#### ORIGINAL RESEARCH

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# Burden of respiratory failure in pediatric patients: Analysis of a prospective multicenter cohort in Bogotá, Colombia

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#### Abstract

**Background and Aims:** The approach to the burden of disease is a demographic, economic, and a health problem, which requires the design and application of specific measures of cost of the disease, such as disability-adjusted life years (DALYs), to establish better public health policies in the pediatric population. The aim of this study is to approach the burden of disease in children with acute respiratory failure (ARF) through the calculation of DALYs.

**Methods:** This study was conducted in the framework of a prospective, multicenter cohort in Bogotá, Colombia. Inclusion criteria were all pediatric patients admitted to the emergency department, hospitalization, and intensive care unit with respiratory distress; eligible patients were all those who developed ARF between April 2020 and December 2021. They were followed-up during hospitalization, at 30 and 60 days after admission. The Infant/Toddler Quality of Life Questionnaire and KIDSCREEN quality of life scales were applied for follow-up according to the age group. The results were used to calculate DALYs

**Results:** Six hundred and eighty-five eligible patients, 296 (43.08%) developed ARF, of these 22 (6.08%) patients died (mortality rate = 7.43%). The total DALYs was 277.164 years. For younger than 9 years, the DALYs were 302.64 years, while for older than 10 years were 40.49 years.

**Conclusion:** ARF is one of the main causes of preventable mortality in pediatrics, its progression to respiratory failure is a highly prevalent condition in pediatric age, a condition that has a great impact on mortality, morbidity, and disability in our patients.

#### KEYWORDS

burden of disease, child mortality, disability-adjusted life years, respiratory failure, years of life potentially lost

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#### 1 | INTRODUCTION

Respiratory diseases are the most frequent cause of morbidity and mortality in the world, especially acute respiratory infection (ARI), responsible for nearly two million deaths each year.<sup>1-3</sup> In Colombia, ARI are among the three leading causes of death in children under 5 years of age, with viral ARI being responsible for 90% of ARI.<sup>4</sup> ARI encompasses a wide variety of conditions that can lead to acute respiratory failure (ARF), which is the leading cause of cardiorespiratory arrest and subsequent death in the pediatric population.<sup>5</sup> The incidence of ARF varies between 1.4 and 9.5 cases per 100. In pediatric patients with acute respiratory distress syndrome who develop ARF, there is an annual incidence of 2.3% of admissions to the pediatric intensive care unit (PICU) and a mortality between 2.4% and 3.4%.<sup>6</sup> In Colombia, for 2018, mortality due to ARI was 3.3 cases per 100,000 children, and the etiologic agent in more than 65% of cases was respiratory syncytial virus.<sup>4</sup> By 2019, more than 17,000 hospitalizations in the PICU for severe ARI were recorded.<sup>6,7</sup>

Since December 2019, there has been a change in the etiology of ARI, given the emergence and progression to pandemic of the new SARS-CoV-2 coronavirus.<sup>8-10</sup> The burden of disease by COVID-19 has not yet been established.<sup>11</sup>

Respiratory diseases represent an immense health burden worldwide. The literature shows that children admitted to PICU have increased morbidity, including decreased quality of life, and that the impact on parents in children receiving mechanical ventilation is significant.<sup>12</sup> Research is essential and increases understanding of disease processes to improve diagnosis and treatment.<sup>3,13</sup>

To measure the burden of disease, different indicators are implemented, such as the quality-adjusted life year for the costeffectiveness analysis of the health effect; the disability-adjusted life year (DALY), which measures the burden of disease suffered by a population due to established causes; the years of life lost (YLL), which measures premature death; and the years of life lived with disability (YLD).<sup>14</sup> The measurement of these indicators in a disease such as ARF will make it possible to measure the burden of disease and physical damage in units with which to evaluate the cost-effectiveness of health interventions. An analysis of DALYs from deaths due to respiratory failure disease will be carried out by analyzing variables through the application of scales such as the Infant/Toddler Quality of Life Questionnaire (ITQOL), which is the only generic measure of health status in children from 2 months to less than 8 years of age.<sup>15</sup> The KIDSCREEN scale is an instrument for measuring health-related quality of life and subjectively assessing the health and well-being of children over 8 years of age and adolescents.<sup>16</sup>

Respiratory diseases are a huge drain on resources, so in a low/middle-income country such as ours it becomes necessary to estimate the overall burden of disease from health-related quality of life and ARI mortality in children. Therefore, it is necessary to demonstrate the impact of ARI in Colombia to better understand the disease, prevent, diagnose, and treat patients with ARI and reduce the impact generated by this pathology in our pediatric population, which continues to have an impact on the Colombian health system.

#### 2 | METHODOLOGY

#### 2.1 | Cohort

The FARA (its acronym in Spanish) project was a multicentric cohort study conducted in three hospitals: Hospital Universitario Fundación Santa Fe de Bogotá, Clínica Infantil Colsubsidio, and Instituto Roosevelt, in Bogotá, Colombia, from April 2020 to December 2021. The objective was to estimate mortality and describe mortality risk factors, severity, mechanical ventilation in children, and approach the burden of disease in children with ARF. It was conducted as part of a supervised collaborative research initiative within the pediatrics residency program at Universidad de los Andes. The cohort study represents a significant contribution to the knowledge of high-altitude ARF, providing updated and accurate information that serves as a reference guide for its prevention, approach, and treatment in Colombia and in regions with similar contexts.

The investigators and coinvestigators identified candidate subjects to enter the study, verifying inclusion and exclusion criteria for entry into this study, applying informed consent, and filling out the data collection and patient follow-up forms.

Eligible patients were children older than 1 month and younger than 18 years with respiratory distress at the time of admission, either in the emergency room, hospitalization, or PICU of the three participating institutions. Eligible patients were asked to participate in the study, the informed consent form was filled out by their caregivers, and in patients with 8 years of age or older, it was also filled out by the patient. The only exclusion criterion for the study was teenage pregnancy.

#### 2.2 | Instruments

ARF was 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.<sup>17</sup> 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 above sea level). For our study, patients with ARF who received management with HFNC were chosen and followed-up. If the eligible patient developed ARF, data were collected from the moment they needed high-flow oxygen, 48 h later, and upon discharge from the institution. Follow-up to evaluate quality of life was done by a telephone call at 30 and 60 days after

discharge, through the application of two instruments according to the age of the patients: ITQOL for those under 8 years of age and KIDSCREEN for those who were older. All variables were collected from primary sources under four main categories: demographic variables, clinical variables during hospital stay and after hospital discharge, hemodynamic and laboratory variables, and oxygenation and ventilation variables.

To estimate DALYs associated with ARF in eligible patients, measurements related to incidence, mortality, and disability due to ARF were used, as well as quality of life indexes (i.e., KIDSCREEN and ITQOL scales of the instrument) previously calculated in the framework of this research. These scores were necessary for the calculation of the YLL and YLD. To calculate the YLL, the data from the deaths of individuals in the FARA cohort were used.

To calculate the YLD, the severity of the disabilities was weighted, taking into account the results of the follow-up of the patients 60 days after discharge from hospitalization, according to the impact of the disease on the physical environment (use of home oxygen, requirement of new hospitalizations) and social environment (absenteeism of the parents from their work activity and school absenteeism of the individual), as well as the results obtained from the ITQOL quality of life scales and KIDSCREEN. This allowed us to create disability severity categories and score them according to Global Burden of Disease study (GBD) of 2019. The scoring procedure used for the KIDSCREEN and ITQOL questionnaires were made following the steps described in the respective manuals for both questionnaires.<sup>15,18</sup>

#### 2.3 | Data analysis

The formulas needed to calculate these measures can be found in the original bibliography written by Murray.<sup>14</sup> Subsequently, an uncertainty analysis will be performed from a Monte Carlo simulation propagation to calculate the uncertainty intervals for each of the previously selected parameters. Finally, a global sensitivity analysis was carried out to identify the parameters that have the greatest contribution to generating uncertainty. With these values identified, the synthetic measurements were calculated.

The main bias in the study was the risk of selection bias, which is in direct relation to the attrition rate. This was controlled by following the standardized protocol, inclusion, and exclusion criteria; likewise, the researchers were governed by the procedure manual for the implementation of the study activities, which mainly helped to control information bias.

For the sample size and to answer the four research questions posed and achieve a confidence level of 95% and a statistical power of 80%, the openEpi program and the sample size formula for a proportion were used to calculate the sample size in each case; a p-value of less than 0.05 was considered statistically significant.

Data collection was performed using the Kobo toolbox data capture electronic application; STATA Version 17 (StataCorp LLC) was used to perform all statistical analyses.

#### 3 | RESULTS

#### 3.1 | Demographics

Within the FARA cohort, of the 685 eligible patients, 296 (43.20%) developed respiratory failure, and of these 22 (7.43%) patients died.

Of the deceased patients, 20 died during hospitalization and the corresponding data were completed up to the day of death; they were not followed-up at 30 and 60 days (2 of them died during follow-up for causes different from ARF). Of the 296 who developed respiratory failure, 263 follow-ups at 30 days and at 60 days from hospital discharge have been performed so far (Figure 1). The demographic features from eligible patients are found in Table 1.

Of the 22 deceased patients, 9 (40.91%) were female and 13 (59.09%) were male. The distribution by age group was as follows: Infants 59.09%, schoolchildren 22.73%, preschoolers 9.09%, and adolescents 9.09%. The main demographic features from this group are list in Table 2.

#### 3.2 | Burden of disease

Of the 296 patients who developed respiratory failure, 25.55% of the patients were discharged with home oxygen. During the 30-day followup after discharge from hospitalization, 47.97% continued with supplemental oxygen requirements. Since discharge, the average number of days of oxygen requirements was 18.87 days, with a maximum of 30 days and a minimum of 1 day, and during the 60 days follow-up, 15.71% continued with home oxygen.

Of the 263 patients at 30-day follow-up, 9.58% required a new hospitalization after the discharge; the main cause of hospitalization was a respiratory condition (36%) followed by cancer therapy 16.00%, urinary tract infection 12.00%, and seizures 8.00%. Regarding parental absenteeism from work, 37.78% had to be absent from work during the patient's hospitalization, 39.08% of the parents were not working during the hospitalization, and 24.14% did not have to abandon their activities. The average number of days absent from work was 19.65 days (SD = 21.96), with a maximum of 150 days and a minimum of 2 days. When analyzing the absenteeism from the school activities of the patients, it was found that 59.07% of the patients were not in school at the time of hospitalization, 24.32% of the patients had to miss school during hospitalization, and 16.60% did not have to be absent from school. The average number of days absent from school was 12.68 days (SD = 8.64), with a maximum of 30 days and a minimum of 1 day.

As shown in Table 3, from the 60-day follow-up, 8.43% required a new hospitalization; the main causes were 36.36% respiratory conditions, 22.72% cancer therapy, 18.18% seizures, and 13.63% urinary tract infection. Regarding parental absenteeism from work, 33.72% continued being absent from work during follow-up, 33.33% of the parents were not employed during follow-up, and 32.95% did not have to abandon their activities. The average number of days absent from work was 22.92 days (SD = 26.1), with a maximum of 150 days and a minimum of 2 days. When analyzing the absenteeism from the school activities of the patients, it was found that 28.68% continued to be absent from school at



FIGURE 1 Flowchart of number of patients followed in FARA cohort.

this point of follow-up, 51.94% of the patients were not at school, and 19.38% did not have to be absent from school.

In the population younger than 8 years, after the 60-day followup, the results for ITQOL score were the following: high health-rate quality of life (HRQoL) 51.33%, moderate HRQoL 42.96%, low HRQoL 5.70%. In the population older than 8 years, according to the interpretation of KIDSCREEN, 85.00% had a normal *t*-value, which means they have a high HRQoL, while 15.00% were below the threshold and were rated as low HRQoL (Table 4).

#### 3.3 | YLL, YLD, and DALY

The average YLL was 254.424 years, with a maximum of 635.222 years and a minimum of 6.242 years. The YLL adjusted by sex and death diagnosis are represented in Table 5.

Of the 13 patients who died due to respiratory failure itself, 8 had ARI (bronchiolitis 37.50%, pneumonia 37.50%, croup 12.50%, and infection by SARS-CoV-2 12.50%).

Of the 6 patients who died due to shock, the main cause was sepsis in 66.60%, other causes were hemorrhage and congenital heart disease.

Considering the results obtained in the 60-day follow-up for the two scores used, we calculated the individual YLD and the average for the complete group. The YLD was 22.74 years, with a minimum 0.64 and maximum 99.62 days. The YLD adjusted by sex and diagnosis are represented in Table 6.

The total DALYs was 277.164 years. For the population under 9 years the DALYs was 302.64 years, while for the population over 10 years the DALYs was 40.49 years.

#### 4 | DISCUSSION

ARF is considered one of the main causes of preventable mortality in pediatrics.<sup>19</sup> Infant mortality is underestimated compared to other age groups; mainly, the moments of adulthood and old age where there is a higher prevalence of mortality associated with cardiovascular,

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#### TABLE 1 Demographic features of eligible patients.

Characteristics	Eligible patients N = 296	Hight quality N = 135	Moderate quality N = 113	Low quality N = 15
Sex				
Female	147 (49.66%)	66 (48.80%)	45 (39.82%)	9 (60.00%)
Male	149 (50.34%)	69 (51.11%)	68 (60.17%)	6 (40.00%)
Age (years)				
Infant/toddler (<2)	135 (45.27%)	56 (41.48%)	54 (47.78%)	6 (40.00%)
Preschooler (2-5)	74 (25.00%)	25 (18.51%)	32 (28.31%)	3 (20.00%)
School-aged child (6-12)	52 (17.81%)	36 (26.66%)	24 (21.23%)	6 (40.00%)
Adolescent (13-18)	35 (11.82%)	18 (13.33%)	3 (2.65%)	-
Socioeconomic stratum <sup>a</sup>				
1	51 (17.23%)	20 (14.81%)	15 (13.27%)	6 (40.00%)
2	141 (47.64%)	31 (22.96%)	20 (17.69%)	2 (13.33%)
3	79 (26.69%)	15 (11.11%)	14 (12.38%)	4 (26.66%)
4	15 (5.07%)	35 (25.92%)	36 (31.85%)	3 (20.00%)
5	7 (2.36%)	20 (14.81%)	20 (17.69%)	-
6	3 (1.01%)	14 (10.37%)	8 (7.07%)	-
Recruitment place				
Intensive care unit	163 (55.07%)	13 (9.62%)	25 (22.12%)	9 (60.00%)
Emergency room	66 (22.30%)	34 (25.18%)	32 (28.31%)	3 (20.00%)
Intermediate care unit	43 (14.62%)	66 (48.88%)	15 (11.11%)	2 (13.33%)
Hospitalization	19 (6.42%)	22 (16.29%)	29 (21.48%)	1 (6.66%)
Other	5 (1.69%)	-	12 (8.88%)	-
Perinatal history**				
Negative perinatal history	35 (11.82%)	20 (14.81%)	15 (11.11%)	2 (13.33%)
Positive perinatal history	21 (7.09%)	15 (11.11%)	17 (15.04%)	3 (20.00%)
Hospitalization at NICU	10 (3.37%)	6 (4.44%)	20 (17.69%)	4 (26.66%)
OTI requierements	86 (29.05%)	25 (18.51%)	15 (13.27%)	3 (20.00%)
Respiratory distress syndrome	2 (0.67%)	9 (6.66%)	12 (8.88%)	2 (13.33%)
Supplementary oxygen	142 (47.97%)	60 (44.44%)	34 (30.08%)	1 (6.66%)
Comorbidities				
Yes	205 (69.25%)	45 (33.33%)	60 (53.09%)	10 (66.66%)
No	91 (30.74%)	90 (66.66%)	53 (39.20%)	5 (33.33%)
Neurological condition	43 (14.52%)	6 (13.33%)	9 (15.00%)	6 (60.00%)
Respiratory condition	73 (24.66%)	32 (71.11%)	32 (53.33%)	4 (40.00%)
Gastrointestinal condition	25 (8.44%)	2 (4.44%)	15 (25.00%)	-
Genetic condition	22 (7.43%)	1 (2.22%)	1 (1.66%)	-
Cardiiology condition	11 (3.71%)	3 (6.66%)	2 (3.33%)	-
Renal condition	8 (2.70%)	-	1 (1.66%)	-
Other	23 (7.77%)	1 (2.22%)	-	-

(Continues)

#### TABLE 1 (Continued)

Eligible patients N = 296	Hight quality N = 135	Moderate quality N = 113	Low quality N = 15
263 (88.85%)	128 (94.80%)	98 (86.72%)	6 (40.00%)
33 (11.14%)	7 (5.18%)	15 (13.27%)	9 (60.00%)
	Eligible patients N = 296 263 (88.85%) 33 (11.14%)	Eligible patients         Hight quality           N = 296         N = 135           263 (88.85%)         128 (94.80%)           33 (11.14%)         7 (5.18%)	Eligible patients         Hight quality         Moderate quality           N = 296         N = 135         N = 113           263 (88.85%)         128 (94.80%)         98 (86.72%)           33 (11.14%)         7 (5.18%)         15 (13.27%)

Abbreviations: NICU, neonatal intensive care unit; OTI, orotracheal intubation.

<sup>a</sup>Socioeconomic strata as defined by National Department of Statistics (DANE) of Colombia: 1 (very low) to 6 (high).

\*\*Perinatal history refers to all patient events after birth and during the first month of life.

**TABLE 2**Demographic features of deceased patients.

Characteristic	Frequency (n)	Percentage (%
Sex		
Female	9	40.91
Male	13	59.09
Age (years)		
Infant/toddler (<2)	13	59.09
Preschooler (2-5)	2	9.09
School-aged child (6–12)	5	22.73
Adolescent (13-18)	2	9.09
Socioeconomic stratum <sup>a</sup>		
1	4	18.18
2	12	54.55
3	1	4.55
4	3	13.64
5	1	4.55
6	1	4.55
Perinatal history <sup>b</sup>		
Negative perinatal history	11	50.00
Positive perinatal history	11	50.00
Hospitalization at NICU	6	27.27
OTI requirements	5	22.73
Respiratory distress syndrome	4	18.18
Supplementary oxygen	1	4.55
Comorbidities <sup>b</sup>		
Yes	14	63.64
Neurological condition	10	71.43
Respiratory condition	6	42.86
Gastrointestinal condition	6	42.85
Genetic condition	4	28.57
Cadia condition	3	21.43
Renal condition	3	21.43

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Characteristic	Frequency (n)	Percentage (%)
Other	2	14.28
No	8	36.36
Complete immunization status		
Yes	17	77.27
No	5	22.73
Death causes		
Acute respiratory insufficiency	13	59.09
Shock	6	27.27
Neoplasm	2	9.09
Meningitis	1	4.54

Abbreviations: NICU, neonatal intensive care unit; OTI, orotracheal intubation.

<sup>a</sup>Socioeconomic stratum as defined by National Department of statistics (DANE) of Colombia: 1 (*very low*) to 6 (*high*).

<sup>b</sup>There are cases in which a patient had more than one comorbidity or perinatal history, which is why the sum of subjects per category is greater than the total of subjects for comorbidity/perinatal history.

oncological, and external causes, occupy the first places in the global mortality analyses.  $^{\rm 13}$ 

In 2018 in Bogotá, the main causes of mortality in children under 1 year were respiratory disorders and congenital malformations; in children under 5 years the causes were congenital malformations followed by pneumonia; and between 5 and 18 years the main cause of death was cancer.<sup>20</sup> For this reason, acute respiratory insufficiency and its progression to respiratory failure is a highly prevalent condition in pediatric age, a condition that has a great impact on mortality, morbidity, and disability in our patients.

The main findings of this study are the characterization of the survival population and deceased population, and the calculation of YLL, YLD, and DALY according to age and sex.

We found an incidence of ARF of 43.20% and a mortality rate of 7.43%. These results emphasize the importance of prevention measures that have an impact on mortality; as a significant percentage of mortality was attributed to respiratory causes,

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<b>TABLE 3</b> Variables at 30 and 60 day follow-up.		
Patients who developed respiratory failure (n = 296)	30 day follow-up discharge from hospitalization	60 day follow-up discharge from hospitalization
Supplemental oxygen requirements at home	47.97%	15.71% continued with home oxygen
Average number of days of oxygen requirements	18.87	
	Maximum of 30 days and a minimum of 1 day	
Hospitalization after the discharge	9.58%	8.43%
	Main causes	Main causes
	Respiratory condition (36%)	Respiratory condition (36.36%)
	Cancer therapy 16.0%	Cancer therapy 22.72%
	Urinary tract infection 12.00%	Urinary tract infection 12.00%
	Seizures 8.00%	Seizures 8%
Parental absenteeism from work during hospitalization	37.78% during the patient's hospitalization	33.72% continued being absent
	39.08% of the parents were not working	33.33% of the parents were not employed
		32.95% did not have to abandon their activities
Absenteeism from the school activities of the patients at the time of hospitalization	59.07% of the patients were not in school	28.68% continued to be absent from school at this point
	24.32% of the patients had to miss school during hospitalization	51.94% of the patients were not at school
	16.60% did not have to be absent from school	19.38% did not have to be absent from school

these have a large socioeconomic impact, since the pediatric population has a high potential for productive life.

Analyzing the causes that impact premature mortality in populations and the causes that lead to living with disabilities are essential functions of public health.<sup>21</sup> In this study, these indices were calculated using the YLL and the YLD for the most relevant causes of ARF in the pediatric population belonging to the FARA cohort.

Before analyzing each of the aspects that make up DALYs, the demographic characteristics that could influence the outcomes of the disease were taken, such as age, sex, socioeconomic status, and the main causes that led to development of respiratory failure and causes of mortality.<sup>22</sup> Additionally, for deaths, comorbidities, prenatal history, and immunization status of patients were recorded. YLL represents death that occurs before reaching maximum life expectancy and measures the length of time lost due to premature mortality.<sup>23</sup> In Colombia, in a study published by Rojas et al. in 2020,<sup>24</sup> YLL for all causes for the population between zero and 19 years of age in women was 74.4 years, and in men it was 103 years. In our study, the rate of YLL was higher, with an increase of 74.50% and 55.60% for men and women, respectively. Women represent a total of 291.317 years of life potentially lost, while men 231.720, implying that women died at younger ages, contributing to more years lost.

In our study, the pathologies that most contribute to the loss of potential years of life were shock secondary to various pathologies (septic, hypovolemic, and cardiac shock) and ARF itself, ARI (bronchiolitis, pneumonia, and croup) being the main cause that led to respiratory failure.<sup>22</sup> It should be considered that 63% of the patients had some comorbidity, and this could influence the life expectancy of these patients. However, this analysis is not part of the objectives of our study.

The quality-of-life scales used, and the questions aimed at quantifying the impact on the family, on schooling, and recurrence of hospitalizations allowed us to classify the severity of the disability, in trying to cover different dimensions of a person's life.

Conducting this study during the COVID-19 pandemic allowed observation of different aspects of ARF during an unprecedented event, and it helps to understand the impact of this pandemic on pediatric patients. 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. The respiratory disease continues to be the main cause of ARF in this study, finding within this group the most frequent asthma, bronchiolitis, pneumonia, and given the current pandemic conditions, infection by COVID-19.<sup>22</sup> For each of them, the averages of YLD were established, with infection by COVID-19, pneumonia, and acute respiratory insufficiency the pathologies that contributed the most to the total YLD although obstruction of lower respiratory tract (bronchiolitis and asthma) contribute as well to the burden of YLD, because those pathologies were the most prevalent in the whole respiratory group. When differentiating by sex, we see that the results were very similar for

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 TABLE 4
 Results for ITQOL and KIDSCREEN score 60 days follow-up.

	Health-rate quality of life (HRQoL)
Younger than 8	ITQL score
years	High HRQoL 51.33%
	Moderate HRQoL 42.96%
	Low HRQoL 5.70%
Older than 8	KIDSCREEN score
years	85.00% had a normal t-value, which means they have a high health-rate quality of life, while
	15.00% were below the threshold and were rated as low HRQoL

Abbreviation: ITQOL, infant/toddler quality of life questionnaire.

**TABLE 5**Years of life lost, FARA cohort.

Variable	Frequency (n)	Individual YLL rate <sup>a</sup>
Sex		
Female	9	291.31
Male	13	231.72
Death diagnosis		
Acute respiratory insufficiency	13	294.11
Shock	6	343.24
Neoplasm	2	15.79
Meningitis	1	6.24

Abbreviation: YLL, years of life lost.

<sup>a</sup>Average YLL in years.

**TABLE 6** Years of life lost for disability, FARA cohort.

Variable	Frequency (n)	Adjusted YLD
Sex		
Female	66	21.33
Male	61	24.26
Diagnosis		
Bronchiolitis	40	18.88
Asthma	42	17.98
Acute respiratory infection	16	26.07
Pneumonia	18	22.76
COVID-19 infection	3	64.84
Others <sup>a</sup>	5	30.41

Abbreviation: YLD, years of life lived with disability.

<sup>a</sup>Others: Subglottic infection, tracheal diseases, diseases caused by other respiratory atypical microorganisms, foreign body, pulmonary hypertension. Average disability-adjusted life years (ADL). both men and women, with a total average of 24.6 and 21.3 years, respectively.

Even though in our study the percentage of patients affected by COVID-19 was low, having a COVID-19 infection did represent a significant burden in our population. There are currently few studies on the burden of disease from pediatric COVID-19 infection worldwide; however, in the same study by Rojas et al., the YLL for COVID-19 was calculated for 1000 inhabitants, with a YLL rate of 3.3 for children under 19 years.<sup>24</sup> When the last GBD report is analyzed in children under 9 years of age, lower respiratory infection is the second pathology that contributes the most to the percentage of DALYs in 11.60%, while asthma occupies the 19th position, with 0.50% of the percentage of DALYs in this age group.<sup>13</sup> Among the population aged 10-24 years, respiratory infections and asthma have a lower contribution to the percentage of DALYs worldwide (1.40% and 1.30%, respectively).<sup>13</sup> Extrapolating these results to our work was difficult because the few existing studies evaluate the overall disease burden without taking into account the different severity spectra, in this case it would be ARF, the intension from this study is to update the existing data on the burden of disease of these pathologies when they have the most severe presentation, that is. ARF.

The estimation of the DALYs for our study was performed using the YLL and the YLD determined by the deceased population during the duration of the study and the follow-up of the survivors at 60 days. The result of the DALYS for the population aged 0-9 and 10-19 was lower than expected compared to the GBD 2020 results. For the GBD, the value of a young adult within the family and society is highest in the third decade of life and the burden of the disease is greater if the disability occurs between 20 and 25 years, and less at the extremes of life.<sup>13</sup> However, in our study, for the population under 9 years of age, the DALYs were of greater magnitude than in older children and teenagers, which implies a greater burden of the disease in those under 9 years of age. This is probably due to the YLL, considering the life expectancy for the patient age group. Besides, most of our population with respiratory failure belonged to the group of infants and preschoolers who have a particular vulnerability to the development of respiratory pathologies secondary to lower lung compliance, as well as increased probability of airway obstruction due to secretions, inflammation, and foreign bodies, secondary to smaller airway dimensions and an immature immune system.<sup>25</sup>

While the average DALY was lower compared to that shown by other international studies, we must understand the impact that premature deaths and YLD have on the health needs of populations. Infant mortality shows the degree to which the right to life and health is exercised in a society.<sup>26</sup> It is an indicator of the availability, use, and access to health systems by the population and especially children, and also of their nutritional situation.<sup>26,27</sup> The fact that one of the main causes of death is respiratory disease, a preventable disease, makes it necessary to implement strategies and interventions to prevent and manage this disease properly. Improving access to health, hygiene conditions, adequate nutrition, and reducing exposure to air pollutants, among others, can reduce respiratory infections and their severity.

Some limitations found in our study include the events that were occurring at the time of collection; carrying out this study during the pandemic implied that the normal behavior of respiratory infections could be altered. Another limitation was the short follow-up time; we found that the follow-up time must be longer to be able to evaluate other outcomes that may occur in the long term due to this disability.

With the results obtained, we can conclude that despite the low mortality found in our study, mortality cases continue to have a very high socioeconomic cost and cause a great burden of disease. Followup of patients allows establishing a rapid recovery, but those who remain with sequelae of ARF have a high cost to the system and their caregivers. Finally, respiratory failure is an important cause of mortality, more than early disability, and within its multiple etiologies, viral infections have the highest impact both in direct mortality and in overall disease charge.

#### AUTHOR CONTRIBUTIONS

Laura Hernández-Corredor: Conceptualization; formal analysis; investigation; methodology; validation; writing-original draft; writing-review and editing. Rocio Plazas-Pachón: Conceptualization; formal analysis; investigation; methodology; supervision; writingoriginal draft; writing-review and editing. Fernanda Argote-Bolaños: Conceptualization; formal analysis; investigation; methodology; validation; writing-original draft; writing-review and editing. Pedro Barrera-Lopez: Conceptualization; investigation; methodology; project administration; supervision; writing-original draft; writingreview and editing. Melisa Naranjo Vanegas: Conceptualization; data curation; methodology; resources; software; validation; writingoriginal draft; writing-review and editing. Sergio Moreno-Lopez: Conceptualization; data curation; investigation; methodology; software; supervision; validation. Paola Rueda-Guevara: Conceptualization; data curation; investigation; methodology; software; supervision; visualization. Juan G. Piñeros: Methodology; project administration; resources; supervision; validation. Olga Lucía Baquero Castañeda: Project administration; resources; supervision; validation; writing-review and editing. Carolina Bonilla: Conceptualization; formal analysis; investigation; supervision; validation; writing -original draft. Luz M. Mejía: Conceptualization; formal analysis; investigation; methodology; supervision; validation; writing-original draft. María L. Mesa: Conceptualization; investigation; methodology; supervision; validation; writing-original draft. Sonia Restrepo-Gualteros: Conceptualization; investigation; methodology; supervision; validation; writing-original draft. Andrea Ramírez Varela: Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; software; supervision; validation; writing-original draft.

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#### CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

#### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author, Laura Jimena Hernández Corredor, upon reasonable request.

#### ETHICS STATEMENT

All the authors declare that the work submitted to *Health Science Reports* has been done in accordance to these guidelines and that it has been performed in an ethical and responsible way, with no research misconduct, including data fabrication and falsification, plagiarism, image manipulation, unethical research, biased reporting, authorship abuse, redundant or duplicate publication, and undeclared conflicts of interest. This study was approve by the ethical committee from all three participant institutions, as no risk study. All participants' parents filled out the informed consent form and, for those over 8 years of age, informed assent together with the consent form. All the author are willing to maintain the confidentiality of the peer review process and declare any competing interests.

#### TRANSPARENCY STATEMENT

The lead author Laura Hernández-Corredor 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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#### APPENDIX A

ITQOL score

# INFANT AND TODDLER QUALITY OF LIFE QUESTIONNAIRE (ITQOL-SF47) CUESTIONARIO SOBRE LA CALIDAD DE VIDA DE LOS BEBÉS Y NIÑOS PEQUEÑOS PARENT SHORT FORM – 47 SPANISH (COLOMBIA)

INSTRUCCIONES: Este cuestionario contiene preguntas sobre la salud física y emocional de su hijo pequeño o bebé. Sus respuestas personales se mantendrán bajo la más estricta confidencialidad. No hay respuestas correctas o incorrectas. Si no está seguro de cómo responder a una pregunta, por favor dé la mejor respuesta posible. Por favor responda a todas las preguntas. Por favor use tinta negra o azul.

Las marcas correctas: 🔳 🕱 🗹 🚍

SECCIÓN 1: LA SALUD EN GENERAL DE SU HIJO						
		Excelente	Muy buena	Buena	Regular	Mala
1.1	En general, diría que la salud de su hijo es:					

#### SECCIÓN 2: LAS CAPACIDADES FÍSICAS DE SU HIJO

2.1	Considerando su edad y sus capacidades, ¿ha estado limitado su hijo en alguna de las siguientes actividades a causa de problemas de salud o aprendizaje?	Sí, muy limitado	Sí, algo limitado	Sí, un poquito limitado	No, no ha estado limitado	Todavía no hace eso
	a. Tomar el tetero/ tomar el pecho/comer					
	b. Dormir					
	c. Agarrar algo					
	d. Darse la vuelta					
	e. Jugar					
	f. Dar pasos o caminar					

#### SECCIÓN 3: SATISFACCIÓN CON EL CRECIMIENTO Y DESARROLLO TOTAL DE SU HIJO

3.1	En general, ¿qué tan satisfecho está usted con:	Muy satisfecho	Algo satisfecho	Ni satisfecho ni insatisfecho	Algo insatisfecho	Muy insatisfecho
	<ul> <li>a. el crecimiento y desarrollo físico de su hijo (tal como la estatura o el peso)?</li> </ul>					
	<li>b. su desarrollo motor (tal como intentar alcanzar o agarrar algo, darse la vuelta, sentarse o caminar)?</li>					
	<li>c. su reacción hacia otros (tal como responder con una sonrisa, voltearse hacia el sonido de una voz familiar o responder a preguntas)?</li>					
	<li>d. su desarrollo lingüístico (tal como balbucear, hablar)?</li>					
	<ul> <li>su capacidad de aprendizaje o desarrollo cognoscitivo?</li> </ul>					

#### SECCIÓN 4: MOLESTIAS/DOLORES DE SU HIJO

4.1 Durante las últimas 4 semanas, ¿cuánto malestar o dolor (a causa de gases, dentición, lesión, enfermedad) ha tenido su hijo en alguna parte del cuerpo?

Ninguno	Poco	Regular	Mucho	Muchísimo

4.2 Durante las últimas 4 semanas, ¿con qué frecuencia ha tenido su hijo malestar o dolor en alguna parte del cuerpo?

Nunca	Algunas veces	Con cierta frecuencia	Con mucha frecuencia	Siempre

#### SECCIÓN 5: EL TEMPERAMENTO Y EL HUMOR DE SU HIJO

5.1	¿Cuánto tiempo, durante las últimas 4 semanas, su hijo:	Siempre	Casi siempre	Algunas veces	Casi nunca	Nunca
	a. ha estado menos activo que de costumbre?					
	b. ha estado irritado o molesto?					
	c. "no ha sido el mismo de siempre"?					
	d. ha estado alegre?					
	e. se ha enojado fácilmente?					
	f. ha estado alerta?					

- 2

#### ¿TIENE SU HIJO POR LO MENOS 1 AÑO DE EDAD O MÁS?

- NO (Pase a la página 4, sección 8)
- SÍ (Continúe aquí con la sección 6)

#### SECCIÓN 6: EL COMPORTAMIENTO GENERAL DE SU HIJO

6.1	¿Cuánto está usted de acuerdo/en desacuerdo con cada afirmación en relación a su hijo?	Totalmente de acuerdo	De acuerdo	No estoy seguro	En desacuerdo	Totalmente en desacuerdo
	<ul> <li>El comportamiento de mi hijo es a veces difícil de controlar.</li> </ul>					
	<li>Mi hijo parece portarse mal con más frecuencia que otros niños que conozco.</li>					
	<li>c. La gente me ha felicitado por el comportamiento de mi hijo.</li>					
	d. Otros se han quejado del comportamiento de mi hijo.					

6.2 En comparación con otros niños de su edad, diría usted que el comportamiento de su hijo es:

Excelente	Muy bueno	Bueno	Regular	Malo

#### SECCIÓN 7: SU COMPORTAMIENTO CON OTROS

7.1	¿Con qué frecuencia, durante las últimas 4 semanas, su hijo:	Con mucha frecuencia	Con cierta frecuencia	Algunas veces	Casi nunca	Nunca
	a. ha tenido un comportamiento difícil de controlar?					
	b. se ha llevado bien con otros niños?					
	c. ha tenido rabietas?					
	d. ha reaccionado de forma positiva a muestras de afecto?					
	e. se ha aislado?					
	f. se ha comportado acorde con su edad?					
	g. ha prestado atención o seguido instrucciones?					

#### SECCIÓN 8: LA SALUD DE SU HIJO

8.1	¿Qué tan cierta o falsa es cada afirmación en el caso de su hijo?	Absoluta- mente cierta	Bastante cierta	No estoy seguro	Bastante falsa	Absoluta- mente falsa
	<ul> <li>Parece que mi hijo es menos saludable que otros niños que conozco.</li> </ul>					
	b. Mi hijo no ha estado nunca gravemente enfermo.					
	<li>Cuando alguna enfermedad anda por ahí, mi hijo siempre se contagia.</li>					
	<ul> <li>Tengo la expectativa de que mi hijo tendrá una vida muy saludable.</li> </ul>					
	<ul> <li>Yo me preocupo por la salud de mi hijo más de lo que otra gente se preocupa por la salud de sus hijos.</li> </ul>					

#### ¿TIENE SU HIJO POR LO MENOS 1 AÑO DE EDAD O MÁS?

- NO (Pase a la página 5, sección 9)
- SÍ (Continúe aquí)

#### 8.2 En comparación con hace 1 año, ¿cómo calificaría la salud de su hijo ahora?

Mucho mejor ahora	Algo mejor ahora	Más o menos igual	Algo peor ahora	Mucho peor ahora
que hace 1 año	que hace 1 año	ahora que hace 1 año	que hace 1 año	que hace 1 año

#### SECCIÓN 9: EL EFECTO DE SU HIJO EN USTED

9.1	Durante las últimas 4 semanas, ¿CUÁNTA ansiedad o preocupación le ha causado a USTED cada uno de lo siguiente?	Ninguna en absoluto	Un poquito	Alguna	Bastante	Mucha
	a. La salud física de su hijo					
	<ul> <li>El bienestar emocional/el comportamiento/el temperamento de su hijo</li> </ul>					
	<ul> <li>La capacidad de aprendizaje o el desarrollo cognoscitivo de su hijo</li> </ul>					
	d. La capacidad de su hijo para interactuar con los demás					
9.2	Durante las últimas 4 semanas, ¿ha estado LIMITADO en el tiempo que USTED disponía para sus propias necesidades personales a causa de problemas con?		Sí, muy limitado	Si, bastante limitado	Sí, un poco limitado	No, nada limitado

necesidades personales a causa de problemas con ?	limitado	limitado	limitado	limitado
a. La salud física de su hijo				
<ul> <li>El bienestar emocional/el comportamiento/el temperamento de su hijo</li> </ul>				
<ul> <li>La capacidad de aprendizaje o el desarrollo cognoscitivo de su hijo</li> </ul>				
d. La capacidad de su hijo para interactuar con los demás				

9.3 A veces las familias pueden tener dificultades para que sus miembros se lleven bien unos con otros. Éstos no siempre se ponen de acuerdo y pueden enojarse. En general, ¿cómo calificaría la capacidad de su familia para llevarse bien unos con otros?

Excelente	Muy buena	Buena	Regular	Mala

1. Physical Activities and Health

#### APPENDIX B

Kidscreen, children's version

#### In general, how would you say your health is? 1. O excellent O very good Ogood O fair O poor Thinking about the last week... not at al slightly extremely noderately herv not at all derate slightly extremely very 2. Have you felt fit and well? 0 0 0 0 0 not at all noderate extremely Have you been physically active (e.g. light/ very 3. running, climbing, biking)? 0 0 0 0 0 not at all slightly moderately very extremely 4. Have you been able to run well? 0 0 0 0 0 Thinking about the last week .... very often always never seldom guite often seldom quite often very often always never 5. Have you felt full of energy? 0 0 0 0 0

### 2. General Mood and Feelings about Yourself

	Thinking about the last week					
	<u> </u>	not at all	slightly	moderately	very	extremely
	Hee year life heen enjoughte?	not at all	slightly	moderately	very	extremely
1.	has your life been enjoyable?	0	0	0	0	0
		never	seldom	quite often	very often	atways
		never	seidom	quite otten	very otten	amays
2.	Have you been in a good mood?	never	seidom	drare orreu	very otten	armays
	,	0	0	0	0	0
3	Have you had fun?	never	seldom	quite often	very often	always
σ.	nuvo you nuu nun:	<u> </u>	A 1	~	~	$\sim$

	Thinking about the last week					
		never	seldom	quite often	very often	always
4.	Have you felt sad?	never	seldom	quite often	very often	always
	nave jee len eas.	0	0	0	0	0
5.	Have you felt so bad that you didn't	never	seldom	quite often	very often	always
	want to do anything?	0	0	0	0	0
6.	Have you felt lonely?	never	seldom	quite often	very often	always
•.		0	0	0	0	0
7	Have you been happy with the way	never	seldom	quite often	very often	atways
	you are?	0	0	0	0	0
					JV	
3.	Family and Free Time		1.	VI		
			V			
	Thinking about the last week	<u></u>				
		never	seldom	quite often	very often	always
	Have you had enough time for	never	seldom	quite often	very often	always
1	yourself?	0	0	0	0	0
	Have you been able to do the things	never	seldom	quite often	very often	always
2.	that you want to do in your free time?	0	0	0	0	0
~	Have your parent(s) had enough time	never	seldom	quite often	very often	always
3.	for you?	0	0	0	0	0
4	Have your parent(s) treated you fairly?	never	seldom	quite often	very often	always
	nave your parent(s) realed you raily.	0	0	0	0	0
5	Have you been able talk to your	never	seldom	quite often	very often	always
υ.	parent(s) when you wanted to?	0	0	0	0	0
	Have you had enough money to do	never	seldom	quite often	very often	always
0.	the same things as your friends?	0	0	0	0	0
7	Have you had enough money for your	never	seldom	quite often	very often	always
1.	expenses?	0	0	0	0	0

## 4. Friends

	Thinking about the last week					
		never	seldom	quite often	very often	always
1.	Have you spent time with your	never	seldom	quite often	very often	always
	friends?	0	0	0	0	0
2	Have you had fup with your friends?	never	seldom	quite often	very often	Always
۷.	have you had full with your menus?	0	0	0	0	0
2	Have you and your friends helped	never	seldom	quite often	very often	always
э.	each other?	0	0	0	0	0
	Have you been able to rely on your	never	seldom	quite often	very otten	always
4.	friends?	0	0	0	0	0
5.	School and Learning	<b>P</b> not at all	slightly	moderately	Very	extremely
1		not at all	slightly	moderately	very	extremely
1.	Have you been happy at school?	0	0	0	0	0
-	Line of the second second second	not at all	slightly	moderately	very	extremely
2	Have you dot on well at school?					

	Thinking about the last week						
		never	seldom	quite often	very often	always	
3.	Have you been able to pay attention?	never O	seldom	quite often	very often O	always O	
4.	Have you got along well with your teachers?	never O	seidom O	quite often O	very often O	always	

Kidscreen, parents' version

#### 1. Physical Activities and Health In general, how would your child rate her/his health? 1. O excellent O very good O good O fair O poor Thinking about the last week ... not at all slightly moderately extremely very moderately not at all slightly very extremely 2. Has your child felt fit and well? 0 0 0 0 0 extremely not at all Has your child been physically active slightly derals very 3. (e.g. running, climbing, biking)? 0 0 0 0 0 lis to fon slightly extremely moderately very Has your child been able to run well? 4. 0 0 0 0 0 Thinking about the last week ... seldom always never quite often very often seldom guite often never very often always 5. Has your child felt full of energy? 0 0 0 0 0

## 2. General Mood and Your Child's Feelings

	Thinking about the last week	not at all	slightly	moderately	very	extremely
1.	Has your child felt that life was enjoyable?	not at all	slightly O	moderately O	very O	extremely O
	Thinking about the last week	never	seldom	quite often	very often	always
2.	Has your child been in a good mood?	never O	seldom O	quite often	very often O	ahvays O
3.	Has your child had fun?	o	seldom	quite often	very often	ahvays O

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	Thinking about the last week					
		never	seldom	quite often	very often	always
	Hee your shild fall and?	never	seldom	quite often	very often	always
4.	has your child feit sad?	0	0	0	0	0
-	Has your child felt so bad that he/she	never	seldom	quite often	very often	always
5.	didn't want to do anything?	0	0	0	0	0
6	Has your shild falt longly?	never	seldom	quite often	very often	always
•.	has your child felt lonely?	0	0	0	0	0
7	Has your child been happy with the	never	seldom	quite often	very often	always
1.	way he/she is?	0	0	0	0	0

# 3. Family and Your Child's Free Time

	Thinking about the last week	<u></u>	1		1	
		never	seldom	quite often	very often	always
	Has your child had enough time for	never	seldom	quite often	very-often	always
- <u>-</u> -	him/herself?	0	0	0	0	0
	Has your child been able to do the		reliam	mile chen	very often	alama
2.	things that he/she wants to do in his/her free time?	0	0	0	0	0
3.	Has your child felt that his/her	DEVER	seldom	quite often	very often	always
	parent(s) had enough time for him/her?	0	0	0	0	0
	Has your child felt that his/her	never	seldom	quite often	very often	always
4.	parent(s) treated him/her fairly?	0	0	0	0	0
	Has your child been able to talk to	0.004	reliam	mile often	very often	always
5.	his/her parent(s) when he/she wanted to?	0	0	0	0	0
	Has your child had enough money to	never	seldom	quite often	very often	always
6.	do the same things as his/her friends?	0	0	0	0	0
-	Has your child felt that he/she had	never	seldom	quite often	very often	always
7.	enough money for his/her expenses?	0	0	0	0	0

	Thinking about the last week					
		never	seldom	quite often	very often	always
1.	Has your child spent time with his/her friends?	never O	seldom O	quite often O	very often O	always O
2.	Has your child had fun with his/her friends?	o	seldom O	quite often	very often	Always O
3.	Have your child and his/her friends helped each other?	O	seldom O	quite often	very often O	ahrays O
4.	Has your child been able to rely on his/her friends?	never O	seidem O	quite often	very atten	always O
			V			

# 5. School and Learning

-	Thinking about the last week					1.1
		not at all	slightly	moderately	very	extremely
1.	Has your child been happy at school?	not at all	slightly	moderately O	very	extremely O
2.	Has your child got on well at school?	not at all	slightly O	moderately O	Very	extremely O

	Thinking about the last week	]				
		never	seldom	quite often	very often	always
3.	Has your child been able to pay attention?	never O	seldom O	quite often	very often O	ahvays O
4.	Has your child got along well with his/her teachers?	never O	seldom O	quite often O	very often O	always O