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ORIGINAL RESEARCH

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Severity and mortality of acute respiratory failure in pediatrics: A prospective multicenter cohort in Bogotá, Colombia

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Abstract

Background and Aims: Acute respiratory failure (ARF) is the most frequent cause of cardiorespiratory arrest and subsequent death in children worldwide. There have been limited studies regarding ARF in high altitude settings. The aim of this study was to calculate mortality and describe associated factors for severity and mortality in children with ARF.

Methods: The study was conducted within a prospective multicentric cohort that evaluated the natural history of pediatric ARF. For this analysis three primary outcomes were studied: mortality, invasive mechanical ventilation, and pediatric intensive care unit (PICU) length of stay. Eligible patients were children older than 1 month and younger than 18 years of age with respiratory difficulty at the time of admission. Patients who developed ARF were followed at the time of ARF, 48 h later, at the time of discharge, and at 30 and 60 days after discharge. It was conducted in the pediatric emergency, in-hospital, and critical-care services in three hospitals in Bogotá, Colombia, from April 2020 to June 2021.

Results: Out of a total of 685 eligible patients, 296 developed ARF for a calculated incidence of ARF of 43.2%. Of the ARF group, 90 patients (30.4%) needed orotracheal intubation, for a mean of 9.57 days of ventilation (interquartile range = 3.00–11.5). Incidence of mortality was 6.1% (n = 18). The associated factors for mortality in ARF were a history of a neurologic comorbidity and a higher fraction of inspired oxygen at ARF diagnosis. For PICU length of stay, the associated factors were age between 2 and 5 years of age, exposure to smokers, and respiratory comorbidity. Finally, for mechanical ventilation, the risk factors were obesity and being unstable at admission.

Conclusions: ARF is a common cause of morbidity and mortality in children. Understanding the factors associated with greater mortality and severity of ARF might allow earlier recognition and initiation of prompt treatment strategies.

KEYWORDS

acute respiratory failure, mechanical ventilation, mortality, pediatric intubation, respiratory therapy

1 | INTRODUCTION

Acute respiratory failure (ARF) is the most frequent cause of cardiorespiratory arrest and subsequent death in children worldwide. Therefore, several efforts have been made to better understand its etiology and risk factors for further progression.[1–4] The following are the two presumptions upon which this research is based: the immense burden of ARF in children and the few number of studies regarding ARF in Colombia and in cities at high altitude.

Acute respiratory infection (ARI) accounts for one-fifth of the mortality in children under 5 years of age worldwide, mainly due to pneumonia, and is responsible for nearly two million deaths per year in developing countries.[1,5,6] It is estimated that more than 700 million episodes of ARI occur annually, of which 52 million are episodes of pneumonia and 11.9 million are severe ARIs resulting in numerous hospitalizations worldwide, including in the pediatric intensive care unit (PICU).[7,8] The incidence of ARF varies from 1.4 to 9.5 cases per 100,000 children and adolescents per year worldwide, and mortality is estimated to be approximately 30%, depending on associated comorbidities.[3,4]

ARF has had many different definitions, especially regarding the specific etiology that led to ARF. Some authors define ARF according to specific results on arterial blood gas analysis, while others consider other hemodynamic markers.[1,4,9] However, ARF can be understood as any failure of the respiratory system to achieve adequate oxygenation and ventilation that requires respiratory support with high-flow oxygen through any of the available devices.[2,4,9–12] ARF can be classified as hypoxemic when oxygen saturation (SaO_2) is less than 90%, ARF with respiratory distress (due to increased work of breathing and elevated or decreased expected respiratory rate according to age), or hypercapnic ARF (due to partial pressure of carbon dioxide [PCO_2] greater than 60 mmHg or by an arterial pH of less than 7.2).[10,11]

In Colombia, during 2021, 7.2% of all hospitalizations in intensive care units were registered for children; of these, 7.9% were in children under 1 year of age, 2.4% under 5 years of age, and 1.9% in children older than 5 years of age.[13] The age groups most affected nationally by influenza-like illnesses were children under 1 year of age (34.56%), from 1 to 4 years (27.75%), and older than 5 years (10.27%) for the same period.[13] According to the Colombian National Institute of Health, by November 2021, 11 deaths were reported to be associated with ARI in children under 5 years of age, with evidence of an increase in the number of cases compared to the same period in 2020. During the year 2021, the highest proportion of emergency room (ER) visits due to ARI occurred in children aged 1 year (20.1%), followed by children aged 2–4 years (16.7%).[14]

In Colombia, about 20% of the population (approximately 10 million people) live at altitude between 2500 and 3500 m above sea level (masl).[15] As altitude increases, barometric pressure and inspired oxygen pressure decrease, leading to a decrease in alveolar and arterial pressure of oxygen. This causes a compensatory increase in ventilation with a reduction in arterial partial pressure of carbon dioxide. Consequently, the respiratory characteristics of children residing at high altitudes are likely to differ from those described at sea level.[15]

In Bogotá, Colombia, where our study was conducted, from 2007 to 2020, 400 deaths were recorded in children under 5 years of age due to ARI, with mortality rates between 1.8 and 9.7 cases per 100,000 children under 5 years of age, and with a downward trend during the study period.[16] For the same period, a total of 858 deaths in children under 5 years of age due to pneumonia were reported, with mortality rates between 2.6 and 21 cases per 100,000 children under 5 years of age. The highest number of deaths associated with ARI occurred in male children under 1 year of age (0–6 months of age).[16]

Considering these reports and the burden of ARF in children, our objective was to calculate the incidence of mortality and determine the factors associated with the severity and mortality of ARF in children older than 1 month and younger than 18 years in three hospitals in Bogotá.

2 | MATERIALS AND METHODS

This study was conducted within a prospective multicentric cohort that evaluated the natural history of pediatric ARF in three hospitals in Bogotá, Colombia (a city at 2600 masl) from April 2020 to July 2021.[17] The three institutions included in the cohort were Hospital Universitario Fundación Santa Fe de Bogotá, Clínica Infantil Colsubsidio, and Instituto Roosevelt. These were included since they are all part of the Pediatrics Residency Program at Universidad de los Andes. Severity was measured as the need for invasive mechanical ventilation (IMV) and PICU length of stay. The cohort profile and the general cohort methods can be found elsewhere. The cohort was conducted under a collaborative modality among the group of pediatric residents at Universidad de los Andes. The topic addressed was ARF in pediatrics from which four research questions were addressed. First, to characterize ARF, its incidence, and etiology.[17,18] Second, the use and indications of high-flow nasal cannula (HFNC).[19] Third, the burden of ARF (in the process of publication). And finally, the question addressed in the present study.

2.1 | Eligible patients

Eligible patients were children older than 1 month and younger than 18 years of age with respiratory difficulty at the time of admission either to the ER, the inpatient ward, or the PICU at one of the three participating institutions. Respiratory difficulty was defined as the presence of at least one of the following: tachypnea or bradypnea (according to the normal respiratory rate for each age group)[20] gasping breathing, or the presence of retractions. All eligible patients were asked to participate in the study, and informed consent was signed by their caregivers; informed assent was signed by children aged 8 years or older as well. The only exclusion criterion that was considered was an ongoing pregnancy. ARF was defined as the need for high-flow oxygen by any of the available devices (from HFNC, Venturi, and nonrebreather mask, to noninvasive and IMV). If any of the eligible patients developed ARF, data was obtained at the moment of high-flow oxygen initiation, 48 h later, and at the time of hospital discharge. Follow-up for the ARF group was conducted by a telephone call at 30 and 60 days after discharge (Figure 1).

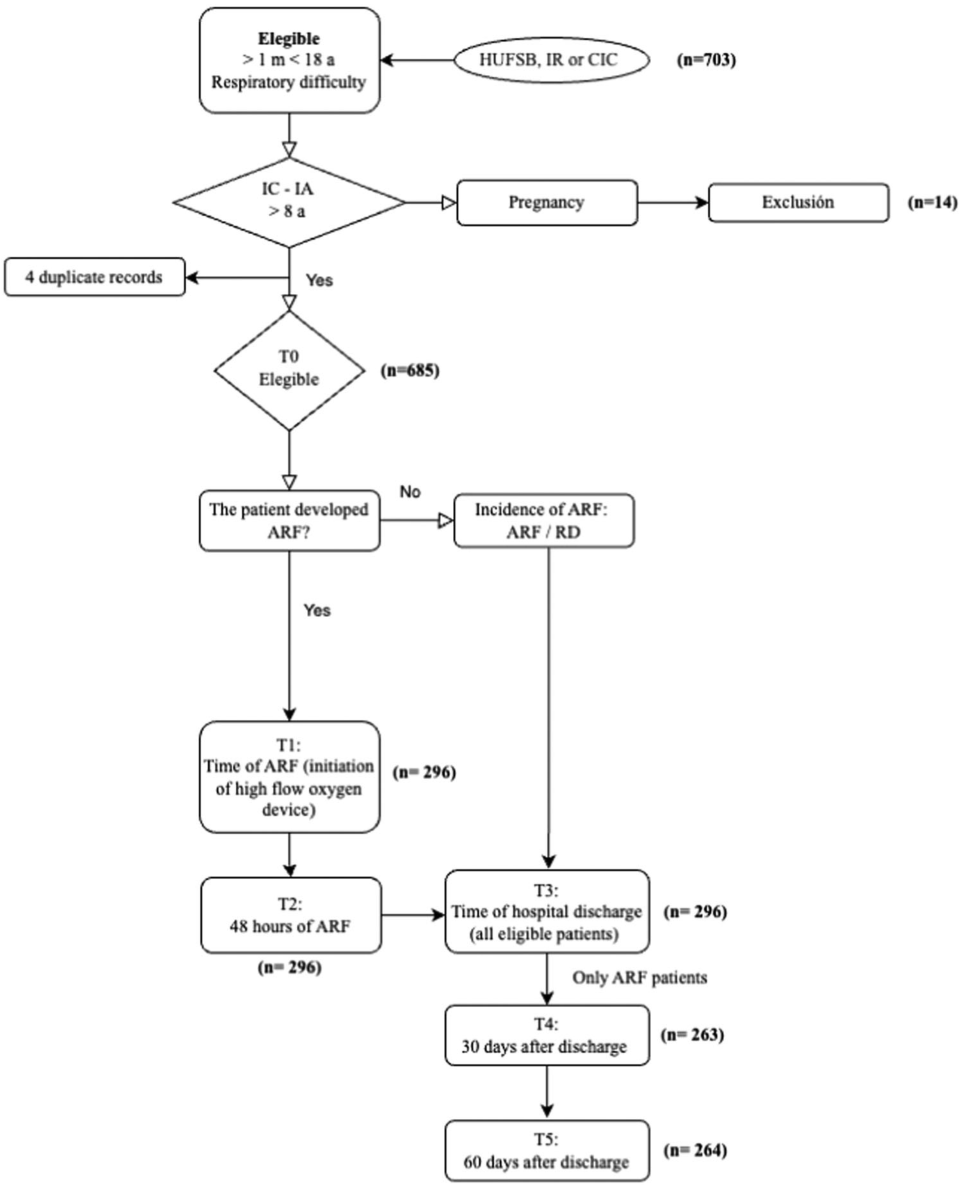

FIGURE 1 Cohort flowchart. ARF, acute respiratory failure; CIC, Clinica Infantil Colsubsidio; HUFSFB, Hospital Universitario Fundación Santafe de Bogotá; IR, Instituto Roosevelt; PICU, pediatric intensive care unit; T0–5, times 0–5 of data collection.

2.2 | Sample size

To calculate the sample size for the cohort, we first identified the incidence of ARF in the three institutions where the study was carried out. Then the Peduzzi formula, adjusted to a finite population, was used to obtain the sample size necessary to make associations, obtaining a minimum of 477 patients. An additional 20% was added to consider the attrition rate in a cohort.

2.3 | Instruments and variables

All variables were collected from primary sources within the three participating institutions. Four main categories were considered: demographic variables, clinical variables during hospital stay, hemodynamic and laboratory variables, and oxygenation and ventilation variables. Nutritional status was assessed at admission and classified according to Resolution 2465 of the Colombian Ministry of Health; malnutrition defined as less than −2 SD in weight for height in children younger than 5 years, thinness as less than −2 SD in body mass index for age in children older than 5 years; and obesity was defined as more than +3 SD in weight for height in children younger than 5 years and more than +2 SD in body mass index for age in older than 5 years. Clinical severity at the time of ARF diagnosis was assessed through the pediatric assessment triangle.

2.4 | Analytic strategy

A descriptive analysis was performed, with qualitative variables described as absolute and relative values and quantitative variables as central tendency and dispersion statistics.[21] A Shapiro–Wilk test was performed to determine normal distribution. A bivariate analysis was performed for the primary outcomes (mortality, PICU length of stay, and IMV). With quantitative variables, a Kruskal–Wallis or Mann–Whitney *U* test was performed, depending on each variable; when they were qualitative, a χ^2 test or Fisher's exact test was performed. Mortality density rate was calculated for ARF patients and stratified by sex and age group. Bivariate and multivariate analyses were conducted to explore associated factors to the three main outcomes; those included in the models were considered according to biological plausibility as well as associations previously published in the literature. Additionally, variables were included when a significant relationship was found in a χ^2 or Fisher test (p value < 0.02).

A logistic regression model was conducted for mortality and PICU length of stay. For IMV, a Poisson regression was conducted for relative risk (RR) estimation. For PICU length of stay, a Kaplan–Meier survival estimate analysis was conducted. The goodness-of-fit test for the models was evaluated using a linearity test and a Hosmer–Lemeshow test. The collinearity of the explanatory variables was verified within the regression model. A cross-validation exercise was carried out to eliminate the influencing data identified from Cook's distance. A p value of less than 0.05 was considered statistically significant. STATA v17 was used to conduct all statistical analysis.

2.5 | Risk of bias

The main bias present during the study as well as the strategies to reduce their impact, are mentioned as follows. The risk of selection bias is in direct relation to the attrition rate; therefore, the main strategy to prevent selection bias was the prevention of loss of follow-up. Information and interviewer bias during data collection pose a considerable risk in the context of a prospective cohort. This was controlled by training all participating investigators (the majority members of the residency program, as previously mentioned).

3 | RESULTS

The demographic characteristics of all patients with ARF are presented in Table 1, and Figure 1 shows a flow diagram with the number of patients at each stage of the recruitment phase. A total of 685 eligible patients were identified with respiratory difficulty, of which 296 developed ARF, for a calculated incidence of ARF of

TABLE 1 Demographic characteristics of ARF patients.

Variable	ARF *n* = 296 *n* (%)
Sex female	147 (49.7)
Age in years, median (IQR)	4.5 (0.47–7.43)
Age group	
Infant (<2 years)	135 (45.6)
Preschoolers (2–5 years)	74 (25.0)
School children (6–12 years)	52 (17.5)
Adolescents (13–18 years)	35 (11.8)
Presence of comorbidities	135 (45.6)
Neurological comorbidity	43 (31.9)
Respiratory comorbidity	73 (54.1)
Incomplete vaccination schedule	32 (11.1)
Environmental exposure smokers	44 (14.9)
Nutritional assessment	
Malnutrition[a]	48 (16.2)
Obesity	11 (3.7)

Abbreviations: ARF, acute respiratory failure; IQR, interquartile range.
[a]Classified according to Resolution 2465 of the Colombian Ministry of Health as less than −2 SD for weight for height in less than 5 years and body mass index for age in greater than 5 years.

TABLE 2 Clinical characteristics.

Variables	n = 296 n (%)
Etiology of ARF	
Asthma	81 (27.8)
Bronchiolitis	68 (23.4)
Pneumonia	45 (15.3)
Non-lung-related sepsis	10 (3.4)
Convulsive episode	12 (3.8)
Shock	12 (3.8)
Pediatric assessment triangle	
Stable	64 (21.6)
Potentially unstable	201 (67.9)
Unstable	31 (10.5)
RSV infection	56 (19.2)
SARS-CoV-2 infection	18 (6.19)
OTI	90 (30.4)
Average time of IVM in days, median (IQR)	9.57 (3.00–11.5)

Abbreviations: ARF, acute respiratory failure; IQR, interquartile range; IVM, invasive mechanical ventilation; OTI, orotracheal intubation; RSV, respiratory syncytial virus; SARS-CoV-2, severe acute respiratory syndrome-related coronavirus.

TABLE 3 Mortality.

	Person-year	Rate	CI
Mortality density rate	1.0	17.2	10.89–27.4
By sex			
Female	0.2	29.1	13.08–64.81
Male	0.8	14.3	8.16–25.30
By age group			
Infants	0.6	19.5	10.83–35.34
Preschoolers	0.07	13.52	1.905–96.03
School children	0.06	49.8	16.0–154.42
Teenagers	0.11	18.2	4.56–73.02

43.2%. In the ARF group, 49.7% were female (*n* = 147), with a median age of 4.5 years (interquartile range [IQR] = 0.47–7.43), and most patients were younger than 5 years of age (younger than 2 years *n* = 134, 45.3%; and 2–5 years *n* = 74, 25.0%). Effective follow-up was achieved in 88.9% (263) at 30 days and in 89.2% (264) at 60 days.

Regarding the patients' history, almost half of the ARF patients were reported to have comorbidities at the time of admission (*n* = 135, 45.6%), 54.1% (*n* = 73) were respiratory, and 31.9% (*n* = 43) were neurological. Additionally, 11.1% (*n* = 32) had an incomplete vaccination schedule, and 14.9% (*n* = 44) were reported to have had environmental exposure to smokers. Malnutrition was found in 16.2% (*n* = 48) of patients with ARF, and obesity was in 3.7% (*n* = 11) of patients.

Clinical characteristics of patients with ARF are shown in Table 2. At the time of ARF diagnosis, 21.6% (*n* = 64) of cases were considered stable (pediatric assessment triangle), 67.9% (*n* = 201) as potentially unstable, and 10.5% (*n* = 31) as unstable. The most frequent etiology was asthma exacerbation in 27.8% (*n* = 81). SARS-CoV-2 infection was documented in 6.2% of cases (*n* = 18). Ninety patients (30.4%) needed orotracheal intubation (OTI) and IMV for a median of 9.6 days of ventilation (IQR = 3.00–11.5).

Incidence of mortality during hospitalization was 6.1% (*n* = 18), with a mortality density rate of 17.2 (1.04 person/year). Mortality rates stratified by sex and age group are shown in Table 3. At 30 days after discharge, there were no deaths, and at 60 days, there was one death due to ARF (1.0%).

Supporting Information S1: Table 4 shows the variables included in the bivariate analysis. In the adjusted model for mortality, the factors that had a statistically significant relationship were a history of a neurologic comorbidity (RR = 8.02, 95% CI: [2.91–22.1], *p* = 0.001), a higher fraction of inspired oxygen at ARF diagnosis (RR = 1.03, 95% CI: [1.01–1.06], *p* = 0.001) and being unstable according to the pediatric assessment triangle (RR = 5.13, 95% CI: [1.44–18.20], *p* = 0.011, see Supporting Information S1: Table 1 in Supporting Information digital content).

For PICU length of stay, a significant relationship was found for patients between 2 and 5 years of age (hazard ratio [HR] = 1.75, 95% CI: [1.26–2.42], *p* = 0.001), environmental exposure to smokers (HR = 1.58, 95% CI: [1.11–2.26], *p* = 0.0011), and the presence of respiratory comorbidity (HR = 1.63, 95% CI: [1.19–2.24], *p* = 0.002; see Supporting Information S1: Table 2). The Kaplan–Meier survival estimate curve is presented in Supporting Information S1: Figure 1 (both in Supporting Information digital content).

Finally, the variables associated with OTI and IMV were obesity (RR = 1.73, 95% CI: [1.10–2.72], *p* = 0.017), an evaluation at ARF diagnosis as unstable according to the pediatric assessment triangle (RR = 2.19, 95% CI: [1.29–3.75], *p* = 0.004), and the presence of anemia at diagnosis of ARF (RR = 1.59, 95% CI: [1.07–2.36], *p* = 0.02). Other associations are shown in Supporting Information S1: Table 3 (in Supporting Information digital content).

4 | DISCUSSION

ARF is a common problem in PICU of a wide variety of causes and etiologies. This study was conducted at a high altitude. Physiologically, when the altitude is higher, the atmospheric barometric pressure decreases, which in turn decreases the partial pressure of oxygen (PO_2), causing tissue hypoxia or hypobaric hypoxia. Above 1500 masl, the carotid bodies detect the decrease in PO_2 in arterial blood, increasing the frequency and depth of respiration. Therefore, signs and symptoms vary in relation to altitude, which makes the diagnosis of respiratory diseases more difficult.[22,23] Although there is a described adaptive capacity for residents at high altitude, this relative hypobaric hypoxia is more relevant in pathologic conditions and in younger and older patients, just as in our cohort.[22]

The main findings regarding severity and mortality of ARF in this cohort were (a) a high incidence of ARF (43.2%), (b) the incidence of mortality in ARF (6.1%), (c) the frequency of neurologic comorbidities before ARF diagnosis and its relationship to mortality, (d) the main factors associated with IMV (obesity and the pediatric assessment triangle at time of ARF diagnosis), and (e) the main factors associated with PICU length of stay (exposure to smokers and age between 2 and 5 years of age).

4.1 | Incidence of ARF

The specific incidence of ARF has varied significantly in the literature, especially concerning the specific cause, but it can range from 1% to 4% when caused by acute respiratory distress syndrome.[9] In our cohort, the incidence of ARF was higher; however, there are several factors that may play a role in this finding. First, children with chronic diseases were treated at home and might have delayed consultation to avoid COVID infection, which can lead to a higher risk of complications, such as ARF, due to viral or bacterial infections, as well as the consequence of chronic diseases.[24,25] Pediatric care facilities considered nonessential or elective care shifted patient care protocols or were displaced to increase the capacity to attend to adult COVID patients.[25] On the other hand, during the 2020 pandemic, infectious causes of respiratory disease, and therefore ARF, decreased significantly as children stayed home from school and multiple safety protocols were implemented.[25] According to a study conducted during the first part of 2020 in China, there was a reduction in pediatric outpatient consults of 60% and 57% compared with the same period in 2018 and 2019, respectively.[26] Regarding the incidence of respiratory infections, they reported reductions of 66% and 59% compared with the incidences in 2018 and 2019, respectively.[26]

4.2 | Incidence of mortality in ARF

In the cohort, the mortality due to ARF was 6.1%. However, when comparing it to other mortality rates reported in the literature, it is highly variable since it is usually reported regarding a specific cause that led to the ARF. Nonetheless, it can range from 18% to 22%, according to some authors, even up to 51% with specific etiologies.[5,27] There are few studies in Latin America regarding the incidence of ARF mortality; however, our mortality rate might be lower than reported due to the unusual epidemiological characteristics during the COVID-19 pandemic. This may be related to an increase in the use of HFNC and in the high-quality standards of care for these patients, both of which have brought better results and decreased the mortality rate. However, further studies are required to confirm this.

4.3 | Neurologic comorbidity and mortality in ARF

As mentioned, the presence of a neurologic comorbidity previous to an ARF diagnosis was found to be relevant, especially in terms of mortality in ARF. It is important to mention that one of the institutions included in our study has a large volume of patients with neurological comorbidities; therefore, 32.0% of our patients had this condition. Previous studies have documented an increase in mortality in the presence of neurological comorbidity, this being one of the main causes of death in patients with ARF during the first 7 days of the disease.[27–29] Consequently, patients with a neurological comorbidity in our cohort had an OR of 9.12 for mortality in ARF.

4.4 | OTI and IMV

Regarding mechanical ventilation, the literature reports that OTI is among the most common procedures implemented in the PICU, necessary in approximately 30.0% (20.0%–60.0%) of patients.[30] This is important, as many of the patients admitted to the PICU who are intubated can have complications associated to IMV; an Australian prospective cohort study reported complications in 24% of 500 patients requiring respiratory support.[30] In our cohort, 30.4% of ARF patients required IMV, which correlates to that reported in previous studies.[30] As for the mean duration of mechanical ventilation, compared to previous reports with a duration varying from 2–7 to 21–28 days, our cohort reported a mean of 9.57 days of ventilation.[31] It has been well-described that obesity is an inflammatory state of malnutrition that can impact disease severity and outcomes, especially in adults.[32–34] In our cohort it was found to increase the risk of OTI and IMV (RR = 1.73, 95% CI: [1.10–2.72], $p = 0.017$). In other series, it has been shown to increase the time of OTI but not necessarily increase mortality in patients with ARI and ARF, such as in our cohort.[32] Moreover, within the model, patients' instability is a variable that proves to be statistically significant in relation to IMV and OTI (RR = 1.73, 95% CI: [1.10–2.72], $p = 0.017$), with an evaluation at ARF diagnosis as unstable (RR = 2.19, 95% CI: [1.29–3.75], $p = 0.004$). This has been documented from the initial evaluation of the patient with the pediatric assessment triangle, which allows a rapid evaluation of the patient's stage of physiological compromise to establish urgent treatment measures.[35]

4.5 | PICU length of stay

It has been well established that the need for PICU hospitalization significantly increases morbidity and mortality in pediatric ARF.[8,24,36,37] When analyzing age groups in our cohort, similarly to that reported previously, incidence of ARF and severity (measured PICU length of stay, HR = 1.75) was greater in children between 2 and 5 years of age.[7]

Finally, environmental exposure to smoking was found to increase the risk of greater PICU length of stay (HR = 1.58, 95% CI: [1.11–2.26], p = 0.0011). This relationship, although not directly explored in the literature, has been reported in relation to other respiratory outcomes.[38,39] Additionally, exposure has been related to a higher incidence of chronic respiratory symptoms, frequent respiratory infections, and the need for hospitalization.[38,39] Furthermore, the severity of respiratory infections, pneumonia, influenza, and asthma exacerbations has been associated with secondhand smoke exposure, mainly during infancy.[40–42] The specific relation to PICU length of stay has not been specifically described, but PICU length of stay is a measure of disease severity that is increased with tobacco exposure.[40–42]

5 | STRENGTHS AND LIMITATIONS

This study is part of a large multicentric cohort that had the privilege of observing different aspects of ARF during an unprecedented event, namely, the COVID-19 pandemic. Additionally, a study of respiratory disease at 2600 masl is rarely published in the literature. Nonetheless, the decrease in respiratory infections and thus the risk of ARF during most of 2020 and 2021 changed in many ways the usual characteristics of pediatric ARF. Regarding mortality, the logistic regression models were limited by the number of deaths observed in the cohort. Moreover, the three hospitals that were included are large high-volume reference pediatric centers where highly complex pathologies are treated. Thus, the behavior of mortality and severity, as well as the incidence of ARF, might differ when evaluating only respiratory infections that cause ARF.

For this study, a sample size calculation was made based on the documented incidence in the study institutions, as well as on the calculation of a sample that would allow associations to be made. A literature review was performed in search of factors documented as possible risk factors or predictors of severity in ARF and thus were included in the statistical models performed. We also used a universal definition of ARF based on the criteria of the American Heart Association. The study was conducted in Bogota. However, patients from the Roosevelt Institute, which sees patients from all over Colombia, were included. Despite the above, it is possible that the sample analyzed contains specific characteristics of a local population with a limited geographical scope. Results must be considered with this in mind. Even so, this population has conditions similar to those of populations in many other middle-income countries.

6 | CONCLUSIONS

ARF is a common cause of morbidity and mortality in children. The presence of a neurologic comorbidity before ARF diagnosis was associated with mortality. Obesity and being unstable, according to the pediatric assessment triangle, were associated with IMV. Finally, exposure to smoking and age between 2 and 5 were associated with greater PICU length of stay.

AUTHOR CONTRIBUTIONS

Catalina Vargas-Acevedo: Conceptualization; data curation; formal analysis; supervision; validation; writing—original draft. **Mónica Botero Marín**: Conceptualization; data curation; supervision; writing—original draft. **Catalina Jaime Trujillo**: Conceptualization; data curation; supervision; validation; writing—original draft. **Laura Jimena Hernández**: Data curation; formal analysis; writing—original draft; writing—review and editing. **Melisa Naranjo Vanegas**: Data curation; formal analysis; investigation; resources; supervision; validation; writing—original draft; writing—review and editing. **Sergio Mauricio Moreno**: Data curation; formal analysis; methodology; software; validation; writing—original draft; writing—review and editing. **Paola Rueda-Guevara**: Data curation; methodology; validation. **Olga Baquero**: Conceptualization; writing—original draft; writing—review and editing. **Carolina Bonilla**: Conceptualization; supervision; writing—original draft; writing—review and editing. **María L. Mesa**: Conceptualization; supervision; writing—original draft; writing—review and editing. **Sonia Restrepo**: Conceptualization; supervision; writing—original draft; writing—review and editing. **Pedro Barrera**: Conceptualization; supervision; writing—review and editing. **Luz M. Mejía**: Conceptualization; supervision; writing—original draft; writing—review and editing. **Juan G. Piñeros**: Conceptualization; funding acquisition; supervision; writing—original draft; writing—review and editing. **Andrea Ramírez Varela**: Conceptualization; formal analysis; funding acquisition; investigation; methodology; project administration; supervision; validation; writing—original draft; writing—review and editing. All authors have read and approved the final version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data sets used and/or analyzed during the current study are available from the corresponding author upon reasonable request. The authors confirm that the data supporting the findings of this study are available within the article. The corresponding author had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

ETHICS STATEMENT

This project was presented and approved by the institutional review boards at each of the three participating institutions (Institutional Ethics Board: Clínica Infantil Colsubsidio # 264-1, Fundación Santa Fe de Bogotá # CCEI 11815-2020 and 11899-2020, and Instituto Roosevelt # 2020041401-003). Written informed consent was obtained from all participants before study inclusion.

TRANSPARENCY STATEMENT

The lead author María L. Mesa affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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