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Microbiological study of empyema thoracis among children in a tertiary care hospital

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ABSTRACT

Background: Empyema thoracis is a condition resulting in the accumulation of purulent fluid in the pleural cavity. It is a common source of illness among young children and is the most common sequela of bacterial pneumonia. **Aims and Objectives:** This study was to determine the clinico-microbiological profile, causative agents, and antimicrobial susceptibility patterns of the isolates of the study population. **Materials and Methods:** Prospective observational study was done in the Department of Microbiology, S. C. B. M. C. H., Cuttack. The study group comprised a total of 105 cases of empyema thoracis between the age group of 0–14 years, diagnosed by aspiration of pus from the pleural space. Complete histories of cases in detail were noted. **Results:** A total of 41% of patients were in the age group of 5–9 years with M: F ratio of 1.1:1. Maximum cases 36 (34.3%) were seen in the spring season. Fever, cough, and breathlessness were the most common complaints. Bronchopneumonia 56 (53.3%), impetigo, and skin lesions 29 (27.6%) were the major predisposing factors. Right-side empyema 71 (67.6%) was more common than the left side 34 (32.4%). Culture revealed *Staphylococcus aureus* as the most common etiologic agent 26 (36.1%), of which 30.8% were methicillin-resistant *S. aureus*, followed by *Mycobacterium tuberculosis* complex 13 (18.1%). Finally, 103 (98.2%) empyema cases were recovered by antibiotics and tube thoracostomy. **Conclusion:** Empyema thoracis is more prevalent in the lower socioeconomic population which can be prevented by an early diagnosis of pneumonia. Effective methods to treat empyema thoracis in children include the administration of proper antibiotics and tube thoracostomy in resource-poor settings.

Key words: Pleural pus; Tube thoracostomy; Pneumonia in children; Empyema thoracis

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INTRODUCTION

Empyema is a condition where there is the accumulation of purulent fluid or pus formation in the pleural cavity. It is a common entity in developing countries, along with the high incidence of pneumonia, due to multiple factors. Empyema may cause significant morbidity in children but not mortality. However, there is a lack of evidence from pediatric trials and it would be inappropriate to look at adult data to understand empyema in children as adult and pediatric pleural infections are different. Since children rarely experience an underlying lung disease, the final outcome is almost always excellent. Furthermore, adult empyema carries a 20% mortality rate due to comorbidity (i.e., malignancy, immunodeficiency, prolonged hospital stays, and nosocomial infections).[1-3]

In developed countries, the microbial profile has changed with the increasing incidence of penicillin-resistant *Streptococcus pneumoniae* and methicillin-resistant *Staphylococcus spp.*[4,5] However, the situation is very different in the developing countries, where empyema is associated with significant

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morbidity and the consumption of lesser sources from the hospitals. Incidence of empyema constitutes about 0.8% of the total pediatric admissions. Moreover, effusions occur in at least 40% of bacterial pneumonias with up to 60% of effusions resulting in the formation of empyema in all age groups.[2] It occurs in 5–10%of children with bacterial pneumonia and in up to 86% of children with necrotizing pneumonia. It commonly occurs as a sequel of bacterial pneumonia. The pathologic manifestation of empyema thoracis is that of a dynamic condition. The American Thoracic Society has described three stages of empyema, namely exudative, fibrinopurulent, and organized. The exudative phase (1–3 days) is caused by an increased permeability of the inflamed pleura, the fibrinopurulent phase (4–14 days) is characterized by an accelerated fibrin deposit, which will become purulent and lead to empyema and loculation. Finally, the organizing stage (after 14 days) is characterized by a thickened pleura producing an inelastic membrane, which restricts lung movement; this is termed as a trapped lung.[6]

Malnutrition, poor host defense, poor socio-economic status, partial treatment with inadequate or improper antibiotics, and poor housing are the contributory factors behind this condition.[6] *Staphylococcus aureus*, *S. pneumoniae*, *Haemophilus influenzae*, *Escherichia coli*, *Klebsiella* spp., and *Pseudomonas* spp. are the most commonly implicated organisms.[6,7] Among these, *S. pneumoniae* is the most common organism responsible for empyema in developed countries. In India, *S. aureus* is the most common organism in patients of all ages.[8,9] Anaerobes such as *Bacteroides fragilis, Porphyromonas spp*. Porphyromonas spp., and *Fusobacterium nucleatum* are also commonly involved. The symptoms generally include profound weight loss, fever and often present themselves after aspiration pneumonia or poor dental hygiene.

In about 12–34% of cases of empyema, anaerobes are associated with mixed infection and in 14% of cases, as a single etiological agent.[10] Moreover, tubercular empyema cases occur in about 2–5% of empyema thoracis cases. Tuberculous empyema originates in the discharge of the bacilli into the pleural space from a subpleural pulmonary focus or caseated lymph nodes. Tuberculous empyema is usually unilateral but it can also be bilateral in certain cases.

The knowledge regarding the isolated organisms and their antimicrobial susceptibility patterns will guide clinicians in selecting the appropriate antimicrobial agent for better treatment outcomes.

Aims and objectives

The knowledge regarding the isolated organisms and their antimicrobial susceptibility patterns will guide clinicians in selecting the appropriate antimicrobial agent for better treatment outcomes.

MATERIALS AND METHODS

Study design

It was a hospital-based observational prospective study conducted in the post-graduate department of Microbiology, S.C.B.M.C.H, Cuttack, in collaboration with the Department of Pediatrics, S.C.B.M.C.H, S.V.P.P.G.I.P of Pediatrics, Cuttack and the State anti-TB Demonstration and Training Centre, Cuttack, with the approval of the Institutional Ethical Committee (IEC/IRBNo.-701/Dt27.11.2018).

Study period

This study was carried out for a period of 2 years from September 2016 to August 2018.

Study population

The study group comprised a total of 105 cases of Empyema thoracis between the age group of 0–14 years.

Permission and patient consent

This study was approved by the Institutional Ethical Committee (IEC/IRBNo.-701/Dt27.11.2018). Appropriate procedures were followed to obtain informed consent from the patients.

Inclusion criteria

All patients belonging to the age group of 0–14 years and clinically diagnosed cases of Empyema thoracis.

Exclusion criteria

Patients aged >14 years, whose consent was not obtained or not willing to participate in the study. Those were transudative causes of pleural effusions, post-surgical empyema and post-traumatic empyema.

All the 105 clinically suspected cases of empyema thoracis were evaluated by their detailed history after admission, with emphasis on the duration of symptoms, previous medication, contact history of tuberculosis, and the course of illness before admission. The patients were examined thoroughly for vital signs, nutritional status, and the respiratory signs. Suspected cases were confirmed after chest X-ray and ultrasonography. All clinically suspected cases, diagnostic thoracentesis was performed under local anesthesia with 2% xylocaine, using a sterile disposable syringe (needle size: 18 g), which was introduced through the 5th intercostals space in the mid-axillary line or the area of maximal dullness. The appearance of pus clinched the diagnosis. Pleural pus was aspirated before the administration of antibiotics by a sterile syringe and

was collected in three sterile vials, one for aerobic culture; the second one for the culture of *Mycobacterium tuberculosis complex,* and the third in a special anaerobic transporting vial for anaerobic culture. After that, all the three vials were sent to the laboratory for processing.

Microscopy was conducted in one of two ways: (a) Gram staining: Gram-stained preparation of the pus samples was observed for the presence of polymorphonuclear (PMN) cells and bacteria; and (b) Ziehl–Neelsen (Z-N) Staining: Pus samples were also observed for the presence of acid-fast bacilli.

Culture methods

Aerobic Culture Methods[11-13]

The flow chart showing steps of aerobic culture methods in the present study as follows (Figure 1).

Anaerobic Culture Method[14]

The flow chart showing steps of anaerobic culture methods in the present study as follows (Figure 2).

RESULTS

The prevalence of empyema among hospitalized children was as follows: Out of the 13,897 cases admitted, 105 (0.8%) cases had empyema. There were 56 (53.33%) males and 49 (46.66%) females. The male-to-female ratio was 1.1:1.

Seasonal distribution, clinical manifestations, and predisposing factors of the study population were studied. Most cases were clustered in the spring season (January–March) and decreased incidence was observed in the summer. In the present study, bronchopneumonia, impetigo, and other skin lesions were major predisposing factors and some cases had a history of tuberculosis.

Out of the 105 pleural pus samples processed for bacteriological culture 58 (55.2%) showed mono-microbial growth, 7 (6.7%) experienced poly-microbial growth and no growth was observed in 40 (38.1%) cases.

Aerobic bacteria and *M. tuberculosis* complex (MTBC) were isolated in 55.2% and 12.4% cases respectively. Nontuberculous mycobacteria were isolated only in one case (1%) and no anaerobic organisms were isolated in the present study (Table 1, Figures 1 and 2).

Among all isolated organisms, *S. aureus* (36.1%) was the predominant organism followed by *M. tuberculosis* complex (18.1%). Out of 26 cases of *S. aureus*, 8 (30.8%) were MRSA (methicillin-resistant *S. aureus* (Table 2 and Figure 1).

Table 1: Bacterial growth and organisms isolated in the study population

Bacterial growth	Number of cases (n)	Percentage
Mono-microbial	58	55.2
Poly-microbial	7	6.7
No growth	40	38.1
Organisms isolated		
Only aerobic bacteria	51	48.5
Only MTBC	7	6.7
MTBC+aerobacteria	6	5.7
NTM+aerobacteria	1	1
Anaerobacteria	0	0
No growth	40	38.1

MTBC: *Mycobacterium tuberculosis* complex

Table 2: Number of bacterial isolates in the study population

Organisms	Number of isolates		Percentage	
Staphylococcus spp.	26	MRSA= 8/26	36.1	30.8
Mycobacterium tuberculosis complex	13		18.1	
Escherichia coli	9		12.5	
Klebsiella spp.	7		9.7	
Pseudomonas aeruginosa	7		9.7	
Acinetobacter spp.	5		6.9	
Enterococcus spp.	3		4.2	
Citrobacter freundii	1		1.4	
NTM	1		1.4	
Total	72		100	

All isolated Gram-positive cocci were 100% susceptible to vancomycin, teicoplanin, and linezolid. Isolates belonging to the Enterobacteriaceae family were 100% susceptible to Imipenem. All isolated nonfermenters were 100% susceptible to polymyxin B, Colistin, and Imipenem (Table 3 and Figure 1).

Among 29 Gram-negative isolates, 9 (31%) were ESBL producers. Maximum ESBL producers were *Klebsiella* spp. (42.8%), followed by *Acinetobacter* spp. (40%) (Table 4 and Figure 1).

Out of the 105 samples tested for *M. tuberculosis* complex, CBNAAT was positive in 12 samples, microscopy was positive in 11 samples, and culture was positive in 13 samples, which were confirmed by smear and ICT test. Those 11 samples that were microscopically positive were directly processed for line probe assay (LPA) and found to be sensitive to both rifampicin and isoniazid. Two cases that were microscopically negative but culture positive and ICT positive were processed for anti-tubercular drug susceptibility testing and found to be sensitive to isoniazid, rifampicin, ofloxacin, and kanamycin. Hence, all *M. tuberculosis* complex cases were sensitive to both Isoniazid and Rifampicin (Table 5 and Figure 3).

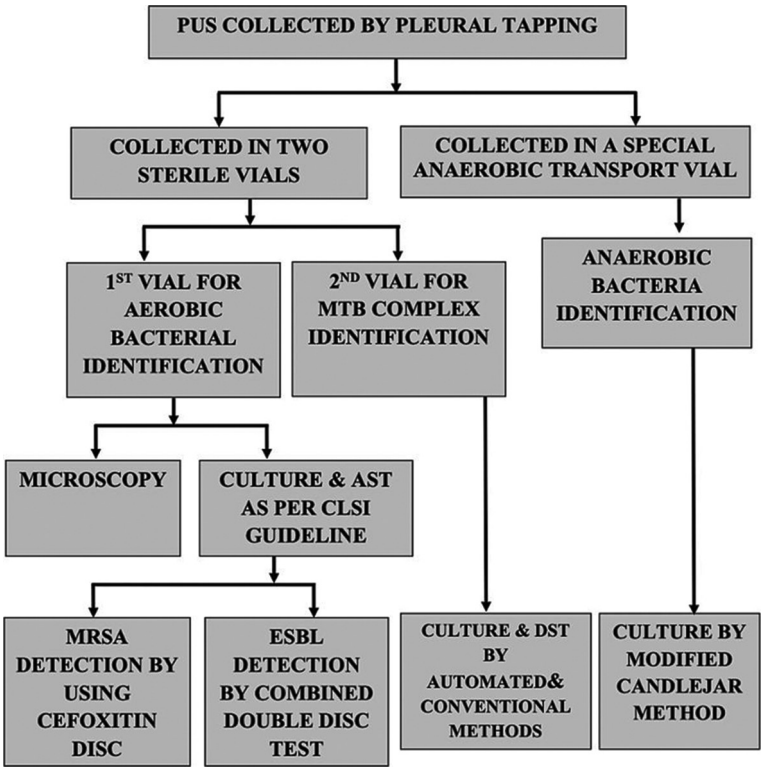

Figure 1: Specimen collection and processing for bacterial culture, identification, antimicrobial susceptibility testing, methicillin-resistant *Staphylococcus aureus*, and extended-spectrum beta-lactamases detection

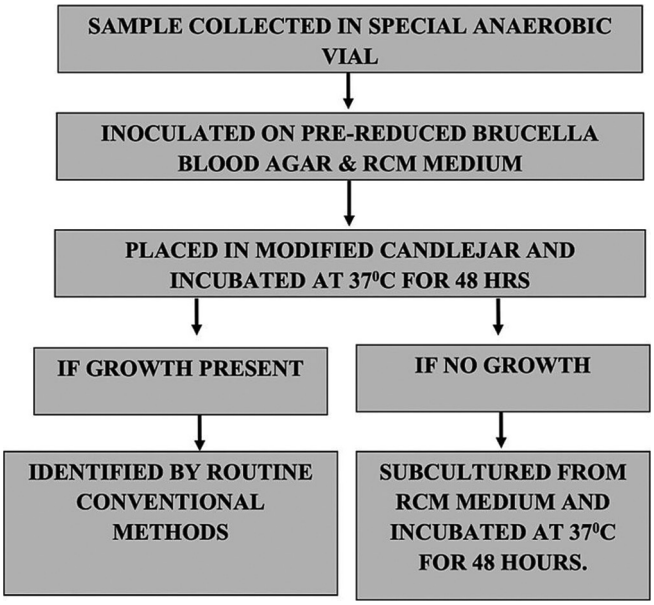

Figure 2: Anaerobic culture method: *Mycobacterium tuberculosis* complex identification and drug susceptibility testing[15]

DISCUSSION

Lower respiratory tract infections are a leading cause of morbidity and mortality in children throughout the world. In developing countries, poverty, HIV infection, and the lack of universal access to new vaccines contribute to the high incidence of severe and complicated pneumonia. Para pneumonic effusion and empyema most frequently occur as a complication of bacterial pneumonia.[16] Due to the delay in seeking medical opinion and indiscriminate use of antibiotics, it is very difficult to isolate microorganisms in the Indian set up. In the present study 105 children with empyema were evaluated over 24 months for the clinical course of the disease, bacteriological profile, and various treatment options.

In the present study, male preponderance was more with M: F ratio 1.1:1, which was similar to the study by Narayanappa et al.,[8,9] The role of male gender as a risk factor for immune-compromise and trauma may partially explain the predisposition to staphylococcal, Gram-negative, anaerobic and mycobacterial infections. Varied opinions regarding the seasonal prevalence were noted in the past studies. In the current study, cases were presented in January to March (spring). This indicates that the majority of cases have been presented during winter and early spring. This differed from Baranwal et al.,[17] as they found most cases in summer. Earlier studies had reported most cases in winter and early spring probably due to the increased spread of infections from overcrowding, ill ventilation, chilling breeze, and soak in grains.[18,19]

The classical picture of a child with empyema used to be that of a very sick, breathless child, running a high fever, and looking haggard, presenting late in the fibrin purulent

Table 3: Drug sensitivity of Gram-positive cocci and nonfermenting microorganisms

Organisms	GEN	VA	TEI	LZ	CFS	PIT	IPM	PB	CL
Staphylococcus aureus (n=26)	65	100	100	100					
Enterococcus spp. (n=3)	-----	100	100	100					
Escherichia coli (n=9)	67				100	78	100		
Klebsiella spp. (n=7)	71	----	----		86	86	100		
Citrobacter freundii (n=1)	100				100	100	100		
Pseudomonas aeruginosa (n=7)						71	100	100	100
Acinetobacter spp. (n=5)	40				80	--	100	100	100

Table 4: Frequency of ESBL producers in the study population

Organisms	Isolated	ESBL producer	Percentage
Escherichia coli	9	3	33.3
Klebsiella spp.	7	3	42.8
Pseudomonas aeruginosa	7	1	14.3
Acinetobacter spp.	5	2	40
Citrobacter freundii	1	0	0
Total	29	9	31

Extended-spectrum beta-lactamases

Table 5: *M. tuberculosis* complex positivity by various diagnostic methods and drug sensitivity pattern

Diagnostic methods	Positive	Negative	DST
CBNAAT	12	2-S (I, R, O and K)	S (H and R)
Microscopy	11	2-S (I, R, O and K)	S (H and R)
Culture	13	00	S (H and R)
LPA S (R/I)	11	2	S (H and R)

S: Sensitivity H: Isoniazid, R: Rifampicin, O: Ofloxacin, K: Kanamycin, DST: Drug sensitivity test, CBNAAT: Cartridge-based nucleic acid amplification test and LPA: Line probe assay is a rapid technique based on polymerase chain reaction (PCR) that is used to detect *Mycobacterium tuberculosis* (MTB) complex and drug sensitivity to rifampicin (RPM) and isoniazid (INH) by the Revised National Tuberculosis Control Programme (RNTCP) of India

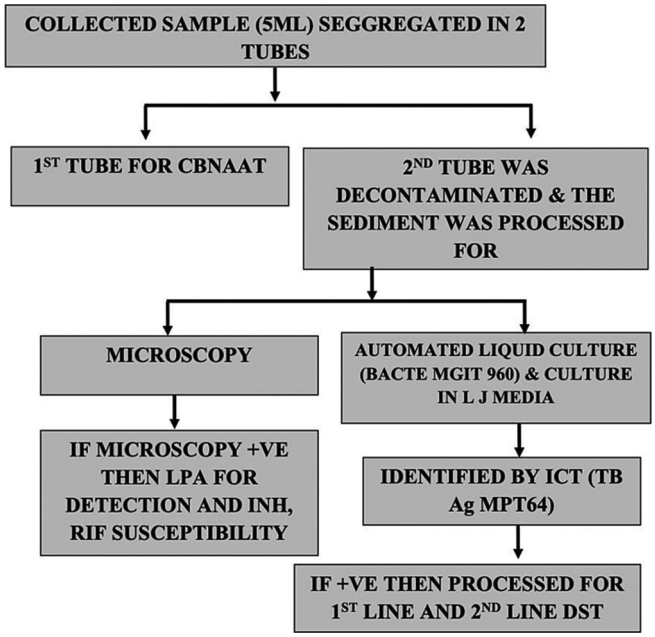

Figure 3: *Mycobacterium tuberculosis* complex identification and drug susceptibility testing

stage. In contrast, the present clinical picture revealed that 8 children were not in frank respiratory distress at the time of presentation. The most common presenting symptoms of patients were fever and cough in all 105 cases, while 97 patients showed hurried respiration and 34 were experiencing chest pain. This simulates well with the study by Lingayat and Wankhede[20] Further, the absence of frank breathlessness may be due to prior treatment with antibiotics.

In the current study, bronchopneumonia predisposed to the empyema cases, and next to it were Impetigo and other skin lesions in 29 cases. A history of tuberculosis and measles were seen in some cases. The present study correlates with that of Lingayat and Wankhede.[20,21]

Right-side empyema was seen in 71 cases and was more common than the left, which was observed in 34 cases. In general, the right, middle, and the lower lung lobes are the most common sites affected due to the larger caliber and more vertical orientation of the right main stem bronchus.

In the present study, the isolation rate of aerobic bacteria was 55.2%. Among them, the most commonly isolated organism was *S. aureus* (36.1%), followed by *M. tuberculosis complex* (18.1%). The isolation rate of *S. aureus* in the present study was similar to the study by Lingayat and Wankhede[20] but it differed from Jain and Banavaliker[22] where *Pseudomonas aeruginosa* was the most common causative organism. In the tropical zone, excessive sweating and moist skin favor the growth of cutaneous flora, thereby leading to the high incidence of staphylococcal pyoderma. This pyoderma developed into pneumonia and parapneumonic empyema through a hematogenous route. Due to the importance of *Staphylococcus* spp. in causing parapneumonic empyema in tropical areas, the first line treatment should be anti-staphylococcal agents in cases of severe pneumonia.

In this study, the percentage of MRSA isolates was 30.8%, which was similar to the study by Narayanappa et al.,[9] but

it differed from Jain and Banavaliker[22] where it was found to be 79.3%. Nowadays, due to the rise in use of β lactam antibiotics in the community, more dissemination of MRSA occur, which is a cause of concern and further investigation is required for the same.

All Gram-positive cocci isolated in our study were sensitive to linezolid, vancomycin, and teicoplanin, which is similar to that reported by Narayanappa et al.,[9] In the present study, 31% of all isolated Gram-negative bacilli were ESBL producers. This differed from a study by Jain and Banavaliker[22] who found the percentage of ESBL producers among to be 41.8%.[22] ESBL production was the highest in *E. coli*, followed by *Klebsiella* spp. as observed in various reports worldwide.[23] The current study showed that ESBL production was maximum in *Klebsiella* spp. (42.8%) and *Acinetobacter* spp. (40%). This rising ESBL production poses a daunting challenge toward Gram-negative antibiotic resistance, which is indicative of an ominous trend of more and more isolates acquiring resistance mechanisms.

Tubercular etiology was detected in 13.4% of cases in the present study, which is similar to the results found by Ramireddy and Krishna.[24] However, this finding differs from Jain and Banavaliker[22] where the incidence of tuberculous empyema was 27.2%. Tuberculosis was usually diagnosed by clinical features, X-ray findings, and laboratory results. Direct examination of pleural fluid and Ziehl–Neelsen staining required bacillus concentrations of 10,000/mL and, therefore, has a low sensitivity. Culture is more sensitive but requires 2–6 weeks due to high doubling time. In this study, conventional methods (Ziehl–Neelsen stain and culture of pleural pus in LJ Media) as well as modern methods (CBNAAT, Automated Liquid Culture [BACTECMGIT960] and LPA) were implemented. In this study, 13/105 (12.4%) samples were culture positive in both Lowenstein-Jensen egg-based solid medium and the automated culture method for *M. tuberculosis complex*. Soe et al.,[25] from Malaysia found only 5.6% of cases to be culture positive. In this study, only 11 (10.5%) samples, which were microscopy positive, were processed for LPA. The current study showed that LPA is a rapid and sensitive method but highly technical and expensive. It also requires expertised workforce.

CBNAAT detected MTB in 12 out of 14 culture-positive cases (85.7%). Two false negatives were CBNAAT negative but culture positive because one culture sample was positive for MOTT (mycobacterium other than tuberculosis) and CBNAAT only detects MTB. In the other samples, although MTB growth was in the culture, it is possible that the bacterial load may have been too low for the CBNAAT to detect the DNA from the MTB complex. It shows that a patient with a negative CBNAAT can still have TB with MTB or MOTT as per Agarwal et al.[26]

Intercostal drainage and antibiotic therapy was the mainstay in terms of treating empyema thoracis. Complicated patients require other treatment modalities like Video Assisted Thoracoscopic Surgery (VATS) and decortication surgery. In the present study, the majority of patients have responded to antibiotics and intercostal drainage, while two patients required decortication. These treatment outputs were similar to the study performed by Satpathy et al.,[2] In this study, anaerobic isolates were not detected, which was similar to Jain and Banavaliker[22] who conducted the study at Rajan Babu Institute of Pulmonary Medicine and Tuberculosis (RBIPMT) in Delhi.

Limitations of the study

The limitation of the present study regarding not obtaining an anaerobic isolate could be due to the technical difficulty in the collection and transportation of specimens and growth of anaerobes. Though aspiration pneumonia was a major predisposing factor for anaerobic infection, there was no aspiration pneumonia cases predisposed to empyema thoracis.

CONCLUSION

The prevalence of pediatric empyema is more in those belonging to the lower socioeconomic strata due to improper use of antibiotics and the delay in seeking medical advice. By knowing the infective organism and its antibiotic pattern in the early stages, it helps the clinician treat the patient effectively. It is important in preventing the development of empyema and reduces the rate of morbidity and mortality. Further, antibiotics and tube thoracostomy are the effective methods to treat empyema thoracis in children within resource-poor settings.

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Authors Contribution:
SD and LM- Definition of intellectual contents, literature survey, implementation of study protocol, data collection and data analysis. **DPM-** Prepared first draft of Manuscript prepare and submission of manuscript. **JRC-** concept design, clinical protocol, manuscript revision: **MKD-** Design of study, statistical analysis and interpretation; **DPM-** Review of manuscript and preparation of figures: **DNM-** Final revision of manuscript coordination and manuscript.

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