

## **Review Article**

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

### **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.

**Methodology:** A narrative literature review method was adopted, with research carried out in the following databases: Google Scholar, 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<sup>1</sup>. This is an important public health issue, affecting all age groups, resulting in high morbidity and mortality<sup>2</sup>. 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<sup>3</sup>. It is known that community-acquired pneumonia 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<sup>4</sup>. 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<sup>5,6</sup>.

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, in addition, it is the second cause of hospitalization and one of the main ones due to **prolonged hospitalization** in Pediatric Intensive Care Units<sup>7</sup>.

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<sup>8</sup>. 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<sup>9,10</sup>.

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<sup>11</sup>.

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 and quantitative 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, 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", "Pediatría" 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<sup>12,13,14</sup>. 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<sup>15</sup>.

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<sup>16,17</sup>.

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*<sup>4,5,18,19</sup>. 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<sup>20,21</sup>.

In addition, knowing the local epidemiology and the etiological spectrum and its possible resistance are the basic points for managing pneumonia<sup>22,23</sup>. 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<sup>15,24</sup>.

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<sup>25,26,27</sup>.

### 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<sup>1,5,6,28</sup>.

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<sup>29,30,31,32</sup>. 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<sup>1,5,6</sup>. 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<sup>9,33,34</sup>.

Table 1. Most prevalent etiological agents of Community Acquired Pneumonia

| study          | etiological agent   |
|----------------|---|
| Viral etiology |   |
| Chiu YT (2021) | Human rhinovirus/enterovirus; Adenovirus;<br>Parainfluenza virus; Respiratory syncytial virus;<br>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 virus sincicial respiratório and Influenza A; Influenza A.  |
| Rios Proaño(2021)         | Human rhinovirus; Respiratory syncytial virus Influenza A; Adenovirus   |
| <b>bacterial etiology</b> |   |
| le Roux (2017)            | <i>Streptococcus pneumoniae</i> ; <i>Haemophilus influenzae</i> type B  |
| Ebruke (2020)             | <i>Streptococcus pneumoniae</i> ; <i>H. influenzae</i> ; <i>Moraxella catarrhalis</i>   |
| Garcés MP(2021)           | <i>Streptococcus pneumoniae</i> ; <i>Staphylococcus aureus</i> ; <i>mycobacterium tuberculosis</i>  |
| Zhang R(2022)             | <i>Streptococcus pneumoniae</i> ; <i>Haemophilus influenzae</i> ; <i>Moraxella catarrhalis</i> ; <i>Staphylococcus aureus</i>                       |

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<sup>35</sup>. 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<sup>1,5,6,36,37,38</sup>.

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<sup>39,40</sup>.

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%)<sup>41</sup>.

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<sup>5,6,42,43,44</sup>.

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<sup>4</sup>. 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<sup>4,45,46,47,48</sup>.

### 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<sup>49</sup>. 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 atypical viral or bacterial pneumonia, in the latter, *Mycoplasma pneumoniae* is more prevalent<sup>1</sup>.

In addition, it was observed that inflammatory markers, such as CRP and 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<sup>50,51</sup>. 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<sup>9,24</sup>.

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<sup>9</sup>.

#### 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.

#### CONSENT

All authors declare that written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal.

#### REFERENCES

1. Mena Galviz LS, Carreño Almanzor FR, Cala Vecino LL, Mena Galviz LS, Carreño Almanzor FR, Cala Vecino LL. Etiological diagnosis of pneumonia: a problem in pediatric clinical practice. *Medical UIS* [Internet]. 2020 Apr;33(1):39–52. Accessed 23 May 2023. Available: [http://www.scielo.org.co/scielo.php?script=sci\\_arttext&pid=S0121-03192020000100039](http://www.scielo.org.co/scielo.php?script=sci_arttext&pid=S0121-03192020000100039)
2. Torres, A. et al. pneumonia. *Nature Reviews Disease Primers*, [S.L.], v. 7, no. 1 p. 1-7, 8 Apr. 2021. Springer Science and Business Media LLC. Accessed 15 June 2023. Available: <https://pubmed.ncbi.nlm.nih.gov/33833230/>. 3.
3. Mathur S, Fuchs A, Bielicki J, Van Den Anker J, Sharland M. Antibiotic use for community-acquired pneumonia in neonates and children: WHO evidence review. *Pediatrics and International Child Health.*;38(sup1):S66–75. Accessed 23 May 2023. Available: [https://www.who.int/selection\\_medicines/committees/expert/21/applications/s6\\_p\\_aed\\_antibiotics\\_appendix4\\_sepsis.pdf](https://www.who.int/selection_medicines/committees/expert/21/applications/s6_p_aed_antibiotics_appendix4_sepsis.pdf)

4. Brito R de CCM de, Guerra TCM, Câmara L de HLD, Mattos JDPG de, Mello MJG de, Correia J de B, et al. Clinical characteristics and outcomes of acute community acquired pneumonia in children at a reference public hospital in Pernambuco State, Brazil (2010-2011). *Brazilian Journal of Maternal and Child Health* [Internet].;16(3):247–57. Accessed 23 May 2023. Available: <https://www.scielo.br/j/rbsmi/a/3H3mdm7ZYTCZ5rkQHFvgyVJ/?lang=en>
5. Sánchez OV, González PGP, Astudillo NEP. Prevalence of Complicated Pneumonia in Pediatric Patients Hospitalized at the José Carrasco Arteaga Hospital. January 2014 to December 2017. *Ecuadorian Journal of Pediatrics*. 2020 Dec 31;21(3). Accessed 23 May 2023. Available: <https://pesquisa.bvsalud.org/portal/resource/pt/biblio-1146527>
6. Magana M, Pushpanathan M, Santos AL, Leanse L, Fernandez M, Ioannidis A, et al. The value of antimicrobial peptides in the age of resistance. *The Lancet Infectious Diseases* [Internet]. 2020 Sep 1;20(9):e216–30. Accessed 23 May 2023. Available: [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30327-3/fulltext#:~:text=Antimicrobial%20peptides%20have%20clear%20advantages](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30327-3/fulltext#:~:text=Antimicrobial%20peptides%20have%20clear%20advantages)
7. Tirado-Soler M, García-Bell H, Batista-Lucas Y. Community-acquired pneumonia in a Pediatric Intensive Care Unit. *Rev inf cient* [Internet]. 2021;1–11. Accessed 15 June 2023. Available: <https://pesquisa.bvsalud.org/portal/resource/pt/biblio-1156706>
8. Nascimento-Carvalho CM. Community-acquired pneumonia among children: the latest evidence for an updated management. *Journal of Pediatrics*. 2019 Sep;96(1). Accessed 15 June 2023. Available: <https://www.sciencedirect.com/science/article/pii/S0021755719304930?via%3Di%3Dhub>
9. Matthew JL. Etiology of Childhood Pneumonia: What We Know, and What We Need to Know! *Indian Journal of Pediatrics* [Internet]. 2018;85(1):25–34. Accessed 23 May 2023. Available: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7090409/>
10. Aurilio RB, Sant'Anna CC, March M from FBP. CLINICAL PROFILE OF CHILDREN WITH AND WITHOUT COMORBIDITIES HOSPITALIZED WITH COMMUNITY-ACQUIRED PNEUMONIA. *Paulista Journal of Pediatrics*. 2020;38.. Accessed 15 June 2023. Available: <https://www.scielo.br/j/rpp/a/rfrF33ZC9fJhBsfJ5znQdzy/?lang=en>
11. UNICEF. Committing to Child Survival: A Promise Renewed. Accessed 15 June 2023. Available: <https://www.selounicef.org.br/>.
12. Lodha R, Kabra SK, Pandey RM. Antibiotics for community-acquired pneumonia in children. *Cochrane Database of Systematic Reviews*. 2013 Jun

4;(6). Accessed 20 June 2023. Available:  
<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD004874.pub4/full>

13. Fuchs Bahlis L, Diogo L, De Souza Kuchenbecker R, Fuchs S, Fuchs L. Please refer to correspondence. *J bras pneumol* [Internet]. 2018 Aug;44(04). Accessed 20 June 2023. Available:  
[https://www.scielo.br/pdf/jbpneu/v44n4/pt\\_1806-3713-jbpneu-44-04-00261.pdf](https://www.scielo.br/pdf/jbpneu/v44n4/pt_1806-3713-jbpneu-44-04-00261.pdf)

14. Gaspar MAR, Barros PHS, Costa ASV, Soares FA, Oliveira BLCA de. Social inequality and hospitalizations due to pneumonia in children under five years of age in the State of Maranhão, Brazil. *Brazilian Journal of Maternal and Child Health* [Internet]. 2020 May 11;20:81–9. Accessed June 20, 2023. Available:  
<https://www.scielo.br/j/rbsmi/a/MtvWvKSRk9YSRW4mTdrfFJw/abstract/?lang=p>

15. Corrêa A, Costa B, Lundgren F, Michelim<sup>4</sup>, Figueiredo E, Holanda F, et al. Recommendations for the management of community-acquired pneumonia 2018. *www.jornaldepneumologia.com.br* [Internet]. 2018;44(5):405–23. Accessed 20 June 2023. Available:  
<https://www.jornaldepneumologia.com.br/details/2853/en-US/recomendacoes-para-o-manejo-da-pneumonia-acquired-in-the-community-2018>

16. Meira J, Daniel, Alves R, Andrade L, Araujo PF, Figueiredo L, et al. Climate seasonality and lower respiratory tract diseases: a predictive model for pediatric hospitalizations. 2022 Jan 1;75(2). Accessed 20 June 2023. Available:  
<https://pubmed.ncbi.nlm.nih.gov/36134811/>

17. March M de F, Galvão A. Community-acquired pneumonia in children and 10-valent pneumococcal vaccination: update. *SOPERJ Pediatric Journal*. 2018;18(3). Accessed 22 June 2023. Available:  
<https://cdn.publisher.gn1.link/residenciapediatrica.com.br/pdf/v11n3aop196.pdf>

18. Community-acquired pneumonia in childhood. Scientific Department of Pulmonology of the Brazilian Society of Pediatrics. 2018;3:1-8. Accessed 02 May 2023. Available:  
[https://www.sbp.com.br/fileadmin/user\\_upload/Pneumologia\\_-20981d-DC-\\_Pneumonia\\_acquired\\_na\\_comunidade-ok.pdf](https://www.sbp.com.br/fileadmin/user_upload/Pneumologia_-20981d-DC-_Pneumonia_acquired_na_comunidade-ok.pdf).

19. Kuitunen I, Jääskeläinen J, Korppi M, Renko M. Antibiotic treatment duration for community acquired pneumonia in outpatient children in high-income countries – a systematic review and meta-analysis. *Clinical Infectious Diseases*.

2022 May 17;76. Accessed 23 May 2023. Available:  
<https://pubmed.ncbi.nlm.nih.gov/35579504/>

20. Passos SD, Maziero FF, Antoniassi DQ, Souza LT de, Felix AF, Dotta E, et al. ACUTE RESPIRATORY DISEASES IN BRAZILIAN CHILDREN: ARE CAREGIVERS ABLE TO DETECT THE FIRST WARNING SIGNS? *Revista Paulista de Pediatria* [Internet]. 2018 Jan 15;36(1):3–9. Accessed 23 May 2023. Available:  
<https://www.scielo.br/j/rpp/a/3MhQrZ8KS9GXRh4ZtmPCzqG/?lang=pt&format=pdf>

21. Rodríguez HRC, Álvarez BS, Bencomo DR, Risco EE del. Complications of community-acquired pneumonia. *Camagüey Medical Archive* [Internet]. 2015;9(4). Accessed 23 May 2023. Available:  
<https://revistaamc.sld.cu/index.php/amc/article/view/2968>

22. Iroh Tam PY. Approach to Common Bacterial Infections. *Pediatric Clinics of North America*. 2013 Apr;60(2):437–53. Accessed 23 May 2023. Available:  
<https://pubmed.ncbi.nlm.nih.gov/23481110/>

23. Xavier SP, Victor A, Cumaquela G, Vasco MD, Rodrigues OAS. Inappropriate use of antibiotics and their predictors in pediatric patients admitted to the Central Hospital of Nampula, Mozambique. *Antimicrobial Resistance & Infection Control*. 2022 Jun 2;11(1). Accessed 23 May 2023. Available:  
<https://aricjournal.biomedcentral.com/articles/10.1186/s13756-022-01115-w>

24. KATZ, Sophie E.; WILLIAMS, Derek J.. Pediatric Community-Acquired Pneumonia in the United States. *Infectious Disease Clinics Of North America*, [S.L.], v. 32, no. 1, p. 47-63, Mar. 2018. Elsevier BV. Accessed 22 June 2023. Available:  
<https://pubmed.ncbi.nlm.nih.gov/29269189/>

25. Jarovsky D, Berezin EN. Impact of PCV10 on pediatric pneumococcal disease burden in Brazil: time for new recommendations? *Journal of Pediatrics*. 2022 Dec. Accessed 22 June 2023. Available:  
<https://www.scielo.br/j/jped/a/MS5xvTvCKYqR4KbpWwN4BpB/>

26. Rappuoli R, De Gregorio E, Costantino P. On the mechanisms of conjugate vaccines. *Proceedings of the National Academy of Sciences*. 2018 Dec 21;116(1):14–6. Accessed 22 June 2023. Available:  
<https://www.pnas.org/content/116/1/14>

27. Warren, Joshua L et al. Impact of Pneumococcal Conjugate Vaccines on Pneumonia Hospitalizations in High- and Low-Income Subpopulations in Brazil. *Clinical Infectious Diseases*, [S.L.], v. 65, no. 11, p. 1813-1818, 22 Jul. 2017. Oxford University Press (OUP). <http://dx.doi.org/10.1093/cid/cix638>. Accessed 15 June 2023. Available: <https://academic.oup.com/cid/article/65/11/1813/4004801>.

28. Fuentes FG, Cedeño O, Abreu SG, Fuentes FG, Cedeño Osorio O, Abreu SG. Community-acquired pneumonia by patients between 1 month and 18 years of age. *Cuban Journal of Pediatrics*. 2021 Jun 1;93(2). Accessed 15 June 2023. Available: [http://scielo.sld.cu/scielo.php?script=sci\\_arttext&pid=S0034-75312021000200002](http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S0034-75312021000200002)

29. Chiu YT, Tien N, Lin HC, Wei HM, Lai HC, Chen JA, et al. Detection of respiratory pathogens by application of multiplex PCR panel during early period of COVID-19 pandemic in a tertiary hospital in Central Taiwan. *Journal of Microbiology Immunology and Infection*. 2021 Oct 6;55(6):1144–50. Accessed: 15 June 2023. Available: <https://pubmed.ncbi.nlm.nih.gov/34674956/>

30. Obaid SR. Viral Pneumonia Causative Agents Diagnosis by using Indirect Immune Fluorescent Assay. *Research Review*. 2022 Jun 30;5(6). Accessed 15 June. 2023. Available: <https://jmrhs.info/index.php/jmrhs/article/view/598>

31. Mendes ET, Paranhos HL, Santos ICM, Souza LB de, Aquino JLB de, Leandro-Merhi VA, et al. Prognosis of hospitalized children under 2 years of age with co-detection of influenza A and respiratory syncytial virus at the healthcare facility. *Brazilian Journal of Mother and Child Health*. 2021 Jun;21(2):531–7. Accessed 20 June 2023. Available: <https://www.scielo.br/j/rbsmi/a/DDTrnwZtDVmTSG4WWxGgWDQ/?format=pdf&lang=pt>

32. Ríos Proaño LC. Prevalence of respiratory viruses detected by DNA/PCR in children with acute respiratory infection hospitalized at Hospital Roberto Gilbert año 2019. 2021 Jun 1. Accessed 15 June 2023. Available: <http://repositorio.ucsg.edu.ec/bitstream/3317/16882/1/T-UCSG-POS-EGM-PE-84.pdf>

33. von Mollendorf C, Berger D, Gwee A, Duke T, Graham SM, Russell FM, et al. Aetiology of childhood pneumonia in low- and middle-income countries in the era of vaccination: a systematic review. *Journal of Global Health*. 2022 Jul 23;12. Accessed 15 June 2023. Available: <https://pubmed.ncbi.nlm.nih.gov/35866332/>

34. Ebruke BE, Maria DK, Haddix M, Syed, Prospero C, Feikin DR, et al. The Etiology of Pneumonia From Analysis of Lung Aspirate and Pleural Fluid Samples: Findings From the Pneumonia Etiology Research for Child Health (PERCH) Study. *Clinical Infectious Diseases*. 2020 Jul 25;73(11):e3788–96.

35. le Roux DM, Zar HJ. Community-acquired pneumonia in children — a changing spectrum of disease. *Pediatric Radiology*. 2017 Sep 21;47(11):1392–8. Accessed 15 June 2023. Available:<https://pubmed.ncbi.nlm.nih.gov/29043417/>

36. Taffarel P. Severe *Staphylococcus aureus* infection in three pediatric intensive care units. Analysis of cases of necrotizing pneumonia. *Archivos Argentinos de Pediatría*. 2014 Feb 15;112(2). Accessed 15 June 2023. Available:<https://pubmed.ncbi.nlm.nih.gov/24584792/>

37. Zhang R, Wu Y, Deng G, Deng J. Value of sputum Gram stain, sputum culture, and bronchoalveolar lavage fluid Gram stain in predicting single bacterial pathogen among children with community-acquired pneumonia. *BMC Pulmonary Medicine*. 2022 Nov 19;22(1). Accessed 20 June 2023. Available:<https://bmcpulmed.biomedcentral.com/articles/10.1186/s12890-022-02234-1>

38. Małgorzata W, Maj D, Waclawska M, Ewelina WG. Most common aetiology of pneumonia among children hospitalized in the University Children's Hospital in Lublin, Poland, 2010–2020. *Medycyna Ogólna i Nauki o Zdrowiu*. 2022 Jun 13;28(2). Accessed 23 June 2023. Available:<https://www.proquest.com/openview/1104b30a28074a8f23cfd49064a4ee52/1?pq-origsite=gscholar&cbl=5221235>

39. Dean P, Florin TA. Factors associated with pneumonia severity in children: A systematic review. *Journal of the Pediatric Infectious Diseases Society*. 2018 May 30;7(4). Accessed 20 June 2023. Available:<https://pubmed.ncbi.nlm.nih.gov/29850828/>

40. Garcés MP, González EA, Betarte CM, Cabrera ED, Fernández AIÁ. Comportamiento de las neumonías graves en el Hospital Pediátrico Borrás-Marfán. 2015-2019. *Revista Habanera de Ciencias Médicas*. 2021 Jun 9 ;20(3):3539. Accessed 23 June 2023. Available:<https://revhabanera.sld.cu/index.php/rhab/article/view/3539/2884>

41. Ferreira S, Sant'Anna CC, March M de FBP, Santos MARC, Cunha AJLA. Lethality by pneumonia and factors associated to death. *Jornal de Pediatria*. 2014;90:92–7. Accessed 23 June 2023. Available:<https://www.scielo.br/j/jped/a/JFMRjFLw4fqyHGtyWvQH8ww/?lang=en>

42. Shim JY. Current perspectives on atypical pneumonia in children. *Clinical and Experimental Pediatrics*. 2020 Jun 10;63(12). Accessed 23 June 2023. Available:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7738772/>

43. Ma YJ, Wang SM, Cho YH, Shen CF, Liu CC, Chi H, et al. Clinical and epidemiological characteristics in children with community-acquired mycoplasma pneumonia in Taiwan: A nationwide surveillance. *Journal of Microbiology, Immunology and Infection* [Internet]. 2015 Dec 1;48(6):632–8. Accessed 23 June 2023. Available:

<https://www.sciencedirect.com/science/article/pii/S1684118214001716#fig1>

44. YU, Yun et al. Atypical pathogen infection in community-acquired pneumonia. *Bioscience Trends*, [S.L.], v. 10, n. 1, p. 7-13, 2016. International Research and Cooperation Association for Bio & Socio-Sciences Advancement (IRCA-BSSA). <http://dx.doi.org/10.5582/bst.2016.01021>. Accessed 23 June. 2023. Available: <https://pubmed.ncbi.nlm.nih.gov/26961211/>. Acesso em: 15 jun. 2023.

45. Chandran L, Boykan R. Chlamydial Infections in Children and Adolescents. *Pediatrics in Review*. 2009 Jul 1;30(7):243–50. Accessed 23 June 2023. Available: <https://pubmed.ncbi.nlm.nih.gov/19570922/>

46. Vervloet LA, Marguet C, Camargos PAM. Infection by *Mycoplasma pneumoniae* and its importance as an etiological agent in childhood community-acquired pneumonias. *Brazilian Journal of Infectious Diseases*. 2007 Oct;11(5):507–14. Accessed 23 June. 2023. Available: <https://www.scielo.br/j/bjid/a/8RyDXqFBDG9786x9yRLb6ZF/?lang=en>

47. Ma YJ, Wang SM, Cho YH, Shen CF, Liu CC, Chi H, et al. Clinical and epidemiological characteristics in children with community-acquired mycoplasma pneumonia in Taiwan: A nationwide surveillance. *Journal of Microbiology, Immunology and Infection* [Internet]. 2015 Dec 1;48(6):632–8. Accessed 23 June 2023. Available:

<https://www.sciencedirect.com/science/article/pii/S1684118214001716#fig1>

48. Juana del VM, Silva-Caso W, Cornejo-Tapia A, Fiorella OP, Verne E, Ugarte C, et al. Molecular etiological profile of atypical bacterial pathogens, viruses and coinfections among infants and children with community acquired pneumonia admitted to a national hospital in Lima, Peru. *BMC Research Notes*. 2017 Dec 6;10(1). Accessed 23 jun. 2023. Available: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5718007/>

49. Menezes RAM, Pavanitto DR, Nascimento LFC. Distribuição espacial das taxas de internação de crianças por pneumonia no Sistema Único de Saúde, nos municípios do estado de São Paulo. *Revista Brasileira de Epidemiologia*. 2019;22. Accessed 23 jun. 2023. Available: <https://www.scielo.br/j/rbepid/a/mjqmTqxnc3WD3T7g64MDw7N/?lang=pt>

50. Hammitt LL, Feikin DR, Scott JF, Zeger SL, Murdoch DR, O'Brien KL, et al. Addressing the Analytic Challenges of Cross-Sectional Pediatric Pneumonia Etiology Data. *Clinical Infectious Diseases*. 2017 May 29;64(suppl\_3):S197–

204. Accessed 23 jun. 2023. Available:  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5447845/>

51. Kwon JH, Kim JH, Lee JY, Kim YJ, Sohn CH, Lim KS, et al. Low utility of blood culture in pediatric community-acquired pneumonia. *Medicine*. 2017 Jun;96(22):e7028. Accessed 23 jun. 2023. Available:  
<https://pubmed.ncbi.nlm.nih.gov/28562556/>