



Submitted on: 05/20/2024

Approved on: 10/17/2024

ORIGINAL ARTICLE

Comparison of clinical outcomes and treatments of complicated and uncomplicated community-acquired pneumonia in children at a maternal and child referral hospital

Raul José Almeida Albuquerque¹, Camila Esteves Paredes¹, Ana Carolina de Souza Vasconcelos¹, Renê Elias Gonçalves², Ítalo José Sampaio Vieira da Cruz², Vitória Souza Araújo², Ilka Juliana Ferreira Rodrigues³, Yuri Francilane Carvalho Dos Santos⁴

Keywords:

Pneumonia,
Streptococcus
pneumoniae,
Pleural Effusion,
Vaccination Coverage,
Hospitalization.

Abstract

Objective: To analyze data on clinical progression and treatment to improve understanding and management of Complicated Community-Acquired Pneumonia. **Methods:** A prospective and cross-sectional study conducted with children hospitalized for community-acquired pneumonia in a tertiary public hospital, a maternal and child reference center, over a period of 6 months. **Results:** A total of 130 patients were analyzed over 6 months. Of these, 97 (74.6%) patients presented only with uncomplicated pneumonia (CAP), while 33 (25.4%) developed complicated pneumonia (CCAP) or had complications upon admission. Among CCAP patients, pleural effusion was the most common complication (90.4%). Diagnostic tools used to elucidate complications included radiography (93.9%), ultrasonography (57.6%), and computed tomography (42.4%). The predominant treatment was empirical antibiotic therapy, primarily with third-generation cephalosporins. Surgical interventions were frequently performed in patients with complications (75.8%), such as thoracic drainage (92%), with a mean drainage duration of 11.3 days, which prolonged hospitalization to an average of 18 days ($p=0.048$). Regarding outcomes, 93.9% of the patients were discharged, 3.0% died, and 3.0% were transferred. **Conclusions:** The study concludes that CCAP results in prolonged hospital stays and additional healthcare costs. These findings highlight the severity of the disease and underscore the need for a broader therapeutic approach, including more effective pneumococcal vaccines to reduce complications.

¹ Hospital Dom Malan, Residência em Pediatria - Petrolina - Pernambuco - Brazil.

² Universidade Federal do Vale do São Francisco, Curso de Medicina - Petrolina - Pernambuco - Brazil.

³ Hospital Santo Antônio/ Obras Sociais Irmã Dulce, Hematologia pediátrica - Salvador - Bahia - Brazil.

⁴ Universidade Federal de Pernambuco, Pediatra - Recife - Pernambuco - Brazil.

Correspondence to:

Raul José Almeida Albuquerque.

Hospital Dom Malan, Residência em Pediatria - Petrolina - Pernambuco - Brasil. Rua Joaquim Nabuco, s/nº, Centro, Petrolina, PE, Brazil. E-mail: rauljose1993@gmail.com

INTRODUCTION

Community-acquired pneumonia (CAP) is a leading cause of morbidity and mortality in children under 5 years of age, especially in developing countries. According to the World Health Organization (WHO), pneumonia is responsible for approximately 15% of all deaths in this age group, resulting in more than 800,000 deaths annually. In Brazil, CAP in patients aged 0 to 19 years, from January to September 2017, was the leading cause of hospitalizations, responsible for 243,364, in line with figures from other developing countries^{1,2}.

Complicated community-acquired pneumonia (CCAP) is a severe progression of the disease that develops even with adequate antibiotic use, such as lung abscess (LAB), necrotizing pneumonia (NEC), parapneumonic effusion (PE) and pleural empyema (PEM)¹. PEM and PE are distinct stages of the same pathophysiological condition, in which the inflammatory process in the pleura leads to the buildup of fluid in the pleural cavity. NEC occurs due to tissue liquefaction and should be considered in cases of prolonged fever and septic symptoms, with the diagnosis confirmed by chest X-ray or tomography. LAB results from the buildup of inflammatory cells and tissue destruction or necrosis, leading to the formation of one or more pulmonary cavities³.

In most cases, initial treatment is empirical, since the most prevalent etiological agent is still *Streptococcus pneumoniae* and the lack of etiological investigation in the initial management of the disease. Although there are divergences in the literature, several Brazilian studies indicate that the systematic adoption of guidelines for the treatment of CAP in hospitalized patients showed a significant reduction in the 30-day mortality rate, in-hospital mortality, length of hospital stay and time required to achieve clinical stability, in addition to a decrease in associated complications^{4,5}.

Regarding surgical treatment, it serves as an adjuvant to antimicrobial treatment in situations where CAP evolves into some complication, with no consensus on the best surgical model or the ideal time for each procedure¹.

Since Complicated Community-Acquired Pneumonia (CCAP) is a disease characterized by the worsening of CAP, one of the main causes of mortality and morbidity in the world, especially in Pediatrics. Furthermore, there is currently an increase in complicated cases of pneumonia among children in Brazil, with few studies on CCAP. The objective of this study is to collect and analyze data that contribute to the knowledge and reporting of CCAP in the region, so as to enable improvements in the management of this disease and a reduction in morbidity and mortality records in this group.

MATERIALS AND METHODS

This is a descriptive, cross-sectional study with prospective data collection, consisting of 130 children hospitalized for

community-acquired pneumonia in a tertiary maternal and child hospital, a reference in emergency care in 54 municipalities. The collection period was from June 1 to December 31, 2022.

The inclusion criteria were children hospitalized with a clinical and/or radiological diagnosis of CAP and/or CCAP, age under 10 years and a Free and Informed Consent Form (FICF) signed by the guardian. The collection was carried out in the children's emergency room and in the general pediatric ward. Parents and/or guardians were invited to participate in the study when the patient was hospitalized and were then interviewed by the main researchers or previously trained medical students from the Federal University of Vale do São Francisco (UNIVASF).

A questionnaire was used as an instrument, consisting of 23 questions about epidemiological and demographic characteristics, clinical manifestations, treatment instituted and progression of the disease until the final outcome. The data obtained were coded in a standardized manner, transferred to a database created in the Microsoft Excel 2007 spreadsheet editor and statistically analyzed using Jamovi 2022 - version 2.3. The patients were divided into 2 groups: 1) uncomplicated CAP and 2) complicated CAP. Depending on the variables analyzed, parametric (Student's t-test) and nonparametric (Chi-square, Fisher's exact test) tests were used. A significance level of 0.05 was considered to reject the null hypothesis. The project was approved by the Research Ethics Committee of the Professor Fernando Figueira Institute of Integral Medicine, under substantiated opinion CAAE: 60399922.3.0000.5201.

RESULTS

The medical records of 130 patients who met the inclusion criteria were analyzed over a 6-month period. Of these, 97 (74.6%) patients persisted with only uncomplicated pneumonia (CAP) (Group A) and 33 (25.4%) developed complicated pneumonia (CCAP) or already had complications at admission (Group B) (Table 1).

The most common signs and symptoms on admission for CAP (Group A) were fever (94.9%), cough (91.8%), respiratory distress (77.6%), runny nose (72.4%), tachypnea (62.2%), abdominal pain (22.4%), chest pain (15.3%) and 16.3% had O₂ saturation below 94%. Regarding patients with CCAP (Group B), they were fever (90.9%), cough (90.9%), respiratory distress (63.6%), runny nose (54.5%), tachypnea (51.5%), abdominal

Table 1. Epidemiological distribution of sex according to groups.

Sex	Group A		Group B		Total	
	N	%	n	%	n	%
Males	52	57.1%	18	54.5%	70	56.5%
Females	39	42.9%	15	45.5%	54	43.5%

Source: the authors.

pain (36.4%), chest pain (27.3%) and approximately 21.2% had O2 saturation below 94% (Table 2). When comparing the groups regarding signs and symptoms upon admission, a statistical difference ($p < 0.05$) was shown in relation to fever, cough, chest pain and abdominal pain (Table 2).

Table 2. Comparison of signs and symptoms among patients with pneumonia.

Signs and symptoms	Group A*		Group B**		p-value***
	n	%	n	%	
Fever	93	94.9%	30	90.9%	0.02
Cough	90	91.8%	30	90.9%	0.01
Runny nose	71	72.4%	18	54.5%	1
Tachypnea	61	72.2%	17	71.5%	0.03
Respiratory distress	76	77.6%	21	63.6%	0.6
SatO2 <94%	16	16.3%	7	21.2%	0.2
Chest pain	15	15.3%	9	27.3%	0.02
Abdominal pain	22	22.4%	12	36.4%	0.01

*Uncomplicated Community-acquired pneumonia;

**Complicated Community-acquired pneumonia

*** p -value < 0.05 were considered relevant

Source: the authors.

The mean duration of fever after the start of antibiotic treatment in patients with CAP was 1.3 days. However, in patients with CCAP, fever continued for approximately 6 days, while in necrotizing pneumonia, fever persisted for approximately 9 days.

The diagnosis of CCAP was mostly clinical and radiographic, with imaging tests, such as chest X-ray, performed on admission (93.9%), in addition to thoracic ultrasound (57.6%) and chest tomography (42.4%) to investigate complications.

In patients with CAP who developed complications after hospitalization, 66.7% maintained the initial use of Ampicillin, 16.7% had their antibiotic regimen changed to Ceftriaxone, and 16.7% to Ceftriaxone associated with Oxacillin. The reasons that led to this antibiotic replacement were: Complications (58.3%), Persistent fever (20.8%), Clinical worsening (12.5%) and Medication deescalation (8.3%).

On the other hand, the initial choice of antibiotic therapy for patients diagnosed with CCAP upon arrival at the service was that 13.3% started intravenous treatment with Ampicillin, 13.3% with Ampicillin-Sulbactam and 73.4% with Ceftriaxone associated with Oxacillin. However, 33.3% had their initial regimen modified, as they developed pulmonary necrosis; of these, 75% were switched to Ceftriaxone with Clindamycin and 25% to Meropenem with Vancomycin.

Analyzing the need for oxygen supplementation, 30.6% of CAP and 42.5% of CCAP patients used it ($p = 0.584$). Regarding the devices used in patients with CAP, 76.6% used a nasal cannula (NC), 63.3% non-rebreathing mask (NRM),

16.6% non-invasive ventilation (NIV) and 3.3% mechanical ventilation by orotracheal intubation (MV-OTI), with an overall average use of supplemental oxygen of 3 days. Regarding the devices used in patients with CAP, 71.4% used NC, 21.4% NRM, 14.3% NIV and 14.3% MV-OTI, with an overall average use of supplemental oxygen of 4 days.

Among the complications presented, 90.9% of the patients had pleural effusion, 27.3% pulmonary necrosis, 15.1% empyema and 3.0% lung abscess. After diagnosis, 75.8% required surgical intervention, which included: 92% thoracic drainage (with an average of 11.3 days of drain in place); 12% thoracentesis; 4% thoracotomy; and 4% lobectomy.

In general, patients in Group B spent an average of 18 days in the hospital; while patients in Group A spent an average of 6 days in hospital ($p < 0.001$). Finally, 100% of patients with CAP were discharged from the hospital. In contrast, 93.9% of patients with CCAP were discharged from the hospital, 3.0% died, and 3.0% were transferred.

DISCUSSION

Among the individuals analyzed in the study, there was an incidence of 25.4% who presented complications from CAP upon admission (45.5%) or developed complications after an average time of 3.4 days for complications (54.4%). The most common complication was Pleural Effusion (PE), present in most individuals with CCAP (90.4%), followed by Pulmonary Necrosis, Empyema, and Lung Abscess. The data corroborate previous studies conducted using data from other populations, such as the one conducted by Krapiec et al. (2022)³, in a hospital in Curitiba, in the south of the country, which demonstrated a prevalence of complications (27%) and the most frequent types of complications very close to the results obtained in this study.

The symptoms of community-acquired pneumonia (CAP) can manifest in different ways, resulting in different clinical presentations, which vary according to the individual characteristics of the patient and, in certain cases, the microorganisms involved⁶. In our study, a statistically significant relationship was observed regarding the association of clinical symptoms and the diagnosis of pneumonia, in which children with cough, fever, tachypnea, chest and abdominal pain suggest a diagnosis of pneumonia, complicated or not. The World Health Organization (WHO)^{7,8,9,10} has recommended that attention be paid to coughing and tachypnea as signs that suggest pneumonia in children under five years of age.

Although the diagnosis of CAP is predominantly clinical, chest radiography is an important tool for assessing severity, extent of lung involvement, and complications^{11,12}. The results found by Ferrero et al demonstrated that alveolar infiltrate was the most sensitive finding in the radiographic evaluation of CAP, and that upper lobe involvement and pleural effusion were associated with invasive pneumococcal infections. Other studies also indicate the presence of consolidations and other infiltrates as evidence of this pathology^{13,14}.

USG is essential in the evaluation of CAP, being the most sensitive imaging modality for evaluating the pleural space in children and superior to CT because it does not use ionizing radiation, as well as in its ability to demonstrate internal components of the effusion, such as loculations and the presence of fibrin. CT, on the other hand, is gold standard in pulmonary necrosis, as it is capable of identifying parenchymal changes not visible on chest radiography^{1,9}. In this study, CAP diagnoses were mostly made clinically, but chest radiography (93.9%), USG (57.6%) and/or CT (42.4%) were used in the selected cases in order to investigate possible complications.

It is noteworthy that most patients were treated with intravenous 3rd generation cephalosporin and beta-lactam antibiotics during hospitalization, and all of them showed a positive therapeutic response, regardless of the group they received, thus following the recommendations of the Brazilian Society of Pediatrics (SBP) and the World Health Organization^{1,12}.

Due to the urgency of starting treatment, treatment of pneumonia, specifically, whether complicated or not, is initiated empirically. This means that the choice of medications is based on factors such as the patient's age, resistance patterns in the region, clinical circumstances, the patient's immunological status, and the results of imaging tests^{15,16}. In children with complicated pneumonia, intravenous therapy with crystalline penicillin G or ampicillin is appropriate^{7,15}. If the patient has previously used antibiotics or is dealing with severe pneumonia with an unfavorable progression to the use of Penicillin, the use of ampicillin-sulbactam, ceftriaxone or ceftriaxone together with oxacillin or clindamycin may be considered, due to the risk of infection by *Staphylococcus aureus* or its community-acquired methicillin-resistant variant (CA-MRSA)^{6,16,17,18}. Regarding treatment duration, antibiotic therapy for CAP is carried out for a period of 5 to 10 days and, for the complicated form, it is extended for 4 weeks, or at least for 2 weeks after the patient becomes afebrile and shows improvements in their clinical condition^{1,15,19,20}. The SIREVA (Regional Vaccine System)²¹, a surveillance program that monitors the distribution and resistance of bacteria "*in vitro*", showed that *Streptococcus pneumoniae* was more prevalent between 1 and 5 years of age in children diagnosed with bacterial pneumonia (12-23 months: 36.6%; 24-59 months: 47.3%), with the main serotype being type 19A, with Penicillin susceptible to all serotypes except 4, 6A, 6B, 9V, 18C, 19F and 23A (19A susceptible to only 5.2%); in relation to Ceftriaxone, it has susceptibility in 68.3% in children under 12 months, 58.5% between 12 and 23 months, and 56.5% between 2 and 5 years. Regarding *Haemophilus influenzae*, almost 15% of children under 5 years of age diagnosed with CAP presented it as a pathogen, with Ampicillin being susceptible in 73.8% of children under 12 months and 85% between 12 and 23 months, but 100% were susceptible to Ceftriaxone.

With regards to fever, it is important to know that it can persist for an average period of 4 to 8 days, especially in cases

of necrotizing pneumonia, which, despite adequate treatment, presents as a prolonged inflammatory response. Therefore, additions or modifications to the appropriately chosen antibiotic therapy should be avoided, if the patient does not present clinical/radiological deterioration^{18,19,22}.

The WHO recommends the use of supplemental oxygen only for individuals with saturation below 90%, while the SBP recommends its use in children with saturation below 92% in room air^{7,23}. Among the children hospitalized during the study period with CCAP, almost half received supplemental oxygen at some point during their hospitalization, most often by NC, followed by MRI. In the present study, there was no statistical relationship between the need for supplemental oxygen and the diagnosis of CAP or CCAP. The types of surgical treatments most frequently performed for complications are in agreement with the records of other studies^{16,19,24}. Chest drainage was performed in 92% of the individuals, and its most common indication was the presence of symptomatic pleural effusions or those that were loculated. The remaining surgical interventions were thoracentesis (14%), thoracotomy (4%) and lobectomies (4%). A 2005 meta-analysis showed that primary surgical therapy, compared with non-surgical therapy, was associated with a lower in-hospital mortality rate (0% vs. 3.3%) and reintervention rate (2.5% vs. 23.5%). In addition, primary surgical therapy was associated with a shorter hospital stay (10.8 vs. 20 days), chest tube days (4.4 vs. 10.6 days) and antibiotic therapy (12.8 vs. 21.3 days), respectively. However, in the present study, the length of hospital stay was longer in patients who underwent some type of surgical procedure (19 vs. 13)^{1,7,25}. In this sense, it was observed that the presence of complications from CAP prolonged the length of hospital stay of patients by approximately 11 days, a factor that significantly increases the costs related to healthcare from the Unified Healthcare System (SUS)^{4,26}. Furthermore, the hospitalization periods found are longer than those provided by the SUS and recommended by the WHO for the treatment of pneumonia, which is 5 days⁸.

The mortality rate in our study was 3% (n=1) among patients with CCAP and 0% among those without complications. The occurrence of deaths due to CAP is rare in Europe and North America, especially after early childhood, due to advances in vaccination, early access to medical care, and the availability of effective antimicrobial treatment. In most healthy children, recovery occurs without complications or sequelae. Historically, mortality is higher in very young children, such as the patient in our study who died at 1 year and 4 months of age, without comorbidity. It is important to emphasize that the incidence of mortality may be higher in children with underlying medical conditions, such as malnutrition, neuromuscular disorders, or cystic fibrosis, or in cases of infection with MRSA or multidrug-resistant organisms¹⁵.

The main limitations of this study were the difficulty in identifying the cause of pneumonia, due to the absence of a service that processed blood or pleural fluid material for

culture, and the relatively small number of patients included in the study. However, the predominant practice in the treatment of complicated or uncomplicated pneumonia still involves the use of empirical antibiotic therapy based on criteria such as the patient's age and clinical and radiological findings.

We conclude that CCAP resulted in prolonged hospitalizations and additional healthcare costs. These results highlight the importance of the disease, emphasizing the need for a comprehensive therapeutic approach and tools, such as more comprehensive pneumococcal vaccines, to prevent complications.

REFERENCES

1. Sociedade Brasileira de Pediatria. Departamento Científico de Pneumologia. Pneumonias Adquiridas na Comunidade Complicadas. (atualização) 2022 [citado em 14 de dezembro de 2023]. Disponível em: https://www.sbp.com.br/fileadmin/user_upload/23053i-DC-Pneumonias_Adquiridas_Complicadas.pdf.
2. TabNet Win32 3.2 [Internet]. Morbidade hospitalar do SUS - por local de internação - Brasil. DATASUS; 2017 [citado em 07 de janeiro de 2024]. Disponível em: <http://tabnet.datasus.gov.br/cgi/tabcgi.exe?sih/cnv/niuf.def>.
3. Krapiec AB. Complicações da pneumonia adquirida na comunidade em crianças: fatores associados e a associação com falha terapêutica. Resid Pediatr. 2022 [citado em 10 de janeiro de 2024];12(1):1-4 DOI: <https://doi.org/10.25060/residpediatr-2022.v12n1-237>.
4. Cupurdija V, Lazic Z, Petrovic M, Mojsilovic S, Cekerevac I, Rancic N, et al.. Community-acquired pneumonia: economics of inpatient medical care vis-à-vis clinical severity. J bras pneumol. 2015 [citado em 15 de janeiro de 2024];41(1):48-57. DOI: <https://doi.org/10.1590/S1806-37132015000100007>.
5. Silveira CD, Ferreira CS, Corrêa R de A. Adesão a diretrizes e impacto nos desfechos em pacientes hospitalizados por pneumonia adquirida na comunidade em um hospital universitário. J bras pneumol. 2012 [citado em 11 de novembro de 2023];38(2):148-57. DOI: <https://doi.org/10.1590/S1806-37132012000200002>.
6. Nascimento-Carvalho CM. Community-acquired pneumonia among children: the latest evidence for an updated management. J Pediatr (Rio J). 2020 [citado em 15 de novembro de 2023];96:29-38. DOI: <https://doi.org/10.1016/j.jped.2019.08.003>.
7. Sociedade Brasileira de Pediatria. Departamento Científico de Pneumologia. Abordagem diagnóstica e terapêutica das pneumonias adquiridas na comunidade não complicadas. 2021. [citado em 11 de agosto de 2023]. Disponível em: https://www.sbp.com.br/fileadmin/user_upload/23054d-DC-Pneumonias_Adquiridas_Nao_Complicadas.pdf.
8. Nunes SEA, Minamisava R, Vieira MA da S, Itria A, Pessoa VP, Andrade ALSS de, et al.. Hospitalization costs of severe bacterial pneumonia in children: comparative analysis considering different costing methods. einstein (São Paulo). 2017 [citado em 21 de novembro de 2023];15(2):212-9. DOI: <https://doi.org/10.1590/S1679-45082017GS3855>.
9. Harris M, Clark J, Coote N, Fletcher P, Harnden A, McKean M, Thomson A; British Thoracic Society Standards of Care Committee. British Thoracic Society guidelines for the management of community acquired pneumonia in children: update 2011. Thorax. 2011 [citado em 15 de setembro de 2023];66 Suppl 2:ii1-23. DOI: <https://doi.org/10.1136/thoraxjnl-2011-200598>.
10. Lima EJDF. Pneumonia comunitária em menores de cinco anos na era pós-vacina pneumocócica conjugada - características clínicas e fatores de risco [Internet]. Instituto de Medicina Integral Professor Fernando Figueira; 2014 [citado em 01 de março de 2024]. Disponível em: <http://higia.imip.org.br/handle/123456789/177>.
11. Kimberlin DW, Brady MT, Jackson MA, Long SS. Pneumococcal infections. In: Red book: 2015 report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village (IL): American Academy of Pediatrics; 2015. 626.
12. March MFBP, Ferreira S, Ribeiro JD, Souza ELS. Pneumonias comunitárias. In: Campos Jr D, Burns DAR, Lopez FA. Tratado de Pediatria. 3. ed. São Paulo: Manole; 2013. p. 2549-58.
13. Ferrero F, Nascimento-Carvalho CM, Cardoso MR, Camargos P, March MFP, Berezin E, et al. Radiographic findings among children hospitalized with severe community-acquired pneumonia. Pediatr. Pulmonol. 2010 [citado em 07 de dezembro de 2023];45:1009-1013. DOI: <https://doi.org/10.1002/ppul.21287>.
14. Cherian T, Mulholland EK, Carlin JB, Ostensen H, Amin R, de Campo M, et al. Standardized interpretation of paediatric chest radiographs for the diagnosis of pneumonia in epidemiological studies. Bull World Health Organ. 2005;83(5):353-9. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/15976876/>.
15. Mani CS. Acute Pneumonia and Its Complications. Principles and Practice of Pediatric Infectious Diseases. 2018 [citado em 11 de janeiro de 2024];238-249. e4. DOI: <https://doi.org/10.1016/B978-0-323-40181-4.00034-7>.
16. Marchi E, Lundgren F, Mussi R. Derrame pleural parapneumônico e empiema. J bras pneumol. 2006 [citado em 11 de janeiro de 2024];32:S190-6. DOI: <https://doi.org/10.1590/S1806-37132006000900005>.
17. Pereira LMD, Azevedo MM de, Filho ARI. Derrame pleural como complicação de pneumonia em paciente pediátrico. Cam Clin. 2022 [citado em 09 de fevereiro de 2024];1(01). Disponível em: <https://revistas.unifoa.edu.br/caminhos/article/view/4035/3076>.
18. Nascimento-Carvalho CM. Community-acquired pneumonia among children: the latest evidence for an updated management. J Pediatr (Rio J). 2020 [citado em 11 de dezembro de 2023];96:29-38. DOI: <https://doi.org/10.1016/j.jped.2019.08.003>.
19. Bini AC. Perfil e evolução dos pacientes internados por pneumonia com derrame pleural em hospital de referência do sul do Brasil [Internet]. 2021 [citado em 01 de março de 2024]. P. 1-33 Disponível em: <https://repositorio.ufsc.br/bitstream/handle/123456789/230362/TCC.pdf?sequence=1&isAllowed=y>.
20. Amorim PG, Morcillo AM, Tresoldi AT, Fraga A de MA, Pereira RM, Baracat ECE. Fatores associados às complicações em crianças pré-escolares com pneumonia adquirida na comunidade. J bras pneumol. 2012 [citado em 11 de setembro de 2023];38(5):614-21. DOI: <https://doi.org/10.1590/S1806-37132012000500011>.
21. Secretaria de Estado de Saúde (SES). Coordenadoria de Controle de Doenças Instituto Adolfo Lutz. SIREVA. Informação da vigilância das pneumonias e meningites bacterianas. 2023 [citado em 11 de junho de 2023];3. Disponível em: http://www.ial.sp.gov.br/resources/insituto-adolfo-lutz/publicacoes/sireva_2023_v3_2.pdf.
22. Westphal FL, Lima LCD, Ferreira CA, Carvalho MAD. Tratamento cirúrgico de pneumonia necrosante: análise de quatro casos. J Pneumologia. 2000 [citado em 05 de março de 2024];26(1):1-4. DOI: <https://doi.org/10.1590/S0102-3586200000100002>.
23. Pocket Book of Hospital Care for Children: Guidelines for the Management of Common Childhood Illnesses. 2nd edition. Geneva: World Health Organization; 2013. [citado em 11 de março de 2023]. Disponível em: <https://www.ncbi.nlm.nih.gov/books/NBK154447/>.
24. de Benedictis FM, Kerem E, Chang AB, Colin AA, Zar HJ, Bush A. Complicated pneumonia in children. Lancet. 2020 [citado em 11 de março de 2023];396(10253):786-798. DOI: [https://doi.org/10.1016/S0140-6736\(20\)31550-6](https://doi.org/10.1016/S0140-6736(20)31550-6).
25. Avansino JR, Goldman B, Sawin RS, Flum DR. Primary operative versus nonoperative therapy for pediatric empyema: a meta-analysis. Pediatrics. 2005 [citado em 17 de abril de 2023];115(6):1652-9. DOI: <https://doi.org/10.1542/peds.2004-1405>.
26. Tan SS, Rutten FF, van Ineveld BM, Redekop WK, Hakkaart-van Roijen L. Comparing methodologies for the cost estimation of hospital services. Eur J Health Econ. 2009;10(1):39-45. DOI: [10.1007/s10198-008-0101-x](https://doi.org/10.1007/s10198-008-0101-x).