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St. Paul's Hospital Millennium Medical College

**Magnitude and treatment outcome of empyema thoracis in children admitted to St. Paul's
Hospital Millennium Medical College from 2015 to 2022**

By: Eyerusalem Legesse (MD, Pediatric Resident)

**A Research Thesis to be submitted to the Department of Pediatrics for the Partial
Fulfillment of the Requirements for Postgraduate Diploma in Pediatrics and Child Health**

Addis Ababa Ethiopia

January 2024



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Abstract

Background: Empyema thoracis is an accumulation of pus in the pleural space. Parapneumonic effusion and Empyema thoracis are the terms used to describe complications of pneumonia. Around forty percent of bacterial pneumonia are said to be complicated by parapneumonic effusions, 10% of whom would evolve into empyema. Although, many studies were done worldwide, few in Africa; there is scarce data on the magnitude, associated factors, and treatment outcome of empyema thoracis in Ethiopia. This study assessed the clinical profile of children with empyema, the treatment practice and their outcome.

Objective: - To determine the magnitude, associated factors and treatment outcome of Empyema among pediatric patients admitted to St. Paul Hospital Millennium Medical College.

Methods: A retrospective chart review was conducted on children who were diagnosed with empyema thoracis that were admitted to St. Paul's Hospital Millennium Medical College (SPHMMC) pediatrics departments over 8 year from January 2015 to December 2022. The total number of children admitted with the diagnosis of Empyema during the study period was 88. Data were collected using a structured questionnaire. Data was entered to SPSS version-27 and cleaned before analysis. Frequency and percentage descriptive statistics were used to describe the characteristics of the variable. Data analysis includes descriptive analysis, chi-square test and Binary Logistic regression was done to look for association between variables.

Result: The incidence of childhood empyema in this series was 12/1000 admissions accounting for 5.3% of the cases of pneumonia, which is significantly higher compared to a previous data from Ethiopia. The associated factors that determine the outcome of empyema patients through Univariate analysis were gender, place of admission, the level of respiratory support needed, WBC count, the pleural fluid amount and initiation of anti-TB during the treatment with a P value of <0.05 . However none of the variables were found to be significant with multivariable analysis. Antibiotic therapy with chest drain insertion $\pm$ intra-pleural fibrinolysis were the modality of treatment in most children with empyema thoracis (73%) and surgical intervention was rarely performed. A significant number of patients (28%) developed complication during

treatment for empyema thoracis . The most common complications were pericarditis followed by pneumothorax and necrotizing pneumonia . The majority (83%) recovered fully on hospital discharge while 15 were discharged with sequelae . There was no in-hospital death reported with in the 8 year study period but the outcome of 6 patients was not known .

Conclusion: A significant increase in the incidence of empyema thoracis was noted in children especially in the last two years. Antibiotic therapy with chest drain insertion $\pm$ intra-pleural fibrinolysis is an effective treatment of empyema thoracis in children and surgical intervention was rarely performed. The overall outcome pediatric empyema thoracis was found to be very good in our setting .

Key words: Children, Empyema, Ethiopia, outcome

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Acronyms and Abbreviation

- CHD Congenital Heart Disease
- CXR Chest x-ray
- DM Diabetes Mellitus
- Dx Diagnosis
- ER Emergency Room
- HMIS Health Management Information System
- Hx History

- IRB Institutional Review Board

- PICU Pediatric Intensive Care Unit
- PCV Pneumococcal Vaccine
- TB Tuberculosis
- SPHMMC St. Paul's Hospital Millennium Medical College
- VATS Video Assisted Thoracotomy
- WHO World Health Organization

1. Introduction

1.1 Background

Paranemonic effusion and Empyema thoracis are the terms used to describe complications of pneumonia; whereas Parapneumonic effusion is defined as an exudative pleural effusion associated with lung infection (pneumonia). (1)

Around 28 % of children requiring hospitalization for pneumonia may have an associated effusion. It occurs in 5–10% of children with bacterial pneumonia and in up to 86% of children with necrotizing pneumonia.(2)

Early in the disease course, the effusion usually is free-flowing (also known as a "simple" effusion) and sterile. Complicated parapneumonic effusion or Empyema occur with changes in the plural fluid due to the bacterial invasion in the plural fluid and defined as the presence of bacterial organisms on culture, gram stain and/or grossly purulent fluid in the pleural cavity. (1)

Empyema thoracis is most frequently encountered in infants and preschool children. It is most often associated with pneumonia caused by *Streptococcus pneumoniae* although *staph aureus* is most common in developing nations, as well as in posttraumatic empyema. The relative incidence of *Haemophilus influenzae* empyema has decreased since the introduction of the H. influenzae type b vaccination. Group A streptococcus, Gram-negative organisms, tuberculosis, fungi, viruses, and malignancy are less common causes. The disease can also be produced by rupture of a lung abscess into the pleural space, by contamination introduced from trauma or thoracic surgery, or, rarely, by mediastinitis or the extension of intra-abdominal abscesses (2)

Classically empyema thoracis is classified into 3 different phases which describe the progression of disease, namely purulent phase, fibrinopurulent phase and organizing phase based on the contents of pleural cavity. Early empyema (stage 1) may respond to parenteral antibiotics with or without tube thoracostomy usually < 10mm thickness is being used as reference. However, when loculation and septae developed (stage 2) with the formation of thick fibrous cap and thickened pleural (stage 3), nonsurgical treatment such as tube thoracostomy with/without intrapleural fibrinolytic therapy is being practiced in most of developing countries. (2)

Treatment of children with empyema is associated with significant utilization of healthcare resources. Most children with empyema require prolonged hospitalization, undergo multiple invasive procedures, require multiple radiologic studies, and receive prolonged courses of antimicrobial, analgesic, and sedative medications (3)

1.2 Statement of the problem

The World Health Organization (WHO) has reported that pneumonia continues to be a significant cause of mortality in the pediatric age group for children under five years of age, where it accounts for nearly one-fifth of childhood deaths worldwide(4). Around forty percent of bacterial pneumonias are said to be complicated by parapneumonic effusions, 10% of whom would evolve into empyema. Empyema thoracis is more common in young children with rates of 3.7, 3.9, and 1.3 cases per 100,000 population among children <2 years, 2 to 4 years, and 5 to 17 years. In untreated cases of empyema, mortality rates can be as high as 30%(5).

From a paper published in 2018 a 10 year period retrospective chart review study in Australia has shown the incidence rate of 8.5 per 100000 in all children and under 5 years age group had the highest rate (24.5; 95% CI: 24.4–24.6) There was a progressive rise in incidence during the 10-year period, with the highest incidence of 15.2 (95% CI: 15.1–15.2) occurring in 2016(6).

Another global report on 2008 from Asia on large representative pediatric hospitals in China, Korea, Taiwan and Vietnam with study period of 10 years has shown the increase in the incidence of empyema in young children as well as male preponderance was noted in all countries (62% in China and Korea and 57% in Taiwan and Vietnam), and majority of the patients in all countries were under 5 year of age also around 71% of empyema patients were culture negative(7).

Based on Health Management Information System (HMIS) registry log book of the department, as compared to the previous 3 or 4 years, lately there has been an increasing influx of patients with empyema in our hospital where the reasons for this rise remain not fully explained. To the best of our knowledge, there lacks prior researches to explain this issue in Ethiopia. This study

will add more insight to the topic; address associated factors and treatment strategies applied so that it will help in the future to decrease the impact and occurrence of the disease.

Controversies exist worldwide regarding the optimal treatment for empyema in children. Infection should be controlled with antibiotics and drainage of the pleural cavity. Intrapleural fibrinolysis and video assisted thoracoscopic surgery (VATS) are modern interventions widely used in high-income countries, but mostly unavailable in the developing world(8)

1.3 Significance of study

To the best knowledge of the investigators, in our country , there are no adequate studies on the current extent of empyema in children. Furthermore, diagnosis and management of empyema in resource-limited settings like ours represent a major challenge; burden to the healthcare system as well as it became major morbidity and mortality for the patients.

The aim of this study is to describe the base line data on empyema thoracis regarding the incidence, etiological distribution, clinical characteristics, laboratory evaluation, associated factors, treatment practice and outcome of pediatric patients admitted to SPHMMC pediatric ER, ward and ICU.

We hope that the study results will be used to modify our practice and help to inform future policies that will enhance the quality of care given to these patients plus it will add knowledge on Empyema. It will also serve as a basis for appropriate further advanced research.

2. Literature Review

2.1 Magnitude of pediatric empyema

A nationwide surveillance study done over 7 years in Germany hospitals showed an increase in number of patients over the study period in children admitted under the age of 18yr.; over 7 years around 1447 patients were found to have plural empyema with annual incidence varies from 14-18 PE per million children(9).

Another similar retrospective chart review study done in a large Australian tertiary children's hospital done over 7 years period showed the significant increase in incidence of empyema cases from 1.7/1000 to 7.1/1000 admissions(10).

In contrast in 2015 University of the Witwatersrand, Johannesburg, South Africa a prospective study over 5 year chart review study showed around 142 patients with empyema with a 50% reduction in the incidence of empyema following post PCV vaccination. (11). However another research conducted in 2017 at Red Cross War Memorial Children's Hospital, University of Cape Town the increase incidence of empyema is thus closely linked to the epidemiology of invasive *S. pneumonia* and nasopharyngeal carriage of disease causing *S. pneumoniae* serotypes in childhood populations(12).

On the other hand in Ethiopia, Addis Ababa, a 4 year study conducted at Ethio-Swedish Children's Hospital in Nov 2000, there were 944 cases of pneumonia admitted during the period among which the incidence of childhood empyema was 2.7/1000 admissions(13).

2.2 Clinical profiles and associated factors

A prospective etiological based study done in England on risk factors for the development of empyema in children were reported as there is no significant difference in age and sex; and

according to the study causative pathogen where identified in 61% of the cases among which 31% were viruses and 17.5% were bacteria's and are strongly associated with development of empyema's and the rest 12% where mixed infections (14). On the other hand a study conducted in USA Texas on the risk factors of pediatric parapneumonic empyema showed children with empyema were older than 3 years of age and no significant difference between sex or race and regarding the clinical presentation fever was the most common presenting feature which usually have longer duration with chest pain and dyspnea. Upon their microbiologic report pathogenic bacteria recovered from 42% of patients with empyema and *S.pneumoniae* was the most identified cause for empyema(15).

A retrospective study over 13 years in China reported from 153 cases of pleural TB 27 of the cases developed tuberculous empyema where adolescent males predominate around 13% of them had TB contact history and the most common symptoms where fever followed by cough dyspnea and sputum production(16). Likewise a 2 year study from South Africa reported culture-confirmed TB empyema in 10% of all empyema cases, the third most common etiology after *S. pneumoniae* and *S. aureus*. So the relatively higher incidence of empyema caused by *M. tuberculosis* was unexpected finding and as shown in these studies, it can be concluded as in areas where there is high TB prevalence settings and of TB co infection, therefore, be considered in the differential diagnosis of empyema as the presentation can mimic that of acute bacterial empyema (11).

A cross-sectional study conducted in tertiary care center in India; Bangalore revealed other than the above risk factors, they found malnutrition as a significant risk factor for the development of empyema in children (17). A comparable study from South Africa University of Cape Town published in 2015 among 133 empyema cases 35% of them were malnourished (18).

2.3 Treatment practice and outcome

A treatment practice and outcome in one of the tertiary hospital in India from a retrospective 4 year study reported all of the patients were treated with chest tube insertion and IV antibiotics (ampicillin and cloxacillin) and antibiotics were changed to PO amoxicillin when patient condition stabilizes and cessation of pus drainage usually in 1-3 week. Average day of chest tube drainage is from 3-35 days. From the total number of patients around 60% of the cases were treated with chest tube and antibiotics the others require fibrinolytics administration,

decortication was needed for 9.3% of the cases. The average hospital stay during the study time was 25 days. The commonest complication observed during the study period were collapse (18%), thickened pleura (16.7%), pericardial effusion (8%), cardiac tamponade (3.3%) and bronchopleural fistula (3.3%). 3.3% of the patients died of persistent sepsis, post-operative septic shock and ventilator associated complications. However; most of the cases showed complete clinical improvement and full lung expansion during follow-up(19).

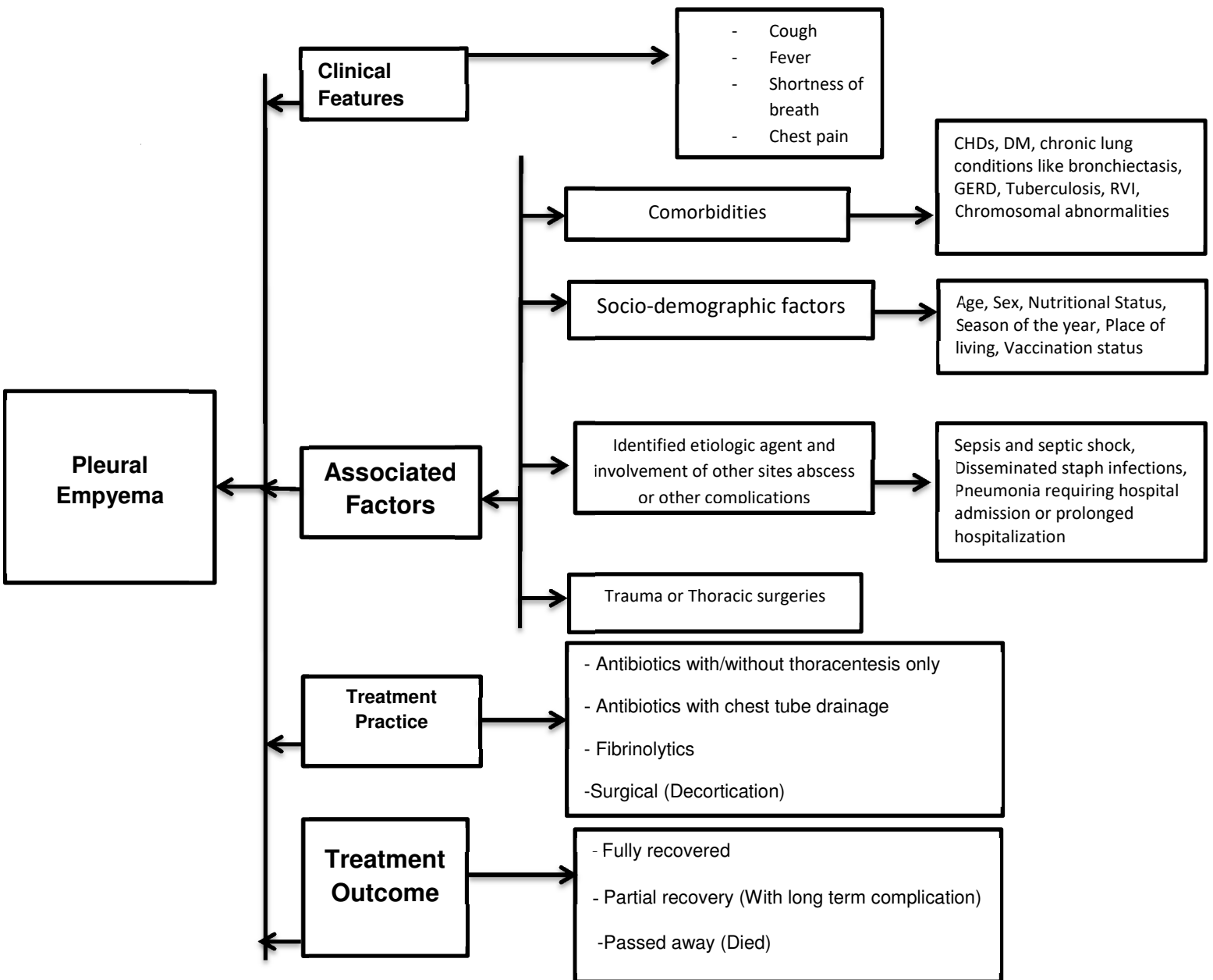
A comparative multicenter retrospective cohort study was done in University of Pennsylvania School of Medicine, USA on 2011 which compares the outcome of patients who was managed with chest tube drainage with and without fibrinolytics and VATS. Outcomes were similar in patients undergoing initial chest tube placement with or without fibrinolysis. Those undergoing VATS received fewer additional drainage procedures but had no differences in LOS compared with other strategies (3).

A treatment practice in Ethiopia Addis Ababa a decade back were reflected by one study conducted over 4 year in one of the referral hospital in Addis Ababa showed that all the empyema cases were treated with antibiotics from the total 38 patients around 74% of patients receive cloxacillin and the rest 16% receive penicillin plus chloramphenicol. Chest tube drainage was applied on 71% of patients where as 29% of patients were managed with antibiotics plus thoracentesis alone. Decortication and sequestrectomy was done on 1 patient and there average hospital stay was 32 days and 2/3rd of patients stayed more than 3 weeks and 45% of patents develop complications. The commonest complications were chest wound infection, pneumothorax and superinfection of empyema. From those who had clinical recovery (32 patents) around 47% of them had normal chest findings and from this only 39% of them had normal CXR recovery. Death were reported on 6 of the patients(13).

2.4 Conceptual frame work

Several different factors attribute for patients to develop Pleural empyema. These factors also could be interrelated to each other. This conceptual frame work is developed on the perceived factors leading to pleural empyema based on the literature review.

Fig 1: Conceptual Framework



3. Objectives

3.1 General Objective

- To determine the magnitude, clinical profile, associated factors and treatment outcome of Empyema thoracis among pediatric patients admitted to St. Paul Hospital Millennium Medical College in Addis Ababa Ethiopia.

3.2 Specific objective

- Document the Clinical profile of children with empyema at SPHMMC over a 8 year admission period.
- Determine the incidence of Empyema thoracis among pediatric patients admitted to St. Paul Hospital Millennium Medical Collage Addis Ababa Ethiopia.
- Identify factors associated with outcome of Empyema thoracis among pediatric patients in the study area.
- Assess treatment outcome of admitted pediatric cases with Empyema thoracis at discharge.
- Identify the microbiologic pattern of admitted pediatric cases of Empyema thoracis patients at the study area..

4. Methods and Materials

4.1 Study area

This study was conducted at St. Paul Hospital Millennium Medical College pediatrics department on those admitted pediatric patients in the ER, ward and ICU. The hospital was established in 1969 by the late emperor Haile Selassie. It is one of the largest public teaching hospitals in Ethiopia receiving a large amount of patients from different parts of the country. The hospital has dedicated pediatric department which was established and started teaching residents and medical students since 2007 with the opportunity to gain clinical experience in the field of pediatrics. The department has grown over years to encompass various pediatric subspecialists. The Pediatric surgical unit which was established in 2010, making it relatively young department, provides a comprehensive range of surgical services supported by highly experienced pediatric surgeons and residents to ensure that children receive the best possible care. Also the department collaborates with other specialties to provide comprehensive care for pediatric patients who need interdepartmental consultations.

In our hospital the management pleural empyema involves a multidisciplinary team; however the primary healthcare providers are pediatricians, pediatric residents and pediatric surgeons who are involved in the diagnosis and treatment of childhood pleural empyema to ensure the best possible outcome for the child. The setting required for the management of childhood pleural empyema depends on the severity of the condition and the child's overall health. In general, children with pleural empyema require hospitalization in a medical facility, either in emergency or pediatric ward or a pediatric intensive care unit (PICU), for close monitoring and management of their condition.

4.2 Study period

The study was commenced after department and IRB approved the proposal where data collection was done till November 2023. Then data entry and analysis was carried out starting from December with final report done in Jan 2024. The study included empyema patients admitted from Jan 2015 to Dec 2022 where data source of HMIS registry log book and patient medical cards are available.

4.3 Study design

Hospital based retrospective medical chart review was conducted with structured questionnaire filled by trained data collectors from the information on the charts.

4.4 Study Population

All children admitted to the ER, ward and pediatric ICU with the diagnosis of parapneumonic empyema from Jan 2015 to Dec 2022 that fulfills the inclusion criteria.

4.4.1 Eligibility criteria

4.4.1.1 Inclusion Criteria

- All pediatric patients admitted with the diagnosis of empyema thoracis

4.4.1.2 Exclusion Criteria

- Children with incomplete data of the critical variables (e.g. unknown information like treatment modalities and outcome)
- Children treated for empyema clinically but with no pleural tap and analysis

4.5 Sample size

All patients who are below 15 years and diagnosed with empyema thoracis from Jan 2015 - December 2022 were included.

4.6 Study Variables

4.6.1 Dependent variable

- Treatment outcome

4.6.2 Independent variable

- Socio-demographic factors: Age, Sex, vaccination status, nutritional status, season of year.
- Clinical Presentation: Cough, fever, Shortness of breath, Chest Pain
- Treatment Modalities: antibiotic therapy along with chest tube drainage, fibrinolytic therapy, decortication.

4. 7 Operational Definition

Empyema Thoracis : Criteria to define empyema thoracis are at least one of the following

- (i) Grossly purulent fluid;
- (ii) Positive Gram stain or culture and
- (iii) White blood cell count >10,000 mm³ with predominant polymorphs.
- (iv) Short of pleural tap analysis, chest US or CT imaging suggestive of complicated effusion characterized by presence of loculation , thick fluid and / debris in a child with typical clinical features of complicated pneumonia and effusion on chest x-ray.

Empyema grading based on the degree of pleural involvement on CXR :

- (a) Small – some costophrenic angle blunting;
- (b) Medium – involving up to half of the hemithorax and;
- (c) Large – involving over more than half of the hemithorax with/without mediastinal shift

Based on the amount of volume on chest ultrasound volume estimate, empyema was classified as:

- a. Small volume : when pleural fluid collection is less than or equal to 10mm in depth
- b. Moderate volume : when pleural fluid collection is between 10mm and 30mm in depth
- c. Large volume : when pleural fluid collection is greater than 30mm in depth

4.8 Data collection tool and procedure

The study was conducted by reviewing medical records of admission and discharge diagnosis of empyema who were admitted to pediatric department during the study period of Jan 2015 to Dec 2022. First MRN of empyema patients was retrieved from the HMIS, and admission and discharge log book of ER, Ward and PICU then the patient charts was collected from the archive room.

The information on the patients' demographic characteristics, clinical presentations, treatment modalities and the outcomes of patients with empyema was collected using structured questioner by a year 2 pediatric residents. Completeness and consistency of collected data was checked throughout data collection period by principal investigator.

4.9 Data processing and analysis

The collected data was using Epi-info version 7, cleaned and then was exported to SPSS version 25 for the required analysis. Frequencies and percentages were calculated to all the variables that were related to the objectives. Descriptive statistics are presented using cross tabulations. For comparison of data chi- square probability test was performed. For each analytical test $p < 0.05$ was considered significant between independent variable and outcome of empyema patients.

4.10. Data quality assurance

Quality of the data was insured by carefully prepared extraction checklist and the selected data collector team (year 2 pediatric residents) was trained on the purpose of the study and how it will be conducted and supervised on regular basis. The collected data was also continuously reviewed for accuracy and completeness by the principal investigator. The investigator was responsible for monitoring the overall data collection process and providing supportive supervision on the spot.

The data collected was carefully entered and cleaned before analysis.

4.11. Ethical consideration

An Ethical clearance was obtained from the Ethical review committees of research & publication of the Department of public health, SPHMMC after approval by the research advisor before data collection. Permission to collect data was obtained from the department head of Pediatrics and child health, SPHMMC and quality office. Data were collected after obtaining the MRN of empyema cases from the admission discharge HMIS log book of ER, pediatric ward and pediatric ICU. Confidentiality was kept by avoiding recording of names of clients on data collection format, client records was available to the investigator and data collectors and returned to its place after completion of data entry. The data collected were used only for the intended purpose of the study.

4.12. Dissemination of results

After being completed the research paper will be submitted and presented in the department of Pediatrics and child health, SPHMMC. After incorporation of comments and suggestions, If possible, the findings will be presented in different seminars, meetings and workshops and will be also published in peer reviewed international and national journals.

5. Results

5.1 Socio-demographic Variables

During the study period there were 88 children treated for Empyema thoracis in SPHMMC. Among them 59 of them were male (67%) with male to female ratio 2:1. Age at presentation ranged from 25 days to 15 year and the median age for the development of pleural empyema in this study was 3 year IQR (1-4 years). Patients were categorized in to four age groups as shown in table 1. Majority of the children (46%) were in the range of 5-12 years with mean age be 2. 9 (± 0.8) years. The seasonal distribution of empyema cases was similar in each season of the year (Table 1.)

The total numbers of children admitted to the hospital during the study period were 7133 with 1643 cases (23%) of non-tuberculous pneumonia. The incidence of childhood empyema in this series was 12/1000 admissions accounting 5.3% of the cases of pneumonia. Marked increase in the number of empyema cases is seen from 2020 onwards.(Figure 1)

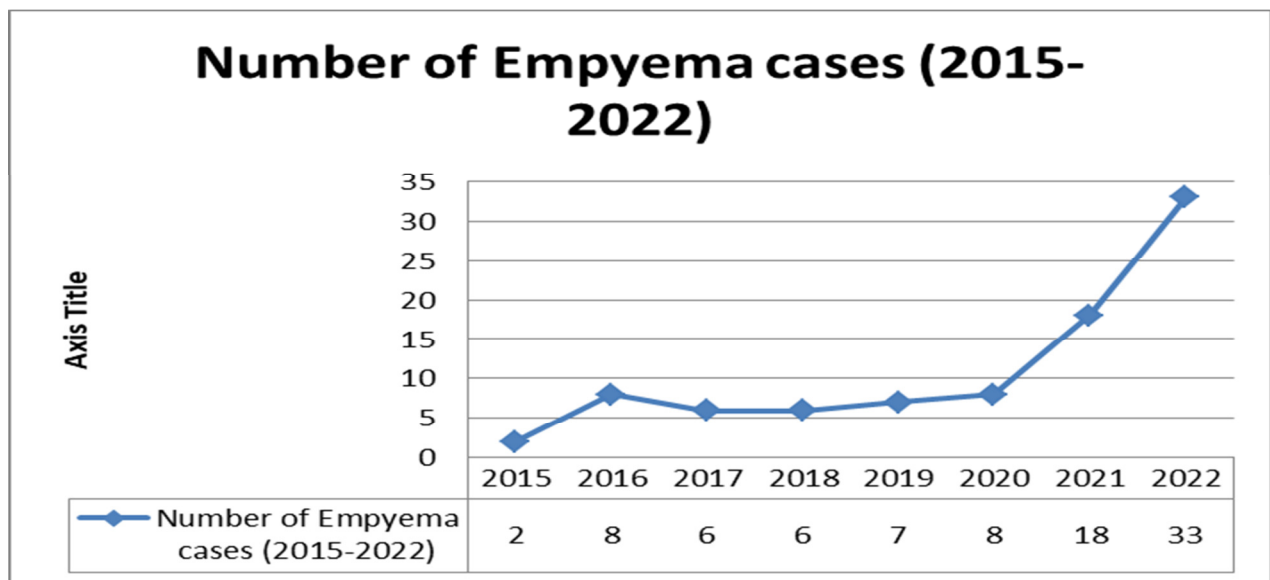


Figure 1: Number of Empyema cases (2015-2022)

Many of the patients were from Oromia region which account 60% of the admissions and 33% were from Addis Ababa. Six of the patients were having severe acute malnutrition making 6.8% of the whole empyema admission. There were nine unvaccinated cases (10.2%) and five were partially vaccinated (5.7%) and none were HIV infected.

Table 1: Socio-demographic characteristics of empyema thoracis patients

Variable		Frequency (N)	Percent (%)
Age in years	< 1 year	7	8.0
	1-5 year	27	30.7
	5-12 year	40	45.5
	12-15 year	14	15.9
Gender	Male	59	67
	Female	29	33
Address	Oromia region	53	60.2
	Addis Ababa	29	33.0
	Amhara region	5	5.7
	SNNPR	1	1.1
Nutritional Status	Normal	71	80.7
	MAM	11	12.5
	SAM	6	6.8
Vaccination status	Fully vaccinated	74	84.1
	Partially Vaccinated	5	5.7
	Unvaccinated	9	10.2
RVI status	Negative	86	97.7
	Positive	0	0
	Not known	2	2.3
Seasonal distribution	Spring	22	25
	Summer	20	22.7
	Autumn/fall	26	29.5
	Winter	20	25
Place of Admission	ER	5	5.7
	Pedi ward	63	71.6
	PICU	20	22.7

5.2 Clinical Profile

The median duration of illness before admission was 9.5 days IQR (2-60 days). From the total number of patients 63(71.6%) of them had cough as the chief complaint, and 41 (46.6%) of the patients had prior upper respiratory tract infection. Six patients (6.8%) had history of contact with TB patient. None of the children with empyema after 2019 tested positive for COVID-19 virus. Among the total 88 empyema cases, 19(21.6%) report history of chest trauma prior to illness and only 1 patient had penetrating chest trauma for which she stayed in Abet Hospital and chest tube was inserted, received ceftriaxone for 10 days prior to transfer to our side, the other 18 of them were blunt chest trauma.

Sixty three (70.5%) of the 88 patients were admitted to pediatrics ward and twenty of the patients (22.7%) were admitted to pediatric ICU and among those seven of them were intubated. The minimum oxygen saturation recorded at presentation was 62% at room air.

There were eleven cases with previous chronic illness accounting 12.5% of the total empyema admissions. Among them there were 4 preschool asthma, 2 Atrial-septal defects with severe pulmonary hypertension and 1 down-syndrome patient. The rest were congenital lung lesions (1 congenital lobar emphysema, 2 Bronchogenic cyst, and 1 pulmonary hypoplasia).

The diagnosis of empyema was made on the basis of physical findings, pleural tap analysis, chest x-ray and chest ultrasound and/or chest CT findings when available. 42 of the patients (47.7%) had all the investigation modalities except chest CT, Chest CT was done for 19 of the patients (19.3%). Majority of the patients had unilateral empyema with right lung being commonly affected in 55.7% (49/88) compared to the left lung (28.4%). Involvement of both lungs was observed in 14 of the patients (15.9%). 50% of the patients were graded as moderate sized empyema and 30 of the patients (34.1%) were having massive empyema. Chest x-ray's showed obliteration of CPA in all of cases with concomitant findings of pneumonia in (46.5%).

5.3 Laboratory data

Routine investigations like Hemoglobin, total WBC and differential , platelet and ESR were done for all patients but CRP wasn't done for most patients. On CBC white cell count ranged from 2300 -23400, majority of the patients had leukocytosis (WBC count of greater than 14500) with neutrophil predominance (54.5%), 28.4% had higher platelet count at presentation ($>450 \times 10^3$). Thirty-One out of 88 (35.3%) patients were anemic. The minimum ESR recorded at the time of admission was 26mm/hr and the maximum was 160mm/hr and most follow-up ESR's were in the normal range on discharge from follow up.

Table 2: Anemia Incidence

Hemoglobin	Number of patients	Percentage %
Hgb>10mg/dl	57	64
Hgb 7-10 mg/dl	29	33
Hgb <10 mg/dl	2	2.3
Total	88	100

5.4 Pleural fluid analysis

Complete pleural fluid analysis was done for 63 of the 88 cases and in the rest of 25 cases pleural fluid analysis was not done. From 25 of the cases; gross pus mixed with blood were seen on chest tube insertion in 10 of the cases, full of pus cells were reported from 3 of the pleural fluid and there were 3 lost samples documented on the chart. The rest of 9 empyema cases they were having dry tap. The other finding regarding pleural fluid analysis was 17 samples with only pleural cytology reports of empyema(from 63 cases).

Pleural fluid cell count was divided in to four categories listed below in table 2. Majority of the patients had pleural fluid cell count above 10,000. Pleural fluid gram stain was positive in 14 cases among those 12 were gram positive and 2 were gram negative bacteria. The causative organism was identified in 14 samples, the most common pathogen identified was *S.aures* in 7/14 cases (50%), followed by *Acitinobacter* 5/14 (35.7%) cases and *Streptococcus* 2/14 (14.3%) cases.

Table 3: Pleural fluid cell count

Pleural fluid cell count	Frequency	Percentage
<4,000	7	8
4,000-10,000	14	15.9
>10,000	42	47.7
Dry tap/tap not done	25	28.4
Total	88	100

5.5 Management

Prior to admission to SPHMMC ; thirty three (37.5%) of the patients had prior hospital admission before coming to SPHMMC for similar complaint and 40 of the 88 patients (45.5%) received antibiotics (at regional referring hospital or at private clinic), Ceftriaxone was frequently prescribed IV medication in 65% of the cases followed by vancomycin in combination with ceftriaxone in 6 of the 40 cases.

After being admitted to SPHMMC; all children admitted with empyema thoracis were treated with intravenous antibiotics during hospitalization. In general first line empiric antibiotics were ceftriaxone with vancomycin. In early study periods 2015 to 2019 ceftriaxone mono therapy or with penicillin without vancomycin was practiced. Eleven of the children (12.5%) had started Anti-TB in addition to antibiotics where majority (7 of the 11) of them started because of lack of response to antibiotics while the rest of 4 patients were started on Anti TB from the referring hospital. Fourteen of the eighty-eight patients (16%) were treated with only antibiotics without thoracentesis.

Along with the antibiotics 74 of the patient have had chest tube inserted (82.9%) and among them twenty three received fibrinolytic therapy and decortication was done for only 3 patients. There were 2 empyema cases referred to BLH for surgical management and ICU admission and 2 patients were advised for decortication but they went against medical advice. The average duration of chest tube placement was 15.1 days.

Table 4: Modes of treatment for Pediatric Empyema form 2015 to 2022, SPHMMC

Local treatment	Frequency	Percentage
Antibiotics without thoracentesis	14	15.9
Antibiotics with thoracentesis	2	2.3
Antibiotics with chest tube drainage	43	48.8
Antibiotics+ chest tube drainage with intrapleural fibrinolytic (streptokinase)	22	25
Surgical management (Decortication)	7	7.95
Total	88	100

The median length of stay in the hospital was 26.8 days (IQR 8 -62 days). The mean duration of hospital stay in those treated with Antibiotics plus chest tube drainage was 29.3 days whereas in those with addition of fibrinolytic was 26.3days.

5.6 Treatment outcome and complications

Twenty five of the 88 patients developed complications during their hospital stay (Table 6). Among them 6 of the patients outcome was not known (4 went against medical advice, whereas 2 of them were advised for surgical management but family refused and the other 2 of the patients were deteriorating; on double vasopressor and one was on MV, the other was also requiring maximum respiratory support) 2 of the 6 patients referred to BLH for surgical intervention). Fifteen of the patients were discharged with sequel, the rest of 4 of the 25 patients recovered fully from their complications and discharged home.

Table 5: Complications during treatment

Complications	Frequency	Percentage
Pneumothorax	3	12.0
Necrotizing pneumonia	3	12.0
Pericarditis	7	28.0
Lung abscess	2	8.0
Pneumothorax and pericarditis	2	8.0
Septic arthritis	2	8.0
Septic Shock	2	8.0
Atelectasis	1	4.0
Meningitis with suppurative pericarditis	1	4.0
Meningitis	1	4.0
PSGN	1	4.0
Total	25	100

5.7 Factors associated with outcome of children treated for empyema thoracis

Among the independent variables that were analyzed with univariate analysis; gender, estimated fluid amount, admission place, level of respiratory support, WBC count and initiation of anti TB were found to have P value of <0.05. However with multivariable analysis none of the independent variable was found to have significant association with patient outcome.

Table 6: Univariate and Multivariable logistic regression of factors associated with Plural Empyema among pediatric patients admitted to SPHMMC from 2015-2022

Variable		Treatment outcome at discharge		COR (95% CI)	P- value	AOR (95% CI)	P- value
		Fully recovered at discharge	Discharged with complication				
Gender	Male	53	6	.252(0.079-0.798)	0.019	0.029(0-6.25)	0.196
	Female	20	9	0.45			
Estimated fluid amount	Small	14	0		0.085		0.951
	Moderate	39	5	0	0.998		0.996
	Large	20	10	0.256(0.77-0.852)	0.026	1.815(0.046-71.994)	0.751
Admission Place	ER	4	1		0.013		0.305
	Ward	57	6	0.375(0.35-3.999)	0.417	0.261	1.00
	PICU	12	8	0.158(0.046-0.539)	0.003	0.047(0.001-2.306)	0.124
Level of respiratory support at admission	None	16	0		0.022		0.515
	INO2 <3 LPM	42	5	0	0.998	0	1.0
	INO2 3-5 LPM	5	4	0.5536(0.089-3.212)	0.495	0	
	Face mask	1	4	3.6(0.478-27.11)	0.214	0	1.356
	CPAP	9	2	18(1.242-260.918)	0.034	0	8.536
WBC count	< 4000	0	3		0.461		0.537
	4000-12000	23	6	1.737(0)	0.999	0.000	1.0
	12000-14000	7	2	2.804(0.718-10.956)	0.138	8.707(0.065-1167.16)	0.387
	>14000	43	4	3.071(0.471-20.047)	0.241	42.144(0.292-6086.02)	0.140
Anti TB initiation	Initiated	7	4	0.292(0.073-1.164)	0.081	3.942(0.044-349.546)	0.549
	Not initiated	66	11	1.959	0.604		

6. Discussion

Empyema thoracis is the most common complication of bacterial pneumonia faced in pediatric age group. In this study there were 88 empyema patients treated over a period of 8 years at SPHMMC. An increase in incidence of empyema cases has been reported by different authors (9, 10). The reason for this phenomenon is not clear but possible explanations could be being unvaccinated, delayed hospital visit and most importantly the emergence of antibiotic resistant bacteria making it more difficult to effectively treat infections potentially leading into more severe cases and increase in empyema. The incidence of empyema in this study is 12/1000 admissions which is significantly higher compared to a previous study from Ethio-Swedish pediatric hospital in Ethiopia which was 2.7/1000 admissions. But the incidence with respect to the number of nontuberculous bacterial pneumonia cases which is 5.3%, is comparable to 4% reported in the study by S.Hailu et al. (13)

The median age for the development of pleural empyema in this study was 3 year IQR (1-4 years) and the age range was from 25 days to 15 years of age with male predominance of M:F 2.03:1. Univariate analysis showed that male sex likely to have favorable outcome, even though the multivariable analysis failed to show any association. This result is almost similar with other studies conducted in Ethiopia and Belgium (13, 20). This study has shown higher prevalence in age group 5-12 year where bacterial pneumonia is prevalent above 5 years of age in which our finding is consistent with the general agreement. Previously known risk factors such as nutritional status, vaccination and identified etiologic agents could not be demonstrated to be independent in this series. However studies from south Asia demonstrate malnutrition as predisposing factor for development of pleural empyema (21), another study done in central Europe showed un-vaccination associated with development of parapneumonic effusion and empyema (22). Apart from a possible difference in host-agent interaction, this could partly be explained by the fact that the number of cases in this study was small.

Regarding the place of admission of empyema patients, 20 of the 88 patients were admitted to pediatric ICU where all of them were managed with chest tube drainage only 2 of the patients required decortication and none of those patients who were given fibrinolytics required PICU admission this is similar to prospective study in tertiary care hospital in Canada (23)

As opposed to studies conducted in Israel and America (13, 15, 24) where fever with prolonged duration were the presenting symptom in our study cough (71.3%) is the main presenting symptom which usually have longer duration prior to presentation. The study also revealed that the initial level of respiratory support is associated with the treatment outcome of pleural empyema patients much of the patients who require less respiratory support are likely to have full recovery and early hospital discharge ($P=0.042$).

Those who didn't have prior hospitalization history (61.9%) have good treatment outcome than those who have history of hospitalization. However; there prior antibiotic use doesn't affect the treatment outcome ($P>0.05$) which can be supported by a study done in Israel showing no significant association between the use of prior antibiotics and the risk of developing empyema.(24). In contrary Brington et al who did find significant association between the two factors (25). Those who have chronic illness are likely to have prior hospitalization history ($P<0.017$) but no significant lengthy stay in the hospital. Although An increased risk of pleural empyema occurrence was observed in adult study with chronic illness like asthma with frequent hospitalization, antibiotic use and length of stay (26).

From those patients pleural fluid culture done(63/88) pathogenic bacteria recovered in only 14 of the samples where *S.aures* accounted 50% of etiologies. This finding is similar with the local data series done by S.Hailu et al (13) followed by *Acinetobacter* in 35.7% of the culture positive cases this finding is against most literatures as *Streptococcus pneumonia* is the predominant cause for empyema(12,15,22). In addition to the frequent antibiotic use prior to culture as noted in most of our patients. Culture negative empyema cases may also be sometimes due to anaerobic organisms which can be improved by the use of improved bacteriologic techniques.(13)

Those patients with leukocytosis were found to have favorable outcome. However leukocytosis is unreliable marker of pleural empyema where in this study 5 of the culture positive results didn't show leukocytosis on their initial CBC profile. In our study anemia were seen in 31 of the 88 empyema patients (35%); In addition, anemia was found by several investigators to be a risk factor for the development of invasive pneumococcal disease, including pneumonia, as well as being a marker for increased morbidity and mortality(27-29). However our study did not reveal any association between treatment outcome and anemia.

All of the empyema thoracis patients received antibiotics and most of the patients were treated with chest tube drainage 72/88 (81.8 %); among those who were treated with antibiotic and chest tube drainage without fibrinolytic (46/88) 28 of the patients recover fully similarly; a comparative study done in Tunisia in 2022 intensive medical management with adequate chest tube drainage and appropriate antibiotics will result in full resolution for most patients(30). The median duration of chest tube removal in this study was 15.1 days which is comparable to a prospective study from India(8) however in this study with addition of fibrinolytic there was no significant shortening of hospitalization unlike the findings done in a retrospective study in India and London (8, 31). Surgical intervention (decortication) was planned for seven patients however; it was done for only 3 patients (where 2 patients were referred to BLH for lack of ICU bed, 2 of the patients family refused the procedure) which is a small number when compared to other studies(11, 12).

A number of patients had complications most of the complications are local site complications like pericarditis (28%) pneumothorax (12%) Necrotizing pneumonia (12%) and 2 patients developed lung abscess (8%). Among the distant complications were meningitis (8%), septic shock(8%) and septic arthritis(8%). Although there is no in-hospital mortality was recorded in this study yet there were 2 cases that deteriorated prior to self-discharge, they are discharges against medical advice. A delayed presentation was generally present in our current study as well. Despite this, mortality is decreased as compared to the previous local data by S. Hailu et al where it was 16%, despite the rise in incidence.(11, 12) However the improved medical and surgical interventions, as well the improved living conditions and the awareness of individuals about early detection that has evolved over the years can be the rationale behind this finding.

7. Strength and Limitation of study

7.1 Strength

To the best of our knowledge there is no study conducted over the past 20 years in Ethiopia that assessed the magnitude and associated factors of empyema thoracis in children admitted with pneumonia.

The longer time coverage with a relatively larger sample size is another strength of the study.

7.2 Limitation

This study has some limitations. First, as a retrospective review, our data collection, analysis and reporting were restricted to that available in hospital databases or logbooks. Thus, for some years of data, incomplete patient information precluded further analysis. Additionally as it is an institution based study it cannot be generalized to the general population.

8. Conclusion and Recommendation

8.1 Conclusion

Empyema thoracis is becoming prevalent complication of bacterial pneumonia; the incidence has been increasing since the past 24 years. The majority of empyema patients in this study 82.9% recovered without complication. Antibiotic therapy with chest drain insertion $\pm$ intra-pleural fibrinolysis is an effective treatment of plural empyema and surgical intervention is rarely practiced.

8.2 Recommendations

As retrospective studies have significant limitations and the empyema thoracis required a prolonged prospective study with improved diagnostic modalities. This will help in setting up a management protocol that is relevant to our particular setting and identifying specific etiologies with details of sensitivity pattern and predisposing factors to improve the prevention of empyema before occurrence.

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