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Clinical characteristics and outcomes of empyema thoracis in 117 patients: A comparative analysis of tuberculous vs. non-tuberculous aetiologies

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KEYWORDS
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Summary
Background: Empyema thoracis remains a major problem in developing countries. Clinical outcomes in tuberculous empyema are generally believed to be worse than in non-tuberculous aetiologies because of the presence of concomitant fibrocavitary parenchymal disease, frequent bronchopleural fistulae and poor general condition of patients. We performed a prospective study over a 2-year period with the objective of comparing the clinical characteristics and outcomes of patients with tuberculous vs. non-tuberculous empyema.
Methods: Prospective study of all cases of non-surgical thoracic empyema seen at a tertiary care centre in North India over a 2-year period. A comparative analysis of clinical characteristics, treatment modalities and outcomes of patients with tuberculous vs. non-tuberculous empyema was carried out. Factors associated with poor outcomes were analysed using multivariate logistic regression.
Results: One hundred and seventeen cases of empyema were seen in the study period of which 95 had non-tuberculous and 41 had tuberculous empyema. Malnutrition and bronchopleural fistulae (BPF) were more common and duration of symptoms longer in the tuberculous empyema group. Time to resolution of fever, duration of pleural drainage and pleural thickening >2 cm were significantly greater as well. Eight (10.5%) patients with non-tuberculous empyema and four (9.8%) with tuberculous empyema succumbed. Presence of a BPF was significantly associated with poor outcomes on multivariate logistic regression analysis.

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Conclusions: Tuberculous empyema remains a common cause of thoracic empyema in India though it ranked second amongst all causes of empyema after community acquired lung infections in this study. Tuberculous empyema is associated with longer duration of symptoms, greater duration of pleural drainage and more residual pleural fibrosis.

Introduction

Thoracic empyema remains a common problem both in the developed as well as developing world. In the former pulmonary infections and thoracic trauma are the usual causes while pulmonary infections including tuberculosis account for the majority of cases in the latter. 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 aetiologies because of the presence of concomitant fibrocavitary parenchymal disease, high bacillary load, frequent development of bronchopleural fistulae and poor general condition of patients. To the best of our knowledge no study so far has directly compared clinical features and outcomes of patients with tuberculous empyema with those of non-tuberculous causes of empyema. We performed a prospective study over a 2-year period with the objective of comparing the clinical characteristics and outcomes of patients with tuberculous vs. non-tuberculous empyema.

Material and methods

Study design

This study was a prospective analysis of all cases of non-surgical thoracic empyema seen by/admitted under the Department of Pulmonary and Critical Care Medicine of the Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India over a 2-year period between January 2003 and December 2004.

Patient selection

Inclusion criteria. Patients aged more than 12 years with clinical evidence of infection as assessed by the treating physician on the basis of clinical indicators such as fever, an elevated white-cell count, and an elevated serum level of *C*-reactive protein, and pleural effusions that fulfilled at least one of the following criteria were included in this study: (i) frank pus or purulent appearing fluid on diagnostic pleural aspiration, (ii) positive pleural fluid culture, and (iii) positive pleural fluid gram stain. Empyema arising secondary to the performance of the following procedures were also included: diagnostic or therapeutic thoracentesis, pleural biopsy and tube thoracostomy for spontaneous pneumothorax or malignant pleural effusion. Written informed consent was taken from all patients and the study was cleared by the Institute's ethics committee.

Exclusion criteria.

(i) empyema secondary to penetrating or blunt trauma chest,
(ii) empyema secondary to any surgical procedure, e.g. esophagectomy, pneumonectomy, etc.

Study procedure

Detailed demographic and clinical parameters were evaluated in all patients fulfilling the inclusion criteria: age and sex, symptoms and their duration (fever, cough, expectoration, haemoptysis, chest pain, dyspnoea, and loss of appetite and weight). The presence of any comorbid illness was documented including chronic lung disease, diabetes mellitus, HIV infection, rheumatoid arthritis, chronic renal failure, chronic liver disease and malignancy. Chest radiographs were obtained in all patients while ultrasound (USG) and computed tomography (CT) were carried out when deemed necessary by the treating physician. Pleural fluid was collected under strict asepsis by thoracentesis and total leukocyte count (TLC), differential leukocyte count (DLC); protein, sugar; gram stain and culture sensitivity were performed in all patients unless pleural fluid was grossly purulent in which case only the latter investigation was sent. Mycobacterial smear and culture was sent in patients with suspected tuberculous empyema. Complete blood counts, renal and liver function tests and blood culture were sent in all patients. Other clinically relevant investigations (e.g., arterial blood gas analysis, HIV serology, ultrasound and/or CT abdomen, amoebic serology) were also performed if indicated.

Aetiology of empyema was decided based on the history, physical examination, radiology, empyema fluid analysis as well as other clinically relevant investigations. A diagnosis of tuberculous empyema was defined as definite if pleural fluid smear and/or culture was positive for acid-fact bacilli (AFB)/*Mycobacterium tuberculosis* on two or more occasions. Probable tuberculous empyema was defined as empyema in patients in who had radiological evidence of active pulmonary tuberculosis on CT scans (nodular consolidation in apical segments/tree-in-bud appearance/mediastinal lymphadenopathy with central necrosis) or concomitant positive sputum smears for AFB. Patients who had radiological features suggestive of past/inactive TB (apical fibro-calcific lesions, parenchymal bands or thin-walled cavities alone without surrounding areas of consolidation or tree-in-bud appearance) were not deemed to have tuberculous empyema. Bronchopleural fistula (BPF) was diagnosed if the CXR prior to tube thoracostomy revealed pyopneumothorax and air leak through the tube thoracostomy persisted for more than 24 h after tube insertion.

Empyema fluid was drained by either a tube thoracostomy or, if fluid was either loculated or difficult to approach by conventional tube thoracostomy, by the placement of a pigtail catheter under ultrasound guidance. All patients received antibiotic therapy, intravenous for 7–14 days followed by an equivalent oral agent for 2–4 weeks depending on the clinical response. The most commonly administered agents were a combination of a third generation cephalosporin and clindamycin or a β-lactam-β-lactamase inhibitor alone. Antibiotics were changed if culture revealed a resistant organism or empirically if there was no clinical response (defined as persistent fever and purulent drainage) by day seven after tube thoracostomy. Intrapleural streptokinase (STK) was used in selected patients with empyema if financial constraints were not present in whom drainage of pus by tube thoracostomy or pigtail catheter had declined to less than 50 ml of pus on two consecutive days and there was evidence of persistent sepsis and undrained pleural fluid on ultrasound of the chest.

The following parameters were monitored to assess the progress and outcomes of patients: time to fever resolution, duration of pleural drainage, duration of hospitalisation, need for surgery, extent of pleural thickening (defined as the largest linear dimension of pleural thickening in centimeters, more than or less that 2 cm on CXRPA at the time of tube/catheter removal), and mortality. Poor outcomes were defined as duration of pleural drainage greater than 14 days, need for surgery, and/or death.

Statistical analysis

Statistical analyses were performed using the SPSS version 10.0 (SPSS inc., Chicago, IL) software for MS-Windows. Descriptive frequencies were expressed using mean (standard deviation) and median (range). Differences between continuous variables were compared using the Mann Whitney *U* test and Friedman's test, as applicable, and that of categorical variables with the χ^2-test. Risk factors for poor outcomes were evaluated using multivariable logistic regression analysis. Initially the variables were analysed using univariate analysis to derive crude odds ratio and if found significant ($P<0.1$) these variables were then entered in a multivariate logistic.

Results

Patient characteristics

One hundred and seventeen cases of empyema were encountered during the study period. Their ages ranged from 13 to 81 years (mean 40.9, SD 16.2). Most cases ($n = 48\%$, 41%) were in the age group of 21–40 years. Co-morbid illnesses (Table 1) were present in 59 (50.4%) patients of which the commonest were chronic pulmonary parenchymal disease and diabetes mellitus. Patients with tuberculous empyema were significantly more likely to have diabetes mellitus than those with non-tuberculous aetiologies. More than one co-morbid illness was present in 14 patients. Malnutrition and BPF were more common and duration of symptoms longer in the tuberculous empyema group. In addition, percentage polymorphs in pleural fluid were lower and pleural fluid protein level was significantly higher.

Bacteriologic spectrum

Pleural fluid gram stain was positive in 21 (18.1%) patients while 72 bacteria were isolated in 55 patients on pleural fluid bacterial cultures (Table 2). Thirteen patients grew two organisms, and two grew three organisms in pleural fluid. Acid-fast bacilli were identified in pleural fluid from 20 patients. In five of these patients, *Mycobacterium tuberculosis* was isolated on culture. In addition one patient's pleural fluid repeatedly grew *Aspergillus fumigatus* during his hospital stay and he was administered 1.2 g of amphotericin B.

Two categories of pleural space infection were identified: (i) primary infection in which an organism was isolated from the culture sent at initial presentation and (ii) superinfection in which the initial culture was sterile but a culture sent at a later date during the hospitalisation was positive. In cases with primary infection aerobic organisms were isolated on 41 occasions while four pleural fluid cultures grew anaerobic bacteria. Twenty-six organisms were isolated as superinfections, the majority of which were gram-negative bacilli. Patients who developed superinfection were younger (mean age 35 years vs. 43 years, $P<0.05$), more likely to be female, malnourished (BMI $<18.5\,kg/m^2$ in 62.9% vs. 30%; <0.05), and have a tuberculous aetiology of empyema than those who did not (51.9% vs. 30%).

Aetiology of empyema

Five broad categories of disorders were identified in the aetiology of empyema (Table 3) of which the largest was that of empyemas secondary to broncho-pulmonary infection (87 cases, 74.3%). Community acquired bacterial infections (44 cases, 37.7%) including 32 (27.4%) pneumonias and 12 (10.3%) lung abscesses were the commonest causes overall, closely followed by tuberculosis in 41 cases (35%). A definite diagnosis of tuberculous empyema was made in 20 patients by demonstration of acid-fast bacilli on pleural fluid examination while the remaining cases either had radiological evidence of active pulmonary tuberculosis on CT scans (nodular consolidation in apical segments/tree-in-bud appearance/mediastinal lymphadenopathy with central necrosis) or positive sputum smears for AFB and were labeled as probable tuberculous empyema. Twenty-four patients with tuberculosis also had microbiological evidence of co-existent bacterial infection. Interestingly, four of the 76 patients with non-tuberculous empyema had evidence of old healed pulmonary TB on CT scans. They were deemed not to have tuberculous empyema as AFB/*M.TB* could not be demonstrated on repeated pleural fluid or sputum samples and they responded satisfactorily to antibiotics. Twenty-eight of the 41 patients with tuberculous empyema were tested for HIV infection by ELISA and all were found to be negative. Pleural fluid adenosine deaminase levels were checked in 36 patients (those who did not have frankly purulent pleural fluid) including 11 who were subsequently proven to have tuberculous empyema and ranged between 12 and 164 IU/ml with a mean of 67 IU/ml (SD 42). There was

Table 1 Comparison of clinical and demographic characteristics of patients with tuberculous vs. non-tuberculous empyema.

Clinical characteristic	Non-tuberculous empyema ($n = 76$)	Tuberculous empyema ($n = 41$)
Age in years (mean (SD))	43 (17)	38 (14)
Male sex (*n* (%))	28 (68.3)	57 (75)
Co-morbid illness		
Chronic lung disease (*n*, %)	13 (17.1)	18 (43.9)
Post-TB fibrocavitary disease	4 (5.3)	13 (31.7)
COPD	7 (9.2)	5 (12.2)
Others	2 (2.6)	0
Diabetes mellitus* (*n*, %)	4 (5.3)	16 (39)
Malignancy (*n*, %)	6 (7.9)	1 (2.4)
Lung	5 (6.6)	1 (2.4)
Oesophagus	1 (1.3)	0
Alcohol-related liver disease (*n*, %)	3 (3.9)	2
Immunosuppression (*n*, %)	4 (5.2)	2 (4.9)
Drug related	3 (3.9)	2 (4.9)
HIV infection	1 (1.3)	0
Miscellaneous (*n*, %)	4 (5.2)	2 (4.9)
Duration of symptoms* (median, days)	15	37.5
BMI $<$ 18.5 kg/m(n (%))*	22 (28.9)	23 (56.1)
SIRS (*n* (%))	66 (86.8)	35 (85.4)
BPF* (*n* (%))	17 (22.4)	32 (78.1)
Massive effusion (*n* (%))	13 (17.1)	9 (22)
Pleural fluid TLC per mm^3 (median)	9600	8000
Pleural fluid percentage polymorphs (median)	90	75
Pleural fluid protein (mean (SD), g/dl)	4.3 (1.7)	5 (1.9)
Pleural fluid sugar (mean (SD), g/dl)	36 (40)	37 (47)
Pleural fluid culture positivity (*n* (%))	38 (50)	16 (39)
Hemoglobin (mean (SD), g/dl)	10.4 (2.3)	10.4 (2.3)
TLC per mm^3 (mean (SD))	15,516 (7415)	14,968 (11,536)
Serum albumin (mean (SD); g/dl)	2.9 (0.5)	2.9 (0.6)
PaO_2 (mean (SD), mm Hg)	61 (11)	61 (12)

*$P < 0.05$.

no statistically significant difference in ADA level in tuberculous vs. other causes of empyema.

No cause was identifiable in 12 cases of empyema even after extensive investigation, including CT of the chest and these cases were therefore labeled idiopathic or primary empyema.

The aetiologic spectrum of the 49 cases with BPF was as follows: tuberculosis in 32 (65.3%), community acquired pneumonia/lung abscess in 11 (22.5%), superinfection of pre-existing spontaneous pneumothorax in 5 (10.2%) and as a complication of amebic liver abscess in one (2%) patient.

Modalities of treatment

All patients received broad-spectrum intravenous antibiotics for periods ranging from 7–28 days followed by appropriate oral antibiotics for 14–30 days. Anti-tubercular therapy was administered to the 41 patients with tuberculosis for periods ranging from 6–9 months depending on clinical, radiological and microbiologic improvement. Intercostal tube drainage (ICTD) was used for pleural drainage in 95 patients, while 22 patients underwent primary pigtail catheter drainage. Sixteen patients required both procedures. Median time of insertion of ICTD following symptom onset was 10 days and median duration of ICTD was 20 days. Intra-pleural streptokinase (STK) was used in 20 patients (18 with non-tuberculous and 2 with tuberculous empyema). Successful drainage defined as subjective and objective clinical improvement, adequate pleural drainage and radiological resolution was seen in 17 (85%) patients. There were no complications. Decortication by surgical thoracotomy was performed in 6 (5.2%) patients (three each with tuberculous and non-tuberculous empyema) who had severe restriction on spirometry. Median time to surgery following symptom onset was 55 days. The median duration of post-operative pleural drainage by ICTD was 22.5 days.

Significantly more patients with non-tuberculous empyema received intrapleural STK. Among the outcome measures studied, time to resolution of fever, duration of pleural drainage and pleural thickening >2 cm were significantly greater in the tuberculous empyema group. All patients with

Table 2 Bacteria isolated in pleural fluid of patients with non-tuberculous empyema.

Bacteria	*n* (%)
Primary infection	45 (38.4)
Aerobic bacteria	41 (35)
Gram positive organisms	17 (14.5)
S. aureus	9 (7.7)
Viridans streptococci	5 (4.3)
S. pneumoniae	1 (0.9)
S. pyogenes	1 (0.9)
Enterococcus fecalis	1 (0.9)
Gram negative organisms	24 (20.5)
P. aeruginosa	7 (6)
K. pneumoniae	7 (6)
E. coli	6 (5.1)
E. aerogenes	3 (2.6)
P. mirabilis	1 (0.9)
Anaerobic bacteria	4 (3.4)
Peptostreptococci	3 (2.5)
Bacteroides sp	1 (0.9)
Superinfection	27 (23.1)
Gram positive cocci (MRSA)	1 (0.9)
Gram negative bacilli	26 (22.2)
A. anitratus	15 (12.8)
P. aeruginosa	7 (6)
Alcaligenes fecalis	2 (1.8)
P. mirabilis	1 (0.9)
A. lwoffi	1 (0.9)

Table 3 Spectrum of aetiologic conditions responsible for empyema.

Aetiologic condition	*n* (%)
Bronchopulmonary infection	87 (74.3)
Tuberculosis	41 (35)
Community acquired pneumonia	32 (27.4)
Aspiration/ lung abscess	12 (10.3)
Ruptured hydatid cysts	1 (0.9)
Pulmonary infarction	1 (0.9)
Iatrogenic	8 (6.8)
Post ICTD for pneumothorax/malignant pleural effusion	7 (6)
Post-pleural biopsy	1 (0.9)
Infra-diaphragmatic sepsis	6 (5.1)
Amoebic liver abscess	5 (4.4)
Acute pancreatitis	1 (0.9)
Idiopathic/primary	12 (10.3)
Miscellaneous	4 (3.4)
Septicemia	3 (2.5)
Ludwig's angina	1 (0.9)

positive acid fast bacilli on pleural fluid became negative after a mean of 27.5 days (range 7–51). Eight patients with non-tuberculous empyema and four with tuberculous empyema succumbed. These latter four patients succumbed within 3 weeks of the start of anti-tubercular therapy. Causes of death in the former were septic shock in five, disseminated malignancy in two and respiratory failure in one, while all patients with tuberculous empyema died due to severe respiratory failure. Necropsy was performed in three patients with tuberculous empyema (two probable and one definite case) and revealed features of active TB in all (extensive caseating AFB positive epitheloid cell granulomas in the pulmonary parenchyma and pleura).

Discussion

The fact that empyema remains a common clinical problem in India is highlighted by the large number of cases (117 over a 2-year period at a single center) included in this series in comparison to other studies both from India as well as the West some of which were multi-center studies carried out over much longer periods of time.[1–7,9–12]

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 in the West. Surgical trauma ranks as the second most frequent cause.[1–8] In contrast most studies from India reveal that tuberculosis accounts for a large number of empyemas with figures ranging from 29% to 85.1% of all cases.[10–12,13–15] In fact till the mid-1980s tuberculosis was the commonest aetiology of thoracic empyema in India. However more recent studies including ours indicate that tuberculosis now ranks second to bacterial pneumonia as a cause for empyema.[10,12] This may be due to the wider availability of anti-tubercular drugs and an increasingly effective tuberculosis control programme.

Tuberculous empyema thoracis usually occurs when caseous material from a superficial parenchymal cavity ruptures into the pleural space. It may also develop secondary to paratracheal lymph node involvement, by direct extension of a paravertebral cold abscess, progression of a primary tuberculous pleural effusion itself or from haematogenous spread of infection.[15,16] Though it is often expected that tuberculous empyema should be teeming with mycobacteria, this may not be the case in clinical practice as *M. 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.[17] This was the case in 20 of our patients with tuberculous empyema, only five of whom were culture positive. However technical factors may have also contributed to this low culture positivity rate. We used the standard NALC–NaOH (*N*-acetyl *L*-cystine sodium hydroxide) method of concentration and decontamination of specimens.[18] The specimens (5 ml) were mixed with an equal quantity of NALC–NaOH and left for 20 min of exposure. We then added 20 ml of PBS pH 6.8 to neutralise the alkalinity, and centrifuged the mixture. The deposit was used to inoculate two vials of LJ medium incubated for up to 4 weeks aerobically at 37 °C. This method is considered by some experts to be too harsh and can lead to loss of viability of mycobacteria to an extent of up to 80%. Many workers recommend assessing the load of contamination by an initial

gram stained smear and expose the specimens with mild degree of contamination to shorter lengths of time (5–10 min) to the NALC–NaOH to preserve mycobacterial viability. However, ours is a referral centre in a country with a very high specimen load of samples for *M.TB* and, since this was a prospective, ''real-life'' study it was difficult to give customised attention to each specimen. In addition, BACTEC was not available during the study period and samples were inoculated onto conventional culture media (LJ medium) which have a lower sensitivity compared to the former.[19] In the remaining 21 patients who had pleural empyema with co-existent pulmonary tuberculosis (diagnosed on the basis of positive sputum smears for AFB, CT evidence of active TB and clinical as well as microbiological response to anti-tubercular therapy), three smears of the pleural fluid were negative for AFB. To make a definitive diagnosis of tuberculous empyema in these patients one would have had to demonstrate simultaneous positivity for AFB/*M.TB* in both sputum and pleural fluid samples, and therefore these cases were considered to have probable tuberculous empyema (Table 4).

Measurement of pleural fluid adenosine deaminase (ADA) is diagnostically useful in differentiating tuberculous effusions from other causes of exudative effusions. Unfortunately it is of less value in empyema as levels tend to be high in empyema of any aetiology.[20] This was the case in our study as well, with no statistically significant difference in values between tuberculous and non-tuberculous aetiologies of empyema.

Tuberculous empyema remains a major problem in developing countries despite the availability of potent anti-tubercular drugs and improved surgical techniques. The invariable presence of concomitant fibrocavitary parenchymal disease, high bacillary load, frequent development of bronchopleural fistulae and poor general condition of patients combine to ensure significant morbidity and mortality for this disease.[16] In the present study clinical characteristics and outcomes of patients with tuberculous empyema were compared with non-tuberculous causes of empyema. In concordance with other authors we found that tuberculous empyema most often afflicts young male patients.[15,21,22] This is primarily due to the high incidence of pulmonary tuberculosis in this age group. Not surprisingly, duration of symptoms and frequency of malnutrition were significantly greater in patients with tuberculous empyema. Tuberculous empyema is typically chronic as compared to pyogenic causes, which often have a dramatic and sudden onset with severe systemic symptoms.[16] Most patients with PTB are chronically ill with fever, cough, expectoration and dyspnoea due to underlying fibrocavitary disease and the supervention of pleural involvement often is clinically silent. In some patients the inflammatory process may go on for months or years with a paucity of clinical symptoms. This prolonged asymptomatic course may be explained by the formation of a thick pleural rind that virtually isolates the tubercle bacilli to the pleural space.[23] In addition, the frequent co-existence of malnutrition also may decrease the severity of the systemic inflammatory response syndrome, further masking the onset of this complication.

Intrapleural streptokinase could only be administered in two patients with tuberculous empyema in our study while 18 patients with non-tuberculous empyema received the drug. Almost 80% of the patients with tuberculous empyema had bronchopleural fistulae and in such patients the administration of STK is contraindicated due to the risk of spill over of the agent into the lung parenchyma. In addition, median duration of symptoms in patients with tuberculous empyema was 37.5 days, meaning that most patients were already in the fibrino-purulent or organising stage of empyema in which the effectiveness of STK is expected to be markedly reduced.

Most outcome variables studied including duration of hospitalisation, duration of pleural drainage and time to fever resolution were significantly longer in the tuberculosis group. There are several explanations for this. First tuberculous empyema is usually chronic and most patients have significant pleural fibrosis which limits the entry of drugs into the pleural space. In addition, the frequent presence of septations due to the chronic nature of the empyema makes pleural drainage with a single tube difficult.[24] Second, the concomitant presence of BPF predisposes to continued contamination of the pleural space

Table 4 Comparison of treatment modalities and outcomes of patients with tuberculous vs. non-tuberculous empyema.

	Non-tuberculous empyema ($n = 76$)	Tuberculous empyema ($n = 41$)
Treatment and outcomes		
Intrapleural streptokinase (n (%))*	18 (23.7)	2 (4.9)
Pigtail catheter drainage (n (%))	16 (21)	6 (27.3)
Duration of hospitalization (median, days)	16	14
Duration of pleural drainage (median, days)*	14	55
Resolution of fever ($n = 86$)(median, days) *	5	7
Surgery (n (%))	3 (4)	3 (7.3)
Pleural thickening		
<2 cm (n (%))	28 (36.8)	2 (4.9)
>2 cm(n (%))*	48 (63.2)	39 (95.1)
Mortality (n (%))	8 (10.5)	4 (9.8)

*$P<0.05$.

Table 5 Analysis of factors affecting outcome in empyema patients by logistic regression.

	Poor outcome ($n = 77$)	Good outcome ($n = 40$)	Crude OR (95% CI)	Adjusted OR (95% CI)
Age, mean (SD)	39.4 (15.9)	43.9 (16.5)	1.01 (1.003–1.02)	0.99 (0.97–1.01)
Female gender (*n*, %)	25 (78.1)	7 (21.9)	3.57 (1.54–8.25)	4.15 (0.97–17.68)
Duration of symptoms (days, mean (SD))	32.94 (29.3)	23.06 (22.3)	1.02 (1.007–1.03)	0.98 (0.95–1.01)
Diabetes mellitus (*n*, %)	13 (65)	7 (35)	1.86 (0.74–4.6)	—
Other comorbid illness	39 (70.9)	16 (22.1)	3.14 (1.34–7.36)	1.56 (0.35–6.95)
Current smokers (*n*, %)	17 (53.1)	15 (46.9)	1.13 (0.56–2.27)	—
Alcoholism (*n*, %)	11 (78.6)	3 (21.4)	3.67 (1.02–13.14)	2.72 (0.38–19.57)
BMI $< 18.5\,kg/m^2$ (*n*, %)	36 (80)	9 (20)	4.00 (1.93–8.30)	2.13 (0.61–7.36)
Large effusion (*n*, %)	16 (72.7)	6 (27.3)	2.67 (1.04–6.81)	1.02 (0.26–3.89)
Bronchopleural fistula (*n*, %)	45 (91.8)	4 (8.2)	11.25 (4.05–31.28)	6.65 (1.55–28.47)
Tuberculous aetiology (*n*, %)	35 (85.3)	6 (14.7)	5.83 (2.45–13.86)	5.73 (0.91–36.27)
Culture positivity (*n*, %)	39 (72.2)	15 (27.8)	2.60 (1.43–4.71)	1.41 (0.51–3.91)
Streptokinase administration (*n*, %)	10 (50)	10 (50)	2.23 (1.45–3.43)	0.76 (0.23–2.52)

with both mycobacteria and other respiratory pathogens. This is illustrated by the finding of superimposed bacterial infection in 24 out of 41 (58%) cases of tuberculous empyema in the present series which was statistically significantly more than in non-tuberculous empyema. Finally, as seen in other studies patients with this affliction were more likely to be malnourished and thus have compromised host defenses.

The mortality in patients with tuberculous empyema reported in the present study 4/41 (9.8%) is comparable to that seen in other studies and is similar to that of non-tuberculous etiologies of empyema.[12,15,21,24] Patients with tuberculous empyema are frequently debilitated and have concomitant pulmonary parenchymal disease making them poor surgical candidates. In addition, they are more prone to develop post-operative complications like secondary bacterial infections, respiratory failure and bronchial stump dehiscence. Surgery is also technically complex because of the obscuration of traditional anatomic landmarks by the fibrocalcific pleura. The low mortality seen in our study with conservative management in the form of prolonged tube-thoracostomy or pigtail drainage suggests that high-risk patients may be successfully managed without resorting to more invasive procedures like thoracotomy.

Poor outcomes, defined as duration of tube thoracostomy for more than 14 days and/ or death were seen in 77 (65.8%) patients. Risk factors for poor outcomes were evaluated initially using univariate analysis to derive crude odds ratio, and if found significant ($P < 0.1$) these variables were then entered in a multivariate logistic (Table 5). The presence of a bronchopleural fistula was significantly associated with poor outcomes on multivariate logistic regression analysis while two other factors that approached significance were female gender and tuberculous aetiology. Female patients in India and other developing countries often present late to hospital due to social circumstances and this may be an explanation for relatively poorer outcomes. The reasons for expecting worse outcomes in tuberculous empyema have already been dealt with above, and it is possible that if larger numbers were present in our study, some of the risk factors for poor outcomes may have assumed statistical significance.

References

1. Smith JA, Mullerworth MH, Westlake GW, et al. Empyema thoracis: 14 year experience at a teaching center. *Ann Thorac Surg* 1991;**51**:39–42.
2. Alfageme I, Munoz F, Pena N, Umbria S. Empyema of the thorax in adults. Etiology, microbiologic findings and management. *Chest* 1993;**103**:839–43.
3. Maskell NA, Davies MDCWH, Nunn AJ, et al. UK Controlled Trial of Intrapleural Streptokinase for Pleural Infection. *New Engl J Med* 2005;**352**:865–74.
4. Brook I, Frazier EH. Aerobic and anaerobic microbiology of empyema. A retrospective review in two military hospitals. *Chest* 1993;**103**:1502–7.
5. Ferguson AD, Prescott RJ, Selkon JB, et al. The clinical course and management of empyema. *Q J Med* 1996;**89**:285–9.
6. Alfageme I, Munoz F, Pena N, Umbria S. Empyema of the thorax in adults. Etiology, microbiologic findings and management. *Chest* 1993;**103**:839–43.
7. Weissberg D, Refaely Y. Pleural empyema: 24-year experience. *Ann Thorac Surg* 1996;**62**:1026–9.
8. Chapman SJ, Davies RJO. Recent advances in parapneumonic effusion and empyema. *Curr Opin Pulm Med* 2004;**10**:299–304.
9. Chen KY, Hsueh PR, Liaw YS, Yang PC, Luh KT. A 10-year experience with bacteriology of acute thoracic empyema: emphasis on *Klebsiella pneumoniae* in patients with diabetes mellitus. *Chest* 2000;**117**:1685–9.
10. Gupta SK, Kishan J, Singh SP. Review of 100 cases of empyema thoracis. *Ind J Chest Dis All Sci* 1989;**31**:15–20.
11. Singh RP, Katiyar SK, Singh KP. Conservative management of empyema thoracis and bronchopleural fistula. *Ind J Chest Dis Allied Sci* 1994;**36**:15–9.
12. Banga A, Khilnani GC, Sharma SK, Dey AB, Wig N, Banga N. A study of empyema thoracis and role of intrapleural streptokinase in its management. *BMC Infect Dis* 2004;**4**:19–24.
13. Aggarwal SK, Ray DC, Jha N. Empyema thoracis: a review of 70 cases. *Ind J Chest Dis Allied Sci* 1985;**27**:17–22.
14. Jha VK, Singh RB. Empyema of the thorax. *Ind J Chest Dis* 1972;**14**:243–8.

15. Sharma TN, Jain NK, Madan A, Sarkar SK, Durlabhji P. Tubercular empyema thoracis: a diagnostic and therapeutic problem. *Ind J Chest Dis Allied Sci* 1983;**25**:127–31.
16. Sahn SA, Iseman MD. Tuberculous empyema. *Semin Respir Infect* 1999;**14**:82–7.
17. Murray PR, Baron EJ, Pfaller MA, Tenver FC, Yolken RH, editors. Mycobacterium Chapter 31. In: Manual of clinical microbiology, 6th ed. Washington DC: ASM Press; 1995. pp. 409–11.
18. Baron EJ, Finagold SM. In: *Bailey and Scott's Diagnostic Microbiology.* 9th ed. St Luis: The CV Mosby Company; 1994. p. 590–633.
19. Pfyffer GE, Cieslak C, Welscher HM, Kissling P, Rusch-Gerdes S. Rapid detection of mycobacteria in clinical specimens by using the automated BACTEC 9000 MB system and comparison with radiometric and solid-culture systems. *J Clin Microbiol* 1997;**35**:2229–34.
20. Ernam D, Atalay F, Hasanoglu HC, Kaplan O. Role of biochemical tests in the diagnosis of exudative pleural effusions. *Clin Biochem* 2005;**38**:19–23.
21. Rosha D, Panda BN. Successful management of tubercular bronchopleural fistula with pyopneumothorax by saline irrigation. *Lung India* 1998;**16**:56–9.
22. Al-Kattan KM. Management of tuberculous empyema. *Eur J Cardiothorac Surg* 2000;**17**:251–4.
23. Bai KJ, Wu IH, Yu MC, et al. Tuberculous empyema. *Respirology* 1998;**3**:261–6.
24. Elliot AM, Berning SE, Iseman MD, et al. Failure of drug penetration and acquisition of drug resistance in chronic tuberculous empyema. *Tubercle Lung Dis* 1995;**76**:463–7.