

Hospitalized Children and Adolescents with Community-Acquired Pneumonia: Clinical and Epidemiological Profile After the Introduction of the 10-Valent Pneumococcal Conjugate Vaccine

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What is already known on this topic?

- Community-acquired pneumonia (CAP) is a major cause of childhood hospitalization and mortality worldwide.
- The introduction of the 10-valent pneumococcal conjugate vaccine (PCV10) in Brazil has successfully reduced hospitalization rates for CAP and invasive pneumococcal disease in children.

What does this study add on this topic?

- Despite high PCV10 vaccination coverage, CAP requiring hospitalization still occurs, predominantly in children under 5 years and those with underlying comorbidities. This highlights the potential value of higher-valent vaccines.
- In children already hospitalized with CAP, the presence of a neurological disorder or a complication like pleural effusion were the strongest predictors of a prolonged hospital stay, whereas vaccination status alone did not significantly shorten the hospitalization length in this specific group.

Abstract

Objective: To characterize the clinical, radiological, and epidemiological profile of patients hospitalized with community-acquired pneumonia (CAP), compare the characteristics of vaccinated and unvaccinated children and identify factors associated with prolonged hospitalization.

Methods: A retrospective, monocentric cohort study was conducted at the Instituto de Puericultura e Pediatria Martagão Gesteira (IPPMG), a University Pediatric Hospital affiliated with the Universidade Federal do Rio de Janeiro (UFRJ), from January 2013 to December 2018. The study included children and adolescents aged 29 days to 14 years hospitalized with CAP. Data on demographics, clinical presentation, radiological findings, vaccination status, comorbidities, and hospitalization outcomes were analyzed. Bivariate and multivariate logistic regression analyses were performed to identify factors associated with prolonged hospitalization (>10 days).

Results: Among 185 patients analyzed, 58.9% were male and 89.7% were under 5 years of age. Comorbidities were present in 61.5% of patients, with neurological disorders being the most frequent (22.0%). 10-valent pneumococcal conjugate vaccine (PCV10) vaccination coverage was 75.6%. Vaccinated patients had significantly higher median age (22 vs. 15 months; $P = .048$) and daycare attendance (32.5% vs. 7.7%; $P = .012$), but lower occurrence of neurological disorders (17.8% vs. 33%; $P = .041$) and other comorbidities (13.6% vs. 30.8%; $P = .014$). Alveolar consolidation was the most common radiological finding, and pleural effusion was the most frequent complication (21.9%). The median hospitalization duration was 11 days. In the multivariate analysis, neurological disorders and pleural effusion were independent predictors of prolonged hospitalization (>10 days).

Conclusion: Despite high PCV10 vaccination coverage, severe CAP requiring hospitalization continues to occur, particularly in patients with underlying comorbidities. Neurological disorders and pleural effusion were significant predictors of prolonged hospitalization.

Keywords: Children, community acquired pneumonia, epidemiology, hospitalized, pneumococcal vaccines

Introduction

Community-acquired pneumonia (CAP) represents one of the most significant causes of morbidity and mortality in pediatric populations worldwide. According to the World Health Organization, CAP accounts for approximately 15% of all deaths in children under 5 years of age globally, making it a leading cause of childhood mortality.^{1,2} In Brazil, respiratory diseases, particularly CAP, constitute a major public health concern, with substantial impacts on healthcare systems and families.³

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The epidemiological landscape of pediatric CAP has undergone significant transformation following the introduction of pneumococcal conjugate vaccines. *Streptococcus pneumoniae* has historically been recognized as one of the primary bacterial pathogens responsible for severe CAP in children, particularly those under 5 years of age.⁴ The organism's virulence and propensity to cause severe and invasive disease have made it a priority target for vaccination strategies worldwide.⁵

In March 2010, Brazil became the first country to introduce the 10-valent pneumococcal conjugate vaccine (PCV10; Synflorix, G laxoSmithKline) into its national immunization program, making it available to all children under 2 years of age.⁶ Several studies employing hospital-based surveillance or population-based data from other regions of Brazil have shown declines in invasive pneumococcal disease following PCV10 introduction.⁷ The implementation of PCV10 vaccination has also been associated with substantial reductions in hospitalization rates for CAP among children in various Brazilian states.^{8,9} An ecological study demonstrating the remarkable cost-effectiveness of PCV10 and its considerable positive impact on public health outcomes supports its use in Brazil's routine vaccination program.¹⁰

However, the impact of PCV10 vaccination on hospitalized pediatric patients with CAP requires continued surveillance and analysis. While the PCV10 has had a significant impact on reducing the burden of pediatric pneumococcal disease in Brazil since its introduction in 2010, its overall effectiveness has been continuously challenged by the phenomenon of serotype replacement.^{9,11,12}

This study aims to characterize the clinical, radiological, and epidemiological profile of children hospitalized with CAP at a University Pediatric Hospital in Rio de Janeiro, Brazil, encompassing 6 years of data collection in the post-PCV10 vaccination era. Other secondary aims are to compare the characteristics of vaccinated and unvaccinated children within this hospitalized cohort and to explore factors associated with a prolonged hospital stay in this population.

Methods

This retrospective cohort study was conducted at the Instituto de Puericultura e Pediatria Martagão Gesteira (IPPMG), a University Pediatric Hospital affiliated with the Universidade Federal do Rio de Janeiro (UFRJ), located in Rio de Janeiro, Brazil. The study period extended from January 2013 to December 2018.

Participants and Diagnostic Criteria

The diagnosis of CAP was established based on a combination of clinical presentation (e.g., acute fever, abdominal pain, cough, tachypnea, respiratory distress, decreased breath sounds, and crackles or rales) and confirmatory radiological findings (presence of infiltrate, consolidation, or pleural effusion on chest radiograph), following the Brazilian guidelines for CAP in pediatrics.¹³ Inclusion criteria comprised children and adolescents aged 29 days to 14 years who were admitted to the general pediatric ward with a primary diagnosis of CAP during the study period. Exclusion criteria included patients previously admitted for the same episode of pneumonia (only the first admission was considered), admitted to the Pediatric Intensive Care Unit at any point during the hospitalization, with hospital-acquired pneumonia (defined as pneumonia occurring ≥ 48 hours after hospitalization), immunocompromised states (excluding those with HIV with normal CD4 counts), or with incomplete medical records lacking essential data for analysis.

Data Collection and Variable Definitions

Data were extracted from electronic and physical medical records using a standardized, pre-piloted form. Variables included:

- Demographics: Age (categorized as ≤ 12 , 13-59, ≥ 60 months) and gender.
- Exposure: Daycare attendance (defined as regular attendance at a collective child education facility outside the home, part-time or full-time), household smoking (regular smoking ≥ 1 cigarette/day by at least 1 household member), and exclusive breastfeeding (duration in months, stratified into absent, 1 to 4 months or 5 months to 6 months of age).
- Medical history: Comorbidities (pre-existing chronic conditions recorded in the medical chart, categorized per Table 1).
- Vaccination status: PCV10 vaccination was considered "complete" if the child was up-to-date for their age according to the Brazilian National Immunization Program schedule.¹⁴ Status was ascertained from documented medical history, vaccination cards, or the national immunization registry when available. Unvaccinated or incompletely vaccinated children were grouped as "unvaccinated."
- Clinical outcomes: Radiological findings (based on official reports by staff pediatric radiologists), complications (including pleural effusion, pneumothorax, pneumatocele, lung abscess, or atelectasis), length of hospitalization (LOS) in days (from admission to discharge). Prolonged LOS was defined as >10 days. This cutoff was selected based on the median LOS of the cohort (11 days) and aligns with the median LOS found in other pediatric CAP studies.¹⁵

Statistical Analysis

Data analysis was performed using SPSS software, version 26 (IBM SPSS Corp.; Armonk, NY, USA). Continuous variables are

Table 1. Comorbidities of Hospitalized Pediatric Patients with CAP. IPPMG-UFRJ, 2013-2018

Comorbidity	n = 182	%
General comorbidity	112	61.5
Neurological disorders	40	22.0
Sickle cell anemia	16	8.8
Genetic syndromes	14	7.7
Heart diseases	12	6.6
Asthma	11	6.0
Bronchopulmonary dysplasia	11	6.0
HIV/AIDS	7	3.8
Nephropathies	7	3.8
Endocrinopathies	4	2.2
Leukemia	3	1.6
Hemoglobinopathies	2	1.1
Tuberculosis	2	1.1
Other comorbidities	33	18.1

%, percentage; AIDS, acquired immunodeficiency syndrome; CAP, community-acquired pneumonia; HIV: human immunodeficiency virus; n, frequency.

described using median and interquartile range (IQR), as their non-normal distribution was confirmed by the Shapiro–Wilk test and graphical inspection of histograms. Categorical variables are summarized using frequencies and percentages (n, %).

Group comparisons (e.g., vaccinated vs. unvaccinated) were performed using the Mann–Whitney *U*-test for numerical variables and the Chi-square test or Fisher’s exact test for categorical variables, as appropriate.

To identify factors associated with prolonged hospitalization (>10 days), bivariate analyses were first conducted using the Mann–Whitney *U*-test (for comparisons involving 2 groups), the Kruskal–Wallis test (for 3 or more groups), or Spearman’s rank correlation coefficient for numerical variables.

Variables yielding a *P*-value <.20 in these bivariate analyses were considered candidates for inclusion in a multivariate binary logistic regression model. Given the exploratory nature of this analysis, a backward stepwise selection procedure was employed to identify a parsimonious model, using a threshold of *P* <.05 for variables to remain in the final model. The goodness-of-fit of the final model was assessed using the Hosmer–Lemeshow test, and multicollinearity was evaluated by calculating variance inflation factors (VIF); all VIF values were below 2.0, indicating no substantial multicollinearity.

Results of the logistic regression are presented as odds ratios (OR) with their respective 95% CI. A 2-tailed *P*-value <.05 was considered statistically significant throughout the analysis.

Ethical Considerations

The waiver of the informed consent form was justified because the study was a retrospective, observational analysis that utilized only existing data from medical records and institutional systems without employing biological material. All data were handled and analyzed anonymously, with no nominal identification of the research participants, and the resulting findings were presented in an aggregated format that prevented individual identification. Furthermore, the study was non-interventional, meaning it did not alter clinical routines or treatments and consequently added no risks to the participants’ well-being. The researchers committed to using the data solely for the described purposes and to complying with all regulatory guidelines for data confidentiality.

This study was approved by the the Instituto de Puericultura e Pediatria Martagão Gesteira (IPPMG), a University Pediatric Hospital affiliated with the Universidade Federal do Rio de Janeiro (UFRJ) ethics committee (Approval No.: 07017018.8.3001.5264; Date: September 19, 2019)

Results

Patient Characteristics

The initial search yielded 207 admissions. After excluding 22 readmissions, 185 unique patients were eligible for analysis. Vaccination status was retrievable for 160 (86.5%) patients. Among these, 121 (75.6%) were fully vaccinated with PCV10 according to age (Figure 1).

The cohort was predominantly male (58.9%) and young, with 89.7% under 5 years of age (Table 2). Comorbidities were present in 112/182 patients (61.5%). Neurological disorders were the most frequent comorbidity (22.0%), with cerebral palsy being the most common diagnosis (Table 1).

Comparison Between Vaccinated and Unvaccinated Children

Comparisons were made within the subset of 160 patients with known vaccination status. Vaccinated children were significantly

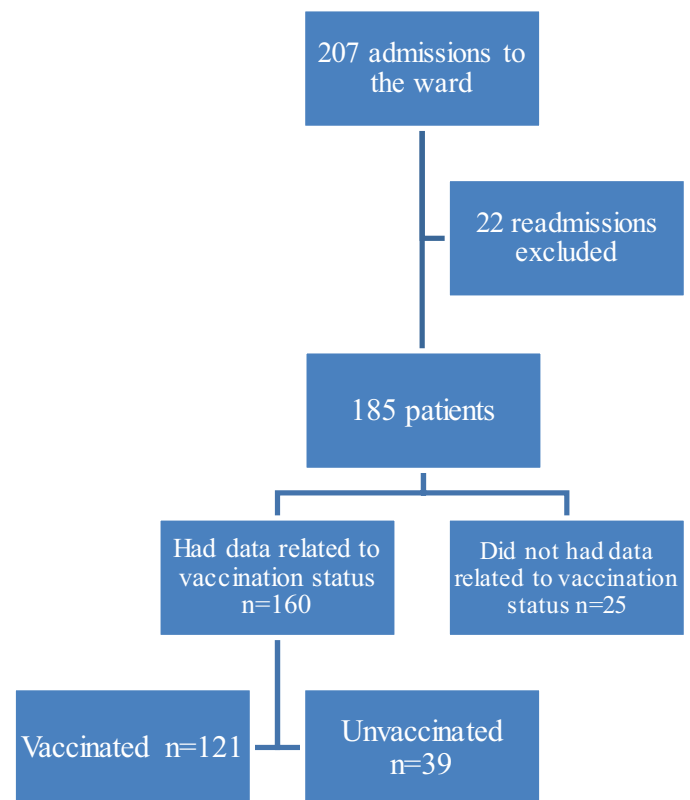


Figure 1. Patient flow.

older (median 22 vs. 15 months, *P* = .048) and had a higher frequency of daycare attendance (32.5% vs. 7.7%, *P* = .012). Conversely, the vaccinated group had a significantly lower prevalence of neurological disorders (17.8% vs. 33.3%, *P* = .041) and other comorbidities (13.6% vs. 30.8%, *P* = .014) (Table 3 and 4). There were no significant differences in gender, household smoking, or breastfeeding history.

Clinical Course and Radiological Findings

Radiological evaluation was available for 178 patients. Alveolar consolidation was the most frequent finding (96/178, 53.9%). Pleural effusion was the most common complication, affecting 39/178 patients (21.9%). The median LOS for the entire cohort was 11 days (IQR: 7-17). The median LOS was not significantly different between vaccinated and unvaccinated children (11 vs. 12 days, *P* = .41).

Factors Associated with Prolonged Hospitalization (>10 days)

In bivariate analysis, age 13–59 months (*P* = .033), presence of neurological disorders (*P* = .0009), and pleural effusion (*P* = .001) were associated with prolonged LOS. Vaccination status, gender, and other comorbidities were not significant.

In the multivariate logistic regression model (Hosmer–Lemeshow test *P* = 0.72, indicating good fit), only 2 variables remained as independent predictors of prolonged hospitalization: neurological disorders (OR = 7.3; 95% CI: 2.9-18.8; *P* < .0001) and pleural effusion (OR = 4.6; 95% CI: 2.4-13.2; *P* = .0001). Vaccination status was not retained in the final model.

Discussion

This study describes the profile of children hospitalized with CAP in a tertiary center in Brazil over the course of 6 years after

Table 2. Epidemiological Variables of Hospitalized Pediatric Patients with CAP (IPPMG-UFRJ 2013-2018)

Variable	n	%
Age (months)	n total: 185	
≤ 12 months	69	37.3
13-59 months	97	52.4
≥ 60 months	19	10.3
Sex	n total: 185	
Male	109	58.9
Female	76	41.1
PCV10 vaccination	n total: 160	
Yes	121	75.6
No	39	24.4
Comorbidities	n total: 182	
Yes	112	61.5
No	70	38.5
Daycare attendance	n total: 115	
Yes	31	27.0
No	84	73.0
Smoking at home	n total: 150	
Yes	47	31.3
No	103	68.7
Exclusive breastfeeding (months)	n total: 152	
Absent	51	33.6
1-4 months	52	34.2
5-6 months	49	32.2
Median (Q1-Q3)	2.5 (0-5)	

n, frequency; %, percentage; PCV10, 10-valent pneumococcal vaccine.

PCV10 introduction. The key findings are the high prevalence of comorbidities (61.5%), particularly neurological disorders, and the identification of neurological disorders and pleural effusion as strong, independent predictors of a hospital stay longer than 10 days. It is crucial to note that the comparison between vaccinated and unvaccinated children pertains only to this specific hospitalized cohort; it should not be interpreted as a measure of vaccine effectiveness, which requires population-level data.

The predominance of males and children under 5 years aligns with global epidemiology of pediatric CAP.^{16,17} Differences in genetics and immunity have been proposed as explanations for such differences; however, it is likely that a complex interplay of sex steroid hormones, host immunity, genetics, anatomical variation, and lung physiology, in addition to sociocultural and behavioral factors, influences the observed sex differences in respiratory infections.^{18,19,20} However, analysis of the epidemiological literature on CAP in children reveals a complex picture regarding

Table 3. Epidemiological, Demographic, and Clinical Variables According to PCV10 Vaccination in Pediatric Patients with CAP (IPPMG-UFRJ, 2013-2018)

Variable	Vaccination with PCV10				P
	Yes		No		
	n	%	n	%	
Age (months)					
≤ 12 months	38	31	18	46.2	.24
13-59 months	53	44	13	33.3	
≥ 60 months	30	25	8	20.5	
Median (Q1-Q3)	22 (10-58)		15 (6-27)		.048
Sex					
Male	58	48	22	56.4	.36
Female	63	52	17	43.6	
Presence of comorbidities					
Yes	70	59	27	69.2	.27
No	48	41	12	30.8	
Presence of comorbidities					
Yes	26	33	2	7.7	.012
No	54	68	24	92.3	
Household smoking					
Yes	31	30	9	29	.91
No	72	70	22	71	
Presence of comorbidities					
Absent	30	29	16	43.2	.2
1-4 months	36	35	13	35.1	
5-6 months	36	35	8	21.6	
Median (Q1-Q3)	3 (0-6)		2 (0-4)		.076

CAP, community-acquired pneumonia; PCV10, 10-valent pneumococcal conjugate vaccine.

gender differences. Many studies suggest a male predominance, but specific quantitative data are limited and often inconsistent across populations and pathogens.^{17,21}

The prevalence of CAP in children under 5 years is well documented, with this age group being particularly vulnerable due to immature immune systems and smaller airway calibers, which can lead to more severe complications.^{22,23}

The high burden of comorbidities, especially neurological conditions, reflects the tertiary, referral nature of the hospital and underscores that children with chronic diseases remain a vulnerable population for severe CAP despite vaccination as observed by other authors.²⁴

The 75.6% PCV10 coverage in the cohort mirrors the successful implementation of Brazil's national program.^{25,7} The observed differences between vaccinated and unvaccinated children within the hospital—namely that vaccinated children were older,

Table 4. Comorbidities Found in 160 Pediatric Patients with CAP According to PCV10 Vaccination (IPPMG-UFRJ, 2013-2018)

Variable	PCV10		No PCV10		P
	n	%	n	%	
General comorbidities					
Yes	70	59.3	27	69.2	.270
No	48	40.7	12	30.8	
Sickle cell anemia					
Yes	14	11.9	1	2.6	.072
No	104	88.1	38	97.4	
Leukemia					
Yes	0	0	0	0	NSA
No	118	100.0	39	100.0	
HIV/AIDS					
Yes	2	1.7	3	7.7	.098
No	116	98.3	36	92.3	
Heart diseases					
Yes	9	7.6	3	7.7	.610
No	109	92.4	36	92.3	
Hemoglobinopathies					
Yes	2	1.7	0	0	.560
No	116	98.3	39	100.0	
Asthma					
Yes	8	6.8	0	0	.095
No	110	93.2	39	100.0	
Tuberculosis					
Yes	1	0.8	0	0	.750
No	117	99.2	39	100.0	
Neurological disorders					
Yes	21	17.8	13	33.3	.041
No	97	82.2	26	66.7	
Genetic diseases					
Yes	11	9.3	3	7.7	.520
No	107	90.7	36	92.3	
Pulmonary bronchodysplasia					
Yes	9	7.6	2	5.1	.460
No	109	92.4	37	94.9	
Nephropathies					
Yes	6	5.1	1	2.6	.440
No	112	94.9	38	97.4	

Table 4. Comorbidities Found in 160 Pediatric Patients with CAP According to PCV10 Vaccination (IPPMG-UFRJ, 2013-2018) (Continued)

Variable	PCV10		No PCV10		P
Endocrinopathies					
Yes	1	0.8	2	5.1	.150
No	117	99.2	37	94.9	
Other comorbidities					
Yes	16	13.6	12	30.8	.014
No	102	86.4	27	69.2	

The data were expressed as frequency (n) and percentage (%). Chi-square test or Fisher's exact test. AIDS, acquired immunodeficiency syndrome; HIV, human immunodeficiency virus.

more often attended daycare, but had fewer comorbidities—likely reflect a combination of factors. Daycare attendance is a known risk factor for CAP exposure but, in this cohort, is also an indicator of children who are more likely to be fully vaccinated. There are indirect factors by which daycare centers can promote vaccination, such as requiring a vaccination card for enrollment. In Brazil, many public and private daycare centers require an up-to-date vaccination card as part of the enrollment documentation, which encourages parents to update their children's vaccination status before enrollment.²⁶ On the other hand, the lower vaccination rate among children with neurological disorders suggests potential barriers to healthcare access or specific vaccine hesitancy in this high-risk group, a critical area for public health intervention.

The central finding that vaccination status was not associated with higher LOS in this cohort requires careful interpretation. This does not question the established effectiveness of PCV10 in preventing CAP hospitalizations at a population level.^{8,9,25} Rather, it suggests that among children who develop CAP severe enough to require hospitalization despite vaccination, the subsequent in-hospital disease trajectory is driven more powerfully by the presence of complications (e.g., pleural effusion) and the patient's underlying health issues (e.g., neurological disorder) than by their vaccination status. In this cohort, the vaccine did not alter the hospital LOS, which was also found by other authors.²⁷ The possibility of serotype replacement after PCV introduction could not be investigated, and this prevents us from concluding that there is no change in clinical outcomes after immunization.

The results strongly align with clinical intuition and previous studies identifying pleural complications as markers of prolonged LOS. Patient hospital LOS was also found to be positively associated with time until procedural drainage.²⁸ In this cohort, it was not possible to determine if there was a linear relationship between LOS and time until drain insertion after identification of pleural effusion.

The powerful association of neurological disorders with prolonged LOS (OR = 7.3) is particularly notable. This may be due to factors such as severe motor impairment that limits mobility and cough effectiveness; chronic aspiration from dysphagia or reflux; poor nutritional status which weakens immune response; spinal deformities with lung expansion restriction; ineffective airway clearance and difficulty managing secretions; and the presence of comorbidities such as uncontrolled seizures or significant drooling. Together, these issues impair the ability to clear infections

and regain baseline respiratory health, often resulting in extended recovery periods.²⁹

Limitations

This study has limitations inherent to its retrospective, single-center design. Data reliance on medical records can lead to information bias and missing data (e.g., 25 patients without vaccination records). PPSV23 status was not assessed in older, high-risk children, which is a potential confounder. Furthermore, conducting the study at a referral hospital introduces selection bias towards more severe or complex cases, limiting generalizability to community hospitals. The definition of prolonged LOS (>10 days), while based on the cohort's median and similar studies, is somewhat arbitrary. Furthermore, the use of a stepwise procedure for variable selection in the multivariate model, while practical for exploratory analysis, is known to potentially yield unstable model configurations and optimistic *P*-values. Although the final predictors (neurological disorders and pleural effusion) are clinically highly plausible and the model showed adequate fit, these findings should be interpreted as hypothesis-generating and warrant validation in future studies.

Conclusions

Despite high PCV10 coverage, CAP leading to hospitalization persists, predominantly affecting young children and those with comorbidities, in a tertiary care setting. Neurological disorders and pleural effusion were the strongest predictors of prolonged hospitalization. While vaccination status did not influence LOS in this specific hospitalized cohort, likely because disease course was dominated by complications and baseline health, this finding underscores that PCV10's primary benefit is in preventing hospitalizations. Efforts should focus on ensuring complete vaccination, especially in high-risk groups like children with neurological disorders, and on the prompt recognition and management of complications to improve outcomes for hospitalized patients.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Instituto de Puericultura e Pediatria Martagão Gesteira (IPPMG), a University Pediatric Hospital affiliated with the Universidade Federal do Rio de Janeiro (UFRJ) (Approval No.: 07017018.8.3001.5264; Date: September 19, 2019).

Informed Consent: Due to the retrospective nature of the study, the requirement for informed consent was waived by the ethics committee.

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