Epidemiological surveillance of the influenza virus in Ecuador: a bibliographic review

Moreira Zambrano, Ronaldo Andrés[1], Lascano Álvarez, Karla Alejandra[2], Poveda Paredes Francisco Xavier[3]

[1]Facultad de ciencias médicas, Universidad Regional Autónoma de los Andes, Ambato, Email: ma.ronaldoamz25@uniandes.edu.ec Ecuador. https://orcid.org/0000-0001-6789-6698

[2]Facultad de ciencias médicas, Universidad Regional Autónoma de los Andes, Ambato, Email: ma.karlaala25@uniandes.edu.ec Ecuador. https://orcid.org/0000-0001-6659-6095

[3]Facultad de ciencias médicas, Universidad Regional Autónoma de los Andes, Ambato, Email: ua.franciscopoveda@uniandes.edu.ec Ecuador. https://orcid.org/0000-0002-2009-3502

Abstract

The influenza virus is a respiratory disease that affects the nose, throat, bronchial tubes, and lungs. Generally, the virus tends to spread in the form of seasonal epidemics, especially in winter. However, Ecuador experiences two peaks of infection in January-March and July-August. Since people with comorbidities are at higher risk of complications, since 2006 Ecuador has offered an annual vaccination campaign that begins in December and ends in mid-March. These quadrivalent vaccines are designed from four strains of influenza to help build the immune system and its rapid response to contact with an infected person. The objective of this study is to carry out a bibliographic analysis of the epidemiological surveillance of the country in order to highlight the usefulness of the investigation against new strains of influenza.

Keywords: "influenza", "epidemiological surveillance", "Ecuador"

1. Introduction

The flu virus causes a contagious respiratory illness that can be mild or severe. This mainly affects the nasal cavity, throat, bronchi and sometimes the lungs. It has a high transmissibility, a person can be infected through contact with the droplets of an infected person, either by coughing or sneezing (Pan American Health Organization, 2021).

Before the contagion by influenza, the symptomatology appears with respiratory manifestations such as nasal congestion, sore throat. The characteristic debut of influenza presents with episodes of fever, chills, muscle aches, headache, fatigue, weakness, asthenia (Gómez et al., 2022; Pan American Health Organization, 2021). In children it is common for them to present nausea and vomiting accompanied by diarrhea (Lozano, 2019)

Influenza is an RNA virus characterized by remarkable genetic variability. This can be classified into types A, B, C and D, the first three, causing pathologies in humans. From this classification, influenza A is responsible for causing epidemics, especially in a specific season of the year, winter. This is due to its mutagenic capacity and easy spread among the population. Influenza A is characterized by the presence of two proteins that act as antigens: hemagglutinin (varies from H1 to H18) and neuraminidase (can be from N1 to N11), and therefore would have different combinations thanks to the redistribution of the virus. Through this process it can exchange genetic material, this happens when two different combinations of influenza infect the same host, which would explain the ease of mutation. (Centers for Disease Control and Prevention, 2021; Rao et al., 2019; Vircell Microbiologist, 2020)

The aforementioned proteins are what we call antigens, at the time of entering the body, these are recognized by the immune system what we call antigenic property. The immune response develops antibodies for each antigen. However, it is necessary to remember that the high genetic variability of this virus causes that the immunity developed for one subtype of influenza A is not fully effective in counterattacking the invasion of another virus of the same type. We usually find subtypes A(H1N1) and A(H3N2) of the influenza virus. (Centers for Disease Control and Prevention, 2021; Rao et al., 2019; Vircell Microbiologist, 2020)

Influenza A is the protagonist of five pandemics from 1890 to 2009 and each year triggers epidemics (Harrington et al., 2021). Since the late nineteenth century, the so-called Russian flu appeared due to the influenza A (H3N8) virus with which at least 1 million people lost their lives (Castañeda et al., 2021). The following century, at the beginning of March 1918 a wave of flu was recognized in a US army camp that meant the first wave, the second occurred in mid-October of the same year during this period the highest mortality rate was recorded among 50 to 100 million people, the symptoms were not different from those typical of the common cold, However, complications appeared suddenly,

tachypnea, angina pectoris, dry cough, delirium and in some cases cyanosis for what was known as purple death. The so-called 1918 Spanish flu is due to the influenza A (H1N1) virus (Harrington et al., 2021; Mora & Rojas, 2022).

A second pandemic was identified by place of onset in Singapore in May 1957 that from its appearance until the late 1960s caused the death of between 1 and 3 million people at which time the virus stopped spreading, its transmissibility was very high, but less severe compared to that of 1918. This second pandemic is known as the Asian flu, given by the influenza A (H2N2) virus (Harrington et al., 2021; Hochman, 2021). Almost a decade later, a new strain of influenza A is evident, this would be the A (H3N2), responsible for the death of around 1 million inhabitants, known as the Hong Kong flu, due to its geographical location that affected Hong Kong, Singapore, India, Australia, the United States, and others (Gómez et al., 2022; Harrington et al., 2021). In the twenty-first century, during the year 2009, in the summer there was a pandemic of influenza A (H1N1) being the first pandemic of the new millennium. Since that date, WHO has been responsible for care through annual vaccination campaigns, in addition to establishing prevention and early diagnosis measures combining surveillance knowledge and laboratory work with the aim of controlling the overall potential pandemic risk (Harrington et al., 2021).

Surveillance is the best strategy to identify new strains of influenza, these arise from the interactions of ecology, humans and animals, especially avian and swine species. In 2010, CDC created the Influenza Risk Assessment Tool (IRAT) that takes into account different points for the future. Meanwhile, WHO in 2016 developed the same strategy, the Influenza Risk Assessment Tool (TIPRA) to determine the risk of emerging influenza pandemics (Harrington et al., 2021).

Epidemiological surveillance is based on the systematic and continuous collection of data on a specific health problem, for subsequent analysis, interpretation and use in the planning, implementation and evaluation of health programs. This type of surveillance aims at the early detection of health impacts, the identification of groups sensitive to certain risks, and the adaptation of the plan to the individual. (Ministry of Public Health, 2014)

Important instruments in the area of salt canbe applied to different areas, such as: occupational medicine, which controls and monitors the influence of working conditions on workers' health; analyzing climate change and its relationship with dengue; in the monitoring of emerging and re-emerging diseases such as HIV/AIDS, pulmonary tuberculosis, corona virus disease, among others. (Quijije, 2021)

This work aims to carry out the bibliographic analysis of the epidemiological surveillance of the influenza virus in Ecuador in order to highlight the usefulness of studies in the face of the appearance of new influenza strains in addition to proposing strategies that would benefit surveillance in the country.

2. Materials and methods

This bibliographic review is a retrospective observational analytical study where priority is given to the collection of data from high-impact scientific articles, meta-analysis, cohort studies, updated data on confirmed cases of influenza by health entities, among others. The search yielded a total of 50 articles of which 18 were chosen to explain the influenza virus and epidemiological surveillance in Ecuador. Scientific opinion articles were discarded as they have no scientific evidence.

3. Results

Virus de Influenza Tipo A

Influenza is a highly contagious virus, so an infected person can transmit the virus to another host at a distance of about two meters, without neglecting the droplets or "flush" that occurs when talking, coughing or sneezing. The contagion period is longer during the first days, infections have also been evidenced even one day before the symptoms are noticeable which begins about two days after contact with the virus and transmissibility continues up to 7 days after the onset of the disease. Individuals with a weakened immune system may be a source of transmission for more than 7 days thereafter (Centers for Disease Control and Prevention, 2021; Rao et al., 2019).

Diagnóstico

At first, a clinical diagnosis is made according to the patient's symptoms such as fever, chills, headache and muscle pain characteristic of the disease. For laboratory tests, different factors must be taken into account, all of which have limitations. The sensitivity will depend on each one and the type of sample, these must be taken (before 48 or 24 hours before the patient presents symptoms), from the respiratory tract to obtain the greatest number of hair epithelial cells, so the samples will be taken as swabs from the deep nostrils, pharynx, nasopharynx and bronchial aspirate (Tchounwou, 2022).

The most common are rapid influenza diagnostic tests (RIDT), these detect antigens, their result is obtained between 10 to 15 minutes after the test, but they are not as reliable (1) (Centers for Disease Control and Prevention, 2021). They are mainly used in developing countries that do not have access to RT-PCR tests, however, they are considered useful in outpatients, but not in hospitalized patients (Tchounwou, 2022).

Molecular detection: Nucleic acid amplification tests (NAATs) responsible for detecting viral genetic material and their waiting time for results varies between 15 and 20 minutes and are more accurate. Standard diagnostic methods such as antigen detection, serology, and virus isolation, but are limited by time, analysis, and low specificity or

sensitivity (Centers for Disease Control and Prevention, 2021; Tchounwou, 2022).

In order to determine a type of virus, amplification techniques can be used, other methods such as RT-PCR, next-generation sequencing, DNA microarray and loop-mediated isothermal amplification (LAMP) technique are also chosen. Most tests take a maximum of 4 hours and demonstrate greater specificity and sensitivity than conventional ones (11) (Tchounwou, 2022). PCR (polymerase chain reaction) has high specificity and is fast, RT-PCR is a variant. RT-PCR multiplex is responsible for detecting virus A subtypes H1 and H3, while RRT-PCR (RT-PCR in real time) is better for detecting virus A of subtypes H5 and H7.

Viral culture is the traditional technique due to its high sensitivity and specificity, this method is not used for clinical management, however, it is mainly used for epidemiological surveillance. The advantage of this is that the viability and ineffectiveness of the virus can be confirmed (11) (Saha & Davis, 2022; Tchounwou, 2022).

On the other hand, we have immunological detection, serological methods allow the detection of virus-specific antibodies through different assays: complement fixation, enzyme-linked immunosorbent assay (ELISA), hemagglutination inhibition (HAI), virus neutralization (VN), simple radial hemolysis (SRH) and Western blot. The use of these is aimed at retrospective seroepidemiological and population seroprotection studies (Tchounwou, 2022).

Table 1. Laboratory diagnostic methods for influenza viruses. (Angulo Valdivia & Torrico Villarroel, 2019)		
Methods	Sample	Time for results
RIDTs	Nasopharyngeal swab or washing, throat swab, throat wash	Up to 30 minutes
NAATs	Nasopharyngeal swab, throat, nasal lavage, endotracheal aspirate and sputum	4-6 hours
Viral culture	Nasopharyngeal swab or wash, throat swab, aspirate, and sputum	3 to 14 days
Immunofluorescence	Nasopharyngeal swab or lavage, nasal and bronchial lavage, aspirated	1-4 hours
Immune screening	Blood samples	several weeks

Treatment

Treatment of pathology is prescribed according to the severity of the disease. People who are uncomplicated, the goal is the relief of symptoms, on the other hand, the most serious patients should be treated with antiviral medications, in either case, in both cases it is recommended to rest and constant hydration to avoid fluid loss in addition to general measures such as avoiding contact with other people, using tissues when coughing or sneezing and frequent hand washing (Centers for Disease Control and Prevention, 2021).

Antiviral drugs are a good choice for treating influenza, according to the CDC, patients with comorbidities are likely to develop complications. Some of the FDA-approved drugs are neuraminidase inhibitors (INA) such as oseltamivir, zanamivir, peramivir, acid endonuclease polymerase inhibitors such as baloxamivir, marboxil and M2 proton channel antagonists such as amantadine.

Amantadine blocks M2 proton channels thus inhibiting the process of viral replication of influenza A. Amantadine hydrochloride is used for the treatment of influenza orally, this drug should be cautioned in patients with renal pathologies, for this reason it has ceased to be a drug of choice since 2006 (Tchounwou, 2022).

At present the most recommended drugs are the INA, as a representative oseltamivir, its mechanism of action is the inhibition of viral replication. In general, this group of drugs is recommended to use 48 hours prior to the onset of the clinical picture, or, in other words, between the second and third day after having been in contact with the virus because at this time the replication peak occurs. Given the case, it can also be used until the fifth day after the onset of symptoms (Tchounwou, 2022).

Similarly, baloxavir marboxil is a prodrug that inhibits virus replication by binding the RNA polymerase complex of the RNA that depends on RNA to the PA protein (Tchounwou, 2022).

The preventive treatment with which the complication and mortality rate of the population has been significantly reduced. This stimulates the activation of the immune system that in response gives the production of antibodies that will be effective during a season, so the inoculation of annual vaccines is necessary. Vaccines are usually tri- or quadrivalent combining different strains such as A and B. It is a type of inactivated vaccine with which caution should be exercised with patients allergic to egg protein, since for its preparation the selection of the virus is injected into the chicken egg. To date, it is the most effective treatment (Vidal, 2020).

Epidemiological surveillance of influenza in Ecuador

The concept of epidemiological surveillance is the result of a long evolution, whose origins date back to antiquity. Because, the habit of observing, recording, collecting, analyzing the facts and deciding from there what actions to take can be attributed to different authors. However, its codification began to take shape during the bubonic plague and other epidemics that Europe faced in the fourteenth and fifteenth centuries. Now it can be applied to the analysis and observation of specific diseases in the community such as malaria, yellow fever, among others. (Ministry of Public Health, 2014; Pan American Health Organization, 2002)

For a disease to be monitored, it must constitute a public health problem due to its high prevalence, incidence or mortality, and preventive or treatment measures must be taken available to health services. Different types of epidemiological surveillance

systems are available to implement these measures. (Pan American Health Organization, 2002; Quijije, 2021)

Passive Surveillance: In this case, health institutions routinely and periodically record information about the events under surveillance. Sources include statistical yearbooks, medical records, outpatient reports, notifiable disease registries, direct access to information systems, death certificates, autopsy and forensic protocols. (Pan American Health Organization, 2002)

Active Surveillance: Occurs when health services search for specific information for surveillance purposes. This is independent of whether the patient uses health services or records data regularly. The sources of this type of surveillance are prevalence surveys, outbreak surveys, epidemic surveys, socio-economic surveys, ethnographic and entomological surveys. (Pan American Health Organization, 2002)

Professional or Sentinel Epidemiological Surveillance: It is the surveillance that is carried out on specific health problems in which there are international commitments or national priorities, eradication campaigns, epidemics of individual notification, etc. This type of monitoring can use both passive and active surveillance elements. In addition, it is characterized by rapid detection, immediate action and specific prevention. (Pan American Health Organization, 2002)

In this work, epidemiological surveillance of influenza is carried out. In 2018 and 2019, influenza A (H1N1) predominated in North America, and influenza A (H1N1) and A (H3N2) circulated in Europe. In Western and South Asia, some countries achieved medium and high levels of influenza cases. In parts of the Southern Hemisphere, influenza activity remained at interseasonal levels, with the exception of parts in Australia. In Ecuador, the development of epidemiological surveillance focuses mainly on communicable diseases. At the end of 2001, the process of developing an Integrated Epidemiological Surveillance System (SIVE) began. In 2013 it is rethought and two components are established: indicator-based surveillance and event-based surveillance. (Quijije, 2021)

Until June in Ecuador 617 cases of respiratory diseases through a National Sentinel Surveillance System for severe acute respiratory infections by the Ministry of Public Health in association with sixteen institutions: General San Vicente de Paul Hospitals (zone 1), Riobamba General Teaching Hospital (zone 3), Verdi Cevallos Hospital (zone 4), Homero Castañer Crespo Hospital, Vicente Corral Moscoso Hospital (Zone 6) Hospital of infectology and dermatological, Luis Vernaza Hospital, Naval Hospital, Roberto Gilbert Pediatric Hospital (zone 8), Carlos Andrade Marin Hospital, Baca Ortiz Children's Hospital, Dr. Francisco Icaza Bustama Children's Hospital, Enrique Garces Southern Hospital, Eugenio Espejo Hospital, Pablo Arturo Suarez Hospital, Vozandes Hospital (zone 9). (Ministry of Public

Health, 2022)
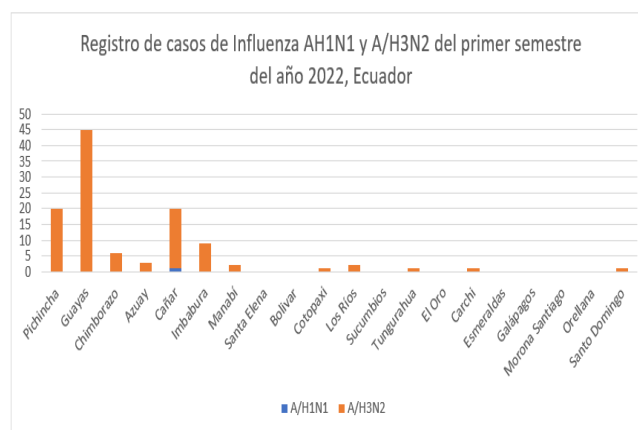
Figure 1. Of the 110 registered cases of influenza A/H3N2 in the first half of 2022 in Ecuador, the provinces where the highest number of cases were identified were: Guayas with 45, Pichincha with 20, followed by Cañar with 19 cases. It is in the latter where an infected with influenza A/H1N1 was reported. (Ministry of Public Health, 2022)
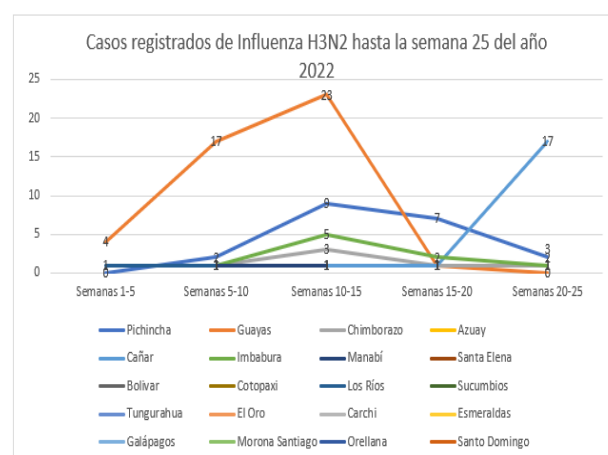
Figure 2. Epidemiological curve of the first semester of the H3N2 influenza virus. An increase in cases can be observed in the period of week 10-15. Likewise, a growth of cases in the province of Cañar in the last record of week 20-25 (Ministry of Public Health, 2022)

4. Discussion

Influenza is considered an endemic disease with a high transmission capacity. The subtypes registered in Ecuador are: type A/H1N1 and A/H3N2. Type A/H1N1 is now considered a seasonal influenza strain. Until the first semester there has been an increase in cases in the periods of January-March, reaching its peak in March. According to information recordedin 2019, it is estimated that 10% of individuals who acquire the influenza virus may present a severe watery respiratory infection (SARI) and may require hospitalization.

In order to reduce the incidence of the disease and avoid possible complications in the population, immunization strategies are carried out annually based on the seasonality records of the circulation of the virus. In Ecuador the national vaccination scheme has been in force since 2006, usually vaccination campaigns begin in December until around March the supply of the same is guaranteed by the

Revolving Fund of the Pan American Health Organization (PAHO). The vaccination plans are aimed at all population groups, even more so priority groups, pregnant women, children under 5 years of age, the elderly, patients with comorbidities and health personnel, which are recommendations of the WHO Strategic Advisory Group of Experts on Immunization (SAGE) and the PAHO Technical Advisory Group on Vaccine-Preventable Diseases (TAG) (Ministry of Public Health, 2022) .

While the MSP of Ecuador included in this group people between 50 and 64 years old, it is suggested because in the years 2013-2014 the rate of infections of this group increased. Due to the various mutations generated in the virus, annual vaccination is recommended.

In addition to immunization strategies, identification data is recorded in the population that has acquired the virus, which are subject to continuous updating that depend on the onset of symptoms and the national reference laboratory report. For this type of surveillance, 14 hospitals work together under the regulations ofthe Integrated Epidemiological Surveillance System, in which all severe acute respiratory infection confirmed under standardization criteria are recorded. However, it should be said that due to the low number of hospitals that manage to identify and register influenza cases, the information that is known is an estimated value.

5. Influenza

- Type of surveillance: Passive surveillance
- Definition of disease: The influenza virus causes a contagious respiratory illness that can be mild or severe. This mainly affects the nasal cavity, throat, bronchi and sometimes the lungs.
- Risk factors: Priority groups: Pregnant women, Children under 5 years of age, the elderly, patients with comorbidities Having been in contact with infected people, not following biosecurity measures such as the use of disposable tissues when coughing or sneezing and washing hands frequently. In addition, have contact with surfaces contaminated with this virus.
- Reason for Surveillance: The influenza virus is a virus of high mutagenic variability and represents complications to priority attention groups, although there is a vaccine that is placed annually, the rate of infections remains high at specific times of the year, in Ecuador in the months of January-March and July-August.
- Symptoms of a suspected case: A person who has been in a country with cases of influenza or in contact with someone infected and presents the following symptoms: Fever 38 °C, Severe headaches, muscle and joint pain, sore throat, runny nose.

Table 2. Health entities and their functions in Ecuador. (Ministry of Public Health, 2022)			
Influenza Code: J11.1			
Objective	*Functions*	*Activities*	*Responsible*
Have an influenza surveillance system that allows for regular and systematic recording of information.	Registration of data of diagnosed and treated patients.	Diagnostic confirmation of the disease.	-Attending physician who diagnoses the patient. -Health centers
		Training medical professionals who treat patients.	Ministry of Public Health.
Define the guidelines for the surveillance, regulation and control of the entities of the sector and implement strategies to safeguard the health of the population	Surveillance of epidemiological control of diseases	National epidemiological prevention and control of influenza virus.	Vice-Ministry of Governance and Health Surveillance
Determine the relationship between risk factors and diseases to prevent their spread	Incorporate computer technology for the epidemiological notification and capture system	Study of social determinants, act in prevention and socialize experiences	National Directorate of Epidemiological Surveillance
Formulate control projects and interventions that affect the health of Ecuadorians	Generate information to guide public policies	It covers all epidemiological surveillance systems where the possible risks faced by the population are notified	Integrated Epidemiological Surveillance System
Propose immunization programs at the national level	Manage models for the institutional management of the expanded program of immunizations	Designs and provides information on immunization programs based on scientific evidence	Advisory Commission on Immunization Practice
Analyze the behavior of diseases from their causative agent in the epidemiological week	Application of techniques for the characterization of respiratory viruses	Be alert to the possible appearance of new strains of influenza that would put the health of Ecuadorians at risk.	National Institute for Public Health Research

Each entity performs a joint work since each one has its function as detailed in table 2. From the collection of data they can establish the cases of contagion, analyze and interpret their statistics, in this way they can carry out the development of proposals that

improve the models, tools and techniques to achieve a more assertive epidemiological surveillance for the benefit of the population in general.

6. Conclusions

Epidemiological surveillance is one of the most important functions carried out by the Ministry of Health of Ecuador in conjunction with other entities such as the National Institute for Public Health Research (INSPI) with other entities related to public health. From the collection, analysis and interpretation of data, these entities have the obligation to disseminate timely information about a health problem. In this case, influenza is one of the most common viruses that cause respiratory diseases, which is in our day to day. The proper registration of cases helps decision-making in Public Health, so it is the duty of the health personnel in charge to report positive cases, this will help to propose and improve strategies that benefit the population.

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