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# The deadly impact of COVID-19 among children from Latin America: The case of Ecuador

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**Background:** The SARS-CoV-2 pandemic remains a critical global health concern, with older adults being the most vulnerable group. Nonetheless, it is crucial to recognize that COVID-19 has caused numerous deaths in children worldwide. Emerging evidence indicates that infants and breastfeeding children, particularly those aged below one year, face a greater risk of hospitalization and mortality than older children with COVID-19.

**Objective:** This study aimed to describe the epidemiology of COVID-19 among children during the early phase of the pandemic in Ecuador.

**Methods:** We conducted a country-wide population-based analysis of the epidemiology of COVID-19, using incidence and mortality data reported from Ecuador between February 15, 2020 and May 14 2021. Measurements of frequency, central tendency, dispersion, and absolute differences were calculated for all categorical and continuous variables.

**Results:** At least 34,001 cases (23,587 confirmed cases, 5,315 probable and 5,099 suspected) and 258 COVID-19 related deaths have been reported among children in Ecuador during the first 16 months of the pandemic. The overall incidence rate was 612 cases per 100,000 children, the mortality rate was 3 per 100,000, while the case fatality rate was 0.76%. The highest risk group for infection was children and adolescents between 15 and 19 years of age; however, the highest mortality rate occurred in children under one year of age. The largest provinces, such as Pichincha, Guavas and Manabí, were the ones that reported the highest number of cases, 27%, 12.1% and 10.8%, respectively.

**Conclusions:** This study is the first to report on COVID-19 epidemics among children in Ecuador. Our findings reveal that younger children have a lower risk of SARS-CoV-2 infection, but a higher risk of mortality compared to older children and adolescents. Additionally, we observed significant disparities in infection rates and outcomes among children living in rural areas, those with comorbidities, and those from indigenous ethnic groups.

## KEYWORDS

COVID-19, SARS-CoV-2, children, pediatric population, adolescent, epidemiology, latinamerica, Ecuador (country)

# 1. Introduction

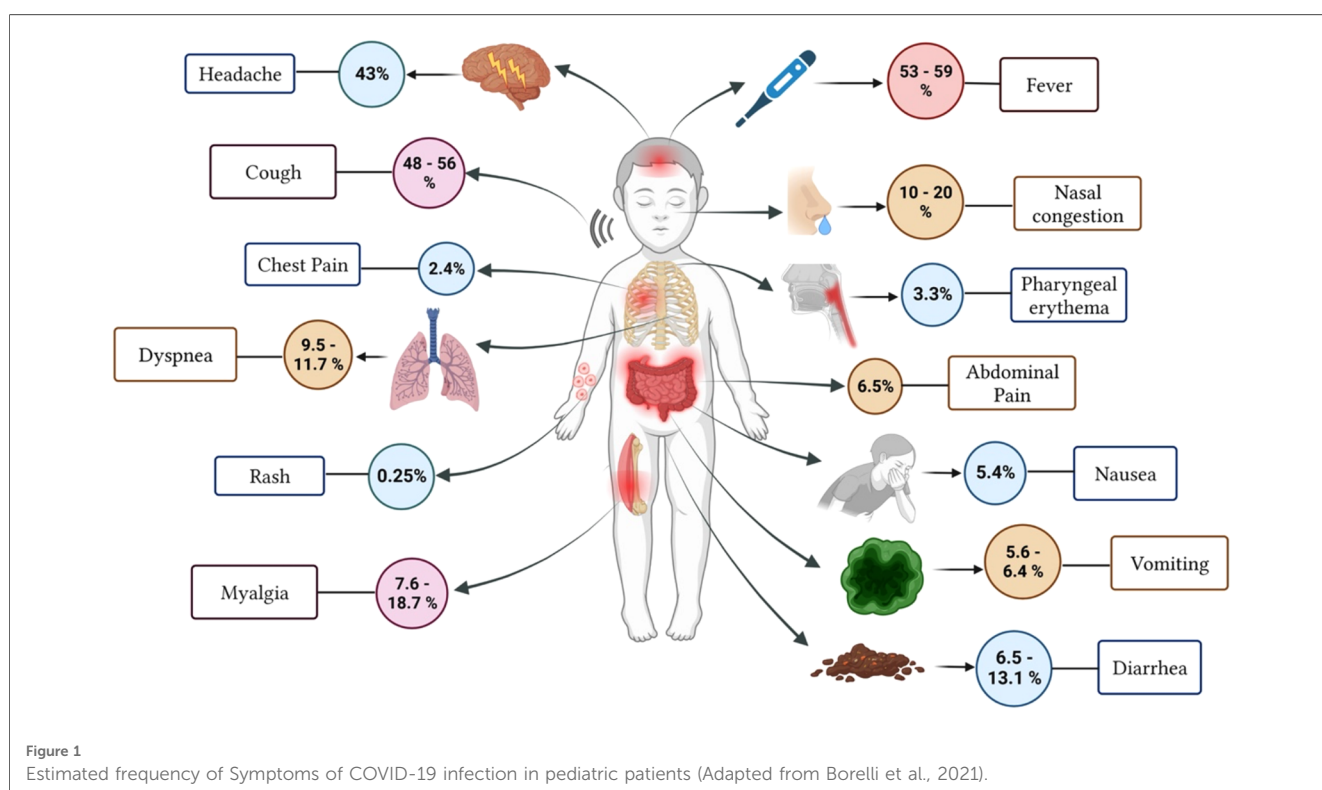
Since December 2019, at least 658 million cases and arguable more than 6.6 million deaths have been attributed to the SARS-CoV-2 virus (1-5). In the early phase of the pandemic, we learned that the most affected populations were the elderly, those with comorbidities, and those with adverse social determinants (6). However, with the deployment of vaccines, the unvaccinated and those with incomplete vaccination schemes became the most affected population in terms of severity and mortality (7). While there are increasing reports globally on the effects of COVID-19 among children and adolescents, there is still limited knowledge on the impact of the disease on children in developing countries (8).

Since the first pediatric case of COVID-19 was reported on January 20, 2020 in China, there have been numerous reports worldwide attempting to address the issue of COVID-19 among this population (9-11). Evidence suggests that, in comparison to older populations, children are less likely to die from COVID-19, exhibit significantly lower case fatality rates, experience milder symptoms, and have a quicker recovery time than adults (12-15). Nonetheless, children comprise between 1% and 2% of the overall pool of positive cases and 0.4% of the total number of COVID-19 related deaths worldwide (16). Although current literature confirms that among adults, the proportion of deaths is equal between men and women, deaths are more likely to occur in men. In children, however, it seems like younger female children might have a slightly higher risk of dying and a consistent positive correlation between age and the likelihood of getting COVID-19 (17-19).

According to Patel's et.al systematic review, there is an increased risk of illness among older children, although mortality rates decrease as the child enters adolescence (19). Viner et al., 2021, reported that children without symptoms made up anywhere from 14.6% to 42% of the studied population (20). The most prevalent symptoms were also fever, varying from 46% to 64.2% and cough, from 32% to 55.9% (20). The frequency of all other symptoms and indicators, such as rhinorrhea, headache, fatigue/myalgia, and gastrointestinal problems including diarrhea and vomiting, represented from 10% to 20% of the pediatric population (20) (Figure 1).

In terms of mortality rates, children are less likely to develop severe cases, nevertheless, reports worldwide vary from 0.1% up to 1% (21, 22). Data suggest that newborns and children, especially those under one year of age are more likely to develop severe disease (21, 22). Like adults, children with comorbidities have a higher risk for developing symptomatic COVID-19 infection and have poorer prognosis than healthy children. Shekerdemian et al. (2020) found that 40 out of 48 children who required life support within the pediatric intensive care unit (PICU) had underlying conditions (genetic abnormalities, immunosuppression, cancer, malignancy, other congenital heart disease, obesity and chronic kidney diseases) (23). The epidemiological, sociodemographic, and clinical features of children with COVID-19 are known within the develop world; however, very few investigations involving children from low and middle-income countries, particularly from Latin America have been published.

The objective of this study was to describe the epidemiology of COVID-19 among Ecuadorian children.



## 2. Methodology

### 2.1. Study design

We conducted a country-wide population-based analysis of the epidemiology of COVID-19 among children from 0 to 19 years of age.

### 2.2. Setting

The study was conducted in Ecuador, a country located in South America, bordering with Colombia to the North, Peru to the South/East and the Pacific Ocean to the West. The 2020 population projections estimated a total of 17.5 million people for 2020, having a pediatric and adolescent population of 5.9 million (24).

### 2.3. Data sources and description

A country-wide comparison of the data from the 24 provinces and 221 cantons was performed using the complete dataset from the Ministry of Public Health's national databases on overall mortality and hospital discharge data from February 2020 to May 2021. The 2020 population census data from the National Institute of Census and Statistics (INEC) were used to compute age and sex adjusted rates.

All cases of COVID-19 were classified according to the International Classification of Diseases 10th Revision (ICD-10). ICD-10 codes reflecting intentional self-harm (U07) were included in the analysis.

Cases were identified according to guidelines from the Ministry of Public Health, which define three categories of cases.

A case was identified as confirmed by a positive RT-PCR test, regardless of symptoms, or a positive rapid antigen detection test and meeting the criteria for a probable or suspected case. This included asymptomatic or symptomatic individuals who have had contact with a confirmed or probable case and test positive.

A case was defined as probable when a person met the clinical criteria for a suspected case and had been a contact of a confirmed or probable case, had imaging findings suggestive of COVID-19 disease, had recent onset of anosmia or ageusia or respiratory symptoms without another explanation, or has unexplained death with respiratory distress and had contact with a confirmed or probable case or were linked to an identified COVID-19 cluster.

A suspected case was identified by meeting the clinical criteria, including an acute onset of fever and cough, as well as three or more of several other symptoms such as headache, sore throat, or gastrointestinal symptoms. The epidemiological criteria included residing or working in an area with a high risk of virus transmission, having high-risk contact with a confirmed or probable case of COVID-19, traveling to a country with community transmission, or working in a healthcare facility.

The presence of comorbidities was assessed based on the diseases and conditions reported by patients, including but not

limited to: arterial hypertension, chronic kidney disease, asthma, diabetes, chronic hepatic disease, psoriasis, cancer, chronic vascular disease, COPD, rheumatoid arthritis, tuberculosis, hepatic cirrhosis, pulmonary fibrosis, obesity, and hypothyroidism.

### 2.4. Data analysis

The overall incidence and mortality rate, as well as age and sex specific case fatality rate (CFR) percentage were computed according to the entire children and adolescent population at risk (by canton and province). Measurements of frequency (counts, absolute and relative percentages), central tendency (median), dispersion (interquartile range) and absolute differences were calculated for all categorical and continuous variables using a methodology previously reported (25). In our study, we computed the CFR by using the number of cases officially reported as COVID-19 related deaths.

In our analysis, we considered deaths as a binary variable, meaning that individuals were categorized as either alive or dead. We used this variable as an outcome to calculate the CFR percentage, which is determined by dividing the number of deaths reported as COVID-19 related by the number of confirmed COVID-19 cases.

We used two-pronged approach to analyze the multivariate relationship between infection and death rates. First, we conducted an ANOVA test on linear models that consider both cases and deaths. This helped us to identify the variables that were associated with these features. Second, we conducted a principal component analysis of all variables to determine which ones were related to the main features of cases and deaths. Through these methods, we aimed to gain a deeper understanding of the factors that contributed to infection and death rates.

We analyzed and described every variable using the IBM SPSS statistics version 24.0. We designed figures and other graphics using the prism 9 data visualization software and Piktochart infographic online app. References and citations were managed by Zotero Open-Source Software version 4.0.11.

### 2.5. Study size and sample size calculation

We have included every confirmed, probable, and suspected COVID-19 case reported to the Public Health Surveillance System (ViEpi) in Ecuador. According to the MoH of Ecuador, during the first 454 days of the duration of the pandemic (February 15th, 2020 to May 14th, 2021), a total of 473,937 cases and 23, 803 COVID-19 related deaths were reported in Ecuador. From these, 34,001 cases and 258 COVID-19 related deaths were registered among children and adolescents.

### 2.6. Ethics statement

This study involved a secondary data analysis of anonymized and unidentifiable information, which received ethical approval

(#EOP-200301-001) from the Universidad de las Americas Ethics Committee CEISH on March 10th, 2020. To ensure data privacy and confidentiality, the Minister of Public Health robustly anonymized the data, and no personal identifiable data was shared. We obtained authorization to access the countrywide level data from the former Minister of Health through N. MSP-MSP-2021-1523-O. Our research was conducted in compliance with local and international ethical standards and all ethical principles for medical research involving human subjects, including the Helsinki Declaration. We took every measure to avoid potential ethical issues and prevent any selection or information bias that could compromise the integrity of our findings.

### 2.7. Bias

To minimize selection and information bias, we obtained the secondary dataset directly from the MoH shared file. EOP, RFN, and JSI analyzed the data independently, and in cases where the results were not consistent, we reviewed the entire dataset and considered automated measures and appropriate data codification to prevent potential human errors. Through these measures, we aimed to ensure the accuracy and reliability of our findings.

## 3. Results

In Ecuador, during 454 days of the total analysis period, from February 15, 2020 to May 14, 2021, at least 34,001 cases and 258 COVID-19 related deaths were registered among children and adolescents from 0 to 19 years of age within the national surveillance system.

### 3.1. Sex differences

Within all the age categories, at least 17,336 (51%) cases were reported among the female pediatric population and 16,665 (49%) among males (Table 1)

### 3.2. Age differences

Among the analyzed cases, the median age for males was 14 years (IQR 9–17 years) and 15 years (IQR 10–17 years) for females. While regarding deaths recorded, the median age in the male group was one year (IQR 0–11.5 years) and two years (IQR 0–12.5 years) for females.

In Ecuador, at least 14.9% ( $n = 5,054$ ) of the COVID-19 new cases were reported among pre-scholar group (0 to 5 years), 2,392 (47.3%) in female children and 2,662 (52.7%) among males. Through the adolescents' group (12 to 18 years), the subgroup with the highest risk of infection is over 16 years of age, who combined account for 41.6% ( $n = 14,154$ ) of the entire cohort, 7,468 female (21.9%) and 6,686 (19.6%) male adolescents (Table 2).

### 3.3. Mortality and CFR (%) among children and adolescents

During the first 454 days of the pandemic in Ecuador, 127 female (49%) and 131 male (51%) children and adolescents died due to COVID-19. In the same period, we found that most deaths were reported among children from 0 to 1 year of age, representing 44% ( $n = 114$ ) of the total number of deaths reported (Figure 2).

### 3.4. Risk analysis among children and adolescents with COVID-19 in Ecuador

After using the population with the lowest risk of dying from COVID-19 (15 to 19 years old) as a reference, we found that infants (less than one-year-old) have the highest odds of dying from COVID-19 among the entire pediatric population (Table 3).

Male and female children with comorbidities showed a higher risk of dying from COVID-19 (OR: 12.6; 95% CI: 8.35–18.99, and OR: 21.8; 95% CI: 14.92–31.79, respectively).

TABLE 1 Female and male COVID-19 cases reported among children and adolescents in Ecuador from 2020 to 2021.

Age category	Sex	Confirmed cases	Probable cases	Suspected cases		COVID-19 cases	Discarded cases			Deaths
		<i>N</i>	<i>n</i>	<i>N</i>	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)
0–4 years	Female	1,052	467	524	2,043	47%	5,689	47%	70	48%
	Male	1,157	547	581	2,285	53%	6,494	53%	77	52%
5–9 years	Female	1,464	390	360	2,214	48%	4,909	48%	17	52%
	Male	1,531	446	398	2,375	52%	5,226	52%	16	48%
10–14 years	Female	3,082	637	539	4,258	50%	7,504	50%	15	44%
	Male	3,002	621	576	4,199	50%	7,387	50%	19	56%
15–19 years	Female	6,480	1,259	1,082	8,821	53%	16,935	54%	25	57%
	Male	5,819	948	1,039	7,806	47%	14,274	46%	19	43%
Subtotal	Female	12,078	2,753	2,505	17,336	51%	35,037	51%	127	49%
	Male	11,509	2,562	2,594	16,665	49%	33,381	49%	131	51%
<b>Total</b>		<b>23,587</b>	<b>5,315</b>	<b>5,099</b>	<b>34,001</b>	<b>100%</b>	<b>68,418</b>	<b>100%</b>	<b>258</b>	<b>100%</b>

TABLE 2 Age related sex differences between children and adolescents from 0 to 19 years of age.

Age (year)	Female				Male				
	<i>n</i>	(%)	Deaths	CFR	<i>n</i>	(%)	Deaths	CFR	CFR Diff.
0	645	4%	57	8.8%	785	5%	57	7.3%	1.6%
1	404	2%	6	1.5%	473	3%	12	2.5%	-1.1%
2	328	2%	1	0.3%	365	2%	4	1.1%	-0.8%
3	337	2%	3	0.9%	339	2%	1	0.3%	0.6%
4	329	2%	3	0.9%	323	2%	3	0.9%	0.0%
5	349	2%	5	1.4%	377	2%	5	1.3%	0.1%
6	388	2%	7	1.8%	433	3%	1	0.2%	1.6%
7	412	2%	0	0.0%	472	3%	2	0.4%	-0.4%
8	509	3%	3	0.6%	514	3%	4	0.8%	-0.2%
9	556	3%	2	0.4%	579	3%	4	0.7%	-0.3%
10	598	3%	1	0.2%	664	4%	3	0.5%	-0.3%
11	730	4%	2	0.3%	706	4%	2	0.3%	0.0%
12	843	5%	5	0.6%	840	5%	2	0.2%	0.4%
13	959	6%	4	0.4%	919	6%	6	0.7%	-0.2%
14	1,128	7%	3	0.3%	1,070	6%	6	0.6%	-0.3%
15	1,353	8%	4	0.3%	1,120	7%	5	0.4%	-0.2%
16	1,607	9%	4	0.2%	1,337	8%	4	0.3%	-0.1%
17	1,820	10%	6	0.3%	1,538	9%	3	0.2%	0.1%
18	1,865	11%	4	0.2%	1,748	10%	2	0.1%	0.1%
19	2,176	13%	7	0.3%	2,063	12%	5	0.2%	0.1%
<b>Total</b>	<b>17,336</b>	<b>100%</b>	<b>127</b>	<b>0.7%</b>	<b>16,665</b>	<b>100%</b>	<b>131</b>	<b>0.8%</b>	<b>-0.1%</b>

CFR, case fatality rate.

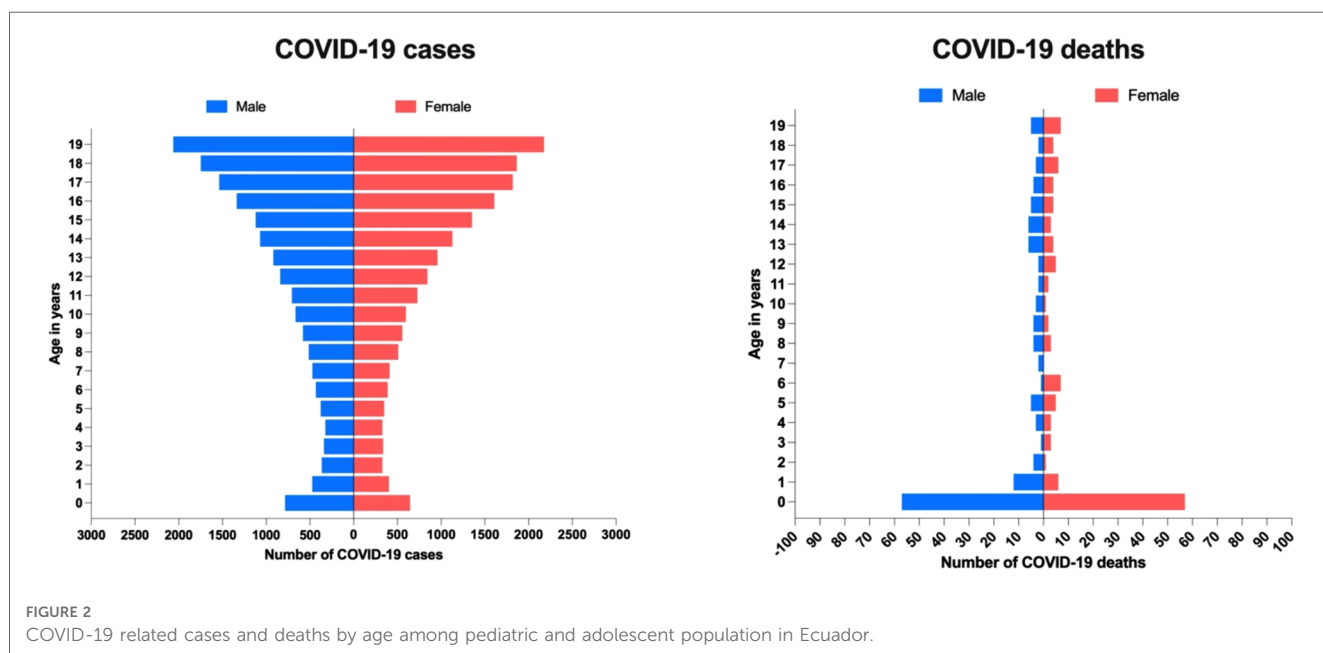


FIGURE 2 COVID-19 related cases and deaths by age among pediatric and adolescent population in Ecuador.

We found that the CFR is 305% higher among infants younger than 12 months of age than those older than one year, 1,057% higher than those from two to three years, 1,250% from those three to four years, and 3,140% higher than 19 years old adolescents (Table 2). In comparison with adults, CFR increases dramatically with age, especially after the age of 50, where CFR increases from 5,5% at 55

years up to almost 20% when reaching the late 80's (Supplementary File S1).

Our findings from a multivariate analysis conducted on the risk of infection and mortality among individuals. Our results indicate that ethnicity and sex did not show any significant association with the risk of infection, as measured by infection rate. However, we found that the presence of a comorbidity was positively

TABLE 3 Analysis of risk and probability of infection and death among children and adolescents with COVID-19 in Ecuador.

		Sex	Cases <i>n</i>	Deaths <i>n</i>	CFR %	OR	CI 95%	<i>P</i> Value
Age (years)	0–4	Female	2,043	70	3.4%	12.5	7.88–19.75	<b>0.0001</b>
		Male	2,285	77	3.4%	14.3	8.63–23.66	<b>0.0001</b>
	5–9	Female	2,214	17	0.8%	2.7	1.46–5.05	<b>0.0015</b>
		Male	2,375	16	0.7%	2.8	1.42–5.41	<b>0.0026</b>
	10–14	Female	4,258	15	0.4%	1.2	0.65–2.36	0.500
		Male	4,199	19	0.5%	1.9	0.98–3.52	0.055
15–19	Female	8,821	25	0.3%	ref	ref	ref	
	Male	7,806	19	0.2%	ref	ref	ref	
Comorbidities	No	Female	16,883	83	0.5%	ref	ref	ref
		Male	16,209	97	0.6%	ref	ref	ref
	Yes	Female	453	44	9.7%	21.8	14.92–31.79	<b>&lt;0.0001</b>
		Male	456	34	7.5%	12.6	8.35–18.99	<b>&lt;0.0001</b>
Ethnicity	Afro	Female	83	2	2.4%	3.8	0.88–14.99	0.0661
		Male	68	0	NA	1.1	0.06–17.07	0.9725
	White	Female	36	0	NA	2.1	0.12–34.18	0.6071
		Male	39	0	NA	1.8	0.11–29.83	0.6743
	Indigenous	Female	542	4	0.7%	1.1	0.41–3.09	0.8026
		Male	447	10	2.2%	3.3	1.71–6.38	<b>0.0004</b>
	Mestizo	Female	15,232	99	0.6%	ref	ref	ref
		Male	14,560	100	0.7%	ref	ref	ref
	Montubio	Female	127	1	0.8%	1.2	0.16–8.76	0.8481
		Male	116	0	NA	0.6	0.03–10.00	0.7344
	Mulato	Female	13	0	NA	5.6	0.33–95.41	0.2311
		Male	14	0	NA	4.9	0.29–83.74	0.2666
	Other	Female	1,303	21	1.6%	2.5	1.55–4.02	<b>0.0001</b>
		Male	1,421	21	1.5%	2.2	1.35–3.48	<b>0.0014</b>
<b>Total</b>			34,001	258	0.8%			

CFR, case fatality rate; OR, Odds ratio; OR, Odds ratio; CI 95%, Confidence intervals.

associated with the likelihood of becoming infected among confirmed cases (Table 4).

rate (41/100,000), followed by Tena (27/100,000) and Pastaza (12/100,000) (as shown in Figure 3B).

### 3.5. Geographical differences

In Ecuador, the largest provinces, such as Pichincha, Guavas, Manabí, were those where the highest number of cases were reported, i.e., 27%, 12.1% and 10.8%, respectively. However, in terms of CFR percentage, it is noteworthy that the province of Napo and Chimborazo were the ones that reported the highest mortality, 3.1% and 1.7%, respectively. In terms of infections per population at risk, the province of Galapagos (1,685/100,000), followed by Carchi (1,347/100,000) and Morona Santiago (858/100,000), reported the highest number of cases per 100,000 inhabitants. Concerning mortality per 100,000 inhabitants, Napo (18/100,000), followed by Pichincha (10/100,000) and Pastaza (10/100,000), were the provinces with the highest number of cases per 100,000 inhabitants (Table 5).

The geographic analysis revealed that among pediatric patients, the highest rate of COVID-19 infection was observed in Atahualpa (4,312/100,000), Guachapala (3,995/100,000), Portobelo (3,784/100,000), Aguarico (3,712/100,000), and Isabela in the Galapagos Islands with 3,382/100,000 (as shown in Figure 3A). Meanwhile, in terms of mortality by canton, Penipe had the highest mortality

### 4. Discussion

To the best of our knowledge this is the first epidemiological report of COVID-19 among Ecuadorian children and adolescent. We found a high incidence and mortality rate within this population during the early phase of the pandemic. A total of all 34,001 cases (confirmed, probable, suspected) and 258 COVID-19 related deaths were reported in the pediatric population, a significantly higher burden than the one reported elsewhere (26, 27).

Within the Latin-American context, only Brazil reported a greater CFR than Ecuador. Oliveira et. Al found that among 11,613 children infected with SARS-CoV-2, at least 886 children died due to COVID-19 (CFR 7.6%) (28), however, the overall crude mortality rate in Ecuador (1.4/100,000) was three times higher than in Brazil (0.4/100,000). In the neighboring country of Colombia, a 0.16% CFR was found (29). If we compare our results with European children, Ecuador reported a much higher CFR than Spain (CFR = 0.02%) (30), or Italy (CFR = 0.10%) (31).

During the study period in Ecuador, the predominant variant of the COVID-19 virus was the ancestral variant, with other variants such as Alpha, Gamma, Delta, Iota, Lambda, and Mu appearing in lower percentages as of January 2021 (Table 6).

TABLE 4 Pediatric COVID-19 cases and deaths per province.

Province	Cases (n)	Deaths (n)	Pop. At Risk (n)	CFR (%)	IR per 100,000	MR per 100,000	Cases (%)	Deaths (%)
Azuay	1,716	7	318,092	0.4%	539	2	5.0%	2.7%
Bolivar	732	1	91,892	0.1%	797	1	2.2%	0.4%
Cañar	352	0	113,906	0.0%	309	0	1.0%	0.0%
Carchi	917	1	68,087	0.1%	1,347	1	2.7%	0.4%
Chimborazo	411	7	203,710	1.7%	202	3	1.2%	2.7%
Cotopaxi	906	2	203,155	0.2%	446	1	2.7%	0.8%
El Oro	1,910	7	259,299	0.4%	737	3	5.6%	2.7%
Esmeraldas	787	3	288,605	0.4%	273	1	2.3%	1.2%
Galapagos	207	0	12,284	0.0%	1,685	0	0.6%	0.0%
Guayas	4,131	31	1,596,161	0.8%	259	2	12.1%	12.0%
Imbabura	1,477	6	181,429	0.4%	814	3	4.3%	2.3%
Loja	1,500	6	199,990	0.4%	750	3	4.4%	2.3%
Los rios	1,081	5	373,930	0.5%	289	1	3.2%	1.9%
Manabi	3,666	24	600,199	0.7%	611	4	10.8%	9.3%
Morona santiago	816	3	95,154	0.4%	858	3	2.4%	1.2%
Napo	353	11	61,889	3.1%	570	18	1.0%	4.3%
Orellana	291	0	76,976	0.0%	378	0	0.9%	0.0%
Pastaza	398	5	50,248	1.3%	792	10	1.2%	1.9%
Pichincha	9,189	117	1,115,305	1.3%	824	10	27.0%	45.3%
Santa elena	301	2	166,342	0.7%	181	1	0.9%	0.8%
Santo Domingo	1,076	12	182,081	1.1%	591	7	3.2%	4.7%
Sucumbios	603	4	97,474	0.7%	619	4	1.8%	1.6%
Tungurahua	1,000	3	205,905	0.3%	486	1	2.9%	1.2%
Zamora Chinchipe	181	1	55,412	0.6%	327	2	0.5%	0.4%
<b>Total</b>	<b>34,001</b>	<b>258</b>	<b>6,617,525</b>	<b>0.6%</b>	<b>612</b>	<b>3</b>	<b>100.0%</b>	<b>100.0%</b>

CFR, case fatality rate; IR, incidence rate; MR, mortality rate.

TABLE 5 Multivariate analysis.

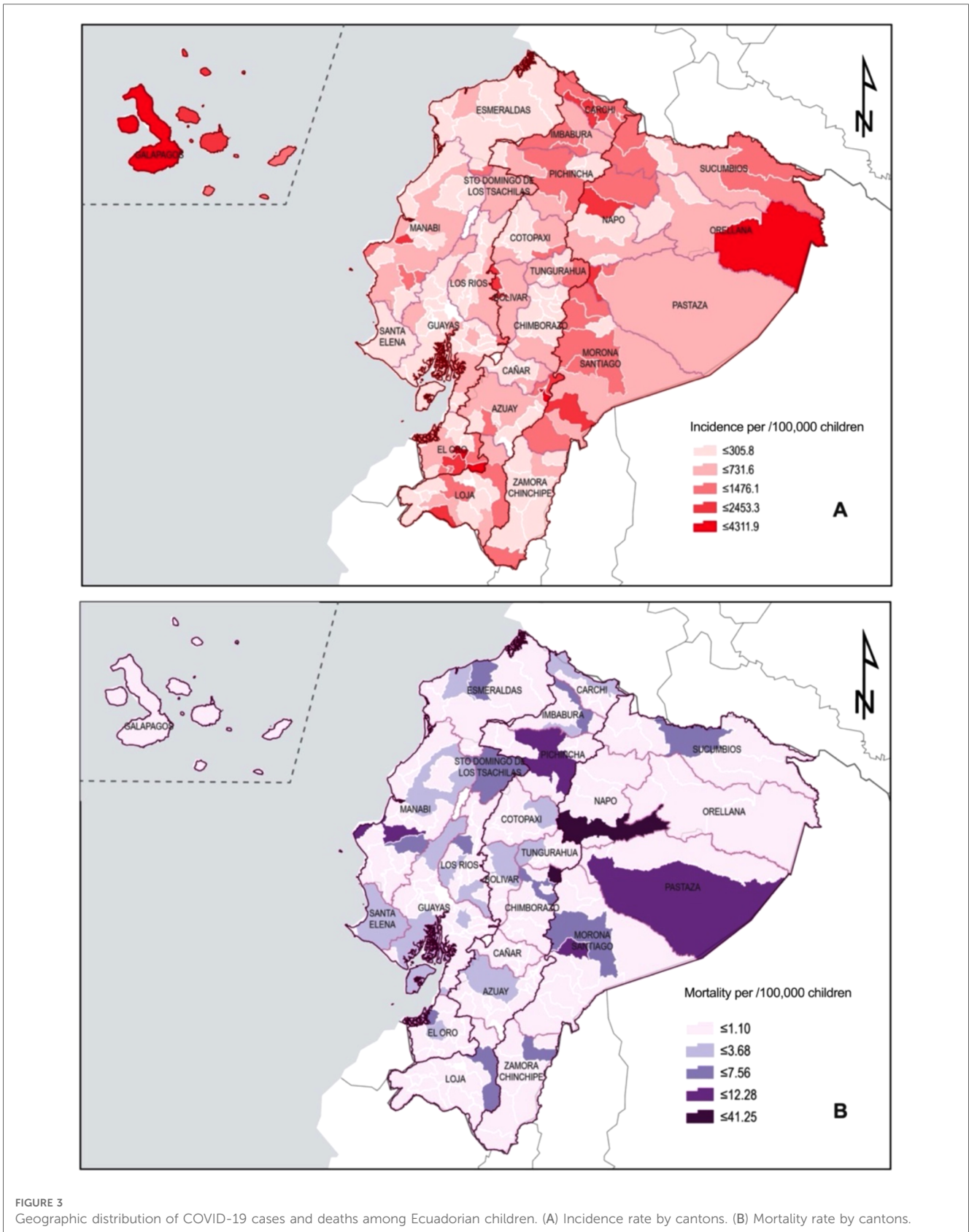
Independent Variable		COVID-19 cases				COVID-19 Deaths			
		df	Mean Sq	F	Sig	df	Mean Sq	F	Sig
Comorbidities	No	1	773,723	47.691	.0001	1	192.734	2.626	.0001
	Yes	1	1,244	7.667	.0001	1	68.353	9.313	.0001
Ethnic Category	Mestizo	1		2.034	0.652	1		0.000	0.9989
	Other	1		42.200	0.924	1		50.243	0.9828
	Montubio	1		8.600	0.926	1		50.243	0.9436
	Indigenous	1		92.030	0.923	1		0.000	0.9885
	Afro-Ecuadorian	1		13.543	0.907	1		0.000	0.9832
Age	Age	1		4.222	0.040	1		1.000	0.9204
	Residuals	438				439			

However, the fatality rates in the pediatric population associated with the different variables did not show significant differences after the arrival of variants other than the ancestral variant (Supplementary File S2) (32).

It is possible that the lack of natural immunity to the virus and the absence of pre-existing treatments or vaccines contributed to the high infectiousness of the ancestral variant, which made COVID-19 so lethal at the beginning of the pandemic (33). In addition, overwhelmed healthcare systems and the vulnerability of certain populations also contributed to the severity of the pandemic.

The burden of COVID-19 among children is significantly lower than adults and the elderly. In terms of symptomatology and severity, milder cases are often compared to common endemic viral infections of childhood such as those caused by adenovirus

or respiratory syncytial virus (34, 35). The reasons behind differences in severity and prognosis between children and adults could be explained by several factors (21). Zimmermann and Curtis, 2020, have summarized them in: age-related endothelial changes, higher density and increased affinity for transmembrane serine protease-2 and angiotensin converting enzyme-2 receptors; pre-existing coronavirus antibodies and T cells as well as immunosenescence and lower viral loads due to host-specific factors (36). Although most of the few available epidemiological analyses on COVID-19 in children have shown that fatal outcome of the infection occurs in very low frequencies (12, 30, 37), in this study we observed that in Ecuador, the mortality triggered by SARS-CoV-2 in children had a dramatic toll on deaths per 100,000 people, comparable only with those reported in Brazil (28).



In adults the sex-linked effects of COVID-19 are characterized by similar infection rates between males and females, and more severe cases along with mortality in males (38, 39), on the other

hand, no sex-related differences in COVID-19 mortality have been demonstrated in children (29, 37, 40–42). In this context, in Ecuadorian children, the overall incidence and mortality from



TABLE 6 SARS-CoV-2 variants circulating in Ecuador from 2020 to May 2021.

	Month	SARS-CoV-2 variant (%)						Pediatric COVID-19		
		Ancestral	Alpha	Gamma	Iota	Lambda	Mu	Cases (n)	Deaths (n)	Fatality rate (%)
2020	February	100.0	0.0	0.0	0.0	0.0	0.0	16	3	18.8
	March	100.0	0.0	0.0	0.0	0.0	0.0	529	25	4.7
	April	100.0	0.0	0.0	0.0	0.0	0.0	797	26	3.3
	May	100.0	0.0	0.0	0.0	0.0	0.0	1,394	29	2.1
	June	100.0	0.0	0.0	0.0	0.0	0.0	2,499	18	0.7
	July	100.0	0.0	0.0	0.0	0.0	0.0	3,632	22	0.6
	August	100.0	0.0	0.0	0.0	0.0	0.0	3,004	16	0.5
	September	100.0	0.0	0.0	0.0	0.0	0.0	2,381	19	0.8
	October	100.0	0.0	0.0	0.0	0.0	0.0	1,954	13	0.7
	November	100.0	0.0	0.0	0.0	0.0	0.0	1,698	17	1.0
	December	100.0	0.0	0.0	0.0	0.0	0.0	1,828	21	1.1
	2021	January	80.5	14.6	0.0	4.9	0.0	0.0	2,703	15
February		100.0	0.0	0.0	0.0	0.0	0.0	3,033	13	0.4
March		63.2	16.8	8.4	9.5	2.1	0.0	3,558	17	0.5
April		57.1	17.1	3.4	15.6	6.3	0.5	3,794	3	0.1
May		56.4	11.8	3.5	18.1	8.4	1.9	1,181	1	0.1

COVID-19 between males and females was very close; however, in 1-year-old girls, the CFR was slightly higher in boys (Table 2).

Regarding the age of the pediatric population, the highest number of COVID-19 cases was observed in populations older than 15 years. This high risk is comparable to data published by the CDC and explained by the fact that older children and adolescents socialize more than toddler and younger children (43). Interestingly, the highest CFR (Table 2) was observed among children younger than one year of age, having a higher likelihood of dying than older children (male OR: 12.5; 7.88–19.75, and female OR: 14.3; 8.63–23.66). These findings are similar to other reports (30, 44). Harwood et al. (2022), taking as a reference children from one to four years of age, found that infants (one year and under) are at increased risk of death (OR: 2.08; 1.57–2.86) (42).

The influence of ethnicity on children infected with COVID-19 has not been extensively studied. Oliveira et al. reported that when taking white children as a reference, children of indigenous ethnicity had a higher risk of dying from COVID-19 (HR: 3.36; 2.15–5.24) (28). In this context, we decided to take children of mestizo ethnicity as a reference because it is the most representative ethnic group in Ecuador (45). We found that male indigenous children are at higher risk of dying when compared to other groups (OR: 3.3; 1.71–6.38). This may be due to different factors, including socioeconomic and educational dynamics among this group. In 2018, Ecuador reported that 50.6% of its indigenous population lived in poverty, compared to 20.9% of the non-indigenous population (24). Nationwide data have also reported a 30% higher mortality and 63% higher hospital admission rates than their non-indigenous counterparts (46). In a recently published work, Ortiz-Prado et al., 2022 have found a 12 times greater risk of dying due to water borne diseases among indigenous children when compared them to self-determined white populations (47). Another important factor is the cultural barrier that indigenous people face. Indigenous groups have ancestral practices and views away from doctors, generating conflict between the traditional healer's believe who has the respect of the community and the tradition doctor who may

sound distant, arrogant, and detached from the tribe's worldview (48). This could be partly associated with the massive contagion in Ecuador that also affected indigenous groups, regardless of their province or canton of residence (48).

Two of the three provinces with the highest number of COVID-19 cases belong to the coastal region of Ecuador (Guayas and Manabí), we believe that this observation is probably due to the massive contagion that occurred in the coastal region in the initial stage of the pandemic (25). Within the same context, as we have mentioned, we also consider that the highest rates of COVID-19 infection noted in the specific region of Ecuador was due to the largest number of tests that have been performed in provinces such as of Pichincha, Guayas, and Manabí, the ones close to major urban areas in Ecuador such as Quito, Guayaquil, and Manta, respectively. Additionally, to this, the highest number of deaths per 100,000 inhabitants are in urban-marginal or rural cantons, where the most severe cases probably ended in higher hospitalization and mortality rates as well as superspreading events (48–50).

The low prevalence of COVID-19 infection among children in Ecuador is consistent with the findings of previous studies from other countries, suggesting that children are less susceptible to COVID-19 infection than adults (51). However, the study also found that children with comorbidities were more likely to develop severe disease, indicating that children with underlying health conditions should be closely monitored for COVID-19 infection.

To reduce the impact of COVID-19 on vulnerable populations in Ecuador, several recommendations can be implemented. First, healthcare access in rural areas should be improved, and healthcare facilities should be equipped with necessary resources. Second, targeted public health interventions, such as outreach programs, health education, and culturally sensitive messaging, should be implemented to reduce disparities in infection and mortality rates among children with comorbidities and those belonging to indigenous ethnic groups. Third, a robust surveillance and reporting system should be implemented to track the spread of the virus accurately. Fourth, vaccination

campaigns should prioritize the most vulnerable populations, such as children under one year of age, those with comorbidities, and those belonging to indigenous ethnic groups. Finally, policies tackling poverty, social exclusion, and access to basic services such as water and sanitation should be implemented to address systemic inequalities that put vulnerable populations at a higher risk of infection and mortality.

## 5. Limitations

While our study provides important insights into the clinical characteristics of pediatric COVID-19 cases in Ecuador, it is important to acknowledge several inherent limitations in its design. One such limitation is the potential underestimation of asymptomatic cases, as our analysis relied solely on reported symptoms. However, it should be noted that during the early months of the pandemic in Ecuador, diagnostic testing was required as part of the healthcare process, which may have reduced the likelihood of missing asymptomatic cases. Another limitation is the lack of information on comorbidities and length of hospital stay for the included children, which may have influenced our findings. Despite these limitations, our study provides valuable information on the presentation and outcomes of pediatric COVID-19 cases in Ecuador, highlighting the need for further research in this area.

Limitations such as underreporting of COVID-19 cases, inadequate diagnostic capability, and disease misclassification could impact the accuracy and validity of our conclusions. We recognize the need to acknowledge and address these limitations to ensure the reliability of our study findings. In future research, we will strive to ensure comprehensive reporting of COVID-19 cases, accurate diagnosis, and proper disease classification to reduce the risk of bias.

Another limitation is the possibility of false positive and false negative results, which could have led to misclassification of patients as either infected or uninfected. Additionally, this study design did not allow for a follow-up process of the registered cases, which would have been optimal to understand the long-term outcomes and potential sequelae of COVID-19 in the pediatric population. Therefore, our findings should be considered as descriptive only, and future studies should aim to address these limitations by using more accurate diagnostic tests and incorporating follow-up assessments to better understand the impact of COVID-19 on pediatric patients.

## 6. Conclusion

This study, the first of its kind in Ecuador, reveals that children have a high likelihood of contracting SARS-CoV-2, with those under one year of age facing the highest risk of mortality. Furthermore, our findings highlight significant disparities in infection and mortality rates among children living in rural areas, those with comorbidities, and those belonging to indigenous ethnic groups. The observed variations in mortality and infection rates across cantons and provinces of Ecuador

suggest the existence of systemic inequalities, particularly in impoverished rural regions of the Coast and Amazon areas. These results underscore the need for targeted public health interventions to mitigate the disproportionate impact of COVID-19 on vulnerable populations in Ecuador.

## Data availability statement

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding authors.

## Author contributions

EOP was responsible for the idea and conception of the project. He wrote the first draft, analyzed the data in its entirety and was responsible for the creation of some figures in the manuscript. JIC was partially responsible for the project and contributed to the writing, analysis, and discussion of the manuscript. MRN, and MGDR were responsible for obtaining the data and reviewing the final version, providing valuable feedback to improve the quality of the analysis. JVG, DRB, and DHQ were responsible for writing part of the introduction, helping with the analysis of the available references and verifying that the latest version complies with the international standards of the STROBE guidelines. Finally, RFN was the one who helped us with the analysis of the data and the barcoding of some of the images used in this manuscript. All authors contributed to the article and approved the submitted version.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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## Supplementary material

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fped.2023.1060311/full#supplementary-material>.

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