Received: 23 November 2022 | Revised: 2 March 2023 | Accepted: 8 March 2023

DOI: 10.1002/hsr2.1182

ORIGINAL RESEARCH

Health Science Reports Open Access WILEY

Use of high-flow cannula in pediatric patients with respiratory failure: A prospective cohort study in three high-altitude hospitals

Natalia Ante-Ardila[1] | Camilo Novoa Garnica[1] | Paola Mora Umaña[1] | Olga Lucía Baquero Castañeda[2,3] | Alexandra Jiménez Cháves[3] | Melisa Sofía Naranjo[2] | Juan G. Piñeros[1,2,4] | Carolina Bonilla[2,4] | Luz M. Mejía[2,5] | María L. Mesa-Rubio[1,2] | Sonia Restrepo-Gualteros[2,4] | Pedro Barrera[2] | Sergio Moreno-Lopez[2] | Paola Rueda-Guevara[2] | Andrea Ramírez Varela[2] | FARA Group

[1]Department of Pediatrics, Universidad de los Andes, Bogotá, Colombia

[2]Faculty of Medicine, Universidad de los Andes, Bogota, Colombia

[3]Pediatrician Clínica Infantil Colsubsidio, Bogotá, Colombia

[4]Fundación Santa Fe de Bogotá, Bogota, Colombia

[5]Instituto Roosevelt, Bogota, Colombia

Correspondence

Natalia Ante-Ardila, Practice Center, Faculty of Medicine, Universidad de los Andes, Carrera 7# 116-05, fourth floor, Bogotá, Colombia.
Email: natalia.ante@hotmail.com

Funding information

Department of Pediatrics HU-FSFB; Universidad de los Andes

Abstract

Background and Aims: Acute respiratory failure (ARF) is a common cause of morbimortality, and a frequent reason for admission to the pediatric intensive care unit (PICU). It requires a high-flow oxygen device as treatment. Our aim is to determine the frequency and main indications for the use of high-flow nasal cannula (HFNC), and the prevalence of HFNC failure and its main causes, in three hospitals

Methods: It is a multicenter prospective cohort study, developed in three hospitals in Bogota. Eligible patients were children older than 1 month and younger than 18 years who presented ARF and required management with an HFNC. The study was carried out between April 2020 and December 2021. The follow-up was carried out at 1, 6, and 48 h after starting the management.

Results: Of 685 patients included in the study, 296 developed ARF. The prevalence of patients with ARF who required management with HFNC was 48%. The frequency of the pathologies that cause the ARF was: Bronchiolitis was the most frequent pathology (34.5%), followed by asthmatic crisis (15.5%) and pneumonia (12.7%). The average time of use of HFNC was 81.6 h. Regarding treatment failure with HFNC, 15 patients presented torpid evolution and required invasive mechanical ventilation, with a prevalence of therapeutic failure of the HFNC of 10.6%.

Conclusion: The use of HFNC is more frequent in patients with bronchiolitis, in children under 2 years of age and in males, which is in line with what has been reported in the literature. In addition, the failure rate of HFNC is low (10.6%), and it may be useful in other pathologies besides bronchiolitis, such as asthma, pneumonia,

among others. It opens the possibility to continue evaluating the role of HFNC in pediatric pathology in new studies.

KEYWORDS
critical care medicine, emergency medicine, pediatrics and adolescent medicine, respiratory medicine

1 | INTRODUCTION

Acute respiratory failure (ARF) is defined as a respiratory insufficiency, characterized by a diffuse lung injury of acute onset, which leads to increased pulmonary vascular permeability and loss of functional aerated lung tissue.[1] This is an important cause of morbidity and mortality in pediatric patients and hospitalization in a pediatric intensive care unit (PICU).[1–3] In the literature, it is reported as the main cause of cardiorespiratory arrest, and subsequent death, in the pediatric population.[4,5] Regarding its etiology, it is considered to have multifactorial origin, given the anatomic and physiological changes that occur throughout the pediatric age. Thus, there are microbiological, pathological, social, demographic, nutritional, and in-hospital factors, among others, that contribute to the risk of developing ARF.[6]

In the global literature, it is estimated that the prevalence of admissions to pediatric intensive care secondary to ARF is approximately between 2.4% and 2.7%. However, most studies have been conducted in developed countries.[3] In Colombia, a developing country, at the three hospitals where the study was carried out (Hospital Universitario Fundación Santa Fe de Bogotá [HUFSFB], Clínica Infantil Colsubsidio [CIC], Instituto Roosevelt [IR]), ARF is presented as a prevalent pathology, estimated to be between 7.8% and 9% of all the admissions to the PICU, which is higher than the world estimated prevalence. During 2018 at HUFSFB, 497 patients were admitted to the PICU. Half of these patients had respiratory failure, of which 85% required management with a high-flow nasal cannula (HFNC) and 9.7% with invasive mechanical ventilation (IMV). For the case of the CIC, in the same year, around 1545 patients were treated in the PICU, where 30% required mechanical ventilation and 43% were treated with an HFNC. At IR, for the year 2018, 1560 patients were treated in the PICU. Of these, 403 patients had respiratory failure (25%), 234 required support with an HFNC (15%), and 156 patients required mechanical ventilation (10%). As described in the world literature, ARF is one of the main causes of admission to PICU even in a developing country, such as Colombia.

It is important to carry out studies in cities at high altitudes since the effects of altitude on pulmonary physiology are known. At higher altitudes above sea level, the atmospheric pressure decreases, and, therefore, there is a reduction in the partial pressure of oxygen in the inspired air. This generates hypobaric hypoxia, which in turn causes alveolar hypoxia and hypoxemia.[7] Differences in pulmonary physiology at high altitudes can affect the clinical evolution of patients and their treatment, that is why more studies are required, both at sea level and at high altitudes, to determine adequate diagnostic and therapeutic methods.

On the other hand, the management of patients with ARF requires ventilatory support that can provide them a high-flow oxygen supply (invasive and noninvasive).[1,3–8] There are few high-altitude city studies about the indications and frequency of HFNC use in ARF in pediatric patients. Most studies on the use of high-flow cannula in pediatric patients have been carried out in developed countries, in sociodemographic and environmental contexts different from our local contexts. One study carried out in 2019, in Bogota, by Vásquez-Hoyos et al., concluded that ARF treatment with HFNC has a good clinical response, with few complications and a low failure rate.[9]

The aim of this study is to evaluate the prevalence of HFNC use in ARF in patients older than 1 month and younger than 18 years, in three hospitals in Bogota, located at an altitude of 2600 m above sea level. As well as to evaluate the most frequent causes of ARF that required the use of HFNC and to determine the frequency of HFNC failure therapy, defined as the deterioration of patient clinical status and the need for IMV after HFNC.

2 | MATERIALS AND METHODS

2.1 | Study design and data collection

This is a multicenter prospective cohort study, conducted in three hospitals in Bogota, Colombia: HUFSFB, IR, and CIC. Data collection was performed between April 2020 and December 2021.

2.2 | Inclusion and exclusion criteria

Patients between 1 month and 18 years of age with respiratory distress, defined as tachypnea, increased respiratory effort due to retractions and/or inadequate respiratory effort due to slow or agonal breathing. Patients admitted to the emergency department, hospital, PICU, and/or pediatric intermediate center were included. Of these patients, those presenting ARF, defined as failure of gas exchange manifested as hypoxemia or pump failure established by hypercapnia due to central depression, mechanical defect or fatigue, which leads patients to require treatment with a high-flow ventilation system to maintain adequate gas exchange.[10] Patients with ARF were considered to be those who had entered the study due to respiratory

distress, and who, despite being managed with a low-flow oxygen device (conventional nasal cannula), continued with clinical signs of respiratory distress (tachypnea, use of accessory muscles of respiration, nasal flaring), and/or low oxygen saturation (defined as less than 90% for the city of Bogotá, at an altitude of 2600 m above sea level). For our study, patients with ARF who received management with HFNC were chosen and followed-up.

Eligible patients and their families were invited to participate in the study. All participants were required to have an informed consent signed by their parents and/or legal guardian. In patients aged 8 years or older, in addition to the informed consent, there was an informed assent signed by the children, in which they agreed to participate in the study. The only exclusion criterion was an ongoing pregnancy, regardless of whether the patient had other chronic comorbidities, so we included all patients in the study, except those who were pregnant.

Patient information was collected in different surveys elaborated through the digital tool Koboo. These surveys recorded patient information and identified each patient with a unique assignment number. For our study, a first survey called "Moment 1," which identified patients with ARF, was evaluated (please see Supporting Information: Field 1). A second survey, called "Moment 2," was conducted, which followed-up at 1, 6, and 48 h after initiating management with a high-flow oxygen device (please see Supporting Information: Field 2).

The main sources of information were the clinical history, laboratory results, as well as information provided by the patient and/or caregiver.

2.3 | Variables

Among the variables selected we have dependent variables and independent variables. The dependent variables are respiratory failure classified as pulmonary and pump failure. Likewise, it was verified within these types of variables, if the patient presented signs of severe respiratory distress or respiratory failure and patients with altered respiratory function. The independent variables were taken from the clinical history of the patients, such as history, admission laboratories, images, use of airway devices, scales to predict ARF, admission diagnosis, stay in PICU, total hospital stay, among others.

These variables were chosen to determine those patients presenting ARF, their cause and their clinical and paraclinical status.

2.4 | Outcomes

The primary outcome assessed was the prevalence of HFNC use in patients presenting with ARF in the three hospitals.

As secondary outcomes, we estimated the frequency of the different etiologies requiring HFNC in the three hospitals. Likewise, we determined the frequency of HFNC failure, determined by the number of patients treated with HFNC who subsequently required IMV, and classified the etiologies of ARF that did not respond to treatment with HFNC between respiratory and non-respiratory causes.

2.5 | Analysis

The STATA technological tool (version 16; StataCorp LLC) was used for data analysis. For the analysis of the baseline measurements, which refers to the moment of detection of ARF in an eligible patient and corresponds to the first moment of application of the survey in any of the three institutions, descriptive statistics were used for all instrument variables collected during Moments 1 and 2. Quantitative variables were summarized using measures of central tendency and dispersion (i.e., mean) appropriate according to their distribution (i.e., normal or non-normal), and qualitative variables were presented using frequency tables and percentages over the total number of evaluable responses. A descriptive analysis of the sociodemographic and clinical variables was performed.

To estimate the prevalence of the use of HFNC in the management of ARF, the numerator corresponds to the number of ARF patients who were treated with HFNC, and the denominator is all ARF patients. To estimate the frequencies of clinical indications in patients with ARF treated with HFNC, the denominator is patients with HFNC, and the numerator corresponds to the number of ARF patients treated with HFNC with the same clinical indication. As many frequencies were calculated as clinical indications were observed in the cohort.

We also estimated the frequency of treatment failure with HFNC in the management of ARF at 48 h after hospital admission. We choose this follow-up period, because according to the literature, most children who do not have an adequate response with HFNC fail in the first 48 h.[11] The denominator of this measure corresponds to the number of eligible patients who developed ARF and were treated with HFNC during each patient's hospitalization period, and the numerator is the number of patients treated with HFNC who required IMV after the use of HFNC therapy.

2.6 | Bias

The standardized protocol and inclusion and exclusion criteria were followed to avoid different biases presented below:

- Selection bias: This arises when there are losses in the exposed groups, generating false associations between exposure and disease, since they may be underestimated or overestimated. To prevent this, follow-up activities and strategies such as surveys developed through Koboo tool were carried out. In cases of refusal to participate in the study, a "refusal form" was applied.
- Information bias: This type of bias occurs at the data collection stage, and produces a distorted estimated effect, either

measurement error or misclassification. To avoid this, all the researchers who participated in the data collection had training sessions before the start of the collection, to do it in a systematic and unified manner, avoiding errors. Likewise, the collected information was monitored and verified, in case of finding any inconsistencies.

- Interviewer bias: Occurs when the interviewer has not been adequately trained and therefore may induce some type of responses from the interviewee. To prevent this bias, the only persons trained to apply the surveys and the established tools to the patients and their relatives were the researchers. In addition, during the interview, most of the questions were closed, in such a way that the possibility of inducing the answer was reduced. On the other hand, random and programmed reviews of the application of the instruments with immediate feedback were performed.
- Voluntary participant bias: Occurs when the study participants agree to participate looking for some economic or material incentive, among others. In this study all participants did so voluntarily, without the use of any type of incentive, whether monetary or in-kind.
- Diagnostic suspicion bias: The clinician who knows that a patient has a prognostic factor of presumed importance may carry out more frequent or detailed searches for relevant prognostic results. The specific control of this bias is based on strict adherence to previously defined recruitment, inclusion, and exclusion criteria.

3 | RESULTS

The collaborative study of ARF (FARA), was conducted between April 1, 2020, and December 1, 2021, during the pandemic of COVID-19. In the sample, we completed 703 eligible patients; 14 of them rejected to participate in the study and 4 patients were duplicated. Finally, 685 patients with respiratory distress were included in the study. 296 of these patients developed ARF, and 142 patients required HFNC management with an estimated prevalence of 48% of the total patients who developed ARF (see Figure 1). In Colombia, every patient with HFNC has an indication to be managed in the PICU, so each of the patients who required management with HFNC was admitted to the PICU in this study.

SARS-CoV-2 infection was suspected, and tests were requested according to national guidelines. Since the study was carried out during the Covid-19 pandemic, in Colombia according to the guidelines of the Colombian National Ministry of Health, for the year 2020, before having access to vaccines in the country, a test of SARS-CoV-2 (antigen or polymerase chain reaction) to all patients with respiratory symptoms. After the application of the vaccine, the indication changed, a test was taken from all patients under 3 years of age, or over 60 years of age, or who were not in that age group but had some risk factor for severe disease (e.g., immunosuppression, asthma, lupus, obesity, hypothyroidism, among others), or who was not vaccinated with the full immunization schedule. Additionally, since the patients who entered the study all had respiratory distress, they all underwent a SARS-CoV-2 test, following the guidelines of

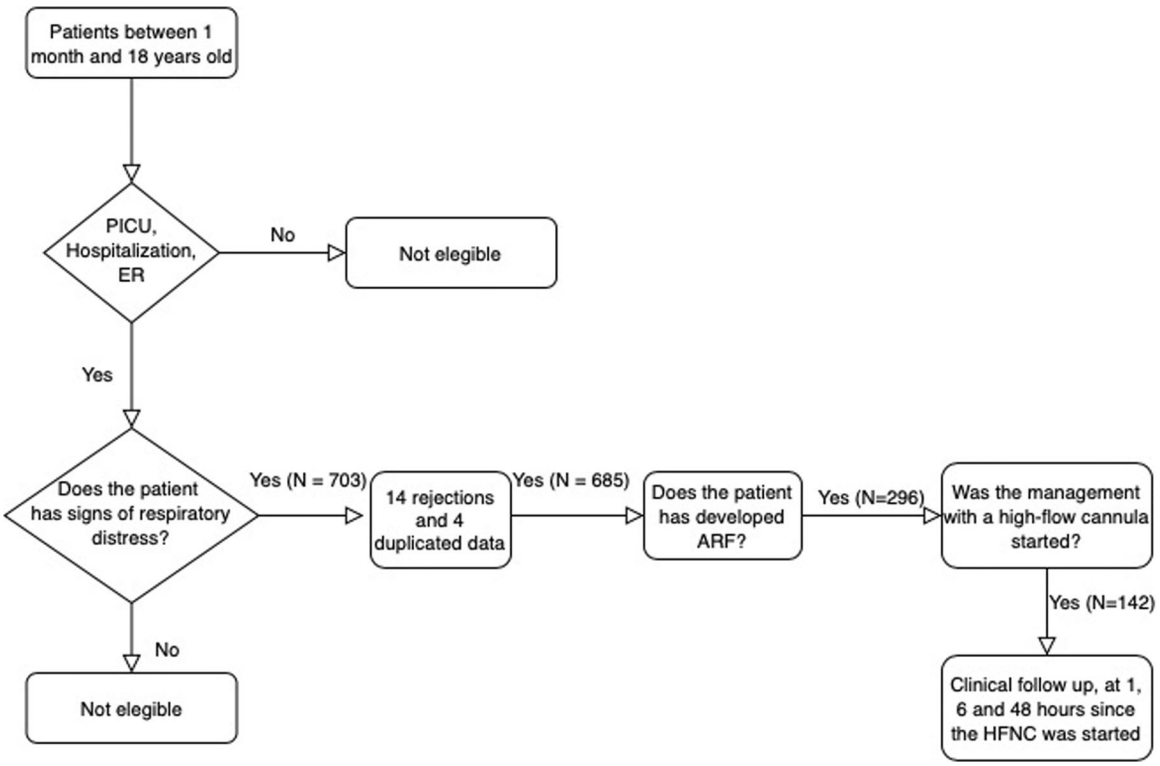

FIGURE 1 Patient eligibility flow-diagram. ER, emergency room; HFNC, high-flow nasal cannula; PICU, pediatric intensive care unit.

TABLE 1 Characteristics of patients who presented with ARF.

Variable	ARF *n* = 296
Sex female, *n* (%)	147 (49.6)
Age in years, median (IQR)	4.47 (0.47–7.43)
Age group, *n* (%)	
Infant (<2 years)	134 (45.3)
Preschoolers (2–5 years)	74 (25.0)
School children (6–12 years)	53 (17.9)
Teenagers (13–18 years)	35 (11.8)
Etiology of ARF	
Respiratory	238 (80.4%)
Neurological	23 (7.8%)
Cardiological	4 (1.3%)
Metabolic	3 (1.0%)
Other*	23 (7.8%)

Abbreviation: ARF, acute respiratory failure.

*Other: renal, hematological, rheumatologic, musculoskeletal, otorhinolaryngological.

each hospital. Out of the 685 patients with respiratory distress, 66 patients had confirmed SARS-CoV-2 infection.[12,13]

Of the total patients who developed ARF (296), 50.3% were male (149) and 49.6% female (147), the majority being under 2 years of age (45.2%), followed by preschoolers (25%), school children (17.9%), and adolescents (11.8%) (see Table 1). The prevalence of HFNC use in ARF in these hospitals was 48.0%. The patients requiring management with HFNC were male, at 55.6%, versus 44.4% of females. The age group with the highest frequency of high-flow cannula use was children under 2 years of age (58.4%), followed by patients 2–5 years of age (20.4%), in third place patients of 6–12 years of age (12%), and finally children 13–18 years of age (9.2%) (see Table 2).

There are different indications for the use of HFNC in pediatrics described in the literature, as hypoxemic ARF, preoxygenation in the orotracheal intubation, management after extubation, oxygen therapy during invasive procedures, ARF secondary to non-pulmonary disease, heart failure, and palliative care.[14,15] In our study the main cause of ARF corresponded to respiratory pathology (80.4%), with 19.4% corresponding to non-respiratory pathologies. The most frequent causes of ARF that required the use of HFNC were bronchiolitis (34.5%), asthmatic crisis (15.5%), and pneumonia (12.7%). Other etiology in patients with ARF treated with HFNC were suspected SARS-CoV-2 infection, status epilepticus, and pulmonary septic shock in 4.9% of cases. The average time of use of HFNC was 81.6 h (3.4 days).

On the other hand, the frequency of therapeutic failure of the HFNC in this study was estimated at 10.6%; where 15 patients required IMV after the use of HFNC. Of these patients, 53.3%

TABLE 2 Clinical characteristics and evolution in ARF patients treated with HFNC.

Characteristics	Total
HFNC therapy at the diagnosis of ARF	
Yes	142 (48.0%)
No	154 (52.0%)
Sex	
Male	79 (55.6%)
Female	63 (44.4%)
Age	
Age in years, median (IQR)	4.47 (0.47–7.43)
Age groups	
Infant (<2 years)	83 (58.4%)
Preschoolers (2–5 years)	29 (20.4%)
School children (6–12 years)	17 (12.0%)
Teenagers (13–18 years)	13 (9.2%)
Etiology in ARF patients treated with HFNC	
Bronchiolitis	49 (34.5%)
Asthma	22 (15.5%)
Pneumonia	18 (12.7%)
SARS-CoV-2 infection suspicion	7 (4.9%)
Septic shock of pulmonary origin	7 (4.9%)
Status epilepticus	7 (4.9%)
Crup	5 (3.5%)
Postsurgery status	4 (2.8%)
Urinary sepsis	2 (1.4%)
Septic shock of abdominal origin	1 (0.7%)
Other[a]	20 (14.1%)

Abbreviations: ARF, acute respiratory failure; HFNC, high-flow nasal cannula.

[a]Other: hematological, rheumatologic, musculoskeletal, otorhinolaryngological, neurological, oncological.

corresponded to respiratory pathology and 46.7% with non-respiratory pathology.

Finally, the cumulative incidence of mortality secondary to ARF during the study period corresponded to 7.4%, taking into account that of the total of 296 patients with ARF in the study, 22 died, and of the patients who died, 8 had been started on HFNC.

4 | DISCUSSION

ARF is a prevalent pathology, with an important cause of morbidity and mortality in pediatric patients and in those hospitalized in a PICU.[4,16] In our study, the prevalence of HFNC use in ARF was 48%,

similar to the prevalence found in the year 2018, before the pandemic in the same institutions. At the beginning of the pandemic, there was concern regarding the use of HFNC, since it is a system that could increase the generation of aerosols, it was feared that it could increase the nosocomial contagion of COVID-19, therefore it was recommended that these patients were managed in rooms with negative pressure and that all the staff had their complete personal protection elements.[17–19] However, in Colombia, at the three hospitals where the study was carried out, during the years 2020 and 2021, there were no negative pressure rooms for the management of HFNC in covid-positive pediatric patients, which could limit their use in the initial stage of the study, and could influence a change in the choice of respiratory support systems due to the nature of the virus, the shortage of devices, and the uncertainty regarding the contagion of personnel. When compared with the literature, studies conducted in adults, in China and Japan, in patients with covid-19 respiratory infection, who did not respond to management with a conventional nasal cannula, the high-flow cannula was the first-line oxygen device used. During the third wave of the pandemic, the use of HFNC in adults increased from 12% to 49% in Japan (a prevalence similar to that found in our study of 48%) and in China, it is estimated that up to 66% of adults required management with HFNC.[17,20,21]

During the COVID-19 period, there were several limitations, which implied mandatory isolations, causing children not to attend schools or kindergartens and thus decreasing the transmission of other viral infections (respiratory syncytial virus, influenza, among others). This could influence the prevalence of the different pathologies that caused ARF in our study, which differs from what is described in the literature, where respiratory viral infections are the main cause of ARF in children. Also, these years were characterized by a decrease in pediatric hospitalization, as evidenced by Kruizinga et al. in the multicenter analysis and by a review of the literature showing that some countries reported decreases in pediatric emergency admissions between 30% and 89%, as well as a decrease in respiratory infections between 52% and 98%.[22] In CIC hospital, the decrease in the number of patients admitted to the emergency department was 85% and in the hospitalization department 20.5%, for the same period of time compared to previous years.

ARF has a multifactorial etiology, being the most common etiology due to respiratory infections. It is estimated that there are more than 700 million cases of acute respiratory infection per year.[23,24] One of the risk factors for developing ARF is age. The world literature reports that age groups between 1 and 3 years have a higher risk of acquiring respiratory tract infections and developing ARF,[19] and this was evident in our study because the highest prevalence of respiratory failure was the age group under 2 years of age, followed by the group between 2 and 5 years of age.

The use of HFNC is important for the management of respiratory failure since it is an alternative oxygenation treatment thanks to the humidification, heating, and interface system used in it, with fixed flows and dynamic pressures that improve the clinical behavior of the patient and fundamental processes such as oxygenation and ventilation. People who lived at high altitudes are exposed to hypobaric hypoxia leading to chronic hypoxia, above 2500 m above level sea, barometric pressure and inspired oxygen pressure decrease and the result is alveolar hypoxia and hypoxemia; also the temperature and humidity are lower compared to people living above sea level, and wind and solar radiation are higher, which generates drier environments.[25] The potential benefit of high flow nasal cannula can be explained by the following mechanisms: decrease of anatomical dead space, a lower PEEP (Positive End Expiratory Pressure) that decreases alveolar collapse, decreases the use of accessory muscles, humidifies the airways, and improves mucus rheology, generates greater patient comfort compared to other noninvasive ventilation systems and significantly improves lung compliance [26]

Additionally, patients with HFNC present greater tolerance and comfort with evident improvement in their clinical evolution.[27–29] One of its main indications accepted in pediatrics is in the management of severe bronchiolitis, however, it could be useful in other causes of ARF.[28] HFNC is also considered a therapeutic option in multiple etiologies that cause ARF, such as asthma, pneumonia, and septic shock, among others. Although the indications for HFNC have been described, it is possible that more could exist.

The main objective of HFNC is to reduce the need for endotracheal intubation, a ventilatory assistance technique associated with different risks such as barotrauma, ventilator-associated pneumonia, and endotracheal trauma.[24,30,31] However, treatment with HFNC may have some complications such as the possibility of tension pneumothorax, epistaxis, and delayed the decision making of orotracheal intubation.[32]

This study found a higher frequency of use of HFNC in patients with bronchiolitis, in children under 2 years of age and male, which is in relation to what is reported in the literature.[9,15] There are few high-altitude city studies about the indications and frequency of HFNC use in ARF in pediatric patients. An observational study was conducted in Colombia and developed between 2013 and 2016, in which information was collected from a sample of patients between 1 month and 18 years of age who were admitted to the PICU with a clinical diagnosis compatible with respiratory failure that initially required support with HFNC. In that study, a follow-up was performed at baseline, 1, 6, and 24 h. Of the patients, 84.2% continued with HFNC at 24 h, and there was evidence of improvement in heart rate and respiratory rate over the hours. There was a therapeutic failure in 53 patients (9.8%, similar to the result that we obtained for HFNC failure of 10.6%); 21 were before 24 h and 35 were after this time, and it was evidenced that the initial respiratory rate is an independent predictor of failure.[27–29,33,34]

In Colombia, about 20% of the population (approximately 10 million people) live at altitudes between 2500 and 3500 m above sea level, a level classified as high altitude. As altitude increases, barometric pressure and inspired oxygen pressure decrease, resulting in a decrease in PaO_2, leading to a compensatory increase in ventilation with a decrease in $PaCO_2$. Consequently, the respiratory characteristics of children living at high altitude are likely to differ

from those described at sea level, so it is important to develop further studies in high-altitude cities regarding the use of HFNC.

This study is valuable because it shows the outcome of high-flow cannula use in three institutions during the COVID-19 pandemic, with a low failure rate. This opens the possibility of evaluating the role of high-flow cannula in other pathologies such as asthma and pneumonia and as therapeutic support, in patients without respiratory pathology.

The limitations of this study, as mentioned before, are based on the fact that it was developed during the COVID-19 pandemic years 2020 and 2021, which led to the lack of the respiratory peak of infections, that is usually recorded annually in the months of April, May, and June, and which further generated changes in viral circulation in the city and in the number of patients with acute respiratory infection and therefore risk of ventilatory failure. The use of high-flow cannula was also restricted during the initial pandemic stage, because it presents a high level of aerolization.

5 | CONCLUSIONS

The use of HNFC is more frequent in patients with bronchiolitis, in children under 2 years of age and in males, which is in line with what has been reported in the literature. In addition, the failure rate of HNFC in our study was low, and it may be useful in other pathologies besides bronchiolitis, such as asthma, pneumonia, and septic shock. In addition, we believe that our study opens the possibility of further evaluating the role of HFNC in pediatric pathology in future studies, including respiratory and non-respiratory etiologies. Given that most studies of HFNC have been conducted at sea level, this study, which was conducted in Bogotá, a city located more than 2600 m above sea level, it is one of the first studies of ARF and HFNC in a pediatric population in high-altitude cities.

AUTHOR CONTRIBUTIONS

Natalia Ante-Ardila: Conceptualization; data curation; formal analysis; investigation; methodology; supervision; validation; writing—original draft; writing—review & editing. **Camilo Novoa Garnica**: Conceptualization; data curation; formal analysis; investigation; methodology; writing—original draft; writing—review & editing. **Paola Mora Umaña**: Conceptualization; formal analysis; investigation; methodology; writing—original draft; writing—review & editing. **Olga Lucía Baquero Castañeda**: Conceptualization; formal analysis; funding acquisition; investigation; methodology; project administration; supervision; writing—original draft; writing—review & editing. **Alexandra Jiménez Cháves**: Data curation; formal analysis; writing—original draft; writing—review & editing. **Melisa Sofía Naranjo**: Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; software; supervision; validation. **Juan G. Piñeros**: Funding acquisition; project administration; resources; supervision; validation. **Carolina Bonilla**: Conceptualization; formal analysis; supervision; visualization. **Luz M. Mejía**: Conceptualization; investigation; methodology; project administration; supervision. **María L. Mesa-Rubio**: Conceptualization; supervision; validation. **Sonia Restrepo-Gualteros**: Conceptualization; investigation; supervision; validation. **Pedro Barrera**: Conceptualization; data curation; supervision; validation. **Sergio Moreno-Lopez**: Data curation; formal analysis; software; supervision; validation. **Paola Rueda-Guevara**: Conceptualization; data curation; formal analysis; supervision. **Andrea Ramírez Varela**: Conceptualization; formal analysis; funding acquisition; investigation; methodology; project administration; resources; software; supervision.

ACKNOWLEDGMENTS

We thank the entire work team of the FARA Group, the Hospital Fundación Santa Fe de Bogotá, Instituto Roosevelt, and Clínica Infantil Colsubsidio. We also thank the Universidad de los Andes, all the residents of the pediatrics program and our professor María Adelaida Córdoba. The study was funded by the specialization program in pediatrics at the Universidad de Los Andes, and the Department of Pediatrics at HUFSFB. The sponsors were not directly involved in the study, meaning that they had no role in the study design, data collection, data analysis, interpretation, analysis of the results, report writing, the decision to submit the report for publication, or publication of the article.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data supporting the findings of this study are available from the corresponding author upon reasonable request and through the supplementary documents. If you require the data, or if you wish to review the protocol, you can contact the author via email: natalia.ante@hotmail.com. The data set on which this paper is based is too large to be retained or publicly archived with available resources. Documentation and detailed methods of the FARA cohort, used to support this study are available from doi:10.3389/fped.2022.1009375.

ETHICS STATEMENT

The protocol was approved by the ethics committee of each hospital (Comité Corporativo de Ética de Investigación Fundación Santa fe de Bogota [CCEI-11815-2020]; Comité de ética en Investigación—Instituto Roosevelt [No 2020041101-003]; Comité de bioética Colsubsidio [264–1]). It was considered a low-risk study since no modification or intervention was made in the management received by the patient in clinical practice.

TRANSPARENCY STATEMENT

The lead author Natalia Ante-Ardila 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.

ORCID

Natalia Ante-Ardila http://orcid.org/0000-0002-3036-4062
Camilo Novoa Garnica http://orcid.org/0000-0002-9278-947X
Melisa Sofía Naranjo http://orcid.org/0000-0002-8794-2871

REFERENCES

1. Wolfler A, Calderini E, Iannella E, et al. Evolution of noninvasive mechanical ventilation use: a cohort study among Italian PICUs. *Pediatric Critical Care Med*. 2015;16(5):418-427.
2. Wong JJM, Loh TF, Testoni D, Yeo JG, Mok YH, Lee JH. Epidemiology of pediatric acute respiratory distress syndrome in Singapore: risk factors and predictive respiratory indices for mortality. *Front Pediatr*. 2014;2(Jul):16-19.
3. Friedman ML, Nitu ME. Acute respiratory failure in children. *Pediatr Ann*. 2018;47(7):e268-e273.
4. Yadav B, Bansal A, Jayashree M. Clinical profile and predictors of outcome of pediatric acute respiratory distress syndrome in a PICU: a prospective observational study. *Pediatric Critical Care Med*. 2019;20(6):e263-e273.
5. Wolfler A, Raimondi G, Pagan de Paganis C, Zoia E. The infant with severe bronchiolitis: from high flow nasal cannula to continuous positive airway pressure and mechanical ventilation. *Minerva Pediatr*. 2018;70(6):612-622. https://www.ncbi.nlm.nih.gov/pubmed/30334625
6. Leticia Yánez P, Michelangelo Lapadula A, Carmen Benavente R, Bettina Von Dessauer G, Marcos Emilfork S. Ventilación de alta frecuencia en infección respiratoria grave por VRS. *Rev Chil Pediatr*. 2010;81(3):221-227.
7. Penaloza D. Efectos de la exposición a grandes alturas en la circulación pulmonar. *Rev Esp Cardiol*. 2012;65(12):1075-1078.
8. Cavari Y, Sofer S, Rozovski U, Lazar I. Non invasive positive pressure ventilation in infants with respiratory failure. *Pediatr Pulmonol*. 2012;47(10):1019-1025.
9. Vásquez-Hoyos P, Jiménez-Chaves A, Tovar-Velásquez M, et al. Factores asociados al fracaso de la terapia con cánulas nasales de alto flujo en pacientes pediátricos con insuficiencia respiratoria en dos unidades de cuidados críticos pediátricos a gran altitud. *Medicina Intensiva*. 2021;45(4):195-204.
10. De Luca D, Piastra M, Chidini G, et al. The use of the Berlin definition for acute respiratory distress syndrome during infancy and early childhood: multicenter evaluation and expert consensus. *Intensive Care Med*. 2013;39(12):2083-2091.
11. Kang YS, Choi SM, Lee J, et al. Improved oxygenation 48 hours after high-flow nasal cannula oxygen therapy is associated with good outcome in immunocompromised patients with acute respiratory failure. *J Thorac Dis*. 2018;10(12):6606-6615. doi:10.21037/jtd.2018.10.110
12. Salgado FC, Socarras YF, Gallego MC. Lineamientos para el uso de pruebas diagnósticas para SARS-CoV-2 (COVID-19) en Colombia. *Minsalud*. 2020;9-18. https://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/VS/PP/ET/gips21-lineamientos-uso-pruebas-diagnosticas-sars-cov-2-covid19-2021.pdf
13. Vargas Muñoz SM, De Vivero Haddad S, Beltran AM, et al. Incidence, etiology, sociodemographic and clinical characterization of acute respiratory failure in pediatric patients at a high-altitude city: a multicenter cohort study. *Front Pediatr*. 2022;10:1009375.
14. Bradshaw ML, Déragon A, Puligandla P, Emeriaud G, Canakis AM, Fontela PS. Treatment of severe bronchiolitis: a survey of Canadian pediatric intensivists. *Pediatr Pulmonol*. 2018;53(5):613-618.
15. Masclans JR, Pérez-Terán P, Roca O. Papel de la oxigenoterapia de alto flujo en la insuficiencia respiratoria aguda. *Medicina Intensiva*. 2015;39(8):505-515. doi:10.1016/j.medin.2015.05.009
16. Divecha C, Tullu MS, Chaudhary S. Burden of respiratory illnesses in pediatric intensive care unit and predictors of mortality: experience from a low resource country. *Pediatr Pulmonol*. 2019;54(8):1234-1241. doi:10.1002/ppul.24351
17. Gupta S, Angurana SK, Kumar V. Respiratory care in children with COVID-19. *J Pediatr Intensive Care [Internet]*. 2021;1:3-5. doi:10.1055/s-0041-1723036
18. Vargas F, Saint-Leger M, Boyer A, Bui NH, Hilbert G. Physiologic effects of high-flow nasal cannula oxygen in critical care subjects. *Respir Care*. 2015;60(10):1369-1376.
19. Segovia B, Velasco D, Jaureguizar Oriol A, Díaz Lobato S. Terapia combinada en pacientes con insuficiencia respiratoria aguda: alto flujo por cánula nasal y ventilación mecánica no invasiva. *Arch Bronconeumol*. 2019;55(3):166-167.
20. Tomii K, Terada J, Chin K. Increased usage of the high flow nasal cannula in COVID-19 cases in Japan—from the online questionnaire survey by the Japanese Respiratory Society. *Respiratory Investigation*. 2021;59(5):666-669. doi:10.1016/j.resinv.2021.05.009
21. Agarwal A, Basmaji J, Muttalib F, et al. High-flow nasal cannula for acute hypoxemic respiratory failure in patients with COVID-19: systematic reviews of effectiveness and its risks of aerosolization, dispersion, and infection transmission. *Canadian J Anesthesia/J canadien d'anesthésie*. 2020;67(9):1217-1248 doi:10.1007/s12630-020-01740-2
22. Kruizinga MD, Peeters D, van Veen M, et al. The impact of lockdown on pediatric ED visits and hospital admissions during the COVID19 pandemic: a multicenter analysis and review of the literature. *Eur J Pediatr*. 2021;180(7):2271-2279.
23. Díaz-Lobato S, Alonso JM, Carratalá JM, Mayoralas S. High-flow nasal oxygen is not an oxygen therapy device. *Revista Portuguesa de Pneumologia (English Edition)*. 2017;23(1):51-52.
24. Kelly GS, Simon HK, Sturm JJ. High-flow nasal cannula use in children with respiratory distress in the emergency department. *Pediatr Emerg Care*. 2013;29(8):888-892.
25. Santos-Martínez LE, Gómez-Tejada RA, Murillo-Jauregui CX, Hoyos-Paladines RA, Poyares-Jardim CV, Orozco-Levi M. Exposición crónica a la altura. Características clínicas y diagnóstico. *Arch Cardiol Mex*. 2022;91(4):500-507. doi:10.24875/ACM.20000447
26. Mauri T, Turrini C, Eronia N, et al. Physiologic effects of high-flow nasal cannula in acute hypoxemic respiratory failure. *Am J Respir Crit Care Med*. 2017;195(9):1207-1215. doi:10.1164/rccm.201605-0916OC
27. Ali Mir A, A I, Fazili A, Iqbal J, Jabeen R, Salathia A. Prevalence and risk factor analysis of acute respiratory tract infections in rural areas of Kashmir valley under 5 years of age. *Int J Med Public Health*. 2012;2(3):47-52.
28. Moreel L, Proesmans M. High flow nasal cannula as respiratory support in treating infant bronchiolitis: a systematic review. *Eur J Pediatr*. 2020;179(5):711-718.
29. Kamit F, Anil M, Anil AB, Berksoy E, Gokalp G. Preemptive high-flow nasal cannula treatment in severe bronchiolitis: results from a high-volume, resource-limited pediatric emergency department. *Pediatr Int*. 2020;62(12):1339-1345.
30. Oto A, Erdoğan S, Boşnak M. Oxygen therapy via high flow nasal cannula in pediatric intensive care unit. *Turk J Pediatr*. 2016;58(4):377-382.
31. Wax RS, Christian MD. Practical recommendations for critical care and anesthesiology teams caring for novel coronavirus (2019-nCoV) patients. *Canadian J Anesthesia/J canadien d'anesthésie*. 2020;67(5):568-576. doi:10.1007/s12630-020-01591-x
32. Simioli F, Annunziata A, Polistina GE, Coppola A, Di Spirito V, Fiorentino G. The role of high flow nasal cannula in COVID-19 associated pneumomediastinum and pneumothorax. *Healthcare*. 2021;9(6):620. doi:10.3390/healthcare9060620
33. Ballestero Y, de Pedro J, Portillo N, Martinez-Mugica O, Arana-Arri E, Benito J. Pilot clinical trial of high-flow oxygen therapy in children with asthma in the emergency service. *J Pediatr*. 2018;194:204-210. doi:10.1016/j.jpeds.2017.10.075

34. Kawaguchi A, Yasui Y, Decaen A, Garros D. The clinical impact of heated humidified high-flow nasal cannula on pediatric respiratory distress. *Pediatric Critical Care Med*. 2017;18(2):112-119.

SUPPORTING INFORMATION

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

How to cite this article: Ante-Ardila N, Garnica CN, Umaña PM, et al. Use of high-flow cannula in pediatric patients with respiratory failure: a prospective cohort study in three high-altitude hospitals. *Health Sci Rep*. 2023;6:e1182. doi:10.1002/hsr2.1182