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Original Research Article

COMPARATIVE ANALYSIS OF CLINICO-ETIOLOGY, DIAGNOSTIC EVALUATION AND TREATMENT OUTCOME OF TUBERCULAR AND NON-TUBERCULAR BACTERIAL EMPYEMA: FIRST STUDY FROM KUMAOUN REGION

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Abstract

Background: Empyema thoracis is a common benign pathology of the pleural sac causing high morbidity and mortality rates. It can be caused by M. tuberculosis as well as other pathogenic bacteria. To analyze the comparison between clinical, etiological, diagnostic and treatment outcome of tubercular and non-tubercular empyema. **Materials and Methods:** Clinical presentation and history were recorded of participating patients. Chest radiography was performed as per requirement. Pleural fluid was collected aseptically and processed for microbiological evaluation such as AFB staining and culture. Sputum was processed for AFB staining. CBNAAT was performed for pleural fluid and sputum specimens. Clinical outcome for six months was recorded. **Result:** Out of total of 67 cases of empyema, tubercular empyema (58.2%) was found more frequent than non-tubercular empyema cases (41.8%). Antibiotics and intercostal drainage for treatment were required for 61.5% of tubercular empyema and 50% of non-tubercular cases. Antibiotics and serial thoracentesis were required for 39.3% of non-tubercular empyema and 10.3% of tubercular cases. Surgical treatment post-ICD was required for 28.2% of cases with tubercular empyema and 10.7% of cases with non-tubercular empyema. Outcomes for tubercular empyema were recorded as cured (79.5%), follow-up lost (10.2%), re-expansion after surgery (7.7%), and died (2.6%). The outcome for non-tubercular empyema cases was cured (82.1%), follow-up lost (7.2%), and died (10.7%). **Conclusion:** Tubercular empyema is more frequent in India and differs from non-tubercular cases in clinical presentation, as well as is difficult to manage and has more unfavorable outcomes. Timely and precise diagnosis can lead to better management of empyema thoracis.

INTRODUCTION

Empyema thoracis (ET) is a collection of purulent fluid in the pleural space that mainly occurs with pneumonia or secondary to chest trauma/surgery. Approximately half of the patients with pneumonia develop pleural effusion, and 5–10% of patients may develop empyema thoracis after antibiotic treatment.[1] Patients may have a fever, chest pain, and cough in the early stage, whereas dyspnea may occur in the late stage. Treatment includes antibiotics, chest tube drainage, surgical intervention with video-assisted thoracoscopic surgery (VATS), or open thoracotomy.[2]

Despite the use of antibiotics and different pneumococcal vaccines in clinical care, and improvement of the minimally invasive surgical techniques; empyema remains the most common complication of pneumonia with a reported mortality rate between 10% and 20%.[3] There are four stages in the development of empyema (i) The pleuritis sicca stage (ii) The exudative stage (iii) The fibropurulent stage and (iv) The organizational stage.

In developed countries, non-mycobacterial pulmonary infections constitute the majority of thoracic empyema cases. Staphylococci and Pneumococci are the commonest organisms isolated from the pleural pus. The rest of the isolates include gram-negative organisms and anaerobes. Gram-negative organisms are frequently isolated, presumably because of high incidence of resistance

of these organisms to commonly used antibiotics in the early phase of empyema.[4] On the other hand, in the developing countries, tubercular infections account for a substantial number of cases.[5]

Mycobacterium tuberculosis is an aerobic bacterium and the acidic and anaerobic pleural environment of patients with empyema may hinder its growth thus resulting in positive smears but negative cultures.[6] Pleural infection always results in fluid collection in the pleural space with pleural thickening and loculation, regardless of bacterial etiology which forms the basis of radiological findings in empyema cases.[7] Typical pulmonary changes caused by M. tuberculosis include centrilobular nodules, tree-in bud appearance, consolidation and cavitation.[8]

Pulmonary infections including community-acquired pneumonia, aspiration pneumonia as well as suppurative lung diseases like bronchiectasis and lung abscess are the commonest causes of thoracic empyema followed by surgical trauma in the West. In contrast, majority of studies from India revealed that tuberculosis accounts for a large number of empyemas ranging from 29% to 85.1% of all cases. Despite the availability of potent anti-tubercular drugs and improved surgical techniques tuberculous empyema remains a major problem in developing countries responsible for considerable morbidity and mortality. Clinical outcomes in tuberculous empyema are generally believed to be worse than in non-tuberculous etiologies because of the presence of concomitant fibrocavitary parenchymal disease, high bacillary load, frequent development of bronchopleural fistulae and poor general condition of patients.[9] The differential diagnosis of tuberculous pleural infections from other pleural infections is difficult, as the diagnosis of TB is based on polymerase chain reaction (PCR) testing and acid fast bacilli (AFB) staining, and culture of pleural effusion specimens is not always available. There are no data available from the Kumaoun region of Uttarakhand on tubercular and non-tubercular empyema, so the present prospective study was designed to observe the current trends in etiology, clinical presentation, treatment and its outcome in cases of empyema thoracis and to analyze the comparison between tubercular and non-tubercular cases in a tertiary care hospital.

MATERIALS AND METHODS

A prospective hospital based observational study was conducted from January 2021 to September 2022 at Government Medical College, Haldwani & associated hospitals. A prior approval to perform the study was taken from Institutional Ethical Committee. A verbal as well as written consent were taken from the study participants. The participants included in the study were the patients diagnosed as Empyema Thoracis either Tubercular or Non-Tubercular by laboratory investigations & radiologically, visiting OPD or admitted in the department of Respiratory Medicine of the study institute. Patients below the age of 16 years were excluded from the study. Empyema secondary to injury or surgical procedure were also not considered for the study.

The clinical parameters including age, gender, symptoms (fever, weight loss, cough, sputum, hemoptysis, shortness of breath, chest pain) and duration of stay were evaluated in all patients. Presence of any comorbidity like diabetes mellitus, HIV infection, seizure disorder, liver abscess, rheumatoid arthritis, and malignancy were documented. Chest radiographs were obtained in all patients at the admission, after intercostal tube drain (ICTD) insertion, ICTD removal and at discharge, while ultrasound (USG) and computed tomography (CT) of chest were done if necessary.

Pleural fluid was collected aseptically by thoracentesis and if macroscopically purulent was submitted for Gram stain, culture (aerobic), and smear for AFB. Nonpurulent fluid was studied additionally for total leukocyte count (TLC), differential leukocyte count (DLC), protein, sugar, and LDH. Anaerobic culture was carried out if there seemed a suspicion of anaerobic empyema (in those with h/o aspiration, alcoholism, seizure, periodontal disease). Mycobacterial culture of pleural fluid was not performed in this study owing to non-availability of automated system such as MGIT (BD, USA) and facilities for drug-sensitivity testing. Complete blood counts, renal and liver function tests, blood for HIV serology, blood sugar (fasting and postprandial), and sputum for AFB smear were sent in for all patients.

Outcome assessment: A follow up observation for six months was performed for each patient. Outcome was categorized as:

(i) Improved (Complete resolution of symptoms, normalization of laboratory markers of infection/inflammation, and complete lung expansion with residual pleural thickening of <2 cm in chest X-ray PA).

(ii) Treatment failure (Recurrence or persistence of BPF after medical and surgical management).

(iii) Death (During the course of illness due to the disease process)

Statistical Analysis

Data was entered into Microsoft excel and analysed using Statistical Package for the Social Sciences (SPSS) version 19. Bio-statistical test were used to compare means with the help of biostatistician. A difference with p value <0.05 was considered statistically significant.

RESULTS

A total of 200 cases of pleural effusion were observed during the period of study. Out of total, 67 cases of empyema were included in the study. The male to female ratio was recorded 4.6:01.

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Majority of patients aged between 41-60 years group.

Table 1: Demographical distribution of the patients on the basis of gender, age and etiology.

Characteristics	Number	Percentage
Female	12	17.9
Male	55	82.1
Age groups		
<20 years	8	11.9
21-40 years	18	26.9
41-60 years	31	46.3
>60 years	10	14.9
Aetiology		
Tubercular	39	58.2
Non tubercular	28	41.8

Table 2: Comparative analysis of tubercular and non-tubercular cases on the basis of clinical characteristics, comorbidieties, radiological features, management and treatment outcome.

	Tubercular Cases (N=39)	Non-Tubercular Cases (N=28)	P Value
Clinical Characteristic			
Fever	39 (100%)	28 (100%)	-
Cough	36 (92.3%)	27 (96.4%)	0.4886
Chest Pain	10 (25.6%)	7 (25%)	0.9559
Dyspnoea	31 (79.5%)	25 (89.3%)	0.2890
BPF	24 (61.5%)	4 (14.3%)	0.0001
Co-morbidities			
Diabetes Mellitus	8	4	
Hypertension	4	3	
COPD	5	1	
CKD	0	1	
Hepatitis	2	0	
AIDS	1	0	
Malignancy	0	1	
CVA	0	1	
Chest X-Ray Finding			
No Lesion	2 (5.1%)	2 (7.1%)	0.7345
Mild	11 (28.2%)	4 (14.3%)	0.1815
Moderate	20 (51.3%)	18 (64.3%)	0.2931
Far Advanced	6 (15.4%)	4 (14.3%)	0.9016
Treatment			
Antibiotics + ICD (Inter-Costal Drainage)	35 (89.7%)	17 (60.7%)	0.0053
Antibiotics + Serial Thoracentesis	4 (10.3%)	11 (39.3%)	0.0053
Required Surgical Treatment	11 (28.2%)	3 (10.7%)	0.0845
Outcome			
Cured	31 (79.5%)	23 (82.1%)	0.7922
Lost To Follow Up	4 (10.2%)	2 (7.2%)	0.6736
Re-Expansion After Surgery	3 (7.7%)	0 (0%)	0.1359
Death	1 (2.6%)	3 (10.7%)	0.1712

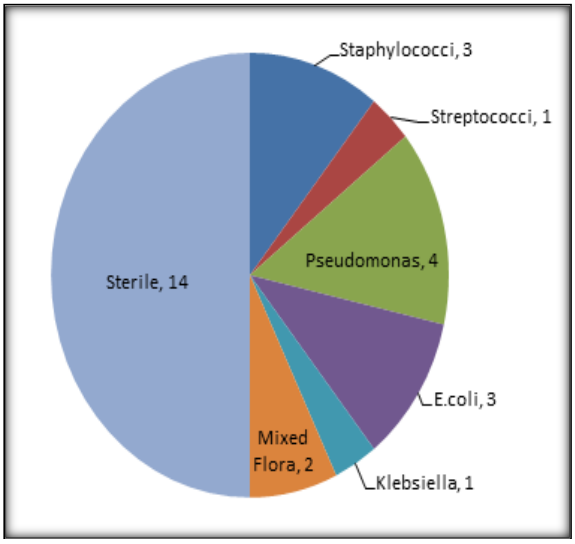

Figure 1: Distribution of Bacterial Pathogens isolated from the non-tubercular empyema patients.

DISCUSSION

Most patients that develop an empyema thoracis are frail with significant co-morbidity, immunocompromise or have had recent thoracic instrumentation. In recent years, there has been a surge in empyema incidence in both children and adults, the causes of which remain speculative.[10,11]

In the present study among the 67 participants, the mean age of the study participants was 43.58 ± 15.45 years which is comparable to mean age of participants in study done by Malhotra P et al, who found mean age to be 40.9 ± 16.2 years.[9] Majority of patients belonged to 41-60 years age group (46.3%), followed by 21-40 years age group (26.9%). This is well supported by a study of Singh GV who also reported maximum number of participants from 41-60 years age group.[12] Male (82.1%) predominance was observed in present

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study in comparison to females (17.9%) which is similar to many previous studies.[9,12,13]

In the current study tubercular etiology was recorded in 58.2% while remaining 41.8% were cases of non-tubercular bacterial etiology. Similar data of etiology has been published by Pulle MV et al.[13]

The clinical features were very similar in both types of etiologies. Only difference was seen in BPF which was higher among the tubercular cases. Fever was common in all the cases while cough was second most common clinical feature. Fever and cough are usually present for longer duration among the tuberculosis empyema, probably due to the nature of disease progression & pathology related to nature of etiological agent.[14-16]

In the present study, the comorbidities among the tubercular empyema cases included 8 cases with diabetes mellitus, four cases with hypertension, five cases with COPD, two cases with hepatitis and one case with AIDS while among non-tubercular empyema cases four cases with diabetes mellitus, three cases with hypertension and one case each with COPD, CKD, malignancy and CVA. These results are well supported by a previous study by Kundu S et al.[5]

The culture positivity rate for pleural infection ranges between 40-60% by conventional method which limits the usage of narrow spectrum antibiotics. Therefore, successful empirical treatments can be achieved with better knowledge of predominant pathogens.[17] In the current study, the culture positivity rate was recorded 50% among non-tubercular cases. Previous studies have reported culture positivity rate of 40-70%.[12,13,18] This variation in culture positivity rate can be explained by various reasons such as delayed presentation, prior antibiotic intake, difference in culture techniques, exclusion of anaerobic culture and study population.

Among the non-tubercular cases Pseudomonas species were found in 14.3% cases. E. coli and Staphylococcus species were reported in 10.7% cases each. Mixed flora grown in 7.1% cases. Streptococcus species and Klebsiella species were reported in 3.6% cases each. The present study showed comparatively more cases with Gram-negative bacteria. Streptococcus species and Pneumococci accounted for most empyema cases in early 1940s. With the advent of antibiotics and their widespread usage, S. aureus emerged as the most frequent pathogen causing empyema in the 1960s. Gradually, Gram negative bacterial infections have markedly increased and succeeded in the other pathogens. This above pattern emphasizes the trend of dominance of Gram-negative organisms in the causation of empyema.[19-21]

Out of total 39 tubercular empyema cases, 48.7% were sputum smear positive for AFB and 7.7% were smear positive for pleural fluid AFB. There were 64.1% cases each with pleural fluid and sputum CBNAAT positivity. Mantoux test was positive in 82.1% cases. In study by Singh GV et al, pleural fluid smear for AFB was positive in 9 cases (21.5%), sputum smear was positive in 11 of the patients (26%).[12]

No significant difference was noted in chest radiography findings of both categories. Majority of cases (51.3%) with tubercular empyema showed moderate lesion, 28.2% showed mild lesions, 15.4% showed far advanced lesions and 5.1% showed no lesion. On the other hand, 64.3% cases with non-tubercular empyema showed moderate lesion, 14.3% showed mild lesions, 14.3% showed far advanced lesions and 7.1% showed no lesion.

Significant difference was noticed in the management (except surgical interventions) of both categories of cases. Therapy for tubercular empyema consists of prompt drainage of infected pleural space, effective anti-tubercular treatment regimen and treatment of associated secondary infection of pleural space. Greater number of cases with tubercular empyema required antibiotics and intercostal drainage for treatment as compared to non-tubercular cases (89.7% v/s 60.7%) in the present study. Majority of cases with non-tubercular empyema required antibiotics and serial thoracentesis for treatment as compared to tubercular cases (39.3% v/s 10.3%). Surgical treatment post- ICD was required in 28.2% cases with tubercular empyema and 10.7% cases with non-tubercular empyema.

In the present study, the mean duration of ICD in tubercular empyema was 54.71 ± 43.08 days and non-tubercular empyema was 40.53 ± 21.52 days. The mean duration of ICD was observed to be longer in tubercular empyema cases as compared to non-tubercular empyema cases which is in concordance with study done by Kundu S et al,[5] It suggests that tuberculous empyema has more chronicity not only in terms of symptom presentation, but also treatment course. Longer duration of ICD can be explained by delayed healing of peripheral alveolar leaks due to active tuberculosis.[13]

No statistically significant difference was seen in treatment outcome of both groups of patients. Majority of cases with tubercular empyema were cured (79.5%), 10.2% were lost to follow up, 7.7% showed re-expansion after surgery and 2.6% died. On the other hand, 82.1% cases with non-tubercular empyema were cured, 7.2% were lost to follow up and 10.7% died. The outcome among both groups were different with non-tuberculous empyema showing good response and almost complete resolution in most cases with appropriate antibiotics and therapeutic procedures like serial thoracocentesis and intercostal drainage but in tubercular group, despite ATT and ICDT, the duration and course of the disease was longer, hospital stay and mean duration of ICDT was longer with more cases presenting with BPF and resolution rate was less compared to non-tubercular group.

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Limitation

Unavailability of automated culture and drug susceptibility testing of Mycobacterium tuberculosis in the study centre.

CONCLUSION

Tuberculous empyema remains a significant cause of empyema thoracis in India and it differs from non-tuberculous empyema in clinical presentation, difficult management and significantly poorer outcome. Accurate diagnosis with minimum turnaround time can aid in effective management of empyema cases. Further studies with larger sample size are required to validate the findings of this study.

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