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Predictors of Severity and Mortality in Children Hospitalized With Respiratory Syncytial Virus Infection in a Tropical Region

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Summary

Introduction—Respiratory syncytial virus (RSV) is one of the leading causes of acute lower respiratory infection (ALRI) in infants and young children. Although ALRI is a major public health problem in developing countries located in tropical areas, studies about RSV epidemiology in these regions are scarce.

Methods—In a retrospective cohort study, we investigated the epidemiology and predictive variables that reflect disease severity and mortality in young children hospitalized with ALRI due to RSV in Colombia, South-America, during a 2-year period (2009–2011).

Results—Of a total of 6,344 children with a diagnosis of ALRI, we selected 2,147 (33.8%) that were positive for RSV. After controlling for pre-existing conditions, we found that independent predictors of severe disease in our population included age <6 months (RR 2.01; CI 95% 1.70–2.38; $P < 0.001$), prematurity (RR 1.61; CI 95% 1.20–2.17; $P = 0.001$), congenital heart disease (RR 2.03; CI 95% 1.16–3.54; $P = 0.013$), and mixed RSV-adenovirus infection (RR 2.09; CI 95% 1.60–2.73; $P < 0.001$). Multivariate analysis identified that cancer (RR 31.60; CI 95% 5.97–167.13; $P < 0.001$) is a predictor of mortality in our RSV-infected pediatric population independently of age and other co-morbidities.

Conclusions—RSV is an important cause of ALRI in infants and young children living in tropical regions, especially during the rainy season. The identified predictors of severe disease and mortality should be taken into account when planning interventions to reduce the burden of ALRI in young children living in these regions.

Keywords

respiratory syncytial virus; acute respiratory infection; pediatrics

INTRODUCTION

Acute lower respiratory infection (ALRI) is one of the most important causes of morbidity and mortality among children under 5 years-of-age throughout the world.¹ Although ALRI is the most common cause of morbidity in high-income countries, it is an even greater health problem in low- and middle-income countries (LMIC).² For instance, it has been calculated that in developing countries, every 7 sec a child <5 years-of-age dies because of an ALRI, usually pneumonia.^{3,4} As a result, ALRI is still considered by far, the leading cause of death among infants and children living in the developing world.²

Respiratory syncytial virus (RSV) is one of the most significant causes of ALRI in infants and young children worldwide.⁵ Nonetheless, it has been estimated that 96% of these infections occur in developing countries.³ Interestingly, although a considerable amount of epidemiological RSV research has been, and continues to be, conducted in high-income countries, only a limited amount of information is available about the pediatric epidemiology of RSV infections in other areas of the globe. Accordingly, there is a critical need for studies that investigate the seasonality and risk factors for severe RSV-induced lower respiratory tract infection in tropical LMIC. The latter is essential for predicting epidemics and planning preventive measures, especially for high-risk pediatric groups. In this regard, prior studies have already suggested that RSV infections have unique characteristics in countries located in tropical areas.⁶ For example, the timing of epidemics, and overall severity of the infections caused by this virus, can vary widely among different climatic regions.⁷ In fact, in contrast to temperate climates where outbreaks of RSV occur during the fall, winter, and/or spring months, in the equatorial zones and in other areas with a tropical weather, RSV infections are more often associated with the rainy season,⁶ although the seasonality of RSV in the tropics is not as marked as in temperate regions.⁶

The aim of the present study was to investigate the epidemiology and predictive factors of RSV severity and mortality in a large cohort of Colombian children <3 years-of-age hospitalized due to ALRI, and by doing so, provide new insights into the pathobiology of RSV infection in infants and children living in LMIC with a tropical climate.

MATERIALS AND METHODS

Study Site

Bogota, the capital city of Colombia, is located at an elevation of about 2,650 m (8,660 ft.) above sea level, on a mountain-rimmed plateau high in the Andes Mountains, laying only

4°36' north of the equator. Its average annual temperature is 14.8°C, with daily variations that range between 1 and 26°C. The average annual precipitation in the city is about 672 mm and the average annual wind speed is 1.5 m/sec. Two main seasons that are recognized in the city are the *dry season*, running from December to March and from June to August; and the *rainy season*, running approximately from March to May and from September to November. Yearly emissions by fixed sources of air pollution in Bogota are about 2,198 tons of dust, 6,503 tons of SO₂, and 1,687 tons of NO₂.⁸ Industrial kilns and furnaces represent 75% of fixed sources of air pollution. The technological deficiencies of small and medium industrial enterprises have been associated with high levels of industrial pollution in the city.⁸ The *Fundación Hospital La Misericordia* is a tertiary care University-based Children's Hospital located in the metropolitan area of Bogota. The hospital has 287 beds, and serves the city of Bogota (7,363,782 inhabitants), as well as other cities of the country. For the latter, it mainly functions as a referral center that admits about 12,000 children, and registers more than 60,000 emergency room visits per year.

Study Design and Procedures

In a retrospective cohort study, we examined a consecutive sample of pediatric patients, aged <36 months, who were hospitalized in the Fundación Hospital La Misericordia between May 1, 2009 and April 30, 2011 with a diagnosis of ALRI, and underwent nasopharyngeal aspirates (NPA) testing for RSV and adenovirus. After reviewing the electronic medical records, we collected the following demographic and clinical data: date of admission, age, primary diagnosis at admission, presence of comorbidities, number of days with respiratory symptoms, and month and year of NPA sampling. Likewise, we collected variables related to outcomes of care or disease-severity parameters such as need of hospitalization, oxygen supply, need for home oxygen administration, Pediatric Intensive Care Unit (PICU) admission, length of stay in the PICU, need for endotracheal intubation, use of antibiotics, length of hospital stay, and mortality.

In our institution, while bronchodilators are used at the discretion of the attending physician, systemic steroids are not routinely used during the hospitalization of patients with ALRI. Additionally, children hospitalized due to ALRI with the following conditions are transferred to the PICU: worsening hypoxemia or hypercapnia, worsening respiratory distress, continuing requirement for more than 50% oxygen, hemodynamic instability, or apnea. We also recorded whether it was a community-acquired or nosocomial-acquired VSR infection. RSV infections were judged to be community acquired if the virus was isolated within 48 hr after admission; nosocomial acquired was assumed when the organism was identified 48 hr or longer after admission. NPA for virus detection was taken immediately upon admission to the emergency department or within 48 hr of admission using a standardized technique, and was processed immediately or stored at 4°C until the next working day (in phosphate-buffered saline transport medium at 2–8°C for 24 hr or at –70°C for more than 24 hr). Children screened were tested for RSV antigen using a rapid immunoassay method (Abbott Test Pack RSV Rapid Diagnostic Kit, Abbott, IL), and for adenovirus using a rapid immunochromatographic test method (Adeno Respi-Strip; Coris BioConcept, Gembloux, Belgium). NPA data for other viruses (i.e., rhinovirus and influenza) were not consistently available as it was not routinely conducted in our institution

during the study period (2009–2011). If more than one sample of a patient tested positive for RSV, it was considered that there were different RSV episodes when the dates of the tests were separated by more than 4 weeks or if at least one negative test was recorded in between. The study protocol was approved by the local ethics board.

Statistical Analysis

Continuous variables are presented as mean $\pm$ standard deviation (SD) or median (interquartile range), whichever is appropriate. Categorical variables are presented 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 were analyzed using Chi-square test or Fisher's exact test, whichever was appropriate. To identify factors independently associated with severe disease and with mortality, we used Poisson regression with robust error variance. This regression technique allows for a conservative estimation of the relative risk when the outcome of interest occurs more than 10% of the time, as in the case of severe disease in this analysis.⁹ We defined severe disease as requirement of PICU admission. The predictive variables included in the models were: age, presence of comorbidities, month of the year of NPA sampling, and the presence of mixed RSV-adenovirus infection. All statistical tests were two-tailed, and the significance level used was $P < 0.05$. The data were analyzed with the Statistical Package Stata 11.0 (Stata Corporation, College Station, TX).

RESULTS

Study Population

A total of 6,344 children with a diagnosis of ALRI were tested during the study period, of whom 2,147 (33.8%) were selected for study because they were positive for RSV. During the periods 2009–2010 and 2010–2011 there were 1,065 and 1,082 cases of RSV bronchiolitis, respectively. The RSV positive group patients were younger compared with the RSV negative group patients, but this difference did not reach statistical significance (9.18 ± 8.46 months vs. 9.59 ± 9.0 months, $P = 0.07$). The age group distribution was: 1,060 (49.4%) < 6 months, 489 (22.8%) between 7 and 12 months, 433 (20.2%) between 13 and 24 months, and 165 (7.7%) between 25 and 36 months. The median (interquartile range [IQR]) of the number of days with respiratory symptoms before admission was 3 (2–5) days. Regarding the clinical diagnosis at admission, 1,602 patients were diagnosed as having bronchiolitis (74.6%), 281 as pneumonia (13.1%), and the remaining 264 (12.3%) as other diagnoses such as viral laryngotracheitis (croup), apparent life threatening event (ALTE), and acute viral nasopharyngitis. In terms of comorbidities, we found that 930 children (43.3%) showed comorbid conditions: 714 patients (33.3%) had some pre-existing respiratory condition (previous wheezing episodes, asthma symptoms, or pneumonia), 98 patients (4.6%) had a previous history of prematurity, 26 patients (1.2%) had a previous history of a congenital heart disease, 18 patients (0.8%) had some pre-existing renal disease, 10 patients (0.5%) had a previous cancer diagnosis, and the remaining 64 patients (2.9%) had other comorbidity conditions such as malnutrition and epilepsy. RSV infection was acquired in the community in 2,065 cases (96.2%) and it was transmitted nosocomially in the remaining 82 cases (3.8%).

RSV Infection Seasonality in Tropical Climate

On analyzing the data about seasonal distribution of the RSV infections, we found that 1,385 infections (64.5%) occurred during the 3-month period from March to May, and 180 infections (8.3%) occurred during the 3-month period from September to November, periods corresponding to the two rainy seasons in Colombia. Figure 1 shows the monthly number of RSV infections, along with monthly variation of average precipitation. Interestingly, the monthly number of RSV infections was positively correlated with rainfall, measured as the average monthly precipitation ($r = 0.76$, $P < 0.001$). Additionally, there was a seasonal pattern for mortality, with most of the deaths attributed to RSV infection occurring during April, which is the wettest month of the first rainy season in Colombia, and the remainder of deaths occurring in December, February, March, June, and September. No deaths were registered during January, July, and August, the driest months of the year.

RSV Infection Severity: Role of Co-Morbidities and Adenovirus Co-Infection

Regarding the severity of the respiratory disease, 474 (22.1%) children were admitted to the PICU. Out of the total number of children hospitalized with RSV infection, 2,031 (94.6%) required supplemental oxygen use, 107 (5%) required endotracheal intubation, 75 (3.5%) were given antibiotics, and 995 (46.3%) required home oxygen administration. Children who were admitted to the PICU, compared to children who did not require PICU admission, were significantly younger (4.0 [1.0–9.0] vs. 7.0 [3.0–15.0] months, $P < 0.001$), had a significantly higher number of days with supplemental oxygen use (12.0 [9.0–17.2] vs. 7.0 [4.0–9.0], $P < 0.001$), were more likely to be given antibiotics (RR, 3.09; CI 95%, 2.66–3.60; $P < 0.001$), were more likely to have a comorbidity (RR, 1.42; CI 95%, 1.21–1.67; $P < 0.001$), and were more likely to require home oxygen administration (RR, 2.03; CI 95%, 1.72–2.40; $P < 0.001$).

In 75 cases of children with RSV (3.5%), a concomitant infection with Adenovirus was present. A comparison of the cases with mixed RSV-adenovirus infection, and the cases with only RSV infection, showed statistically significant differences in age (8.0 [4.0–15.0] vs. 6.5 [2.2–13.7] months, $P = 0.04$), and in some parameters that reflect disease severity such as length of hospital stay (10.0 [6.0–17.0] vs. 8.0 [5.0–11.0] days, $P = 0.006$), number of days with supplemental oxygen use (9.0 [5.0–17.0] vs. 7.0 [5.0–11.0] days, $P = 0.02$), PICU admission, and need for endotracheal intubation (Table 1). Multivariate analysis was conducted to determine predictive factors of severe RSV infection. Our predictive model included age, comorbidities, month of the year of NPA sampling, and the presence of mixed RSV-adenovirus infection. After controlling for these potential confounders, we found that age <6 months, history of prematurity, pre-existing respiratory conditions, previous history of congenital heart disease, and mixed RSV-adenovirus infection, were independent predictors of severe disease in our sample of patients (Table 2).

RSV Infection Mortality

The mortality rate of RSV infection during the 2-year period was 1.1%. The median age (IQR) of the patients who died statistically was not significantly different than the age of children who survived from their disease (6.0 [2.5–14.0] vs. 7.0 [3.0–14.0] months, $P = 0.42$). A greater proportion of patients with the presence of a comorbidity died compared

with those without any comorbidity (RR, 2.32; CI 95%, 1.03–5.24; $P = 0.036$). As illustrated in Table 3, comparative analysis of the underlying conditions in children included in the study, differentiated by live versus dead, revealed that cancer was significantly more common in children with death attributed to RSV infection. Multivariate analysis conducted to control for age, NPA sampling time, presence of comorbidities and mixed RSV-adenovirus infection, identified that cancer as comorbidity, was an independent predictor of mortality in children with RSV infection (Table 4).

DISCUSSION

The present study shows that RSV is a significant cause of ALRI in infants and young children in tropical low-middle income countries (LMIC), especially during the first rainy season, which is defined as the 3-month period from March to May in Colombia. Additionally, the findings of the present study suggest that in tropical areas more severe forms of RSV are seen in children aged <6 months, and in those with history of prematurity, respiratory disease, congenital heart disease, and concomitant infection with adenovirus. Moreover, our data identified that children with cancer have a higher risk of death due to RSV infection in our study population.

The present findings could have important consequences for the application of passive immunization for high-risk infants, and for establishing a threshold for admission to the hospital for RSV-infected children. Since passive immunization with palivizumab is a high-cost intervention,¹⁰ it is essential to identify those high-risk groups of patients who are most likely to benefit from it. In addition, it is crucial to determine when to start this immunization and when to discontinue it in tropical LMIC where healthcare resources are limited. Although most countries have developed guidelines on when to start passive immunization against RSV and when to discontinue it, in other countries guidelines mention “local seasonality” as the starting date, leaving open the possibility that RSV passive immunization can be started in any month of the year.¹¹ As this approach is quite costly, epidemiological monitoring is crucial. Our current findings suggest that RSV passive immunization in tropical LMIC should coincide with the raining season given the abrupt increase in RSV infections during this period of time.

Although the difference did not reach statistical significance, the mean age of RSV cases was lower than that of non-RSV cases. This is consistent with other studies in which younger infants were shown to be at higher risk for RSV infection.^{12–14} Likewise, as shown in the literature,¹⁵ in our study young age was independently associated with more severe forms of the disease, although not with increased mortality. This may be attributed to lower levels of cellular immunity and poor antibody response during the acute phase of RSV infection in young infants, primarily due to immaturity of the young infant’s immune system.¹⁶ In addition to young age, our study also identified prematurity, respiratory disease, congenital heart disease, cancer, and adenovirus co-infection as independent predictors of worse outcomes during RSV ALRI in our study population. Accordingly, these variables should be considered as criteria for lowering the threshold for admission to the hospital in acute cases of RSV ALRI in infants and young children living in a tropical LMIC.

In agreement with other studies done in tropical and sub-tropical regions with seasonal rainfall, the present study shows that the seasonality of RSV is associated with the rainy period of the city.⁶ On analyzing the absolute numbers of positive RSV cases, a clear and abrupt increase in the incidence of RSV cases was found during the 3-month period from March to May, the first rainy season of the year in Colombia. These findings also agree with previous research showing that the peak of RSV incidence below the equatorial line commonly occurs in May¹⁷ and also agrees with local epidemiological surveillance reports (Secretary of Health of Bogota) showing that, although RSV can be isolated throughout the entire year, there is an increase in the number of cases beginning in about epidemiological-week 10 and ending in approximately epidemiological-week 23.¹⁸ The reason for the association between RSV cases and the raining season in tropical and sub-tropical regions is unclear. Although it could be due to factors directly related to the climate (e.g., increase in absolute humidity), it could also be affected, at least in part, by changes in social behaviors and by interactions with other infections that are seasonally determined.⁶ Independently of the exact mechanisms for this association, this finding is essential for predicting epidemics and planning for preventive interventions, especially for the high-risk children.

In regard to predictors of severe disease, although our findings are consistent with other studies in which young age, prematurity, chronic lung disease, and congenital heart disease were risk factors associated with severe RSV infection,^{19,20} we also identified that cancer was an independent risk factor for RSV mortality in our study population (Table 4). Interestingly, the pathobiology of RSV infections in children with cancer is still not well understood. El Saleeby et al.²¹ reported that among children with cancer, profound lymphopenia and young age were significant risk factors for RSV-related death, suggesting a role of lymphopenia as a critical risk factor for severe RSV disease in immunocompromised patients. However, reports of mortality rates associated with RSV infections are quite variable and conflicting. While early reports described mortality rates as high as 83% for ALRI in adult patients with leukemia,²² Simon et al.²³ in a prospective study, found no increased mortality due to RSV among hospitalized children with cancer. In our study, the mortality rate for RSV-infected children with cancer was 20% and multivariate analysis demonstrated that cancer was independently associated with increased mortality in our population of RSV-infected children. Possible explanations for these discrepancies in the reported mortality rates of this population might be diversity in the degree of immunosuppression, criteria differences for ordering RSV diagnostic tests, variability in therapeutic interventions, and lack of standardization for the definition of death attributed to RSV disease.²¹ Although our findings require confirmation in controlled studies, treatment and prophylaxis for RSV in high-risk oncological patients, as identified in this study, should be carefully considered.

Another important finding of our study was the potential role of adenovirus in modifying RSV disease severity. In this regard, previous studies have not found significant differences between respiratory infections caused by a single viral agent and those caused by two or more viral agents, either for hospitalized children or ambulatory patients.^{24,25} Likewise, it has been reported that concomitant infections with RSV and adenovirus, mainly detected during the winter RSV epidemics, were not any more severe than those caused by adenovirus alone.²⁶ In contrast with these findings, we found that relative to patients with

only RSV infection, patients with mixed RSV-adenovirus infection had worse outcomes in variables that reflect disease severity such as length of hospital stay, number of days with supplemental oxygen use, PICU admission, and need for endotracheal intubation. Moreover, multivariate analysis found that concomitant infection with adenovirus was independently associated with more severe forms of RSV disease. This greater severity of mixed RSV-adenovirus infections compared to single RSV infections was suggested by a previous study in hospitalized infants,²⁷ which reported that mixed viral infections (of which a significant proportion had mixed RSV-adenovirus infections) were associated with longer hospital stays compared to single RSV infections.²⁷ Possible reasons for these variability in the reported outcome of mixed RSV-adenovirus infections are differences in environmental, host (e.g., genetic immune response, previous immune condition, infected target cells), and viral factors (e.g., serotypes).²⁸ Another possible reason could be that adenovirus alone produces a more severe disease with no additional severity of a RSV infection. Although this concept may be supported by the prominent effects of adenovirus on mononuclear cell activation and release of pro-inflammatory cytokines compared to RSV,²⁹ at the present time, there is no clear evidence demonstrating that adenovirus causes more severe respiratory disease in children than RSV.²⁸

The main limitations of the present study are its retrospective design, the small number of predictor variables included in the multivariate analysis, the technique used for the diagnosis of RSV infection, and the fact that it was conducted in a specialized, tertiary referral hospital. With respect to the first point, because the data were taken from electronic medical records, and the majority of variables analyzed are hard variables, it is unlikely that its retrospective design significantly compromised the validity of data collected. Second, although in the multivariate analysis we included a small number of predictor variables, we considered that we included the majority of variables that have been reported in the literature as potential confounders. However, as is the case in other observational epidemiologic studies, residual confounding cannot be excluded, so interpretation of our results needs to be cautious. Third, although the technique used for the diagnosis of RSV infections in our study has been reported to have low sensitivity for detecting cases of RSV infection, this low sensitivity has been described as occurring especially in older children and adults.³⁰ Therefore, because the study was conducted with patients younger than 3 years old, it was considered that the sensitivity of the technique used to detect cases of RSV infection was acceptable. Additionally, the positive predictive value of the test used for the diagnosis of RSV infection could be reduced during the months when the prevalence of this viral infection is low. However, as RSV was not detected during an unusual period, confirmatory testing of positive results was not done. Finally, the fact that the study was conducted in a specialized, tertiary referral hospital makes it likely that the patients included represent the extreme of the spectrum of severity of all patients with RSV infection, which could limit the generalization of results to other contexts. However, the similarity of the results of the seasonality of RSV with previous surveillance epidemiologic reports in the city that included patients with the entire spectrum of disease severity suggests that the results of this study could be extrapolated to other contexts. The main strengths of this study are the inclusion of a large number of samples analyzed, a sample size greater than that of similar epidemiological reports, and the inclusion of a large number of patients with RSV infection,

thus reducing random error and increasing the accuracy of the estimates. Additionally, patient samples were analyzed over a period of 2 years, allowing comparison of the consistency of trends in seasonality of RSV between the two periods analyzed, which increases the reliability of the findings.

In conclusion, RSV is an important cause of ALRI in infants and young children in tropical low-middle income areas, especially during the rainy season. The identified predictors of severe disease and mortality attributed to RSV in infants and children should be taken into account when planning the interventions to reduce the burden of ALRI in young children living in these regions.

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Fig. 1.

Monthly number of RSV infections, along with monthly variation of average precipitation*. *The X-axis shows the date (covering the period from May 2009 through May 2011). The Y-axis shows the monthly number of RSV infections. The Y-axis also shows the average monthly precipitation (mm).

TABLE 1

Clinical Characteristics of the Children Differentiated by Unique (RSV) or Mixed (RSV-Adenovirus) Respiratory Infection

Clinical characteristic	Children with unique RSV infection, n = 2,072 (%)	Patients with mixed RSV-adenovirus infection, n = 75 (%)	P-value
Supplemental oxygen use	1,958 (94.5)	73 (97.3)	0.43
PICU admission	166 (8.0)	12 (16.0)	<0.001*
Need of endotracheal intubation	99 (4.8)	8 (10.7)	0.021*
Use of antibiotics	529 (25.5)	26 (34.7)	0.07
Mortality	23 (1.1)	2 (2.7)	0.21
Home oxygen administration	963 (46.5)	32 (42.7)	0.51
Presence of a comorbidity	1,179 (56.9)	38 (50.7)	0.28

PICU, Pediatric Intensive Care Unit.

* *P* value < 0.05.

TABLE 2

Predictors of Severe Respiratory Syncytial Virus (RSV) Disease in Multivariate Analysis

Variable	Relative risk (RR) (95% CI)	P-value
Age <6 months	2.01 (1.70–2.38)	<0.001*
Prematurity	1.61 (1.20–2.17)	0.001*
Pre-existing respiratory disease	1.41 (1.19–1.66)	<0.001*
Congenital heart disease	2.03 (1.16–3.54)	0.013*
Renal disease	1.54 (0.70–3.40)	0.277
Malnutrition	1.63 (0.44–6.01)	0.458
Cancer	1.18 (0.28–4.87)	0.820
Other comorbidities	1.22 (0.77–1.95)	0.395
NPA sampling during March to May ^a	0.93 (0.79–1.09)	0.390
Mixed RSV-adenovirus infection	2.09 (1.60–2.73)	<0.001*

^aNasopharyngeal aspirates (NPA) during the 3-month period from March to May, the period of the first rainy season in Colombia.

* *P* value < 0.05.

TABLE 3

Underlying Conditions in Children Included in the Study, Differentiated by Live Versus Dead

Type of underlying condition	Alive children, n = 2,122 (%)	Dead children, n = 25 (%)	P-value
Respiratory disease	704 (33.2)	10 (40)	0.47
Prematurity	97 (4.6)	1 (4)	1.00
Congenital heart disease	26 (1.2)	0 (0)	1.00
Renal disease	18 (0.8)	0 (0)	1.00
Cancer	8 (0.4)	2 (8)	0.006*
Malnutrition	4 (0.2)	0 (0)	1.00
Epilepsy	1 (0.0)	0 (0)	1.00

*
P value < 0.05.

TABLE 4

Predictors of Mortality in Patients With Respiratory Syncytial Virus (RSV) Infection in Multivariate Analysis

Variable	Relative risk (RR) (95% CI)	P-value
Age <6 months	1.11 (0.51–2.41)	0.782
Prematurity	1.36 (0.17–10.58)	0.767
Pre-existing respiratory disease	1.90 (0.77–4.69)	0.164
Cancer	31.60 (5.97–167.13)	<0.001*
Other comorbidities	1.26 (0.32–5.29)	0.695
Mixed RSV-adenovirus infection	1.76 (0.37–8.47)	0.479

*
P value < 0.05.