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Pediatric pneumonia across altitudes in Ecuador: a countrywide, epidemiological analysis from 2010–2021

Esteban Ortiz-Prado[1,4*], Maria V. Cortez-Silva[1], Jorge Vasconez-Gonzalez[1], Juan S. Izquierdo-Condoy[1], Javier Peñafiel[1], Benjamin T. Crookston[2] and Ginés Viscor[3]

Abstract

Background In Ecuador, pneumonia is a significant pediatric health challenge and a leading cause of infant mortality. Little is known about the contribution of altitude to trends in pneumonia incidence and mortality. The objective of this study was to examine the how the disease burden of pneumonia varies across substantial changes in altitude in a large population over time.

Methods A nationwide descriptive ecological analysis of the burden of pediatric pneumonia was conducted using secondary data from hospital discharges spanning 2010 to 2021. Patients aged 0 to 18 years with ICD-10 diagnoses related to pneumonia were included. The data were stratified by altitudes using the two main classifications available: The classical categorization (low < 2,500 m and high altitude > 2,500 m), and the classification offered by the International Society of Mountain Medicine (low altitude (< 1,500 m), moderate altitude (1,500 m – 2,500 m), high altitude (2,500–3,500 m). Disease frequency, prevalence, and the burden of disease were analyzed in relation to altitude.

Results Between 2010 and 2021 in Ecuador, there were 268,895 pediatric hospitalizations and 4,669 deaths due to lower respiratory tract infections. The incidence was higher among males (54.3%), who had a mean age of 1.4 years during their hospital stay. In comparison, females accounted for 45.7% of cases and had a slightly higher mean age of 1.6 years. The incidence rate in low altitude areas (< 2,500 m) was 341.6 per 100,000 with 173,305 cases, whereas high altitude areas (> 2,500 m) had a rate of 467.4 per 100,000 with 95,590 cases. The mortality rate was disproportionately high in very high-altitude regions at 34.2 per 100,000, despite lower incidence rates.

Conclusions In Ecuador, pneumonia incidence notably increases at altitudes above 2,500 m, while mortality rates were higher at elevations exceeding 3,500 m. This increment in mortality may be attributed to reduced access to medical services in higher altitudes, leading to fewer individuals seeking early medical intervention and underreporting of incidence rates. The multifaceted nature of these findings underscores the necessity for tailored health strategies that prioritize improved healthcare accessibility, widespread vaccination programs, to mitigate the impact of pneumonia across varying altitudes.

*Correspondence:
Esteban Ortiz-Prado
e.ortizprado@gmail.com

Full list of author information is available at the end of the article

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Introduction

According to the World Health Organization (WHO) data, pneumonia remains the leading cause of infant mortality worldwide, particularly evident in developing countries [1]. In recent years, pneumonia was responsible for 14% of deaths in children under 5 years worldwide and 22% in those aged 1–5 years [2]. The Global Burden of Diseases (GBD) study 2021 estimated that in 2021, lower respiratory infections (LRIs), including pneumonia and bronchiolitis, accounted for approximately 344 million incident episodes worldwide. These infections disproportionately affected children under five years old, with 502,000 deaths in this age group, and adults over 70, who experienced the highest mortality rates [3].

The GBD study identified Oceania as the continent with the highest incidence of lower respiratory tract infections, particularly among children under 15 years [4]. Additionally, the study reported a mortality rate of 89.1 per 100,000 people for children under 5 years old [4]. In Latin America, the results demonstrated that mortality rate affected 80.5 per 100,000 people, while approximately 150,000 children under 5 in the Americas succumbed to pneumonia [4]. The global burden of pneumonia is so severe that UNICEF (United Nations International Children's Emergency Fund) reports a child dies from the disease every 39 s [5].

While the risk factors for pneumonia are multiple and include poverty, malnutrition, indoor air pollution, lack of immunization, and pre-existing respiratory conditions, non-traditional or confounding factors, such as exposure to high altitude, have been less studied. In this context, chronic hypoxia, as experienced in mountainous regions, has been linked to an increased incidence of pneumonia [6]. A study conducted in Pakistan revealed that the incidence of pneumonia in children aged 2 to 35 months living at altitudes higher than 1980 m was greater compared to those living at lower altitudes [7]. Furthermore, Choudhuri et al. found that the hospitalization rate for respiratory syncytial virus increased by 25% among infants under 1 year of age and by 53% among children aged 1 to 4 years for every 1000-meter increase in altitude [8].

Children living at high altitudes who developed pneumonia had significantly lower oxygen saturation, more cyanosis, lower systolic blood pressure, and higher hemoglobin levels [9]. The pediatric population residing at high altitudes takes longer to reach normoxia compared to those living at lower altitudes (5.25 vs. 0.75 days; $P < 0.0001$) [9]. In Mexico, it was found that children living at altitudes between 2000 and 2499 m had a pneumonia mortality rate three times higher [10]. Lastly, one study conducted in La Paz, Bolivia, analyzed 1,214 mortality records from 2017 to assess the leading causes of death in high-altitude residents (3,600–4,150 m above sea level). The results revealed that respiratory diseases were the third leading cause of mortality in this population, with pneumonia emerging as the primary respiratory-related cause of death, accounting for 40.5% of cases [6].

While previous studies have highlighted the increased incidence and severity of pneumonia at high altitudes in various countries, including Pakistan, Mexico, and Bolivia, no such epidemiological research has been conducted in Ecuador. The country's diverse topography, ranging from sea level to high-altitude regions above 4,000 m, presents a unique opportunity to examine how altitude influences pneumonia burden. Understanding these variations is essential for developing targeted public health interventions. Therefore, this study aims to assess how pneumonia burden varies across different altitudes in Ecuador over time, using a disease burden approach, with disability-adjusted life years (DALYs) as the primary indicator to quantify its impact on public health [11, 12].

Materials and methods

Study design

We conducted a cross-sectional, countrywide ecological study over a 11-year period (2010–2021) to determine the demographic and spatial distribution patterns of pneumonia among Ecuadorian children, using hospital discharge and in-hospital mortality data as proxies for incidence and mortality.

Sample and setting

The study was conducted in Ecuador, a country located in the northern region of South America with an area of 283,561 km2. The Ecuadorian territory is divided into four geo-climatic regions: the Coast, Andes (Highlands), Amazonia, and the Galápagos Islands. Politically, it is segmented into 24 provinces, each further subdivided into cantons. Currently, Ecuador comprises a total of 223 cantons, with 141 located at low altitude (< 1,500 m), 28 at moderate altitude (1,500-2,500 m), 41 at high altitude (2,500-3,500 m), and 13 at very high altitude (3,500-5,500 m).

Population

In 2019, Ecuador's population in the 0 to 18 age group consisted of approximately 6,648,436 individuals, representing a significant portion of the total population of 17,082,730, with a slight female predominance (51%). This demographic includes 330,105 under 1 year, 1,321,687 aged 1 to 4 years, 1,666,259 between 5 and 9

years, 1,685,209 from 10 to 14 years, and 1,645,176 in the 15 to 18 age group. While specific ethnic and altitude distribution data for this age group are not available, the overall patterns suggest a majority of mestizo (79.3%), followed by Afro-descendants (7.2%), indigenous (7.1%), white (6.1%), and other groups (0.4%), with 60% living at low altitude, 10% at moderate altitude, 27% at high altitude, and 3% at very high altitude [13, 14].

Data source and description

This study examined hospitalization records of pediatric patients from 0 to 18 years old residing in Ecuador, diagnosed with lower respiratory tract infections resulting in pneumonia upon hospital discharge. These conditions were identified through 22 distinct etiologies as per the International Classification of Diseases, Tenth Revision (ICD-10), including: Influenza due to identified zoonotic or pandemic influenza viruses (J09), Influenza due to identified seasonal influenza viruses (J10), Influenza due to other identified influenza viruses, not elsewhere classified (J100), Influenza with other respiratory manifestations, not elsewhere classified (J101), Influenza with other manifestations, other (J108), Influenza, virus not identified (J11), Influenza with pneumonia, seasonal influenza virus identified (J110), Influenza with other respiratory manifestations, seasonal influenza virus identified (J111), Influenza with other manifestations, seasonal influenza virus identified (J118), Viral pneumonia, not elsewhere classified (J12), Pneumonia due to Streptococcus pneumoniae (J13), Pneumonia due to Haemophilus influenzae (J14), Bacterial pneumonia, not elsewhere classified (J15), Pneumonia due to other infectious organisms, not elsewhere classified (J16), Pneumonia, organism unspecified (J18) and COVID-19 (U07.1 and U07.2).

Inclusion criteria

Using the 10th Revision of the International Classification of Diseases (ICD-10), the study included pediatric patients from 0 to 18 years old diagnosed with lower respiratory tract infections resulting in pneumonia upon hospital discharge. This encompassed 22 distinct etiologies, including various forms of influenza (J09, J10, J100, J101, J108, J11, J110, J111, J118), viral pneumonia (J12), pneumonia due to Streptococcus pneumoniae (J13), Haemophilus influenzae (J14), other bacterial pneumonia (J15), pneumonia due to other infectious organisms (J16), unspecified pneumonia (J18), and COVID-19 (U07.1 and U07.2).

Exclusion criteria

Excluded from the analysis were pediatric cases diagnosed with upper respiratory tract infections, asthma, COPD, as well as other conditions not classified under the specified ICD-10 codes for lower respiratory tract infections resulting in pneumonia. This ensured a focused study on the specified pneumonia conditions in the pediatric population.

Bias

To minimize the potential for selection bias and ensure the integrity of the data, three researchers (EOP, MVC and JIC) independently analyzed the dataset. Data verification focused on confirming the diagnoses as per the inclusion criteria and ensuring that the patients were within the specified age range and diagnosed with the relevant lower respiratory tract infections. Additionally, the "place of residence" variable was used to confirm that the patients were residing at different altitudes in Ecuador, rather than basing this on the "place of medical attention," thus providing a more accurate reflection of the population under study.

Hypothesis

Null hypothesis (H_0) There is no significant difference in the incidence and mortality rates of pediatric pneumonia across different altitude levels in Ecuador.

Alternative hypothesis (H_1) There is a significant difference in the incidence and mortality rates of pediatric pneumonia across different altitude levels in Ecuador, with higher altitudes exhibiting increased incidence and mortality rates compared to lower altitudes.

Exposure

The association between altitude exposure and the incidence and mortality of pneumonia was analyzed. Altitude classifications were used as a key variable, with a cut-off point of < 2,500 m for low altitude and > 2,500 m for high altitude. The more detailed classification by the International Society of Mountain Medicine, categorizing altitudes as low (< 1,500 m), moderate (1,500–2,500 m), high (2,500–3,500 m), and very high (3,500–5,500 m), was utilized to assess prevalence odds ratios across different elevations. These analyses are crucial given the range of pneumonia etiologies, including those due to various influenza viruses and bacterial agents.

Outcome

Age, sex, and altitude-adjusted incidence and mortality rates for pneumonia were calculated using hospital admissions data and death records in Ecuador from 2010 to 2021. This includes cases classified under 22 distinct etiologies as per ICD-10, encompassing various types of influenza and pneumonia caused by different pathogens, including Streptococcus pneumoniae, Haemophilus influenzae, other bacterial and viral agents, and COVID-19 (U07.1 and U07.2).

Data analysis

The study analyzed sex, age, month, etiology, type of hospital, province and canton of residence, elevation, and date of hospital admission. Incidence and mortality rates were standardized by sex and age, utilizing projection data from the 2010 census.

Percentage differences in incidence and case fatality rates (CFR%) across age groups and genders were calculated using the equation for percentage change = [(New Value – Old Value)/ Old Value] ×100%.

Incidence was calculated by dividing the number of new cases per year by the total population at risk during each year for each age group. Incidence and mortality rates by age, sex, geographic location, and corresponding population were calculated. The classification of low altitude < 2,500 m and high altitude > 2,500 m was used as a cut-off point for exposure to altitude. The analysis was also carried out using the classification offered by the International Society of Mountain Medicine (ISMM) which includes low altitude (< 1,500 m), moderate altitude (1,500 m – 2,500 m), high altitude (2,500–3,500 m), and very high altitude (> 3,500 m) [15].

Ethical consideration

The study was granted an exemption from ethical review by the Institutional Review Board (IRB) of the Ethics Committee at Universidad de las Américas (UDLA), Quito, Ecuador, acknowledging the ethical compliance of the research methodology. This exemption, officially coded as 2023-EXC-008, was formally issued on May 8, 2023.

The dataset employed in this study was sourced from the publicly accessible databases of the National Institute of Statistics and Census (INEC) of Ecuador. These databases contain only anonymized, non-identifiable information, ensuring adherence to stringent confidentiality standards and the preservation of ethical integrity concerning the subjects involved. The use of such anonymized datasets aligns with international Good Clinical Practice (GCP) guidelines and adheres to the ethical principles set forth in the Declaration of Helsinki. The ethical acceptability of employing these datasets stems from their capability to safeguard individuals from harm while maintaining robust confidentiality protocols.

Results

Age and sex analysis

Based on hospital admission and mortality data from 2010 to 2021, Ecuador experienced 268,895 hospitalizations and 4,669 fatalities in children and adolescents aged 0 to 18 due to lower respiratory infections. Males accounted for 54.3% of admissions, with 146,103 reported cases and an incidence rate of 383.2 per 100,000 individuals. Females comprised 45.7% with 122,792 cases and an incidence rate of 335.0 per 100,000. The average age at hospitalization was similar across genders. The mean age of patients with any type of pneumonia was 1.4 years (±1.4) for males and 1.6 years for females (±1.5) (Fig. 1).

Incidence rates by age group

Pre-school children exhibited the highest incidence rate for unspecified pneumonia (J18), with 7,549 cases per 100,000, accounting for 79.4% of the total burden.

School-age children showed a significant incidence in bacterial pneumonia (J15), with a rate of 426.9 per 100,000, contributing to 14.3% of the cases. Influenza virus infections (J09, J10, J11) were more prevalent in pre-school and school-aged children, with rates of 8.8 and 4.6 per 100,000 for zoonotic or pandemic influenza (J09), and 47.4 and 22.7 for seasonal influenza (J10), respectively. Adolescents presented lower rates across all categories, with the highest incidence observed for COVID-19 (U07) at 36.5 cases per 100,000 (Table 1).

Mortality rate

In the 0–4 years age group, males exhibited a notably higher incidence rate of infections at 1,108.5 per 100.000, which is approximately 12.2% greater than the incidence rate for females at 988.4 per 100.000, with both genders sharing an equal CFR of 1.6%. The disparity in CFRs becomes more evident in the 15–19 years cohort, where males experienced a CFR that is 375% higher at 7.6% compared to the 1.6% for the 0–4 years group, despite the incidence rate plummeting to 29.1 per 100.000. Similarly, females in the 15–19 years group faced a CFR of 5.7%, marking a 256.3% increase from the CFR in the 0–4 years category, alongside a reduced incidence rate of 27.7 per 100.000 (Table 2). Overall, despite the total incidence rates for males and females being 383.2 and 335.0 per 100.000, respectively, a consistent CFR of 1.7% was observed across both genders. Additionally, the data indicates an extreme contrast in incidence rates between the youngest (0–4 years) and oldest (15–19 years) age brackets, with males and females in the younger age group having a 3,706.5% and 3,467.8% higher incidence rate, respectively, compared to their counterparts in the oldest age group (Table 2).

Pneumonia distribution according to the diagnosis

Our study records a cumulative tally of 4,669 deaths, with the highest number attributed to J189 (Pneumonia, organism unspecified) at 2,881 deaths, indicating a significant impact of this condition on mortality. U07, which is associated with COVID-19, accounts for 223 deaths. Other respiratory conditions such as J15 (Bacterial pneumonia, unspecified) also show a notable number of deaths at 305. The highest CFR is observed in J156 (Pneumonia due to other aerobic Gram-negative bacteria) at

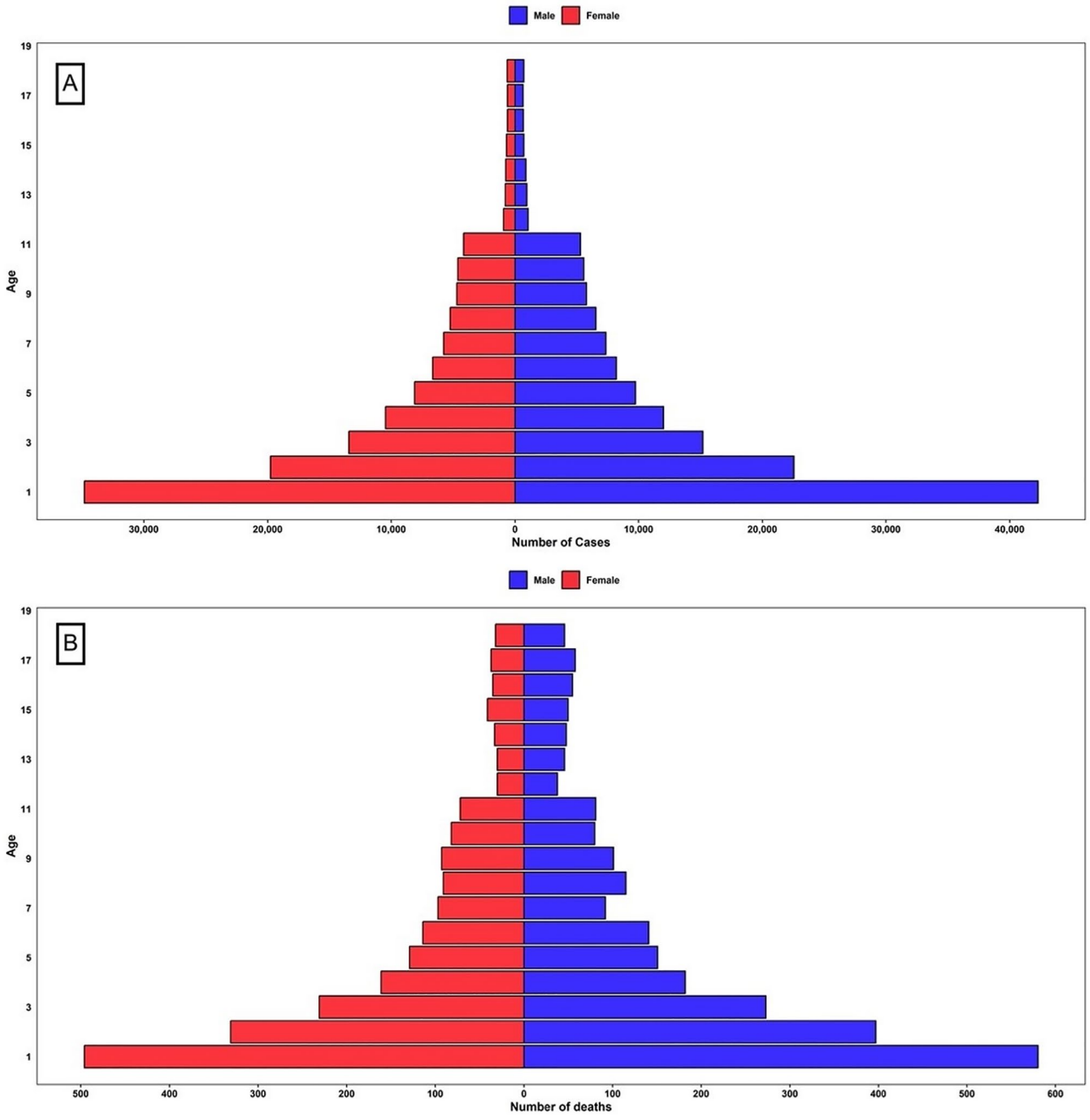

Fig. 1 Comparative Age and Gender Distribution of Lower Respiratory Tract Infection Cases and Deaths in Ecuador from 2010 to 2021. (**A**) A population pyramid showing the total number of cases by gender, with females (red) on the left and males (blue) on the right, across age groups 1 to 18 on the y-axis and number of cases on the x-axis, highlighting a predominance in younger age groups. (**B**) A bar chart illustrating the total number of deaths by gender for the same age groups, maintaining the color scheme with females (red) and males (blue), emphasizing the mortality distribution across different age categories

15.9%, with J152 (Pneumonia due to staphylococcus) closely following at 8.5%. Notably, J189 (Pneumonia, unspecified organism) accounts for the most substantial number of cases (150,071 alive) but has a relatively low CFR of 1.9%. The data for COVID-19 indicates a CFR of 5.8% for U071 (COVID-19, virus identified) and 5.4% for U072 (COVID-19, virus not identified), with more survivors than fatalities reported (Supplementary Table 1).

Trends by province

The province of Morona Santiago experienced the highest incidence rates due to codes (J09, J10, J11, J12, J13, J14, J15, J16, J17, J18 and U07) per 100,000 inhabitants

Table 1 Incidence rates of lower respiratory tract infections leading to pneumonia in pediatric age groups classified by ICD-10 codes, with distribution percentages across Pre-School, School-Aged, and adolescent populations in Ecuador from 2010 to 2021

ICD-10 Code	Pre school		School		Adolescent		% Distribution
	(*n*)	(Rate/100k)	(*n*)	(Rate/100k)	(*n*)	(Rate/100k)	
J09 - Influenza due to identified zoonotic or pandemic influenza virus	176	8.8	108	4.6	50	1.9	0.10%
J10 - Influenza due to identified seasonal influenza virus	944	47.4	534	22.7	116	4.5	0.60%
J11 - Influenza, virus not identified	1427	71.7	537	22.8	162	6.2	0.80%
J12 - Viral pneumonia, not elsewhere classified	5,999	301.2	2,058	87.3	177	6.8	3.10%
J13 - Pneumonia due to Streptococcus pneumoniae	208	10.4	53	2.2	12	0.5	0.10%
J14 - Pneumonia due to Hemophilus influenzae	74	3.7	25	1.1	5	0.2	0.00%
J15 - Bacterial pneumonia, not elsewhere classified	27,067	1,359.1	10,060	426.9	1,191	45.8	14.30%
J16 - Pneumonia due to other infectious organisms, not elsewhere classified	284	14.3	103	4.4	25	1	0.20%
J17: Pneumonia in diseases classified elsewhere	41	2.1	20	0.8	2	0.1	0.00%
J18 - Pneumonia, organism unspecified	150,349	7,549.6	57,134	2424.4	5,962	229.3	79.40%
U07 - COVID-19	1,814	91.1	1,229	52.2	949	36.5	1.50%
Total	188,383	859.9	71,861	277.2	8,651	30.2	100.00%

Table 2 Age-specific incidence rates and case fatality rates (CFR%) for lower respiratory tract infections in male and female pediatric and adolescent populations in Ecuador. The table delineates the number of cases and deaths, along with the calculated incidence rates (per 100,000 population) and CFR% for both genders across different age groups: 0–4 years, 5–9 years, 10–14 years, and 15–19 years. Incidence rates are presented with confidence intervals in brackets. The total for each gender across all age groups is also provided, summarizing the overall burden and mortality risk of the infections studied

Age Groups (years)	Male				Female			
	Cases (n)	Incidence Rate	Deaths (n)	CFR%	Cases (n)	Incidence Rate	Deaths (n)	CFR %
0–4	92,076	1,108.5 [1,069.7 to 1,147.4]	1,432	1,60%	78,550	988.4 [952.5 to 1,024.3]	1,219	1,60%
5–9	37,604	363.4 [350.0 to 376.8]	600	1,60%	30,500	307.8 [296.8 to 318.8]	524	1,70%
10–14	13,718	136.5 [32.7 to 140.3]	293	2,10%	11,244	116.6 [112.9 to 120.3]	247	2,20%
15–19	2,705	29.11 [8.43 to 29.79]	209	7,60%	2,498	27.7 [26.84 to 28.5]	145	5,70%
Total	146,103	383.2 [211.7 to 554.7]	2534	1,70%	122,792	335.0 [182.7 to 487.4]	2,135	1,70%

according to the registered place of residence with an adjusted incidence rate at 1,295.5 per 100,000, though this province had a lower relative mortality, contributing to only 1.1% of total deaths. Following Morona Santiago, Pastaza and Napo provinces also demonstrated significant incidence rates of 755.71 and 621.15 respectively. In terms of mortality, Pastaza reported the highest rate at 18.82 per 100,000, with Chimborazo and Napo following at 15.03 and 12.3, respectively.

From 2010 to 2021, provincial incidence and mortality rates per 100,000 for a certain condition varied significantly. Azuay recorded 16,206 cases with an incidence rate of 454.74 and a mortality rate of 6.55. Morona Santiago had the highest incidence rate at 1295.5 but only 1.1% of deaths. Pichincha had the most cases (21.6%) and deaths (22.9%), with an incidence rate of 482.51. Chimborazo had a high mortality rate of 15.03, with 7.3% of deaths. Bolivar and Guayas had mortality rates of 11.22 and 7.52, respectively, while the Galapagos reported no deaths. Across all provinces, there were 268,895 cases and 4,669 deaths (Supplementary Table 2).

Trends by cantons

The analysis of the dataset reveals significant disparities in the incidence and mortality rates of pneumonia among children below the age of 18 across different cantons. Specifically, the canton of Napo - Quijos has the highest recorded incidence rate at 837.74 cases per 100,000 individuals. This is closely followed by the cantons of Azuay - Paute and Tungurahua - Píllaro, with rates of 829.91 and 769.78 per 100,000, respectively (Fig. 2).

The analysis of mortality data among cantons reveals a range of mortality rates due to a specified condition, being those cantons located at higher altitudes the ones having higher mortality. For Instance, El Tambo (3,170 m) reports a rate of 102.42 per 100,000 [95%CI: 99.15; 105.69], indicating a relatively lower variance in mortality estimates. Tisaleo (3,514 m) and Patate (3,468 m) exhibit slightly higher rates of 102.98 [95%CI: 102.88; 103.08] and 107.23 [95%CI: 84.72; 129.74] respectively, suggesting greater variability in Patate. The data shows a progressive increase in mortality rates with Pimampiro (3,358 m) at 112.91 [95%CI: 86.18; 139.65] (Fig. 2).

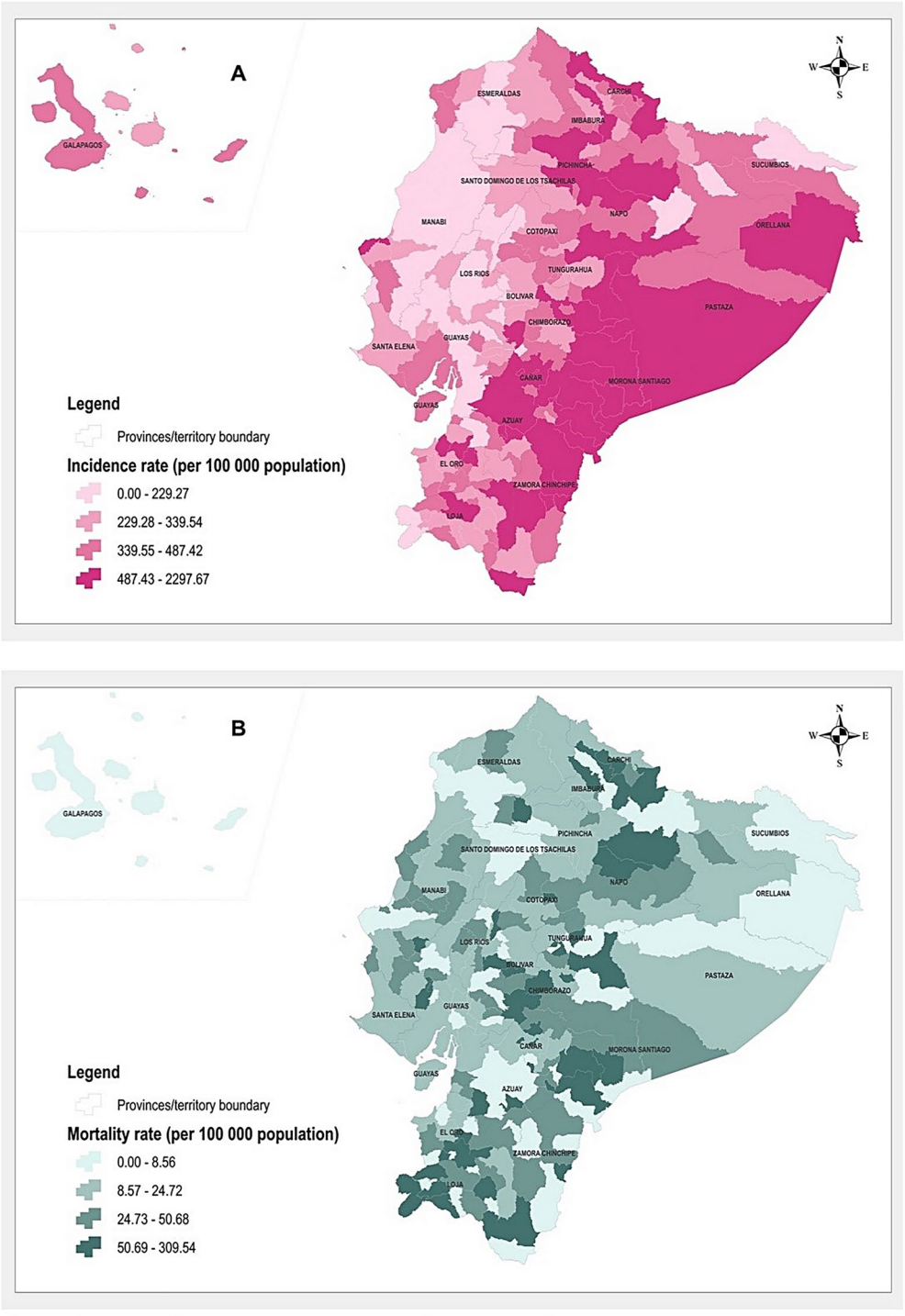

Fig. 2 Map of incidence and mortality pneumonias by cantons of Ecuador

Analysis according to elevation

Classic classification

The study examined how pneumonia incidence and mortality rates varied by altitude. Regions were delineated in low altitude (< 2500 m) and high altitude (> 2500 m). The analysis comprised a sample of 173,305 cases from low altitude regions, accounting for 64.5% of the total, with an adjusted incidence rate of 341.6 per 100,000 [95%CI: 329.8–353.5]. These regions also reported 2,723 deaths, representing 58.3% of the total, with an adjusted mortality rate of 10.16 per 100,000 [95%CI: 9.96; 10.37]. Conversely, high altitude regions encompassed 95,590 cases, which is 35.5% of the sample, with a significantly higher adjusted incidence rate of 467.4 per 100,000 [95% CI:

Table 3 Distribution of cases and deaths due to lower respiratory tract infections and pneumonia by altitude classification

Altitude Classification	Cases (*n*)	%	Adjusted Incidence rate	Deaths	%	Adjusted Mortality rate
Low	173,305	64,5%	341.6 [CI95% 329.8–353.5]	2,723	58,3%	10.16 [9.96;10.37]
High	95,590	35,5%	467.4 [95% CI 450.3–484.6]	1,946	41,7%	11.94 [11.59;12.29]
ISMM Classification						
Low	139,675	51,9%	322.2 [311.1-333.4]	2,298	49,2%	10.2[10.0-10.4]
Moderate	33,630	12,5%	455.0 [439–471.1]	421	9,0%	9.7[9.5–9.9]
High	91,321	34,0%	484.7 [466.8-502.5]	1,822	39,0%	11.6[11.2–11.9]
Very High	4,269	1,6%	267.1 [257.9-276.4]	128	2,7%	34.2[33.3–35.0]

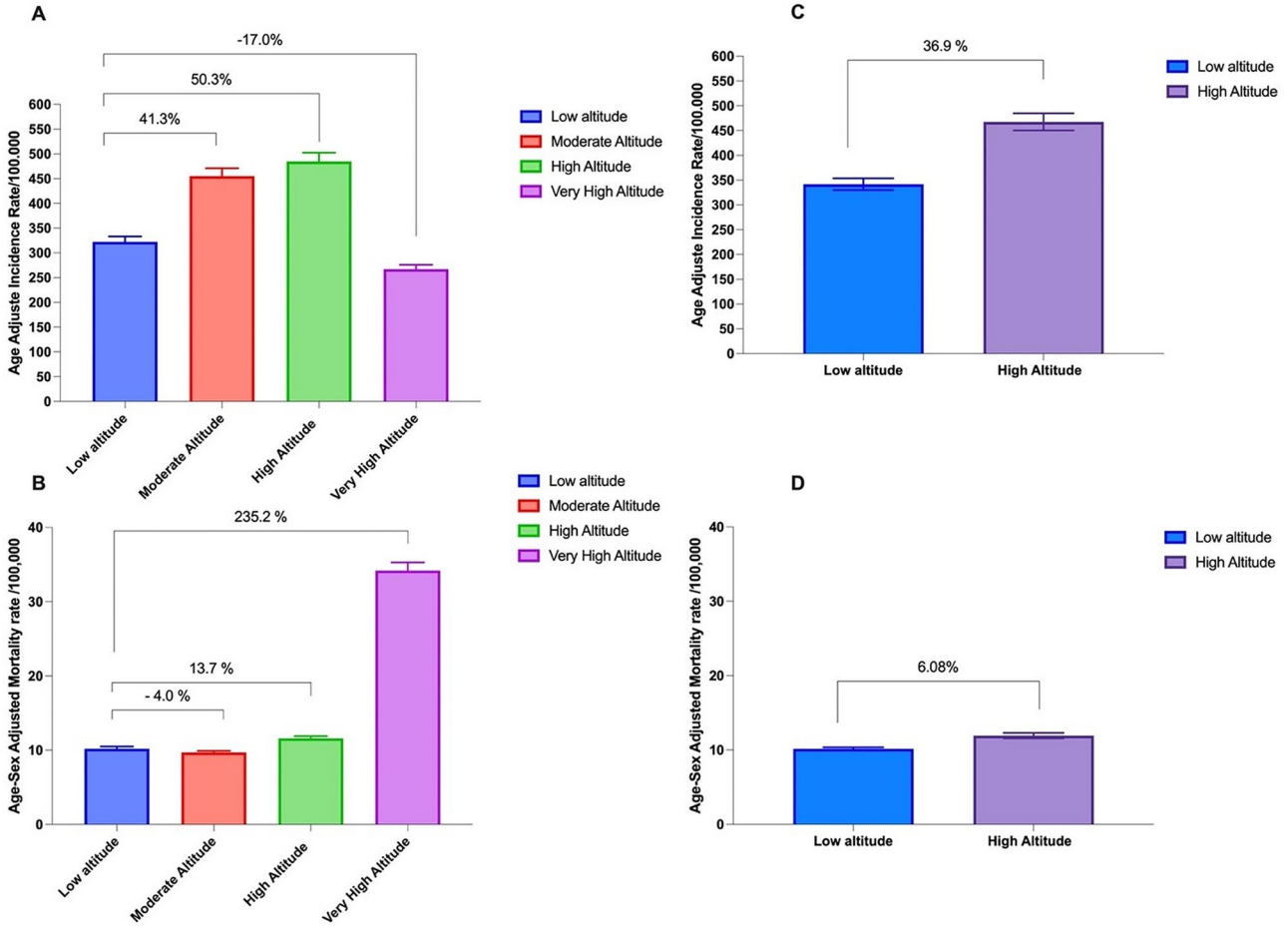

Fig. 3 Is composed of four subfigures that delineate the influence of altitude on respiratory infection outcomes. Subfigure **A** presents age-adjusted incidence rates per 100,000 people across altitude strata: low altitude in blue, moderate altitude in orange, high altitude in green, and very high altitude in purple. Subfigure **B** correlates these altitudes with mortality rates per 100,000. Subfigure **C** simplifies the categories into two groups: low altitude (< 2500 m) in blue, illustrating incidence rates, and high altitude (> 2500 m) in purple, depicting mortality rates. Subfigure **D** mirrors this two-tiered approach, highlighting mortality rates

450.3–484.6] and 1,946 deaths, constituting 41.7% of the total, with an adjusted mortality rate of 11.94 per 100,000 [95%CI: 11.59; 12.29] (Table 3).

Further classification using the ISMM classification (low, moderate, high, and very high altitude) zones show that the majority of cases (51.9%) and nearly half of the deaths (49.2%) were in low altitude areas, with an incidence rate of 322.2 per 100,000 [95%CI: 311.1-333.4] and a mortality rate of 10.2 per 100,000 [95%CI: 10.0-10.4], respectively. Moderate altitude regions reported an incidence rate of 455.0 per 100,000 [95%CI: 439–471.1] and a mortality rate of 9.7 per 100,000 [95%CI: 9.5–9.9] (Fig. 3).

High altitude areas had an incidence rate of 484.7 per 100,000 [95%CI: 466.8-502.5] and a mortality rate of 11.6 per 100,000 [95%CI: 11.2–11.9]. Notably, the very high-altitude regions, despite constituting only 1.6% of the cases, had a markedly lower incidence rate of 267.1 per 100,000 [95%CI: 257.9-276.4], but the mortality rate

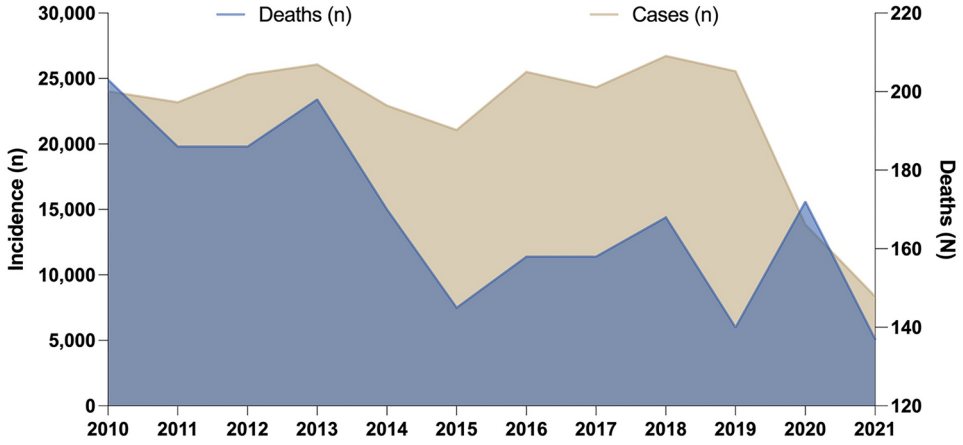

Fig. 4 Trends in pneumonia incidence and mortality in Ecuador (2010–2021). The graph illustrates the annual number of pneumonia cases (beige) and deaths (blue) among pediatric patients. A decline in hospitalizations is observed in 2020 and 2021, coinciding with the COVID-19 pandemic, while mortality remained relatively stable with a slight increase in 2020

was significantly higher at 34.2 per 100,000 [95%CI: 33.3–35.0].

Trends by year

Between 2010 and 2021, pneumonia incidence and mortality in Ecuador fluctuated. Hospitalizations remained stable from 2010 to 2019 (21,000–26,000 cases annually) but dropped sharply in 2020 (13,851) and 2021 (8,355), likely due to COVID-19-related healthcare disruptions and preventive measures. Mortality declined from 203 deaths in 2010 to 137 in 2021, though a slight increase in 2020 (172 deaths) may reflect pandemic impacts. These trends underscore the need to evaluate changes in treatment, vaccination, and healthcare access (Fig. 4).

Discussion

The burden of pneumonia on children in Ecuador varies with altitude and sex. At lower altitudes, total YLL is higher, especially in boys. Adjusting for population, boys, and girls at lower altitudes experience 5,454 and 4,600 YLL per 100,000, respectively. While higher altitudes report fewer total YLL, the per capita burden remains significant. COVID-19 has further contributed to the disease burden, with over 200 YLL per 100,000 in identified cases, emphasizing its impact on child health.

Pneumonia accounted for 15% of all deaths in children under 5 years of age in Ecuador in 2015 [13]. The disease disproportionately affects socially marginalized populations, including ethnic minorities, low-income families, individuals with limited education, and those residing in remote areas with restricted healthcare access [16]. Despite the burden, pneumonia is classified as a preventable disease with accessible and affordable treatment [17].

During the study period, over 268,000 children in Ecuador were hospitalized for pneumonia, with more than 4,600 fatalities. Mortality was attributed to various causes, including unspecified diagnoses, bacterial pneumonia, nonspecific pneumonias, and viral pneumonias without molecular confirmation. Limited access to an organized healthcare system for accurate disease etiology diagnosis likely contributed to these figures. The absence of diagnostic testing has been a persistent challenge in Ecuador, further highlighted during the COVID-19 pandemic [18]. Diagnosing pneumonia etiologies often requires molecular methods and invasive measures to collect sputum or lung tissue, reducing opportunities in areas with scarce health services, like communities at very high altitudes [19].

In high-income countries, pneumonia incidence rates range between 10 and 15 cases per 1,000 children annually, with hospitalization rates of 1 to 4 per 1,000 [20]. This study found significantly higher rates of 20 to 28 cases per 1,000 children annually, which may be attributed to differences in healthcare access and immunization coverage [21, 22].

Approximately 79.1% of pneumonia cases were of unknown etiology, likely due to systemic constraints on confirmatory testing [20]. Identifying pneumonia etiology is challenging even in high-income settings, as children are not reliable sputum producers, and less than 10% of pneumonia cases present with bacteremia. Serology is unreliable in infants under one year, and antigen detection tests have variable sensitivity [23]. Nasopharyngeal aspiration provides the most reliable method for identifying viral pneumonia through virus isolation. However, molecular detection requires specialized laboratories, which are often unavailable in remote areas [24].

Most pneumonia cases occurred in children under one year old, aligning with global trends in disease burden. Mortality decreased with age. In socioeconomically disadvantaged populations, undernutrition is prevalent

among women and children, negatively impacting breastfeeding practices and increasing pneumonia risk [25, 26]. Given the underdeveloped immune systems of infants, they remain highly vulnerable to severe respiratory infections [27]. This population should be prioritized in public health strategies, including vaccination campaigns, to mitigate morbidity and mortality.

During the study period, COVID-19 pneumonia in Ecuador resulted in fewer than 2,000 hospitalizations and under 30 deaths attributed to SARS-CoV-2. However, these figures likely underestimate the true burden, as approximately 88,000 deaths occurred during the pandemic [18]. While SARS-CoV-2 was not the leading cause of pneumonia overall, it was associated with high mortality rates among infants, as reported in previous studies [28].

Regarding ethnicity, Afro-descendant girls exhibited the highest pneumonia-related mortality rates compared to other ethnic groups. Conversely, children self-identified as "white" had higher pneumonia incidence, potentially reflecting greater access to healthcare and diagnostic services, alongside lower mortality rates due to improved health determinants and reduced risk factors [29, 30]. Disparities in pneumonia outcomes by ethnicity may be linked to differences in healthcare access, socioeconomic status, and possible genetic or immunological factors [25, 26, 31].

This study contributes to the limited literature on disease burden by elevation. Higher altitudes are associated with lower partial oxygen pressure, reducing oxygen availability [32]. In adults, physiological adaptations to hypoxia may mitigate pneumonia severity, as observed with COVID-19 [33]. However, geographic isolation and healthcare accessibility challenges in high-altitude areas may increase pneumonia-related mortality due to delayed medical intervention.

While defining an altitude threshold for elevated pneumonia mortality remains difficult, higher elevations generally correlate with reduced healthcare access. Previous research in Ecuador found a similar distribution of medical centers and hospital beds per capita at different elevations [14]. This study observed that pneumonia morbidity declines at higher altitudes, whereas mortality and disease burden increase. However, causality cannot be established. Factors such as geographic isolation, limited healthcare access, and long distances from urban centers may contribute to this trend. It is hypothesized that physiological adaptations to chronic hypoxia at high altitudes may be insufficient to counteract the acute hypoxemia caused by pneumonia, exacerbating disease severity and mortality risk in children.

Limitations

Most data in this study were grouped under 'unspecified pneumonia,' primarily due to difficulties in identifying the etiological causes of pneumonia and errors in coding the disease. This grouping results in a loss of detailed information that could be crucial for developing targeted health interventions focused on prevention.

Furthermore, standardized data on the level of disability caused by pneumonia in Ecuador is unavailable. Consequently, calculating Disability-Adjusted Life Years (DALYs) was not feasible. Without a comparable population dataset, extrapolating the results was also not possible. This lack of data significantly hampers the accurate estimation of the disease's burden.

Lastly, the hospital discharge system lacks data on several key aspects, including the educational level of the patients' families, the children's places of origin, the treatments received, and instances of recurrence or hospital readmissions. The absence of this information limits the comprehensiveness of our understanding of the factors influencing pneumonia outcomes.

Conclusions

This study reveals that the burden of pneumonia in Ecuadorian children is significantly influenced by altitude and sex. It highlights the importance of incorporating altitude considerations into public health strategies addressing pneumonia, alongside socio-economic factors. The interplay between geographic location and socio-economic status is critical for understanding and improving child health outcomes. Therefore, future research should focus on exploring this intersection to inform more effective public health interventions and policies. Such efforts are essential for mitigating the impact of pneumonia on vulnerable populations, particularly in areas with challenging geographical and economic conditions.

Abbreviations

WHO	World Health Organization
GBD	Global Burden of Diseases
UNICEF	United Nations International Children's Emergency Fund
DALYs	Disability-adjusted life years
CFR	Case fatality rates
IRB	Institutional Review Board
UDLA	Universidad de las Américas
INEC	National Institute of Statistics and Census
GCP	Good Clinical Practice

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Author contributions
EO-P conceived the idea, formulated the research paper, and was responsible for data acquisition, having gained full access to data from the National Statistical Institutes in Ecuador. EO-P also played a pivotal role in the conception and design of the entire project, ensuring the completeness and accuracy of the work, and took primary responsibility for all aspects of the study. MVCS and JP conducted the analysis under the supervision of EO-P and were instrumental in writing the initial draft of the manuscript. JV-G, and JSI-C contributed to data collection, as well as to the review of the relevant literature and the preliminary drafting of the text. JSI-C, along with EO-P, were involved in the statistical analysis, reinforcing the internal validity of the research. GV and BC provided a critical appraisal of the manuscript, revising it thoroughly to produce the final version. All authors have meticulously reviewed and given their consent to the final version of the manuscript before submission.

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Data availability
The data used comes from the public access databases of the National Institute of Statistics and Census (INEC) https://www.ecuadorencifras.gob.ec/camas-y-egresos-hospitalarios/.

Declarations

Ethical approval
The study was granted an exemption from ethical review by the Institutional Review Board (IRB) of the Ethics Committee at Universidad de las Américas (UDLA), Quito, Ecuador. This exemption, officially coded as 2023-EXC-008, was formally issued on May 8, 2023.

Consent for publication
Not Applicable.

Competing interests
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.

Author details
[1]One Health Research Group, Faculty of Health Science, Universidad de Las Americas, Quito, Ecuador
[2]Department of Public Health, Brigham Young University, Provo, USA
[3]Departament de Biologia Cel·lular, Fisiologia iInmunologia, Universitat de Barcelona, Barcelona, Spain
[4]One Health Research Group, Universidad de las Américas Quito, Ecuador Calle de los Colimes y Avenida De los Granados, Quito 170137, Ecuador

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