**Section: Pediatrics** 



# **Original Research Article**

# CLINICAL AND MICROBIOLOGICAL PROFILE OF EMPYEMA IN CHILDREN: A PROSPECTIVE OBSERVATIONAL STUDY

Munigangaiah Lalitha<sup>1</sup>, Niranjan Biswal<sup>2</sup>, Sujatha Sistla<sup>3</sup>

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### **Corresponding Author:**

Email: drnbiswal@yahoo.com

**Dr. Niranjan Biswal,**Professor, Department of Pediatrics,
JIPMER, Pondicherry, India.

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### ABSTRACT

**Background: Objective:** To study the etiological agents of empyema and their antibiotics sensitivity.

**Materials and Methods:** In this prospective observational study, children diagnosed with empyema were recruited. Clinical, laboratory and radiological profile of patients were analysed.

**Results:** Out of 37 cases, 27 cases were in under five age group. The most common symptom was fever (89%) followed by cough, respiratory distress and chest pain. Among 14 pleural fluid culture positive cases, the most common organism was Staphylococcus aureus followed by Pseudomonas aeruginosa. The cases with culture positivity had longer duration of intercostal drainage (p<0.05).

**Conclusion:** Staphylococcus aureus still remains the predominant causative organism of empyema thoracis in developing nations. Isolation of MRSA has been in rising trend. If managed effectively, the children recover without much long term effects.

Keywords: Empyema, children, pneumonia.

### INTRODUCTION

Acute respiratory tract infection (ARI) is the leading cause of childhood morbidity and mortality in both developing and developed countries. Incidence of ARI in under five age group is 15-21 % in developing countries as per WHO.<sup>[1]</sup> Pneumonia and Empyema Thoracis (ET) are associated with substantial level of morbidity and mortality despite advances in their management.<sup>[2]</sup> Microbiological profile of empyema has changed over the past decades. Staphylococcus aureus being the predominant organism in developing countries. In developed and developing countries there is increasing incidence of penicillin resistant Streptococcus pneumoniae and methicillin resistant Staphyloccus aureus (MRSA).<sup>[3,4]</sup>

Different protocols with varieties of antibiotic combinations had been used to treat ET with no consensus on a preferred combination of antibiotics due to lack of evidence from pediatric trials. Identification of causative organisms and their

antibiotic sensitivity pattern may help in suggesting an effective empiric antibiotic regimen for ET.

# MATERIALS AND METHODS

This was a prospective observational study conducted from January 2014 to Feb 2015 in the department of pediatrics, JIPMER, a tertiary care centre in South India. Approval from the Institute Ethics committee was obtained. Informed consent was taken from the parents. The primary objective was to study etiological agents causing Empyema Thoracis (ET) in children. The secondary objectives were to estimate the duration of hospital stay, the duration of intercostal drainage and the proportion complications. All the cases of pleural effusion in the age group of 1 month-12 years diagnosed as ET were included in the study based on the following criteria:1) Frank pus on thoracocentesis or 2) Pleural fluid showing predominantly polymorphonuclear cells or 3) Pleural fluid showing positive gram stain or AFB stain or culture or 4) Pleural fluid glucose <40

<sup>&</sup>lt;sup>1</sup>Department of Pediatrics, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Pondicherry, India.

<sup>&</sup>lt;sup>2</sup>Professor, Department of Pediatrics, JIPMER, Pondicherry, India.

<sup>&</sup>lt;sup>3</sup>Department of Microbiology, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Pondicherry, India.

mg/dl and/or pleural fluid protein >3g/dl. Appropriate antibiotics and supportive treatment was given according to the unit protocol. Intercostal tube drainage (ICD) was carried out under aseptic precautions in cases of ET. Depending on the clinical response and culture sensitivity report antibiotics was changed. With progressive clinical improvement and reduction of ICD drainage to <15 ml, ICD tube was removed. Surgical management was considered when there was persistence of clinical symptoms, persistent effusion 10days after ICD, loculated effusion, restrictive pleural thickening with collapse of lungs. Switching over to oral antibiotics from parenteral antibiotics was done after the case was afebrile and clinically improved. Cases were followed up at 1month and 3 months after discharge.

### RESULTS

37 cases were enrolled in the study of which 13 (35%) children were in the age group between 1 to 12 months and 14 (38%) children in the age group between 1-5 years. The median age was 30 months (3months-12yrs). Many of the children with empyema had grade I and grade II malnutrition (32%). The most common symptom was fever (89% cases), followed by cough (76%) and respiratory distress (78%), chest pain (21.6%) and abdominal pain (8%). The median duration of fever was 8 days (range: 4-15 days). On clinical examination majority of the children had chest retractions (70%), tachypnea (65%) who also had stony dull note on percussion (97%) (Table: 1).

Pleural fluid Gram stain was positive in 5 cases (14%). Culture was positive in 14 cases (38%). The organisms isolated were: Staphylococcus aureus in 10 cases (27%), beta hemolytic streptococci in 1 case (3%), Pseudomonas aeruginosa in 2 cases (5%) and Acinetobacter baumannii in 1 case (3%) (Table 2). Among the isolates of Staphylococcus, 7 were methicillin sensitive and 3 were methicillin resistant.70% of the isolates of Staphylococcus was

from the infants. MSSA was sensitive to gentamicin, cloxacillin and vancomycin in all the cases.57% isolates were sensitive to erythromycin and clindamycin. All the MRSA isolates were sensitive to vancomycin and resistant to ciprofloxacin, penicillin and erythromycin. Sensitivity to clindamycin was observed in 2 isolates.

Beta hemolytic Streptococci were sensitive to tetracycline, penicillin and erythromycin. Both the isolates of Pseudomonas were sensitive to amikacin and meropenem, whereas they were resistant to cefoperazone and ceftazidime. Acinetobacter was sensitive to amikacin, gentamicin and meropenem (Table 3). 21 patients required ICD in addition to antibiotics while 11 patients needed tube thoracostomy and decortication.

The various antibiotic combinations were used for empirical therapy based on unit protocol .16 patients required change of antibiotics based on the clinical improvement and culture reports (Table 4). The median duration of parenteral therapy was 14days (7-42 days). The median duration of total treatment was 28 days (21-49 days). The median duration of hospital stay was 14 days (6-42 days). The median duration of intercostal drainage was 7 days (0-29 days). The median time taken for defervescence was 7 days (1-32days).On comparison of the outcomes between culture positive group and culture negative group, the duration of intercostal drainage was significantly higher in culture positive cases(p=0.02). However, there was no significant difference in length of hospital stay, time taken for defervescence and the proportion of complications.

The complications observed were respiratory failure in 9 cases (24%), shock in 7 cases (19%), (out of which 4 were in culture positive cases), pneumothorax in 3 cases, rib osteomyelitis in one case (Table 5). There was mortality in one case due to septic shock. On 3 months follow up of 36 cases, there was radiologic clearance in 95% of the cases and they were all asymptomatic. 3 cases had pleural thickening with no symptoms.

Table 1: Demographic and	clinical p	rofile of c	hildren v	vith en	npyema 1	horacis

Parameters	Number (n=)	Percentage (%)
Agewise distribution		
< 1year	13	35
1-5 years	14	38
5-12 years	10	27
Male	19	51
Female	18	49
Predisposing factors		
Malnutrition (grade I & II)	12	32
Partial immunization	9	24
Contact with tuberculosis	3	8
Congenital heart disease	2	5
Infection at other sites	2	5
Others #	7	21
Symptoms		
Fever	33	89
Respiratory distress	29	78
Cough	28	76
Chest pain	8	22
Signs		
Stony dull note (percussion)	36	97

Chest retractions	26	70
Tachypnea	24	65
SpO2< 94%	14	38

# - T cell acute lymphoblastic leukemia, Cerebral palsy, Down syndrome, Ataxia telangiectasia, Nephrotic syndrome, Organic academia, Infection in other sites (one case in each)

Table 2: Organisms isolated from pleural fluid culture

Organism	Frequency(n=)	Percentage (%)
Staphylococcus aureus	10	27
Pseudomonas aeruginosa	2	5
Beta hemolytic streptococci	1	3
Acinetobacter baumannii	1	3
No growth	23	62
Total	37	100

Table 3: Comparison of antibiotic sensitivity pattern between MSSA and MRSA

Antibiotic	Organism	Sensitivity (n=; %)	Resistance (n=; %)
Gentamicin	MSSA (n=7)	7(100)	0(0)
Gentalmeni	MRSA (n=3)	1(33)	2(67)
Penicillin	MSSA (n=7)	1(17)	6(83);
Penicinii	MRSA (n=3)	0(0)	3(100)
E4h	MSSA (n=7)	4(57)	3(43)
Erythromycin	MRSA (n=3)	0(0)	3(100)
Tates avalina	MSSA (n=7)	2(29)	5(71)
Tetracycline	MRSA (n=3)	1(33)	2(67)
Vancomycin	MSSA (n=7)	7(100)	0(0)
	MRSA (n=3)	3(100)	0(0)
Clindamycin	MSSA (n=7)	4(57)	3(43)
Cindanycii	MRSA (n=3)	2(67)	1(33)
Cimusfloyeein	MSSA (n=7)	2(29)	5(71)
Ciprofloxacin	MRSA (n=3)	0(0)	3(100)

Table 4: Requirement of second line antibiotic in various empirical antibiotic combinations

First line antibiotic	Received	Second line antibiotic		Total	n volue*
First line antibiotic	Received	Yes (n=;%)	No (n=;%)	Total	p value*
Ox+Ci	Yes	5(28)	13(72)	18	0.065
OX+CI	No	11(58)	8(42)	19	0.003
Ci+Va	Yes	2(100)	0(0)	2	0.096
CI+ va	No	14(40)	21(60)	35	0.090
Ak+Ox	Yes	2(33)	4(67)	6	0.592
AK+OX	No	14(45)	17(55)	31	0.392
Pt+Va	Yes	1(50)	1(50)	2	0.84
rt+va	No 15(43	15(43)	20(57)	35	0.64
Others	Yes	6(67)	3(33)	9	0.107
Oulers	No	10(36)	18(64)	28	0.107

Ox-cloxacillin, Ci-ceftriaxone, Va-vancomycin, Ak-amikacin, Pt-piperacillin+tazobactam.

Table 5: Comparison of outcomes between pleural fluid culture positive and culture negative cases

Outcor	ne	Culture positive (n=14)	Culture negative (n=23)	p value*
Median duration of ICD days		9(3-29)	5(0-11)	0.020
Median time taken for defervescence		7(3-32)	7(0-21)	0.660
Median duration of hospital stay		20(7-38)	14(6-32)	0.059
aomaliantian	Yes	8	12	0.769
complication	no	6	11	0.769
0114004W.	yes	5	6	0.713
surgery		9	17	0.713

<sup>\*</sup>p<0.05 was considered as significant.

### What this study adds?

- Though Staphylococcus aureus still remains as the predominant organism causing empyema thoracis in developing, MRSA has been in rising trend.
- Anti staphylococcal agent must be considered in the initial antibiotic combination to treat empyema.

<sup>\*</sup>p value < 0.05 is significant

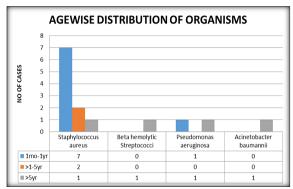


Figure 1: Age wise distribution of organisms isolated from pleural fluid

# **DISCUSSION**

Empyema thoracis is one of the common complications of bacterial pneumonia in children. It was more common in in the age group of less than 5 years(73%) which was comparable with other studies. [5,6] The occurrence of empyema was distributed equally among the males and females. No gender preponderance was found in few studies by Satpathy et al and Goyal et al.<sup>[7,8]</sup> However many other studies showed that the incidence of empyema is more prevalent in males. [9] There was no significant difference in the outcome between those cases who were malnourished and cases who were not malnourished. However the previous study conducted in our institute by Padmini et al. found that malnutrition affects the adverse outcome in patients with empyema.<sup>[7]</sup>

The most common symptom was fever followed by cough and respiratory distress similar to the findings in few studies, [8,9,10] 57% of the cases in this study had received antibiotics prior to admission which is comparatively twice the number compared to the study done Baranwal et al.<sup>[5]</sup> This probably reflects the increasing awareness of pneumonia and early health care seeking behavior. Leucocytosis was present in 21 patients (59%) and Neutrophilia in 19 cases (51%). It was comparatively higher compared to a study by Hardie et al.[11] Though bacterial pneumonia and empyema are more often expected to have neutrophilic leucocytosis, nearly 30-60% may not have it at admission. No organisms were isolated from blood culture taken from all these cases. The pleural fluid culture yield in our study was 38%. This was comparable with the recent study by Narayanappa et al.<sup>[5]</sup> Low culture yield of bacteria from pleural fluid and blood culture might be due to less number of bacteria in exudate and blood with prior antimicrobial use.

Out of 14 culture positive cases, the commonest organism isolated in our study was Staphylococcus aureus (27%), followed by Pseudomonas aeruginosa(5%).Out of 10 cases of Staphylococcus aureus, 3(30%) were MRSA. It was similar to study done in India by Narayanappa et al. where 30% organisms isolated were staphylococcus. In the

developing countries, staphylococcus has remained the commonest cause of empyema, however the isolation of MRSA has been rising (30% Vs 6% in prior study). [4] Also Pneumococcus is a less common cause of empyema thoracis in children unlike developed countries. [12] Among MRSA, all the isolates were sensitive to vancomycin, 67% were sensitive to clindamycin, 33% were sensitive to gentamicin and tetracycline. The clinical outcome did not significantly vary between patients with MSSA and MRSA(p<0.05).

Tubercular empyema was seen in 2 cases (5%) with frank pus and AFB stain was positive in 2 cases. TB PCR and mycobacterial culture were negative. Gene expert was positive in one case. ADA was more than 40 U/L in both the cases. Tuberculous empyema can have an acute presentation. It should kept in mind especially when treating older children with normal leucocyte count with lymphocytic exudate. [13]

Among the various empirical antibiotic regimens, commonly used were ceftriaxone with cloxacillin (49%) and cloxacillin with amikacin (16%). Second line antibiotics were used based on clinical response and culture report. Of the cases who received ceftriaxone and cloxacillin as first line therapy, 27% needed 2nd line antibiotics in contrast to 33 % of receiving cloxacillin and amikacin. There was no significant difference in the requirement of second line antibiotics on comparison of various antibiotic regimens. Padmini et al observed that 72% of cases receiving cloxacillin and gentamicin could be discharged within 4 weeks in comparison to only 36% cases treated with penicillin and gentamicin.

Since staphylococcus was the predominant organism in our study and in other studies in tropical countries as well, [5,6,14] we suggest that anti staphylococcal agent must be administered in the initial antibiotic regimen as the empirical therapy in tropical countries like India. Aminoglycoside especially amikacin may be added for its synergistic effect. The empirical choice of antibiotics should be based on the local culture and sensitivity pattern and should be directed against Staphylococcus aureus. Early shifting over to oral antibiotics from parenteral therapy after defervescence and clinical improvement would help in reducing the cost of treatment and also the duration of hospital stay.

This study emphasizes that early stages of empyema could be treated with antibiotics and or ICD for 4-6 weeks without the need of surgical intervention and these patients do not develop any complications on follow up.<sup>[14]</sup> Hence the morbidity related to empyema is less in children. Most of the children with empyema thoracis recover without any long term effects.

The limitation of the study was clinical outcomes between various organisms could not compared since sample size was less.

### **CONCLUSION**

**Ethics clearance:** Institutional Ethics committee, JIPMER; No.JIP/IEC/SC/2014/1/470, dated 04/03/2014

Contributors: ML and NB: Designed the study, analysed the data and drafted the manuscript; KS: collected the data and reviewed the literature. NB: conceptualized the study and critically reviewed the manuscript; SS: provided guidance regarding laboratory evaluation and also critically reviewed the manuscript. All authors approved the final version of the manuscript.

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