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Research Article

Duration of fever in pediatric patients hospitalized with Community Acquired Pneumonia in a reference center for infectious diseases

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Abstract

Introduction: Community acquired pneumonia (CAP) is an important cause of global morbidity and mortality, especially in developing countries, more frequently affecting children under 5 years of age. Few studies in the region have analyzed the total duration of fever days in relation to the presence of complications of the disease.

Objective: To determine the total fever days in patients admitted to the Institute of Tropical Medicine with a diagnosis of CAP, in relation to the presence of complications such as pleural effusion.

Material and methods: Retrospective, descriptive, cross-sectional study, including clinical records of pediatric patients under 16 years of age, admitted to the Institute of Tropical Medicine from January 2015 to December 2017. Epidemiological, clinical, and laboratory data were included and evolutionary.

Results: 433 patients with a diagnosis of CAP were included. The mean age was 32.6 ± 38.3 months. The age distribution was presented as follows: from 0 to 23 months, 252 (58.2%) patients, from 24 to 59 months, 97 (22.4%) and ≥ 60 months, 84 (19.4%) patients. Two hundred thirteen patients (49.2%) were female and 220 (50.8%) were male (1:1 ratio). The presence of pleural effusion was verified in 17.3% of patients (75/433). The average white blood cell count was 16102 ± 11549 cel/mm^3; the hemoglobin and hematocrit averages were 10.5 ± 2.1 g / dL and 32 ± 5.8%, respectively. Platelets presented a mean of 397911 ± 186023 / mm^3 with C-reactive protein positive in 318 patients (73.4%). The presence of bacteremia was verified in 28 (6.5%) patients. Severe hemodynamic compromise, verified by the presence of shock on admission, was found in 69 (15.9%) of the patients, requiring hospitalization in the Pediatric Intensive Care Unit (PICU) 149 patients (34.4%). The requirement of mechanical respiratory assistance occurred in 21.9% (95/433) of the cases, the average stay in assisted ventilation being 3.2 ± 5.3 days. The presence of comorbidities was 13.4% (58/433). The mortality found was 6.5% (28/433). Some microorganism was isolated in 12.7% of cases (55/433). Pneumococcus was found in 12/55 (21.8%), *Staphylococcus aureus* in 27/51 (49.1%) patients. The presence of bacteremia was verified in 28 (6.5%) patients. In pleural fluid, the germ was identified in 32.7% of cases (18/55) patients. In relation to fever, 79% (342/433) of the patients presented it, the total duration of the fever being 4.5 ± 4.6 (Range: 1 - 32), yielding the same value in cases with effusion pleural (4.6 ± 4.6 days Range: 0-27) and in cases of bacteremic pneumonia (4.6 ± 4.6 days Range: 1-27) (p> 0.05).

Conclusion: Community-acquired pneumonia represents high morbidity and mortality, with greater involvement in children younger than 5 years, with a significant requirement for intensive care. Fever is very frequent, not observing a difference in its duration in relation to the presence of pleural effusion or bacteremia.

Introduction

Community-acquired pneumonia (CAP) is the most common cause of death in children worldwide, accounting for 15% of deaths in children under 5 years of age [1].

According to data from UNICEF and the World Health Organization (WHO), in developing countries, CAP represents the cause of at least 20% of deaths in children fewer than 5 years of age [2]. In developed countries this represents around 2%, which the world mortality due to pneumonia in this age

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group would be 19% worldwide [3]. In Paraguay, mortality from CAP in children between 28 days to 12 months of age amounts to 11.4% and in children from 1 to 4 years of age it is around 4% [4].

Almost 1 in 500 children will be hospitalized by NAC, creating a substantial financial burden. Therefore, diagnosing CAP is important, as well as treating it appropriately. While viral causes of CAP are the most common, differentiating viral versus bacterial etiologies can be difficult. This leads to excessive use of antimicrobial drugs, as well as increased pressure to prescribe them [5]. Furthermore, broad-spectrum, but less effective, antimicrobial agents are sometimes prescribed when more favorable, lower-spectrum pharmacokinetics are available [6].

Thus, the adverse effects of the excessive treatment of CAP in those in whom the treatment is not fully justified, influences the morbidity of this process, given the side effects of the drugs, their action on antimicrobial resistance and the microbiome [7].

CAP is defined as an acute lower respiratory tract infection. Associated symptoms include fever, cough, dyspnea, and tachypnea with supporting evidence of infection and inflammation of the parenchyma, diagnosed according to findings on chest auscultation or the presence of focal opacity seen on chest radiographs [8].

Focal opacity on chest radiographs is often maintained as a reference standard; however, some viral processes and pulmonary atelectasis can also cause focal radiological findings (although atelectasis traditionally resolves within 48–72 hours). Furthermore, radiographic manifestations can be delayed with respect to clinical symptoms [9].

Viral pneumonitis is the cause of most respiratory infections, especially in children younger than 5 years old. Unfortunately, the constellation of symptoms or clinical signs (fever, tachypnea, hypoxemia, breathing work) do not show good sensitivity and specificity for radiographic findings of pneumonia, except for the severity of symptoms and poor appearance, which are correlated with focal infiltrates [9].

Combinations of radiographic and physical findings are often used to decide to treat a patient for bacterial pneumonia. The decision on whether or not to hospitalize a patient is made by weighing various factors such as age less than 3 months, underlying comorbid conditions, toxic appearance, complicated pneumonia, respiratory distress, lack of response to outpatient treatment, social risk, recurrent pneumonia or saturation. less than 92% (ambient air) [8,9].

When to perform the image in cases of acute pneumonia is also not well defined, although some general rules apply, such as those indicated in patients with severe respiratory distress, in addition to those who meet hospitalization criteria. It is especially valuable in evaluating the presence of focal parenchymal opacities, as well as detecting complications, such as pleural effusion or pleural empyema, especially in patients who do not respond to antibiotic treatment. It is also useful to identify other causes of auscultatory or respiratory disorders, such as foreign bodies, pneumothorax, pleural disease, heart disease) [10].

Chest radiography is also indicated in febrile infants younger than 12 months without apparent cause, with leukocytosis. In contrast, in patients with evidence of lower respiratory tract infection (fever, cough) without hypoxemia or compatible lung examination, suitable for outpatient treatment, chest radiographs are usually not indicated [11].

Laboratory tests are considered for all hospitalized patients with suspected bacterial pneumonia. These can commonly include blood cultures, inflammatory markers, complete blood cell count, and nasopharyngeal virus swabs (PCR). Blood cultures rarely yield positive results in CAPs, and should not be performed in patients treated on an outpatient basis or in hospitalized patients with uncomplicated disease. However, in patients with severe disease, the performance ranges from 10 to 18%, so its use is strongly considered [12].

Regarding the aetiology of CAP, viral is the most frequent in children under 5 years of age, with viruses responsible for up to 62% of CAP cases, among which respiratory syncytial virus (RSV) is the most common in children under 2 years[7]. *Streptococcus pneumoniae* is the most frequently identified bacteria at any age, with a prevalence of 37% to 44%, with *Staphylococcus aureus* (although it has increased in recent years) and *Haemophilus influenzae* type b (Hib) being less common, especially, after the implementation of the conjugated anti-Hib vaccine. Bacteria such as *Mycoplasma pneumoniae* and *Chlamydiophila pneumoniae* acquire importance at school age, and in different series they constitute the etiology of 14% and 9% of pneumonia, respectively [13].

In relation to the treatment of CAP there are various clinical scenarios and contexts, suitable according to age range that expose the best therapeutics, in relation to the expected germ in infection and the local resistance pattern. It should be remembered that the use of antibiotics such as penicillin or clindamycin are notably influenced by the pattern of sensitivity of bacteria to these antimicrobials, which in those years underwent major transformations and will probably continue to undergo it, forcing specialists to review frequently therapeutic schemes, in order to optimize the cost-benefit ratio and above all obtain satisfactory results [14].

Although fever is a frequent finding in patients with CAP, Latin American studies such as that of Paz F et al. Found no differences in the time of fever according to the surgical resolution or not of the pleural empyemas [15].

Objective

To determine the total fever days in patients admitted to the Tropical Medicine Institute with a diagnosis of CAP, in relation to the presence of complications such as pleural effusion.

Materials and methods

Observational, retrospective, cross-sectional study, carried out with clinical records at the Institute of Tropical Medicine,

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a reference hospital for infectious diseases located in the city of Asunción, which receives patients derived from various locations throughout Paraguay.

Patients under the age of 16 with a diagnosis of community-acquired pneumonia, both by clinical and radiological parameters, were recruited from January 2015 to December 2017.

Epidemiological, clinical and laboratory data were obtained, as well as evolutionary data, including fever days, both during hospitalization, and totals.

Definition of variables

Community-acquired pneumonia: pathology diagnosed in the context of a patient with a clinical history, compatible semiological and radiographic data, presented up to 72 hours after hospital admission.

Exclusion criteria: patients with an incomplete medical record, age over 15 years or data outside the period established in this study, as well as patients whose pulmonary infectious symptoms developed during hospitalization (onset of symptoms after 72 hours, or within 7 days after hospital discharge).

Ethical considerations: The sources of information are the clinical files stored in the Archive of the Institute of Tropical Medicine, obtaining the corresponding permission for their use. The identity of the patients is respected.

Results

From January 2015 to December 2017, 433 patients with a diagnosis of community-acquired pneumonia were included.

The mean age was 32.6 ± 38.3 months. The age distribution was presented as follows: from 0 to 23 months, 252 (58.2%) patients, from 24 to 59 months, 97 (22.4%) and ≥ 60 months, 84 (19.4%) patients. In the present series, 213 (49.2%) patients were female and 220 (50.8%) were male. 1:1 ratio. The presence of pleural effusion was verified in 17.3% of the patients (75/433). (Table 1).

Some microorganism was isolated in 12.7% of cases (55/433). Pneumococcus was found in 12/55 (21.8%), *Staphylococcus aureus* in 27/51 (49.1%) patients (Table 2).

The average white blood cell count was 16,102 ± 11,549 cel / mm3. The hemoglobin and hematocrit averages were 10.5 ± 2.1 g / dL and 32 ± 5.8%; respectively. Platelets presented an average of 397911 ± 186023 / mm3. 318 (73.4%) had positive C-reactive protein values.

The presence of bacteremia was verified in 28 (6.5%) patients. Severe hemodynamic compromise, confirmed by the presence of shock on admission, was found in 69 (15.9%) of the patients. The admission requirement in the Pediatric Intensive Care Unit was 34.4% (149 patients).

The requirement of mechanical respiratory assistance occurred in 21.9% (95 patients) of the cases. Being the average stay in assisted ventilation of 3.2 ± 5.3 days.

The presence of comorbidities was verified in 58 patients, representing 13.4%.

Table 1: General Characteristics of Pediatric Patients Hospitalized with Community Acquired Pneumonia Hospitalized at Tropical Medicine Institute.

Variable	N= 433	%
Age (months)	32,6 ± 38,3	
0-23	252	58,2
24-59	97	22,4
≥ 60	84	19,4
Sex		
Male	213	49,2
Female	220	50,8
Fever	342	79
Pleural effusion	75	17,3
Comorbidity	58	13,4
PICU	149	34,4
MRA*	95	21,9

*Mechanical respiratory assistance

Table 2: Microbiological Characteristics of Pediatric Patients Hospitalized with Community Acquired Pneumonia Hospitalized at Tropical Medicine Institute.

Clinical and evolutionary characteristics	N= 433	%
Isolated germ	55	12,7
Staphylococcus aureus	27	49,1
Streptococcus pneumoniae	12	21,8
Others	16	29,1
Bacteremia	28	6,5
MRSA	17	60,7
MSSA	1	3,6
Streptococcus pneumoniae	5	17,9
Others	5	17,9
Pleural fluid	18	32,7
Staphylococcus aureus	6	31,6
Streptococcus pneumoniae	9	50
Others	3	16,7

The mortality found was 6.5% (28 patients).

Some microorganism was isolated in 12.7% of cases (55 patients). *Streptococcus pneumoniae* was found in 12/55 (21.8%), *Staphylococcus aureus* in 27/55 (49.1%) patients. The presence of bacteremia was verified in 28 (6.5%) patients. In pleural fluid, the germ was identified in 32.7% of cases (18/55 patients).

The average number of fever days prior to hospitalization was 3.2 ± 3.6 (Range: 1-30); while after it the average was 1.8 ± 2.9 (Range: 1–23). Thus, the total duration of fever was 4.6 ± 4.6 (Range: 1–32).

Regarding children with pneumonia complicated with pleural effusion, the average number of fever days prior to hospitalization was 3.3 ± 3.6 days (Range: 0–20); during hospitalization they presented fever on average 1.7 ± 2.6 days (Range: 0–16); the total duration of fever days being 4.6 ± 4.6 (Range: 1–27).

The patients who presented bacteremia had an average of 3.3 ± 3.7 days (Range: 1–20); during hospitalization an average

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of 1.8 ± 2.8 (Range: 1-16); the total duration of the days being 4.6 ± 4.7 days (Range: 1-27) (Table 3). No difference was found between patients without complications (bacteremia, pleural effusion) 4.6 ± 4.6 days.

No difference was found between patients without complications (bacteremia, pleural effusion) 4.6 ± 4.6 days. Patients with pleural effusion had a higher frequency of shock, requiring mechanical ventilation, anemia (Hb>9 g/dL) and bacteriemia significantly, although there was no difference in mortality (Table 4).

Discussion

The present study puts into discussion a situation little addressed in our country, in relation to a known topic, but which always brings controversies regarding various aspects of its management, which is community-acquired pneumonia. The morbidity and mortality of the disease is known and the impact of this disease on the pediatric population has been analyzed in different national and international studies.

It was carried out in a national reference center for infectious diseases, so the population could in that sense contain a selection bias, since many serious cases are derived from it. As well as most of the patients included in the series came from urban centers, among them from the Central Department, most of them came from them.

Table 3: Laboratory, clinical and evolutionary characteristics of Pediatric Patients Hospitalized with Community Acquired Pneumonia Hospitalized at Tropical Medicine Institute.

Characteristics	N= 433	%
White blood cells > 15000	205	47,3
White blood cells < 5000	31	7,2
Hemoglobin < 9	88	20,3
Shock	69	15,9
MRA*	95	21,9
Death	28	6,5
Bacteremia	28	6,5
Blood and pleural fluid	4	0,9
Total fever days	4,6 ± 4,6	
Fever days in patients with bacteremia	4,6 ± 4,7	

*Mechanical respiratory assistance

Table 4: Laboratory, clinical and evolutionary characteristics related to pleural effusion in Pediatric Patients Hospitalized with Community Acquired Pneumonia Hospitalized at Tropical Medicine Institute.

Characteristics	Pleural effusion		No pleural effusion		P	OR
	N= 75	%	N= 358	%		
White blood cells	16131 ± 11617		16102 ± 11549		-	-
White blood cells > 15000	47	62,7	158	44,1	0,003	0,5 (0,3-0,8)
White blood cells < 5000	8	10,7	23	6,4	0,19	0,6 (0,2-1,3)
Hemoglobin < 9	30	40	57	15,9	<0,05	0,3 (0,2-0,5)
Shock	20	26,7	23	6,4	<0,05	0,2 (0,1-0,4)
MRA*	25	33,3	27	7,5	<0,05	0,2 (0,1-0,3)
Death	6	8	12	3,4	0,067	0,2 (0,1-1,1)
Bacteremia	16	21,3	3	0,8	<0,05	0,0 (0,0-0,1)
Blood and pleural fluid	4	5,3	0	0	-	-
Total fever days	4,6 ± 4,6		4,6 ± 4,6		-	-

*Mechanical respiratory assistance

The mean age of the patients included in the present study was 32.6 ± 38.3 months; reinforcing the high prevalence of CAP in children under 5 years old, a fact verified in different studies in both national and international publications. Thus, Arbo A. et al. In a study that included patients hospitalized between 2006 and 2018 in a national referral center, 79.1% were younger than 5 years[3]. In the present study, 80.6% (349/433) patients corresponded to this age group. Breaking down the distribution by age range in the present series, it was verified that it was as follows: 0 to 23 months 252 (58.2%) patients, 24 to 59 months 97 (22.4%) and ≥ 60 months 84 (19.4%) patients. Pathology in infants is important, representing in this series the largest group, this recalling the character of the hospital as a reference center, so this fact could influence the data found.

The male: female ratio was 1:1; thus also translating a population with adequate representativeness in relation to said characteristic, coinciding with the fact that prevalence in favor of any sex was not found in both national and foreign studies.

Complications are frequent in CAP, especially in the predominant age group in this study, with pleural effusion being one of the most frequently encountered complications. In the present series, pleural effusion was evidenced in 17.3% of patients (75/433). This is comparable to national studies, such as the series by Arbo A. et al., Where they verified this complication in 10.1% of patients[3].

The average white blood cell count was 16,102 ± 11,549 cel / mm3. It should be borne in mind that most of the patients were younger than 5 years, so that the leukocyte values could be significantly higher ordinarily than in other patients of older ages. 318 (73.4%) had positive C-reactive protein values. Many of these data were qualitative, with positive or negative results. North American and other studies relate the value of CRP with the bacterial etiology of pneumonia, placing values above 100 mg/L as highly predictive of it; it is a limitation of the present series the lack of quantitative measurements of said acute phase reactant.

The presence of bacteremia was verified in 28 (6.5%) patients, coinciding with global series. The presence of shock at admission was verified in 69 (15.9%) of the patients, relatively high in relation to multicenter series, taking into account that this was developed in a reference center for infectious diseases, where many patients are referred due to its severity or poor evolution. The requirement for hospitalization in the Pediatric Intensive Care Unit was 34.4% (149 patients), which is consistent with the above, in addition to the age group of risk of many of the patients.

The requirement for mechanical respiratory assistance occurred in 21.9% (95/433 patients) of the cases. The average stay in assisted ventilation being 3.2 ± 5.3 days, similar to different studies, with greater severity in developing countries, as highlighted by studies such as those of McCulloh et al[11].

The presence of comorbidities was verified in 48 patients, representing 11.1%. Likewise, the mortality found was 6.5% (28/433 patients), similar to various series3.

Regarding the etiology, some microorganism was isolated in 12.7% of the cases (55 patients), a fact that coincides with

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the literature, although the new molecular methods increase the performance of the isolation. *Streptococcus pneumoniae* was found in 12/55 (21.8%), *Staphylococcus aureus* in 27/55 (49.1%) patients; In different series, staphylococcus increased in frequency over time, so this fact also probably influences the high need for PICU found in this series, considering that various studies, including one developed by Arbo A. and collaborators in the same hospital center3, speak of the greater severity of *Staphylococcus aureus* pneumonia in relation to that caused by pneumococcus. In pleural fluid, the germ was identified in 32.7% of the cases (18/55) patients.

Fever is a frequent symptom in pathology, finding that 342/433 patients (79%) presented it in the development of the disease. This fact is replicated in most series globally. In the patients in general of the present series, it was evident that the average number of fever days prior to hospitalization was 3.2 ± 3.6 (Range: 1 - 30) days; once the patient was admitted, the average was 1.8 ± 2.9 (Range: 1-23). Thus, the total duration of fever was 4.6 ± 4.6 (Range: 1–32). Various studies highlight the fact that complicated pneumonia, with pleural effusion being one of the most frequent complications, conditions the prolongation of fever days in the evolution; thus, in local series by Lovera D and Arbo A and collaborators, these pneumonias were documented with 10 to 14 days of fever, without necessarily representing a nosocomial infection.

In this sense, in the present series, the children with pneumonia complicated with pleural effusion, presented an average of 3.3 ± 3.6 days (Range: 0–20) days of fever prior to hospitalization; in addition, during hospitalization, they presented an average of 1.7 ± 2.6 days (limits: 0–16) of fever; the total duration of fever days being 4.6 ± 4.6 (Range: 1–27). In this way, no difference was found regarding the duration of fever in relation to the presence or absence of pleural effusion.

The patients who presented bacteremia had an average of 3.3 ± 3.7 days (Range: 1–20) of fever prior to hospitalization; during hospitalization an average of 1.8 ± 2.8; the total duration of the days being 4.6 ± 4.7. No difference was found in the total fever time in relation to the presence or absence of pleural effusion. Thus, there is also no difference in the duration of total fever in relation to the evidenced presence of bacteremia.

Various guidelines show the serious nature of complicated pneumonia with pleural empyema[14]. In the present study, it was verified in patients with pleural effusion, a higher frequency of shock, a requirement for mechanical ventilation, anemia (Hb < 9 g / dL) and bacteremia in a significant way, although there was no difference in terms of mortality.

Conclusion

Community-acquired pneumonia represents a prevalent disease in children under 5 years of age, with an important requirement for admission to intensive care. No difference was found in terms of total fever days in the course of the disease according to the presence or absence of pleural effusion.

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