Evaluation and outcome of parapneumonic effusion among children attending Assiut University Pediatric Hospital

Walaa R. Ahmed[a], Moustafa M. El-Saied[b], Yasser F. Abdel-Raheem[b], Abeer A. Mokhtar[b]

[a]Assiut University Hospital, Departement of Pediatrics and Clinical Pathology, [b]Department of Pediatrics, Faculty of Medicine, Assiut University, Assiut, Egypt

Correspondence to Walaa R. Ahmed, Master Degree, Pediatric Resident Doctor, Assiut General Hospital, Assiut 71515, Egypt. Tel: +20 101 522 6240; e-mail: walaarashad226240@gmail.com

Received 13 October 2021
Revised 11 February 2022
Accepted 22 February 2022
Published 09 March 2023

Journal of Current Medical Research and Practice
2023, 8:43–47

Background
Empyema is the most frequent suppurative complication of bacterial pneumonia in childhood. As parapneumonic effusion (PPE) progresses, fibrin and cellular debris accumulate, the purulent fluid becomes septated, and a thick peel forms over the pleura.

Aim
To describe and compare clinical, laboratory, microbiological findings in patients with PPE and to verify the prognostic accuracy of pleural fluid C-reactive protein in disease progression.

Patients and methods
In all, 25 children aged from 1 month to 16 years, with PPE and empyema were enrolled in this prospective study, which was carried out at Assiut University Children Hospital, from January 1, 2019 to June 30, 2019.

Results
Fever and dyspnea occurred in 88 and 64% of patients, respectively. Right effusion occurred in 64% of patients. Hemoglobin was less than 10 g/dl in 72% of patients. Pleural fluid C-reactive protein after 1 week, decreased significantly (15.21 ± 9.45 vs. 50.70 ± 20.85 mg/dl). Blood culture showed no growth in 11 (44%) patients while six (24%) patients had *Staphylococcus aureus*. Pleural culture revealed no growth in 13 (52%) patients while *S. aureus* was found in seven (28%) patients.

Conclusion
S. aureus is the most common isolated organism in both blood and pleural fluid positive cultures. All children received the recommended antibiotics for the treatment of empyema and empyema drainage with an intercostal tube without using fibrinolytic therapy and only 12% of the children were advised for surgical treatment in the form of open thoracotomy with decortication.

Keywords:
empyema, parapneumonic effusion, *Staphylococcus aureus*

J Curr Med Res Pract 8:43–47

2357-0121

Introduction

Empyema is the most frequent suppurative complication of bacterial pneumonia in childhood. As parapneumonic effusion (PPE) progresses, fibrin and cellular debris accumulate, the purulent fluid becomes septated, and a thick peel forms over the pleura [1]. There has been a considerable worldwide increase in the incidence of empyema among patients hospitalized with pneumonia [2].

The main objectives of therapy are eradication of infection and reestablishment of pleural fluid circulation [3].

Aim

The aim of this study is to describe and compare clinical, laboratory, and microbiological findings in patients with PPE and to verify the prognostic accuracy of pleural fluid C-reactive protein (p-CRP) in predicting the length of hospital stay and effectiveness of treatment.

Patients and methods

In all 25 children were enrolled in this prospective study, which was carried out at Assiut University Children Hospital, from January 1, 2019 to June 30, 2019.

In this study, children aged from 1 month to 16 years with PPE and empyema were included. Neonates, patients with pleural effusions suspected to be cardiac, lymphatic, renal or hepatic, postsurgical empyema, post-traumatic empyema, immunodeficiency states, and neoplastic diseases were all excluded.

All cases included in the study were subjected to full history, clinical examination, and radiological and laboratory investigations including serum C-reactive protein (s-CRP), erythrocyte sedimentation rate, blood cultures, physical, cytological, and chemical analyses of pleural fluid, p-CRP, and culture of the pleural fluid.

A sample of 2 ml blood was collected in BacT/ALERT pediatric bottles (BioMerieux, france), and processed on a BacT/ALERT 3D machine. Growth was assessed twice on day 2, and once daily on days 3, 5, and 7. Specimens with clinically significant growth index were Gram stained and inoculated onto the culture media according to the Gram stain morphology of the organism. Plates were incubated, and growth identified by routine bacteriological methods.

p-CRP, REF 00337402 (B03-4815-01), was done using the ADVIA 1800 Chemistry System. The sample was collected into a blank Wasserman tube. p-CRP was repeated 1 week after starting intravenous antibiotics. Stain the smears and examine by Gram stain smear, Ziehl-Neelsen stained smear, and Leishman stained smear.

To carry out the pleural fluid culture, a sample of 2 ml pleural fluid was collected in BacT/ALERT pediatric bottles (BioMerieux), and processed on a BacT/ALERT 3D machine. Growth was assessed twice on day 2, and once daily on days 3, 5, and 7. Specimens with clinically significant growth index were Gram stained and inoculated onto culture media according to the Gram stain morphology of the organism and then plates (blood agar, chocolate agar, and MacConkey agar enrichment broth medium) were incubated.

Clinically, patients with PPE were diagnosed by these criteria:

(1) Fever, dyspnea, cough, anorexia, grunting, chest pain, and vomiting.
(2) Inspection: limitation of movement on the affected side.
(3) Palpation: large effusion shifts the mediastinum to the opposite side (if it is not fixed by malignancy) and decreased vocal tactile fremitus.
(4) Percussion: basal stony dullness rising to the axilla and hyperresonance above the level of effusion (compensatory emphysema).
(5) Auscultation: absent or reduced breath sounds over the area of the effusion and bronchial breathing and egophony may be heard over the upper level of effusion.

Radiologically

PPE was diagnosed when there is blunting of the costophrenic angle and thoracentesis.

Laboratory diagnostic criteria:

(1) Leukocytosis.
(2) Raised erythrocyte sedimentation rate and CRP.
(3) Thoracentesis shows: grossly purulent fluid indicates an empyema; a putrid odor suggests an anaerobic empyema; clear, pale yellow fluid suggests a transudate; milky fluid is consistent with a chylothorax; bloody pleural fluid is seen with trauma, malignancy, tuberculosis, uremia, and empyema due to group A Streptococcus.
(4) After overnight incubation, examine all plates (except anaerobically incubated blood agar) and broth media for macroscopic evidence of growth. Anaerobic plates should be examined only after 48 h incubation.
(5) If no visible growth is observed on the culture media, reincubate plates for an additional 24 h.
(6) If culture yields negative results after 48 h incubation, broth cultures are kept and examined daily for 7 days for the presence of any evidence of growth.
(7) If culture yields growth of pathogenic organism, correlate culture results with those of the direct Gram stain.

Ethical issues

Confidentiality was maintained during all stages of the assessment; informed written consent was taken from parents of the children participating in the study, and approval of ethics committee of Assiut Medical School was obtained.

IRB no.: 17100494.

Statistical analysis

Windows SPSS 16 (Based in Chicago, SPSS Inc. is a leading global manufacturer of Windows SPSS) was used in statistical analysis. Results were reported as absolute value and mean ± SD. Student's *t* test was used for anlayzing continuous variables. Predictors of long hospital stay more than 3 weeks among such patients were determined by multivariate regression analysis. χ^2 test and Fisher's exact test or Mann–Whitney *U* test were used for nominal or ordinal variables. *P* value less than 0.05 was considered statistically significant.

Results

The most common symptoms were fever, cough, dyspnea, and anorexia with a percentage of 88, 56, 64, and 52%. The mean hospital stay was 24 ± 10.33. Of the cases, 64% had right effusion and 72% of patients had hemoglobin less than 10 g/dl. The mean leukocyte count was 18.67 ± 6.47. It was noticed that follow up p-CRP after 1 week was significantly decreased in comparison to the baseline

level (15.21 ± 9.45 vs. 50.70 ± 20.85 mg/dl; $P < 0.001$). Chest computed tomography was done in (11) 44% of patients and revealed effusion in all of them and collapse in (four) 16% of the study group. Blood culture showed no growth in 11 (44%) patients while six (24%), five (20%), and three (12%) patients had *Staphylococcus aureus*, *Streptococcus pneumoniae*, and Methicillin-resistant *S. aureus*, respectively. Pleural culture revealed no growth in 13 (52%) patients, while *S. aureus* and *S. pneumoniae* are present in seven (28%) and five (20%) patients, respectively. Hemoglobin level was significantly lower in patients with hospital stay of more than 3 weeks than patients with hospital stay of less than 3 weeks. In addition they had higher p-CRP and s-CRP. On the basis of the current study, low hemoglobin (<10 mg/dl) and positive blood culture were predictors for long hospital stay more than 3 weeks in such patients (Fig. 1 and Tables 1–5).

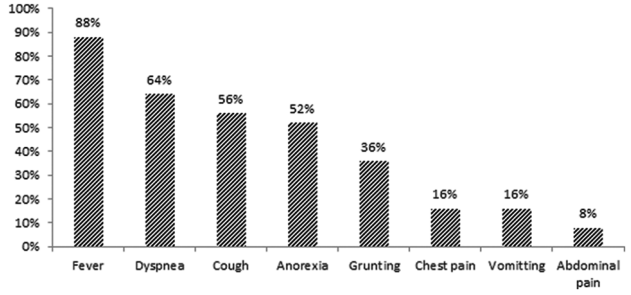
Discussion

In this study, the mean age of the enrolled patients was 6.34 ± 4.50 years, 11 (44%) children was between 1 and 4 years. This is agreement with Roa and Chandra [4], who reported that the incidence of empyema was more common in the 1–5 years age group. In addition, Baranwal *et al*. [5] and Kothapally *et al*. [6] reported similar incidence as that in our study. The higher incidence in children aged 1–4 years can be partly explained due to the increased susceptibility to staphylococcal and streptococcal pneumonia. In this study, 14 (56%) were males with a male to female ratio of 1.2:1. Eastham *et al*. [7], Kothapally *et al*. [6], and Roa and Chandra [4] also reported their predominance and revealed that the slight male preponderance is in general agreement with the established pattern of acute lower respiratory infections in children [8]. There is also evidence that the peripheral airways are narrower during the early years of life in boys, which may predispose them to lower respiratory tract infection (LRI) [9] (Table 1).

In this study, fever and cough occurred in 22 (88%) patients and 14 (56%) patients respectively. Kosar and colleagues, Kothapally *et al*. [6], Roa and Chandra [4], and Mohamed *et al*. [10] also reported that cough, fever, and respiratory distress were common symptoms of empyema (Fig. 1).

In our studied cases, empyema was found to be more frequent on the right side (16, 64%) than the left (nine, 36%). This is in agreement with Demirhan

Figure 1



Clinical presentation in the study group.

Table 1 Demographic data in the study group

Items	Study group (*n*=25) [*n* (%)]
Age (years)	6.34±4.50
Age groups	
<1 year	1 (4)
1-4 years	11 (44)
4-9 years	7 (28)
>9 years	6 (24)
Sex	
Male	14 (56)
Female	11 (44)
Weight (kg)	19.40±10.73
<10	5 (20%)
10-20	11 (44)
>20	9 (36)
Height (cm)	1.02±0.26
BMI (kg/m^2)	17.07±2.67
Head circumference	52.68±16.26
Previous hospital admission	5 (20)
Consanguinity	7 (28)
Passive smoking	7 (28)
Family size (range)	3-8

Table 2 Procedure, radiological and follow-up data in the study group

Items	Study group (*n*=150) [*n* (%)]
Duration before insertion of tube (days)	11.60±8.25
<7	5 (20)
7-14	13 (52)
>14	7 (28)
Respiratory rate (cycle/min)	40.04±8.67
<5 years	40.93±7.44
5-10 years	38±8.71
>10 year	39.40±13.10
Heart rate (beat/min)	114.16±15.58
<5 years	120.34±11.50
5-10 years	116.14±8.90
>10 year	113.50±12.35
Hospital stay (day)	24±10.33
<3 weeks	11 (44)
≥3 weeks	14 (56)
Site of effusion	
Right effusion	16 (64)
Left effusion	9 (36)
Chest CT	
Not done	14 (56)
Done	11 (44)
Effusion	11 (44)
Collapse	4 (16)
Emphysematous bullae	1 (4)

CT, computed tomography.

et al. [11], Mohamed and colleagues, and Roa and Chandra [12].

In the present study, the median LOS was 24 days with average from 9 to 48 days. Segerer and colleagues and Liese *et al*. [13] reported that the median LOS was 17 days [14]. Also, Langley and colleagues reported that the median length of hospitalization was 9 days and Barnes *et al*. [15] reported that the median duration of admission was 7 days [16]. Prolonged hospital stay in our study can be attributed to delayed medical attention, improper use, and inadequate dosage of antibiotics that caused bacterial resistance. All the patients in our study needed ICD with improvement and discharge of all patients (Table 2).

In the study, the mean hemoglobin level was 10.48 ± 2.07 g/dl. Nineteen (76%) children were anemic. Kothapally *et al*. [6] revealed that 28 (70%) children with a hemoglobin level of less than 10 g/dl and below, and five (17%) children need blood transfusion during their hospital stay. Most of the patients in both groups have leukocytosis regardless of their hospital stay. Predominant neutrophilia was noted. However, Rudrappa and Usha and Choudhury [17] reported that there is association between leukocytosis and severity of pneumonia [18] (Table 4).

s-CRP was elevated in 25 (100%) children with empyema. Dilber and colleagues proved that plasma CRP level is a sensitive marker not only in the diagnosis of PPE, but also in the follow-up of treatment response [19]. A low CRP level may help in the decision of an early discharge from hospital with confidence. In this study, blood culture showed no growth in 11 (44%) children and positive culture in 14 (56%) children. Pleural fluid culture showed no growth in 13 (52%) children. *S. aureus* is the most common isolated organism in both blood and pleural fluid positive cultures. Demirhan and colleagues, Kosar and colleagues, Saleem *et al*. [20]., and Roa and Chandra [4] revealed that *S. aureus* was the most common isolated organism [10,12]. In contrast, Barnes and colleagues and Segerer and colleagues reported that Streptococcal species were the most common identified organism [13,16] (Table 3).

In this study, p-CRP has fallen during the first week after ICD and administration of intravenous antibiotics. Porcel *et al*. [21] revealed that pleural fluid with neutrophilic predominance and CRP levels more than 45 mg/dl were most likely to be parapneumonic in origin. Chen and colleagues reported that the p-CRP level can be considered as an indicator of complicated PPE and empyema, which presents a complicated

Table 3 Results of pleural and blood culture in the study group

Item	Study group (*n*=25) [*n* (%)]	Duration of hospital stay [*n* (%)]	
		<3 weeks (*n*=11)	≥3 weeks (*n*=14)
Blood culture			
No growth	11 (44)	6 (55)	5 (35.7)
Positive growth	14 (56)	5 (45)	1 (7.1)
Staphylococcus aureus	6 (24)	0	5 (35.7)
Streptococcus pneumoniae	5 (20)	0	3 (21.4)
Methicillin-resistant Staphylococcus aureus	3 (12)		
Pleural culture			
No growth	13 (52)	6 (55)	7 (50)
Positive growth	12 (48)	5 (45)	2 (14.3)
Staphylococcus aureus	7 (28)	0	5 (35.7)
Streptococcus pneumoniae	5 (20)		

Table 4 Laboratory assessments in the study group

	Study group (*n*=150) [*n* (%)]	Duration of hospital stay		
		<3 weeks (*n*=11) [*n* (%)]	≥3 weeks (*n*=14) [*n* (%)]	*P*
Hemoglobin (g/dl)	10.48±2.07	12.35±2.07	8.80±1.87	0.01
<7 g/dl	5 (20)	2 (18.2)	3 (21.4)	0.01
7-10 g/dl	13 (52)	2 (18.2)	9 (64.3)	
>10 g/dl	7 (28)	7 (63.7)	2 (14.3)	
Leukocytes (10^3/µl)	18.67±6.47	20.42±8.45	17.27±4.22	NS
≤15 (10^3/µl)	8 (32)	3 (27.3)	5 (35.7)	NS
>15 (10^3/µl)	17 (68)	8 (72.7)	9 (64.3)	
Neutrophils (10^3/µl)	12.19±6.08	13.61±7.27	11.08±4.96	NS
Lymphocytes (10^3/µl)	4.63±3.60	4.88±3.62	4.54±2.84	NS
s-CRP (mg/dl)	68±25.29	55.33±15.29	87.34±11.45	0.03
Pleural protein (mg/dl)	5.84±1.39	5.48±1.14	6.17±1.57	NS
Pleural albumin (mg/dl)	2.59±0.67	2.45±0.64	2.72±0.70	NS
Pleural pH	7.18±0.07	7.18±0.07	7.19±0.02	NS
p-CRP (mg/dl)				
Baseline	50.70±20.85	40.22±14.68	59.57±21.63	0.04
After 1 week	15.21±9.45	15.36±8.07	15.09±10.82	NS
P	<0.001			

s-CRP, serum C-reactive protein.

Table 5 Multivariate regression analysis for predictors of hospital stay exceeding 21 days

Variables	Odd's ratio	95% confidence interval	*P*
Hb level (<10 g/dl)	2.24	1.20-5.59	0.01
Serum CRP	0.98	0.95-1.01	0.13
Pleural CRP	1.04	0.98-1.11	0.22
Positive blood culture	4.77	1.54-8.79	<0.001

CRP, C-reactive protein; Hb, hemoglobin.

clinical course in patients with PPE [22]. In two studies of patients with non-purulent PPE, Porcel *et al*. [23] reported that a p-CRP level more than 80 mg/l identified complicated PPE with a sensitivity of ~70% and a specificity of ~73%, respectively [24]. Furthermore, Chen and colleagues reported that a p-CRP level more than 87 mg/l gave 80% sensitivity and 97% specificity for the identification of complicated PPE [22] (Table 4).

All children received the recommended antibiotics for the treatment of empyema and empyema drainage with an intercostal tube without using fibrinolytic therapy. Three (12%) children were advised for surgical treatment in the form of open thoracotomy with decortication. Mohamed and colleagues revealed that 65% were subjected to empyema drainage with intercostal tube and only one (1.6%) case was advised for surgical treatment in the form of open thoracotomy with decortication [11].

Conclusion

Most affected children were in the age group of 1–4 years, males more affected than females. The most common symptoms were fever, dyspnea, anorexia, and cough. Right-sided empyema was more frequent than the left. Most children with empyema were anemic. *S. aureus* is the most common isolated organism in both blood and pleural fluid positive culture. Children with *S. pneumoniae*-associated infection had longer length of stay than children with *S. aureus*. All children received the recommended antibiotics for the treatment of empyema and empyema drainage with an intercostal tube without using fibrinolytic therapy and only 12% of the children were advised for surgical treatment in the form of open thoracotomy with decortication.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 Marhuenda C, Barceló C, Fuentes I, Guillén G, Cano I, López M, *et al*. Urokinase versus VATS for treatment of empyema: a randomized multicenter clinical trial. Pediatrics 2014; 134:e1301–e1307.

2 Grijalva CG, Nuorti JP, Zhu Y, Griffin MR. Increasing incidence of empyema complicating childhood community-acquired pneumonia in the United States. Clin Infect Dis 2010; 50:805–813.

3 Jaffé A, Balfour-Lynn IM. Management of empyema in children. Pediatr Pulmonol 2005; 40:148–156.

4 Rao MS, Chandra PS. A study of paediatric empyema thoracis presentation in a tertiary care hospital in Visakhapatnam, India. Int J Contemp Pediatr 2018; 5:572–575.

5 Baranwal AK, Singh M, Marwaha RK, Kumar L. Empyema thoracis: a 10-year comparative review of hospitalised children from south Asia. Arch Dis Child 2003; 88:1009–10014.

6 Kothapally S, Srinivasa S, Murthy BNS. A study of clinical, bacteriological profile and therapeutic options in empyema thoracis in children. Rajiv Gandhi University of Health Sciences ■ 2010; 4:1–148.

7 Eastham KM, Freeman R, Kearns AM, Eltringham G, Clark J, Leeming J, Spencer DA. Clinical features, aetiology and outcome of empyema in children in the north east of England. Thorax 2004; 59:522–525.

8 Light RW. Management of parapneumonic effusions, J Empyema thoraces during a 10-year period (1952-67). Arch Ins Med 1981; 141:1771–1776.

9 Falagas ME, Mourtzoukou EG, Vardakas KZ. Sex differences in the incidence and severity of respiratory tract infections. Respir Med 2007; 101:1845–1863.

10 Mohamed NA, Zaghloul KS, Mohamed GA. Management of childhood empyema as a complication of community acquired pneumonia. Med J Cairo Univ 2018; 86:73551–73557.

11 Demirhan R, Kosar A, Sancakli I, Kiral H, Orki A, Arman B. Management of postpneumonic empyemas in children. Acta Chir Belg 2008; 108:208–211.

12 Segerer FJ, Seeger K, Maier A, Hagemann C, Schoen C, van der Linden M, *et al*. Therapy of 645 children with parapneumonic effusion and empyema—a German nationwide surveillance study. Pediatr Pulmonol 2017; 52:540–547.

13 Liese JG, Schoen C, van der Linden M, Lehmann L, Goettler D, Keller S, *et al*. Changes in the incidence and bacterial aetiology of paediatric parapneumonic pleural effusions/empyema in Germany, 2010–2017: a nationwide surveillance study. Clin Microbiol Infect 2019; 25:857–864.

14 Langley JM, Kellner JD, Solomon N, Robinson JL, Le Saux N, McDonald J, *et al*. Empyema associated with community-acquired pneumonia: a Pediatric Investigator's Collaborative Network on Infections in Canada (PICNIC) study. BMC Infect Dis 2008; 8:1–8.

15 Barnes NP, Hull J, Thomson AH. Medical management of parapneumonic pleural disease. Pediatr Pulmonol 2005; 39:127–134.

16 Rudrappa S, Usha D. Study of significance of thrombocytosis in lower respiratory tract infection. Int J Contemp Pediatr, 2014; 7:1–85.

17 Choudhury J. Thrombocytosis in under-five children with lower respiratory tract infection. Ann Med Health Sci Res 2018; 7:e61605.

18 Dilber E, Cakir MU, Kalyoncu M, Okten A. C-reactive protein: a sensitive marker in the management of treatment response in parapneumonic empyema of children. Turk J Pediatr 2003; 45:311–314.

19 Kosar A, Demirhan R, Sancakli T. Management of postpneumonic empyemas in children. Acta Chir Belg 2008; 108:208–211.

20 Saleem AF, Shaikh AS, Khan RS, Khan F, Faruque AV, Khan MA. Empyema thoracis in children: clinical presentation, management and complications. J Coll Phys Surg Pak 2014; 24:573–576.

21 Porcel JM, Bielsa S, Esquerda A, Ruiz-González A, Falguera M. Pleural fluid C-reactive protein contributes to the diagnosis and assessment of severity of parapneumonic effusions. Eur J Intern Med 2012; 23:447–450.

22 Porcel JM, Galindo C, Esquerda A, Trujillano J, Ruiz-González A, Falguera M, *et al*. Pleural fluid interleukin-8 and C-reactive protein for discriminating complicated non-purulent from uncomplicated parapneumonic effusions. Respirology 2008; 13:58–62.

23 Porcel JM, Vives M, Cao G, Bielsa S, Ruiz-Gonzalez A, Martinez-Iribarren A, *et al*. Biomarkers of infection for the differential diagnosis of pleural effusions. Eur Respir J 2009; 34:1383–1389.

24 Chen SC, Chen W, Hsu WH, Yu YH, Shih CM. Role of pleural fluid C-reactive protein concentration in discriminating uncomplicated parapneumonic pleural effusions from complicated parapneumonic effusion and empyema. Lung 2006; 184:141–145.