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## Clinical features, management and outcomes of pediatric pleural empyema: A retrospective, multicenter cross sectional study

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### ABSTRACT

**Objectives:** To evaluate clinical features, treatment strategies, and outcomes of pleural empyema for children who were treated at referral pediatric hospitals in 8 provinces of Iran.

**Methods:** In this retrospective, multicenter cross sectional study, we retrospectively retrieved patients' data from 8 teaching hospitals during 2010 and 2017. A questionnaire was applied and filled, and all data were statistically and descriptively analyzed.

**Results:** In total, 191 children (109 males and 82 females) were included. Their mean age was 4.95 years and ranged from 11 months to 16 years. The majority of cases (45.1%) were 1-4 years old. Fever (70.3%), cough (65.6%), tachypnea (53.1%), chest pain (14.6%), and abdominal pain (12%) were the most common manifestations at admission. The mean length of admission in hospital was 16.4 d. Consequently, 27 patients (14.1%) were admitted into the pediatric intensive unit because of severe illness, and 15 patients (7.9%) died. Logistic regression analysis showed that younger age (less than 12 months) and presence of underlying diseases (such as cardiovascular disease, immune deficiencies, malignancies, and neuro-developmental delay) significantly increased the mortality rate of patients with pleural empyema ( $P=0.004$  and  $P=0.001$ , respectively).

**Conclusions:** Pleural empyema children of younger age and with underlying diseases are at higher risks of death. In addition, guidelines for treating pleural empyema should be developed.

**KEYWORDS:** Pleural empyema; Pediatric; Diagnosis; Treatment; Outcome

### 1. Introduction

Empyema is defined as the presence of bacterial organisms or purulent fluid in the pleural space secondary to bacterial pneumonia, chest trauma, or chest surgery. Empyema is a rare complication of acquired pneumonia, and it is reported that 0.6% of children with pneumonia grew empyema[1]. Despite recent advances in antibiotics, the incidence of empyema seems to have increased, especially in the developed world, owing to antibiotic resistance or changes in microbial strains due to vaccination against *Streptococcus pneumoniae* and *Haemophilus influenzae* type b[2-4]. In essence, empyema develops as a result of interaction between the host immune system and bacterial virulence[5].

Children under 2 years account for the bulk of the empyema cases. Other risk factors include spring and winter, underlying diseases such as immune-deficiencies, malignancies, cerebral palsy and cystic fibrosis, late treatment, inappropriate antibiotic therapy, and low socioeconomic status and malnutrition. Empyema has significant morbidity, including persistent fever and prolonged

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hospital stay, high health care costs, and burden of disease. Despite current management, it has a high mortality (6%-24%). To reduce mortality and morbidity we should make a proper and rapid diagnosis, implement effective treatment, as well as find and eliminate risk factors for poor prognosis<sup>[6,7]</sup>.

The aim of the study is to evaluate the clinical features, treatment strategies, and outcomes of pleural empyema in children treated in referral pediatric centers in 8 provinces of Iran.

## 2. Materials and methods

### 2.1. Ethical approval

This study was reviewed and approved by the Ethics Committee of Shahid Beheshti Medical University (Ethics number: IR.SBMU.REC.1393.699).

### 2.2. Data collection and screening

In this descriptive cross sectional study, we retrieved patients' data from the record of teaching hospitals of 8 provinces in Iran during 2010 and 2017. International Classification of Diseases Codes was used to search computerized hospital discharge record database in each collaborating hospital. Records of all patients who were discharged with the diagnostic code corresponding to pyothorax with fistula (J86.0), pyothorax without fistula (J86.9), or pleural effusion (J90), and pleural empyema were evaluated.

For each patient, the information questionnaire includes demographic information, signs, and symptoms of the patient at the time of admission, underlying diseases, and laboratory tests and imaging results, history of treatment, duration and outcomes of admission were recorded. The content of the questionnaire was confirmed by 3 pediatric infectious disease subspecialists and a methodologist.

A child who aged 2 months to 16 years old and was under following conditions was defined as empyema: (1) Positive smear or positive culture; (2) Two from three markers: Glucose<40 mg/dL, lactic acid dehydrogenase>1000 IU/L, pH<7.2; (3) WBC>10000/mL + polymorphonuclear leukocytes>90%

### 2.3. Statistical analysis

The obtained data were analyzed by using IBM SPSS software, version 21.0. Descriptive data were expressed as frequency and percentage. Logistic regression analysis was conducted to analyze the risk factors of mortality rate. The significance of this test was set at  $\alpha=0.05$ .

## 3. Results

During the study period (2010-2017), 191 children (109 males

and 82 females) were included. The mean age of the children was 4.95 years, ranging from 11 months to 16 years with a median age of 3.6 years. The age group of 1-4 years (45.1%) comprised the largest proportion of all cases. Fever (70.3%), cough (65.6%), tachypnea (53.1%), chest pain (14.6%), and abdominal pain (12%) were the most common manifestations at admission (Table 1). The mean duration of symptoms before admission was 13.7 d and the median was 10 d. Besides, 106 patients (55.2%) took oral antibiotics before hospital admission. We found 38 cases (19.9%) had underlying diseases including congenital heart disease (11.3%), malignancy (3.8%), immune deficiency (3.2%), neuro-developmental delay (1.1%), and myopathies (0.5%) (Table 1).

The chest X-rays of patients at the time of admission showed 143 cases of unilateral effusion (89.4%) and 17 cases of bilateral effusion (10.6%). Other abnormalities in their chest X-rays were abscess formation in 8 patients (5%), pneumothorax in 36 patients (22.5%), and pneumatocele in 4 patients (2.5%). The records of the chest X-ray of 31 patients were missed.

The report of chest ultrasonography was done for 94 patients (49.2%). Free fluid in pleural space was shown in 63 patients (67.0%) within 72 h of admission, while loculated pleural effusion in 32 patients (34.0%), air-fluid level in 12 patients (12.8%) and thickening of pleura in 11 patients (11.7%).

The median of patients' erythrocyte sedimentation rate was 62 mm/h, and a positive C-reactive protein test was found in 65.6% of the patients. The result of the blood culture test was not found in 53 patients (27.7%) but the existing results showed 126 negative (91.3%) and 12 positives (8.7%) blood cultures. The pleural fluid culture was positive in 14% of patients.

**Table 1.** Baseline information at admission.

Variables	N	Percentage (%)
Gender		
Male	109	57.1
Female	82	42.9
Signs and symptoms		
Fever	135	70.6
Cough	126	66.0
Tachypnea	102	53.4
Respiratory distress	71	37.2
Vomiting	28	14.7
Abdominal pain	23	12.0
Chest pain	28	14.7
Decreased respiratory sounds	124	64.9
Rales	46	24.1
Wheezing	10	5.2
Hepatomegaly	9	4.7
Presence of underlying disease		
No	148	77.5
Yes	40	20.9
Type of underlying disease		
Congenital heart disease	21	11.0
Malignancy	8	4.2
Immune deficiency	6	3.1
Neuro-muscular diseases	5	2.6

**Table 2.** Relationship between chronic diseases and immune deficiencies and the mortality rate.

Variables	B	S.E.	Wald	df	Sig.	Exp (B)	95%CI for EXP (B)	
							Lower	Upper
Chronic diseases and immune deficiencies	2.255	0.583	14.939	1	0.000	9.533	3.039	29.910
Constant	-3.353	0.455	54.327	1	0.000	0.035	-	-

**Table 3.** Relationship between younger age (less than 12 months) and the mortality rate .

Variables	B	S.E.	Wald	df	Sig.	Exp (B)	95%CI for EXP (B)	
							Lower	Upper
Younger age (less than 12 months)	-1.981	0.695	8.113	1	0.004	0.138	0.035	0.539
Constant	-1.099	0.471	5.431	1	0.020	0.333	-	-

Treatment of patients was done in the form of monotherapy (only antibiotics) or combination therapy [antibiotics with surgical interventions such as thoracentesis, chest tube drainage with intrapleural fibrinolytic and video-assisted thoracoscopic surgery (VATS)]. All children were treated with antibiotics. The most commonly used antibiotic was the third generation of cephalosporin (131 cases), vacomycine (124 cases), clindamycine (67 cases), and imipenem (43 cases). The mean duration of antibiotic therapy was 5.57 d (median: 5 d; minimum: 1 d; and maximum: 60 d). Surgical interventions were performed for 49 (25.7%) patients. Decortications were performed in 21 patients (42.9%), lobectomy for 13 patients (26.5%), VATS for 10 patients (20.4%), and debridements in 5 patients (10.2%).

The mean length of admission in the hospital was 16.4 d and the median was 15 d. This duration in patients with surgical therapy was longer than others. The mean date of the surgery was 8th day of admission (median: 7; minimum: 1; and maximum: 32).

Altogether, 27 patients (14.8%) were admitted to the pediatric intensive unit because of severe illness and 15 patients (7.8%) died. In logistic regression analysis, younger age (less than 12 months) and presence of underlying diseases (such as chronic diseases and immune deficiencies) were significantly increased mortality rate in patients ( $P=0.004$  and  $P=0.001$ ) (Table 1 and Table 2).

#### 4. Discussion

Defined by the American Thoracic Society Classification, empyema is a dynamic process that progresses through 3 fairly distinct stages. The mainstay of pleural empyema treatment is the diagnosis based on clinical and para-clinical findings for controlling this situation.

Unfortunately, there is no specific symptom for the diagnosis. The most common presentation of empyema in our patients was fever (70.3%), cough (65.6%), and respiratory distress (37%). Similarly, Almaramhy *et al.*[8] reported cough (88.7%), fever (80.6%), and dyspnea (74.2%); Aydogan *et al.*[9] and Waheeb *et al.*[10] reported cough and fever as the most common symptoms of empyema. For the reason why we didn't see any specific presentation in our patients, it is maybe the delay in diagnosis and long duration of symptoms before admission (13.7 d). Besides, other researchers reported this period has been as long as 10.6 -11.4 d. Same with

our results, most studies also showed that males accounted for the bulk of the empyema cases. Further study is needed to verify significant sex differences in the development, progression, and complications of respiratory tract infections.

In the study of Cohen *et al.* most patients were managed with a chest tube (62%), where 79% of them received fibrinolysis; none of them were treated with VATS, and none of the patients was surgically treated[2].

In our study the mean length of admission in hospital was 16.4 d and median was 15 d. The mean duration of admission in patients with surgical therapy was longer than other patients. The reason may lie in more severe or complicated disease and no response to medical therapy in surgical-treated patients[11]. Despite our results, the study of Safi *et al.* and the study of Goyal *et al.* showed lower morbidity, shorter hospital stay, and better long-term outcome in patients with pleural empyema who treated with early surgical treatment[12,13].

Near 20% of our cases had an underlying disease and it was 15.4% in other studies[3]. This data is an alarm for underlying-disease-suffered children presenting the symptoms of prolonged cough and fever, and complicated pneumonia should be considered while making a diagnosis.

The presence of underlying diseases, the clinical severity of pneumonia and pleural empyema, the virulence of the etiologic organisms, and the protocol for hospital admission and discharge are different among the various studies, and treatments only based on the results of studies are not reasonable[14].

As outlined by Mayo *et al.*, the goals of treatment in patients with pediatric empyema are (1) Save lives; (2) Eliminate the empyema; (3) Re-expand the trapped lung; (4) Restore mobility of the chest wall and diaphragm; (5) Return respiratory function to normal; (6) Eliminate complications or chronicity; (7) Reduce the duration of hospital stay[15]. To achieve these goals, the development of therapeutic protocol or guidelines for treatment of pediatric pleural empyema is necessary. This survey showed to us, unfortunately we don't have specified guideline and equal approach to pediatric pleural empyem in Iran. Our recommendation to health policymakers in our country is to develop care pathway or guideline for pediatrics' illnesses as soon as possible.

## 5. Conclusion

Pleural empyema is an important cause of morbidity in children[16]. This study demonstrated the status of pleural empyema and its incidence during the last 8 years, as well as the diagnosis and therapeutic action, in the referral hospital of Iran. According to the results of most studies, fever, cough, and chest pain were the most common symptoms of empyema[6]. Thus, determining a diagnosis and treatment protocols, selection of the best management approach according to the underlying disease, including supportive care, selection of proper antibiotics, and invasive approaches if required can result in favorable outcomes[3]. Antibiotic therapy with chest drain insertion with or without intrapleural fibrinolysis is an acceptable treatment in pleural empyema, and surgical intervention is infrequently needed[17]. According to the results of this study, younger age and presence of underlying diseases affect the mortality rate in pleural empyema patients; so the two groups of patients are high risk and need more attention during treatment. Furthermore, we recommend that guideline development for pediatrics' illnesses at the first opportunity.

## Conflict of interest statement

The authors report no conflict of interest.

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## Authors' contributions

All authors contributed equally to this article.

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