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Retrospective review of empyema and parapneumonic effusions in hospitalized children in Ghana

Sandra Kwarteng Owusu[1], Sheila Agyeiwaa Owusu[2], Obed Ofori Nyarko[3], Richard Kwaku Kwarteng Owusu[4], Haruna Mahama[5], Naomi Dianne Adjetey[5], Birgit Agyeiwaah Baah[6], Isaac Okyere[7], Justice Sylverken[5], Daniel Ansong[1], Marco Zampoli[8]

[1]Department of Child Health, Komfo Anokye Teaching Hospital, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, [2]Department of Pediatrics and Child Health, University for Development Studies/Tamale Teaching Hospital, Tamale, Ghana, [3]Pediatric Cardiovascular Research Laboratory, University of Colorado Denver, Denver, United States, [4]Department of Obstetrics and Gynaecology, 37 Military Hospital, Accra, [5]Department of Child Health, Komfo Anokye Teaching Hospital, [6]Department of Public Health, Komfo Anokye Teaching Hospital, [7]Department of Surgery, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana, [8]Department of Child and Adolescent Health, Division of Paediatric Pulmonology Red Cross War Memorial Hospital/ University of Cape Town, South Africa.

***Corresponding author:**
Sandra Kwarteng Owusu, Department of Child Health, Komfo Anokye Teaching Hospital, Komfo Anokye Teaching Hospital, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.

abenaboamah18@gmail.com

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ABSTRACT

Objectives: Empyema and parapneumonic effusions (PPEs) are common complications of community-acquired pneumonia in children. Both contribute to prolonged hospital stay, increased morbidity, and less frequent mortality. This study aimed to describe the demographics, immunization status, clinical profile, etiology, and outcomes in children admitted with empyema and PPE to the Komfo Anokye Teaching Hospital.

Materials and Methods: This was a retrospective cross-sectional study that reviewed folders and electronic records of children admitted from January 2016 to December 2020. Information on demographic characteristics, immunization status, clinical profile, date of admission, and discharge or death were documented. Information was extracted using Microsoft Excel. Data was then analysed with Stata statistical software package version 16.

Results: Records were available for 51 out of 65 children, the median age was 42 months interquartile range (IQR) (22.5–96) and 68.6% (n = 35) of the children were males. Three of the children 5.9% did not have a chest drain inserted. In all, 60.8% (n = 31) of the children had received all doses of the pneumococcal conjugate vaccine (PCV) up-to-date for age. Four children (7.8%) had oxygen saturation <90%, whereas 43.9% (n = 18) had axillary temperature >38°C. Blood cultures were done for 72.6% (n = 37) of patients, *Staphylococcus aureus* was isolated in 5 patients (13.5%, n = 5/37) and *Streptococcus pneumoniae* was isolated in 1 patient (2.7%, n = 1/37). While the rest, 83.8% (n = 31) had no bacterial growth. The pleural aspirate culture was done in 64.7% (n = 33) of the patients and 6 (18.1%) had *S. aureus* isolated. Common antibiotics administered were amoxicillin clavulanic acid in 33.3% (n = 17) of the patients, and ceftriaxone in 31.4% (n = 16) of the patients. Three (5.9%) children died. The median length of hospital stay was 9 days IQR (7–14).

Conclusion: Empyema and PPE occurred more commonly in children older than 1 year, with a low mortality rate among the children. Most children with empyema were full immunised with PCV-13.

Keywords: Pneumonia, Parapneumonic effusion, Empyema, Children, Community-acquired pneumonia

INTRODUCTION

In children with community-acquired pneumonia (CAP), a small percentage will develop complications.[1,2] The most common complications of CAP are empyema and parapneumonic effusions (PPEs), while necrotizing pneumonia and lung abscesses occur less

frequently.[1] Empyema and PPE which result from episodes of bacterial pneumonia constitute different stages of the same pathophysiological processes resulting in the accumulation of fluid-containing bacteria and pus cells in the pleural cavity as a result of inflammation and infection extending to the pleural membranes.[3] Empyema and PPE contribute to increased length of hospital stay and are less frequently associated with mortality.[3]

The valency of a conjugate vaccine may influence the occurrence of episodes of complicated pneumonia in children. The introduction of the 13-valent pneumococcal conjugate vaccine (PCV-13) led to a decline in the incidence of empyema and PPE in the last decade.[4] However, the first conjugate vaccine PCV-7 introduced over two decades ago was reported to be associated with a rise in the number of cases of complicated CAP in the year 2007 in Europe.[5,6]

The causative organism in episodes of empyema or PPE is usually not identified using routine culture techniques. Simonsen *et al*. reported that up to 60% of cases of empyema and PPE had no bacterial confirmation in children with complicated pneumonia.[4] In cases, where an organism is isolated, *Streptococcus pneumoniae* (serotypes 1, 3, and 19A) and *Staphylococcus aureus* are the most common organisms seen. Less commonly, *Haemophilus influenzae* type B, *Mycoplasma pneumoniae,* and *Streptococcus pyogenes* are also isolated. In countries with high tuberculosis (TB) burden, *Mycobacterium tuberculosis* may account for up to 14% of cases of pneumonia with empyema.[7-9]

Management of empyema and PPE includes administration of broad-spectrum antibiotics; insertion of intercostal drain; regular wide bore drains or pigtail catheters, intrapleural fibrinolytics, and less commonly video-assisted thoracoscopic surgery.[3,10] One multi-center study in Israel reported that cephalosporins and penicillins were the commonly prescribed antibiotics for children with complicated CAP.[3] In 2011, a South African study found that in addition to routine antibiotics, intrapleural fibrinolytic in the management of complicated CAP may reduce the need for surgical intervention in children with empyema.[7] The survival among children admitted with empyema and PPE remains high with very few cases of mortality reported from different studies.[3,8]

There are no recent reports on empyema and PPE among Ghanaian children admitted with complicated CAP. Thus, the study aimed to describe the demographics, immunization status, clinical profile, etiology, and outcomes of children admitted with empyema and PPE to the Komfo Anokye Teaching Hospital (KATH).

MATERIALS AND METHODS

Study design

This was a retrospective cross-sectional study that reviewed folders and electronic records of children 2 months to 14 years who had been admitted to the Pediatric Emergency and Pediatric Pulmonology Units of KATH from January 2016 to December 2020 with a diagnosis of empyema and PPE.

Study site

The KATH is a tertiary hospital in the Kumasi metropolis and the capital city of the Ashanti region of Ghana. The city of Kumasi and its environs are in the middle belt of Ghana with a population of about four million.[11] It serves as the main referral center for three major regions. The pediatric emergency unit (PEU) of KATH operates a 24-h service and is manned by three senior specialist pediatricians and four specialist pediatricians. All children admitted with medical emergencies are first referred to this unit for assessment and initial emergency management. There is an average monthly admission of 350 patients and a range of 15–20 cases of pneumonia are admitted per month. Children with CAP including those with complications such as empyema and PPE are initially admitted to the PEU and later transferred to the pulmonology unit after stabilization. All children 2 months to 14 years admitted to the PEU or the pulmonology unit with a diagnosis of empyema and PPE who had complete medical records were included in the study. We reviewed 61 records and excluded 14 which were incomplete.

A diagnosis of empyema or PPE was established by the presence of purulent pleural fluid following intercostal drain insertion or evidence of fluid on chest ultrasound or chest X-ray. In children with empyema/PPE with an additional clinical suspicion of TB, a pleural aspirate sample was taken, and where available sputum samples were also taken for GeneXpert. A diagnosis of TB was based on information in the folder or in the electronic records. Information extracted from the patient's records included demographic (age and gender) and anthropometric (weight and height), immunization records, mode of presentation, duration of hospital stay, antibiotics administered, and record of pleural and blood cultures.

Immunization status was captured as being up-to-date for age or not up-to-date for age based on the number of doses of the pneumococcal vaccines received. Other clinical information documented included temperature, respiratory rate, and oxygen saturation at presentation. Information on findings used to confirm the presence of empyema and PPE was documented based on retrospective records of chest examination, chest ultrasound, or chest X-ray findings. The effusion site, chest tube insertion, and date of chest tube removal were noted. Further information on laboratory

parameters obtained were blood culture and pleural aspirate culture results. The outcomes of admission were documented as death or survival. The date of admission and date of discharge were documented for those who survived. All information was captured using a case report form which was entered into Microsoft Excel.

Analysis of data

Stata SE Version16 software – Stata Corp Texas USA (www.Stata.com) was used for the analysis. Descriptive summary statistics of explanatory and outcome variables of the study population were done. Median and interquartile range (IQR) values were determined for numerical variables and percentages and proportions for categorical variables. Ethical approval was given for this study with approval number, KATH/IRB/AP/081/21.

RESULTS

Demographic and clinical profile of children with empyema and PPE

A total of 65 patient records were screened, 51 had complete information on children admitted with empyema or PPE over the period reviewed. The rest of the 14 patients' records were excluded, ten had incomplete records, and four had other diagnoses (lung mass, abdominal lymphoma with pleural effusion, congenital thoracic malformation, and pulmonary hydatid).

Out of the 51 children who had complete records for empyema or PPE, 87.3%, (n = 43) were older than 12 months with a median age of 42 months (IQR 23–102) and 68.6% (n = 35) were males. Three children (5.9%) did not have an intercostal drain inserted. The median WAZ score was −0.89 IQR (−1.89–0.07) and the median HAZ score was −0.43 IQR (−1.02–0.17). Thirty-one children (60.8%) with empyema had received all three doses of PCV-13 on schedule [Table 1].

At presentation, four children (7.8%) had oxygen saturation <90%, 37.3% (n = 19) children had respiratory rate more than 50 breaths/min and 35.3% (n = 18) had an axillary temperature above 38°C. Majority of the children 60.9% (n = 31) did not have any comorbidity. However, among those with comorbidities, five (9.8%) had sickle cell disease, six (11.7%) had human immunodeficiency virus (HIV), five (9.8%) had TB, and four (7.8%) had other conditions. Seven (35.5%) of the children with comorbidity had not received all three doses of the PCV [Tables 1 and 2].

Table 1: Demographic and clinical profile of children with empyema and PPE.

Variable	Frequency (n=51)	Percentage
Age (months)		
<12	8	15.7
12–60	24	47.1
>60	19	37.2
Median (IQR) age	42 (24–96)	
Gender		
Female	16	31.4
Male	35	68.6
Weight (kg)	(n=43)	
Median WAZ (IQR)	−0.8 (−1.89–0.07)	
Height (cm)	(n=21)	
Median HAZ (IQR)	−0.43 (−1.02–0.17)	
Number of doses of conjugate vaccine (PCV-13) received		
Three doses	31	60.8
Less than three doses	20	39.2
Type of comorbidity*		
Sickle cell disease	5	9.8
Tuberculosis	5	9.8
RVI	6	11.7
Malaria	2	3.9
Severe malnutrition	2	3.9
No comorbidity	31	60.9
Mode of presentation		
Oxygen saturation		
<90%	4	7.8
Temperature (°C)		
>38°C	16	31.4
Duration of fever (days)		
Median (IQR)	2.0 (1–5)	
Respiratory rate (CPM)		
>50	19	37.3
Heart rate (bpm)		
>130	32	62.7

PPE: Parapneumonic effusions, IQR: Inter quartile range, kg kilograms, cm: Centimeters, RVI: Retroviral infection, PCV-13: Pneumococcal conjugate vaccine 13, WAZ: Weight for age z-score, HAZ: Height for age z-score, CPM: Cycles per minute, n: number of children

Etiologic and laboratory findings

Blood cultures were done for 72.6% (n = 37) of patients, *S. aureus* was isolated in five patients (13.5%, n = 5/37), and *S. pneumoniae* in one patient (2.7%, n = 1/37). The patient with *S. pneumoniae* on blood culture had received all three doses of the conjugate vaccine. The rest 83.9%, (n = 31/37) had no bacterial growth. The pleural aspirate culture was done for 64.7% (n = 33) of patients and six (18.2%, n = 6/33) had *S. aureus* isolated. The rest (81.8%, n = 29/33) had no bacterial growth. Six (11.8%, n = 6/51) patients were in addition investigated for TB and GeneXpert on pleural aspirate, and sputum samples were all negative [Tables 2 and 3].

Treatment and outcome

The most common antibiotic administered to children with empyema and PPE were amoxicillin clavulanic acid 33.3%, (n = 17) and ceftriaxone 31.4% (n = 16). Three children 5.9%

Table 2: Immunization status of children with comorbidity and positive culture results.

	Immunization with pneumococcal conjugate vaccine		
Variable	**Less than three doses *n* (%)**	**All three doses *n* (%)**	**Total *n* (%)**
Total number with comorbidity *n*=20	7 (35)	13 (65)	20 (100)
SCD	1 (25.0)	4 (75.0)	5 (100)
PTB	3 (60.0)	2 (40.0)	5 (100)
HIV	2 (33.3)	4 (66.7)	6 (100)
Others	1 (25.0)	3 (75.0)	4 (100)
Culture sensitivity			
Blood culture isolate *n*=6			
S. aureus	2 (33.3)	3 (66.7)	5 (100)
S. pneumoniae	-	1 (100)	1 (100)
Pleural aspirate culture isolate *n*=6			
S. aureus	-	6 (100)	5 (100)
S. pneumoniae	-	-	
Outcome of admission			
Survived	16 (33.3)	32 (66.7)	48 (100)
Died	-	3 (100)	3 (100)

SCD: Sickle cell disease, HIV: Human immunodeficiency virus infection, PTB: Pulmonary tuberculosis, *S. aureus: Staphylococcus aureus, S. pneumonia: Streptococcus pneumoniae*, *n*: Number of children

with empyema and PPE died, they were all fully immunized with three doses of conjugate vaccine. The median duration of hospital stay was 9 days, IQR (7–14 days) for all the children. Among those who had a chest tube inserted the median duration of insertion was 7 days IQR (6–9 days) [Tables 2 and 4].

DISCUSSION

This study from one tertiary center showed empyema and PPE occurred more commonly in children older than 1 year. The majority of the children studied had no organism isolated on both blood and pleural aspirate cultures. However, among those with a positive culture, *S. aureus* was the most common bacteria isolated. A greater proportion of the children had received all three doses of the PCV. A few of the children with empyema and PPE had comorbid conditions such as sickle cell disease, HIV, and TB. Only a third of those with comorbidities had received all three doses of the conjugate vaccine a high proportion of the children with empyema and PPE survived.

The majority of children admitted with empyema and PPE were older than 12 months. This finding is comparable to reports by Ghoor *et al*. in Johannesburg, and Erlichman *et al*., in Jerusalem, in Israel.[3,8] In addition, Zampoli *et al*., in a study in 2015, reported a median age of 17 months in children with empyema and PPE.[7] In general, it appears that children presenting with empyema and PPE are older than 12 months of age; however, it is unclear why this trend is seen. This could be due to immune responses to vaccines waning in some children with increasing age.

Table 3: Blood and pleural aspirate cultures and TB GeneXpert results.

Variable	**Frequency (*n*=51)**	**Percentage**
Blood culture		
NBG[¥]	31	60.8
S. aureus	5	9.8
S. pneumoniae	1	1.9
Not done	14	27.5
Pleural aspirate culture		
NBG[¥]	18	35.3
S. aureus	6	11.7
Not done	27	53
TB GeneXpert (pleural aspirate)		
Negative	6	21.8
Not done	45	88.2
GeneXpert (sputum)		
Negative	6	21.8
Not done	45	88.2

[¥]NBG: No bacterial growth. TB: Tuberculosis, *S. aureus: Staphylococcus aureus, S. pneumonia: Streptococcus pneumoniae*

The majority of the children with empyema and PPE had received all three doses of the PCV. Ghana is among the countries with very high immunization coverage in the sub-region. The PCV was introduced into the expanded program on immunization in May 2012, in the year 2019 our vaccine coverage was 87% for all three doses.[12] This may be offering protection against empyema caused by *S. pneumoniae* leading to a very low pneumococcal isolate as was seen in this study. We found sickle cell disease, HIV, and TB as the most common comorbid conditions in our study. The majority of

Table 4: Treatment and outcome in children with empyema and PPE.

Variable	Frequency (*n*=51)	Percentage
Outcome of admission		
Discharged	48	92.5
Died	3	7.5
Length of hospitalization (days)		
Median (IQR)	10 (7–14)	
Chest drain inserted	48	94.1
Duration of tube insertion (days)		
Median (IQR)	7 (6–9)	
Site of effusion		
Left	23	45.0
Right	15	29.4
Bilateral	2	1.3
Not indicated	11	24.3
Antibiotics*		
Amoxiclav	17	33.3
Ceftriaxone	16	31.4
Cefuroxime	12	23.6
Azithromycin	8	15.7
Gentamicin	7	13.4
Ciprofloxacin	6	11.8
Clindamycin	4	7.8

*Multiple responses, SD: Standard deviation, IQR: Interquartile range

the children with comorbidities had received all three doses of the conjugate vaccine. Ghoor *et al*. reported HIV and TB as comorbid conditions in children with empyema and PPE. This observation is likely due to the endemicity of the two conditions in these regions.[8] These conditions are known to predispose to severe forms of pneumonia due to their immunosuppressive potential.

There was no bacterial isolate seen both on blood and pleural fluid cultures in a greater proportion of the patients with complicated pneumonia. This may be due to the timing of culture sample taking in the disease process and prior antibiotic use by the patients. In a limited number of cases, *S. aureus* was isolated from blood or pleural fluid cultures. In the past different studies from Africa and Europe reported *S. pneumoniae* as the leading bacteria isolated on both blood and pleural aspirate cultures followed by *S. aureus* either methicillin-resistant or sensitive. However, centers with long-term data on episodes of empyema and PPE have reported a general decline in empyema caused by *S. pneumoniae* following conjugate vaccine introduction.[7,9] Over the last decade, conjugate vaccine uptake has progressed at different stages in Africa; thus, both serotype replacement and changing virulence factors of the two organisms may explain the etiological pattern seen among children with empyema.[9]

The commonly used antibiotics for children with empyema and PPE in our facility, ceftriaxone and amoxicillin-clavulanic acid are comparable to that reported in the study by Erlichman *et al*., involving a similar population.[3] Sensitivity patterns of etiological organisms may be influencing these choices in clinical settings. In addition, patients referred to tertiary centers commonly receive first-line antibiotics with poor response before being referred. This may therefore necessitate the use of second and third-line antibiotics.

Survival among the children admitted with empyema and PPE was good with a low rate of mortality. It is possible that protection is offered by the PCV contributing to improved survival despite the presence of complication. The duration of intercostal drain insertion and duration of hospital stay in our study were similar to the report by Erlichman *et al*. in Israel.[3] This observation may be due to the fact that patients with complicated forms of pneumonia require a longer hospital stay due to the prolonged morbidity. In addition, the time to drain insertion and removal as well as the post-removal period of observation may all prolong the length of hospital stay.

CONCLUSION

Empyema and PPE in our study were common in children older than 1 year. *S. aureus* is the most common pathogen isolated from pleural aspirate and blood cultures. A high proportion of all the children had received three doses of the PCV on schedule. There was a low mortality rate among children admitted with empyema and PPE to KATH.

Limitations

This study had limitations; being a retrospective study there is a possibility that the true burden of empyema and PPE may have been underestimated due to missing or incomplete information on participants. However, every effort was made to capture all complete records as much as practicable. Second, the true pattern of etiological organisms in children with empyema and PPE may have been underestimated due to the low bacterial isolate on blood and pleural fluid cultures. All efforts were made to present all available records. Thus, this first report is still valuable as a starting point to inform future prospective studies.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Nil.

Conflicts of interest

Dr. Marco Zampoli is on the editorial board of Journal.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The author(s) confirms that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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