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ORIGINAL RESEARCH ARTICLE

Costs of Respiratory Syncytial Virus Hospitalizations in Colombia

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Abstract

Background Several clinical practice guidelines exist for the management of respiratory syncytial virus (RSV) infection, but the use and overuse of medications and medical tests with insufficient evidence of effectiveness remains substantial.

Objective This study aimed to evaluate the medical costs associated with bronchiolitis hospitalizations caused by RSV infection among infants aged < 2 years in Colombia.

Methods This was a prevalence-based cost-of-illness multicentric study performed from the societal perspective during 2016–2017. A case was defined as a laboratory-confirmed RSV infection with hospitalization. All costs and use of resources were collected directly from medical invoices and health records.

Results This study included 193 patients with a diagnosis of RSV. The average hospital stay duration was 5.55 days. The major contributors to hospitalization costs were room costs (31.5%), drugs (21.8%), and indirect costs (14.9%). Medications with the highest costs were nebulization with a hypertonic solution and systemic antibiotics. In total, 96% of β-lactam antibiotics, 90% of bronchodilators, and 86% of corticosteroids and epinephrine were classified as inappropriate.

Conclusion RSV infection in Colombia places a high economic burden on the health system. Generating comprehensive data on healthcare resource use and costs associated with RSV will help to provide valuable information for the development of cost-effectiveness models and to guide RSV-prevention strategies.

Key Points for Decision Makers

An understanding of the cost structure of respiratory syncytial virus (RSV) infection is essential for the assessment of cost-effectiveness studies of interventions for preventing infection.

In total, 35% of the costs per patient per day were attributable to drugs and laboratory tests for which most clinical practice guidelines provide no support or evidence.

Strategies are necessary to increase compliance with guidelines to ensure efficient prescribing practices.

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1 Introduction

Respiratory syncytial virus (RSV) is the most frequent cause of bronchiolitis worldwide [1], with around 33.1 million RSV infections resulting in about 3.2 million hospital admissions and 59,600 in-hospital deaths in 2005 [2]. Globally, RSV pneumonia is the second most common cause of postnatal infant death, after malaria, causing 137,000 deaths each year (6.7% of all newborn deaths) [3].

Although several clinical practice guidelines have been developed [4, 5], a substantial economic burden is associated with the use and overuse of medications and medical tests that have insufficient evidence of effectiveness [6–8]. This phenomenon is accentuated in patients with RSV infection, with previous reports indicating that more medical tests are ordered for these patients and that they receive more drug prescriptions [9, 10]. Studies are scarce, and most economic studies focus on assessing the efficiency of palivizumab for the prophylaxis of RSV infection [11] and are conducted from the payer perspective, rather than the social perspective, and so do not include indirect costs, such as those associated with job loss and family expenses [12, 13]. These methodological limitations mean we do not have clear and unbiased evidence of the resource consumption associated

with this disease. Additionally, no studies have yet evaluated the economic impact of such an infection in developing countries, which have greater problems in terms of morbidity and mortality. This study aimed to evaluate the costs associated with RSV infection-related bronchiolitis hospitalizations and determine which medications and tests are misused/overused among infants aged < 2 years.

2 Methods

This prevalence-based cost-of-illness multicentric study was performed from the societal perspective. We included infants aged < 2 years who were admitted to tertiary centers in Rionegro, Colombia, from January 2015 to December 2016 due to RSV (*International Classification of Disease, Tenth Revision* code J21.0, according to the national clinical guidelines for bronchiolitis [4]). Our country has been characterized as having very little price variation over the last 10 years, especially in health services [14]. Moreover, the proportions of each of the costs remained relatively constant, with few variations in their composition over the last 10 years [15]. The municipality of Rionegro has a total population of 101,046 and is the sixth largest populated area in Antioquia, with two tertiary referral hospitals [16].

Inclusion criteria were defined as children aged < 2 years admitted to the pediatric ward with a diagnosis of RSV confirmed using direct immunofluorescence (Light Diagnostics TM Respiratory Panel 1 DFA, Merck-Millipore Laboratory). We excluded patients who were aged > 2 years, had no lower respiratory compromise, had positive bacterial cultures on admission, had confirmed whooping cough, or were referred from another hospital center. The study protocol was reviewed and approved by the Institutional Review Board of Clinica Somer (no. 281015) and the University of Antioquia (no. 18/2015).

2.1 Study Variables

We collected the following variables from the electronic medical records: age, sex, weight, height, signs and symptoms at admission (e.g., fever, chest indrawing, and chest auscultation abnormalities such as rhonchi or crepitation), history of prematurity, bronchopulmonary dysplasia confirmed by a specialist physician at discharge from a neonatology unit, comorbidities (congenital heart disease, neurological disease), results of chest X-rays or other medical tests, drugs and other treatments, and complications [pneumonia, atelectasis, sepsis, admission to the intensive care unit (ICU)].

2.2 Cost Analysis

All costs and resource use were collected directly from medical invoices and health records. The direct costs considered in the analysis included medical consultation at emergency room, specialist referrals, chest physiotherapy, diagnosis support (laboratory, electrocardiogram, X-ray, etc.), medication (oxygen, nebulization, antibiotics, corticosteroids, bronchodilators, etc.), medical devices, day bed in the ICU, and day bed in the general medical ward. All costs are expressed in $US (exchange rate $US1 = 3000 Colombian peso) [17]. In Colombia, about 50% of the population, especially those with better socioeconomic conditions, have private health insurance, whereas the other 50%, with less favorable socioeconomic conditions, receive health insurance from the government. In the case of RSV infection, given its high frequency, medical costs are assumed by the respective insurance system [Social, 2019 #127]. We used the human capital method to value the indirect costs associated with parental loss of productivity, assuming everyone receives an income of at least a legal minimum wage for formal or informal work. In this, the cost opportunity of the productivity loss at the workplace and for the caregiver was assessed based on the minimum wage without including transportation assistance ($US229.81 per month, year 2016 values). The legal minimum wage approved by the government was taken as a reference and not an average or median wage thereof, given that more than 75% of the population in Colombia has this level of income [18]. Because all included patients were children, we assumed that at least one family member permanently accompanied the patient during hospitalization, since pediatric hospitals in the country usually allow only one companion per patient in the hospital. Costs associated with transportation and food (not including a stay) were assumed to correspond to 50% of the day's cost for productivity loss at the workplace.

All prescription drugs and diagnostic tests used (hemogram, C-reactive protein, urine culture, chest radiography, and blood cultures or other tests) were classified as appropriate or inappropriate according to the national guidelines for bronchiolitis [4]. The use of nebulized hypertonic saline was excluded because these guidelines [4] allow its use to reduce the length of hospital stay. The use of corticosteroids, inhaled β_2 agonists, and epinephrine was deemed appropriate only if they were continued after a positive clinical response to a monitored trial. The use of antibiotics was deemed appropriate in patients with confirmed bacterial infections (blood culture, urine culture, or chest X-rays with lobar consolidation).

2.3 Statistical Analysis

Continuous variables (age, weight, height, etc.) are presented as mean ± standard deviation (SD) or median [interquartile range (IQR)], depending on the normality of the data distribution. Categorical variables (symptoms, auscultation abnormalities, comorbidities, etc.) are presented as percentages. The normality of the distributions of the continuous variables was assessed using the Kolmogorov–Smirnov test. All statistical tests were two-tailed, and the significance level used was $p < 0.05$.

3 Results

During the study period, 193 patients had a diagnosis of RSV. Of these, 113 (58.5%) were males, and the mean ± SD age was 5.6 ± 0.38 months. Approximately 14% had a history of prematurity and 5% any cardiac or chronic neurological comorbidity. Only one patient (with a history of congenital heart disease) had received palivizumab. The majority (92%) required oxygen, and more than half had chest retractions in the emergency department. One in three patients had some radiological abnormality, but only 12% had alveolar consolidation. The average hospital stay duration was 5.55 days. No adverse reactions were reported in the included patients. The frequency of complications associated with bronchiolitis was 19.17% (Table 1).

Overall, the diagnostic tests most frequently requested by the attending physicians were hemogram ($n = 185$; 95.85%) and chest radiography ($n = 178$; 92.22%). The medications most often prescribed were nebulized or inhaled β_2 agonists ($n = 108$; 55.96%) and nebulized hypertonic saline ($n = 180$; 93.26%) (Table 2).

Overall, the major contributors to hospitalization costs consisted of room costs (31.5%), drugs (21.8%), and indirect costs (14.9%). The medications with the highest average costs were nebulization with a hypertonic solution, systemic antibiotics, and parenteral fluids (Table 3). Diagnostic tests of both images and laboratory tests contributed 9.32% of the costs per patient. Among these, chest radiography, blood cultures, and C-reactive protein added the most costs per patient (Table 3). In total, 74% of hemograms, 72% of chest X-rays, 40.4% of C-reactive protein tests, 96% of β-lactam antibiotics, 90% of bronchodilators, and 86% of corticosteroids and epinephrine were classified as inappropriate (Table 4).

Table 1 Sociodemographic and clinical characteristics of patients

Variable	*n* (%)
Age (months), median (ds)	5.66 (0.38)
Male	113 (58.55)
Premature birth	28 (14.51)
Comorbidities (CHD, neurological)	11 (5.71)
Atopy	21 (10.88)
SpO_2, median (ds)	88 (0.93)
O_2 supportive	178 (92.33)
Clinical and laboratory parameters	
Fever	53 (27.46)
Chest indrawing	102 (52.85)
Tachypnea	30 (15.54)
Rhonchi	78 (40.41)
Crepitation	36 (18.65)
Leukocytosis (> 15,000/cmm)	31 (16.76)
Increased C-reactive protein (> 4 mg/L)	59 (44.81)
Chest X-ray	
Normal	22 (12.36)
Peribronchial thickening	63 (35.39)
Hyperinflation	33 (18.54)
Atelectasis	5 (2.81)
Bilateral interstitial infiltrates	33 (18.54)
Alveolar infiltrates	22 (12.36)
Length of hospital stay, median (range)	5.88 (0.39)
Complications	
Pneumonia	23 (11.92)
Sepsis	9 (4.66)
Atelectasis	5 (2.59)
ICU	3 (1.5)

CHD congenital heart defect, ds, *ICU* intensive care unit, *SpO_2* oxygen saturation

4 Discussion

Our study is the first to describe the direct and indirect costs associated with RSV in hospitalized infants aged < 2 years in Colombia. Even though RSV is the most common cause of bronchiolitis, evidence about the cost of RSV illness is limited [1, 15]. An understanding of the cost structure of RSV infection in developing countries is essential for accurate assessment of cost-effectiveness studies of current and future interventions for preventing or treating these respiratory infections.

Medical costs are an essential source of economic burden to families of children with RSV-related illness in developing countries [19–23]. In our study, almost 35% of the cost per patient/day was attributable to drugs, imaging tests, chest therapy, and laboratory tests that have no evidence or support in most clinical practice guidelines [24, 25]. In particular, this high expense for inappropriate practices is generated by antibiotics in the absence of bacterial infection, bronchodilators, and hypertonic solution and by tests such as blood count and C-reactive protein. This inappropriate use of resources has been reported for several years [26, 27], and the clinical guidelines remain explicit in the absence of effectiveness data for drugs, chest therapy, and some medical tests [4, 5,

Table 2 Healthcare resource use associated with respiratory syncytial virus infection

Resource	*n* (%)
GP visits/specialist referrals	193 (100)
Chest physical therapy	127 (66.12)
Bronchodilators	
Albuterol	108 (55.96)
Ipratropium bromide	10 (5.18)
Terbutaline	11 (5.70)
Corticosteroids	
Systemic corticosteroids	23 (11.92)
Inhaled corticosteroids	8 (4.15)
Antibiotics	
β-Lactam antibiotics	51 (61.14)
Aminoglycosides	10 (5.18)
Macrolides	8 (4.15)
Others	6 (3.11)
Nebulized hypertonic saline	180 (93.26)
Epinephrine	23 (11.91)
Diagnostic tests	
Hemogram	185 (95.85)
C-reactive protein	179 (79.79)
Respiratory syncytial virus antigen test	193 (100)
Other diagnostic test	30 (15.54)
Chest X-ray	178 (92.22)
Other imagenologic studies	6 (3.1)

GP general practitioner

Table 3 Costs associated with respiratory syncytial virus infection

Item	Cost/patient/day (95% CI)
Specialist referrals	10.457 (10.117–10.798)
Chest physiotherapy	5.049 (4.805–5.293)
Chest radiography	2.788 (2.643–2.933)
Others diagnostic imaging	0.005 (0.000–0.022)
Complete blood cell counts	1.190 (1.134–1.247)
RSV test	2.892 (2.568–3.215)
C-reactive protein and another test	3.988 (3.914–4.063)
Oxygen	1.463 (1.382–1.544)
Nebulization	20.558 (19.665–21.451)
Parenteral fluids	1.367 (1.334–1.399)
Antibiotics systemics	1.291 (1.193–1.389)
Systemic or inhaled corticosteroids	0.089 (0.000–0.915)
Bronchodilators	0.041 (0.036–0.046)
Medical devices	10.664 (10.138–11.190)
Hospital stay	23.925 (22.745–25.106)
Daily cost for emergency ward	12.833 (12.200–13.467)
Indirect cost day	17.236 (16.386–18.087)

All costs are expressed in $US (exchange rate $US1 = 3000 Colombian peso)

CI confidence interval, *RSV* respiratory syncytial virus

Table 4 Frequency of inappropriate use of medications and medical tests

Category	*n* (%)
Bronchodilators	
Albuterol	97 (89.8)
Ipratropium bromide	9 (90.0)
Terbutaline	10 (90.9)
Corticosteroids	
Systemic	20 (87.0)
Inhaled	7 (87.5)
Antibiotics	
β-Lactam antibiotics	49 (96.1)
Aminoglycosides	2 (70.0)
Macrolides	8 (100)
Other	3 (50.0)
Epinephrine	44 (65.7)
Diagnostic tests	
Hemogram	143 (74.1)
C-reactive protein	78 (40.4)
Other	21 (10.9)
Chest X-rays	139 (72.0)
Other imaging studies	3 (50.0)

28]. Inappropriate use of medications generates higher medical costs and greater health risks. Chen et al. [29] found a relationship between the risk of new-onset asthma and the use of a high dose of an antibiotic in children with bronchiolitis (adjusted odds ratio 3.33; 95% confidence interval 2.67–4.15). This evidence emphasizes the urgency of improving adherence to clinical guidelines, an aspect that—in this study—was highlighted by the use of inappropriate medications and tests and the failure to use drugs such as palivizumab in patients who perhaps had an indication.

Indirect costs are costs of resources for which no payment is made but for which an opportunity cost exists. Guidelines for economic evaluation studies in healthcare recommend the inclusion of indirect costs [30]. The addition of indirect costs usually has a substantial effect on the efficiency ratio, especially in pediatric diseases, where hospitalization involves the whole family, increasing the economic impact of the disease on society. The exclusion of such costs also leads to an underestimate of the real cost of the disease and the effect that preventive interventions may have in reducing the frequency and duration of hospitalizations. In our study, about 15% of the costs generated by RSV infection was attributable to indirect costs. We used the human capital method to estimate this indirect cost. This method is one of the most commonly used in health economic studies because of its simple calculation using wages as a proxy measure of employee output and its broad scope, even though it fails

to account for the possibility that absent workers may be replaced [31].

Our study has the following limitations. The costs used in this study may differ from those in other hospitals in Colombia. However, in Colombia, adherence to the use of health reference cost manuals is adequate, leading to low variability between hospitals in the associated direct costs [32]. Second, we report average values per patient per day (which are influenced by the number of patients included in the study), rather than global values. Third, the study focused only on costs associated with hospitalizations and did not include those arising before admission or after discharge from the hospital, including subsequent morbidity after RSV infection. Fourth, our study was limited to patients hospitalized at a tertiary center, so our findings cannot be generalized to all patients with bronchiolitis. Finally, we were unable to calculate marginal increased costs resulting from patients moving through hospital services of increasing complexity. These limitations warrant further research in other hospitals that also considers the long-term consequences of RSV-bronchiolitis.

5 Conclusion

RSV infection in Colombia places a substantial economic burden on the health system. Generating comprehensive data on healthcare resource use and costs associated with RSV will help to provide valuable information for the development of cost-effectiveness models and help guide prevention strategies against RSV.

Author contributions JAB and DGP contributed equally to all the work, from conception of the work to the publication of results.

Data Availability All information and databases can be freely requested from CIEMTO (the drug and poison research and information center), of the Faculty of Medicine of the University of Antioquia. https://ciemto.medicinaudea.co/

Compliance with Ethical Standards

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Conflicts of interest Jefferson Antonio Buendía and Diana Guerrero Patino have no conflicts of interest that are directly relevant to the content of this article.

Ethical approval The study protocol was reviewed and approved by the ethics boards of Clinica Somer (no. 281015) and the University of Antioquia (no. 18/2015).

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