Original Article

Treatment Outcomes of Tuberculous and Non-tuberculous Empyema Thoracis

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Abstract

Background: Pulmonary tuberculosis remains prevalent in the developing parts of the world. Besides the consequent tuberculous pleurisy, which can be complicated by empyema thoracis, *Mycobacterium tuberculosis* is associated with significant lung parenchymal disease that poses an additional clinical challenge in achieving a successful outcome of management. This study compared the outcomes of management of tuberculous versus non-tuberculous empyema thoracis managed at the Ahmadu Bello University Teaching Hospital (ABUTH), Zaria, Nigeria. **Materials and Methods:** A prospective study of patients being managed for empyema thoracis at the ABUTH, Zaria, within a 22-month study period was conducted. Recruitment into the study included all consecutive patients managed for empyema thoracis in ABUTH, Zaria, after obtaining consent. The required data were collected using a structured proforma. These included data on aetiology, microbial isolates, and initial and total empyema volumes. Sociodemographic data (including age, gender, educational level, and occupation) were also noted. The patients were subsequently managed, and the outcomes of management were noted. These outcomes included the duration of drainage, the duration of hospital stay, complications, lung expansion following drainage, and the need for decortication. Data obtained from the study were analysed using the Statistical Package for the Social Sciences (SPSS) version 20 software (IBM Corp. IBM SPSS Statistics for Windows. Version 20.0. Armonk, NY: IBM Corp.; released 2011) and the statistical differences determined using the chi-square test and the student's *t*-test. **Results:** Eighty-three patients were enrolled in the study, 20 (24.1%) of whom were females. Fourteen (16.9%) patients had tuberculous empyema thoracis, whereas 69 (83.1%) had non-tuberculous empyema thoracis. Patients with tuberculous empyema were significantly older than those with non-tuberculous disease (mean age 37.9 years [standard deviation {SD} = 20.6 years] vs. 26.8 years [SD = 18.2 years], $P = 0.045$). Compared to non-tuberculous empyema, tuberculous empyema thoracis was associated with lower percentage of mean lung expansion (60.9% [SD = 22.7%] vs. 78.4% [SD = 16.8%], $P = 0.001$), more than six-fold increased need for decortication (odds ratio = 6.58 [95% confidence interval = 1.84–23.52], $P = 0.004$), and longer period of hospital stay (36.4 days [SD = 3.8 days] vs. 23.6 days [SD = 16.2 days], $P = 0.004$). **Conclusion:** Tuberculous empyema thoracis was associated with worse outcomes (in terms of percentage of lung expansion, need for decortication, and length of hospital stay) compared to non-tuberculous empyema thoracis.

Keywords: *Complications, empyema thoracis, tuberculous empyema*

Abstrait

Contexte:

La tuberculose pulmonaire reste répandue dans les régions en développement du monde. Outre la pleurésie tuberculeuse qui en résulte qui peut être compliquée par un empyème thoracique, Mycobacterium tuberculosis est associé à une importante maladie du parenchyme pulmonaire qui constitue un défi clinique supplémentaire pour obtenir un résultat positif de la prise en charge. Cette étude a comparé les résultats de la prise en charge de l'empyème thoracique tuberculeux et non tuberculeux géré à l'hôpital universitaire Ahmadu Bello (ABUTH), Zaria, Nigéria.

Méthodologie:

Une étude prospective de patients pris en charge pour empyème thoracique à l'hôpital universitaire Ahmadu Bello (ABUTH), Zaria au cours d'une période d'étude de 22 mois a été menée. Le recrutement dans l'étude a inclus tous les patients consécutifs traités pour empyème thoracique à ABUTH, Zaria, après obtention du consentement. Les données requises ont été collectées à l'aide d'un formulaire structuré. Celles-ci comprenaient des données sur l'étiologie, les isolats microbiens et les volumes d'empyème initiaux et totaux. Les données sociodémographiques (notamment l'âge, le sexe, le niveau d'instruction

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et la profession) ont également été notées. Les patients ont ensuite été pris en charge et les résultats de la prise en charge ont été notés. Ces résultats comprenaient la durée du drainage, la durée du séjour à l'hôpital, les complications, l'expansion pulmonaire après le drainage et le besoin de décortication. Les données obtenues à partir de l'étude ont été analysées à l'aide du logiciel Statistical Package for Social Science (SPSS) version 20 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.) et les différences statistiques ont été déterminées à l'aide de Test du chi carré et test t de Student.

Résultats:

Quatre-vingt-trois patients ont été inclus dans l'étude, dont 20 (24.1%) étaient des femmes. Quatorze (16.9%) patients avaient un empyème thoracique tuberculeux tandis que 69 (83.1%) avaient un empyème thoracique non tuberculeux. Les patients atteints d'empyème tuberculeux étaient significativement plus âgés que ceux atteints d'une maladie non tuberculeuse (âge moyen 37.9 [SD20.6] ans 26.8 [SD18.2] ans, $P = 0.045$). Par rapport à l'empyème non tuberculeux, l'empyème thoracique tuberculeux était associé à un pourcentage d'expansion pulmonaire moyen plus faible (60.9 [SD22,7] % contre 78.4 [SD16.8] %, $P = 0.001$), un besoin de décortication plus de six fois supérieur (rapport de cotes 6.58 [IC à 95% 1.84–23.52], $P = 0.004$), et durée d'hospitalisation plus longue (36.4[SD3.8] jours contre 23.6[SD16.2] jours, $P = 0.004$).

Conclusion:

L'empyème thoracique tuberculeux était associé à de moins bons résultats (en termes de pourcentage d'expansion pulmonaire, de besoin de décortication et de durée d'hospitalisation) par rapport à l'empyème thoracique non tuberculeux.

Motsclés: *Empyème thoracique, empyème tuberculeux, complications*

Introduction

Historical reference to empyema thoracis was made by Hippocrates 460–377 b.c.[1] It is defined as a purulent pleural effusion or any pleural effusion with actively multiplying bacteria.[2-5] It commonly results from bacterial pneumonia complicated by parapneumonic effusion. It can also result from tuberculous pleurisy with superimposed pyogenic infection of the pleura.

Besides the consequent tuberculous pleurisy, which can be complicated by empyema thoracis, *Mycobacterium tuberculosis* is associated with a significant lung parenchymal disease that poses an additional clinical challenge in achieving a successful outcome of management.[6] This study compared the outcomes of management of tuberculous versus non-tuberculous empyema thoracis managed at Ahmadu Bello University Teaching Hospital (ABUTH), Zaria, Nigeria.

Materials and Methods

The study subjects comprised all patients with empyema thoracis admitted to ABUTH, Zaria, within the study period spanning January 2017 to October 2018. Consecutive patients with empyema thoracis diagnosed as per the definition earlier who consented to participate in the study were enrolled. Patients who had tube thoracostomy before referral to our hospital and those with bilateral empyema thoracis were excluded from the study. Ethical approval for the study was obtained from the Health Research and Ethics Committee of ABUTH, Zaria.

Upon admission, the sociodemographic characteristics of the patients were recorded. They included their age, gender, educational level, and occupation. The pleural fluid was subsequently taken for analysis (including aerobic microscopy, culture and sensitivity, acid-fast bacilli, and GeneXpert). Patients who had a positive GeneXpert result or acid-fast bacilli test on pleural fluid analysis (irrespective of other bacteria isolated) were labelled as having "tuberculous empyema thoracis". Those who tested negative to the aforementioned tests were labelled as having "non-tuberculous empyema thoracis". All patients were initially managed with empirical antibiotics, tube thoracostomies, and chest physiotherapy. The antibiotics included parenteral ceftriaxone, metronidazole, and oral doxycycline. Antibiotics were subsequently changed based on the sensitivity pattern. Those with confirmed tuberculous empyema thoracis also had rifampicin, isoniazid, pyrazinamide, and ethambutol for 2 months, with rifampicin and isoniazid continued for the subsequent 6 months. The initial empyema volume was the volume of empyema drained in the first 24 h, whereas the total empyema volume was the total volume of empyema drained from the insertion to the removal of the chest tube. These two volumes were indexed to the body surface area in an attempt to standardize the volumes across all age groups. They were designated the initial empyema volume indexed to the body surface area (IEV/BSA) and the total empyema volume indexed to the body surface area (TEV/BSA). Patients were considered successfully treated for empyema thoracis when there was a resolution of dyspnoea, fever, and chest pain, and at least 75% lung expansion compared to the contralateral lung (measurements were taken from the hilum to the periphery of the lungs on a posteroanterior chest X-ray). Any patient who did not meet the above definition of successful treatment was scheduled for pleural decortication. The data were collected using a structured proforma. These included data on aetiology, microbial isolates, and initial and total empyema volumes. The patients were subsequently managed and observed, and the outcomes of management were noted. These outcomes included the duration of drainage, the duration of hospital stay, complications, lung expansion following drainage, and the need for decortication. The complications noted included tube-site infection, cosmetic deformity of the chest wall, bronchopleural fistula, pneumothorax, and subcutaneous emphysema. Data obtained from the study were analysed using the Statistical Package for the Social Sciences (SPSS) version 20 software (IBM Corp. IBM SPSS Statistics for Windows. Version 20.0. Armonk, NY: IBM Corp.; released 2011). The chi-square test (with odds ratios and 95% confidence intervals) was used to compare categorical variables and the student's *t*-

test to compare numeric variables; differences were considered significant if $P < 0.05$.

Results

Eighty-three patients who satisfied the inclusion and exclusion criteria were enrolled in the study. There were 20 (24.1%) females and 63 (75.9%) males. Fourteen (16.9%) had tuberculous empyema and 69 (83.1%) had non-tuberculous empyema.

Sociodemographic characteristics

The ages of the whole group ranged from 7 months to 90 years, with a mean of 28.68 years (SD = 18.96 years) [Table 1]. The mean age of patients with tuberculous empyema (37.9 years [SD = 20.1 years]) was significantly higher than that of those with non-tuberculous empyema (26.8 years [SD = 18.2 years], $P = 0.045$). Between the two groups, there were no significant differences in sex ratios, level of education, or occupation.

Comorbidities

Three (21.4%) of the patients with tuberculous disease had comorbidities, whereas nine (13.0%) of those with non-tuberculous disease had comorbidities. The difference was not statistically significant ($P = 0.68$, Fisher's exact test). The comorbidities were diabetes mellitus, hypertension, malignancies, cardiac failure, sepsis, and sickle cell disease.

Microbiological isolates

Of the 83 patients managed, 33 (39.8%) patients had no organism isolated on microbiological analysis of pleural fluid. Of the 50 (60.2%) patients who had positive isolates, 43 had one organism isolated, four had two, two had three, and one had four; thus 61 isolates were obtained from the 50 patients. The distribution of isolated organisms is as shown in Table 2, with *Staphylococcus aureus*, *M. tuberculosis*, and *Pseudomonas aeruginosa* being the commonest.

The commonest underlying cause of empyema thoracis was parapneumonic process [Table 3].

Outcomes of management

Tables 4–6 show the effect of aetiology (tuberculous versus non-tuberculous) on the IEV/BSA, TEV/BSA, duration of drainage, lung expansion, length of hospital stay, incidence of complications, and need for decortication. There were no significant differences, between the two groups, in the mean IEV/BSA, mean TEV/BSA, mean duration of empyema drainage, or occurrence of complications.

The aetiology of empyema thoracis, however, significantly impacted the lung expansion, the need for decortication, and the length of hospital stay (*P*-values = 0.001, 0.004, and 0.004, respectively). Thus, patients with tuberculous empyema had a statistically significant lower percentage of mean lung expansion (60.9% vs. 78.4%), longer mean length of hospital stay (31.4 days vs. 23.6 days), and more than six times increased odds of requiring decortication.

Three patients (3.6%) who developed bronchopleural fistulae had tuberculous empyema thoracis. Three (3.6%) mortalities were recorded; two patients had sepsis and the third developed acute respiratory distress syndrome. The three mortalities were

Table 1: Sociodemographic characteristics

	Tuberculous empyema thoracis ($n = 14$)	Non-tuberculous empyema thoracis ($n = 69$)	*P*-value
Age (years)	37.9±20.6	26.8±18.2	0.045
Male gender (%)	12 (85.7)	51 (81.0)	0.500
Educational level			0.051
None	3	16	
Primary	2	28	
Secondary	2	13	
Tertiary	7	12	
Occupation			0.415
Civil servant	2	6	
Trader	2	14	
Child	1	7	
Driver	0	3	
Farmer	1	6	
Housewife	0	5	
Mechanic	0	1	
Retiree	3	2	
Student	4	21	
Unemployed	1	4	

Table 2: Isolated organisms from pleural aspirate

Isolated organisms	Frequency of isolated organism	Percentage of total isolates
Staphylococcus aureus	16	26.2
Mycobacterium tuberculosis	14	22.9
Pseudomonas aeruginosa	10	16.4
Klebsiella spp.	8	13.1
Escherichia coli	3	4.9
Enterobacteriaceae	3	4.9
Proteus vulgaris	2	3.3
Haemophilus influenza	1	1.6
Moraxella catarrhalis	1	1.6
Acinetobacter	1	1.6
Alcaligenes faecalis	1	1.6
Citrobacter	1	1.6

Table 3: Aetiology of empyema thoracis

Aetiology	Number of patients	Percentage
Parapneumonic	56	67.5
Tuberculosis	14	16.9
Odontogenic infection	4	4.8
Needle thoracentesis	4	4.8
Post lung contusion	3	3.6
Post oesophageal trauma	1	1.2
Post chest trauma	1	1.2
Total	83	100

Table 4: Management outcomes of empyema thoracis

Variables	Categories		Mean difference	95% confidence interval		*P*-value
	Non-tuberculous empyema (n = 69)	Tuberculous empyema (n = 14)		Lower	Higher	
Mean IEV/BSA (mls/m^2)	632.8±490.9	609.6±342.7	23.2	−297.5	251.1	0.833
Mean TEV/BSA (mls/m^2)	1851.5±1334.7	1949.6±1460.7	−98.1	−790.1	986.1	0.819
Mean duration of drainage (days)	23.6±30.7	31.4±30.4	−7.8	−25.7	10.1	0.391
Mean lung expansion (%)	78.4±16.8	60.9±22.7	17.5	7.1	27.9	0.001
Mean length of hospital stay (days)	23.6±16.2	36.4±3.8	−12.8	−21.5	−4.1	0.004

IEV/BSA: initial empyema volume indexed to the body surface area, TEV/BSA: total empyema volume indexed to the body surface area

Table 5: Occurrence of complications between patients with tuberculous and non-tuberculous empyema thoracis

	Complication		Total
	Yes	No	
Tuberculous empyema thoracis	7	7	14
Non-tuberculous empyema thoracis	27	42	69
Total	34	49	83

Chi-square value = 0.569, *P*-value = 0.451, odds ratio = 1.56 (95% confidence interval = 0.49–4.93)

Table 6: Incidence of need for decortication between patients with tuberculous and non-tuberculous empyema thoracis

	Need for decortication		Total
	Yes	No	
Tuberculous empyema thoracis	10	4	14
Non-tuberculous empyema thoracis	19	50	69
Total	29	54	83

Chi-square value = 9.864, *P*-value = 0.004 (Fisher's exact test), odds ratio = 6.58 (95% confidence interval = 1.84–23.52)

recorded among the patients with non-tuberculous empyema thoracis.

Discussion

It is known that a good number of patients with empyema have sterile cultures in pleural fluid microbiology likely due to prior repeated exposure to antibiotics.[7,8] This may explain the sterile cultures obtained in 33 (39.8%) of our patients. Our inability to carry out routine anaerobic cultures due to institutional limitations could have impacted negatively on the bacteriological spectrum and the number of organisms isolated. Only seven (8.4%) patients in our study had polymicrobial isolates. Alfageme *et al.* also cultured varying numbers of microbial isolates in patients with empyema thoracis, ranging from sterile cultures through single organisms to multiple organisms.[9] This underscores the fact that empyema thoracis is polymicrobial in some cases.[10]

S. aureus was the most commonly isolated organism in the pleural fluid, similar to Asindi *et al.*'s report from Calabar[11] and corroborated by Kundu *et al.*[6] and others.[12,13] Other significant organisms were gram-negative organisms *like Pseudomonas* spp., *Klebsiella* spp., *Escherichia coli, Proteus vulgaris*, and *Enterobacteriaceae*. Although *S. aureus* seems to be the prevalent organism causing empyema thoracis in Nigeria and other tropical countries, Pneumococcal organisms seem to be the culprit in reports from Europe.[14]

Aetiologically, parapneumonic effusion was the leading cause of empyema thoracis. It occurred in 67.5% (n = 56) of patients. This finding was similar to that of Thomas and Ogunleye who had 49.5% of their patients with chronic empyema thoracis arising secondary to poorly treated chest infection (parapneumonic empyema), with 39.8% being secondary to tuberculosis.[8] This finding was also corroborated by Alfageme *et al.*,[9] Ekpe and Akpan,[15] and Asindi *et al.*[11] Thus, timely and appropriate diagnosis and treatment of pneumonia would reduce the incidence of empyema thoracis in our environment.

Three (3.6%) mortalities were recorded; two patients had sepsis and the third developed acute respiratory distress syndrome. An earlier report by Hassan and Mabogunje from Zaria put the mortality at 4.9%.[16] Alfageme *et al.* also reported that three patients out of 82 (3.7%) died from the direct result of empyema,[9] similar to this study. Thomas and Ogunleye also reported similar findings (3.2% mortality),[8] and Asindi *et al.* reported 6% mortality for childhood empyema thoracis in Calabar.[11] Most authors have put the mortality between 6% and 8.4%.[12,13,17]

Aetiologically, patients with tuberculous empyema had a significantly lower lung expansion, increased risk of requiring decortication, and increased length of hospital stay for successful management of the disease. This occurred because they had more lung parenchymal disease, persistent pleural contamination from bronchopleural fistula, and persistent lung collapse due to the aforementioned reasons.[6] The three patients with bronchopleural fistulae had tuberculous empyema. The above factors constitute the reasons for the higher chances of requiring decortication for successful treatment following tuberculous empyema. Patients with tuberculous empyema were 6.58 times more likely to require decortication compared to those with non-tuberculous empyema. Prakash *et al.*, who studied only patients with tuberculous empyema, without comparing with those with

non-tuberculous empyema, however, noted greater success in managing tuberculous empyema, with only 36% of patients having unsatisfactory lung expansion, who were subsequently managed by open drainage.[18] This set of patients with poor lung expansion, in our study, would have merited decortication. However, Kundu *et al.* who compared the clinical profile and management of patients in both groups noted that tuberculous empyema thoracis was associated with significantly worse outcomes in terms of incidence of bronchopleural fistula (odds ratio = 48.8 vs. 10.9) and duration of illness (171.2 days vs. 20 days), similar to this study.

Conclusion

Tuberculous empyema thoracis was associated with significantly worse outcomes (in terms of percentage of lung expansion, need for decortication, and length of hospital stay) compared to non-tuberculous empyema thoracis.

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Conflicts of interest

There are no conflicts of interest.

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