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The Microbiological Profile of Community-Acquired Pneumonia in Pediatric Patients in Brazil

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Authors' contributions

This work was carried out in collaboration among all authors. Author GVL designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors RRL, SMAO and SMBG managed the results analyses of the study and the literature searches. Author SBF managed the guidance of the review. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Aims: Identifying the main pathogens causing Community Acquired Pneumonia in the pediatric population.
Study Design: It is a narrative review, a qualitative study.
Place and Duration of Study: Multidisciplinary Laboratory of Scientific Design and Writing (LaMDEC), Julio Bandeira University Hospital (HUJB), Cajazeiras, Paraíba, Brazil, from May 2023 to June 2023.

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Methodology: A narrative literature review method was adopted, with research carried out in the following databases: Google Scholar, Scientific Scientific Electronic Library Online (SciELO), PubMed, LILACS and Virtual Health Library (BVS).
Results: A relevant prevalence of the bacterial pathogens *Streptococcus pneumoniae*, *Mycoplasma pneumoniae* and *Staphylococcus aureus*, and the viral etiological agent Respiratory Syncytial Virus, depending on the age of the affected patients, was observed in the literature in the pediatric population.
Conclusion: A relevant prevalence of the bacterial pathogens *Streptococcus pneumoniae*, *Mycoplasma pneumoniae* and *Staphylococcus aureus*, and the viral etiological agent Respiratory Syncytial Virus, depending on the age of the affected patients, was observed in the literature in the pediatric population. However, the means used to confirm the etiology are still lacking in their methodological reliability, a fact that makes it important for the scientific community to develop and adopt more effective methods for the microbiological determination of the causes of pneumonia.

Keywords: Viral pneumonia; bacterial pneumonia; pediatrics; children; differential diagnosis.

1. INTRODUCTION

Pneumonia is an acute respiratory infection that affects the lungs and which, according to the guidelines of the World Health Organization, is characterized by an episode of acute illness with cough or respiratory distress combined with increased respiratory rate [1]. This is an important public health issue, affecting all age groups, resulting in high morbidity and mortality [2]. With regard to the population, according to the World Health Organization (2021), pneumonia is the main cause of death in children up to 5 years of age, but it also affects the elderly and immunosuppressed people with high rates, which shows its importance epidemiological [3]. It is known that Community-Acquired Pneumonia (CAP) is an acute inflammatory disease of the pulmonary parenchyma of infectious origin, which affects people outside the hospital environment or presents itself within 48 hours after hospitalization [4]. In general, they occur at specific times of the year, prevailing in the winter period, when there is a greater occurrence of viral infections, such as the Influenza virus [5,6].

With regard to the pediatric population, acute respiratory infections are the main reason for admissions due to infections in pediatric emergency services, approximately 10% of children with lower respiratory tract infections come from Community-Acquired Pneumonia (CAP), in addition, it is the second cause of hospitalization and one of the main ones due to prolonged hospitalization in Pediatric Intensive Care Units [7].

From the point of view of mortality, CAP was responsible for 5% of deaths in children under 5 years of age, making it the most important cause of infant morbidity and mortality worldwide [8]. In 2013, the worldwide analysis of the Global Burden of Disease (GBD) suggested that CAP could be responsible for approximately 0.9 million child deaths; this translates into more than 14% of all child deaths, and the incidence becomes 15 times higher in underdeveloped countries than in developed countries, since in the former there is greater exposure to risk factors such as: such as malnutrition, basic sanitation and overcrowding of spaces [9,10].

UNICEF considers pneumonia related to factors such as malnutrition and little access to health services, with exclusive breastfeeding, vaccination, adequate nutrition and good hygiene habits, prevention factors, being necessary, in addition to adequate management of the disease, control of these environmental factors [11].

Thus, according to the World Health Organization, the main etiological agents that cause Pneumonia in children are: *Streptococcus pneumoniae* (pneumococcus), and *Haemophilus influenzae*, the Respiratory Syncytial Virus and, in HIV-infected babies, it is *Pneumocystis jiroveci*. Understanding the prevalence of these pathogens that circulate in our country has a direct impact on therapeutic choices and length of hospital stay, since one of the problems observed is the inappropriate use of antibiotics, as well as long hospital stays, which can bring even more complications to the patient. In this regard, the objective of the study in question is to survey the main pathogens that cause Community-Acquired Pneumonia in order to enable a more effective empirical approach.

2. METHODOLOGY

2.1 Research Characterization

This article is characterized by a narrative review, qualitative in nature, descriptive and exploratory, which focuses on studies that bring the microbiological profile of pneumonia acquired in the community, with the most common pathogens in the pediatric population.

2.2 Conducting the Investigation

The research, which was carried out in February and March 2023, used the following databases: Google Scholar, Scientif Scientific Electronic Library Online (SciELO), PubMed, LILACS and Virtual Health Library (BVS); with the following Decs/Mesh descriptors in Portuguese and English: “Pneumonia Bacteriana”, “Pneumonia Viral”, “Child”, Pediatria” and “ Bacterial, Pneumonia”, “ Viral, Pneumonia”, “Child” and “Pediatrics” Decs/Mesh descriptors in Portuguese and English used, respectively, were “Bacterial Pneumonia”, “Viral Pneumonia”, “Child”, Pediatrics” and “Bacterial, Pneumonia”, “Viral, Pneumonia”, “Child” and “Pediatrics” . In addition, the descriptors were crossed with the Boolean operators AND and OR, and temporal clippings were not used.

2.3 Criteria Selection

The criteria used for selecting articles should have in their title, abstract and full text an approach to the etiological agents that cause community-acquired pneumonia in children and adolescents, as well as having been published in the last 10 years. In addition, the bibliographic selection should be in English, Portuguese and Spanish, selecting studies published in full, theses and reviews. In addition, there was exclusion of duplicated materials or that the full text was tangent to the theme proposed in the research. The search made in the database showed 412 results. After an initial reading of the titles and abstracts, as well as the application of the criteria for inclusion and exclusion of the full texts, 12 scientific articles remained.

2.4 Exhibition of Findings and Synthesis of Information

After reading the selected articles in full, important information was collected to meet the research objective. The presentation of the results was carried out through a dissertation, organized through the synthesis and critical analysis of the material. In this way, the findings were correlated with the review objective, with the aim of making the state of the art on the subject. It was not necessary to submit it to the Research Ethics Committee (CEP), since the works used are publicly available for consultation and the research methodology does not apply to human beings.

3. RESULTS AND DISCUSSION

3.1 Definition and Epidemiological Aspects

Pneumonia is one of the most relevant causes of mortality and costly for the government and families, with an incidence of 0.29 and 0.05 episodes per year per child in developed and underdeveloped countries, respectively, that is, the each year there are about 156 million new cases of CAP, with the majority in countries such as India, China and Pakistan [12,13,14]. In relation to Brazil, the mortality rates due to respiratory tract infection decreased significantly, despite the CAP still persisting as the one with the greatest impact on health, being the third cause of mortality, despite having had a 25.5% drop among the years 1990 and 2015 [15].

It is known that community-acquired pneumonia (CAP) is an acute infectious disease that affects the lung parenchyma and may have different etiologies depending on the age group, which is of paramount importance for diagnosis and, consequently, therapy [16,17].

Thus, in those younger than 3 weeks, the etiological agents that cause CAP are those present in the birth canal (Group B Streptococcus, gram-negative bacilli and *Listeria monocytogenis)*; from 3 weeks to 3 months, respiratory viruses (rhinovirus, influenza, parainfluenza) and *Staphylococcus aureus* predominate; from 3 months to 4 years, viruses are still responsible for most pneumonias, but *Streptococcus pneumoniae* (pneumococcus) becomes the main agent of bacterial origin; Finally, in those aged 5 years or older, viruses are no longer predominant, with bacterial pathogens now prevailing, including pneumococcus and *Mycoplasma pneumoniae* [4,5,18,19]. CAP is a disease with flowering symptoms that can vary according to the age group and the etiological agent involved, so the diagnosis can be late identified and the use of antibiotics erroneously prescribed [20,21].

In addition, knowing the local epidemiology and the etiological spectrum and its possible resistance are the basic points for managing pneumonia [22,23]. Besides that, despite the variety of respiratory microbiota, the easy dissemination of pathogens and the overlapping of viral infections, *Streptococcus pneumoniae* remains the most prevalent etiological agent of CAP [15,24].

It is known that pneumococcus, for example, a bacterium that commonly colonizes the nasopharynx, is one of the causes of pneumonia, in addition to meningitis and bacteremia, which are part of the group of preventable diseases through priority vaccination of vaccines, which significantly reduce the number of hospitalizations [25,26,27].

3.2 Etiology and Diagnosis

It is important to emphasize that Community-Acquired Pneumonia is a disease that develops from the most varied types of pathogens, partly responsible for the diversity of signs and symptoms of pneumonia in the pediatric age group.However, although it is difficult to differentiate the etiology through the clinic, it is still possible to notice patterns that indicate the type of causative agent [1,5,6,28].

In this regard, viral pneumonia is associated with the coldest months and affects more children under 5 years of age, especially those under 2 years of age, with a prevalence of up to 64% in this population, with Respiratory Syncytial Virus (RSV) being the most common virus in these cases (Table 1.), followed by parainfluenza, influenza, rhinovirus [29,30,31,32]. Its symptoms are varied, and it is common to present in conjunction with manifestations of the upper airways, such as a runny nose and nasal obstruction. It is also important to note that 20%-30% of ACPs are of mixed origin, that is, viral and bacterial [1,5,6]. It was evidenced, through a multicenter study, carried out in 10 underdeveloped countries, that the culture of blood and pleural fluid for bacteria and culture of nasopharyngeal aspirate for viruses showed that viruses (mainly Respiratory Syncytial Virus) were more prevalent than bacteria in children with lower respiratory tract infection, however, in analysis of pleural fluid culture, a predominance of bacterial etiology was observed [9,33,34].

With regard to pneumonia of bacterial origin, it is possible to divide it into two, typical and atypical. The former is more common, with pneumococcus being the most isolated agent in these cases, however *Haemophilus influenzae* and *Staphylococcus aureus* are frequently found, with predominant symptoms of lower airways, dyspnea, cough and tachypnea [35]. One study showed the estimated prevalence of *Streptococcus pneumoniae* from 37 to 44%, while *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* were identified in 6 to 40% of CAP cases; in that same study, other etiologic agents identified, of lower incidence, were Group A *Streptococcus*, *Staphylococcus aureus* and *Haemophilus influenzae*. Still within typical CAPs, it is important to mention those caused by methicillin-resistant *Staphylococcus aureus*, which have shown an increase in community-acquired infections in Latin America and tend to be more aggressive and evolve with complications such as empyema, abscesses and pulmonary necrosis [1,5,6,36,37,38].

According to Dean, in complicated pneumonias, especially necrotizing pneumonia, characterized by liquefaction and necrosis of the parenchyma and subsequent replacement by air or fluid-filled cavities, lung necrosis and abscesses are usually the result of bacterial pathogens, particularly S pneumoniae and *Staphylococcus aureus*, the latter of which is associated with a more severe disease course [39,40].

A study carried out with 871 patients with severe CAP, evaluating the drug used and the most prevalent pathogen, identified penicillin G as the initial treatment (58.7%) and Pneumococcus as the most frequent pathogen (50.7%) [41].

Finally, atypical pneumonias are caused by *Mycoplasma pneumoniae, Chlamydia pneumoniae* and *Legionella* spp., differing from the typical one by the prolonged clinical picture, at first with subclinical and nonspecific manifestations, such as fever, myalgia, coryza and pharyngitis. Because it deals with an infection resulting from atypical bacteria, they have little clinical response with the use of isolated beta-lactams, requiring the association with macrolides [5,6,42,43,44].

Table 1. Most prevalent etiological agents of community acquired pneumonia

	Study	Etiological Agent
Viral etiology		
	Chiu YT (2021)	Human rhinovirus/enterovirus; Adenovirus; Parainfluenza virus; Respiratory syncytial virus; Coronavirus
	Obaid (2022)	Respiratory syncytial virus; Influenza A; Parainfluenza;Adenovirus; Combined Adenovirus and Parainfluenza; Combined Influenza B and Parainfluenza.
	Mendes (2022)	Respiratory syncytial virus; Combined vírus sincicial respiratório and Influenza A; Influenza A.
	Ríos Proaño (2021)	Human rhinovirus; Respiratory syncytial virus Influenza A; Adenovirus
Bacterial etiology		
	le Roux (2017)	*Streptococcus pneumoniae*; *Haemophilus influenzae* type B
	Ebruke (2020)	*Streptococcus pneumoniae; H. influenzae; Moraxella catarrhalis*
	Garcés MP (2021)	*Streptococcus pneumoniae; Staphylococcus aureus; mycobacterium tuberculosis*
	Zhang R (2022)	*Streptococcus pneumoniae; Haemophilus influenzae;Moraxella catarrhalis; Staphylococcus aureus*

In addition to the insidious symptoms, age group is another factor that helps in the suspicion of atypical pneumonia, since up to one third of CAP in preschoolers have *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* as causative agents. The symptoms of CAP due to *Mycoplasma pneumoniae* are headache, paroxysmal dry cough, otitis, maculopapular rashes and even arthritis. Studies show that *Mycoplasma pneumoniae* is present in more than 50% of cases in children over 10 years of age [4]. However, at any age, the most important bacterial pathogen is *Streptococcus pneumoniae*; on the other hand, by *Chlamydia pneumoniae,* it is preceded by pharyngitis and, after 1 to 4 weeks, there is fever with pulmonary symptoms. According to research by Shrey Mathuer, less frequently, severe pneumonias are caused by *Staphylococcus aureus*, especially after infection by Influenza. Whereas *Pneumocystis jiroveci* fungal infection (PJP) is especially significant in young children with AIDS [4,45,46,47,48].

3.3 Methods for Etiological Diagnosis

When trying to differentiate the etiological types, whether viral or bacterial, other important findings are that typical bacterial infections have greater accuracy in their clinical diagnosis than viral ones [49]. However, it was analyzed that the presentation of symptoms of the upper airways, such as wheezing and low-grade fever, especially at an early age, indicate viral or atypica bacterial pneumonia, in the latter, Mycoplasma pneumoniae is more prevalent [1].

In addition, it was observed that inflammatory markers, such as C-Reactive Protein (CRP) and Procalcitonin (PCT), can aid in the etiological diagnosis, in such a way that elevated inflammatory tests generally speak in favor of bacterial respiratory infections (GALVIZ et al., 2020).

Until today, the identification of the microbial etiology of pneumonia is done through the culture of lung aspirates, considered the gold standard in some hospital services. It is noted that there is greater precision in the amount of pathogens identified by aspirates than in blood cultures, which have relatively low sensitivity [50,51]. A multicenter study (10 underdeveloped countries) which was based on the culture of blood and pleural fluid for bacteria and the culture of nasopharyngeal aspirates for viruses, showed that viruses (mainly Respiratory Syncytial Virus) were more identified than bacteria in children with lower respiratory tract infection [9,24].

However, the previously discussed diagnostic methods are not always reliable and have their numerous limitations. For example, the main pathogens (*S. pneumoniae*, *M. pneumoniae*) involved in pneumonia are also found in the nasopharynx of normal children without necessarily being the cause of the infection. In practice, it is impracticable to collect a sample of lung tissue at the beginning of the infection, but

the choice of bronchoscopy as a method for identifying the main pathogens that cause CAP would be the closest to ideal. Thus, it is discussed whether there is really a need to determine the bacterial etiology in individual cases by such methods with their respective limitations or whether it would be more appropriate to follow a more holistic approach that would bring an epidemiological view with the following variables: the etiological agent, the host and the environment [9].

4. CONCLUSION

Considering the studies analyzed in this present review, it is evident that although there is a consensus in scientific articles for the most common microbiological types in CAP, it is admitted that there are still many limitations in the current methods used for the etiological determination individually and that , perhaps, prioritizing an approach based on the patient's clinical history, age, environment and symptomatological/radiographic characteristics is more appropriate for diagnostic differentiation and treatment.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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