Clinical Profile and Outcome of Children with Parapneumonic Effusion

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KEYWORDS
Parapneumonic effusion, community acquired pneumonia, empyema, pleural effusion,

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ABSTRACT

Parapneumonic effusions frequently occur as complications of pneumonia. Data from developing countries is limited. The purpose of this paper is to review the epidemiological and clinical profile of parapneumonic effusions among children admitted in a tertiary government hospital.

Methodology: Medical records of 72 children diagnosed with parapneumonic effusions from 2005-to-2009 were obtained. Demography, clinical presentations, diagnostics, treatment modalities, outcomes, etiology and antibiotic susceptibilities were analyzed using descriptive statistics. Comparison of purulent effusion and empyema was done using parametric or non-parametric statistics, accordingly.

Results: There were 106 children discharged with a diagnosis of parapneumonic effusion. Of the 96 medical records available, 72 patients fulfilled the criteria for parapneumonic effusions. Only 53 patients submitted pleural fluid for analysis: 29 cases were empyema, while 24 cases were purulent effusion; mean age was 9.66 years. Fever (90.28%), cough (69.44%), and dyspnea (66.67%) were the most common clinical presentations. Forty-four patients underwent thoracentesis while 37 children had closed-tube thoracostomy. Methicillin-resistant *Staphylococcus aureus*(MRSA) was the most commonly isolated organism from the pleural fluid cultures (9.26%) and blood cultures (6.25%). Patients with purulent effusion were treated with a combination of antibiotics and anti-TB meds (75%).Majority of patients with empyema were treated with antibiotics alone (79.31%). Earlier improvement and shorter hospital stay were observed among patients with purulent effusion.

Conclusion: Parapneumonic effusions occurred in 6.80% of hospitalized children with pneumonia; 54.72% of which were empyema and 45.28% were purulent effusion. MRSA was the most commonly isolated organism. Chest imaging, pleural fluid analysis and cultures, and blood cultures were important diagnostic procedures. The mainstays of treatment were medical, surgical or both, depending on the severity of effusion. Prompt diagnosis and management could account for favorable clinical outcomes.

INTRODUCTION

In developed countries, parapneumonic effusions occur in 10%-to-40% of bacterial pneumonia, with up to 60% of effusions resulting in the formation of empyema in all age groups.[1-3] *Streptococcus pneumoniae* is the predominant cause of bacterial pneumonia worldwide and it is commonly implicated as the cause of parapneumonic effusions and empyema in developed countries and in certain middle-income countries such as Brazil.[4] The etiology of empyema is closely correlated with that of community acquired pneumonia (CAP). Community acquired methicillin-resistant *Staphylococcus aureus* (MRSA) has shown a proportional increase as the cause of empyema and parapneumonic effusions.[5-8]

Data from developing countries is limited.

The lack of consensus on the optimal management of purulent effusions and empyema has generated renewed interest in the subject, especially with regard to changes among the etiologic agents causing empyemas in children. This five year experience (2005-2009) from a tertiary, government referral-hospital seeks to re-evaluate the clinical and microbial profile of purulent effusions and empyema in children, and review the existing management guidelines, with emphasis on interventions pertinent to resource-limited settings.

MATERIALS AND METHODS

Study Design: This is a retrospective study of pediatric patients (0-18 years) who were admitted at UP-PGH from 2005 to 2009 and discharged with a final diagnosis of CAP with parapneumonic effusion, pleural effusion, pyopneumothorax, pleurisy or empyema thoracis. Medical records were retrieved based on data obtained from the logbooks of the pediatric wards, medical record section, microbiology research laboratory section and radiology section. The demographic profile (age, sex, residence), presenting signs and symptoms, results of imaging studies, pleural fluid analysis, blood and pleural fluid cultures, antibiotics and surgical interventions were retrieved and recorded. Patient confidentiality was strictly observed by using initials and/or codes.Data were recorded using standardized data recording forms. The study was reviewed and approved by the institution's technical and ethical review board.

Exclusion Criteria: Patients with the following conditions were excluded: (1) those receiving chemotherapy or radiotherapy secondary to malignancy; (2) those diagnosed with effusions secondary to chronic conditions like nephrosis, liver cirrhosis, connective tissue diseases and congestive heart failure; (3) those with effusions caused by trauma and drugs like phenytoin, nitrofurantoin, amiodarone, metrotrexate, and bleomycin; and /or (4) those diagnosed with nosocomial pneumonia.

DEFINITION OF TERMS

The classification of pleural effusion as to ***transudate***, ***purulent effusion*** or ***empyema*** was based on the properties of pleural fluid such as its potential of hydrogen (pH), measurements of glucose (mg/dl), fluid lactose dehydrogenase (LDH), protein fluid /serum ratio, LDH fluid/serum ratio, fluid white blood cells (WBC) and percentage of peripheral mononuclear cells (PMN) and lymphocytes.

Parapneumonic effusionis a general term, referring to any pleural exudative process resulting from an inflammatory process in the lungs,[9] which includes purulent effusion and empyema.

Clinical Improvement **is** evident if there is defervescence, decrease in respiratory rate, improvement in appetite, resumption of activity.

Failureisdefined asdeterioration or no changein respiratory rate, appetite, activity and fever patterns, and death.

Table 1. Evaluation of Transudate, Purulent Effusion and Empyema in the Pleural Fluid.[9]

Appearance	Serous	Thin exudates	Turbid
Mean WBC	1000	5300	25,500
PMN (%)	50	>90	>95
Protein (Fluid/serum ratio)	<0.5	>0.5	>0.5
LDH (Fluid/serum ratio)	<0.6	>0.6	>0.6
LDH (IU/L)		>200	>200
Glucose(mg/dl)	>60	<60	<60
pH	7.4-7.5	7.35-7.45	7.2-7.35

STATISTICAL ANALYSIS

Prevalence of purulent effusion and empyema was computed based on the total number of children who were aged zero-to-18 years, with CAP and admitted at PGH from 2005-to-2009. Descriptive statistics was used to analyze trends in prevalence of purulent effusions and empyema, differences in clinical and microbial profile and outcomes for the covered periods. Data were encoded and tallied in SPSS version 10 for Windows. For nominal data, frequencies and percentages were computed. For numerical data, mean ± SD, median and range were generated. Comparison of the different variables was done using t-test, chi-square test, Mann Whitney U test, or Fisher's exact test as appropriate.

RESULTS

From January 1, 2005 to December 31, 2009, a total of 1059 pediatric admissions were diagnosed to have CAP. Of these cases, 106 patients were discharged with a diagnosis of parapneumonic effusion. There were also 96 (90.57%) charts retrieved and among those, 72 patients (75%) fulfilled the inclusion criteria of parapneumonic effusion. Nineteen cases were not classified because of non-submission of pleural fluid and, thus, were not included in the analysis. Of the 53 patients who submitted pleural fluid for analysis, empyema occurred in 29 (54.72%) while purulent effusion was observed in 24 (45.28%)

Table 2. Demographic and Clinical Profile of Patients with Purulent Effusion and Empyema

	PURULENT EFFUSION Frequency N=24	EMPYEMA Frequency N=29	P-value
Age (years) Mean ± SD	12.39 ± 4.74	7.98 ± 6.49	0.008
Distribution of Age			0.020
<1 y/o	0	6	
1-4	0	5	
5-10	7	5	
11-14	5	3	
15-18	12	10	
Sex			0.160
Male	13	21	
Female	12	8	
Previous consultation Yes	22	26	1.000
No	2	3	
Antibiotics in the last 3 months			0.770
Yes	15	17	
No	9	12	
Duration of Illness prior admission (days) Mean ± SD(Median)	49.42 ± 80.50(15)	28.10 ± 42.26(12)	0.100

The mean age of patients was 9.66 ± 6.41 years with male predominance (62.5%). Purulent effusions were commonly observed in 12.39 ± 4.74 years old while empyema was more common in children aged 7.98 ± 6.49 years. The place of residence, previous consultations, antibiotic intake in the last three months and duration of illness prior admission were not

significantly different in those with purulent effusion or empyema.

Table 3. Conditions identified in patientswith purulent effusion and empyema.

CONDITIONS	PURULENT EFFUSION Mean (%) N=24	EMPYEMA Mean (%) N=29	P-value
PTB Exposure			
With Exposure	12 50.0%)	8 (27.6%)	<0.0001
W/O Exposure	10 (41.7%)	14 (48.3%)	
Unknown	2 (8.3%)	7 (24.1%)	
EPI Immunization			0.190
Complete	8 (33.3%)	12(41.38)	
Incomplete	9 (37.5%)	8(27.59)	
Unknown	7 (29.2%)	5(17.24)	
None	0	4(13.79)	
Underlying Illness			0.920
Present	8	10	
Absent	16	19	

Table 3 shows the conditions that were present in patients who developed purulent effusion and empyema. Overall, 28 patients were exposed to pulmonary tuberculosis (PTB). A higher proportion of patients with purulent effusion were exposed to PTB (50%) compared to those with empyema. Only 19 patients (67.86%) had positive tuberculin skin test (TST). Skin infections were observed to be two times more common in the empyema group, although this was not statistically significant. Complete Expanded Program of Immunization (EPI) means that the patient received one dose of BCG, three doses of DPT, three doses of OPV, three doses of Hepatitis B and one dose of measles vaccine. HIB vaccine was administered to one patient and none had received pneumococcal vaccines. For those with history of immunization, all received BCG. There were four patients with empyema who had not received any vaccination.

Table 4.Signs and symptoms in purulent effusion and empyema.

SIGNS AND SYMPTOMS	PURULENT EFFUSION Frequency N=24	EMPYEMA Frequency N=29	P-Value
Fever	22	28	0.584
Difficulty of breathing	15	24	0.096
Cough	13	19	0.400
Weight loss	10	4	0.022
Chest pain	10	4	0.022
Tachypnea	4	12	0.050
Anorexia	4	8	0.344
Back pain	4	2	0.392
Easy fatigability	3	5	0.715
Weakness	3	2	0.648
Abdominal pain	3	2	0.648
Orthopnea	3	1	0.317
Bipedal edema	2	0	0.200
Cyanosis	1	2	1.000
Irritability	0	2	0.494
Pallor	0	2	0.494

The signs and symptoms of purulent effusion and empyema are presented in Table 4. In general, fever was the most frequent symptom in 65 (90%) cases, followed by coughing in 50 (69%), and difficulty of breathing in 48 (67%). In order of decreasing frequency, tachypnea, anorexia, weight loss and chest pain were also observed. Only weight loss and chest pain were noted to be significantly more common among those with purulent effusion while tachypnea was significantly more common in patients with empyema. Other signs and symptoms were comparable among those with purulent and those with empyema.

There was no significant difference in the number of patients who underwent chest imaging studies among those with effusion and empyema. All patients had chest x-ray. Chest ultrasonography was carried out in 20 of

patients with purulent effusion and24 among those with empyema. Chest CT scans were done in four patients and showed pleural effusion with loculations, septations, endobronchial TB with consolidation, and bronchiectatic changes with atelectasis and consolidation.

Table 5.1.Concomitant chest x-ray findings in purulent effusion and empyema.*

FINDINGS	PURULENT EFFUSION N=24	EMPYEMA N=29	P-Value
Pneumonia	4	4	1.000
Consolidation	0	4	0.117
Atelectasis	0	3	0.242
Pneumohy drothorax	0	3	1.000
Tuberculosis	2	0	0.200
Cyst	0	2	0.494
Loculation	0	1	1.000
Empyema Thoracis	0	1	1.000
Pyopneumo-thorax	0	1	0.452
Emphysema	0	1	1.000

Table 5.2.Concomitant chest ultrasound finding in purulent effusion and empyema.

FINDINGS	PURULENT EFFUSION N=24	EMPYEMA N=29	P-Value
Consolidation	1	10	0.007
Septation	6	8	0.832
Loculation	4	5	1.000
Atelectasis	4	5	1.000
Pneumonia	0	2	0.494
Empyema Thoracis	1	1	000
Pulmonary abscess	0	1	1.000

Chest x-ray results showed pleural effusions in 100% of patients with concomitant findings of pneumonia in 18% (13/72), consolidation in 8.33% (6/72), and atelectasis in 5.56% (4/72). There could be more than two findings in a single radiologic or ultrasonographic reading (Table 5.1). On chest ultrasound, a significantly greater proportion of patients with empyema (10/29) presented with consolidation when compared to those with purulent effusion (1/24) (Table 5.2).

Majority of the patients had unilateral pleural effusions with the right lung more commonly affected in 52.78% (38/72) compared to the left lung in 38.89% (28/72). Involvement of both lungs was observed in 8.33% (6/72). Decreased to absent breath sounds over the affected area were noted in 77.77% (56/72) while rales were heard in 29.17% (21/72). Chest lag was observed in 22.22% (16/72) and decreased tactile and vocal fremitus were elicited in 50% (36/72) of cases.

Although the initial volume drained from patients with empyema was 149.23 ± 238.42 ml compared to 323.96 ± 448.40 ml in cases with purulent effusion, there was no statistical difference between the two groups (p= 0.190).

Overall, there were 132 specimens sent for acid fast bacilli AFB smear. Positive AFB smears were noted in wound discharge (1/1), gastric aspirates (4/18), pleural fluid (3/31), sputum (3/30), and urine specimens (1/22). Among these, sputum or pleural fluid were positive in 2 patients with empyema; and gastric, sputum or wound discharge in 3 patients with purulent effusion. Negative AFB smears were reported in 27 ETA and 3 pericardial fluid/ tissue samples.

Table 6.Pleural fluid analysis results of purulent effusion and empyema

FINDINGS	PURULENT EFFUSION N=24	EMPYEMA N=29	P-Value
Pneumonia	4	4	1.000
Consolidation	0	4	0.117
Atelectasis	0	3	0.242
Pneumohy drothorax	0	3	1.000
Tuberculosis	2	0	0.200
Cyst	0	2	0.494
Loculation	0	1	1.000
Empyema Thoracis	0	1	1.000
Pyopneumo-thorax	0	1	0.452
Emphysema	0	1	1.000

Based on the biochemical evaluation of 53 pleural fluid samples, 24 (45.28%) patients were identified with purulent effusions and 29 (54.72%) cases with empyema. Specimens were not submitted for 19 of

the 72 patients. The measurements of glucose, pH, and lymphocytes were significantly lower in patients with empyema (p<0.0001), while pleural fluid WBC, PMN, LDH and LDH fluid/serum ratio were significantly lower among those with purulent effusion (p<0.0001).

Table 7.1.Culture specimens in purulent effusion and empyema.

CULTURE SPECIMENS	PURULENT EFFUSION No. (%) N=24	EMPYEMA No. (%) N=29	P-Value
Pleural Fluid With			<0.0001
Growth	1(4.17)	15(51.72)	
No Growth	23(95.83)	11(37.93)	
Not Done	0(0)	3(10.34)	
Blood With			0.675
Growth	2(8.33)	5(17.24)	
No Growth	14(58.33)	17(58.62)	
Not Done	8(33.33)	7(24.14)	

Patients with purulent effusion and empyema showed no difference in the yield of organisms from the blood (p=0.675). However, more than 50% (15/29) of empyema cases had isolates from the pleural fluid (p<0.0001).

A total of 48 blood specimens and 53 pleural fluid specimens were sent for cultures. Of the 48 blood samples, 18.75% (9/48) were positive. From the 53 pleural fluid cultures, 30.19% (16/53) were positive: 15 isolates from empyema and one MRSA in thioglycolate from patients with effusion. Only 3 patients had positive cultures from both samples. *Staphylococcussp.* in 14.85% (15/101) was the most commonly isolated organism from both blood and fluid cultures, MRSA comprising 53.33% (8/15) of all *Staphylococcus* isolates. The third most common pathogens were methicillin-resistant *Staphylococcus epidermidis*(MRSE),*Staphylococcus epidermidis*, and *Streptococcus pneumoniae*. TB cultures were done on the following specimens: 25 pleural fluid, 2 sputum, 4 urine, 3 gastric aspirates, one ETA, one pericardial fluid and pericardial tissue; but, all were negative. One patient with purulent effusion grew *Mycobacterium sp.* from wound discharge and the isolate showed sensitivity to streptomycin, isoniazid, rifampicin and ethambutol. The susceptibility patterns of the organisms mostly isolated from blood and fluid cultures are shown in the following tables. (Tables 7.3 and 7.4)

Table 7.2.Isolates of blood and pleural fluids in purulent effusion and empyema.

ORGANISM	BLOOD CULTURES N=48	PLEURAL FLUID CULTURES N=53
	Frequency (%)	Frequency (%)
MRSA	3(6.25)	5(9.26)
Staphylococcus aureus	1(2.08)	2(3.70)
Staphylococcus epidermidis	1(2.08)	1(1.85)
MRSE	1(2.08)	1(1.85)
Streptococcus pneumoniae	1(2.08)	1(1.85)
Enterobacter cloacae	1(2.08)	0
Grp A β Streptococcus	0	1(1.85)
Haemophilusinfluenzae	0	1(1.85)
Stenotrophomonasmaltophilia	0	1(1.85)
Pseudomonas aeruginosa	0	1(1.85)
Acinetobacteriwoffii	1(2.08)	0
Aerococcus	0	1(1.85)
Alkaligenesfaecalis	0	1(1.85)
TOTAL	9(18.75)	16(29.63)
P-Value	0.065	<0.0001

Table 7.3Antibiotic Susceptibility of Blood Isolates

ORGANISM	ANTIBIOTICS	SUSCEPTIBILTY PATTERNS				
MRSA N=3		Sensitive	Intermediate	Resistant	Not tested	Total
	Penicillin	0	0	3	0	3
	Oxacillin	0	0	3	0	3
	Erythromycin	3	0	0	0	3
	Tetracycline	2	0	0	1	3
	Clindamycin	3	0	0	0	3
	Cotrimoxazole	1	0	0	2	3
	Vancomycin	3	0	0	0	3
	Gentamicin	1	0	0	2	3
	Chloramphenicol	1	0	0	2	3
S. aureus N=1	Penicillin	0	0	1	0	1
	Oxacillin	1	0	0	0	1
	Clindamycin	1	0	0	0	1
	Cotrimoxazole	1	0	0	0	1
MRSE N+1	Penicillin	0	0	1	0	1
	Oxacillin	0	0	1	0	1
	Erythromycin	1	0	0	0	1
	Clindamycin	1	0	0	0	1
	Vancomycin	1	0	0	0	1
S. epidermidis N=1	Penicillin	0	0	1	0	1
	Oxacillin	1	0	0	0	1
	Erythromycin	1	0	0	0	1
	Clindamycin	1	0	0	0	1
	Cotrimoxazole	1	0	0	0	1
S. pneumoniae N=1	Penicillin	1	0	0	0	1
	Oxacillin	1	0	0	0	1
	Erythromycin	1	0	0	0	1
	Clindamycin	1	0	0	0	1
	Vancomycin	1	0	0	0	1

Based on antibiotic susceptibility patterns common to both blood and pleural fluid cultures, *S. aureus* was sensitive to oxacillin, clindamycin and cotrimoxazole. *S. aureus* was resistant to penicillin and vancomycin from blood and fluid culture, respectively. *S.epidermidis* isolates showed sensitivity to oxacillin and clindamycin but noted resistance to penicillin. MRSE was sensitive to vancomycin but resistant to penicillin and oxacillin. MRSE from blood culture was sensitive to clindamycin while MRSE from fluid culture showed only intermediate susceptibility to clindamycin. From both culture samples, MRSAwas sensitive to erythromycin, tetracycline, clindamycin, cotrimoxazole and vancomycin but was noted to be resistant to penicillin and oxacillin. Susceptibility to erythromycin and vancomycin was observed for *S. pneumoniae*.

The antibiotics commonly used as empiric treatment in our patients were penicillin (26%), oxacillin (24%), and cefuroxime (8%). Of the 72 patients, 37 (51.4%) received antibiotics alone, 34 (47.2%) patients received both antibiotics and anti-TB drugs while one patient (1.4%) was given solely anti-TB agents. Most of the patients with empyema were managed with antibiotics alone in 79.31% (23/29). A combination of antibiotics and anti-TB drugs were given in 75% (18/24) of patients with effusion.

Table 7.4 **ANTIBIOTIC SUSCEPTIBILTY OF PLEURAL FLUID ISOLATES**

ORGANISM	ANTIBIOTICS	SUSCEPTIBILITY PATTERNS				
MRSA N=5		Sensitive	Intermediate	Resistant	Not tested	Total
	Penicillin	0	1	4	0	5
	Oxacillin	0	1	4	0	5
	Erythromycin	4	0	0	1	5
	Tetracycline	2	0	0	3	5
	Clindamycin	5	0	0	0	5
	Cotrimoxazole	2	0	0	3	5
	Vancomycin	3	0	0	2	5
S. aureus N=2	Oxacillin	2	0	0	0	2
	Erythromycin	2	0	0	0	2
	Clindamycin	2	0	0	0	2
	Vancomycin	0	0	1	1	2
	Ciprofloxacin	1	0	0	1	2
	Cotrimoxazole	1	0	0	1	2
	Chloramphenicol	1	0	0	1	2
MRSE N=1	Penicillin	0	0	1	0	1
	Oxacillin	0	0	1	0	1
	Tetracycline	1	0	0	0	1
	Clindamycin	0	1	0	0	1
	Cotrimoxazole	1	0	0	0	1
	Vancomycin	1	0	0	0	1
S. epidermidis N=1	Penicillin	0	0	1	0	1
	Oxacillin	1	0	0	0	1
	Erythromycin	0	1	0	0	1
	Clindamycin	1	0	0	0	1
	Ciprofloxacin	1	0	0	0	1
	Vancomycin	1	0	0	0	1
S. pneumoniae N=1	Oxacillin	0	0	1	0	1
	Tetracycline	1	0	0	0	1
	Cotrimoxazole	0	1	0	0	1
	Vancomycin	1	0	0	0	1
	Erythromycin	1	0	0	0	1

Overall, thoracentesis was performed for 44 patients (61.11%) while 37 (51.38%) underwent CTT. Thoracentesis was more commonly done for patients with purulent effusions (91.67% or 22/24). CTT was the intervention more commonly used for patients with empyema (93.10% or 27/29). The overall mean duration of antibiotic treatment was 23.32 ± 19.91 days. The duration of antibiotic treatment was significantly longer for the empyema group (31.24 ± 15.35 days) than for the purulent effusion group (17.29 ± 13.06 days). Duration of treatment with anti-TB drugs was not specified.

TREATMENT	PURULENT EFFUSION No. (%) N=24	EMPYEMA No. (%) N=29	P-Value
MEDICAL Antibiotics Anti-TB meds Both	 5(20.83) 1(4.17) 18(75)	 23(79.31) 0 (0) 6(20.69)	<0.0001
SURGICAL Thoracentesis Done Not Done	 22(91.67) 2(8.33)	 17(58.62) 12(41.38)	0.006
Chest Tube Thoracostomy Done Not Done	 5(20.83) 19(79.17)	 27(93.10) 2(6.9)	<0.0001

Table 8. Treatment modalities for purulent effusion and empyema

PARAMETERS	Purulent Effusion Mean ± SD N=24	Empyema Mean ± SD N=29	P-Value
Resolution of Clinical S/S (days)	6.08 ± 5.42 (median=4.5)	11.31 ± 9.90 (median= 10)	0.008
Duration of Hospital Stay days)	18.20 ± 15.52	30.52 ± 17.55	0.009
Clinical Outcomes Improvement Failure(Mortality) Home against advice	No. (%) N=24 20(83.33) 2(8.33) 2(8.33)	No. (%) N=24 27(93.10) 2(6.90) 0(0)	0.273

Table 9.Outcomes of patients with purulent effusion and empyema

Seventy-two patients diagnosed with parapneumonic effusion had prolonged hospitalization with a mean duration of 22.96 ± 9.16 (range= 0.5-80). Overall, onset of clinical improvement was variable, ranging from one day to 53 days (85 ± 9.16 days). Of the 72 patients, majority were discharged (90.28%), while four died (5.55%), and three went home against advice (4.17%). A significant statistical difference was observed between the two groups favoring earlier clinical improvement and shorter hospital stay among those with purulent effusions. With respect to clinical outcomes, there was no significant statistical difference between purulent effusion and empyema group.

DISCUSSION

In the present hospital-based study, parapneumonic effusion was detected in 6.80% (72/1059) of children with community acquired pneumonia which was comparable with studies in some developing countries.[10]The estimated occurrence of empyema among hospitalized children with community acquired pneumonia was 2.74% (29/1059), a finding similar to that in Brazil.[4] Among those with parapneumonic effusions, empyema was identified in 54.72% (29/53) and purulent effusions in 45.28% (24/53), higher than what was previously reported in the local data.[11,13]

In contrast to local studies,[14-16] the mean age of patients with parapneumonic effusion was nine years and younger. This increased mean age is likely due to the fact that previous local studies only reported cases with empyema and excluded purulent TB effusions. In this series, we did not exclude TB effusions and observed that the majority of such patients belonged to older age group. Other demographic factors and clinical profile of patients were not significantly different between patients with purulent effusion and empyema.

Prolonged duration of illness prior to admission was noted in both purulent effusion and empyema. Many of the symptoms associated with pleural processes were caused by underlying disease that precipitated the

effusion, rendering a distinct syndrome difficult to recognize. There are some pathogens that follow a more insidious course, which may obscure the symptoms and lead to delay in seeking consultations. A history should always be obtained for conditions such as immunodeficiency, skin infections, TB exposure, malnutrition and neurologic disorders because other studies identified them as risk factors in the development of effusions.[1, 17-18]

Children with neurologic deficits such as cerebral palsy and seizure disorders are at risk for aspiration pneumonia. In tropical areas, excessive sweating and moist skin favor growth of cutaneous flora leading to a high incidence of staphylococcal pyoderma. Among the concomitant conditions, PTB exposure was the most commonly identified finding among patients who developed purulent effusions. Skin infections, intestinal parasitism and cerebral palsy were common underlying illnesses to both groups. In this study, skin infections were noted in 12.5% (9/72) of cases. Although not significantly different, skin lesions were twice more common in the empyema group. Other underlying conditions observed among patients with empyema were cerebral palsy, otitis media, T and B cell immunodeficiency, CCAM, iron deficiency anemia and intestinal parasitism. In contrast, protein energy malnutrition, cerebral palsy, intestinal parasitism and constrictive pericarditis were noted among those with effusion.

Fever, dyspnea and coughing were the most common clinical presentations. This is consistent with other studies where fever and cough usually occurred in more than 90% of cases with pleural effusion.[9]Auscultatory findings were the same with previous studies.[11,13] Decreased breath sounds and rales were heard from associated pneumonia.[19]In a local study,[14] weight loss was found to be a secondary symptom in 3.33% with effusions. In contrast to this study, almost half of the patients with purulent effusion presented with weight loss. TB exposure was observed in more than 50% of these cases. Previous studies claim no appreciable differences in the history and physical findings of patients with purulent effusion and empyema.[20]In this series, weight loss and chest pain were markedly noted among patients with purulent effusion while tachypnea was experienced more frequently by patients with empyema.

The chest radiograph was the simplest and least expensive method of identifying parapneumonic effusion but it was not specific. Obliteration of the costophrenic angle is the earliest radiological sign of pleural fluid accumulation. A lateral decubitus with the patient lying on the affected side provides valuable information about the quality and quantity of effusion. Chest x-ray was performed in all patients and showed pleural effusion. Ultrasonographic findings were similar to chest x-ray findings in 85.25%, with a greater proportion of empyema patients observed to have consolidation on chest ultrasound. The discrepancy between x-ray and ultrasound findings was due to different time frames when the two examinations were taken. Most of the x-rays were carried out immediately upon admission while chest ultrasounds were done once patients were transferred to wards. A delay of 24-to-48 hours allowed cases of early stage of effusion to proceed to a more organizing stage.[8] Chest ultrasonography provides the advantage in the detection of the amount of fluid as well as presence of loculations and septations. It is also able to indicate the best site for thoracentesis and placement of chest tubes. Chest CT scans were done on four patients with blurred costophrenic angles or obscured diaphragms by infiltrates on either x-ray or chest ultrasound. Ultrasound and CT scan have false negative results on examination of pleural effusion. One study in adults showed that neither ultrasound nor CT scan effectively predicted the stage of the effusion or predicted

surgical outcome.[21] Therefore, the presence or absence of empyema on imaging should not influence therapeutic decisions concerning management of parapneumonic effusions.

Pleural fluid analysis remained an important tool to identify etiology and to classify effusions. Pleural fluid cultures in patients with parapneumonic effusions are frequently negative, even when the fluid is pus.[23] Results of our study showed a low yield of 29.63% comparable to previous data.[23-24]Negative cultures could be possibly due to presence of fastidious organisms like anaerobes, atypical microorganisms such as *Mycoplasma* and *Chlamydia*, or an infection caused by *M. tuberculosis*, in which special culture media were needed. Pleural fluid in TB is rarely AFB smear positive and cultures are positive in only 20% to 40% of cases. [25] In this series, all pleural TB cultures were negative for *Mycobacterium*. Differentiation between purulent effusion and empyema in the pleural fluid was seen significantly in all parameters except for protein fluid-serum ratio. During inflammation, cellular and bacterial metabolism caused consumption of glucose and the excretion of lactate and CO2 which resulted to low pleural fluid glucose and pH;[26] such findings are consistent with empyema. Data were also in concordance with the findings of Light and associates that glucose was appropriate in children for classification of pleural effusion.[22]An increase in pleural WBC, PMNs and LDH in patients with empyema resulted from ongoing cellular metabolic activity brought about by inflammation. The volume drained from patients with empyema was expected to be less compared to the volume in purulent effusion because of thicker consistency in the former, but, this was not significantly observed. Differentiating purulent effusion from empyema identified patients that needed thoracic drainage, and guided antibiotic therapy and duration depending on pathogens, response to therapy and complications. This also predicted the onset of clinical improvement and estimated the duration of hospital stay.

Blood culture is still an important ancillary diagnostic procedure as it may be positive in 10-22% of empyema cases.[5,27]Small effusions can generally resorb, and a 10% to 50% chance of recovering the etiologic organism from blood cultures existed in empyema.[9]This result was comparable to our yield of 19.56%. Prior antibiotic use in the last three months resulted to sterilization in almost 2/3 of pleural fluid and blood samples.

From the previous studies done by Hailu and Mahalu, [5, 27]MRSA was rarely reported and *S. aureus* remained the etiological agent in 20% to 77% of cases.In the local studies by Lim and Suratos,[15-16]MSSA was found to be the most common etiologic agent. In the United States, *S. pneumoniae* serotype 1 accounted for <1% to 2.4% of cases of invasive pneumococcal disease. Other reports suggested a change in the cause of empyema in children including an increase in resistant organisms as well as a decline in the incidence of *S. pneumoniae*.This change was concomitant with the introduction of pneumococcal conjugate vaccine in 2000.[30]Our review showed that *Staphylococcus* remained the most commonly isolated organism from both culture samples but MRSA occurred in 53.33% of staphylococcal isolates.

Empiric antibiotic therapy for parapneumonic effusion include antimicrobials effective against *S. aureus*, *S. pneumoniae* and *S. pyogenes*,[9]similar to the empiric treatment used in the local setting. Majority of cases were treated with penicillin, oxacillin and cefuroxime. The first line antibiotics should include coverage for *S.aureus* because the most commonly isolated organism was still *Staphylococcus*sp. (14.70%).However, due to predominance of MRSA among the staphylococcal isolates, poor clinical response within 72 hours should prompt shifting to antibiotics with MRSA coverage pending culture and susceptibility patterns of the isolate. In this study, MRSA was sensitive to

clindamycin based on the antibiotic susceptibility testing from both culture samples.

Despite negative TB cultures, 75% of patients with purulent effusion and 21% with empyema were treated with both antibiotics and anti-TB agents. TB cultures done in all patients were negative except for one patient with purulent effusion that grew *M. tuberculosis* from wound discharge. Positive AFB smears in 9.09% (12/132) of specimens came from three patients with purulent effusion and two patients with empyema. The low yield of TB microbiologic studies in children can be due to difficulty in expectorating adequate sputum for <10 years old. In addition, tuberculosis in this age group is paucibacillary. Tubercle bacilli usually are relatively few in number which are trapped within the tissues of the lungs and lymph nodes and therefore cannot be recovered easily.

In this series, majority of cases treated as TB effusion or empyema were based on histories of persisting cough, weight loss, household TB exposure and of positive TST results suggestive of TB infection. Fever, cough and difficulty of breathing were the most common clinical presentations. Half of the patients with purulent effusion were exposed to TB and weight loss was markedly noted in this group. According to the 2007 3rd Nationwide TB Prevalence Survey in the Philippines,[29]children <10 years (25.4%) and 10-to-19 years (21.9%) were mostly affected, comparable to our age group treated as probable TB effusion. In a local study by Gallardo between 2002-2004 among pediatric patients enrolled in the TB registry and clinic, weight loss, cough and fever were observed in order of decreasing frequency.[30] These findings were supported by Go, et. Al., in 2007.[31] In the local review of cases by Cheng,[13] TB effusions occurred more frequently than parapneumonic effusions. TB pleurisy may occur as a complication of primary tuberculosis in 2% to 38% of children with pulmonary disease.[32] According to the TB Registry and Clinic by the Section of Infectious and Tropical Diseases in Pediatrics (INTROP) at PGH between 2005 to 2007, TB pleurisy occurred in 4% of cases;[31] If left untreated, it may lead to active extrapulmonary TB.[32-33]Gatmaytan and associates observed TB effusions as the second most common type of effusions in 12%; and 9.4% of cases were accompanied by bacterial infections.[34] Distinguishing between progressive pulmonary TB and a simple TB focus with superimposed acute bacterial pneumonia was difficult. Therefore, this prompted the use of antimicrobials in addition to appropriate anti-TB meds.

Aside from management with appropriate antibiotics, drainage of infected fluid by thoracentesis or closed thoracostomy tube was indicated. Majority of patients with empyema needed thoracic drainage. Thoracoscopy with decortication and deloculation were carried out in five patients with empyema where drainage was considered ineffective. Other treatment modalities implemented in empyema group were: five modified Heimlich valves, and one tube pericardiostomy. On the other hand, only few patients with purulent effusions underwent thoracostomy tube insertions. Additional treatment modalities instituted in three patients with effusions were modified Heimlich valve, thoracoscopy with deloculation and pericardiostomy tube insertion.

Majority of patients improved upon discharge. Most patients with purulent effusion responded well to conservative management with no apparent respiratory sequelae. These patients improved earlier, and hospital stay was shorter. Those with empyema also responded to antibiotics but needed to undergo additional surgical modalities. Thus, clinical improvement was delayed and hospital stay was longer. Two infants with empyema died, one due to respiratory failure secondary to pyopneumothorax (*Enterobacter cloacae*) and the other one due to MRSA empyema

thoracis. Two patients with effusion succumbed to death due to delay in seeking consultation.Causes of death were respiratory failure and multiple organ failure.

LIMITATIONS OF THE STUDY

Our study had limitations such as lack of standardized definitions for pleural effusion. Our data collection was restricted to charts retrieved from the medical record section, as well as hospital logbooks. Therefore, further analysis could not be pursued because of incomplete patient information.

CONCLUSION

Parapneumonic effusions in our institution occurred in 6.80% of hospitalized children with pneumonia. Empyema occurred in 54.72%, and purulent effusion in 45.28% among those who developed parapneumonic effusions. The etiologic organisms associated with parapneumonic effusions had become increasingly resistant. The bacteriologic profile was different from what has been described. MRSA, rarely reported in previous studies, is now a predominant pathogen which showed sensitivity to clindamycin. Patients aged nine years and below with male predominance were observed to be the most frequently affected. Radiographic imaging of the chest, pleural fluid biochemical analysis and cultures, and blood cultures were still important tools for diagnosis. Drainage of infected fluid by thoracentesis or CTT, and treatment of the underlying infection with appropriate antibiotics were the mainstays of treatment. Most of the patients with purulent effusion were treated with a combination of antibiotics and anti-TB meds. While majority of patients with empyema were treated with antibiotics alone. Thoracentesis was commonly used among those with purulent effusion. While CTT insertion was observed in majority of patients with empyema. Patients with purulent pleural effusion favored earlier clinical improvement and shorter hospital stay. However, similar clinical outcomes were observed in patients with empyema and those with purulent effusion.

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