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Severe community-acquired pneumonia in pediatric patients at a high-complexity center in Cali, Colombia

Paola Pérez-Camacho[1,*], Ana María Monsalve[2], Laura Torres-Canchala[3], Inés Elvira Gómez[4], Lina M. Sandoval-Calle[5], Camila Ariza-Insignares[6], Jessica Pino[7], Gerardo Alfredo Guzmán[8], María Teresa Agudelo[9], Diana María Duarte-Dorado[10], Jaime Patiño-Niño[11].

Abstract

Objective: Community-acquired pneumonia (CAP) is one of the leading causes of mortality in the pediatric population. It often leads to pediatric hospitalization, with children under 1-year-old being the most affected and usually requiring management in the intensive care unit. Recent molecular studies indicate that viruses are the most common etiology. The aim of our study was to characterize the pediatric population with severe CAP in a high complexity center in Cali, Colombia, describing demographics, etiologic factors, clinical evolution and outcomes of patients.

Method: We conducted retrospective observational study in a private hospital of high-complexity. Ninety-three patients aged between 1 month and 18 years old with the diagnosis of severe CAP admitted to the Pediatric Intensive Care Unit (PICU) during a 5-year period (2015-2020) were included.

Results: In our population there was no significant gender difference, our median age was 10 months (IQ 3-31), 77% presented respiratory distress and 48% required invasive mechanical ventilation. The most commonly isolated microorganism was *Respiratory Syncytial Virus* (RSV) (n=36), followed by *Rhinovirus/Enterovirus* complex in 41% (n=21), and *Metapneumovirus* 12% (n=6). Viral pneumonia was the most common in our patients (44%, n = 41), followed by viral-bacterial co-infection (13.9%, n=13). Seven fatal cases were reported.

Conclusions: Our study provides epidemiologic evidence of microorganisms that cause severe CAP in the pediatric population in a cohort of pediatric patients prior to Covid-19 pandemic.

Keywords: Community-Acquired infections, Pneumonia, Child, Intensive Care Units, Pediatric

Neumonía grave adquirida en la comunidad en pacientes pediátricos en un centro de alta complejidad en Cali, Colombia.

Resumen

Objetivo: La neumonía adquirida en la comunidad (NAC) es una de las principales causas de mortalidad en la población pediátrica. Con frecuencia conlleva hospitalización pediátrica, siendo los niños menores de 1 año los más afectados y requiriendo habitualmente manejo en la unidad de cuidados intensivos. Estudios moleculares recientes indican que los virus son la etiología más frecuente. El objetivo de nuestro estudio fue caracterizar la población pediátrica con NAC severa en un centro de alta complejidad en Cali, Colombia, describiendo datos demográficos, factor etiológico, evolución clínica y resultados de los pacientes.

Método: Se realizó estudio observacional retrospectivo en un hospital privado de alta complejidad. Se incluyeron 93 pacientes entre 1 mes y 18 años de edad con diagnóstico de NAC grave ingresados a la Unidad de Cuidados Intensivos Pediátricos (UCIP) durante un periodo de 5 años (2015-2020).

Resultados: En nuestra población no hubo diferencias significativas entre sexos, nuestra mediana de edad fue de 10 meses (CI 3-31), el 77% presentó distrés respiratorio y el 48% requirió ventilación mecánica invasiva. El microorganismo más frecuentemente aislado fue el *Virus Sincitial Respiratorio* (VSR) (n=36), seguido del complejo *Rhinovirus/Enterovirus* en un 41% (n=21), y *Metapneumovirus* 12% (n=6). La neumonía vírica fue la más frecuente en nuestros pacientes (44%, n = 41), seguida de la coinfección vírico-bacteriana (13,9%, n=13). Se notificaron siete casos mortales.

Conclusiones: Nuestro estudio aporta evidencias epidemiológicas de microorganismos causantes de NAC grave en la población pediátrica en una cohorte de pacientes pediátricos previa a la pandemia de Covid-19.

Palabras claves: Infecciones adquiridas en la comunidad, Neumonía, Unidad de Cuidados Intensivos, Pediatría.

1 Division of Pediatric Infectious Diseases, Fundación Valle del Lili, Cali, Colombia. Department of Medicine, Icesi University, Cali, Colombia. https://orcid.org/0000-0003-1797-3485
2 Department of Pediatrics, Fundación Valle del Lili, Cali, Colombia. https://orcid.org/0000-0002-3891-9368
3 Department of Medicine, Icesi University, Cali, Colombia. Centro de Investigaciones Clínicas, Fundación Valle del Lili, Cali, Colombia. https://orcid.org/0000-0002-2536-982X
4 Department of Medicine, Icesi University, Cali, Colombia. Centro de Investigaciones Clínicas, Fundación Valle del Lili, Cali, Colombia. https://orcid.org/0000-0001-9314-465X
5 Centro de Investigaciones Clínicas, Fundación Valle del Lili, Cali, Colombia. https://orcid.org/0000-0002-5064-0888
6 Department of Medicine, Icesi University, Cali, Colombia. Centro de Investigaciones Clínicas, Fundación Valle del Lili, Cali, Colombia. https://orcid.org/0000-0002-6989-7587
7 Centro de Investigaciones Clínicas, Fundación Valle del Lili, Cali, Colombia. https://orcid.org/0000-0002-6411-2648
8 Department of Pediatrics, Fundación Valle del Lili, Cali, Colombia. https://orcid.org/0000-0001-9268-7820
9 Pediatric Intensive Care Unit, Fundación Valle del Lili, Cali, Colombia. https://orcid.org/0000-0002-7131-5427
10 Division of Pediatric Pulmonology, Fundación Valle del Lili, Cali, Colombia. https://orcid.org/0000-0002-6081-7050
11 Division of Pediatric Infectious Diseases, Fundación Valle del Lili, Cali, Colombia. Department of Medicine, Icesi University, Cali, Colombia. https://orcid.org/0000-0003-1022-3606
* Autor para correspondencia:
Correo electrónico: paola.perez.ca1@fvl.org.co

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Introduction

Community-acquired pneumonia (CAP) is an entity of multiple etiologies acquired outside the hospital. It is one of the most severe infections in the pediatric population, especially in children under two years old. Different strategies have been stablished to prevent infections and reduce mortality rates, but CAP causes many outpatient and emergency department visits[1]. Since the most frequent bacterial etiologic agents are *Streptococcus pneumoniae* and *Haemophilus influenzae*[2], two immunization strategies have been targeted to reduce their prevalence[3,4]. Multiple studies have shown that respiratory viruses are the leading cause of morbidity and mortality in pediatric patients worldwide. In children under two years of age, 80% of severe CAP is due to viral etiology, with *Respiratory Syncytial Virus* (RSV) being the most frequent, followed by *Adenovirus, Metapneumovirus*, and *Influenza*[5–7].

In 2017, Colombia presented 244,143 hospitalizations in general ward and 20,628 hospitalizations in intensive care units for severe acute respiratory infection, 25%, and 42% respectively corresponded to patients under one year of age[8]. According to the National Health Institute of Colombia, 466 deaths from acute respiratory infection in children under five years of age were reported in 2017. Factors related to mortality were: malnutrition, incomplete vaccination for age, and living in crowded homes[8].

The diagnosis of CAP is clinical and depends on the patient's age. Pneumonia is suspected by the presence of fever and tachypnea. Its severity is determined by the presence respiratory distress, nasal flaring, chest retractions, respiratory grunt, oral cyanosis, and feeding difficulty[9]. Patients with severe CAP usually require ventilatory and/or hemodynamic support at Pediatric Intensive Care Unit (PICU)[10]. The bacteriological diagnosis is made by sputum cultures or bronchoalveolar lavage (BAL). In the last 15 years, molecular detection and sequencing have been introduced to the available diagnostic tools, which have led to an increase in the identification of causative pathogens of respiratory diseases, allowing an early diagnosis and treatment[11]. The first multi-PCR panel approved by the FDA for a large number of respiratory pathogens was introduced in 2008. The FilmArray® respiratory panel evaluates the most common viral and bacterial pathogens that cause respiratory tract infections, which occur with similar symptoms. Several publications report sensibility from 80% to 100% and 100% specificity[10,12].

Severe CAP in pediatrics represents a diagnostic challenge to physicians due to the low sensitivity of traditional diagnostic tests. Therefore, it is essential to know the local epidemiology of pediatric patients to plan preventive interventions and provide pharmacologic treatment that reduces mortality. This study aims to describe the etiology, clinical evolution, and outcomes of pediatric patients with severe CAP who were admitted to the PICU.

Materials and methods

Data Source

We performed a cross-sectional observational study from October 2015 to October 2020 at Fundación Valle de Lili (FVL), a University Hospital in Cali, Colombia. Information was recollected retrospectively from electronic clinical records. FVL has 20 intensive care unit beds for pediatric patients and approximately 207 patients are admitted per year. It is a referral facility for pediatric patients with complex diseases from the southwestern Colombian region.. This study was approved by the Biomedical Research Ethics Committee of the FVL (Protocol No. 886).

Patients

We included pediatric patients older than 30 days and under 18 years of age with a diagnosis of severe CAP admitted to the PICU. Severe CAP was defined as the requirement for admission to the PICU for ventilatory and/or hemodynamic support, based on meeting one of the major criteria for CAP severity of illness in children with CAP of the IDSA management guidelines [13]. We excluded patients with chronic lung disease, cystic fibrosis, tracheostomy, ambulatory mechanical ventilation, hospitalization within the last 30 days; immunosuppressive conditions, and chronic steroid use. Cases were identified by the epidemiological surveillance committee and the statistical service.

Study Variables and Outcomes

Selected variables for statistical analysis included: anthropometric measures and sociodemographic characteristics such as income and city of origin. Healthcare insurance was used as a proxy of socioeconomic status since in Colombia, a patient`s affiliation regime (subsidized or contributory) determines access to clinical services8. Other variables included were: microbiological isolations, days of hospital stay, mortality, requirement of invasive or non-invasive mechanical ventilation, and the presence of complicated pneumonia. The last four were considered outcomes of interest.

Nutritional status was classified according to the WHO growth and development tables[15], considering weight for age in children under five years old because in the majority of cases, there was not height data at admission, and body mass index for age, in children older than five years. Vaccination status was evaluated according to the Colombian national vaccination program. Admission criteria for PICU were: severe CAP with ventilatory and/or hemodynamic support requirements, according to IDSA guidelines and our institutional clinical guideline[16]. Respiratory distress was defined as the presence of chest retractions, nasal flaring, cyanosis, grunting, or apneas[17]. The decision to perform a bronchoalveolar lavage was taken between the treating pediatrician and the Pediatric Infectious Diseases team. Rapid tests for *RSV* and *Influenza* were taken when the patient presented respiratory deterioration, and there was an epidemiological link and clinical manifestations, which would point to these agents as

probable etiology. The FilmArray® Pneumonia Panel was not available at the hospital at the time of the study, and the BioFire® Respiratory Panel (which includes atypical pneumonia bacteria) was not always available. All patients had at least one chest x-ray preformed during their hospital stay.

Statistical Analysis

Descriptive statistical analysis was performed with collected information. According to the normality test, categorical variables were presented as proportions and continuous variables as median with their interquartile range (IQR) or media ± standard deviation (SD). These analyzes were made with the statistical package Stata 14.0 ® (Stata Corp, College Station, TX, USA).

Results

During the study period, 363 patients entered the PICU with a diagnosis of severe CAP, and 270 were excluded. 93 individuals were included. As shown in Table 1, 50,5% were males, median age was ten months (3-31) and 70% (n=65) of patients were less than two years old. Most patients, 87% (n=81), lived in an urban city, 56% (n=52) were affiliated with the contributory healthcare regime, and 67% (n= 3) were referred from another institution. Approximately three-quarters of the patients (74%, n=69) presented an adequate nutritional status at admission according to the parameters used for evaluation. Regarding vaccination status, 87% (n=71) had an age-appropriate vaccination regime against *Streptococcus pneumoniae*, 92% (n=76) against *Haemophilus influenzae,* and 86% (n=47) against *Influenza*.

Regarding the characteristics upon admission to the institution, as shown in Table 2, 52% (n=48) had previously consulted, and 23% (n=21) had received antibiotics in an outpatient visit. The most common symptoms were cough 89% (n=83), fever 77% (n=72), and dyspnea 82%(n=76). Most patients were admitted with respiratory distress 77% (n=72) and 26% (n=24) required orotracheal intubation (OTI). The most common radiological finding was interstitial infiltrates 57% (n=53), and consolidation 51%(n=47).

During treatment at the PICU, as shown in Table 3, 47 patients (48%) required invasive mechanical ventilation and 66 (68%) non-invasive mechanical ventilation. Most patients, (67%, n=62) required these interventions for less than five days, and the median (IQR) of the mechanical ventilation time was one day (0-5). Half of the patients did not develop clinical complications. However, the remaining 37% (n=34) had atelectasis, 23% (n=21) pleural effusion, 5% (n=5) necrotizing pneumonia, and three patients (3%) presented pulmonary abscess. The median hospital stay was five days (RIC 4-5), and 61% (n=57) patients had a total hospital stay greater than ten days. As for fatal cases, seven were recorded. Five of them were children less than one year old, one had an incomplete vaccination scheme. Viral pneumonia was common in fatal cases.

Table 1. Sociodemographic characteristics. N=93

VARIABLE	n (%)
Sex	
Male	47 (50,5)
Female	46 (49,5)
Age in months (Median [IQ])	10 (3-31)
Place of origin	
Urban	81 (87,1)
Rural	12 (12,9)
Healthcare affiliation regime	
Contributory	52 (55,9)
Subsidized	39 (41,9)
Special	2 (2,2)
Referral from other hospital	63 (67,4)
Nutritional Status	
Obesity	3 (3,2)
Overweight	3 (3,2)
Normal	69 (74,2)
Low Weight	9 (9,7)
Malnutrition	1 (1,1)
No data	8 (8,6)
Classification of weight for age (Z score)	
More than +2	6 (6,4)
Between +2 and +1	69 (74,2)
Less than –1	9 (9,7)
More than –2	1 (1,1)
***Streptococcus pneumoniae* immunization regime**	
Complete	71 (87)
Incomplete	6 (7,3)
No data	5 (6,1)
Non-applicable*	11 (11,8)
***Haemophilus influenzae* immunization regime**	
Complete	76 (92)
Incomplete	7 (8)
Non-applicable*	10 (10,7)
Influenza immunization regime	
Complete	47 (85,5)
Incomplete	8 (14,5)
Non-applicable*	38 (40,8)

*****immunization regime non-applicable for patient age.
According to WHO **Classification tables

As for the diagnostic approach, as shown in Table 4, BAL culture was performed in 24 patients (26%), and 29% (n=7) were positive. The most commonly isolated microorganism in BAL was *S. aureus* in three patients (8%), two with methicillin-sensitive strain and one with methicillin-resistant strain. All of the BAL samples were analyzed by GeneXpert to detect mycobacteria of the *Tuberculosis* complex, which was positive in one patient. This was the case of a 2-year-old female with normal nutrition status, complete vaccination scheme and no history of prior use of antibiotics nor pediatric consultation. She presented cough and fever. In her diagnostic images, interstitial, alveolar infiltrates and consolidation were reported. Therefore, she required management in the PICU with NIMV for 2 days and then she was treated in hospital for 3 days. Eight patients required surgery related to pneumonia complications such as thoracotomy, decortication, lobectomy and thoracostomy; and in each of them, cultures of pleural effusion were taken only in these specific cases, of which four were positive–all for *S. aureus.* Orotracheal secretion culture was performed in 19 patients, which was positive in six patients (32%) and the most commonly isolated microorganism was *H. influenzae* (16%, n=3). 74 patients had at least one bloodstream culture, of which only 3 were positive (4%), the bacteria isolated were *Methicillin-sensitive Staphylococcus aureus, Streptococcus pneumoniae and Micrococcus spp.*

Table 2. Characteristics during hospital admission. N=93

VARIABLE	n (%)
Previous Antibiotic Treatment	
Yes	21 (22,6)
No	72 (77,4)
Previous Consultation	
None	45 (48,4)
1 Or 2	45 (48,4)
3 Or More	3 (3,2)
Symptoms During Admission	
Cough	83 (89,3)
Dyspnea	76 (81,7)
Fever	72 (77,4)
Anorexy	13 (14)
Respiratory Distress	72 (77,4)
Endotracheal Intubation Requirement During Admission	24 (25,8)
Radiographic Findings	
Interstitial Opacities	53 (57)
Consolidation	47 (50,5)
Alveolar Opacities	32 (34,4)
Pleural Effusion	16 (17,2)
Diagnosis	
No isolation	22 (24)
Viral Cause of Pneumonia	64 (66)
Bacterial Cause of Pneumonia	12 (12,4)
Viral and Bacterial Cause of Pneumonia	11 (11,8)
Mycotic Cause of Pneumonia	1 (1)

For the study of viral pneumonia, as shown in Table 4, nasopharyngeal RSV detection was performed in 61 patients (66%) and was positive in 39% (n=24). Nineteen patients (20%) were given an influenza test panel, positive in one patient, where AH1N1 *Influenza* was detected. The BioFire® Respiratory Panel was taken in 51 patients (55%); the primary virus isolated was the *Rhinovirus/Enterovirus* complex in 41% (n=21), followed by *RSV* in 24% (n=12), and *Metapneumovirus* (12%, n=6). Pneumonia of viral etiology was the most common in our patients (44%, n = 41), followed by viral-bacterial co-infection (13.9%, n=13). One patient presented purely bacterial pneumonia, and one showed atypical pneumonia due to *Mycoplasma pneumoniae*. In 27 (29%) patients, microbiological isolation was not achieved.

Discussion

Severe CAP is a frequent cause of admission to the PICU in our institution. Our study population included 93 pediatric patients with no previous clinical history admitted with severe CAP over two years.

In our study group, the leading etiological agent were viruses, which agrees with recent literature reviews. In the Etiology of Pneumonia in the Community (EPIC) Study conducted during 2010-2012, based on surveillance of a population of more than 2.300 CAP pediatric hospitalizations in the United States, viruses were the agents identified in more than 70% of the study population, while bacteria were identified in 15% of children[18]. Regarding the specific virus, the *Rhinovirus/Enterovirus* and *RSV* complex were the main viruses isolated in our population, the same as shown in the study by Lanaspa in 2014, where *RSV* was the most detected virus, specifically in children under two years of age, followed by *Rhinovirus*[7].

Co-infections have been the subject of study, specifically the impact that they may have on the patient's clinical findings, such as length of stay in intensive care units and ventilatory support time. Also, the relationship between severe bacterial pneumonia after a viral infection has been identified. Usually, the detected bacteria are *S. pneumoniae, S. aureus, H. influenzae* and *Moraxella catarrhalis*[19]. Our group found viral-bacterial co-infection in 13.9% of patients (n=13) and microorganisms identified in co-infections were *S. aureus* (4 cases) and *H. influenzae* (4 cases). Viruses involved in co-infections were *RSV* (5 cases) and *Rhinovirus* (4 cases). The most common pair was *H. influenzae* with *RSV*, presented in 3 patients. As for co-infections involving only viruses, the most common were *Rhinovirus* (5 cases), *RSV* (4 cases), *Adenovirus*, and *Metapneumovirus* (3 cases each). The most common pair was *Rhinovirus/RSV*.

Table 3. Characteristics during hospitalization (24 hours prior to microbiological isolation). N=93

VARIABLE	n (%)
Invasive Mechanical Ventilation Requirement	
No	47 (48,45)
Yes	46 (47,4)
Non-Invasive Mechanical Ventilation	
Yes	66 (68)
No	27 (27,8)
Days of Mechanical Ventilation Requirement	
0-5	62 (66,7)
6-9	14 (15,1)
More or Equal To 10	17 (18,3)
Days of Requirement of Supplementary Oxygen	
0-5	72 (77,4)
6-9	13 (14)
More or Equal To 10	8 (8,3)
Clinical Complications	
None	47 (50,5)
Atelectasis	34 (36,6)
Pleural Effusion	21 (22,6)
Necrotizing Pneumonia	5 (5,4)
Pulmonary Abscess	3 (3,2)
Days of Stay In PICU	
0-5	41 (44,1)
6-9	23 (24,7)
More or Equal To 10	29 (31,2)
Total Days of Hospitalization	
0-5	6 (6,5)
6-9	30 (32,3)
More or Equal To 10	57 (61,3)
Outcomes	
Alive	86 (92,5)
Dead	7 (7,5)

In Colombia in 2017, the National Institute of Health reported 466 deaths due to acute respiratory infection in children under five years of age. Factors related to mortality were: malnutrition, incomplete vaccination for age, and living in crowded conditions[8]. Children under two years of age have the highest incidence and mortality rate. Seven mortality cases were reported during the study period. Four patients were younger than one year, they had an appropriate weight for age and 57% were female. All of them were transferred from another institution, were admitted with respiratory distress and required management with IMV. All had interstitial infiltrates in chest-x rays, 2 had pleural effusion and 3 presented consolidation. One of these patients had been vaccinated against *Streptococcus pneumoniae* and *Haemophilus influenzae*.

Most patients considered in the study were less than two years old, which means they were at a greater risk of presenting severe respiratory infections, according to several epidemiologic studies published in the last 5 years [4,820]. As Lanaspa and cols show, this age group has a high prevalence of CAP[7]. Jain also demonstrated in his publication on the epidemiology of viral pneumonia that the highest incidence corresponds to children under two years of age[18].

Schematic vaccination has effectively reduced cases of severe pneumonia[4,821]. Vaccination scheme of all patients was evaluated, specifically against *Pneumococcus, H. influenzae,* and *Influenza*, considering that the free national vaccination scheme in Colombia only included the vaccine against *S. pneumoniae* from the year 2011 onwards. Also, only 1 of the 7 fatal cases reported in this study had a complete vaccination regime against *Pneumococcus, H. influenzae* and *Influenza*. The rest of the fatal cases did not have a complete vaccination regime. Due to the fact that inadequate nutritional status has been shown to be a risk factor for pediatric infection and mortality[21,22], weight for age and BMI (Body Mass Index) were evaluated in our patients, who were mostly inadequate nutritional status. Additionally, it is interesting that our only case of tuberculosis in an endemic area presented with symptoms of acute respiratory infection, contrary to the usual silent or subacute course described in the literature[23].

Several pediatric pneumonia management guidelines emphasize that the diagnosis of pneumonia should be based initially on clinical criteria. It has been shown that moderate hypoxemia and increased respiratory work are the signs most associated with pneumonia[24]. The majority of our patients were admitted with symptoms of respiratory distress, and a quarter of them required orotracheal intubation. Even with the different diagnostic methods available, establishing an etiological diagnosis continues to be a challenge[25]. In terms of diagnostic tests, many techniques are currently available such as microscopy, microbiological and viral cultures, antigen detection, and molecular tests[6]. Specific guidelines recommend that some tests should be reserved for cases of severe pneumonia, which requires management in an intensive care unit[16]. Only a few of our patients underwent BAL culture, and in more than 50%, a test was performed to detect respiratory viruses and atypical pneumonia bacteria by PCR. The determination of the culture requirement was made by the pediatric infectious disease team based on the patient's clinical status. However, microbiological isolation was not achieved in all patients. The aim of this study did not include description of antibiotic treatment given to participants. However, it is possible that most of the patients included in this study received antibiotic treatment due to the presentation of clinical severity criteria or clinical findings that suggest bacterial co-infection.

Lastly, we have to mention that by the end of our study the world was undergoing a pandemic, and in Colombia since march of 2020. At that time, the scientific community was taking the first steps in understanding how COVID-19 in-

Table 4. Microbiological isolation

VARIABLE	n (%)
Bronchoalveolar Lavage Culture	**n=24**
Methicillin-sensitive *Staphylococcus aureus* (MSSA)	2 (8,3)
Methicillin-resistant *Staphylococcus aureus* (MRSA)	1 (4,2)
Streptococcus mitis	1 (4,2)
Haemophilus influenzae	1 (4,2)
Mycobacterium tuberculosis	1 (4,2)
Fungi	1 (4,2)
% Positive	7 (29,2)
GeneXpert *Mycobacterium tuberculosis* complex	1 (4,2)
Surgery culture	n=8
Positive	4 (50)
Staphylococcus aureus	4 (100)
Orotracheal Secretion Culture	**n=19**
Positive	7 (36,8)
Haemophilus influenzae	3 (15,8)
Pseudomonas aeruginosa	2 (10,5)
Candida albicans	1 (5,3)
Staphylococcus aureus	1 (5,3)
% Positive	14 (73,7)
Respiratory Syncytial Virus Nasopharyngeal Detection	**n=61**
Positive	24 (39,3)
Negative	37 (60,7)
Influenza Virus Test Panel	**n=19**
Influenza virus A	1 (5,3)
Influenza virus AH1N1	1 (5,3)
% Positive	10,5
BioFire® Respiratory Panel	**n=51**
Rhinovirus/Enterovirus	21 (41,2)
Respiratory Syncytial Virus	12 (23,5)
Metapneumovirus	6 (11,8)
Parainfluenza Virus 3	4 (7,8)
Mycoplasma pneumoniae	4 (7,8)
Coronavirus Oc43	4 (7,8)
Adenovirus	3 (5,9)
Influenza A/H1-2009	3 (5,9)
Parainfluenza Virus 1	4 (7,8)
Coronavirus Hku1	1 (2)
Chlamydophila pneumoniae	1 (2)
Influenza B	1 (2)

*KOH: Potassium Hydroxide

fection affected children, the available systematic reviews agreed that children were less affected compared with adults because predominant asymptomatic and mild cases, mortality, and need of PICU were more associated with MIS-C (Multisystemic Inflammatory Syndrome in Children)[2627,28]. By the end of October 2020, in our center, there were only 13 children reported in the PICU with a positive COVID-19 test, whose cause of admission to ICU was not directly related to COVID-19. 6 of them met exclusion criteria, due to the small and heterogeneous sample size, added to the early stage of the pandemic we decided to not include COVID-19 cases in this study, to conduct in the future specific research for this particular population.

Within the study's limitations, we can mention the retrospective collection of the information; however, duplicate validations were made to all records, comparing them with primary data sources such as clinical records, laboratory records, and those of the institutional Epidemiological Surveillance Committee. In addition, we had an issue with the uniformity of the diagnostic tests; not all the patients had the virus detection test for atypical pneumonia done due mainly to administrative issues from the health system, and not all the cultures for bacterial isolates where taken from the same site and in the same way. This specific issue comes in line with the fact that there is no gold standard diagnostic test in CAP. Another limitation was that the nutritional status was determined with weight for age in children under five years because in the majority of cases, there was no height data upon admission.

As a conclusion, severe pneumonia is a public health problem that affects the pediatric population. Identifying risk factors, immunization programs, specific diagnostic tests, and timely use of antibiotics are required interventions to reduce its prevalence. However, much more research is needed in the development of interventions that reduce hospital stay, mortality, and probability of clinical complications related to CAP. Also, the economic burden in the Colombian healthcare system should be taken into considered when public health interventions are planned and developed. Our study provides epidemiologic evidence of microorganisms that cause severe CAP in the pediatric population in a cohort of pediatric patients prior to Covid-19 pandemic.

Ethical considerations

Conflicts of interest. The authors declare that they did not have a conflict of interest in the execution and writing of this research product.

Ethical board approval. This study was approved by the Fundación Valle del Lili´s Biomedical Research Ethics Committee (Cali, Colombia). No identifying information is exposed in this study.

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Data availability. The data required to reproduce these findings is available upon reasonable request to the correspondence author.

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Authors contribution. P.P, A.M, G.G, M.A, D.D, J.P, Research conceptualization and study design. A.M, L.S, C.A, J.P, Performed the data collection. L.T, I.G, Performed the data analysis and interpretations of results. P.P, A.M, L.T, I.G, L.S, C.A, Wrote the draft and final manuscript. All authors contributed to read and approved the version of the submitted manuscript.

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