

Determinants of Complicated Pneumonia in Hospitalized Pediatric Patients

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Abstract- Pediatric complicated pneumonia (PCOMP) is the leading cause of mortality in children under the age of five. The study was conducted to determine the epidemiological and clinical characteristics of children with PCOMP. A retrospective study was carried out among all pediatric patients who were hospitalized due to complicated pneumonia in Abuzar Hospital (Ahvaz, Iran) during two years. The patients were evaluated in terms of epidemiological and clinical characteristics. A total of 65 hospitalized children and infants were identified. More than half of the patients were females (n=36; 55.3%). Their mean age was 4.21 ± 3.80 years (range six months-15 years), and 64.1% of them (n=42) were under the age of five. There were 12 (19.4%) patients with failure to thrive (FTT). In addition, 58.5% of patients (n=38) had no history of hospitalization, and 66.2% of them (n=43) did not have any underlying disease. The mean length of hospital stay (LOS) was 12.46 ± 6.85 (range 4-45) days. Admission was more common in winter (40%) and autumn (33.8%). Moreover, there were no significant associations between the types of complications and patients' gender, age, FTT, and LOS. Further studies are warranted to identify factors contributing to disease severity and develop appropriate strategies for the prevention and treatment of PCOMP among Iranian children.

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Introduction

Complicated pneumonia is a broad term that is commonly defined as an infection involving the lung parenchyma, which is complicated by one or more of the following: empyema, abscess, pneumothorax, parapneumonic effusion, necrotizing pneumonia, and bronchopleural fistula (1).

Pediatric complicated pneumonia (PCOMP) is characterized by parapneumonic effusion (a transudative pleural effusion associated with pneumonia); necrotizing pneumonia (liquefaction and cavitation of consolidated lung tissue associated with empyema); empyema (purulent fluid in the pleural space); or lung abscess (necrosis of lung parenchyma producing one or occasionally several large thick-walled cavities) (2,3). Pneumonia is the leading cause of mortality in the world among children under the age of five. The incidence varies greatly between developed and developing

countries (4). This disease is leading to hospitalization in children under the age of 17 in the United States (5). In developing countries, it is the main cause of death in children younger than five years (6). Early identification and cure of patients with pneumonia cases are essential to decrease mortality (7).

There are many identified risk factors related to pneumonia, including indoor air pollution, low maternal education, malnutrition, low socioeconomic status (SES), lack of breastfeeding, poor access to care, and concomitant illnesses (8).

PCOMP is one of the most common health problems despite the introduction of new vaccines and disease management recommendations. Increased hospital admissions due to pneumonia have been reported in children with empyema, necrosis, parapneumonic effusion, and lung abscesses in many areas; however, the contributing factors that lead to this issue are unclear and have not been accurately identified (9). There are

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heterogeneous definitions of PCOMP and a lack of accurate data on its etiology. Microbiological diagnosis is often difficult, and it may be hard to interpret microbiological results (10).

PCOMP is one of the leading causes of death and hospitalization among children and its economic burden is significant. Besides that, basic and epidemiological studies on etiological factors and disease prognosis are limited. Therefore, recognizing the characteristics of infected children can be a basis for further identification of the current situation, and it can help to determine the etiological factors and prognosis of the disease. It is important to know the exact characteristics of patients with pneumonia to combat high mortality of this disease in children. Epidemiological reports of a health care unit can assist in strategic decisions to improve the quality of patient care. Inadequate clinical and epidemiological data are available related to PCOMP in Iran as a middle-income country. In this study, we explore epidemiological profiles of hospitalized pediatric patients admitted to Abuzar Hospital (Ahvaz, Iran) with the diagnosis of complicated pneumonia.

Materials and Methods

This retrospective epidemiological study was carried out among all pediatric patients who were hospitalized due to PCOMP in Abuzar Hospital (Ahvaz, Iran) between 2017 and 2019. The Medical Ethics Committee of Ahvaz Jundishapur University of Medical Sciences (AJUMS) approved the current study (IR.AJUMS.REC. 1398.325). Patients between the age range of six months to 17 years were eligible for the study. The medical records of children and infants were evaluated. Complicated pneumonia was considered to include the presence of pleural effusion requiring drainage and the presence of pneumatoceles, necrotizing pneumonia, pneumothorax, parapneumonic effusion, empyema, lung abscess, and bronchopleural fistula. The exclusion criteria were patients with incomplete medical records. After the preparation of a checklist, all pediatric patients' medical records over the 2-year duration were reviewed to extract the required data. Patients' data, including gender, age, body temperature, clinical symptoms, and admission time, preclinical findings, hospitalization period (day), vital signs, height, weight, mortality rate, and underlying disease, were summarized for this study. The consistency and completeness of records were cross-checked and extracted in Excel software.

Statistical analysis

All data were analyzed using the Statistical Package for Social Sciences (SPSS) version 25. The Shapiro-Wilk test was used to identify the normality of the data. Descriptive data were reported as a percentage, frequency, median (interquartile range), and mean (standard deviation). The Chi-square (χ^2) test was applied to find any associations between the categorical variables. The associations between independent and dependent variables were also evaluated using linear and logistic regression tests (Odds ratio with 95% confidence). The $P < 0.05$ was considered as the level of significance.

Results

In the current study, 65 documents of hospitalized children with complicated pneumonia were reviewed. More than half of the patients were females (55.3%; $n=36$). Their mean age was 4.21 ± 3.80 years. The highest rates of hospitalization for complicated pneumonia and mortality were in children under the age of five (64.1%; $n=42$), while 21.9% of them ($n=14$) were between 5-10 years, and 14.1% ($n=9$) were above the age of five.

The mean weight of the patients was 15.82 ± 9.59 (range 3.2-50) kg. There were 12 (19.4%) patients with failure to thrive (FTT). In addition, 58.5% of children ($n=38$) had no history of hospitalization, atopic, and respiratory diseases, while 41.5% of them ($n=27$) had a history of hospitalization due to respiratory disease. The most frequent clinical symptoms were cough ($n=55$; 84.6%), fever ($n=53$; 82.5%), tachypnea ($n=40$; 61.5%), and retraction ($n=28$; 43.07%) at the time of admission. The most common respiratory sounds were crackles ($n=37$; 56.9%), noise reduction ($n=32$; 49.2%), and wheezing ($n=4$; 6.1%) at the time of admission. The most prevalent underlying diseases were immunodeficiency ($n=6$; 9.2%), pulmonary ($n=5$; 7.7%), and neuromuscular ($n=4$; 6%) diseases. However, 43 (66.2%) patients did not have any underlying disease. The majority of complications were related to parapneumonic effusion [non-specific empyema (23.07%; $n=15$); empyema (43.07%; $n=28$)] and atelectasis (29.2%; $n=19$). All the patients had pulmonary complications while 4.6% ($n=3$) had also non-pulmonary complications (Table 1).

The data related to the treatment of patients with pulmonary complications (except for parapneumonic effusion) and non-pulmonary complications displayed that 29.2% ($n=19$) of patients had atelectasis, and they were treated with antibiotics (Table 1). Among 43 patients with parapneumonic effusion, 15 and 16 patients required to cure with antibiotics and chest tube with

fibrinolytic therapy, respectively. Two patients had undergone surgery from the beginning (besides taking antibiotic treatment) due to the severity of symptoms.

Around 23.2% of patients (n=10) underwent surgery due to resistance to antibiotic treatment as well as chest tube and fibrinolytic (Table 2).

Table 1. Frequency of complications and related treatments in patients with complicated pneumonia (n=65)

Complications	n(%)	Antibiotics n	Fibrinolytic therapy+ chest tube n	Surgery n	Combination therapy n	Bronchoscopy n
Pulmonary						
Parapneumonic effusion	43(66.15)	43	16	2	10	--
Atelectasis	19(29.23)	18	--	--	--	1
Lung abscess	6 (9.23)	6	--	--	--	--
Pneumothorax	4 (6.15)	4	4	--	--	--
Acute respiratory distress syndrome (ARDS)	3(4.61)	3	--	--	--	--
Emphysema	1(1.53)	1	--	--	--	--
Sepsis	1(1.53)	1	--	--	--	--
Non-Pulmonary						
Hemolytic-uremic syndrome (HUS)	2(3.07)	2	--	--	--	--

*Some patients had multiple pulmonary complications; thus, the total number of complications was more than 100%

Table 2. Frequency of treatments for patients with complicated parapneumonic effusion (n=43)

Treatment types	n(%)	Complications
Antibiotics	15(34.88)	Parapneumonic effusion (non-specific empyema)
Fibrinolytic therapy +chest tube	16(37.20)	Parapneumonic effusion (empyema) ± pneumothorax
Surgery	2(4.65)	Sever parapneumonic effusion (empyema)
Combination therapy(Antibiotics+ fibrinolytic therapy+ chest tube+ surgery)	10(23.25)	Parapneumonic effusion (empyema) resistance to treatment

The mean length of hospitalization of patients with PCOMP was 12.46±6.85 days (range 4-45). Admission was more common in winter (40%) and autumn (33.8%) compared with summer (12.3%) and spring (10.8%). There was no significant association between the types of complications with the gender of patients ($P=0.28$), their age ($P=0.73$), FTT ($P=0.75\%$), and length of hospitalization ($P=0.13$).

Discussion

In the current study, 65 hospitalized children and infants with PCOMP were evaluated. Their mean age was 4.21±3.80 years (range six months-15 years), 44.6% of the patients were males (n=29), and more than half of them (64.1%; n=42) were under five years of age. A similar study was conducted in Canada to examine

changes in the incidence of hospitalization of 371 children due to PCOMP. Their median age was four years (range 0.25 to 17 years), while 47.2% (175/371) were male (9). In another study among 639 children in Afghanistan, their median age was 5 (interquartile range 2.5 to 9) months, and among malnourished children, the female gender was associated with death (11).

In a study which was conducted in Brazil to define the clinical characteristics and outcomes of acute community-acquired pneumonia in 80 children, severe pneumonia with pleural effusion was more frequent in children under five years of age ($P=0.025$) and was associated with a longer period of fever (19 vs. 15 days) and coughing (17 vs. 13 days) when compared to non-complicated pneumonia cases (12). In another prospective study in Brazil with a similar objective among 452 children, almost 70% were 2-year-old (13).

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In Taiwan, a study was carried out to find nationwide surveillance of the epidemiology and clinical manifestations of community-acquired mycoplasma pneumonia (CAMP) in 127 children. The enrolled patients were divided into two groups before and after the age of 5 years. Children younger than five-year-old had a significantly longer hospitalization, more complications, and higher intensive care unit (ICU) admission rates. They were more frequent to receive oxygen supplementation and even surgical intervention. The white blood cell counts and C-reactive protein levels were higher in children 5-year-old or younger (14). In other studies, children under the age of five were most at risk (11,15), indicating that this age group is a high-risk group that needs major attention to reduce the health burden.

In the present study, the mean weight of the patients was 15.82 ± 9.59 kg. In addition, there were 12 (19.4%) patients with failure to thrive (FTT). Two studies in Afghanistan (11) and Pakistan (16) reported that pediatric patients with PCOMP and malnutrition were at increased risk of death.

In the current study, 38 (58.5%) patients had no history of hospitalization, atopic, and respiratory diseases, while 41.5% of the patients ($n=27$) had a history of hospitalization due to respiratory disease, and only one patient had familial atopy. A study in China among 1,298 children aged 1 to 14 years found a significant association between previous medical history (pneumonia, asthma, allergy, bronchitis) with the rate of recovery and severity of pneumonia (17). Therefore, it is necessary to pay attention to patients with underlying disease and history of respiratory disease to reduce the complication of pneumonia and prevent its related deaths.

In the current study, the most common clinical symptoms were cough ($n=55$; 84.6%), fever ($n=53$; 82.5%), tachypnea ($n=40$; 61.5%), and retraction ($n=28$; 43.07%) at the time of admission. A prospective study in Taiwan aimed to identify the risk factors of progressive pneumonia among 402 children hospitalized with community-acquired pneumonia, in which 57 patients (14.2%) had progressive pneumonia. Independent related factors identified for the development of progressive disease, included age < 2 years, tachypnea, Hb < 10 g/dL, pleural effusion as admission diagnosis, WBC count > 17,500/ml, and duration to defervescence > 3 days (18).

Related to the frequency of observed complications, the most frequent complications were parapneumonic effusion (non-specific empyema (23.07%; $n=15$); empyema (43.07%; $n=28$) and atelectasis (29.2%; $n=19$). There was no significant association between the types of complications with the gender of patients, their age, FTT,

and length of hospitalization. However, in a similar study in Iran, there was a significant association between the patient's gender and the complications of the disease, but there was no association between other demographic variables and the complications of the disease (19).

The main limitation of the study was the retrospective nature of the study. The study was carried out with a relatively small number of patients with PCOMP from a single medical center. Small sample size may have potential impacts on the statistical significance and can give a result, which may not be appropriately powered to identify any differences between the groups. It can overestimate the magnitude of an association or produce false-positive results. Additionally, it may limit the ability to detect smaller differences and may not normally yield precise or reliable estimates; thus, the findings should be interpreted carefully (20).

It is worth emphasizing that the present study is one of a few single-center studies related to PCOMP in Iran. This study improved our insight into the clinical and epidemiological characteristics of children with PCOMP in a middle-income country. The identification of the specific causes of infection prepares a good starting point for the finding of disease attributable to respiratory infection and may provide related data for the development of prevention strategies. In addition, the findings of a recent study related to lower respiratory tract infections (LRTIs) in children which was conducted in the same hospital and area, might be linked to this study (21).

Precise insights into the identification of risk factors of complicated pneumonia diseases, epidemiology, seasonality, and etiology, are essential for successful therapy or prevention programs. These risk factors can be modified with simple strategies such as immunization, parental education, adequate nutrition, environmental sanitation, and avoidance of pollution. Appropriate counseling of caregivers on the impacts of these modifiable risk factors will aid in better patient care and inhibition of further pneumonia in children. Proper legislation should be used, and health care services should focus on the specific reference to its necessary components such as environmental management, immunization, and nutrition. The findings from this study reveal important missing data on the PCOMP in southwest Iran.

This study aimed to offer a brief update on the recent epidemiology of PCOMP in Ahvaz, Iran. The findings of this study can be compared to those reported in other parts of Iran and the world. Awareness of these and other shortcomings, as well as taking necessary measures to

overcome the barriers will help clinicians to improve their care practice for children with pneumonia. New protocols have to be provided to caregivers in a trial to improve the outcome of children's illness. These data may reveal important information for program managers and policymakers at regional and national levels to help priority settings, program planning, and resource allocation and aid in the determination of the most cost-effective treatment and preventive interventions to decrease the problem of PCOMP. In addition, this study suggests that once the diagnosis of pneumonia is established, the patient should be referred to an equipped medical center so that the serious complications of the disease (surgical procedures and death) could be avoided.

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MM and PN conceptualized the study protocol. SM analysed the data and prepared the first draft of manuscript. MM, PN, MA, SB, and SM critically reviewed and revised the manuscript. All authors approved the final version.

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