Original Article

Microbiological profile of tubercular and nontubercular empyemas and its impact on clinical outcomes: A retrospective analysis of 285 consecutively operated cases

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ABSTRACT

Background: Empyema thoracis is an entity seen across all age groups. This study aims at reporting a detailed microbiological profile of "pus and pleural tissue" in patients operated for empyema thoracis and also correlating it with perioperative clinical outcomes. **Materials and Methods:** Patients operated for empyema thoracis between 2012 and 2016 were included in the study. Patients were taken up for surgery after thorough preoperative evaluation. Perioperative outcomes were correlated with the results of microbiological analysis to evaluate their effect on clinical outcomes. **Results:** In the study, 285 patients were operated. There were 215 males (75.4%) and 70 females (24.6%). Tuberculosis (TB) was responsible for 58.2% of the cases (n = 166). Of 166, 32 patients were mycobacterial culture positive, suggesting 19.28% mycobacterial culture positivity rate. 21.8% of the total mycobacterial cultures were multidrug resistant. TB culture-positive patients had a significantly higher incidence of air leak (P = 0.03), inter-costal drain (ICD) duration (P = 0.03), and higher rates of recurrence (P = 0.03). Nontubercular empyema constituted 119 cases (41.8%). Forty-seven (39.5%) cases were culture positive. Gram-negative organisms were cultured in 30 (63.8%). *Pseudomonas aeruginosa* was the predominant isolate. Bacterial culture-positive patients had significantly higher conversions (P = 0.03), prolonged postoperative air leak (P = 0.04), and postoperative wound infections. **Conclusions:** This study highlights the emergence of Gram-negative organisms in bacterial empyema and emergence of multidrug resistance in tubercular empyema. Clinical outcome correlation revealed increased complications in culture-positive cases in both tubercular and nontubercular empyemas.

KEY WORDS: Clinical outcomes, decortication, microbiology, nontubercular empyema, tubercular

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INTRODUCTION

Empyema is a common clinical condition and affects patients across all age groups. While tuberculosis (TB) still continues to be a major cause, the incidence of nontubercular cases has been on the rise in the recent past. With time, the microbiological profile of empyema has also been changing. While Gram-positive organisms were dominant in the preantibiotic era, with the

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introduction of antibiotics, more and more Gram-negative organisms are being encountered[1] with emerging problem of drug resistance.[2] In tubercular empyema also, multidrug resistance is emerging as an important challenge.[3] These microbiological issues are important to choose the appropriate antibiotics and antitubercular medications.

No study of microbiological analysis of "pus and pleural tissue" of patients operated for empyema thoracis reporting its correlation with clinical outcome following surgery has been published till date from India. We herein present the microbiological profile and its correlation with clinical outcome in patients with empyema thoracis undergoing surgical management.

MATERIALS AND METHODS

This retrospective study was conducted at Centre for Chest Surgery, Sir Ganga Ram Hospital, New Delhi, India. Patients who underwent surgical management for empyema thoracis between March 2012 and November 2016 were included in the study. Demographic data, details of present illness, and treatment received including antitubercular treatment were recorded in detail. Preoperative investigations included complete blood count, renal and liver function tests, and contrast-enhanced computed tomography scan of the chest to assess the disease stage. Indications for surgery included pleural peel encasing the lung (trapped lung), multiloculated empyema, inadequate drainage of empyema despite chest tube, and persistent bronchopleural fistula with collapsed lung. Patients were taken up for surgery after thorough preoperative evaluation and adequate physical and nutritional preparation. Intraoperatively, pleural fluid/pus as well as pleural tissue was sent for Gram's stain, bacterial culture, direct fluorescent staining for acid-fast bacilli (AFB), mycobacterial culture, KOH staining for fungus, and fungal culture in all patients. Procedure was chosen according to the disease stage and patient fitness. Procedures performed included video-assisted thoracoscopic surgery (VATS) or open debridement, decortication with or without lung resection, and window thoracostomy.

The patients who were not on any antibiotics when taken up for surgery (usually tubercular empyema) were started on a third-generation cephalosporin and an aminoglycoside combination 1 h before skin incision. Those already on antibiotics (usually postpneumonic empyema) were continued on the same medicines till our culture report was available and necessitated a change of antibiotics. The same was then done as per the sensitivity report. In patients who were already on Anti-Tubercular Therapy (ATT) when presenting for surgery, the same regimen was continued till the results of our investigations were available. Further treatment was based on these results. In patients not on ATT at the time of surgery, the same was started postoperatively by us if there was evidence of TB on pleural pus or tissue studies. Antibiotics or antifungal treatment was modified if cultures showed sensitivity different from the drugs being given. Apart from antibiotics, antitubercular therapy, and chest tube care, postoperative management included nutritional support and supervised, vigorous chest physiotherapy to achieve good lung expansion. The chest drains were removed when there was no air leak and the drainage was not purulent and was <100 ml in 24 h. Patients were discharged from the hospital either after drain removal or with drains if they had prolonged drainage or air leak. Duration of postoperative air leak, duration of chest tube, hospital stay, wound infection, recurrence of disease, and mortality during hospital stay were monitored and recorded. After discharge also, patients were monitored for status of lung expansion and any other complication. Perioperative outcomes were then correlated with the results of microbiological analysis to evaluate their effect on clinical outcomes.

RESULTS

Demography and preoperative variables

During the study period, i.e., March 2012 to November 2016, 285 patients were operated for empyema thoracis. There were 215 males (75.4%) and 70 females (24.6%). Majority of the patients (n = 130) were in the age group of 20–40 years. In 63.4% of the patients (n = 180), the disease affected right chest, in 34.4% (n = 99), it affected left side, while bilateral disease was present in 0.2% of the cases (n = 6) [Table 1].

Microbiology profile and clinical outcomes: Tubercular empyema (n = 166)

TB was the leading cause of empyema in our study, responsible for 58.2% of the cases (n = 166). This diagnosis was based on the presence of any or all of the following criteria:

1. Pleural fluid or tissue staining positive for AFB
2. Pleural fluid or tissue culture positive for mycobacteria
3. Pleural biopsy specimen shows granulomatous inflammation with caseation necrosis.

Table 1: Demography of patients operated for empyema (n=285)

Characteristics	n (%)
Male	215 (75.4)
Female	70 (24.6)
Age group (years)	
≤20	48 (16.9)
21-40	130 (45.8)
41-60	72 (25.3)
>60	35 (12)
Side of disease	
Right side	180 (63.4)
Left side	99 (34.4)
Bilateral	6 (0.2)
Etiology	
Tubercular	166 (58.2)
Nontubercular	119 (41.8)

At presentation to us, 195 patients (68.4%) were on ATT for duration ranging from 2 to 9 months. However, taking the abovementioned criteria, 166 patients were finally labeled as tubercular empyema. The remaining 29 were either nontubercular empyema or had burnt-out disease with no evidence of TB now. Of 166, 32 patients were culture positive for mycobacteria (either pleural fluid or tissue), suggesting 19.28% mycobacterial culture positivity rate. Seven of these 32 (21.8%) mycobacterial cultures were multidrug resistant (MDR). In tubercular group, 15 patients were on MDR drugs at presentation, of which 2 patients were ultimately diagnosed as MDR. Indications of starting MDR treatment in rest of the patients were persistence of AFB positivity in pleural fluid even after 3–4 months of first-line ATT in 5 patients, persistence of hydropneumothorax with collapsed lung in 4 patients, and bronchopleural fistula in 4 patients [Table 2].

On comparison of clinical outcomes, mycobacterial culture-positive patients had a significantly higher incidence of postoperative air leak ($P = 0.03$), prolonged ICD duration ($P = 0.03$), and higher rates of recurrence ($P = 0.03$). No difference was found in terms of conversions, hospital stay, and mortality [Table 3].

Microbiology profile and clinical outcomes: Nontubercular empyema

Nontubercular empyema constituted 119 cases (41.8%) of total case volume. Postpneumonic empyema constituted the single largest group (72 cases, i.e., 60.5%), followed by chronic kidney disease-associated empyema (20 cases, i.e. 16.8%). Major remaining group included 8 cases of posttraumatic hemothorax/empyema and six cases of recurrent empyema that were operated elsewhere [Table 4].

Forty-seven (39.5%) cases were culture positive [Table 5]. Gram-negative organisms were cultured in 30 cases (63.8%) and Gram-positive organisms in 14 cases (29.8%). In the remaining three cases, combined growth of both Gram-negative and Gram-positive organisms was isolated [Table 6]. In the Gram-positive group, 41% (7/17) isolated were *Staphylococcus aureus*, of which three were methicillin-resistant *S. aureus*. The remaining included coagulase-negative *Staphylococcus*, *Streptococcus*, and *Enterococcus* [Table 7]. In the Gram-negative group, *Pseudomonas aeruginosa* and *Escherichia coli* comprised 69.7% cases [Table 8].

On comparison of clinical outcomes, bacterial culture-positive patients had significantly higher conversions ($P = 0.03$), prolonged postoperative air leak ($P = 0.04$), and postoperative wound infections ($P = 0.03$). No difference was found in terms of hospital stay, lung expansion, recurrence, and mortality [Table 9].

Table 2: Analysis of tubercular empyema (*n*=166)

	n (%)
DF stain positivity in pleural fluid and/or pleural peel	61 (36.7)
Only pleural fluid DF stain positive	24 (14.5)
Only peel DF stain positive	28 (16.9)
Both pleural fluid and peel stain positive	9 (5.4)
Overall mycobacteria culture positive	32 (19.28)
Both mycobacterial culture and DF stain positive	17 (10.2)
Mycobacterial culture positive without DF stain positive (peel/fluid)	15 (9)
Overall MDR positivity	7 (4.21)
MDR positivity in total mycobacterial culture positivity	7/32 (21.8)
Number of patients who were on MDR treatment at presentation	15
Finally confirmed as MDR on culture	2
No evidence of drug resistance	13

MDR: Multidrug resistant, DF: Direct Flourescent

DISCUSSION

Empyema thoracis is an age-old disease with continuing morbidity and mortality till today.[4] Aged population, immune-compromised individuals, and hospital-acquired infections with evolving drug-resistant organisms contribute to this persisting complex problem. Irrational use of antibiotics has contributed to the development of antibiotic resistance. With passage of time, even the spectrum of organisms causing empyema thoracis has changed. In the preantibiotic era and starting years of antibiotic usage, Gram-positive organisms predominated.[5] However, later on, anaerobic organisms and Gram-negative organisms became majority.[6]

Tubercular group

In this retrospective study, tubercular cases were more as compared to others (58% vs. 42%). This could be explained by high prevalence of TB in India.[7-9] In our group, mycobacterial culture positivity with either pleural fluid or tissue was 19.28% (32/166) which is in the range of previous studies.

Table 3: Comparison of outcomes between mycobacterial culture-positive and mycobacterial culture-negative cases

Characteristics	Mycobacterial culture positive (*n*=32)	Mycobacterial culture negative (*n*=134)	*P*
Conversion to open	0	11	0.1254
Prolonged air leak	12	26	0.036
Average duration of ICD removal (days)	7.42±3.73	6.29±2.41	0.035
Incomplete lung expansion	0	4	1.0000
Average hospital stay (days)	7.12±3.58	7.0±2.84	0.8388
Postoperative wound infection	1	3	0.5791
Recurrence	2	0	0.0362
Mortality	0	0	1.000

ICD: Inter-Costal Drain

Table 4: Analysis of nontubercular empyema (*n*=119)

Nontubercular empyema	Number of cases, *n*
Postpneumonic	72
CKD-associated empyema	20
Posttraumatic	8
Recurrent empyema	6
Postpneumothorax	4
Postesophageal perforation	2
Post-PCNL	2
Rheumatoid arthritis effusion	2
Subphrenic abscess	1
Postpancreatitis	2

CKD: Chronic kidney disease, PCNL: Per cutaneous nephro lithostomy

Table 5: Nontubercular empyema (*n*=119 cases): Culture report

Characteristics	Number of cases, *n* (%)
Culture positive	47 (39.5)
Culture negative	72 (60.5)

Table 6: Details of bacterial culture-positive cases (*n*=47 cases)

Characteristics	Number of cases, *n* (%)
Gram-positive organisms only	14 (29.8)
Gram-negative organisms only	30 (63.8)
Both Gram-positive and Gram-negative organisms	3 (6.4)

Table 7: Gram-positive organisms (*n*=14)

Characteristics	Number of cases, *n* (%)
Staphylococcus sps.	11 (23.4)
S. aureus	7 (14.9)
MRSA	3/7 (42.9)
VRSA	0
CoNS	4 (8.5)
S. epidermidis	1
S. haemolyticus	2
S. hominis	1
S. mitis	2 (4.2)
Enterococcus	4 (8.4)
VRE	0

S. aureus: *Staphylococcus aureus*, *S. epidermidis*: *Staphylococcus epidermidis*, *S. haemolyticus*: *Staphylococcus haemolyticus*, *S. hominis*: *Staphylococcus hominis*, *S. mitis*: *Streptococcus mitis*, CoNS: Coagulase-negative *Staphylococcus*, VRE: Vancomycin-resistant enterococci, MRSA: Methicillin-resistant *S. aureus*, VRSA: Vancomycin-resistant *S. aureus*

In our study, pleural fluid and pleural peel showed AFB stain positivity in 19.8% and 22.2% of the patients, which was similar to the described literature.[10] Mycobacterial culture positivity with either pleural fluid or tissue was 19.28% (32/166), which is comparable to that reported in the previous study.[11] As per the WHO report, in India, the estimated percentage of MDR TB in newly diagnosed cases was 2.5% and in previously treated cases was 16%.[12] In our series, 4.2% of the patients (7/166) were ultimately diagnosed to be MDR. This percentage is slightly higher than the earlier said report.

Postoperative air leak and ICD duration were observed to be significantly longer in mycobacterial culture-positive patients. This can be explained by delayed healing of peripheral alveolar leaks due to active TB.

Nontubercular group

Among the nontubercular group, postpneumonic group was the majority comprising 60% (72/119). Culture positivity among the nontubercular group was 39.5%. The reported culture positivity rate in the literature varies from 1.4%–89%.[13] This varied culture positivity can be explained by delayed presentation as was the case in our study (72% vases were of more than 8 weeks duration) and with frequent use of antibiotics. This could also be due to differences in techniques, nonscreening of anaerobes, and differences in the study population.

Aerobic Gram-negative bacteria were the predominant isolates in our study group comprising 63.8% ($n = 30$) of all culture-positive cases. *P. aeruginosa* was the most frequent isolate ($n = 14$, 29.8% of the total pyogenic isolates). Earlier studies had also reported similar rates of isolation of *Pseudomonas*.[14] Our results are also comparable with the observations of various researchers who emphasized the emergence of Gram-negative bacteria as a causative factor for empyema thoracis.[15] In the early 1940s, *Streptococcus* and pneumococcus accounted for most empyema cases.[16] With the advent of antibiotics and their widespread usage, *S. aureus* emerged as the most frequent pathogen causing empyema in the 1960s.[17,18] Gradually, GNB 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.

MDR bacteria are defined as having acquired nonsusceptibility to at least one antibiotic in three or more classes.[19] Six of 14 *Pseudomonas* isolates (42.9%) and 2 of 4 *Acinetobacter* isolates (50%) were found to be MDR. This finding of increasing trend in antibiotic resistance among the emerging pathogens is a concern as it would leave us with less choice of antibiotics and limit our ability to treat them.

Further subgroup analysis was done with correlation between growth of organisms and clinical outcome. Among attempted cases of VATS decortication, conversion rates were significantly higher in culture-positive cases as compared to negative ones. The most common reason for conversion was bleeding. A higher rate of conversion could be explained by increased vascularity of the adhesions with active infection with culture positivity. The incidence of prolonged postoperative air leak and postoperative wound infection was higher ($P < 0.05$) among cases with culture positivity. However, hospital stay or overall mortality was not statistically different among both the groups.

CONCLUSIONS

The present study is the largest study in Indian context with microbiological evaluation of 285 cases of surgical

Table 8: Gram-negative organisms (*n*=30)

Characteristics	Number of cases (%)
P. aeruginosa	14 (29.8)
MDR	6/14 (42.9)
Pandrug resistant	0
Acinetobacter sps.	4 (8.4)
Baumannii	2
MDR	2
Pandrug resistant	Nil
Lwoffii	1
Haemolyticus	1
Enterobacteriaceae	12 (25.5)
CRE	5/12 (41.7)
E. coli	9 (19.1)
Carbapenem-resistant *E. coli*	2/9 (22.2)
K. pneumoniae	2 (4.2)
Carbapenem-resistant *Klebsiella*	2/2 (100)
P. mirabilis	1 (2.1)
Carbapenem-resistant *Proteus*	0 (2.1)
E. cloacae	1
Carbapenem-resistant *E. cloacae*	1 (100)
M. morganii	1 (2.1)
A. xylosoxidans	1 (2.1)
S. maltophilia	1 (2.1)

P. aeruginosa: *Pseudomonas aeruginosa*, MDR: Multidrug resistant, CRE: Carbapenem-resistant *Enterobacteriaceae*, *E. coli*: *Escherichia coli*, *K. pneumonia*: Klebsiella pneumonia, P. mirabilis: Proteus mirabilis, *E. cloacae*: *Enterobacter cloacae*, *M. morganii*: *Morganella morganii*, *A. xylosoxidans*: *Achromobacter xylosoxidans*, *S. maltophilia*: *Stenotrophomonas maltophilia*

Table 9: Outcome comparison with culture-positive and culture-negative group among nontubercular empyema

Characteristics	Culture positive (*n*=47)	Culture negative (*n*=72)	*P*
Conversion to open	11	6	0.030
Prolonged air leak	21	19	0.048
Average duration of ICD removal (days)	6.20±2.38	5.78±2.4	0.58
Incomplete lung expansion	1	3	1.0
Average hospital stay (days)	7.44±3.88	7.2±2.56	0.71
Postoperative wound infection	9	4	0.033
Recurrence	2	0	0.15
Mortality	1	2	1.0

ICD: Inter-Costal Drain

specimen of empyema patients with clinical outcome correlation. Our study highlights the emerging nature of GNB as a causation agent in bacterial empyema surpassing Gram-positive organisms and emergence of drug resistance in tubercular patients. Clinical outcome correlation revealed increased complications with culture-positive cases among tubercular and nontubercular empyemas. The study highlights the emergence of Gram-negative organisms in bacterial empyema and emergence of multidrug resistance in tubercular empyema. Clinical outcome correlation revealed increased complications in culture-positive cases in both tubercular and nontubercular empyemas.

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Conflicts of interest

There are no conflicts of interest.

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