



BRIEF REPORT

REVISED Importance of respiratory syncytial virus as a predictor of hospital length of stay in bronchiolitis [version 4; peer review: 2 approved]

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Abstract

Introduction : Bronchiolitis is the leading cause of hospitalization in children. Estimate potentially preventable variables that impact the length of hospital stay are a priority to reduce the costs associated with this disease. This study aims to identify clinical variables associated with length of hospital stay of bronchiolitis in children in a tropical middle-income country

Methods: We conducted a retrospective cohort study in 417 infants with bronchiolitis in tertiary centers in Colombia. All medical records of all patients *admitted through the emergency department* were reviewed. To identify factors independently associated we use negative binomial regression model, to estimate incidence rate ratios (IRR) and adjust for potential confounding variables

Results : The median of the length of hospital stay was 3.68 days, with a range of 0.74 days to 29 days, 138 (33.17%) of patients have a hospital stay of 5 or more days. After modeling and controlling for potential confounders age <6 months, comorbidities (CHD or neurological), BPD, chest indrawing, detection of RSV, and C-reactive protein were independent predictors of LOS

Conclusions : Our results show that in infants with bronchiolitis, detection of RSV, age <6 months, comorbidities (CHD or neurological), BPD, chest indrawing, and C-reactive protein were independent predictors of LOS. As a potentially modifiable risk factor, efforts to reduce the probability of RSV infection can reduce the high medical cost associates with prolonged LOS in bronchiolitis.

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- Mauricio T. Caballero** , INFANT Foundation, Buenos Aires, Argentina
- Joan L Robinson** , University of Alberta, Edmonton, Canada

Any reports and responses or comments on the article can be found at the end of the article.

Keywords

Bronchiolitis, Colombia, respiratory syncytial virus, length of hospital stay , chest indrawing



This article is included in the **Pathogens** gateway.

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REVISED Amendments from Version 3

The term 'CRP level of more than 40 mg/lit' was clarified in the document and in the tables. There are a typo error, CRP> 40 mg/lit was considered increased. All the corrections suggested by the reviewer were modified.

Any further responses from the reviewers can be found at the end of the article

Introduction

Bronchiolitis is the most frequent lower respiratory tract infection in infants^{1,2}. One of the variables with more incidence in the financial burden of this disease is the hospital length of stay (LOS)³. The high medical cost associated with prolonged LOS in bronchiolitis imposes an economic burden, especially in tropical middle-income countries⁴. LOS is a direct measure of the quality of health service⁵.

Some models have identified predictors of LOS such as age, underlying conditions (congenital heart disease, chronic lung conditions, immunocompromised states), low birthweight, male gender, clinical characteristics at admission, prematurity, detection of RSV⁶. However, many of these models lack accuracy⁷ or were made in patients without significant comorbidities^{8,9}. In this context, there is a critical need to explore predictors of LOS, improving their accuracy of current models. This information will allow risk management for healthcare and prioritize care strategies in groups with a high probability of prolonged hospital stay to reduce their impact on hospital costs and morbidity. This study aims to identify clinical variables associated with LOS of bronchiolitis in children in Colombia.

Methods

We conducted a retrospective cohort study that included all infants with bronchiolitis younger than two years of age admitted to tertiary centers in Rionegro, Colombia, from January 2019 to December 2019. The municipality of Rionegro had a total population of 101,046 inhabitants, with two tertiary referral hospitals¹⁰. Inclusion criteria were defined as children younger than two years of age admitted to the pediatric ward diagnosed with bronchiolitis, according to the national clinical guideline of bronchiolitis (first wheezing episode younger than 24 months of age)¹¹. Patients without lower respiratory compromise, with positive bacterial cultures on admission, confirmed whooping cough (culture or PCR) were excluded. The study protocol was reviewed and approved by the Institutional Review Board of the University of Antioquia (No 18/2015). Informed consent was obtained from all parents or caregivers of the patients included in the study, following the clinical research standards in Colombia, and prior approval by the ethics committee.

Procedures

We collected the following variables: age, sex, weight, height, signs, and symptoms on admission (including fever, chest indrawing, chest auscultation, %SpO₂), vaccination scheduled chart for age, exposure to cigarette smoking, history of prematurity and bronchopulmonary dysplasia confirmed by a neonatologist

at the time of discharge from the NICU, comorbidities (congenital heart disease, neurological disease), diagnostic tools as chest X rays, hemograms, etc. Additionally, we collected variables related to outcomes of care or disease-severity parameters such as length of hospital stay. In our hospitals, bronchodilators and systemic steroids are discouraged according to national clinical guidelines of bronchiolitis¹¹. Nasopharyngeal aspirate (NPA) was taken immediately upon admission to the emergency department within 48 hrs of admission using standardize technique. RSV was confirmed using direct immunofluorescence (Light Diagnostics TM Respiratory Panel 1 DFA, Merck-Millipore Laboratory). NPA data for other viruses were not available in our institution consistently.

Statistical analysis

Continuous variables were presented as mean \pm standard deviation (SD) or median (interquartile range [IQR]), whichever appropriate. Categorical variables are shown as numbers (percentage). Differences between continuous variables were analyzed using the unpaired *t*-test or Wilcoxon's signed-rank test, whichever was appropriate. Associations between categorical variables and the outcome variable were analyzed using the chi-square test or Fisher's exact test, as needed. To identify factors independently associated with length of hospital stay, we used a Poisson regression model, or negative binomial regression model in case of the presence of overdispersed count data, to estimate incidence rate ratios (IRR) and adjust for potential confounding variables. We only include initially variables associated with LOS with values of $p < 0.2$ or that change the effect estimate by more than 10% after their inclusion. The variable selection and modeling processes were made following the recommendations of Greenland¹². The goodness of fit of the model was evaluated using Hosmer–Lemeshow test and area under curve in Poisson regression or Akaike information criterion (AIC), Bayesian information criterion (BIC) in negative binomial regression. All statistical tests were two-tailed, and the significance level used was $p < 0.05$. The data were analyzed with Stata v15.0 (Stata Corporation, College Station, TX).

Results**Study population**

During the study period, 417 cases of bronchiolitis were included. A total of 66% of the patient was less than 6 months, most of them males (60%), with supportive O₂ (83%). RSV was detected in 200 patients (48%). Of these, 81 patients had a history of premature birth and 17 of them with BPD. A total of 20 patients had some cardiac or neurological disease and 10 of them with a history of use of palivizumab. **Table 1** presents the clinical characteristics of the population. Deidentified individual-level raw data are available from Zenodo¹³.

The median of the length of hospital stay was 3.68 days, with a range of 0.74 days to 29 days and an interquartile range of 4.06 days. Among all 417 patients, 138 (33.1%) have a hospital stay of 5 or more days

Multivariate analysis of predictors associated with LOS

Univariate analysis is presented in **Table 2**. Due to the significant presence of overdispersed count data was detected

Table 1. Demographic features and clinical information of the patients included in the study.

Variable	n (%)
Age less than 6 month	277(66.4)
Male, n(%)	251(60.3)
Premature birth	81(19.4)
Comorbidities (CHD or neurological)	20(4.8)
BPD	17(4.0)
Atopy	17(4.0)
Previously hospitalization by bronchiolitis	30(7.2)
Exposure to cigarette smoking	49 (11.9)
Exclusive maternal breastfeeding for at least six month	102(24.4)
%SpO ₂ , median(ds)**	89(0.2)
O ₂ supportive, n(%)	347(83.4)
Clinical & laboratory parameters	
Fever	119(28.6)
Chest indrawing	184(44.2)
Tachypnea	48(13.3)
Rhonchi	137(32.9)
Crepitation	137(32.9)
Abnormal X-ray*	109(26.3)
Leucocytosis (>15.000/mm ³)	51(12.2)
RSV positive	200(48.4)
Increased C-reactive protein (> 40 mg/lit.)	327(78.6)

*Atelectasis (n=7), alveolar(n=16) or interstitial (n=48) infiltrates, hyperinflation(n=38) CHD: Congenital heart disease, BPD: Bronchopulmonary dysplasia, RSV: Respiratory syncytial virus

**value on admission without oxygen

(Likelihood-ratio test of $\alpha=0$, $\chi^2=203.97$, $p=0.000$), a negative binomial regression model was used to adjust for potential confounding variables. The predictive variables included in the complete model were age, sex, premature birth, comorbidities, BPD, atopy, previously hospitalization by bronchiolitis, %SpO₂, fever, signs of respiratory distress, RSV, Leucocytosis (>15.000/mm³) and increased C-reactive protein (>40 mg/lit.). After modeling and controlling for potential confounders in the negative binomial regression: age <6 months, comorbidities (CHD or neurological), BPD, chest indrawing, RSV isolation, and C-reactive protein were independent predictors of LOS (Table 3).

Discussion

The main purpose of this study was to determine the independent clinical variables associated with LOS of bronchiolitis in children in tropical middle-income countries. Our study shows

that RSV, age <6 months, comorbidities (CHD or neurological), BPD, chest indrawing, and C-reactive protein were independent predictors of LOS

Our results emphasize the importance of knowing the presence of RSV. While some predictors of LOS, such as age, comorbidities, and potentially initial signs of respiratory distress, can not be modified, others as detection of RSV are potentially modifiable by interventions such as future vaccines or palivizumab in a high-risk population^{14,15}. Previous studies in populations with seasonality had revealed the importance of RSV as a predictor of hospital stay. DeVicenzo *et al.*, in a sample of 141 infants <24 months old without previous chronic cardiac or lung disease or prematurity, in Tennessee described a longer LOS with a higher amount of RSV in secretions. A 1-log higher RSV load was associated with a 0.8-day longer hospitalization, reflects the higher RSV load that occur earlier

Table 2. Demographic features and clinical information of the patients included in the study.

Variable. n(%)	n (%)	Incidence rate-ratio (95% CI)	p
Age less than 6 month	277(66.4)	0.998 (0.9-0.9)	0.000
Male , n(%)	251(60.3)	0.048 (0.9-1.1)	0.218
Premature birth	81(19.4)	1.319 (1.1-1.4)	0.000
Comorbidities (CHD or neurological)	20(4.8)	1.787(1.5-2.0)	0.000
BPD	17(4.0)	1.037(0.8-1,2)	0.738
Atopy	17(4.0)	0.827(0.6-1.0)	0.123
Previously hospitalization by bronchiolitis	30(7.2)	0.750(0.6-0.9)	0.003
Exposure to cigarette smoking	49 (11.9)	1.040(0.9-1.1)	0.563
Exclusive maternal breastfeeding for at least six month	102(24.4)	0.627(0.5-1.0)	0.423
SpO2, median(ds)	89(0.2)	1.007(0.9-1.0)	0.055
O2 supportive , n(%)	347(83.4)	2.227(1.8-2.6)	0.000
Clinical & laboratory parameters			
Fever	119(28.6)	0.834(0.7-0.9)	0.000
Chest indrawing	184(44.2)	1.416(1.2-1.5)	0.000
Tachypnea	48(13.3)	1.181(1.0-1.3)	0.018
Rhonchi	137(32.9)	0.777(0.7-0.8)	0.000
Crepitation	137(32.9)	1.088(0.9-1.1)	0.160
Abnormal X-ray*	109(26.3)	1.055(0.9-1.1)	0.277
Leucocytosis (> 15.000/mm3)	51(12.2)	1.179 (1.0-1.3)	0.010
RSV positive	200(48.4)	1.653(1.5-1.8)	0.000
Increased C-reactive protein (> 40 mg/lit.)	327(78.6)	0.849(0.7-0.9)	0.002

*Atelectasis (n=7), alveolar (n=16) or interstitial (n=48) infiltrates, hyperinflation (n=38) CHD : Congenital heart disease, BPD: Bronchopulmonary dysplasia, RSV: Respiratory syncytial virus

Table 3. Multivariate analysis of predictors associated with length of stay.

	IRR	CI 95%	p
Age <6 months	0.998	0.9-0.9	0.000
Comorbidities (CHD or neurological)	2.119	1.4-3.0	0.000
Chest indrawing	1.322	1.1-1.5	0.001
BPD	1.610	1.0-2.3	0.017
RSV positive	1.593	1.3-1.8	0.000
Increased C-reactive protein (> 40 mg/lit.)	1.005	1.0-1.0	0.006

in the disease¹⁴. Rodríguez-Martínez, in 303 infants with acute bronchiolitis in Bogota, also found that detection of RSV correlated with a hospital stay of 5 or more days (OR 1.92, CI 95% 1.02 to 3.73)³. In Qatar, Janahi *et al.*, detected RSV in 51.2% of in 369 patients admitted to the pediatric ward for bronchiolitis, but no association was found between RSV and LOS¹⁶. Additionally, Masarweh *et al.*, in a retrospective study of 4793 infants with bronchiolitis in a single tertiary medical center in Israel between 2001–2009, found that RSV isolation did not correlate with LOS¹⁷. In this evidence, only the Mansbach study used the PCR assay for viral detection, but the results with immunofluorescence assay with respect to the predictive value of RSV were similar to the PCR assay. Indeed, the main problem of the studies mentioned above was the serious statistical mistakes of analyzing the LOS. While we used a negative binomial regression model, due to the presence of overdispersed count data, to adjust for potential confounding variables to analyze LOS, studies by Rodríguez, Devicenzo, and Mansbach dichotomize the LOS to perform logistic regression, while Masarweh's study performed a linear regression; being both approaches not completely correct. The loss of information from dichotomizing a continuous outcome is well documented in the literature, and even worse, analyzing a variable that does not have a normal distribution with a linear regression invalidates this method of analysis¹⁸. These pitfalls in statistical analysis can explain the lack of accuracy of predictive models⁶. The regression models recommended are median, gamma, or Poisson regression, which have some type I error but avoid the mistakes previously mentioned with the logistic or linear regression model.

Other variable potentially modifiable associated with LOS was age <6 months. Our findings are consistent with previous results reported in the literature and provide further evidence that younger infants are at a greater risk of requiring prolonged LOS³. This can be explained because the smaller caliber of the airways in younger infants and poor innate immune response to RSV in newborns, making younger infants more susceptible to severe forms of viral infections and prolonged LOS^{19,20}. Preventive strategies such as the use of palivizumab in a high-risk population or the use of future vaccines that confer immunity in children under 6 months against RSV; will constitute possibly effective interventions in reducing the economic burden of this disease.

Several predictive models had reports consistently the chest indrawing as predictive of prolonged LOS that is which is biologically plausible and expected due that this sign also is a universal marker of severity of the disease, as well as the presence of underlying conditions (congenital heart disease, chronic lung conditions, immunocompromised states)^{3,6–8,21–23} or C-reactive protein (CRP) as a biomarker of severity and bacterial co-infection in patients hospitalized for bronchiolitis^{24–26}

Our study has limitations. First, since this study was based on medical records review, we cannot include other variables such as environmental pollution and genetic factors, and residual confounding cannot be excluded. Second, respiratory syncytial virus was confirmed using direct immunofluorescence, which may underestimate the real burden of viral infection. However,

despite this possible underestimation, RSV infection was positively associated, and it is possible that the magnitude of the IRR is even greater. The detection of other respiratory viruses was not homogeneous in all patients, so to avoid information bias we decided not to include them in the analysis. We cannot rule out that other respiratory viruses have equal or greater association with our dependent variable in the study. Third, the study was conducted in a tertiary referral hospital, and therefore the patients included represent the high spectrum of severity, limiting the generalization of results to other contexts. However, the similarity of our population in terms of clinical characteristics, risk factors, and seasonality of bronchiolitis in our country with previous reports suggest strength and consistency in our results^{3,4}

Conclusion

Our results show that in infants with bronchiolitis, RSV, age <6 months, comorbidities (CHD or neurological), BPD, chest indrawing, and C-reactive protein were independent predictors of LOS in a tropical middle-income country. As a potentially modifiable risk factor, efforts to reduce the probability of RSV infection can reduce the high medical cost associated with prolonged LOS in bronchiolitis.

Data availability

Underlying data

Zenodo: Importance of respiratory syncytial virus as a predictor of hospital length of stay in Bronchiolitis. <http://doi.org/10.5281/zenodo.4432434>¹³.

This project contains the raw data for each patient assessed in the present study.

Data are available under the terms of the [Creative Commons Attribution 4.0 International license](#) (CC-BY 4.0).

Declarations

Ethics approval

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).

Consent for publication

All authors consent this paper for publication

Abbreviations

incidence rate ratios (IRR)

hospital length of stay (LOS)

respiratory syncytial virus (RSV)

Nasopharyngeal aspirate (NPA)

Bronchopulmonary dysplasia (BPD)

Chronic heart disease (CHD)

Authors' contributions

All the authors contributed in the same way from conception of the work to the publication of results. All Authors read and approved the manuscript.

References

- Nair H, Nokes DJ, Gessner BD, *et al.*: **Global burden of acute lower respiratory infections due to respiratory syncytial virus in young children: a systematic review and meta-analysis.** *Lancet.* 2010; **375**(9725): 1545–55.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Buendía JA, Patiño DG: **Costs of Respiratory Syncytial Virus Hospitalizations in Colombia.** *Pharmacoecon Open.* 2021; **5**(1): 71–76.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Rodríguez-Martínez CE, Sossa-Briceño MP, Nino G: **Predictors of prolonged length of hospital stay for infants with bronchiolitis.** *J Investig Med.* 2018; **66**(6): 986–91.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Rodríguez-Martínez CE, Sossa-Briceño MP, Castro-Rodríguez JA: **Direct medical costs of RSV-related bronchiolitis hospitalizations in a middle-income tropical country.** *Allergol Immunopathol (Madr).* 2020; **48**(1): 56–61.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Anderson ME, Glasheen JJ, Anoff D, *et al.*: **Understanding predictors of prolonged hospitalizations among general medicine patients: A guide and preliminary analysis.** *J Hosp Med.* 2015; **10**(9): 623–6.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Luo G, Nkoy FL, Gesteland PH, *et al.*: **A systematic review of predictive modeling for bronchiolitis.** *Int J Med Inform.* 2014; **83**(10): 691–714.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Corneli HM, Zorc JJ, Holubkov R, *et al.*: **Bronchiolitis: clinical characteristics associated with hospitalization and length of stay.** *Pediatr Emerg Care.* 2012; **28**(2): 99–103.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Weisgerber MC, Lye PS, Li SH, *et al.*: **Factors predicting prolonged hospital stay for infants with bronchiolitis.** *J Hosp Med.* 2011; **6**(5): 264–70.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Rodríguez-Martínez CE, Sossa-Briceño MP, Acuña-Cordero R: **Relationship between meteorological conditions and respiratory syncytial virus in a tropical country.** *Epidemiol Infect.* 2015; **143**(12): 2679–86.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Estadísticas DANE: **Proyecciones de población.** 2018.
[Reference Source](#)
- Colciencias MdSyPS: **Guía de Práctica Clínica Para el diagnóstico, atención integral y seguimiento de niños y niñas con diagnóstico de Asma.** Guía No. 01, 2014.
[Reference Source](#)
- Greenland S: **Modeling and variable selection in epidemiologic analysis.** *Am J Public Health.* 1989; **79**(3): 340–9.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Jefferson: **Importance of respiratory syncytial virus as a predictor of hospital length of stay in Bronchiolitis.** (Version 1) [Data set]. *Zenodo.* 2021. <http://www.doi.org/10.5281/zenodo.4432434>
- DeVincenzo JP, El Saleeby CM, Bush AJ: **Respiratory syncytial virus load predicts disease severity in previously healthy infants.** *J Infect Dis.* 2005; **191**(11): 1861–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Mansbach JM, Piedra PA, Teach SJ, *et al.*: **Prospective multicenter study of viral etiology and hospital length of stay in children with severe bronchiolitis.** *Arch Pediatr Adolesc Med.* 2012; **166**(8): 700–6.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Janahi I, Abdulkayoum A, Almshwesh F, *et al.*: **Viral aetiology of bronchiolitis in hospitalised children in Qatar.** *BMC Infect Dis.* 2017; **17**(1): 139.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Masarweh K, Gur M, Leiba R, *et al.*: **Factors predicting length of stay in bronchiolitis.** *Respir Med.* 2020; **161**: 105824.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Aggarwal R, Ranganathan P: **Common pitfalls in statistical analysis: Linear regression analysis.** *Perspect Clin Res.* 2017; **8**(2): 100–2.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Simon AK, Hollander GA, McMichael A: **Evolution of the immune system in humans from infancy to old age.** *Proc Biol Sci.* 2015; **282**(1821): 20143085.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Alvarez AE, de Lima Marson FA, Bertuzzo CS, *et al.*: **Epidemiological and genetic characteristics associated with the severity of acute viral bronchiolitis by respiratory syncytial virus.** *J Pediatr (Rio J).* 2013; **89**(6): 531–43.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Hasegawa K, Tsugawa Y, Brown DFM, *et al.*: **Trends in bronchiolitis hospitalizations in the United States, 2000-2009.** *Pediatrics.* 2013; **132**(1): 28–36.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- McCallum GB, Chatfield MD, Morris PS, *et al.*: **Risk factors for adverse outcomes of Indigenous infants hospitalized with bronchiolitis.** *Pediatr Pulmonol.* 2016; **51**(6): 613–23.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Davies CJ, Waters D, Marshall A: **A systematic review of the psychometric properties of bronchiolitis assessment tools.** *J Adv Nurs.* 2017; **73**(2): 286–301.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Fares M, Mourad S, Rajab M, *et al.*: **The use of C-reactive protein in predicting bacterial co-infection in children with bronchiolitis.** *N Am J Med Sci.* 2011; **3**(3): 152–6.
[PubMed Abstract](#) | [Free Full Text](#)
- Cebey-López M, Pardo-Seco J, Gómez-Carballea A, *et al.*: **Bacteremia in Children Hospitalized with Respiratory Syncytial Virus Infection.** *PLoS One.* 2016; **11**(2): e0146599.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Lamarão LM, Ramos FL, Mello WA, *et al.*: **Prevalence and clinical features of respiratory syncytial virus in children hospitalized for community-acquired pneumonia in northern Brazil.** *BMC Infect Dis.* 2012; **12**: 119.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)

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One residual problem is that it is not clear what (ds) means in Table 2.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Pediatric infectious diseases

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 3

Reviewer Report 24 December 2021

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Joan L Robinson 

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I am not very happy with the response to my review. The authors simply put the word "corrected" after each of my comments even though some of the comments were not addressed. For example, the discussion still talks about HSV. The authors should tell the reviewer how they addressed each comment.

A CRP of 4 mg/L is completely normal. The authors can still claim that a higher CRP predicted a longer LOS but they need to note that this was not necessarily an elevated CRP.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Pediatric infectious diseases

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 25 Dec 2021

Jefferson Buendia, Universidad de Antioquia., Medellín, Colombia

Dear reviewer.

You can see that all grammar suggestions were corrected according to your advice. When we place in our corrections the word "corrected" it means that the text was changed as required by your advise. We do not consider the need to place the multiple grammar corrections in other text , when these can be see in the text with the track changes in word.

The cut-off of the CPR estimated in our mathematical model associated with our outcome was 4 mg/L, and this just is the value of our paper. This variable was managed continuously and no preset cut-off point (eg dichotomic , etc). As was stated in the discussion these values should be alert to the doctor in conjunction with other variables that may be is a patient with a longer hospital stay or seen another way patient with a lower value together with other variables can help to the pediatrician to predict the lack for examen of intensive use of resources by the patient not having a high risk of prolonged hospital staly

Competing Interests: No competing interests were disclosed.

Version 2

Reviewer Report 29 November 2021

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Department of Pediatrics, University of Alberta, Edmonton, Alberta, Canada

The authors analyzed data from all children less than 2 years of age admitted in 2019 to two hospitals in Columbia to establish factors identifiable at admission that predict a longer length of stay (LOS). The factors that they identified include RSV, age <6 months, comorbidities (CHD or neurological), BPD, chest indrawing, and a higher C-reactive protein.

The main question is whether their findings have practical implications. Some of the risks that they identified are not well established (in particular the higher CRP). They make the point that identification of these risk factors for prolonged LOS may inform their palivizumab program and eventually an RSV immunization program. The risk factors that would be helpful for such programs are age < 6 months and comorbidities, both of which are well recognized as risk factors for RSV hospitalization but less so for LOS. Nonetheless, both are currently widely used in palivizumab programs worldwide.

Minor points:

1. Abstract – What does “admitted to the emergency department” mean. Do the authors perhaps mean “admitted through the emergency department”?
2. “Among inpatients with bronchiolitis, approximately a quarter undergo a prolonged length of stay”. There is no standard definition of prolonged LOS, so it is difficult to know what the authors mean by this.
3. The high medical cost associates with prolonged LOS in bronchiolitis imposes an economic burden, especially in tropical middle-income countries.” Why? Surely it is even a greater burden in low income countries. I do not understand why it is a special problem in “tropical countries”.
4. “Some models have identified predictors of LOS such as age, underlying conditions (congenital heart disease, chronic lung conditions, immunocompromised states), low weight, male gender, clinical characteristics at admission, prematurity, RSV isolation” – I think that the authors mean “low birthweight”. Throughout the paper, I do not know what they mean by “RSV isolation” as almost no centers do viral culture anymore. They need to change it to “detection of RSV”.
5. “Otherwise, in tropical areas in addition to genetic differences, the respiratory syncytial virus (RSV), generates differences in the burden of morbidity and mortality given the non-seasonality of these areas” - I do not know what this sentence means.
6. By “in tertiary centers”, do the authors mean “admitted to tertiary centers”? Patients can also be in the emergency department of a hospital.
7. Do the national guidelines encourage or discourage use of bronchodilators and systemic steroids? I think that most discourage both these days.
8. Please reword “NPA data for other viruses were no available in our institution consistently.” I think that the authors mean “not” rather than “no”.
9. In Table 1, are these parameters at admission? For example, “%SpO₂, median(ds)”, is this the value on admission without oxygen? What does “ds” mean?

10. Throughout the paper, I would round all percentages to the nearest whole number or provide only one decimal point. It makes it easier for the reader and the sample size does not justify two decimal points.
11. Table 3 and the abstract need to specify which CRP was considered to be significant.
12. The DeVicenzo study described a longer LOS with a higher amount of RSV in secretions. This is quite different from showing that RSV itself increases the LOS.
13. "Mansbasch *et al.*, in a prospective cohort of 2207 infants of 16 US hospital without excluding patients previous chronic cardiac or lung disease or prematurity, also found that patients with RSV have a higher proportion of patient with prolonged LOS (>3 days) than patients with only HSV infection, but less than RSV+HRV co-infection (48% vs 28% vs 54%, $p < 0.001$ " – I do not understand why HSV would be compared to RSV.

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

I cannot comment. A qualified statistician is required.

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: pediatric infectious diseases

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 12 Dec 2021

Jefferson Buendia, Universidad de Antioquia., Medellín, Colombia

Response : Reviewer 2

- *The authors analyzed data from all children less than 2 years of age admitted in 2019 to two hospitals in Columbia to establish factors identifiable at admission that predict a longer length of stay (LOS). The factors that they identified include RSV, age <6 months, comorbidities (CHD or neurological), BPD, chest indrawing, and a higher C-reactive protein. The main question is whether their findings have practical implications. Some of the risks that they identified are not well established (in particular the higher CRP). They make the point that identification of these risk factors for prolonged LOS may inform their palivizumab program and eventually an RSV immunization program. The risk factors that would be helpful for such programs are age < 6 months and comorbidities, both of which are well recognized as risk factors for RSV hospitalization but less so for LOS. Nonetheless, both are currently widely used in palivizumab programs worldwide.*
- **Response:** Corrected. It was clarified in the document and in the tables the term (CRP level of more than 4 mg/lit) .

- *Abstract - What does "admitted to the emergency department" mean. Do the authors perhaps mean "admitted through the emergency department"*
- **Response:** Corrected.

- *"Among inpatients with bronchiolitis, approximately a quarter undergo a prolonged length of stay". There is no standard definition of prolonged LOS, so it is difficult to know what the authors mean by this.*
- **Response:** Corrected.

- *The high medical cost associates with prolonged LOS in bronchiolitis imposes an economic burden, especially in tropical middle-income countries." Why? Surely it is even a greater burden in low income countries. I do not understand why it is a special problem in "tropical countries".*
- **Response:** Corrected.

- *"Some models have identified predictors of LOS such as age, underlying conditions (congenital heart disease, chronic lung conditions, immunocompromised states), low weight, male gender, clinical characteristics at admission, prematurity, RSV isolation" - I think that the authors mean "low birthweight". Throughout the paper, I do not know what they mean by "RSV isolation" as almost no centers do viral culture anymore. They need to change it to "detection of RSV".*
- **Response:** Corrected.

- *"Otherwise, in tropical areas in addition to genetic differences, the respiratory syncytial virus (RSV), generates differences in the burden of morbidity and mortality given the non-seasonality of these areas" - I do not know what this sentence means.*
- **Response:** Corrected.

- *By "in tertiary centers", do the authors mean "admitted to tertiary centers"? Patients can also be in the emergency department of a hospital.*
- **Response:** Corrected.

- *Do the national guidelines encourage or discourage use of bronchodilators and systemic*

- steroids? I think that most discourage both these days.*
- **Response:** deleted this sentence.
 - *Please reword "NPA data for other viruses were no available in our institution consistently." I think that the authors mean "not" rather than "no".*
 - **Response:** Corrected.
 - *In Table 1, are these parameters at admission? For example, "%SpO2, median(ds)", is this the value on admission without oxygen? What does "ds" mean?*
 - **Response:** Corrected.
 - *Throughout the paper, I would round all percentages to the nearest whole number or provide only one decimal point. It makes it easier for the reader and the sample size does not justify two decimal points.*
 - **Response:** Corrected.
 - *Table 3 and the abstract need to specify which CRP was considered to be significant.*
 - **Response:** Corrected.
 - *The DeVicenzo study described a longer LOS with a higher amount of RSV in secretions. This is quite different from showing that RSV itself increases the LOS.*
 - **Response:** Corrected.
 - *"Mansbasch et al., in a prospective cohort of 2207 infants of 16 US hospital without excluding patients previous chronic cardiac or lung disease or prematurity, also found that patients with RSV have a higher proportion of patient with prolonged LOS (>3 days) than patients with only HSV infection, but less than RSV+HRV co-infection (48% vs 28% vs 54%, $p < 0.001$ " – I do not understand why HSV would be compared to RSV.*
 - **Response:** Corrected.

Competing Interests: No competing interests were disclosed.

Reviewer Report 12 November 2021

<https://doi.org/10.5256/f1000research.58307.r88922>

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Mauricio T. Caballero 

INFANT Foundation, Buenos Aires, Argentina

The authors have resolved the suggestions made.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Respiratory virus infection in children.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 28 June 2021

<https://doi.org/10.5256/f1000research.43735.r85075>

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Mauricio T. Caballero

INFANT Foundation, Buenos Aires, Argentina

Importance of respiratory syncytial virus as a predictor of hospital length of stay in bronchiolitis is an interesting retrospective study conducted in tertiary centers in Rionegro, Colombia, from January 2019 to December 2019. The study explores variables associated with length of stay due to bronchiolitis in children under two years old. I have few comments regarding the study methods and results.

1. Respiratory syncytial virus was confirmed using direct immunofluorescence, which may

underestimate the real burden of viral infection. How do authors estimate this could impact the results?

2. Authors did not mention if other respiratory viruses were explored and compared as associated to length of hospital stay.
3. Univariable analysis should be shown in an extra table.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

No

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Respiratory virus infection in children.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 30 Jun 2021

Jefferson Buendia, Universidad de Antioquia., Medellín, Colombia

We appreciate your valuable comments.

- *Respiratory syncytial virus was confirmed using direct immunofluorescence, which may underestimate the real burden of viral infection. How do authors estimate this could impact the results?*
- **Response:** Corrected. This limitation was added to the discussion of the paper.
- *Authors did not mention if other respiratory viruses were explored and compared as associated to length of hospital stay.*
- **Response:** Corrected. This limitation was added to the discussion of the paper.
- *Univariable analysis should be shown in an extra table.*

- **Response:** Corrected. Added a new table with the univariate analysis.

Competing Interests: None.

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