

Characterization of rhinovirus/enterovirus complex infection in children living at high altitudes: A cross sectional study

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Abstract

Background: Respiratory tract infections caused by the *rhinovirus/enterovirus* (RV/EV) complex have traditionally been considered to be minor, self-limited infections in children, with few complications. There are no previous studies of patients living at high altitudes that characterize severe cases of this infection.

Methods: This was a cross-sectional study including patients from 1 month to 18 years old who had been hospitalized for acute respiratory tract infections between October 2015 and December 2019, and had had a viral panel with RT-PCR during their hospitalization.

Results: During the study period, 645 RT-PCRs were performed, with the two main etiological agents identified being RV/EV (224) and respiratory syncytial virus (68). The median age of patients with RV/EV complex was 27 months (IQR: 8-70), 55.8% were boys and the average length of hospital stay was 12 days (IQR: 6-24). Severe RV/EV complex infections required more transfers to intensive care (11% vs 47%), showed more viral coinfection (OR: 2.13, 95%CI: 1.42-4.64) and had less bacterial coinfection (OR: 0.55, 95%CI: 0.31-0.98) than RSV infections, with no difference in mortality (2.4% vs. 2.1%, P:0.09). Post-transplant patients (OR: 3.35, 95%CI: 1.10-11.34) and those with comorbidities (OR: 3.97, 95%CI: 2.23-7.08) had the highest risk of RV/EV infection.

The RV/EV group had a higher risk of presenting acute respiratory distress syndrome (ARDS) (OR: 3.6, 95%CI: 1.07-12.18), especially in premature infants (p: 0.05; exp (B), 2.99; 95%CI= 1.01-8.82), those with heart disease (p: 0.047; exp(B), 2.99; 95%CI = 1.01-8.82) and those with inborn errors of metabolism (p: 0.032; exp (B), 5.01; 95%CI= 1.15-21.81).

Conclusions: Respiratory infection due to RV/EV in children who live at high altitudes can frequently be severe, requiring management with intensive care therapy. When compared to RSV, this complex is more frequently associated with viral coinfection and the development of ARDS, especially in risk groups such as those with prematurity, heart disease or inborn errors of metabolism. It is important to see RV / EV as a virus that can have an unsatisfactory course as or more severe than that of other viruses that affect the respiratory tract in children.

Background

Acute respiratory infection (ARI) causes about four million deaths per year in children under five years of age. It is one of the main causes of hospitalization and admission to intensive care in pediatrics. According to the World Health Organization (WHO), it is estimated that between 2–3% of children under two years of age in low- and middle-income countries have had severe pneumonia requiring hospitalization, and ARI mortality rates in these countries range from 60 to 100 cases per 1,000 children under the age of five [1].

In children under two years of age, viruses are the main etiological agents of ARI. Respiratory syncytial virus (RSV) has been considered to be the most common germ and it usually affects children who have

risk factors such as prematurity, heart disease or bronchopulmonary dysplasia [2]. Other viruses such as the rhinovirus / enterovirus complex (RV / EV) are thought to commonly cause uncomplicated acute upper respiratory infections that are usually self-limiting and have a benign course. It has recently been noted that this virus, from the genus Enterovirus and family Picornaviridae, can invade the lower respiratory tract and cause complicated disease in children [3]. Additionally, this virus has been associated with a higher frequency of bacterial coinfection and the presence of complicated pneumonia, and it accounts for up to 14% of acute respiratory distress syndrome (ARDS) in children living in high-income countries.

In low and middle-income countries, there is no registry for RV / EV complex infection, its natural course or associated risk factors. In these countries, the difficulty in accessing health services, chronic noncommunicable diseases, and social inequality, frequently make ARI one of the main causes of morbidity and mortality [1]. Moreover, many of these patients live at moderate or high altitudes, which leads to the development of respiratory compensatory mechanisms to tolerate relative hypoxemia [4]. These children tend to be more prone to frequent upper and lower respiratory tract problems. Therefore, in this study we intend to describe the main characteristics of hospitalized patients with ARI due to the RV / EV complex, the risk factors associated with severe infection and their clinical course compared to RSV infections, in children who live at moderate altitudes.

Methods

A cross-sectional study was carried out in children from 1 month to 18 years old hospitalized at the Fundación Cardioinfantil-Instituto de Cardiología, a tertiary university hospital located in Bogotá, Colombia. Patients who underwent multiple RT-PCR tests (FilmArray® BioMérieux) and who were hospitalized for ARI on the regular hospital floor or in pediatric intensive care between October 2015 and December 2019 were included. According to institutional protocol, children with ARI who are going to be hospitalized should have an RT-PCR taken.

Post-transplant surgery patients who underwent multiple respiratory RT-PCR tests without having symptoms or a diagnosis of ARI were excluded. This study was done in accordance with the Helsinki declaration and approved by the institutional ethics committee and was registered with number PM-35-2020. The informed consent was signed by the parents or legal guardian in all the participants.

The information was taken from the electronic charts of the hospitalized children who had undergone multiple RT-PCRs. The analyte used in this technique for virus detection was Type IA10-2003 Zeptometrix 0810161CF. All the information was entered in a database created for this study, to which only the principal investigators had access.

The multiplex RT-PCR respiratory assay was ordered for patients with upper and lower respiratory symptoms at the discretion of the attending physician. A respiratory therapy specialist took samples from nasopharyngeal aspirates, and they were processed within 30 minutes of collection, according to the institutional standard for sample handling. The RT-PCR detects 17 viruses and 3 bacteria, specifically:

adenovirus, coronavirus OC43, coronavirus NL63, metapneumovirus, HRV / HEV, influenza A, influenza A / H1, influenza A / H1-2009, influenza A / H3, influenza B, parainfluenza 1, parainfluenza 2, parainfluenza 3, parainfluenza 4, RSV, Bordetella pertussis, chlamydia and mycoplasma; with a sensitivity and specificity of 95% and 99%, respectively [5], and is currently the gold standard for detecting these microorganisms [6].

Clinical behavior was evaluated in terms of the main viral respiratory infection complications, such as transfer to the intensive care unit, need for ventilatory support and mechanical ventilation, and length of hospital stay. The clinical manifestations were classified into different diagnoses such as rhinopharyngitis, laryngitis, croup, bronchiolitis, tracheitis, pneumonia or ARDS, according to the criteria of the attending physician. The data on RSV was recorded during the same time period.

The outcome of unsatisfactory clinical behavior during RV / EV infection was defined as the requirement for an intensive care unit and/or mechanical ventilation, and the length of ventilatory support and hospital stay in pediatric patients hospitalized for ARI. Inpatient deaths from any cause in children with a positive RV / EV test were considered.

Severe ARI was defined as the use of oxygen with an inspired oxygen fraction (FiO₂) greater than 40% and the need for non-invasive mechanical ventilation (e.g., high-flow nasal cannula), or invasive mechanical ventilation, including hemodynamic instability requiring vasoactive support. Patients in whom a typified viral infection was identified 48 hours after admission, and who did not have respiratory symptoms on admission, were considered to have a nosocomial infection. Viral coinfection was established if two or more respiratory viruses were isolated in the RT-PCR assay, and bacterial coinfection was determined if blood cultures and / or orotracheal secretion cultures were positive and / or procalcitonin was > 0.5 µg / L.

Statistical analysis

Descriptive statistics were used for demographic variables and a measure of central tendency and dispersion for continuous variables, according to the distribution of the variable defined by the Shapiro Wilk normality test. Absolute and relative frequencies were described for the qualitative variables. For the factors related to disease severity, a bivariate analysis was performed using Student's t test for independent samples when the variable was quantitative and parametric with a normal distribution. A Mann-Whitney U test was used for non-normal distribution.

An exploratory bivariate analysis was performed to compare the two agents, RV /EV and RSV. Hospitalized and intensive care patients were analyzed. For the multivariate analysis, binary logistic regression was performed in order to control for confounding factors, mainly the severity of the disease, evaluated according to the PIM2 scale [7]. The aim of this analysis was to establish the risk factors associated with severe RV / EV infection and determine their association with the outcomes of interest. Statistical analysis was performed using SPSS 25 (IBM 16), and a P = <0.05 was considered statistically significant.

We tried to control biases with various strategies. To control for information bias, an exhaustive search of the electronic chart was carried out; if information was lacking, other sources of information were searched, such as the data recorded in the clinical laboratory history or the nurses' notes. The central laboratory's RT-PCR sample collection and processing procedures were standardized. This research was carried out in a single university center that cares for all kinds of pathologies in the emergency room, due to its complexity and size.

Results

RT-PCR was performed on 645 patients in the study period, of whom 224 were positive for RV / EV and 68 were positive for RSV. The demographic characteristics of the patients are detailed in Table 1. The patients with RV / EV complex infection had a median age of 27 months (IQR: 8–70) and were predominantly male (54.8%). This infection was seen more frequently in patients with solid organ transplantation (10.3%) and prematurity (15.1%) (Supplement 1).

Table 1
Demographic characteristics of patients with typification of RV/EV and VSR included in the study.

Patient characteristics		<i>n</i> = 292 (%)
Sex	Male	160 (54.8)
	Female	132 (45.2)
Age group	Infant < 12 months	121 (41.4)
	Infant 12 m to 24m	35 (12.0)
	Preschool	68 (23.3)
	School-age	18 (6.2)
	Adolescent	50 (17.1)
Nutritional status	Severe malnutrition	56 (19.2)
	Malnutrition	52 (18.2)
	Normal	171 (58.6)
	Overweight	11 (3.8)
	Obesity	1 (0.3)
Comorbidities		
Kidney disease		29 (9.9)
Liver disease		40 (13.7)
Heart disease		58 (19.9)
Prematurity		33 (11.3)
BPD		25 (8.6)
Metabolic disease		20 (6.8)
Transplant		33 (11.3)
Primary immunodeficiency		35 (12.0)
Neoplasm		42 (14.4)
Other comorbidity	Respiratory	49 (16.8)
	Cardiovascular	22 (7.5)
	Neurological	31 (10.6)
	Gastrointestinal	15 (5.1)

Patient characteristics		<i>n</i> = 292 (%)
	Genitourinary	13 (4.5)
	Autoimmune	24 (8.2)
	Dermatologic	8 (2.7)
	Hepatobiliar	11 (3.8)
	Neoplasm	6 (2.1)
	Asthma	16 (5.5)
	CMV infection	7 (2.4)
	Pulmonary hypertension	9 (3.1)
	EBV infection	2 (0.7)
Symptoms on admission	Cough	135 (46.2)
	Dyspnea	110 (37.7)
	Gastrointestinal	45 (15.4)
	Neurological	12 (4.1)
	Temperature (°C) (IQR)	37.7 (35.6–40.1)
Systolic blood pressure (IQR)		96.9 (14–90)
Base excess (mmol/L) (IQR)		5.2 (2.6-6.0)
FiO2 (IQR)		0.4 (0.3 – 0.2)
PaO2 (IQR)		71.0 (31.8–60.0)
Pa/Fi (IQR)		292 (137.7–250.0)
PIM 2 (IQR)		0.9 (0.7–2.8)
Total mortality		13 (4.5)
Cause of death	ARDS	1 (7.7)
	Septic shock	3 (23.1)
	Multiple organ failure	1 (7.7)
	Hypoxemic respiratory failure	1 (7.7)
	Severe sequelae -DNR	1 (7.7)
	Bradycardia and asystole	1 (7.7)
	Refractory shock	5 (38.5)

Most of the patients with RV / EV complex infection had a normal weight (58.6%); nevertheless, 19.2% of the cases had severe malnutrition, and obesity was observed in 11 patients (3.8%). The predominant symptoms were cough (46.2%) and dyspnea (37.7%), with some gastrointestinal (15.4%) and neurological symptoms (4.1%) (Table 1).

The comorbidities found among all patients with isolates included respiratory diseases (16.8%) such as bronchopulmonary dysplasia (8.6%), asthma (5.5%) and pulmonary hypertension (3.1%). Other comorbidities were heart disease (19.9%), prematurity (11.3%), autoimmune diseases (8.2%), kidney (9.9%) or urinary (4.5%) disease, liver disease (13.7%), hepatobiliary (3.8%) or gastrointestinal (5.1%) disease, metabolic disease (6.8%), transplantation (11.3%), primary immunodeficiency (12%), CMV (2.4%) or EBV (0.7%) infection, and malignancies (14.4%).

The final diagnoses of RV / EV and RSV infection patients were pneumonia in 114 cases (39%) and bronchiolitis in 59 cases (20.2%), 35 (12%) of whom developed ARDS. Rhinopharyngitis, asthmatic crisis, and recurrent wheezing occurred in 30 children (10.3%); croup and tracheitis in 10 patients (12%), and severe respiratory infection criteria were identified in more than 50% of the study population, for a total of 162 cases (55.5%). The main viruses found to cause viral coinfection with the RV / EV complex are described in Table 2 and were found in 64 cases (Table 2).

Table 2
Viral coinfection in the study population.

Variable	Category	n (%) n = 292	%
Viral coinfection	Yes	63	21.5
	No	229	78.4
	Total	292	100
Second isolated virus	<i>Respiratory syncytial virus</i>	16	34.1
	<i>Adenovirus</i>	2	4.2
	<i>Human metapneumovirus</i>	4	8.6
	<i>Influenza A/H1</i>	1	2.2
	<i>Influenza A/H31</i>	2	4.2
	<i>Influenza A/H1-2009</i>	2	4.2
	<i>Influenza B</i>	1	2.2
	<i>Parainfluenza virus 1</i>	2	4.2
	<i>Parainfluenza virus 3</i>	12	25.5
	<i>Parainfluenza virus 4</i>	2	4.2
	<i>Mycoplasma pneumoniae</i>	2	4.2
	<i>Coronavirus 229E</i>	1	2.2
	Total	47	100.0
	<i>Respiratory syncytial virus</i>	1	33.3
	Third isolated virus	<i>Parainfluenza virus 3</i>	1
<i>Coronavirus NL63</i>		1	33.3
Total		3	100.0
<i>Chlamydomphila pneumoniae</i>		1	100.0

Of the 292 patients with RV / EV and RSV isolation, 172 (58.9%) had to be transferred to the pediatric intensive care unit (PICU). The use of some type of device for supplemental oxygen support was needed in 79.5% of the cases, with mechanical ventilation required in 157 patients (53.8%). The type of ventilatory support is described in Supplement 2.

The patients with RV / who had to be transferred to the PICU were younger than those who did not need to be transferred [13 months (IQR: 4–49) vs 30 months (IQR: 10–65) (P = 0.004)].(Table 3). The predominant symptoms of the patients transferred to the PICU were more severe from the beginning.

More dyspnea was observed at the time of emergency admission among those who were transferred to the PICU vs those who continued in general hospitalization (64.5% vs 24.4%; $P < 0.001$).

Table 3
Bivariate analysis of patients who were or were not admitted to the PICU.

Variable	Category	Need for PICU				Total		<i>P</i>
		Yes		No		<i>n</i>	%	
		<i>n</i>	%	<i>n</i>	%			
ARDS	<i>Yes</i>	33	19.2%	2	1.7%	35	12.0%	< 0.001
	<i>No</i>	139	80.8%	118	98.3%	257	88.0%	
Total		172	100.0%	120	100.0%	292	100.0%	
Severe ARI	<i>Yes</i>	149	86.6%	13	10.8%	162	55.5%	< 0.001
	<i>No</i>	23	13.4%	107	89.2%	130	44.5%	
Total		172	100.0%	120	100.0%	292	100.0%	
Mortality	<i>Yes</i>	13	7.6%	0	0.0%	13	4.5%	0.005
	<i>No</i>	159	92.4%	120	100.0%	279	95.5%	
Total		172	100.0%	120	100.0%	292	100.0%	

The most common comorbidities in the population admitted to the PICU were heart disease (24.4%), liver disease (15.1%), prematurity (15.1%), and bronchopulmonary dysplasia (13.4%). Other comorbidities included primary immunodeficiency (12.8%), transplantation (9.9%), metabolic disease (8.7%), and kidney disease (8.1%). Some type of neoplasm was present in 12 patients (7.0%) in the PICU vs 30 patients (25%) not in the PICU ($P = < 0.001$). Pneumonia was the predominant cause of admission to the PICU, with 72 patients (41.9%), followed by bronchiolitis with 18%, and asthmatic crisis with 11%. Severe ARI was identified in 86.6% of the cases that were transferred to the PICU, but only in 10.8% of those who were not transferred ($P = < 0.001$).

An analysis of the characteristics of the population with RV / EV s RSV showed that the first group was older (27 m IQR: 8–70 vs 11m IQR: 2–29; $P < 0.001$). At the time of admission, the risk of dying, according to the PIM 2 scale, for both viruses was less than 1% ($P = 0.69$) (see Supplement 3). The length of stay in the PICU for both had a median of 5 days (IQR: 3–12) (IQ: 4–13) ($P = 0.58$), with the need for respiratory support reaching a median of 4 days (IQR: 2–8) and 7 days (IQR: 4–11) ($P = 0.001$), respectively. The presence of RV / EV infection increases the risk of developing ARDS (OR: 3.6 (95%CI: 1.07–12.18) ($P = 0.03$) (Supplement 4 and supplement 5).

In patients with a solid organ transplant, RV / EV infection was more frequently observed than RSV, 10.3% vs 1.0% (OR: 3.35 95%CI: 1-11.34) ($P = 0.04$). Viral coinfection was identified in 55 patients (18.8%) with

RV / EV infection vs 9 patients (3.1%) with RSV (OR: 2.13 95%CI: 1-4.58) (P = 0.04). Bacterial coinfection was observed in 19.5% of patients with RV / EV infection vs 8.9% with RSV (OR: 0.55 95%CI: 0.31–0.98) (P = 0.04), as illustrated in Table 4.

Table 4
Calculated OR, comparison of RV/EV and RSV.

Variable		Causal agent				Total		P	OR	I.C. 95%
		RV/EV		RSV		n	%			
		n	%	n	%					
Transplant	Yes	30	10.3%	3	1.0%	33	11.3%	0.04	3.35	0.99– 11.3
	No	194	66.4%	65	22.3%	259	88.7%			
Total		224	76.7%	68	23.3%	292	100.0%			
Other comorbidity	Yes	179	61.3%	34	11.6%	213	72.9%	< 0.001	3.97	2.23– 7.08
	No	45	15.4%	34	11.6%	79	27.1%			
Total		224	76.7%	68	23.3%	292	100.0%			
Viral coinfection	Yes	55	18.8%	9	3.1%	64	21.9%	0.04	2.13	1.00– 4.58
	No	169	57.9%	59	20.2%	228	78.1%			
Total		224	76.7%	68	23.3%	292	100.0%			
Bacterial coinfection	Yes	57	19.5%	26	8.9%	83	28.4%	0.04	0.55	0.31– 0.98
	No	167	57.2%	42	14.4%	209	71.6%			
Total		224	76.7%	68	23.3%	292	100.0%			
ARDS	Yes	32	11.0%	3	1.0%	35	12.0%	0.03	3.6	1.07– 12.18
	No	192	65.8%	65	22.3%	257	88.0%			
Total		224	76.7%	68	23.3%	292	100.0%			

The need for PICU was more frequently seen in the group with RV / EV infection, with 47.3% of these patients vs 11.6% in RSV (P = 0.09). Acute respiratory distress syndrome developed more frequently in the group with RV / EV infection than in children with RSV infection (11% vs 1%; P = 0.003). When different confounding factors (mainly the severity of the disease measured by the PIM2 scale) were controlled for, ARDS in patients infected by RV / EV was observed more frequently in those with heart disease, premature infants and those with inborn errors of metabolism (Table 5).

Table 5
Exploratory multivariate analysis controlling for confounding factors. Association between ARDS and RV/EV infection. (Logistic regression)

	B	Standard error	Wald	gl	Sig.	Exp(B)
Heart disease	1.095	0.552	3.934	1	0.047	2.99
Prematurity	1.802	0.637	8.011	1	0.005	6.062
Metabolic disease	1.611	0.751	4.61	1	0.032	5.01

Discussion

In this study of children with i RV / EV complex infection living at high altitudes, 47.3% were found to have severe disease that required transfer to pediatric intensive care. Children with comorbidities such as prematurity, heart disease and inborn errors of metabolism were especially prone to severe disease. The clinical course frequently includes ARDS and a mortality similar to RSV, which has traditionally been responsible for a significant burden of disease [8].

The study population's median age was much lower than that reported in the literature in high-income countries. Sapedero et al., in a retrospective cohort study carried out in Baltimore with 519 patients, showed a median age of 2.7 years (very similar to what we found in our group) for those hospitalized for RV / EV with severe infection [9]. In a study in New York with 155 children, Smith et al. found a median age of 4 years [5].

Vásconez-García et al. have linked nutritional risk and the presence of worse outcomes and high mortality during severe viral respiratory infection in Latin American individuals with comorbidities [10–11]. However, in our population, malnutrition was observed in only 41%, a finding consistent with the dietary problems of low- and middle-income countries where the prevalence of chronic noncommunicable diseases such as overweight is progressively increasing [12–15]

Traditionally, severe ARI has been described in patients with comorbidities. Tijerina et al., in a cross-sectional study in Mexico with 295 patients, described a higher rate of hospitalization in patients with prematurity [16] and bronchopulmonary dysplasia, relating it to the lack of coverage in vaccination, abandonment of breastfeeding, poverty, social commitment and the socioeconomic level [11] [17]. In our population, we found that children hospitalized for RV / EV presented significant comorbidities and frequently needed to be transferred to intensive care. As mentioned previously, this virus has generally been thought to cause self-limited upper respiratory infection in most cases [18], but studies like ours show that, in risk groups, this virus can have a similar behavior in terms of severity to others previously described, such as RSV.

We found that younger patients infected with RV / EV required transfer to intensive care more often and had a longer hospital stay. Roeleveld et al., in high-income countries, found that RV / EV infection,

regardless of comorbidities, is not associated with a longer length of hospital stay [19]. The difference in our population can be explained by the greater difficulty in accessing health services in low- and middle-income countries, which often leads to late consultations. This is related to the significant frequency of ARDS seen in our series in children with RV / VE, which is higher than that observed with RSV.

Traditionally, RSV causes significant morbidity / mortality in children under two years of age. The study by Bianchini et al. shows that this virus is the second leading cause of infant mortality and the leading cause of lower respiratory tract infections in children worldwide, with clinical manifestations and severe complications including ARDS [20]. Having seen these results with RV / EV infection, it is striking that this germ had a more aggressive behavior, with a higher frequency of ARDS and viral coinfection and a greater need for respiratory support. This has not been described before in middle-income countries. We consider that it is important to look further into the pathophysiological mechanisms that explain this more severe behavior of RV / EV.

Messacar et al. found that pediatric patients admitted with the RV / EV complex had the same probability of requiring admission to the PICU or mechanical ventilation as children admitted with other respiratory viruses, historically considered to be more severe, such as influenza [21] [22]. In a previous publication by our group, the RV / EV complex was described as the most frequent etiological agent (30%), followed by RSV (19%), parainfluenza (7.4%) and adenovirus (5.7%). Influenza only accounted for 1.2% of the total RT-PCRs taken [23]. In his series, Messacar found that only 18% of the patients with RV / EV required transfer to intensive care, while 60% of our patients were transferred [21]. Socioeconomic factors, comorbidities and limitation of access to health services can explain this situation.

Despite the fact that it has been considered to be a minor infection, the risk of developing ARDS was more frequent with the RV / EV complex than with RSV infection in our population. This is an important fact, and we must consider that children admitted to intensive care with RV / EV infection may have an unsatisfactory course and require more frequent and intense support than those with other viruses such as RSV [5]. Comorbidities such as prematurity, heart disease and inborn errors of metabolism may partially explain this evolution, but this implies that, in these risk groups, RV / EV infection cannot be considered to be a mild infection, and its possible complications must be taken into account [5].

We consider that our study has several limitations. In the first place, it is the experience of a single university center that only evaluated children who, due to their severity, required hospitalization. This may be an explanation of why children with some comorbidities may require more transfers to intensive care. However, RV / EV infection was more severe and frequent in patients with comorbidities than RSV was in the same group. Another limitation of our study is that we did not have a control group with a negative RT-PCR and ARI that required a transfer to intensive care. However, when compared with RSV, we observed that the RV / EV behavior is more severe and has a more aggressive natural course. Additionally, the commercial brand of RT/PCR did not allow us to differentially evaluate the enterovirus and rhinovirus to understand the differences between these viruses from the same family [24]. In general, they are analyzed together in most of the tests available commercially today.

Conclusion

Respiratory infection due to RV / EV in children who live at high altitudes can frequently have a severe course that requires management in intensive care. When compared to RSV, this virus is more frequently associated with viral coinfection and development of ARDS, especially in risk groups such as those with prematurity, heart disease, or inborn errors of metabolism. It is important to consider RV / EV as a virus that can have an unsatisfactory natural course equal to or more severe than other viruses that affect the respiratory tract in children.

Abbreviations

RV/EV, Complejo Rhinovirus/Enterovirus; VSR, Virus Sincitial Respiratorio; RIQ, Rango intercuartílico; DPB, Displasia broncopulmonar; CMV, Virus Citomegalovirus; VEB, Virus Epstein Barr; PaO₂, Presión parcial arterial de oxígeno; FiO₂, Fracción inspirada de oxígeno; PIM 2, Pediatric Index of Mortality-2; ARDS Acute respiratory distress syndrome; ARI:Acute respiratory infections; FiO₂:Fraction of inspired oxygen; RT-PCR:Real time-Polymerase chain reaction.

Declarations

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Authors' contributions

Drs. FSJ, CSC, OE, AJ, BGA, BLP, and BON contributed to designing and performing the study. Drs. CSC, OE, FSJ, and BON participated in data collection. Drs. FSJ, CSC, OE, AJ, BGA supervised study development and data collection. All the authors contributed to drafting the manuscript and reviewing the final article. All the authors approved the final manuscript and agreed with all aspects of the study. None of the investigators declare conflicts of interest. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Availability of data and materials

Datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The ethics committee of the Fundación Cardioinfantil-Instituto de Cardiología approved this study with committee's reference number PM-35-2020 and the parents of the children approved to participate in this study. This study was done in accordance with the Helsinki declaration. The informed consent was signed by the parents or legal guardian in all the participants.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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