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ORIGINAL ARTICLE

BACTERIOLOGICAL ETIOLOGY OF EMPYEMA THORACIS PATIENTS ADMITTED IN A TERTIARY CARE HOSPITAL

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Abstract:

Background: *Empyema thoracis is the most common complication of pneumonia and is associated with severe morbidity and mortality. Management of empyema thoracis is complex and needs a multimodal approach. Antibiotic therapy is very crucial in management of empyema thoracis and to ensure appropriate antibiotic therapy, epidemiological data is essential. This study aimed to explore the bacteriological profile of empyema thoracis in a tertiary care hospital.* ***Methods:*** *This cross-sectional study was carried on 30 patients admitted in the Department of Medicine and Department of Respiratory Medicine, Sir Salimullah Medical College and Mitford Hospital, Dhaka over a period of six months.* ***Results:*** *Mean age of the patients was 38±10.94 (SD) years of age with a male predominance (66.7% male and 33.3% female). Presenting symptoms were cough (86.7%), fever (83.3%), expectoration (76.7%), chest pain (70.0%), loss of appetite (50.0%), malaise (46.7%) and hemoptysis (10.0%). The major etiology was the thoracic empyema (56.7%) followed by pneumonia (16.67%), lung abscess (10.0%), liver abscess (6.7%), lung cancer (3.3%), secondary infection (3.3%) and undetermined cases responding to antibiotics (3.3%). Bacteriological profile showed Mycobacterium tuberculosis (56.7%), S. aureus (6.7%), S. pyogen (6.7%) , E. coli (3.3%), Klebsiella (3.3%) and Pseudomonas (6.7%).* ***Conclusion:*** *It was concluded from the study; more than half of empyema thoracis was etiologically tubercular.*

Key words: *Empyema thoracis, bacteriological profile, tuberculosis*

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Introduction:

Among thoracic diseases, Empyema thoracis (ET) is one of the common which is more prevalent in developing countries. This is an inflammatory process of infection in a pleural cavity where the purulent material accumulates and organizes in that

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cavity.[1]Parapneumonic effusion following bacterial pneumonia is the most common precursor of empyema.[2].ET incidence is steadily rising even with the advancements in the antibiotic treatment era. Mortality and morbidity vary between 3% and 33%. [3–5]Around the globe, the incidence and prevalence of empyema have been increasing both among the pediatric and adult age groups. The causative bacteria are also changing. In 2013, there were 7.15 cases per 100 000 inhabitants which increased to 7.75 cases per 100 000 inhabitants in 2017. Empyema patients have mortality and surgery rates remained consistent at around 14%.[6] Each year in the UK and USA, over 65000 patients suffer from pleural infection. Approximately 15% of these patients die and another 30% require surgical drainage of the pleural space.[7]

The pathophysiology of ET is a gradual process. According to the American Thoracic Society, the ET has three phases: (1) exudative (acute or Stage I), where exudative fluid accumulates without loculation; (2) fibrinopurulent (Stage II), where pleural fluid becomes turbid or purulent with loculation; and (3) organizing (chronic or Stage III), where thickened pus or fibrin peels start to form, and the pleural space start to replace by granulation tissue.[8,9] There are varieties of etiological factors for ET including bacteria, fungi, and amoebas, in association with pneumonia. Other causes include penetrating chest trauma, thoracic surgery, and esophageal rupture.[2]

Among pediatric population, over 50% of ET cases are due to Streptococcus pneumoniae. In case of adult patients, microorganisms varied significantly over time. During pre-antibiotic era, Streptococcus pneumoniae accounted for majority of cases, Streptococcus pyogenes and Streptococcus aureus were prevalent as well.[7]

Clinical manifestations of empyema vary with anatomical location of infection and level of severity.[10]Common clinical features of ET are broad-spectrum and like that of bacterial pneumonia. Patients generally present with fever, fatigue, cough, shortness of breath and chest pain. Infections with anaerobes tend to lead a more insidious clinical course with less pronounced fever and more generalized systemic symptoms, such as poor appetite and weight loss.[11,12]

The management of empyema can be challenging and complex. Coordination of care across multiple disciplines is necessary, functioning as a cohesive interprofessional team, to optimize positive patient outcomes. Since therapeutic options for empyema involve medical and surgical intervention, the involvement of several specialists is prudent in improving morbidity and mortality. Appropriate empiric antibiotic therapy for acute pleural empyema incorporates an understanding of the patient's clinical history, local antimicrobial resistance patterns, institutional antibiotic stewardship, and pharmacologic characteristics of the antibiotics. The best course of treatment is debatable, especially when it comes to the length of parenteral antibiotics and the importance of surgery. The current management of empyema is highly diverse, owing to a variety of clinical presentations and provider experiences. The bacteriological etiology of empyema thoracis, as well as antibiotic sensitivity, will aid us in developing a suitable treatment plan.[10,13]. Considering this, the aim of the study was to assess the bacteriological etiology of patients of empyema thoracis admitted in a tertiary care hospital.

Methods:

This cross-sectional study was conducted in 30 adult (age>18 years) patients of Empyema thoracis admitted in the Department of Medicine and Respiratory Medicine, Sir Salimullah Medical College and Mitford Hospital, Dhaka between March 2021 to September 2021.After arrival of patient of suspected empyema thoracis, detailed history was taken from the patient and examined thoroughly. After initial chest radiograph pus from pleural space was aspirated according to indication and pleural aspirate was investigated for cytology, biochemistry, protein, sugar, Gram staining and culture sensitivity and Acid-Fast Bacilli staining.A total of 30 patients with confirmed empyema thoracis (pleural fluid demonstrated on chest radiograph that contained > 1000 WBC/mm^3 from which organism could be cultured [14])were included in this study. Patients who developed post surgical or post traumatic empyema as well as pregnant and lactating mother were excluded from this study.Written consent was taken from all the patients after informing the necessary information's regarding the research study. Then necessary data were collected in a preformed questionnaire.

After collection, data were checked for consistency and completeness and were cleaned and edited. Statistical Package for Social Sciences (SPSS) 23 was used to analyze the data. Data were presented by tables, diagram, percentage chart etc. The frequency rates of various information were described and compared by using statistical method.

Results:

In this study a total 30 cases were included who had confirmed Empyema thoracis fulfilling clinical, radiological, biochemical and microbiological criteria.

Out of them 20 were male (66.7%) and rest are female(33.3%). The majority of the study population (33.3%) were between 18-30 years of age. The mean age for the study population was 38±10.94(SD) years of age. Age group 31-40 and 41-50 both had 26.7% of population in each. 10% study population were between age 51-60 years and only 3.3% were in more than 61 years age group.

The majority of the study population (30.0%) completed their primary education. Only 6.7% completed their graduation.Among all, 27.0% were housewives, 17.0% were farmer, 17.0% were unemployed or retired, students were 13.0%, 13.0% were labour and 13.0% were in service.The majority of the respondents (60.0%) belonged to middle income family whereas 23.0% were from a poor family and 17.0% were from rich family.

The symptoms of the subjects at the time of admission were documented which is presented in Table I

Table-I

Distribution of the study population by the symptoms (n=30)

Symptoms*	Frequency (n)	Percentage
Fever	25	83.3
Cough	26	86.7
Chest pain	21	70.0
Weight loss	22	73.33
Expectoration	23	76.7
Dyspnea	19	63.3
Hemoptysis	3	10.0
Malaise	14	46.7
Loss of appetite	15	50.0

*Multiple responses considered

The etiology of empyema thoracisof the study population are shown in Table II

Table-II

Distribution of study patients by the etiology (n=30)

Etiology	Frequency (n)	Percentage
Tubercular causes	17	56.67
Non-tubercular causes		
Lung abscess	3	10.0
Lung cancer	1	3.3
Pneumonia	5	16.67
Liver abscess	2	6.7
Secondary infection	1	3.3
Undetermined cases responding to antibiotics	1	3.3

Study populations had several comorbidities which are depicted in Figure 1

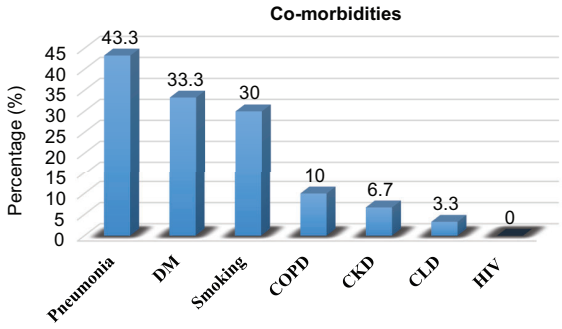

Figure 1: *Distribution of the study population by the co-morbidities and risk factors (n=30)*

TB- Tuberculosis, DM- Diabetes mellitus, COPD-Chronic Obstructive Pulmonary disease, CKD- Chronic Kidney Disease, CLD- Chronic Liver Disease, HIV-Human Immunodeficiency Virus

Lung involvement of the study subjects varied which are shown in Figure 2

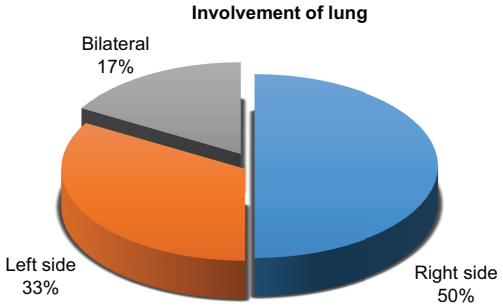

Figure 2: *Distribution of the respondents by the involvement of lungs (n=30)*

Laboratory parameters of the study populations are shown in Table III

Table III

Laboratory parameters of the study patients (n=30)

Parameter	Mean±SD	Range
Hb (gm/dl)	9.49±2.86	4.50-14.0
WBC (Total count) (in cells/mm^3)	8423.33±4444.27	1400-22000
WBC (differential Count)		
Neutrophil (%)	82.9±6.6	75.0-90.0
Lymphocyte (%)	8.1±5.1	3-13.0
RBS (mg/dl)	152.30±96.21	24-510
S.creatinine	0.93±0.40	0.30-1.80
S. Bilirubin (mg/dl)	0.61±0.26	0.10-1.0
Urea (mg/dl)	22.83±14.29	10-60
ESR (in mm 1st hour)	64.83±25.31	20.00-105.00

Table IV delineates the the name of organisms that were identified from the patients' of empyema thoracis

Pleural fluid analysis of the subjects were shown in Table V

Regarding pleural fluid analysis, Total WBC count was 6843.33±11831.01(SD) (in cells/mm^3) , Neutrophil count was 5326.67±11207.29(SD) (in cells/mm^3) , lymphocyte count was 795.10±947.00(SD) (in cells/mm^3), protein was 3.79±0.81(SD) mg/dl and sugar was 61.06±41.15(SD) mg/dl.

Antibiotic sensitivity of the isolated organisms from patients are depicted in Table VI and Table VII

Ciprofloxacin was sensitive to 13.3% gram (+)ve and 33.3% gram (-)ve organism whereas it was resistant to 6.7% gm(+)ve and 46.7% gm (-)ve organisms. Gentamicin was sensitive to 33.3% gm (+)ve and 26.7% gm (-)ve organisms whereas resistant to 40.0% gm (-)ve organisms. Ceftazidime was sensitive to 33.3% gm (+)ve and 30.0% gm (-)ve organisms whereas resistant to 36.7% gm (-)ve organisms. Amikacin was sensitive to 26.5% gm (+)ve and 16.7% gram (-)ve organisms whereas resistant to 56.7% gram (-)ve organisms. Aztreonam was sensitive to 33.3% gm (+)ve and 36.7% gram (-)ve organisms whereas resistant to 30.0% gram (-)ve organisms. Meropenem was sensitive to 20.0% gm (+)ve and 56.7% gram (-)ve organisms whereas resistant to 23.3% gram (-)ve organisms. Netilmicin was sensitive to 16.7% gm (+)ve and 56.7% gram (-)ve organisms whereas resistant to 26.7% gram (-)ve organisms. Cefepime was sensitive to 26.7% gm (+)ve and 46.7% gram (-)ve organisms whereas resistant to 26.7% gram (-)ve organisms. Colistinsulphate was sensitive to 26.7% gm (+)ve and 73.3% gram (-)ve organisms. Tazobactam+Piperacillin was sensitive to 16.7% gm (+)ve and 20.0% gram (-)ve organisms whereas resistant to 3.3% gram(+)ve and 20.0% gram (-)ve organisms.

Among the isolated gram (+)ve organisms, S. Aureus showed highest sensitivity to Gentamicin, Ceftazidime, Amikacin, Aztreonam, Meropenem, Netelmicin, Cefepime and Colistinsulphate, s. Pyogens showed highest level of sensitivity to Gentamicin, Ceftazidime, Amikacin, Aztreonam, Meropenem, Netelmicin, Cefepime, Colistinsulphate and Tazobactam+ Piperacillin. Besides, among the isolated gram (-)ve organisms, E.Coli showed highest level of sensitivity to Colistinsulphate (100%) followed by decreasing order Tazobactam+Piperacillin (75%), Ceftazidime (66.67%) and Meropenem (62.5%), Klebsiella showed highest level of sensitivity to Colistinsulphate (100%) followed by decreasing order Meropenem (80%) and Netelmicin (77.78%), Pseudomonas showed highest level of sensitivity to Colistinsulphate (100%) followed by

Table IV

Distribution of the respondents by the name of organism identified in this study (n=30)

Organisms identified in this study	Frequency (n)	Percentage
MTB	17	56.7
Gram (+)ve		
S. Aureus	2	6.7
S. Pyogens	2	6.7
Gram (-) ve		
Pseudomonus	2	6.7
Klebsiella	1	3.3
E. coli	1	3.3
Polymicrobials	1	3.3
Sterile	4	13.3

MTB- Mycobacterium Tuberculosis, S. aureus- Staphylococcus aureus, S. pyogens-Streptococcus pyogens, E. coli- Escherichia coli,

Table V

Pleural fluid analysis of the study patients(n=30)

Parameter	Mean±SD	Range
WBC (Total count) (in cells/mm^3)	6843.33±11831.01	400-67400
Neutrophil (in cells/mm^3)	5326.67±11207.29	300-64010
Lymphocyte (in cells/mm^3)	795.10±947.00	30-4000
Protein (gm/dl)	3.79±0.81	3.00-5.60
Sugar (mg/dl)	61.06±41.15	25-189

Table VI

Distribution of the study patients by the antibiotic sensitivity and resistance to the organism isolated (n=30)

Name of antibiotics	Gram (+)ve		Gram (-) ve	
	ResistantN(%)	SensitiveN(%)	ResistantN(%)	SensitiveN(%)
Ciprofloxacin	2(6.7)	4(13.3)	14(46.7)	10(33.3)
Gentamicin	0(0.0)	10(33.3)	12(40.0)	8(26.7)
Ceftazidime	0(0.0)	10(33.3)	11(36.7)	9(30.0)
Amikacin	0(0.0)	8(26.5)	17(56.7)	5(16.7)
Aztreonam	0(0.0)	10(33.3)	9(30.0)	11(36.7)
Meropenem	0(0.0)	6(20.0)	7(23.3)	17(56.7)
Netelmicin	0(0.0)	5(16.7)	8(26.7)	17(56.7)
Cefepime	0(0.0)	8(26.7)	8(26.7)	14(46.7)
Colistinsulphate	0(0.0)	8(26.7)	0(0.0)	22(73.3)
Tazobactam+Piperacillin	1(3.3)	5(16.7)	6(20.0)	18(60.0)

Table VII

Distribution of the studied patients by the organism based antibiotic sensitivity (n=30)

Name of antibiotics	Name of Organisms					
(Sensitive %)	S. Aureus	S. Pyogens	E. Coli	Klebsiella	Pseudomonas	MTB
Ciprofloxacin	50%	75%	42.86%	28.57%	50%	100%
Gentamicin	100%	100%	42.86%	37.5%	40.0%	100%
Ceftazidime	100%	100%	66.67%	28.57%	42.86%	100%
Amikacin	100%	100%	25%	16.67%	25%	100%
Aztreonam	100%	100%	60%	50%	57.14%	100%
Meropenem	100%	100%	62.5%	80%	66.67%	100%
Netelmicin	100%	100%	42.86%	77.78%	77.78%	100%
Cefepime	100%	100%	57.14%	60%	70%	100%
Colistinsulphate	100%	100%	100%	100%	100%	100%
Tazobactam+Piperacillin	75%	100%	75%	71.43%	80%	100%

decreasing order Tazobactam+Piperacillin (80%) and Netelmicin (77.78%). MTB showed highest level of sensitivity (100%) to all the antibiotics.

Discussion:

Empyema Thoracic is an infectious disease that causes the accumulation of frank pus in the pleural space of the lungs.[15] It mostly appears as a complication of hospital and community-acquired pneumonia, however, it also occurs due to other causes like thoracic injuries, chest trauma, bronchogenic carcinoma, esophageal rupture, immune-compromised status, and other post-surgical infections.[2,15] The clinical signs and symptoms of empyema include pleuritic chest pain, cough, fever, chills, weight loss, anorexia, dyspnea, and night sweats.[15,16] The diagnosis of empyema is established by the presence of pus and fluid in the pleural space followed by microbiological assay of pleural fluid while gene expert and acid-fast bacilli smear examination are used for the detection of Mycobacterium Tuberculosis.[2] The major aim of empyema treatment is to eliminate the infection and re-expansion of lungs which is usually achieved by eradicating the bacterial growth from the pleural fluid by the use of appropriate antibiotic therapy along with the drainage process.[2,15-17] So this study aimed to assess the bacteriological etiology of empyema thoracis of patients admitted in a tertiary care hospital in Bangladesh.

Among 30 patients of this study, 1/3 rd of the patients were between 18-30 years of age group with mean age 38±10.94(SD) years. Male patients predominated over female patients with a male to female ratio of 2:1. Another similar study found that among 110 patients of empyema, the age varied from 8-74 years of age where 78.2% of the patients were between 11-50 years of age and 7.3% were less than 10 years of age. Male was also predominated over female in this study.[18] Another similar study showed male predominance with mean age 42.07±18.28(SD).[19] Majority of the patients with thoracic empyema were young and middle-aged adults. This age group represents the most productive

years of life and the socio-economic impact is thus tremendous. The high incidence in this age-gender group is attributed to the predilection of pulmonary tuberculosis and community acquired pneumonia in this age gender group.[20,21]

According to this study, two-thirds of the thoracic empyema was due to tubercular causes. Among the non-tubercular causes, 16.67% were due to pneumonia, followed in decreasing order lung abscess (10.0%), liver abscess (6.7%), lung cancer (3.3%), secondary infection (3.3%) and undetermined cases responding to antibiotics (3.3%). Among the western world causes like community-acquired pneumonia, lung abscesses and surgical trauma are the commonest causes of empyema whereas among the south Asian country tuberculosis is one of the most common causes of empyema thoracis.[22-24]

The most common symptoms were cough and cough was among 86.7% of the study population of this study followed in decreasing order fever (83.3%), expectoration (76.7%), chest pain (70.0%), loss of appetite (50.0%), malaise (46.7%) and hemoptysis (10.0%). GajendraVikram Singh et al., and Malhotra et al., also reported almost the same.[24,25] The clinical manifestations of an empyema can vary widely, depending on both the nature of the infecting organism and the competence of the patient's immune system. The spectrum ranges from an almost complete absence of symptoms to a severe illness with systemic toxicity. In general, anaerobic and tubercular empyema usually present with a sub-acute illness, whereas aerobic bacterial infections of the pleural space present with an acute illness.[24]

Regarding co-morbidities and risk factors, H/o pneumonia was among 43.30% of the study population, DM was among 33.30% of the patients, 30% patients had H/o smoking, besides 10% patients had COPD. A similar study in India showed pneumonia as the most common co-morbidities which was among 41% of the study population. Diabetes was among 23.5% of the respondents and 11% of patients had h/o smoking.[25] Co-morbid conditions can make this condition even more troublesome to treat. Early diagnosis, thorough investigations, and early management can help in better outcomes of the patients.

In this current study, for 50% of the respondent's right lung involvement occurred, for 33% of cases left lung involvement occurred whereas for 17% of the patient's bilateral lung involvement happened.

In this study, for 56.7% of the cases, the empyema thoracis was due to tubercular causes. Among the patients with tubercular empyema, 10.0% were sputum positive, 10.0% were plural fluid positive, 13.3% clinico-radiologically positive, 10.0% were both sputum and pleural fluid positive and 13.3% were positive on culture. A similar study in India found that regarding the diagnosis of tubercular empyema, pleural fluid smear for AFB was positive in 21.5% of the patients, sputum smear was positive for 26% of cases which was almost similar to our study.[25]

Among the non-tubercular empyema, S. aureus was among 6.7% cases, S. pyogens were among 13.3% cases, gram-negative bacilli were among 6.7% cases, polymicrobial was found among 3.3% cases and 16.7% cases were sterile. This finding was almost similar to some other Indian studies.[22,25]

Ciprofloxacin was sensitive to 13.3% gram (+)ve and 33.3% gram (-)ve organism whereas it was resistant to 6.7% gm(+)ve and 46.7% gm (-)ve organisms. Gentamicin was sensitive to 33.3% gm (+)ve and 26.7% gm (-)ve organisms whereas resistant to 40.0% gm (-)ve organisms. Ceftazidime was sensitive to 33.3% gm (+)ve and 30.0% gm (-)ve organisms whereas resistant to 36.7% gm (-)ve organisms. Amikacin was sensitive to 26.5% gm (+)ve and 16.7% gram (-)ve organisms whereas resistant to 56.7% gram (-)ve organisms. Aztreonam was sensitive to 33.3% gm (+)ve and 36.7% gram (-)ve organisms whereas resistant to 30.0% gram (-)ve organisms. Meropenem was sensitive to 20.0% gm (+)ve and 56.7% gram (-)ve organisms whereas resistant to 23.3% gram (-)ve organisms. Netilmicin was sensitive to 16.7% gm (+)ve and 56.7% gram (-)ve organisms whereas resistant to 26.7% gram (-)ve organisms. Cefepime was sensitive to 26.7% gm (+)ve and 46.7% gram (-)ve organisms whereas resistant to 26.7% gram (-)ve organisms. Colistin sulfate was sensitive to 26.7% gm (+)ve and 73.3% gram (-)ve organisms. Tazobactam+Piperacillin was sensitive to 16.7% gm (+)ve and 20.0% gram (-)ve organisms whereas resistant to 3.3% gram(+)ve and 20.0% gram (-)ve organisms. In this present study, among the isolated gram (+)ve organisms, S. Aureus showed highest sensitivity to Gentamicin, Ceftazidime, Amikacin, Aztreonam, Meropenem, Netelmicin, Cefepime and Colistinsulphate, s. Pyogens showed highest level of sensitivity to Gentamicin, Ceftazidime, Amikacin, Aztreonam, Meropenem, Netelmicin, Cefepime, Colistinsulphate and Tazobactam+Piperacillin. Besides, among the isolated gram (-)ve organisms, E.Coli showed highest level of sensitivity to Colistinsulphate (100%) followed by decreasing order Tazobactam+Piperacillin (75%), Ceftazidime (66.67%) and Meropenem (62.5%), Klebsiella showed highest level of sensitivity to

Colistinsulphate (100%) followed by decreasing order Meropenem (80%) and Netelmicin (77.78%), Pseudomonas showed highest level of sensitivity to Colistinsulphate (100%) followed by decreasing order Tazobactam+Piperacillin (80%) and Netelmicin (77.78%). MTB showed highest level of sensitivity (100%) to all the antibiotics.

Empyema thoracis is difficult to manage but still presents as a challenge at referral tertiary care hospitals. Besides, co-morbid factors such as diabetes and immunosuppressive retroviral diseases may be implicated as the etiological reason for the resurgence of empyema in the present era of new and effective antibiotics. A high index of suspicion with careful monitoring and pleural fluid aspiration of non-responding parapneumonic effusions cases helps to identify cases of pyothorax at the earliest possible time. Culture sensitivity-based antibiotics and repeat culture tests will offer the best antibiotic choice.

Conclusion:

In this study, in more than half of the patients with empyema thoracis, *mycobacterium tuberculosis* was observed as causative agent. Among the rest, gram positive organism, gram negative organism and polymicrobial organism were observed in a similar frequency. However, further multicentered study should be conducted with a larger sample size to delineate the bacteriological pattern of empyema thoracis in our country.

Limitations:

Like any other study, the present study is not without limitations. Although sample size was calculated statistically, the original sample size was relatively smaller in relation to huge number of population. As the study period was only six months, large sample could not be included.Post surgical & post traumatic empyema thoracis patients were not included in the study. Only one centre (SSMC Mitford Hospital) was enrolled in this study, multiple centers involvement was not only laborious but also expensive.

Acknowledgement:

Thankful to all doctors, nurses and medical stuff of Department of Medicine and Respiratory Medicine, SSMC Mitford Hospital, Dhaka, Bangladesh for their best and kind support for collection of data for this study.

Declaration of Interest:

The authors report no conflict of interest.

Ethical Consideration:

Ethical clearance was obtained from ethical review board of Sir Salimullah Medical College . The objectives of this study along with risks and benefit were fully explained to the subjects in easily understandable local language and then informed written consent was taken from each patient. It was assured that all information and records would be kept confidential and the procedure would be helpful for both the physician and the patient in making rational approach of the case management.

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