

ORIGINAL

## Influenza a pneumonia in the pediatric population in the post-pandemic era

## Neumonía por influenza a en la población pediátrica en la era pospandemia

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**Cite as:** Paredes Lascano P, Toapanta Yugcha I, Mejía Ortiz R, Bravo Paredes L, Aguayo Escobar A. Influenza a pneumonia in the pediatric population in the post-pandemic era. Salud, Ciencia y Tecnología. 2025; 5:1867. <https://doi.org/10.56294/saludcyt20251867>

Submitted: 15-01-2025

Revised: 22-03-2025

Accepted: 01-07-2025

Published: 02-07-2025

Editor: Prof. Dr. William Castillo-González 

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### ABSTRACT

**Introduction:** Influenza A pneumonia is an acute viral infection that affects the respiratory tract and is transmitted through droplets expelled when coughing or sneezing. In the pediatric population, it presents with symptoms such as fever, cough, rhinorrhea, and respiratory distress, which can lead to complications like respiratory distress or bacterial superinfection.

**Objective:** the aim was to identify Influenza A as a cause of pneumonia in children aged 1 year to 10 years in the post-pandemic context.

**Method:** a prospective, observational, and analytical study was conducted in 265 children without previous comorbidities, admitted between 2023 and 2025 at the Ambato General Hospital IESS. Patients aged 1 year to 10 years, diagnosed through nasopharyngeal swabs for Influenza A, were included.

**Results:** 53 % of the cases were female, and 47 % male, with the majority of cases in the 3 to 5 years group (27 %). 82 % had contact with individuals with prior respiratory symptoms. The most common symptoms were cough (23 %), fever (22 %), rhinorrhea (21 %), and respiratory distress (50 %). Radiological images showed hyperinflation (19 %) and interstitial patterns (18 %). Influenza A and Respiratory Syncytial Virus were the predominant etiological agents.

**Conclusions:** Influenza A is a significant cause of pneumonia in children, particularly in those under 5 years old, with a higher incidence in winter months, especially in February. The implementation of epidemiological surveillance protocols and early treatment is recommended to reduce mortality.

**Keywords:** Influenza A; Pediatric Pneumonia; H1N1; Oseltamivir.

### RESUMEN

**Introducción:** la neumonía por Influenza A es una infección viral aguda que afecta las vías respiratorias y se transmite a través de gotitas expulsadas al toser o estornudar. En la población infantil, se manifiesta con síntomas como fiebre, tos, rinorrea y dificultad respiratoria, pudiendo complicarse con distrés respiratorio o sobreinfección bacteriana.

**Objetivo:** el objetivo fue identificar al Influenza A como causa de neumonía en niños menores de 1 año hasta los 10 años en el contexto postpandemia.

**Método:** se realizó un estudio prospectivo, observacional y analítico en 265 niños sin comorbilidades previas, ingresados entre 2023 y 2025 en el Hospital General Ambato IESS. Se incluyeron pacientes de 1 año hasta 10 años, quienes fueron diagnosticados mediante hisopado nasofaríngeo para Influenza A.

**Resultados:** el 53 % de los casos fueron niñas y el 47 % niños, con la mayoría de los casos en el grupo de 3 a 5 años (27 %). El 82 % tuvo contacto con personas con síntomas respiratorios previos. Los síntomas más comunes fueron tos (23 %), fiebre (22 %), rinorrea (21 %) y dificultad respiratoria (50 %). Las imágenes radiológicas mostraron hiperinsuflación (19 %) y patrón intersticial (18 %). Influenza A y el Virus Sincitial Respiratorio fueron los agentes etiológicos predominantes.

**Conclusiones:** la Influenza A es una causa importante de neumonía en niños, particularmente en menores de 5 años, con una incidencia mayor en los meses de invierno, especialmente en febrero. Se recomienda la aplicación de protocolos de vigilancia epidemiológica y tratamiento temprano para reducir la mortalidad.

**Palabras clave:** Influenza A; Neumonía Pediátrica; H1N1; Oseltamivir.

## INTRODUCTION

Influenza A virus pneumonia is a respiratory disease that mainly affects the respiratory tract from the nose, pharynx, larynx, bronchi, and bronchioles, producing complications such as pneumonia and otitis in children under 2 years; it belongs to the family Orthomuxoviridae, whose genome is segmented RNA and its envelope is covered by a hemagglutinin and neuraminidase, which are responsible for generating epidemics as they have the property to change antigenicity.<sup>(1,2)</sup> This virus has caused outbreaks worldwide, such as avian influenza (H5N1) in 1997, swine influenza (H1N1) in 2009, and avian influenza (H7N9) in 2013.<sup>(1,2)</sup>

Influenza A virus is a single-stranded RNA virus; its structure is characterized by a lipid bilayer envelope replete with viral glycoproteins.<sup>(2)</sup> The two major glycoproteins on the viral surface are haemagglutinin (HA) and neuraminidase (NA), which play key roles in the viral life cycle, including adherence, entry, and exit from host cells; in addition, the viral envelope encloses the ribonucleoprotein (RNP) complex that includes viral RNA and associated proteins essential for replication.<sup>(3)</sup>

The influenza A virus genome is composed of eight segments that encode proteins crucial for replication and virulence, including the polymerase subunits (PB2, PB1, and PA), haemagglutinin, neuraminidase, nucleoprotein, and the M1, M2, NS1, and NS2 proteins.<sup>(4)</sup>

The H1N1 subtype contains haemagglutinin type 1 and neuraminidase type 1 in its lipid envelope, a characteristic that determines its ability to bind to sialic acid receptors in the human respiratory epithelium, being responsible for the pandemic potential; the H3N2 subtype contains haemagglutinin type 3 and neuraminidase type 2 in its lipid envelope and is also pathogenic for humans.<sup>(3)</sup>

Worldwide, since 2009, it has been estimated that 34 % to 43 % of H1N1 infections occur in the pediatric population, of which approximately 28 % develop pneumonia as a complication.<sup>(5)</sup>

In Latin America, influenza A infections in the pediatric age group account for 35-40 % of all cases, with hospital admissions for pneumonia reported in 25 % of these cases. In Ecuador, although there are no exact figures for H1N1 pneumonia in the pediatric age group, children under five years of age constitute the majority of reported cases, and this age group is the most affected by pneumonia.<sup>(6)</sup>

Influenza A virus is transmitted by inhalation of respiratory droplets from an infected patient.<sup>(7)</sup> Infection begins when haemagglutinin attaches to sialic acid receptors on hair cells and type II pneumocytes in the respiratory tract. Clathrin-mediated endocytosis leads to the formation of an endosome, whose acidification causes a conformational change in haemagglutinin that facilitates the fusion of the viral and endosomal membranes.<sup>(8)</sup> Once the viral ribonucleocapsids are released into the cytosol, they transit to the nucleus for transcription by viral RNA polymerase.<sup>(9,10)</sup> The new virions assemble at the plasma membrane, and thanks to neuraminidase activity, the sialic acid residues are separated to allow budding and release of the progeny particles.<sup>(10)</sup>

In the early phase of infection, the PB1-F2 protein enhances alveolar macrophage apoptosis. It promotes the release of proinflammatory mediators, whereas the NS1 protein inhibits the production of type I interferon, thereby delaying the innate antiviral response and allowing uncontrolled virus replication in the lower respiratory tract.<sup>(11,12)</sup> Focal necrosis of the bronchiolar epithelium and damage to the alveolar interstitium leads to increased vascular permeability, infiltration of neutrophils, macrophages, the release of cytokines such as interleukin 6, tumor necrosis factor-alpha, and interferon-gamma; This inflammatory environment leads to accumulation of fibrinopurulent exudate in the alveoli and thickening of the alveolar septa, leading to diffuse alveolar damage with formation of hyaline membranes and alveolar collapse, central manifestations of acute respiratory distress syndrome.<sup>(11,13)</sup>

In infants under one year of age, influenza A H1N1 pneumonia typically presents with high fever, refusal of food, lethargy, episodes of apnea, and marked respiratory distress, as evidenced by tachypnea and intercostal retractions.<sup>(14)</sup> In children aged one to five years, headache, rhinorrhoea, dry cough, vomiting, occasional diarrhea, and general malaise are observed; from the age of six and adolescence onwards, symptoms are more

similar to those of adults, with intense myalgia, odynophagia, headache, and productive cough; infants and children under two years of age are at most significant risk of progression to severe forms due to their lower pulmonary reserve and immature immune system.<sup>(15)</sup>

The most relevant complications of influenza A in the pediatric age group include primary viral pneumonia, characterized by extensive inflammation of the lung parenchyma, and progression to acute respiratory distress syndrome with refractory hypoxemia, often requiring invasive mechanical ventilation.<sup>(14)</sup> Secondary bacterial superinfection, especially by *Streptococcus pneumoniae* and *Staphylococcus aureus*, contributes to the development of lobar consolidations, empyema, and lung abscess formation. Sepsis of viral origin may progress to multi-organ failure with cardiovascular and renal dysfunction secondary to viremia and systemic inflammatory response. In rare cases, encephalitis, seizures, myocarditis, and rhabdomyolysis may occur, particularly in patients with comorbidities.<sup>(15)</sup>

The diagnosis of Influenza A pneumonia is based on the integration of clinical, radiological, and laboratory findings. Chest radiography reveals bilateral interstitial infiltrates and ground-glass opacities, while computed tomography (CT) may show consolidation in subpleural areas.<sup>(16)</sup> Polymerase chain reaction (PCR) is the gold standard and is considered positive when the threshold cycle (Ct) values are less than 35, indicating a high viral load; additionally, marked elevations in C-reactive protein (PCR >100 mg/L) and procalcitonin levels between 0,5 and 2 ng/mL are observed in the absence of bacterial co-infections.<sup>(17)</sup>

The differential diagnosis of influenza pneumonia includes viral infections, such as coronavirus disease (COVID-19), the common cold, and seasonal allergies, as well as bacterial infections, including *Mycoplasma pneumoniae* and *Streptococcus pyogenes*. However, respiratory symptoms are common in many of these diseases; the sudden onset of high fever, myalgias, and malaise points to influenza.<sup>(18)</sup> The presence of purulent sputum suggests bacterial etiology, while symptoms such as anosmia or diarrhea are more characteristic of COVID-19. Therefore, specific diagnostic tests are crucial for accurate clinical differentiation.<sup>(17,18)</sup>

Timely management with antivirals such as oseltamivir and timely oxygen therapy is essential to reduce progression to severe forms and minimize mortality, which is high in infants and children with comorbidities such as asthma or heart disease and those with immunosuppression.<sup>(14,19)</sup>

## METHOD

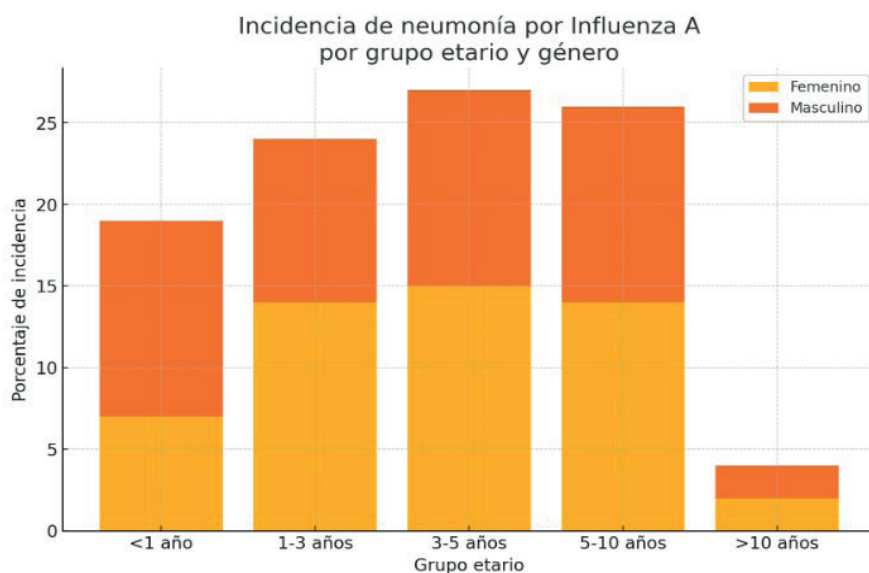
This is a prospective, longitudinal, comparative, comprehensive, and analytical study that evaluated outbreaks of Influenza A in 265 children hospitalized without comorbidities in the Paediatric Department of the General Hospital Ambato IESS, aged between 1 month and 14 years and 4 months. The data were collected from January 2023 to April 2025, and statistical analysis was performed using the SPSS system. The inclusion criteria were patients admitted to the pediatrics department who were registered in the AS400 computer system. Variables such as gender, origin, clinical picture, reason for consultation, aetiological agents, pulmonary radiographic patterns, complementary laboratory tests, and hospital stay were analyzed. Exclusion criteria were children with comorbidities and those in whom nasopharyngeal swabbing for influenza A was not performed.

## RESULTS

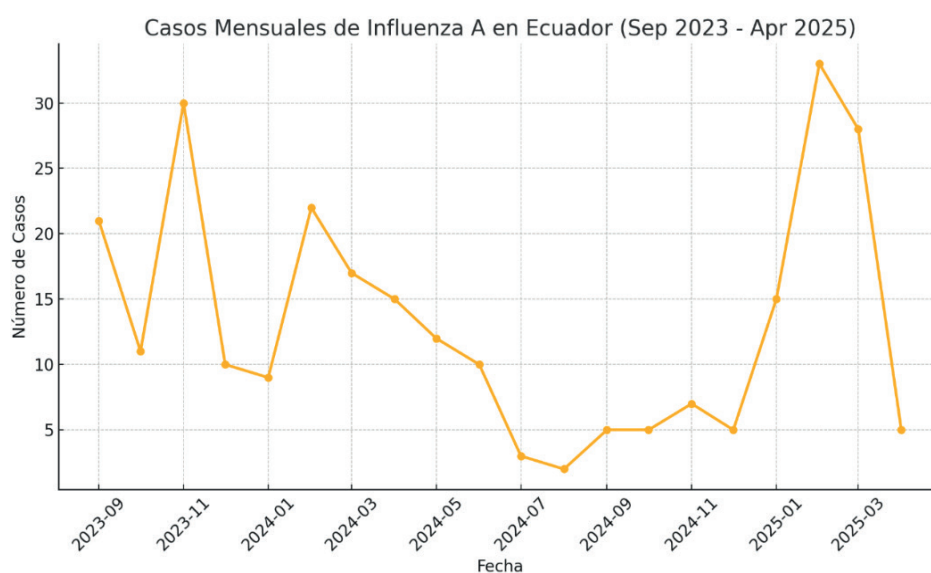
The sample was conducted from 2023 to April 2025, encompassing a universe of 265 patients admitted to the Paediatrics Service of Hospital General Ambato IESS, with a gender distribution of 53 % female and 47 % male. Ninety-seven percent of the patients were from the province of Tungurahua, and 3 % were from the provinces of Cotopaxi, Esmeraldas, Pastaza, Pichincha, and Bolivar. The age group with the highest incidence of Influenza A pneumonia was between 3-5 years old, 27 % (15 % female; 12 % male), between 5-10 years old, 26 % (14 % female; 12 % male), 1-3 years old, 24 % (14 % female; 10 % male), under 1-year-old, 19 % (7 % female; 12 % male) and over 10 years old, 4 % (2 % female; 2 % male).

Between September 2023 and April 2025, the circulation of Influenza A in the central region of Ecuador exhibited an increase during the rainy season, followed by a decrease in the dry season. In November 2023, there was an atypical peak of 30 cases, and in December, 10 cases; for 2024, the incidence was January (9 cases), February (22 cases), remaining high in March and April (32 cases), in May (12 cases), June (10 cases), in July, August and September (10 cases). In September 2024, five cases were observed; by the end of 2024, (5-7 cases). In the first quarter of 2025, January (15 cases), February (33 cases) and March (28 cases), with a sharp drop in April (5 cases).

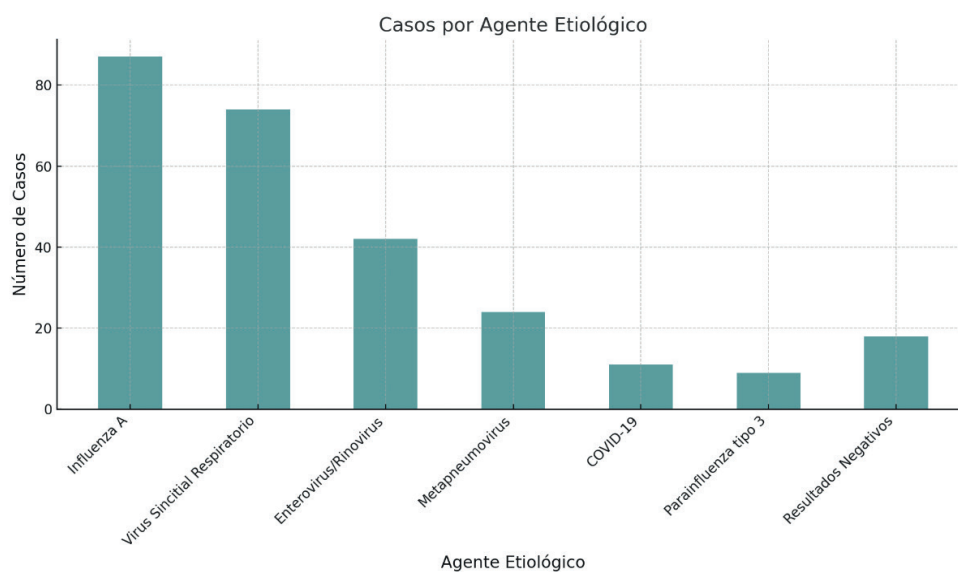
The prodromal period before admission was less than or equal to 3 days in 108 patients (41 %) and more than 3 days in 157 patients (59 %). Regarding the place of infection, 82 % of patients reported contact with respiratory symptomatic patients, and the most frequent place of infection was at home (66 %).



**Figure 1.** Incidence of influenza A pneumonia by age and gender



**Figure 2.** Incidence of cases by season September 2023-April 2025



**Figure 3.** Aetiological agents of pneumonia

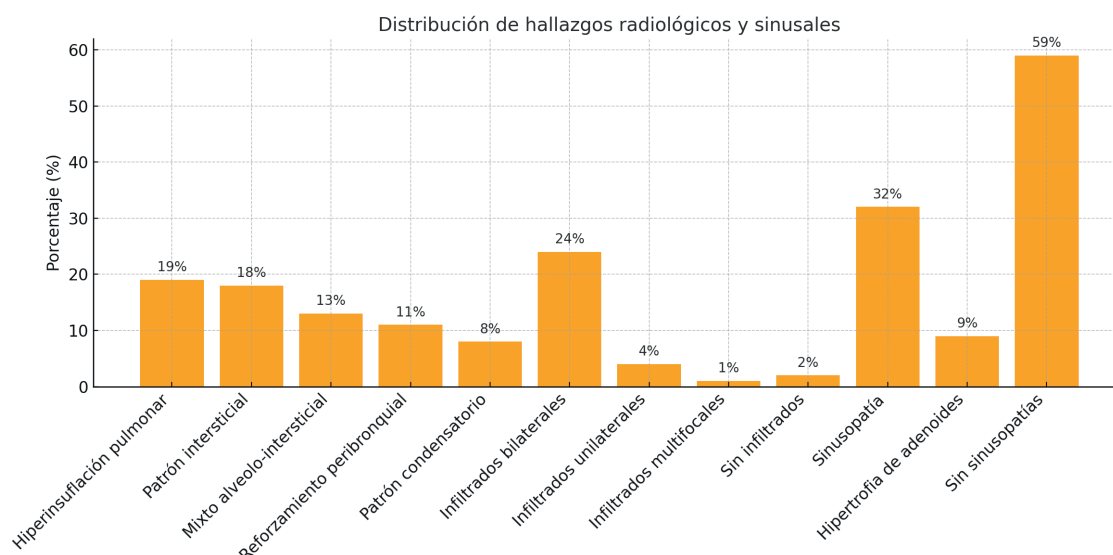


Figure 4. Most frequent radiological patterns

In the laboratory results of acute phase reactants, C-Reactive Protein was  $<5$  mg/l in 174 patients (66 %), 5-50 mg/l, 69 cases (26 %), 50-100 mg/l; 14 cases (5 %), and greater than 100 mg/dl, 8 (3 %). Procalcitonin  $<0,5$  ng/ml, 256 (97 %) and  $>0,5$  ng/ml, 9 (3 %). Interleukin 6 levels were stratified as follows:  $<5$  pg/ml, 195 (74 %); and  $>5$  pg/ml, 70 (26 %).

Blood biometry showed leukocytosis ( $> 10,000/\mu\text{L}$ ) in 44,15 of patients, of which 66 patients exhibited a left shift (56,41 %), while 34 patients showed a right shift (29,06 %), and 17 patients did not exhibit any imbalance (14,53 %).

During treatment, 78 % received combined beta-2-adrenergic agonist and corticosteroid therapy. Triple antibiotic therapy with ceftriaxone, clarithromycin, and azithromycin was used in 5 % of cases. In comparison, ampicillin and sulbactam monotherapy were used in 37 % of cases, and double therapy with ceftriaxone and clarithromycin was used in 58 % of cases.

In terms of length of hospital stay, 21 % were less than 5 days, 77 % were between 5 and 10 days, and 2 % were for more than 10 days. Of all patients, 95 % had no complications during their clinical course, and 5 % had pulmonary hypertension and Epstein-Barr hepatitis, which is why they were transferred to the ICU.

## DISCUSSION

Kanecki Krzysztof, in a retrospective study conducted in Poland by the National Institute of Public Health (NIH) based on the National Hospitalisation Register, with a sample of 8565 patients hospitalized during the period 2015-2019, found that Influenza A pneumonia occurred more frequently in males (55 %) than females (45 %), in children under 1 year of age (46 %) and the seasonal period with the highest incidence was January-March in all years, with a higher number of cases in February (3 247). In the present study, the gender with the highest number of cases was found to be female (53 %), primarily due to cultural and social differences, as well as differences in health systems. Regarding age, the incidence was higher among children aged 3 to 5 years (27 %), a situation that can be attributed to epidemiological factors, differences in vaccination schedules, and childcare habits in each country. The most frequent seasonal period in our study was winter (December to May) (65 %), with February being the month with the highest number of cases, which coincides with the study, as winter weather conditions favor virus transmission.<sup>(20)</sup>

Rukshan Rafeek is a retrospective study conducted in Sri Lanka, South Asia, at Kegalle University Hospital Sri Lanka, with a sample of 500 children hospitalized from May 2016 to June 2018; reported that Influenza A symptomatology in 261 patients was cough (52,2 %), fever in 228 (45,6 %), rhinorrhoea in 251 (50,2 %), dyspnoea in 132 (26,4 %) and wheezing in 17 (3,4 %); In our study of 265 patients admitted to the pediatric ward, the primary symptomatology on admission was wet cough in 171 cases (23 %), fever in 164 (22 %), rhinorrhoea in 155 (21 %), respiratory distress in 133 patients (50 %) and wheezing/rhinorrhoea in 34 (13 %), similar symptomatology that is common to both the series presented and our study.<sup>(21)</sup>

Parralles Cedeño et al., in a retrospective and descriptive study conducted at the Hospital Francisco de Icaza Bustamante in Ecuador, with a sample of 200 pediatric patients admitted with acute respiratory infections aged between 2 months and 15 years, January 2020-December 2023, found that Influenza A virus was the most frequent aetiological agent (35 %), followed by Respiratory Syncytial virus (28 %), Adenovirus (15 %) and Parainfluenza virus (12 %). In the present study, the most frequent aetiological agent was Influenza A virus with

87 cases (33 %), followed by Respiratory Syncytial Virus as the second cause of morbidity with 74 cases (28 %) and less frequently Enterovirus/Rinovirus with 42 cases (16 %), Metapneumovirus with 24 cases (9 %), which shows that Influenza A both on the coast and in the highlands is the primary etiology of hospital admission for pneumonia in the post-pandemic period.<sup>(22)</sup>

Rodríguez Martrus et al., in an analytical literature review that synthesizes the information already existing in the scientific literature on Influenza A, identifies that chest X-rays can show diffuse, multifocal or interstitial pulmonary infiltrates, with or without consolidation; however, there is no pathognomonic radiological pattern that allows differentiation, allowing a typical result to be obtained in the first days of illness or even in severe cases, although it is not an etiological diagnostic method, it helps to monitor progression and detect complications. In this investigation, the most frequent radiological pattern was pulmonary hyperinflation (19 %), followed by an interstitial pattern (18 %), a mixed alveolar-interstitial pattern (13 %), peribronchial enhancement (11 %), and a condensation pattern (8 %). Radiological findings were bilateral and symmetrical in 24 %, unilateral in 4 %, and multifocal in 1 %. This coincides with the imaging results reported.<sup>(23,24)</sup>

Jeffrey Baker et al., in a comparative study of baloxavir and oseltamivir as treatments for influenza infection, with a sample of 173 children aged 1-12 years, showed that administering a single dose of baloxavir was more effective against the H3N2 strain. In contrast, oral oseltamivir twice daily for 5 days was more effective for the H1N1 strain. In our study, oseltamivir was also used, which allowed for a significant recovery without complications. However, in complicated cases, it was necessary to add third-generation cephalosporins and macrolides to the treatment due to bacterial superinfection.<sup>(25)</sup>

Adrienne Randolph et al. observed that children infected with influenza and methicillin-resistant *Staphylococcus aureus* (MRSA) exhibited leukopenia and neutropenia (360/ $\mu$ L) within the first 24 hours despite receiving antibiotic treatment (vancomycin plus clindamycin). In our cohort, 11 % showed leukopenia (< 5000/ $\mu$ L) and 27 % neutropenia (< 40 %), prompting the empirical initiation of broad-spectrum antibiotics, supported by clinical, laboratory, and radiological criteria.<sup>(26)</sup>

Qiong-yu Wang et al., in a retrospective analysis of the clinical features of severe influenza virus-associated pneumonia in children, described a mean hospital stay of 9 days and demonstrated that early administration of neuraminidase inhibitors (within the first 48 h) is associated with a significant reduction in hospitalization time and less need for intensive care. In our study, 21 % of patients stayed in the hospital for less than 5 days, and the majority (77 %) stayed between 5 and 10 days. These results are similar to those of Quiong-yu's retrospective study series.<sup>(27)</sup>

## CONCLUSIONS

The present study demonstrates that Influenza A pneumonia is a significant cause of post-pandemic pediatric hospitalization, particularly in children under 5 years of age, with a higher predominance during the winter seasonal period and a higher incidence in February. These data indicate that the peak season for Influenza A occurs between January and March, highlighting the need to reinforce vaccination and surveillance before February.

From a seasonal perspective, the sharpest increases in cases coincide with the rainy season in the Ecuadorian coastal region (January to April), suggesting that wet conditions favor viral transmission. The atypical peak in November 2023 did not reach high levels. During the dry season (June-September), circulation was minimal, with the lowest values observed in July and August. The last quarter exhibited low activity. Each cycle starts in January, reaches its peak in February-March, and wanes in May-June, underscoring the need to reinforce vaccination before the rainy season.

The most important clinical manifestations for the diagnosis of Influenza A pneumonia are wet cough, fever, and fever.

Pneumonia symptoms include a wet cough, fever, and rhinorrhoea, with respiratory distress being the most alarming clinical sign.

Antiviral treatment with oseltamivir, combined with respiratory support measures and broad-spectrum antibiotics in cases of documented superinfection, improves clinical status, reduces hospital stay, and prevents serious complications, thereby reducing mortality from this pathology.

This research demonstrates the importance of implementing early management protocols and epidemiological surveillance strategies to mitigate the impact of this respiratory infection in the pediatric population.

## ACKNOWLEDGMENTS

The authors would like to thank the Dirección de Investigación y Desarrollo DIDE, Universidad Técnica de Ambato.

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## FUNDING

The authors received no funding for the development of this research.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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