

Tuberculous Empyema Thoracis: Clinical, Bacteriological Features, and Its Medical Management

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Abstract

Background: Tuberculous (TB) empyema is a chronic infection of pleural space which carries a significant morbidity and mortality.

Aims: The aim of this study was to observe clinical, radiological, bacteriological features, and the outcomes obtained by the medical management of TB empyema.

Methodology: A retrospective case analysis of all the adult patients admitted with TB empyema was performed.

Results: Records of 100 patients with TB empyema showed that Cough, expectoration, and chest pain were present in 96%, 94%, and 64% patients, respectively. Direct smear of Pus and sputum showed *acid-fast bacilli* (AFB) in 57 and 46 patients, respectively, whereas 32 patients had smear positivity for both. Mycobacterial culture of pus was positive in 32/100 patients. The chest radiographs had moderate and far advanced parenchymal lesions in 37 patients each. The median duration of hospital stay was 57 (41-97) days. Eight patients were managed using closed needle aspiration, whereas in others intercostals drainage tube was inserted. About 47 patients were discharged after removal of the intercostal tube (ICD) tube, whereas 36 patients had residual empyema space, so was discharged with an open drainage tube. Eight patients died and four left the treatment against advice and 5 were referred for thoracic surgery.

Conclusion: Confirmation of diagnosis by presence of mycobacteria in pus and sputum sample and draining of empyema cavity using ICD tube or closed needle aspiration along with effective anti-tubercular drugs results in healing, and many patients may not requires surgery.

Key words: Antitubercular drugs, Drainage, Empyema tuberculous, Pleural cavity

INTRODUCTION

Empyema thoracis, defined as, a collection of pus in the pleural space, which is an anatomical space bordered by both the visceral and parietal pleura. Empyema is an illness with significant morbidity^{1,2} and mortality.^{3,4} Tuberculosis (TB) of the lung may also lead to formation of pleural

effusion or empyema. TB empyema is a chronic, active infection of the pleural space.

Clinical outcomes of TB empyema are generally believed to be worse compared to those of non-tubercular empyema, because of protracted illness, presence of concomitant fibrocavitary lesions, high bacillary load, development of bronchopleural fistulae (BPF), and requirement for complicated surgeries in face of compromised lung function.⁵ Anti-TB drug treatment alone cannot cure the patients with tubercular empyema and almost all cases require some form of external drainage of pleural pus. The secondary infection of this pus by other pyogenic infections may add to the severity of illness that may prolong the time to cure the illness, as well as increases

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the cost of treatment, in the form of antibiotics that may be required to treat this infection.

In this study, our objectives were to present the clinical features, bacteriological features and to review our experience with mainly medical management (requiring Intercostal drainage or aspiration of pus as only minor surgical procedures) of tubercular empyema by presenting the outcomes.

METHODOLOGY

Study Design

A retrospective case analysis of all adult TB empyema cases admitted at a tertiary care institute for TB and pulmonary diseases from March 2011 to March 2012 was done for the study.

Patient's Population

The patients of empyema suffering from TB confirmed either by, presence of acid-fast bacilli (AFB) in sputum or pus samples, or radiological chest X-ray findings suggestive of TB or diagnosed as TB on clinical grounds in absence of any evidence of TB bacteriologically and radiologically were taken, as cases, for the purpose of study.

Exclusion Criteria

Patients of age younger than 13 years and those with empyema due to other causes were excluded from the study.

Study Procedure

The case files of tubercular empyema patients admitted were reviewed retrospectively. Data with respect to clinical profile, bacteriological status, radiological aspect, and outcomes were recorded. By reviewing the case history recorded in the case file, the presence of cardinal symptoms of chest disease (i.e. cough, expectoration, breathlessness, chest pain, and hemoptysis) and their duration was recorded. Patients reporting constitutional symptoms such as fever, weight loss, and loss of appetite were also recorded. Any associated condition which may cause immunosuppression such as HIV infection or history of intake of corticosteroids for long periods was also recorded. Past history of TB and the treatment received by the patient for it was obtained from case file. As part of the management of these patients, their samples of sputum, and pus is sent for microbiological investigations for the presence of AFB in direct smear in sputum and direct smear and mycobacterial culture in pus sample. The reports of these investigations were recorded for the purpose of the study. The detection of presence of any pyogenic bacteria in aerobic cultures of pus specimen from pleural cavity was also noted for every case. Patients having small volumes of pus (<200 ml) estimated by

ultrasound and without any evidence of bronchopleural fistula (absence of air fluid level) on chest radiograph were managed by therapeutic pus aspiration by closed needle as per the empyema management protocol of the institute. Those with massive pleural collections and presence of bronchopleural fistula were managed by intercostal drainage of pus by tube thoracostomy with underwater seal, by inserting a intercostal tube (ICD) of size 20-32 F, depending on the patient's clinical situation. No negative suction device was applied to ICD during treatment, and the ICD tube was changed every week. By reviewing the case notes, the type of treatment, and length of stay in hospital and outcome of patients were recorded. The anti-TB treatment was given as per Revised National TB Program of India,⁶ under direct supervision of ward nurse to the patients. Patients categorized as newly diagnosed TB were given alternate day regimen with isoniazid, rifampicin, pyrazinamide and ethambutol during intensive phase and rifampicin and isoniazid during continuation phase. The re-treatment category patients received injection streptomycin in addition to the above drugs in Intensive phase. Those with documented secondary infection in pus were given 3 weeks of antibiotics also in addition to anti-tubercular drugs as per the sensitivity testing report. Outcomes of patients were recorded as any one of the following such as patient discharged after successful aspiration of pus by closed needle technique or removing ICD tube and sealing the ICD site, Discharge after removing under water seal drainage and putting small open drainage tube, patients referred for surgery for empyema, death and left against medical advice (LAMA).

The post ICD tube drainage or post closed needle aspiration chest X-ray was considered for evaluation of the parenchymal lesions in tubercular empyema patients. The disease extent radiologically was graded as per the classification of the National TB Association of the USA⁷ which grades TB lesions as:

- Minimal
- Moderately advanced
- Far advanced.

The study was approved by the Institutional Ethics Committee. Informed consent of patients was not recorded as the study was retrospective in nature, done by reviewing only the medical records of patients.

Statistical Analysis

The above information from the performa was tabulated in a Microsoft excel sheet and data analyzed for frequencies and distribution by using statistical software SPSS version 13 (SPSS inc., Chicago, IL) on a personal computer. The results obtained were tested for normality distribution. Intergroup analysis was done by using Chi-square test,

independent *t*-test, Mann–Whitney test or Kruskal–Wallis test as appropriate for the data. The values which were not normally distributed were written as median with inter quartile range. The relationship between two parameters was evaluated by using Pearson correlation coefficient or Spearman rank correlation coefficient, if they were appropriate. The level of significance was set at $P < 0.05$.

RESULTS

One hundred patients of tubercular Empyema were admitted during the study period. Male preponderance was observed in the study group, in which 83 male patients and 17 female patients were enrolled for the study.

The mean age of patients was 31.1 ± 13 years (ranging from 13 to 70 years) with the majority of them belonging to younger age group 15-30 years. General characteristics of the study group and the presence of co-morbid conditions are shown in Table 1.

The majority of patients were chest symptomatics with complaints pertaining to respiratory system such as cough, expectoration, chest pain, and breathlessness. A cough was complained by 96 patients, amongst them 44 had chronic cough of more than 2 months duration. Most of the tubercular Empyema patients also had expectoration with the cough (94%). Chest pain and shortness of breath was present in 64% and 84% patients. Only ten patients had complaint of hemoptysis. 95 patients reported fever, 90 had loss of appetite and 84 had history of significant weight loss.

In this study, it was seen that 53 patients had no past history of intake of anti-tubercular drugs, and 47 patients had reported intake of anti-tubercular treatment for at least 1 month in past. Accordingly, when patients were categorized as per the Revised National TB Control Program (RNTCP) guidelines,⁶ it was found that 53 patients belonged to new, 18 to treatment after default, eight relapse, six failure and 15 to others category. The Mantoux test was done for 62 patients, in which 43 were tuberculin test positive and 19 were tuberculin negative. When the Mantoux test was studied in relation to sputum and Pus for AFB positivity, it was found that 23 patients with Mantoux test positive were sputum positive and 20 were sputum negative. Eight patient each was Mantoux negative, but were sputum positive and Pus culture positive. About 15 patients with pus culture positive were Mantoux positive and 29 were Mantoux positive but Pus culture negative.

Bacteriological Aspect

Among the patients under study, sputum smear for AFB was positive in 46/100 patients. As per WHO classification

of sputum smear⁸ which is based on bacteriological load, it was seen that majority of patients were 1+ (21/46), next common was 3+ (17/46), followed by 2+ (6/46), and scanty +ve (2/46), in that order. The study of AFB in pus smears in patients of tubercular Empyema showed that 57/100 were AFB direct smear positive, with majority having 1+ bacteriological load (25/57), 16/57 were 2+, 10/57 as scanty +ve, and 6/57 were 3+ positive and 43 were reported as smear negative in pus.

Pus sample mycobacterial cultures grew AFB in only 32/100, while 64 samples were reported negative and four samples got contaminated in the process of culture.

When the patients were studied in correlation with sputum smear and pus smear for AFB positivity, it was found that 40/100 patients were positive for AFB in both sputum and pus samples. The results of these correlations are shown in Table 2

Among patients whose pus smear was positive (57/100), 33 reported to be culture negative, whereas eight patients had direct smear negative, but culture had evidence of growth of AFB in pus. In studying the coinfection of pus samples with pyogenic aerobic bacteria's, it was found that 36/100 had documented secondary infection, where as in 64/100 the culture for pyogenic bacteria's was sterile.

Radiological Findings

As per the grading system of Chest X-ray, it was found that 28 patients had mild lesions in lung parenchyma, 37 were graded as moderate and 37 as far advanced, as described

Table 1: General characteristics and co-morbid conditions

Parameter	Value
Age (in years)	31.1±13
Sex ratio (male:female)	4.88 (≈5:1)
BMI in Kg/m ²	16.2±3.2
ATT history (n=100)	47/100
Sputum smear AFB positive (n=100)	46/100
Mantoux test positive (n=62)	43/62
Secondary infection (n=100)	36/100
HIV (n=100)	4/100
DM (n=100)	5/100
On long term steroids (n=100)	1/100

BMI: Body mass index, ATT: Antithrombotic trialists, DM: Diabetes mellitus, AFB: Acid fast bacilli

Table 2: AFB smears status

AFB smear status	Number (n=100)
Sputum +ve, Pus +ve	40
Sputum +ve, Pus -ve	6
Sputum -ve, Pus +ve	17
Sputum -ve, Pus -ve	37

AFB: Acid fast bacilli, +ve: Positive, -ve: Negative

in Table 3. The severity of lung parenchyma involvement on chest radiograph did not had any significant difference in duration of stay or favorable outcomes ($P > 0.05$).

Treatment Outcomes

The median duration of stay was 57 days (41-97 days) for the study group. The median duration of stay in sputum smear negative patients was 42 days (range 33-56 days) and it was significantly lower than those patients who were sputum smear positive for AFB (Median-98.5 days; $P < 0.001$). Duration of stay positively correlated moderately with sputum smear positivity ($r = 0.640$; $P = 0.003$) and weakly with Pus smear ($r = 0.213$; $P = 0.03$) and pus culture positivity ($r = 0.216$; $P = 0.03$). Duration of stay was also seen to be more in patients who had documented secondary infection in pus ($r = 0.261$; $P = 0.009$). The duration of stay did not correlated with any presenting symptoms significantly.

Among the 100 patients of tubercular empyema, 47 were discharged after satisfactory lung expansion, whereas 36 patients had persistent empyema space (incomplete lung expansion), but very minimal or no pus discharge, so open drainage procedure was done in them and discharged from hospital with an advice to attend a special clinics organized once in a weeks.

Eight patients succumbed to their illness. In the study, four patients had decided to quit the treatment against medical advice, so their outcome was recorded as LAMA. Those patients who had pus discharge of more than 100 ml each day through ICD even after completion of an intensive phase of anti-tubercular treatment were referred to other center with thoracic surgery facilities for thoracic surgeons opinion. Five patients were found suitable for thoracic surgery and hence were referred to that center for surgeries and their further progress was not known, so their outcome has been recorded as “referred for thoracic surgery” (Table 4). For the purpose of statistical analysis the outcomes discharged after treatment and open drainage were clubbed as “favorable outcome” and death referred for thoracic surgery and LAMA were clubbed into “not favorable” outcomes. It was found that outcomes correlated weakly with duration of stay ($r = -0.316$; $P = 0.001$) and with age ($r = 0.334$; $P = 0.001$). The outcomes did not correlate with sputum smear or pus smear positivity and Pus culture positivity for AFB (Table 5).

DISCUSSION

TB is a common cause of empyema in countries like India where prevalence of TB is high,⁹ whereas in developed countries post pneumonic and post surgical etiology is

Table 3: X-ray status

X-ray grade	Number of patients (n=100)
No lesion	4
Mild	28
Moderate	37
Far advanced	31

Table 4: Outcomes of patients after minimally invasive treatment approach

Outcomes	Numbers
Discharged after treatment	47
Discharged on open drainage	36
Death	8
LAMA	4
Referred for thoracic surgery	5

LAMA: Left against medical advice

Table 5: Outcomes and its relation with pus smear results

Outcome	Pus smear positive (n=57) (%)	Pus smear negative (n=43) (%)
Discharged after treatment (n=47)	27 (47.3)	20 (46.5)
Discharged on open drainage (n=36)	21 (36.8)	15 (34.8)
Death (n=8)	2 (3.5)	6 (13.9)
LAMA (n=4)	2 (3.5)	2 (4.6)
Referred for thoracic surgery	5 (8.7)	0 (0)

LAMA: Left against medical advice

more common in patients with empyema.¹⁰ TB has been found to be the cause of empyema in approximately 65% of cases in studies reported from high prevalence regions of the world.^{9,11,12}

TB affects the patients commonly in their productive age (21-40 years). In our study also the mean age was 31.1 years, and majority belonged to age group 21-40 years, which was similar to findings in earlier studies.¹¹⁻¹⁴ The studies done in western countries reported the usual age of patients with empyema as 40-50 years, where the etiology of empyema was usually post-pneumonic and post-surgical.^{15,16}

The symptoms in patients of tubercular empyema are similar to that reported by patients of pulmonary TB. Many patients have cough with expectoration and fever (95% cases in our study). Tubercular as well as non-tubercular empyema patients report cough and fever, but these symptoms are present for a longer duration in tubercular patients, prior to their visit to health facility.^{12,14,17} Our study also shows that, as many as 40-45% patients had symptoms of cough, expectoration and fever of more than 2 months duration. Expectoration of blood with sputum was reported by only 10% of patients, although 46% of the patients under study were suffering from

sputum positive pulmonary TB also and studies in past have shown that hemoptysis occurs in 21-27% of patients with pulmonary TB.

Pleural fluid studies of empyema patients have shown high AFB positivity. The pleural fluid (pus) AFB positivity in our study was 57%, which is almost similar to studies done by Kundu *et al.*¹⁸ and Goyal *et al.*,¹² who had found AFB positivity of 71.6% and 50%, respectively. The yield of this test can be increased if a standardized methodology is followed for AFB staining and reporting. In our study, pleural pus direct smear and culture for AFB was done in an intermediate reference lab accredited under RNTCP. Hence, testing of pleural fluid for AFB in a reliable lab may help in actually confirming tubercular etiology rather than the other etiologies of pleural pus in most of the cases. The pus in the pleural cavity may get co infected with secondary bacterial infection through a persistent BPF, but the yield of bacterial culture of pleural fluid in empyema is low with conventional laboratory methods.^{19,20} In our study only 36% patients had documented secondary infection in pus culture.

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.¹⁵ Treatment of these tubercular empyema patients with intercostal drainage for a prolonged period (median 57 days) has resulted in successfully discharging 47 out of 100 patients. Some patients of empyema without bronchopleural fistula can also be managed by closed needle aspirations.¹⁵ Kamat *et al.* had reported shorter duration of hospital stay of 7.9 weeks (55 days) of patients suffering from pyogenic empyema as compared to 12.2 weeks (85 days) in patients with tubercular empyema,¹⁸ similarly, a study done on tubercular empyema patients had shown that majority of cases had duration of stay of 2-4 months.²¹

In our study, it is seen that duration of stay was longer in patients with smear positive for AFB as compared to smear negative. The time taken for the treatment response also depends upon the presence of secondary bacterial infection in pus, as is seen from results in our study in which the duration of stay correlated with the presence of secondary infection.

Discharging patients with persistent empyema space on open drainage, whose lung does not expand further due to formation of adhesions with thickened pleura is an advantageous method of managing an empyema patient conservatively. In the majority of cases simple procedure of chronic open drainage not only allows these debilitated patients to gain independence from tubing's and bottles,

but may also allow a freedom in rehabilitative activities such as doing some lighter kind of jobs as their occupations. In our study, it has been seen that 36 out of 100 patients were discharged on open drainage with advice of regular follow-up visits.

Subjecting all patients to thoracic surgery procedures, the type of surgical procedure and timing of empyema patients to these surgeries remains a matter of debate. Sonmezoglu *et al.*²² in their study have found open drainage better than Eloesser flap and pneumonectomy, in terms of morbidity and complication rates and recommended that these procedures should be avoided wherever possible, where as many studies now recommend performing thoracic surgeries such as video assisted thoracoscopy earlier in cases of empyema. So, it is still not clear whether these surgical procedures should bypass simple medical thoracostomies in all cases of empyema.^{23,24} Ashbaugh reports, decortication is more effective than open drainage in reducing morbidity and mortality when surgical intervention is necessary.¹⁶

In countries such as ours, with limited thoracic surgical facilities and expertise available, it becomes difficult to subject every patient of tubercular empyema with persistent empyema cavity to major thoracic surgical procedure and many times TB patients are chronically ill and therefore, too debilitated (as in our study with mean body mass index of patient only 16.2 kg/m²), so that the general condition of these patients may not permit performing these procedures upon them. A Large number of tubercular empyema patients may not be suitable candidates for surgical therapy also because of involvement of both or the contra lateral lung with TB. Furthermore, the arguments made in favor of subjecting patients early to surgical therapy by shortening the medical management of empyema were based on studies mostly done on patients suffering from parapneumonic effusions, where the empyema is usually acute and also does not carry the extent of morbidity as in tubercular empyema.²⁵⁻²⁸ So, performing studies on tubercular empyema patients for demonstrating benefits of early surgical procedures is needed, such that recommendations on subjecting the patient for surgical therapy may be made.

The mortality from empyema ranges from 11% to 50%.^{12,17} In our study, we had 8% mortality. Many patients are unable to tolerate prolonged treatment required along with the discomfort of chest tubes in situ, hence may decide to leave the treatment, as shown in our study (4%). It was found in a study, that majority of patients decided to quit treatment from the same center after 2.5 months of treatment.¹⁷ In our study, we found that the median duration of stay for patients who had LAMA was 25.5 days.

CONCLUSION

It can be concluded from the above study that, all patients of tubercular empyema have chronic morbidity and may require hospitalization. Closed intercostals drainage is an effective method of draining empyema cavity, therefore resulting in early healing when an effective anti-tubercular treatment regimen is also given in these patients. Many patient of tubercular empyema may not require surgery, but the most important aspect remains to be proper diagnosis of TB as cause of empyema, which can be best confirmed by presence of TB bacteria in pus and sputum samples.

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