-infection and the dynamics of tuberculosis epidemics: local effects in a network model of transmission. J R Soc Interface 2007; 4: 523–531. Abstract.

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ORIGINAL ARTICLE

Laparoscopic Cholecystectomy in patients with mild and moderate Chronic Obstructive Pulmonary Disease (COPD):Our experience in Hepatobiliary & Pancreatic Surgery Division in BSMMU

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Abstract:

Background: *Laparoscopic Cholecystectomy (LC), the gold standard for surgical treatment of many Gall Bladder diseases may render some additional adverse effectsin COPD patients due to the creation of CO_2 pneumoperitoneum in a patient with already reserved pulmonary capability. In our study, the clinical outcome of patients with COPD who underwent LC was compared with the outcome of non-COPD patients to clarify the effects and potential hazards of a CO_2 pneumoperitoneum, if any, in patients with COPD.*

Method: *Twenty patients with COPD (Group-I) and undergoing LC were compared with 25control patients without COPD and also undergoing LC (Group-II). Patient demographics, intraoperative end-tidal CO2 (both before and after CO2 insufflation), and clinical outcome, including surgical duration, length of postoperative hospital stay, and any associated complications, were analyzed.*

Results: *The procedures of 02 Group-I patients were converted to the open method, and these patients wereexcluded from the study. Comprising the COPD group were 20 patients with mild COPDand one patient with moderate COPD. With similar settings of tidal volume and ventilation rate forthe two groups, the measured end-tidal CO2 value was significantly greater for Group-I than forGroup-II patients after the creation of a CO2 pneumoperitoneum (35.4 ± 1.9 vs. 31.5 ± 3.1 mm Hg, P=.012). The duration of surgery was similar for Groups I and II (65 ± 20.7 vs. 58 ± 18.6 minutes), as was the duration of the postoperative hospital stay (4.1 ± 2.2 vs. 4.0 ± 1.6 days; P=.800). No pulmonary complications were noted for any of the patients.*

Conclusion: *Laparoscopic Cholecystectomy (LC) can be safely performed in COPD patients with mild or even a moderate degreeof airway obstruction. Intraoperative CO_2 retention did not complicate the postoperative recoveryin terms of the complication rate or the duration of the postoperative hospital stay.*

Key Words:*LC, Laparoscopic Surgery, COPD, Co_2 Pneumoperitoneum*

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Introduction

In last one decade, increasing worldwide prevalence of COPD can be attributed to smoking, increased life expectancy, and less active lifestyles. For adults older than 40 years, COPD's worldwide prevalence (as defined physiologically) is ~9–10%.[1,2] This high prevalence is putting a burden on both surgeons and anesthesiologists, who are both seeing an increase in the volume of high-risk respiratory patients. These high-risk patients who are undergoing laparoscopic procedures, especially those with COPD, have unique issues that require careful consideration by the surgeons.[3]

Laparoscopic cholecystectomy (LC) was approved for use in 1988, and since then, it has been used as the gold standard treatment method for symptomatic cholelithiasis.[4]During LC, A carbon dioxide (CO2) pneumoperitoneum, the most common means of accomplishing laparoscopic surgery, has been noted to result in net CO_2 retention, arterial hypercarbia, and subsequent arterial acidosis, even for relatively healthy individuals,with associated adverse effects that include increased intracranial pressure and possible cardiac dysrhythmia.[4,5,6] The above-mentioned adverse effects associated with a CO_2 pneumoperitoneum have been shown to occur to a greater degree in patients with chronic obstructive pulmonary disease (COPD), who often exhibit a rather limited cardiopulmonary reserve.[4]

In our study, the clinical outcome of patients with COPD who underwent LC was compared with the outcome of non-COPD patients to clarify the effects and potential hazards of a CO_2 pneumoperitoneum, if any, in patients with COPD.

Materials & Methods:

We prospectively included 22 patients with established COPD(Group-I) who underwentLaparoscopic Cholecystectomy (LC) during the period fromJanuary 2016 to June 2018 in Hepatobiliary & Pancreatic Surgery Division in Bangabandhu Sheikh Mujib Medical University (BSMMU). During the same period oftime, a total of 42 LC procedures were performed on patientswithout COPD. Of these patients, 25 were randomly selected to be a case-matched control group (Group-II). Statistical investigationof the clinical characteristics of these25 patients, including their age, sex, leukocyte count, andsurgical outcome, was undertaken to ensure that they constituted a random and fairly representative subsample ofthe 42 non-COPD patients who had undergone LC(Table 1).

The procedures of two patients in Group-I were convertedto open cholecystectomy because of the presence of sinistroposition of Gall Bladder in one case and difficult anatomy in another case and these patients were excluded fromthe study. Of the remaining 20Group-I patients, elevenwere male and nine were female, with a mean age of 53years (range, 41–67 years). Four of them had hypertension, twodiabetes mellitus, and one congestive heart failure. Nopatient in this group had more than one other concurrentdisease. Indications for LC in these Group-I patients included symptomatic cholelithiasis in thirteen, acute cholecystitis in five, gallbladder polyp in one, and cholelithiasisaccompanied by an impacted choledocholithiasis, whichwas removed before the LC, in one patient. The Group II patientswere comparable with their Group-I counterparts in respect to clinical characteristics, including age, sex distribution, specific disease pattern, and associated diseases(Table 2).

All the patients in Group I had COPD as determinedby appropriate chest specialists according to their history,clinical presentation, and preoperative pulmonary function test results. Following the criteria of the American Thoracic Society, the pulmonary function tests were performed with three acceptable attempts within 5% of one another, under the maximal efforts of each patient. The severity of COPD for each patient was determined according to the widely accepted classification listed in Table 3, primarily by the ratio of the forced expiratory volume at the first second of the test to the

forced vital capacity (FEV1/FVC, expressed as a percentage) and the degree of reduction of the FEV1 in comparison with its predicted value (expressed as percent predicted).[7]

Informed consent was obtained from every patient involved, each of whom was provided with a preoperative explanation of the procedure and rationale behind the study, in addition to training related to appropriate postoperative pulmonary toilet, including cough management and deep inspiration techniques. Postoperative respiratory therapy was provided for the COPD patients and commenced on the first day postoperatively under the instruction of respiratory therapists. Chest physiotherapy mainly consisted of a number of techniques, includingchest percussion, postural drainage, and deep-breathing exercises. Oral medications for preexisting lung diseaseswere resumed as soon as possible. Postoperative pulmonary complications were defined as fever persistingfor more than 1 day with associated clinical evidence of atelactasis or pneumonia, the need for prolonged intubation, or refractory bronchospasm.

LC was performed according to a well-established protocol. In brief, under general anesthesia, a pneumoperitoneum was created by CO2 insufflation until an intra-abdominal pressure of 12 mm Hg had been established. The patient was then kept in the reverse Trendelenburg position with a slight left lateral tilt during the surgical procedure to provide a maximal exposure of the gallbladder and facilitate optimal retraction of the gallbladder fundus. After dissection was complete, the gallbladder was removed via the umbilical port.

The partial pressure of CO_2 measured in exhaled gas (end-tidal CO_2) was continuously monitored during theprocedure, although arterial blood gas analysis (ABG) is not performed as a routine examination during LC in ourinstitution.The tidal volume, minute ventilation, and volume of oxygen flow were all set to a level that was deemed appropriate according to the general condition of each patient. The values of end-tidal CO2 at the time just before the creationof pneumoperitoneum and 15 minutes after insufflation were chosen to represent the pre-insufflation and post-insufflation values of end-tidal CO2. The ventilator settings at both time points were also recorded.

The measured end-tidal CO2 values, clinical demographics, and surgical outcomes, including surgical duration, complications, and length of postoperative stay in the hospital, were compared between groups. Patientswere discharged from the hospital when they were able to tolerate oral intake without the need of parenteral fluid and when they were able to manage bedside activity by themselves.All data were analyzed with Student's *t* test. A *P* value of less than .05 was considered significant.

Results

Among the patients with COPD, two patients' ratio of FEV1 to FVC was 67%, with a predicted FEV1 of 56%. This was categorized as moderate COPD. The remaining patients had FEV1/FVC values between 50% and 70%, but their predicted FEV1 was greater than 80%, and they were categorized as having mild COPD.[7](Table 3)

The tidal volumes for Group I and Group II patients before CO2 insufflation were 587 ± 75.7 and 611. 3±65.2 mL, respectively, and they became 641±121.5 and 687.9 ± 130.0 mL, respectively, after CO2 insufflation. Although the tidal volume for patients in each group generally increased after insufflation, the difference was not statistically significant between the two groups when they were compared either before or after insufflation. The ventilation rates were unchanged before and after insufflation in both groups, which were 11.1/min in group 1 and 11.2/min in Group-II. The measured mean 6 standard deviation end-tidal CO2 values before CO2 insufflation for Group I and Group II patients were 31.2 ± 2.2 and 27.4 ± 3.3mm Hg, respectively (P= .08). A significant increase in the value of end tidal CO2 after CO2 insufflation was observed for both groups of patients, the post-

insufflation value being 35.4 ± 1.9mm Hg for COPD patients (P = .004) and 31.5 ± 3.1mm Hg for non-COPD patients (P=.001).After the creation of a CO2 pneumoperitoneum, however, Group I patients exhibited a significantly greater mean value for end-tidal CO2 when compared with patients from Group II (35.4 ± 1.9vs. 31.5 ± 3.1mm Hg, P=.012) (Table 2).

The duration of surgery was 65 ± 20.7minutes for Group-I patients and 58 ± 18.6minutes for Group II patients (P = .222). Nebulization was given to all patients in Group I, and bronchospasm was well controlled after the use of bronchodilators in all patients. The duration of the postoperative hospital stay was 4.1 ± 2.2days for the COPD group and 4.0 ± 1.6days for the nonCOPD group (P=.800; Table 2). No pulmonary complications, such as prolonged intubation and postoperative ventilator support for hypoxemia, respiratory acidosis, pneumonia, or refractory bronchospasm, occurred in the Group-I patients. Postoperative respiratory therapy was successfully performed by a well-trained staff without any occurrence of clinically significant atelactasis or a complicated pulmonary infection. One patient in Group I had a wound infection that was noted one week after surgery.

Table-I

Clinical Parameter and Outcome of 25 randomly selected Non-COPD Patients of G-II and All Non-COPD Patients.

	G-II (n=25)	All non-COPD Patients (n=42)	P Value
Age (Years)	44.3 ± 13.6	44.0 ± 12.9	.310
M:F	11:14	18:23	-
Leukocyte Count (X 10^9/L)	0.87 ± 2.7	0.79 ± 3.1	.651
Operative Time (Minutes)	65 ± 20.7	58 ± 18.6	.277
Length of Postoperative Stay (Days)	4.0 ± 1.6	4.12 ± 2.14	.589

Table-II

Clinical Parameters and Outcome of COPD (G-I) & Non-COPD (G-II) Patients.

	G-I (n=20)	G-II (n=25)	P Value
Age (Years)	53 ± 11.2	44.3 ± 13.6	.067
M: F	11: 9	11:14	
Length of Postoperative Stay	4.1 ± 2.2	4.0 ± 1.6	.800
Indication (n)			
Cholelithiasis	13	14	
Acute Cholecystitis	4	6	
GB Polyp	1	2	
Choledocholithiasis with Cholelithiasis	2	3	
Tidal Volume (mL)			
Before CO_2 Insufflation	587 ± 75.7	611 ± 65.2	.959
After CO_2 Insufflation	641 ± 121.5	687.9 ± 130	.869
End-tidal CO_2 (mm of Hg)			
Before CO_2 Insufflation	31.2 ± 2.2	27.4 ± 3.3	.08
After CO_2 Insufflation	35.4 ± 1.9	31.5 ± 3.1	.012

Table-III

Classification of COPD by Severity [7] and the number of patients in the COPD Group-I in each stage of severity.

Stage	Characteristics
0: At risk	Normal Spirometry Chronic Symptoms (cough, sputum production)
I: Mild COPD (n=18)	$FEV_1/FVC < 70\%$ FEV_1 e" 80% Predicted With or without Chronic Symptoms (cough, sputum production)
II: Moderate COPD (n=2)	$FEV_1/FVC < 70\%$ 30% d" FEV_1< 80% Predicted (IIA: 50% d" FEV_1< 80% Predicted) (IIB: 30% d" FEV_1< 50% Predicted) With or without Chronic Symptoms (cough, sputum production)
III: Severe COPD (n=0)	$FEV_1/FVC < 70\%$ FEV_1< 30% Predicted, or The presence of respiratory failure[a], or Clinical signs of right-sided heart failure.

[a]Respiratory failure: PaO_2< 8.0 kPa(60mm Hg) with or without PaO_2> 6.7 kPa (50 mm Hg) while breatihing air at sea level.

Discussion

LC has been demonstrated to be superior to open cholecystectomy surgery. With less injury to the abdominal musculature and less intraoperative manipulation of adjacent organs, improved respiratory responses and fewer acute phase responses have been observed, as well as less postoperative pulmonary dysfunction.[8–10] These results, and a reported incidence of postoperative pulmonary complications for patients with COPD following open surgery of 25% to 100%, [11] indicate that it is appropriate to perform cholecystectomy by the laparoscopic technique.However, the considerable systemic adverse effects of the CO2 pneumoperitoneumused in LC have been widely studied and reported; they include the following:[4-12]

1. An increased risk for the development of myocardial ischemia as a consequence of increased myocardial wall tension caused by increased mean arterial pressure and increased systemic venous resistance.
2. The development of cardiac dysrhythmia.
3. The direct vasoconstriction of pulmonary vessels as a consequence of hypercarbia, hypoxemia, and hypoventilation in the context of preexisting lung disease.

Many studies [4,5,10,12] have focused on these changes incirculatory hemodynamics and pulmonary function before and after LC, although the clinical outcome for patients with COPD undergoing LC has not been thoroughly discussed.

In our study, even with similar ventilator settings, we found increased CO_2 retention in patients with COPD after the creation of a CO_2 pneumoperitoneum, as reflected by a significantly increased end-tidal CO_2 pressure. This, however, was not associated with a greater likelihood of postoperative pulmonary complications or a prolonged postoperative hospital stay in comparison with non COPD patients. This observation may be partially explained by the work of Fahyet al.[13]They found that large increases in lung resistance and lung and chest wall stretch, which occur during abdominal CO_2 insufflation before laparoscopic surgery, are largely reversible on abdominal deflation. In addition, Galiziaet al.[14] compared hemodynamic and pulmonary changes during

open CO_2 pneumoperitoneum with those during abdominal wall lifting cholecystectomy. They found that CO_2 insufflation produced a complex hemodynamic and pulmonary syndrome resulting in increased right- and left-sided filling pressures, significant cardiac index reduction, and derangement of the respiratory mechanics, and respiratory acidosis, all of which normalized after desufflation.

LC is superior to its open surgery counterpart in regard to a reduced level of postoperative pulmonary function complications and a faster recovery of normal pulmonary function postoperatively[8,9,15,16] and the noted adverse effects of a CO_2 pneumoperitoneum on respiratory mechanics are largely and quickly reversible following abdominal desufflation. This further supports our conclusions that LC can be safely performed in COPD patients because pulmonary function recovers to normal levels more quickly than with open surgery, and most side effects of a CO_2 pneumoperitoneum are reversible and well-tolerated by patients (mild & moderate COPD).

An alternative explanation of our favorable finding is that patients who undergo LC generally resume their intake of oral medication sooner than those who undergo open cholecystectomy.[17] Thus, their medication for pulmonary disease is likely to be well maintained, without any prolonged interruption or adjustment to an intravenous form. In addition, all but one of our patients have had mild COPD as revealed by their pulmonary function test results; the remaining patient was categorized as having moderate COPD (FEV1/FVC = 68%, predicted FEV1 = 55%).[7] No patients in the COPD group (Group-I) had severe airway obstruction. Hence, it is unclear whether LC in COPD patients with a severe form of airway obstruction would be tolerated as well as it is in patients with a milder form of obstruction.

Based on the previously mentioned criteria for hospital discharge, the mean length of the postoperative stay in both groups was 4 days, which seems longer than that in most other published reports (usual range, 1–2 days). A possible explanation is that some of the patients asked to stay in the hospital longer because they felt discomfort subjectively, even though their general condition had fully reached the criteria for discharge. However, this deviation from the discharge criteria was considered to be acceptable because no negative effects on patient outcome were noted.

In conclusion, there is no contraindication to LC for patients with mild or moderate COPD. Problems with CO2 retention, hypercarbia, and the associated systemic side effects do not complicate the postoperative recovery from LC in terms of frequency of complications and duration of postoperative hospital stay for COPD patients, although the results of LC for patients with severe COPD are still unknown, warranting further study.

Reference

1. Halbert RJ, Natoli JL, Gano A, Badamgarav E, Buist AS, Mannino DM. Global burden of COPD: systematic review and meta-analysis. EurRespir J. 2006;28(3):523–532. doi: 10.1183/09031936.06.00124605.
2. Khetarpal R, Bali K, Chatrath V, Bansal D. Anesthetic considerations in the patients of chronic obstructive pulmonary disease undergoing laparoscopic surgeries. Anesth Essays Res. 2016;10(1):7–12. doi: 10.4103/0259-1162.165500.
3. The Southern surgeons' club: A prospective analysis of 1518 laparoscopic cholecystectomies. N Engl J Med 1991; 324: 1073–1078.
4. Gadacz TR, Talamini MA, Lillemoe KD, Yeo CJ. Laparoscopic cholecystectomy. SurgClin North Am. 1990;70(6):1249–1262. doi: 10.1016/S0039-6109(16)45282-5.
5. Wittgen CM, Andrus CH, Fitzgerald SD, Baudendistel LJ, Dahms TE, Kaminski DL. Analysis of the hemodynamic and ventilatory effects of laparoscopic cholecystectomy. Arch Surg 1991;126: 997–1001.
6. Se-Yuan L, Leighton T, Davis I, Stanley K, Lippmann M, Bongard F. Prospective analysis of cardiopulmonary responses to laparoscopic cholecystectomy. J LaparoendoscSurg 1991;1:241–246

7. Pauwels RA, Buist AS, Calverley PM, Jenkins CR, Hurd SS. Global strategy for the diagnosis,management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. Am J RespirCrit Care Med 2001;163:1256–1276.

8. Schauer PR, Luna J, Ghiatas AA, et al. Pulmonary function after laparoscopic cholecystectomy. Surgery 1993;114: 389–399.

9. Coskun I, Hatipoglu AR, Topaloglu A, Yalcinkaya S, Caglar T. Laparoscopic versus open cholecystectomy: Effect on pulmonary function tests. Hepatogastroenterology 2000;47:341–342.

10. Chumillas MS, Ponce JL, Delgado F, Viciano V. Pulmonary function and complications after laparoscopic cholecystectomy. Eur J Surg 1998;164:433–437.

11. Gass GD, Olsen GN. Preoperative pulmonary function testing to predict postoperative morbidity and mortality. Chest1986;89:127–135.

12. Wahba RNM, Beique F, Kleiman SJ. Cardiopulmonaryfunction and laparoscopic cholecystectomy. Can J Anesth1995;42: 51–63.

13. Fahy BG, Barnas GM, Nagle SE, et al. Changes in lungand chest wall properties with abdominal insufflation ofcarbon dioxide are immediately reversible. Anesth Analg 1996;82:501–505.

14. Galizia G, Prizio G, Lieto E, et al. Hemodynamic and pulmonary changes during open carbon dioxide pneumo-peritoneum and abdominal wall-lifting cholecystectomy. Aprospective, randomized study. SurgEndosc 2001; 15:477–483.

15. Frazee RC, Roberts JW, Okeson GC, et al. Open versuslaparoscopic cholecystectomy—a comparison of postoperative pulmonary function. Ann Surg 1991;213:651–653.

16. Gunnarsson L, Lindberg P, Tokics L, et al. Lung functionafter open versus laparoscopic cholecystectomy. ActaAnaesthsiolScand 1995;39:302–306.

17. Koperna T, Kisser M, Schulz F. Laparoscopic versus opentreatment of patients with acute cholecystitis. Hepato-gastroenterology 1999;46:753–757.

Chest Heart Journal
Vol. 42, No. 1, January 2018

ORIGINAL ARTICLE

Diagnostic Yield of Fiber Optic Bronchoscopy (FOB) in Different Lung Diseases

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Abstract:

Background and Aims: *Fiber optic Bronchoscopy(FOB) is a safe, minimally invasive useful diagnostic &therapeutic tool for the management of pulmonary disease which can be performed on outpatient basis.The purpose of this study is to evaluate utility of FOB in the diagnosis of pulmonary disease & observe the clinical presentation, correlation with radiological finding & demographic characteristics of the patient in SSMC&MH.*

Materials and Methods: *A cross sectional study on 192 patients was done in SSMC &MH from January 2014 to July 2015 over 1 year. The commonest indication are radiological opacity (80.2%) followed by diffuse pulmonary lesion (9.3%).Cough was the commonest symptom seen in 75% patient. Among these patient 71.35% patients were smoker. Out of 192 patient who had undergone FOB.*

Result: *Majority are male (81.25%) & age over 60. The commonest finding of FOB are inflammatory lesion found in 51 patient(26.65%) followed by mass lesion in 41 patient(21.35%). Biopsy taken from 91 patient, malignancy was found in 35 patient(38.46%)followed by tuberculosis in 29 patient(31.86%). In bronchoalveolar lavage(BAL), malignancy was found in 37 patient despite of no growth in FOB. Majority patients didn't have any complication & very few patients had some minor complication.*

Conclusion: *Fiber optic bronchoscopy is a sophisticated investigation by which we can evaluation and diagnosis of variety of lung diseases, inflammatory lung diseases, bronchogenic carcinoma, tuberculosis with significant diagnostic accuracy.*

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Introduction:

Bronchoscopy is an endoscopic technique of visualizing the airways for diagnostic and therapeutic purpose in both in patient and outpatient services[1]. Gustav Killian performed the first bronchoscopy for extraction of a piece of pork bone from the right main bronchus in 1897[2]. FOB allows the physicians to explore the

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tracheobronchial tree for abnormalities such as inflammation, tumors, external compression, bleeding, foreign bodies etc. TBB has a diagnostic yield of 40–90% in sarcoidosis[3], 10–40% in Langerhans cell histiocytosis[4], 88–97% in Pneumocystosis jeroveci pneumonia[3-5]. Therapeutic procedures include removal of bronchial secretion, foreign body, blood etc. Fiber optic bronchoscopy causes less discomfort than the rigid one and can be performed safely under local anesthesia and/or moderate sedation.

Materials and Methods:

All of the procedures were performed in bronchoscopy procedure suite of SSMC&MH with a flexible PENTAX EPK-1000 bronchoscope. Patients were required to fast up to at least 6 hours. At first 0.6 mg Atropine was given intramuscularly as induction. Liquid2% xylocaine was administered on nasopharynx, oropharynx, vocal cord and bronchial tree. The whole procedure was done with the patient on supine position and in some cases on right or left lateral position if required. Flexible fiber optic Bronchoscopewas introduced through trans-nasal route in most cases and oral route for the rests. Few patients were given injectable Midazolam when necessary. Oxygenation was monitored during and after procedures with pulse oxymetry andoxygen was administeredvia nasal cannula to maintain O_2 saturation > 90% if necessary. Bronchial brushing, bronchoalveolar lavage and bronchial biopsy were done as per international guideline and sent for analysis accordingly.

Results:

The analysis was performed in total of 192 patients who underwent fiber optic bronchoscopy. Among the 192 cases, the most common indication was localized radiological opacity, which was seen in 154 patients (80.2%). Others include diffuse pulmonary infiltrate (18 patients, 9.3%), haemoptysis with normal CXR findings (12 patients, 6.2%), unexplained symptoms e.g. persistent cough or shortness of breath, persistent non cardiac chest pain, foreign body (8 patients, 4.1%). [Table I]

Table-I
Indications of FOB

Indications	n (192)	%
Localized radiological Opacity ± effusion	154	80.2 %
Diffuse pulmonary infiltrate	18	9.3 %
Haemoptysis with normal CXR findings	12	6.2 %
Others	8	4.1 %

Out of 192 patients undergone the procedures and evaluated, 156 patients were male (81.25%) and 36 were females (18.75%). [Figure 1]

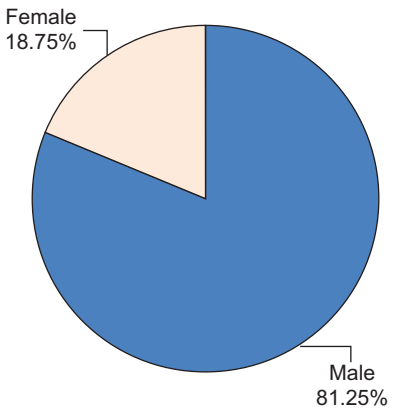

Fig.-1: *Sex Distribution*

Most of our patients were between 51-60 years age group. The oldest is being 95 years and youngest being 19 years old. [Figure: 2]

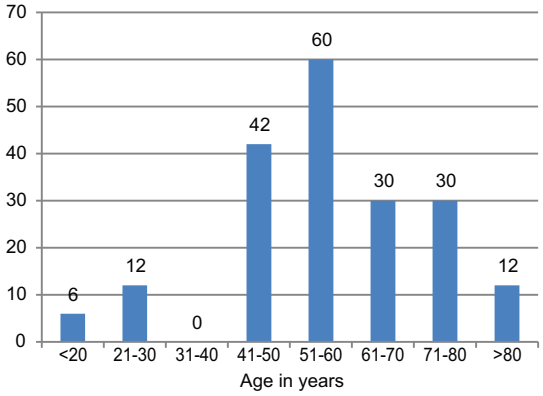

Fig.-2: *Age Distribution*

Cough was the most common presenting symptom in 144 patients (75%), breathlessness in 66 (34.38%), haemoptysis in 60 (31.25%), non-cardiac chest pain in 24 (12.5%), hoarseness of voice in 18 (9.38%), fever in 48 (25%), expectoration in 36 patients (18.75%). [Table II]

Table-II
Clinical symptoms

Clinical symptoms	n (192)	%
Cough	144	75%
Breathlessness	66	34.38%
Haemoptysis	60	31.25%
Non cardiac chest pain	24	12.5%
Hoarseness of voice	18	9.38%
Fever	48	25%
Expectoration	36	36%

Out of 192 patients, 137 (71.35%) were smokers and the rest 55 (28.62%) were non-smokers. [Figure 3]

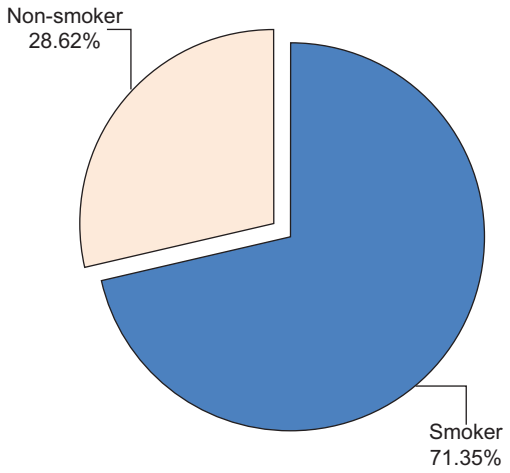

Fig.-3: *Smoking history*

The commonest radiological finding was consolidation, found in 61 patients (35.46%). Others consist of collapse in 33 (19.18%), Perihilar mass in 18 (10.46%), consolidation with effusion in 21 (12.2%), cavitation in 7 (4.06%), collapse with effusion in 14 (8.14%), diffuse pulmonary infiltrate in 18 patients (10.46%). [Table III]

Table-III
Radiological findings

Radiological findings	n (172)	%
Consolidation	61	35.46%
Collapse	33	19.18%
Perihilar mass	18	10.46%
Consolidation with effusion	21	12.2%
Cavitations	7	4.06%
Collapse with effusion	14	8.14%
Diffuse pulmonary infiltrate	18	10.46%

The commonest finding on the fiber optic bronchoscopy was inflammatory lesions, seen in 51 patients (46.68%), Endobronchial growth being the second, seen in 41 patients (37.5%). Bronchoscopy was inconclusive in 27patients (14.06%), whereas in 56 patients (29.16%) it was normal. [Table IV]

Table-IV
Bronchoscopic findings

Bronchoscopic findings	n	%
Normal	56	29.16%
Inflammatory lesions	51	26.65%
Mass lesion	41	21.35%
Secretion	35	18.23%
Inconclusive	27	14.06%
External compression	1	0.52%
Multiple bleeding lesions	2	1.04%

Pathological examination of the specimens obtained by fiber optic bronchoscopy was performed subsequently.

On cytology, malignancy was seen in 37 patients, suspicious malignancy in 19 patients and inflammatory lesions in 49 patients. The cytology was normal in 87 patients.

On histopathological examination of 91 patients, malignancy was found on 35 (38.46%), non-specific inflammation in 16 (15.38%) and tuberculosis in 29 (31.86%), normal in 9(9.8%) and inconclusive in 2 patients (2.1%). [Table V]

Table-V
Histological diagnosis

Histological diagnosis	n (91)	%
Normal	9	9.8%
Inconclusive	2	2.1%
Malignancy	35	38.46%
Tuberculosis	29	31.86%
Non-specific	16	17.58%

Minor bleeding during the procedure was commonest found in 48 patients (25%). Others include hypoxia in 18 (9.38%) and massive bleeding in 12 patients (6.25%). [Table VI]

Table-VI
Complications of bronchoscopy

Complications	n	%
No complication	126	65.63 %
Hypoxia	18	9.38 %
Minor bleeding	48	25 %
Bronchospasm	0	0 %
Pneumothorax	0	0 %
Bradycardia	0	0 %
Massive bleeding	12	6.25 %

Discussion:

Out of 192 patients undergone fiber optic bronchoscopy, majority consists of male (81.25%) and the majority of total patients are from age group of 51-60 years. There is a gradual increase of number of patients requiring bronchoscopy up to 60 years of age with a sharp fall in age group of 31-40 years. Then it decreased but remained static up to 80 years of age.

Cough was the commonest symptoms among the patients (75%)which is similar to a previously published study.

The most important indication for FOB was localized consolidation while others include effusion, unexplained haemoptysis, pleural effusion, collapse. Bronchogenic carcinoma was the more common with unexplained haemoptysis in this study. This is similar to other published studies[6].

The most common finding in bronchoscopy was inflammatory lesions, found in 51 patients (26.65%) followed by mass lesion found in 41 patients (21.35%). Study was found inconclusive in 27 patients (14.06 %).

Histopathological examination of biopsied sample revealed malignancy in 35 patients (38.46 %), followed by tuberculosis in 29 patients (31.86 %) which is prominent in surrounding areas.Some studies shows FOB being superior and minimally invasive for diagnosis of bronchogenic carcinoma.

Among the diagnosed cases of Bronchogenic carcinomas, non-squamous cell carcinoma was the commonest, found in 24 patients (68.57%) and rests were squamous cell carcinoma (31.43%).This was comparable with other studies conducted[7-9] .

All procedures including biopsy, bruising and bronchoalveolar lavage was attempted during the study to increase chances of accurate diagnostic evaluation. In few cases bronchoalveolar lavage and bruising smear can still establish diagnosis while biopsy is negative.

Although various anesthetic and instrumental complications have been reported during the procedure, 126 patients (65.63 %)experienced no complication. Minor bleeding was our commonest found in 48 patients (25%) followed by hypoxia in 12 patients (6.25%). Only a minor portion of our patients (6.25 %)suffered major bleeding. None experienced Bronchospasm, pneumothorax or Bradycardia where some other studies found pneumothorax as a main complicationx .Renalinsufficiency (BUN >30mg/dL and creatinine of >3mg/dL), coagulopathies and pulmonary hypertensionare considered the risk factors for bleeding followingTBBy .

Limitation:

Due to lack of logistic support our study was restricted to diagnostic evaluation only.Moreover,we have no facility to perform transbronchial biopsy that's why we think that we might have missed some diagnosis particularly diffuse parenchymal lung lesion which might be major part of inconclusive patient.

Conclusion:

From our study, we can drag a conclusion that Fiber optic bronchoscopy is a sophisticated and user dependent but yet a safe and smart

instrument when it comes to the evaluation and diagnosis of variety of lung diseases with imaging, for example inflammatory lung diseases, Bronchogenic carcinoma, tuberculosis with significant diagnostic accuracy and also wide opens an array of investigation scopes like biopsy, cytology, culture and sensitivity with least invasiveness. This won't be much to say that it can be a base for further advanced opportunities in more minute evaluation of lung related disorders in the near future.

Reference:

1. Joos L, Patuto N, Chhajed PN, Tamm M. Diagnostic yield offlexible bronchoscopy in current clinical practice. Swiss MedWkly 2006;136(9-10):155–9.
2. Venkateshiah SB, Mehta AC. Role of flexible bronchoscopyin the diagnosis of pulmonary tuberculosis inimmunocompetent individuals. J Bronchal 2003;10:300–8.
3. Becker HD, Killian G: A Biographical Sketch. J Bronchal;1995; 2:77–83.
4. Prakash UBS, Offord KP, Stubbs SE. Bronchoscopy in NorthAmerica: The ACCP survey. Chest 1991; 100: 1668-75.
5. Sawy MS, Jayakrishnan B, Behbehani N, Abal AT, El-Shamy A, Nair MG. Flexible fibreoptic bronchoscopy.Diagnostic yield. Saudi Med J 2004;25(10);1459–63.
6. Sawy MS, Jayakrishnan B, Behbehani N, Abal AT, El-Shamy A, Nair MG. Flexible fibreoptic bronchoscopy.Diagnostic yield. Saudi Med J 2004;25(10);1459–63.
7. Wahbah M. Changing trends in the distribution of thehistologic types of lung cancer: a review of 4,439 cases. AnnDiagnPathol 2007; 11: 89.
8. HernándezBlasco L, Sánchez Hernández IM, VillenaGarrido V, de Miguel Poch E, Nuñez Delgado M, AlfaroAbreu J. Safety of transbronchial biopsy in outpatients. Chest1991;99:562–5.
9. Wahidi MM, Rocha AT, Hollingsworth JW, Govert JA,Feller-Kopman D, Ernst A. Contraindications and safety of the transbronchial lung biopsy via flexible bronchoscopy. Asurvey of pulmonologists and review of the literature.Respiration 2005;72;285–95.

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ORIGINAL ARTICLE

Exploratory laparotomy findings in Polytrauma victims with chest and abdominal injury

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Abstract:

Background: *Poly trauma have the highest incidence of mortality among trauma patients that is now posing a serious public health problem. Prompt diagnosis along with appropriate management is essential for better outcome.*

Objective: *This study was aimed to evaluate pattern of abdominal injury and to investigate factors influencing the management of patients suffering from polytrauma with abdominal injury.*

Methods: *This prospective observational study was conducted in the Department of Casualty and Department of Surgery in Mehalatye District Hospital, Botswana from January 2012 to June 2012.*

Results: *40% of the patients were between ages 21 & 30 years while 85% were males. 60% trauma was caused by penetrating injury and 33% by non-penetrating injury. 55% could reach the hospital within 6 hours and 55% did not receive any primary resuscitation before admission. 54% were haemodynamically unstable of which 37% were in shock when received. 95% presented with abdominal pain and indications for urgent laparotomy were present in more than half of the cases. 84% had associated injuries. 90% were offered operative management in the form of laparotomy. 55% had bowel injury. 33% of the operated patients had uneventful recovery while 66% had complications. Total mortality in the study was 12%.*

Conclusion: *Abdominal injury inflicted by assailant penetrating injury is more severe which needs to be addressed promptly by urgent laparotomy. Both gunshot injury and blunt abdominal trauma from Road Traffic Accident (RTA) usually affect multiple regions of the body.*

Key words: *polytrauma , penetrating injury , laparotomy*

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Introduction:

Trauma remains the most common cause of death for all individuals between the ages of 1 and 44 years and is the 3rd most common cause of death regardless of age and also the number one cause of years of productive life lost.[1] Traditionally, death from trauma has had a 'trimodal' distribution, with 50% of deaths occurring in the pre-hospital environment, 30% during the 'golden hours' and the remaining 20% occurring later. With the advent of better pre-hospital care at present some 50% of deaths occur in the early in-hospital environment.[2]

A central component to the statistical analysis of trauma care is the probability of survival model,

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which predicts outcome of the trauma event taking into account various anatomical and physiological factors. [3]One of the key input information to the survival model is the injury score which forms the cornerstone of trauma epidemiology. There are many scoring systems currently in use, and the Injury Severity Score (ISS) as the anatomical component of the injury in the probability of survival model is a widely used one.[3] Polytrauma is defined via an Injury Severity Score ISS >=17, describing a person being subjected to more than one traumatic injuries.[2]

In polytrauma patients, abdomen arguably presents the greatest diagnostic and therapeutic challenge as manifestations from injuries over other parts of the body are more obvious and early, that demands for accurate diagnosis and definitive therapy.[4] 39% of all trauma deaths can be attributed to major haemorrhage, usually from torso injury.[2] To date unrecognized abdominal injuries continue to be the prime cause of preventable deaths after truncal trauma[5].

Methods:

This prospective observational study was conducted in the Department of Casualty and Department of Surgery in Mehalatye District Hospital, Botswana from January 2012 to June 2012 on 100 trauma victims who were consecutively diagnosed as a case of 'polytrauma' with associated abdominal injury being potential candidates for possible urgent laparotomy owing to the gravity of abdominal injury. Patients dying pre-operatively and with head injury were excluded. Simultaneous assessment according to ATLS guideline and resuscitation of the patients were done after arriving in the hospital. Provisional diagnosis of the patients were mainly based on history of trauma, clinical presentation, and repeated physical examination, supplemented only by some baseline investigations within our limited resources. Indeed in almost half of the patients need for an urgent laparotomy was evident at the initial presentation reduced the need of an accurate preoperative diagnosis.

Operative treatment was offered on the basis of history of impact on abdominal wall, clinical symptoms and signs of peritonitis. Patients who needed massive transfusion and those who had poor haemodynamic conditions despite vigorous resuscitation were operated upon. Almost all of them had exploratory laparotomy. Out of 100 polytrauma patients 90 patients in total were operated upon. There was no negative laparotomy.

The patients were carefully followed up in the post-operative period and if had any complication developed were treated accordingly. Data was collected by structured data sheet, edited in tabulated format and was manually evaluated.

Results:

Table-I

Demographics of the Trauma Patients: (N=100)

Age	Number of Patients
0-10	2
11-20	11
21-30	40
31-40	25
41-50	14
51-60	5
>60	3
Sex	
Male	65
Female	35

The male to female ratio was 5.67: 1

Table-II

Nature of trauma, causes, time elapsed and hemodynamic status during admission and preadmission resuscitation of the Trauma Patients: (N=100)

Nature of Trauma	Number of Patients
Penetrating injury	60
Non penetrating injury	33
Blast injury	4
Crush injury	3
Causes of Injury	
Assault	42
Road Traffic Accident	55
Compression	3
Time Lapsed (Hours)	
0 – 6	55
7 – 12	30
13 – 24	15
Hemodynamic Status	
Normal	6
Stable	40
Unstable	54
Resuscitation before admission	
Received	45
Did not receive	55

Table-III

Clinical presentation of polytrauma victims with abdominal injury (N=100)

Clinical Features	Number of Patients
Abdominal pain	95
Vomiting	13
Dysnpnoea	22
Dehydration	39
Hypotension	43
Anaemia	37
Haematuria	02
Abdominal distension	52
Abdominal rigidity	71
Abdominal tenderness	95
Obliteration of liver dullness	41
Absent bowel sound	65
Evisceration	17
Extra-abdominal injuries	
Thoracic Injury	22
Pelvic Fracture	2
Long Bone Fracture	6
Soft Tissue Injury	54

Table-IV

Nature of organ Injury types and operative procedure done

Organ (Number of injury)	Operative Procedure	Number of Patients
Stomach (3)	Simple repair	2
	Partial Gastrectomy	1
Small intestine (37)	Simple repair	21
	Resection and anastomosis	16
Large intestine (18)	Simple repair	3
	Right hemicolectomy	7
	Left hemicolectomy	3
	Hartmann's Procedure	5
The mesentery (3)	Simple repair	3
Liver (11)	Repair of laceration	10
Spleen (9)	Splenectomy	5
	Repair of laceration	4
Pancreas (2)	A Roux loop with pancreas with gastrojejunostomy	1
	Drainage	1
Kidney (4)	Nephrectomy	1
Urinary bladder (2)	Primary repair with suprapubic drainage	2
RetroperitonealHaematoma (5)	Observation	5
Vascular injury (6)	Repair of Portal vein	1
	Resection & anastomosis for mesenteric vessel injury	3

Table-V

Outcome of the Patients following surgery (N=90)

Outcome	Number of Patients
Uneventful	40
Wound infection	14
Wound dehiscence	06
Intra-abdominal abscess	03
Anastomotic leakage	01
Enterocutaneous fistula	02
Intestinal obstruction	01
Colostomy related complications	02
Pulmonary complications	02
Pyrexia	09
Others e.g. phlebitis, jaundice, UTI etc.	08
Post operative bleeding	05
Death	12
Mode of Death (N=12)	
Major vessel injury	5
Liver injury	1
Post operative bleeding	1
DIC	1
Sepsis	3
Electrolyte imbalance	1

Table-VI

Time interval between accident and operation with its outcome. (N=90)

90% of the Polytrauma victims with abdominal injury required laparotomy.

Time interval (hrs)	No of patients operated	Uneventful recovery	Morbidity	Mortality
0-6	20 (22.2%)	13 (65%)	05 (25%)	01 (05%)
7-12	35 (38.8%)	10 (28.57%)	23 (65.7%)	04(11.4%)
13-24	35 (38.8%)	2 (5.71%)	26 (74.28%)	07(20%)

Discussion

Out of the 100 polytrauma victims the highest incidence (40%) was noted in the age group 21-30 years, the most active period of life then decreasing with age indicating that those who are most involved in outdoor activities and are much active in the working places are more subjected to trauma in their daily life. The sex predominance is also towards male (65%) with a Male: Female of 1.85 : 1. This is due to the fact that males are more involved in outdoor activities hence are more vulnerable to road traffic accidents and occupational accidents and also are more prone to physical assaults.

In this series the majority (60%) of the patients had penetrating abdominal injury whether by sharp instruments or by gunshot injury. 33% patient had non penetrating abdominal injury. 42% of the cases of documented penetrating abdominal trauma were due to gunshot/ bullet injury (10%), followed by stab injury (32%). This indicates urgent need of law and order enforcement. Road Traffic Accident (RTA) was the major (50%) cause of polytrauma with abdominal injury and most common cause of blunt abdominal trauma. In a previous study done in our country by Quader F et al.[6] showed RTA as a major cause of non-penetrating abdominal injury which is also supported by this study.

Only 55% of the patients in the study reached DMCH within 6 hours of the incident. This is quite different from the result in study by *Biswas N*[7] performed in Barisal in 2004 and by *Maniruzzaman M.*[8] performed in Rajshahi in 2000, where the percentage of people arriving before 6 hours was 19%. But *Quader F et al.*[6], who also performed the study in DMCH, showed that the average time lapse is 5 hours. The reason may be due to Dhaka being the capital with better communication system available. Also, this study included patients with polytrauma that needed urgent transfer to a designated trauma center i.e. DMCH.

Transportation time has a direct impact on the outcome of management of traumatic gut injury.[9,10] The patients who were operated between 13-24 hours had the highest morbidity and mortality (74.28%, 20%) and the lowest in those who were operated within 6 hours of the incident (25%, 5%). The result clearly shows that the time taken to start the definitive treatment adversely influences the outcome of management of traumatic gut injury. So, receiving surgical treatment without delay gives better outcome in terms of morbidity and mortality.

More than half of the patients (55%) did not receive any resuscitation before admission and as a result of this and lack of pre-hospital care 54% patients reaching DMCH were haemodynamically unstable and 20% patients were in a state of shock. This is due to lack of operating 'trauma system' as in developed countries.

Haemodynamically unstable patients had worse outcome than those who were stable. 5% among who were in shock at the time of admission died during operation. The overall mortality in the series was 6%. The Massachusetts General Hospital series study by *Claude E.W. et al (1950)*[11] reported that shock is a grave finding and implies extensive concealed haemorrhage contaminated by gastrointestinal contents.

95% patients complained of abdominal pain except those (5 %) that had altered consciousness owing to shocked status. The pain was diffuse and was moderate to severe in intensity.13% had vomiting and 3 patients had hematemesis and 2 patients had haematuria , both having pelvic fracture with associated urinary bladder injury. 17 patients of penetrating injury (32.08%) presented with evisceration of bowel, omentum or both. On examination 39% patients were dehydrated, 43% hypotensive and 37% were anemic. Majority of the patients had abdominal tenderness (95%), abdominal rigidity was present in 71% of cases and abdominal distension was present in 42% of patients; upper border of liver dullness was obliterated in 41% cases. Bowel sound was absent in 65% of patients. In a study by *Hall and Angels* [12], 100% of patients had abdominal pain, 89.3% had tenderness, obliteration of upper border of liver dullness was found in 23.30% of penetrating group and 60% of non-penetrating group, and in all such cases on laparotomy, it was found to have intra-peritoneal gut injury; there were also a good number of cases without obliteration of upper border of liver dullness. These findings are very close to that of our study.

More than half of the patients (84%) had an associated extra-abdominal injury. This finding differs from that of the western series. *Fitzerald, Crawford and DeBakey*[13] found 97% cases to have associated other injuries. All of the RTA patients and bomb blast injury patients had associated injury which is supported by the previous study and also a recent study done by *Miklosh Bala et al*[14].

In this study 90% patients in total were operated upon. There was no negative laparotomy. In our study 55 patients had gut injury whereas only 26 patients had solid organ injury. This indeed supports recent study by *Miklosh Bala et al*[14]. Among 100 patients in the study 37% had injury in small intestine. One case of duodenal injury had associated injury in ascending colon. Large bowel was injured in 18% cases. 2 sigmoid colon injury was associated with pelvic fracture. 10 patients had both small and large bowel injury. Liver was injured in 11 cases from solid organs injured. Among other injuries urinary bladder was found to be injured in 2 cases and all of them had pelvic fracture. 9 patients had splenic injury. Only one was isolated splenic injury while another had associated rib fracture. 7 other had associated gut injury among which 1 also had

associated left renal injury. 4 patients had renal injury. 3 patients had stomach injury, Pancreas was found to be injured in 1 case at its body with duodenal injury; another at the tail. Retroperitoneal hematoma was noticed in 5 cases, 3 having associated retroperitoneal hematoma and 2 having gut injury also. 6 Patients had injury of the major vessel. 1 had injury in the abdominal aorta, 1 at the right renal artery, 3 patients had mesenteric vascular injury and the last patient had injury of the portal vein. It is evident that hollow viscus and liver among the solid organs are most commonly injured organs which shows similar pattern described by *Miklosh Bala et al*[14].

33.3% of operated patients had uneventful recovery. Wound infection and wound dehiscence (22.2%) comprised majority of the post operative complications related to surgical site. Poor nutritional status, absence of asepsis in the hospital environment, excessive handling during operation especially by trainee surgeons - all accounted for the high rate of infection and infective complications.

Mortality rate was high (12%). In a recent review article by *H. Bonatti, and J. F. Calland*[15] showed the mortality among polytrauma victims to be the highest. In our study 6 patients died intraoperatively, 5 having injury of the major blood vessels (1 abdominal aorta injury, 1 renal artery injury, 2 hepatic vein injury, 1 inferior mesenteric artery injury) and 1 having a severely injured liver. Although these patients were taken early for laparotomy but probably due to already compromised hemodynamic status, lack of appropriate speciality and inavailablity of huge amount of blood products, lack of needed facilities; an unfavorable ending could not be avoided. Mortality and morbidity was also high in the patients with polytrauma cases described by *Miklosh Bala et al*[10].

Conclusion

Better outcome of polytrauma patients warrants for a systemic multimodal approach that we lack in our country. Abdominal trauma is often missed and frequently under-estimated in patients with polytrauma as manifestations suffering from injuries over other parts of the body are more obvious and early. This unrecognized injury or uncontrolled bleeding from solid organs or injured vessels is the major cause of high mortality rate. Enforcing law and order to reduce assaults and homicidal injuries ,strict abidance to traffic rules, ensuring fitness of vehicles , improving condition of the plying roads along with increasing awareness is a must to combat the condition.

References

1. Walter L Biffl, Trauma. In: F. Charles Bruncardi, Editor, Schwartz's Principles of Surgery, 9th Ed. McGraw-Hill, United States of America, 2010.
2. Robert Handley. Introduction to Trauma, Trauma to Chest and Abdomen. In: Norman S. Williams, Christopher J.K. Bulstrode, P. Ronan O'Connell, editors. Bailey & Love's Short Practice of Surgery, 25th Ed. Arnold, 2008: 271, 338.
3. Bernice Dillon, Wenbin Wang, Omar Bouamra. A Comparison Study of the Injury Score Models, Eur J Trau ma, 2006, 32:538–47.
4. Hugo Bonatti, MD, James Forrest Calland. Trauma. Emerg Med Clin N Am, 2008, 26, 625–648.
5. American College of Surgeons Committee on Trauma. Advance Trauma Life Support Program for Doctors. Amrican College of Surgeons, Chicago. 8th ed., 2008.
6. Quader F, Hossain M, Iqbal M, Hauque MR, Kalam A, Alam AHMT, Bhuiyan AKMZ.: Blunt trauma abdomen : presentation and outcome – report from a teaching hospital in Dhaka, Bangladesh: J. Dhaka Med. Coll. 1996: 5(2): 75-80.
7. Biswas NP,: Patterns of injury of blunt abdominal trauma in patients attending a teaching hospital- astudy of 100 cases (dissertation). Dhaka: Bangladesh College of Physicians nad Surgeons, 2004.
8. Sarker MM. Intra-abdominal injuries following blunt abdominal trauma (dissertation). Dhaka: Bangladesh College of Physicains and Surgeons, 2002.

9. Chambers LW, Rhee P, Baker BC, Perciballi J, Cubano M, Compeggie M, Nace M, Bahman HR. Initial experience of US Marine Corps Forward Resuscitative Surgical System during operation Iraqi freedom. Archives of Surgery, 2005; 140: 26-32.

10. Jurkovich GJ, Carrico CJ: Trauma: Management of acute Injuries: In: Sabiston Dc. Text book of Surgery. The Biological Basis of modern surgical practice. 14th ed: 1991;258-265.

11. Welche E and Giddings WP: Abdominal Trauma, A clinical study of200 consecutive cases from Massachusetts General Hospital; Am. J. surg: 1950;2:252-258.

12. Hall A and Angels A. "Traumatic injuries of the small intestine" Am Surg. 1969; 35:130-134.

13. Fitzerald JB, Crawford ES, Debakey ME: Surgical consideration of non- penetrating abdominal injuries: An analysis of 200 case: Am. J. surg. 1960; 100:22-29.

14. Miklosh Bala et al. Abdominal Trauma After Terrorist Bombing Attacks Exhibits a Unique Pattern of Injury, *Ann Surg* 2008;248: 303–309.

15. H. Bonatti, J.F. Calland. Trauma. Emerg Med Clin N Am J 2008;26:625–648.

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CASE REPORT

Unilateral Pleural Effusion: An Uncommon Initial Presentation of Acute Lymphoblastic Leukaemia

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Abstract

Hematologic malignancies like acute and chronic leukemia rarely present with or develop pleural effusion during the clinical course of disease. We report a patient with acute lymphoblastic leukemia (ALL), who presented with right sided pleural effusion. There was no symptom related to leukemia at the time of presentation. Radiologically there was moderate right-sided pleural effusion which was exudative, plenty RBC and predominant cell was lymphocytes (80%). Subsequent haemogram, bone marrow aspiration study and flow cytometry analysis confirmed the diagnosis of T-cell lymphoblastic leukaemia (Pro-T variant). Induction chemotherapy was started but the patient developed severe neutropenic sepsis and expired 10 days after starting chemotherapy.

Key words: *Pleural effusion, acute lymphoblastic leukemia (ALL)*

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Introduction

Leukemias are diseases in which abnormal proliferation of haematopoietic cells cause progressively increasing infiltration of the bone marrow, although in certain forms the lymphatic tissues are particularly affected. Acute lymphoblastic leukemia (ALL) involve lymphoid cell line and have an aggressive course.[1]In day-to-day clinical practice, clinicians dealing with pleural effusions discover diverse underlying aetiology. Though it is not an uncommon presentation of different malignancies, unilateral pleural effusion as an initial manifestation of acute lymphoblastic leukemia (ALL) is a rare occurrence. The most common mode of presentation of ALL is anaemia, haemorrhage, infective lesion of mouth, pharynx and respiratory tract, fever, prostration and malaise.[1]Rarely a pleural effusion lead to discovery of an underlying haematological malignancy like ALL.[2]In an area of high tuberculosis burden, a patient presenting with fever and pleural effusion may mislead clinician regarding diagnosis especially where other features of haematological malignancy is absent.

Case study

A 30-year-old man presented with the complaints of cough for two and a half months, low grade fever and gradual weight loss for the same duration, heaviness of right chest and abdominal distension for two weeks. Cough was mostly dry with occasional sputum production, fever was low-grade, and intermittent which subsided with

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taking antipyretics. There was loss of 12 kg weight in preceding months. Two weeks before hospitalization, he felt heaviness in right chest with increasing cough and abdominal distension. There was no history of hemoptysis, bleeding diathesis, skin rash, and history of tuberculosis or contact with active TB patient. There was no significant past medical history. He was a shopkeeper from semi-urban area, married with no history of exposure and use of illicit drug.

On examination, he was apathetic and moderately anaemic, body weight 58 kg, axillary temperature 100^0 F. There was generalized lymphadenopathy involving bilateral cervical, axillary and left epitrochlear region. Nodes were variable sizes, firm in consistency, mobile, non-tender, without any discharging sinus and the largest one 5 cmX3cm in right axillae. There was no bony tenderness. Respiratory system examination revealed diminished breath sound and vocal fremitus with stony dull percussion note over right lower chest, features consistent with right sided pleural effusion. There was mild ascites, enlarged liver with 4.5 cm from right costal margin and mild splenomegaly. Diagnostic tests were performed.

Chest X-ray P/A view showed right sided moderate pleural effusion (Fig-1). Sputum AFB and GeneXpert were negative. Haemogram revealed Hg 7.8 gm/dl (12.5-17.5 gm/dl), ESR 33 mm/1^{st} hr, total leukocyte count 13390/cmm (4000-11000/cmm), with 47% atypical cells and platelet count 70000/cmm (150000-450000/cmm). Peripheral blood film showed many atypical cells in WBC series and reduced platelet count, features suggestive of acute leukemia. Diagnostic pleural fluid aspiration and bone marrow aspiration was planned.

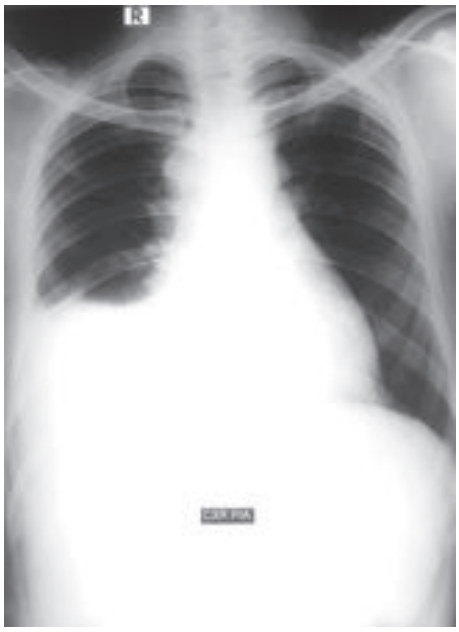
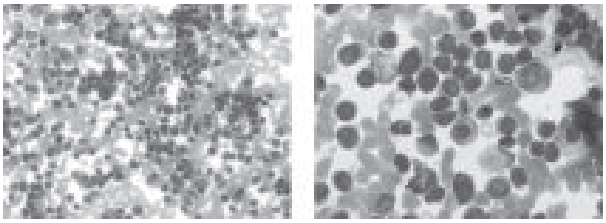


Fig.-1: *Right sided pleural effusion*

About 1200 ml haemorrhaegic pleural fluid was aspirated from right pleural cavity. There was plenty RBC/hpf, total count 200/cmm with 80% lymphocyte, protein 3.9 gm/L, sugar 5-8 mmol/L, ADA 23.9 U/L (0-24 U/L), malignant cell was absent. Bone marrow aspiration revealed features consistent with acute lymphoblastic leukaemia (Fig-2). A clinical diagnosis of ALL with haemorrhagic pleural effusion was made. Haemato-oncologist's opinion was sought and the patient was referred to Haematology department of a multidisciplinary teaching hospital.



A **B**

Fig.-2 (a, b): *Bone marrow aspiration cytology. Arrow indicates blast cell (Leishman stain 400x and 1000x).*

Flow-cytometry of bone marrow was done. On immunophenotyping, it was seen that CD45 slightly dim blastoid population expresses CD7 (strong), CD33 (dim partial) and cCD3. These blastoids were negative for surface CD3, CD5, CD2 and all B-lymphoid and other myeloid markers. Feature was consistent with diagnosis of T-cell lymphoblastic leukaemia (Pro-T variant).

Induction chemotherapy was started with doxorubicin, vincristine, L-asperginase, methotrexate and cytarabin. As there was re-accumulation of pleural effusion and worsening dyspnoea, tube thoracostomy was done after consulting thoracic surgical team. But his condition was deteriorating with persistent high grade fever, with severe neutropenia and

thrombocytopenia and the patient died 10 days after starting chemotherapy due to severe neutropenic sepsis.

Discussion:

Nearly all hematological malignancies can present with or may develop pleural effusion during the clinical course of disease. Among the most common disorders, are

Hodgkin and non-Hodgkin lymphomas, with a frequency of 20 to 30%, especially if mediastinal involvement is present. Acute and chronic leukemia are rarely accompanied by pleural involvement.[3]

Pleural infiltration with malignant cells in acute leukemia is rarely diagnosed during life. It is a common finding at autopsy.[4]Currently, due to increased patient

survival, such cases are being reported. However after an extensive internet search, a very few casereports of malignant pleural effusion that have ledto the diagnosis of ALL are available. Further, due to the rarity of such cases, the underlying etiology of these leukemic effusions is poorly understood.[5]

Leukemic infiltration of lungs may occur as a part of systemic relapse or rarely as an isolated pulmonary leukemic infiltration. Possible pathogenic mechanisms suggested include extramedullary proliferation of a quiescent leukemic clone of cells with subsequent metastasis to bone marrow or alternatively, a subclinical marrow relapse undetected by standard methods with consequent seeding to extramedullary sites.[4]

In leukemic patients, the possibility of other causes responsible for presence of pleural effusion such as bacterial or viral infections, other disseminated solid tumors or complications of chemotherapy should be excluded.Immunocytological examination of cells obtained from pleural effusion, flow cytometry, as well as polymerase chain reaction applied to cytology specimens can contribute to the differential diagnosis. The obtained findings sometimes need to be confirmed by pleuroscopyor thoracoscopicsurgical biopsy.[6-8]

Faiz et al. published the largest series of 111 cases of pleural thoracocentesis in leukemicpatients. In this series, 69 cases were acute myeloid leukemia (AML), 7 were acute lymphoblastic leukemia and 15 were of myelodysplastic syndromes. Major causes attributable to such effusions included associated bacterial or viral infections (47%) and underlying malignancy (36%)[9] Other possible causes may be secondary malignancies, associated autoimmune diseases and treatment toxicities due to chemotherapy, radiation or bone marrow transplant. Desatinib, a tyrosine kinase inhibitor has been found to be linked with exudative pleural effusion.[10]

The prognostic significance of the presence of a pleural effusion at diagnosis with ALL is not easy to determine. Some authors argue that it does not affect the rate of remission or survival. Others report a worse prognosis.[3]Thepleural effusion in patients with ALL usually disappear after induction of chemotherapy. This results in direct improvement of symptoms. However recurrence of pleural exudates is almost inevitable if patients do not achieve remissions. They may present with massive fluid accumulation and respiratory failure. In such case pleurodesis is a treatment option.[11]

Conclusion:

The diagnosis of unilateral pleural effusion as a consequence of haematological malignancy especially acute lymphoblastic leukaemia is always difficult and challenging. Sometimes such pleural effusion may be the first clinical manifestation of an underlying undiagnosed haematological malignancy. Thorough clinical examination and appropriate investigation leads to prompt diagnosis and treatment of theprimary disease.

Conflict of interest: There is no conflict of interest to declare.

Reference:

1. Firkin F, Chesterman C, Penington D, Rush B (editors). de Gruchy's Clinical Haematology in Medical Practice. 5th ed. Oxford: Blackwell Science; 1989.
2. Brunning RD, Matutes E, Harris NL, et al. Acutemyeloid leukaemia: introduction. In:

Jaffe ES, HarrisNL, Stein H, et al (editors). Pathology and genetics of tumours of haematopoietic and lymphoid tissues. 3rded. Lyon, France: IARC Press; 2001. P.77-80.

3. Alexandrakis MG, Passam FH, Kyriakou DS, Bouros D. Pleural effusions in hematologic malignancies. *Chest* 2004; 125: 1546-55.
4. Dix DB, Anderson RA, McFadden DE, Wadsworth LD.Pleural relapse during haematopoietic remission inchildhood acute lymphoblastic leukaemia. *J PediatrHematolOncol.* 1997; 19(5):470-2.
5. Chabbra S, Kalra R, Malik S, et al. Unilateral malignant pleural effusion as an initial manifestation of acute lymphoblastic leukemia: a case report. *Middle East Journal of Cancer* 2015; 6(1): 61-4.
6. Aasebo U, Norum J, Sager G, et al. Intrapleurally instilled mitoxantrone in metastatic pleural effusions: a phase II study. *J Chemother*1997; 9:106-11.
7. Light RW. Malignant pleural effusions. In Light RW, ed. Pleural diseases. Philadelphia PA: Lea &Febiger, 1990; 97-116.
8. Horn KD, Penchansky L. Chylous pleural effusions simulating leukemia infiltrate with thoracoabdominal disease and surgery in infants. *Am J Clinical Pathol*1999; 111: 99-104.
9. Faiz SA, Bashoura L, Lei X, et al. Pleural effusions in patients with acute leukemia and myelodysplastic syndrome. *J Leukemia & Lymphoma* 2013; 54(2): 329-35.
10. Brixey AG, Light RW. Pleural effusions due todesatinib. *CurrOpinPulm Med*. 2010; 16(4): 351-6.
11. BronnerGM, Baas P, Beijnen JH. Pleurodesis inmalignant pleural effusion [Article in Dutch]. *NedTijdschrGeneeskd.* 1997; 141(38):1810-4.