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PANDEMIC INFLUENZA IN A SOUTHERN HEMISPHERE SETTING: THE EXPERIENCE IN PERU FROM MAY TO SEPTEMBER, 2009

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This paper presents a description of Peru's experience with pandemic H1N1 influenza 2009. It is based on data from four main surveillance systems: a) ongoing sentinel surveillance of influenza-like illness cases with virological surveillance of influenza and other respiratory viruses; b) sentinel surveillance of severe acute respiratory infections and associated deaths; c) surveillance of acute respiratory infections in children under the age of five years and pneumonia in all age groups; and d) case and cluster surveillance. On 9 May 2009, the first confirmed case of pandemic H1N1 influenza in Peru was diagnosed in a Peruvian citizen returning from New York with a respiratory illness. By July, community transmission of influenza had been identified and until 27 September 2009, a total of 8,381 cases were confirmed. The incidence rate per 10,000 persons was 4.4 (in the 0–9 year-olds) and 4.1 (in the 10–19 year-olds). During epidemiological weeks (EW)* 26 to 37, a total of 143 fatal cases were notified (a case fatality of 1.71%, based on confirmed cases). The maximum peak in the number of cases was reached in EW 30 with 37 deaths. Currently, the impact of the pandemic in the Peruvian population has not been too severe, and fortunately, healthcare centres have not been overwhelmed. However, the future of this pandemic is uncertain and despite the fact that our country has not been seriously affected, we should be prepared for upcoming pandemic waves.

Introduction

Peru is a South American country that is divided by the Andes Mountains into three distinct natural regions (coastal desert, highlands and jungle region) all extending the entire length of the country. The coastal desert has limited rainfall (<20 cm per year) with temperatures ranging between 15 and 30°C, and Lima, the main and capital city, is located in the central part of this region. The highlands that include cities located over 2,000 m above sea level experience high levels of rainfall and temperatures ranging between -2 and 15°C. Finally, in the jungle region rainfall exceeds 200 cm per year, and cities are located close to sea level with temperature ranging from 18 to 32°C [1].

Since 1998, the Ministry of Health (MoH) of Peru has conducted virological surveillance of influenza and other respiratory viruses,

and in 1999 surveillance of acute respiratory infections (ARI) and pneumonia cases and associated deaths was implemented. In 2006, the MoH established a sentinel surveillance system of influenza-like illness (ILI) cases in all the three regions of the country, in order to strengthen the National Surveillance Network [2]. Through these systems, influenza circulation in Peru has been detected throughout the year in coastal and jungle regions, and seasonal circulation during winter time has been identified in the highland region [3]. As a response of the World Health Organisation's (WHO) global pandemic alert, the MoH established two additional surveillance systems: a case and cluster surveillance, and surveillance for severe acute respiratory infection (SARI) and SARI deaths.

On 9 May 2009, the first confirmed case of pandemic H1N1 influenza in Peru was diagnosed in a Peruvian citizen returning from New York with a respiratory illness. Since then, the influenza A(H1N1)v virus has spread rapidly throughout the country [4]. In this context of preparation and response, this paper presents a description of Peru's experience with the H1N1 influenza pandemic using data from the different surveillance systems in Peru.

Methods

The pandemic was described using data from four different surveillance systems, which are summarised below. All four systems report their data to the MoH. Case and cluster investigation was temporarily carried out at the beginning of the epidemic.

Sentinel surveillance of influenza-like illness cases and virological surveillance

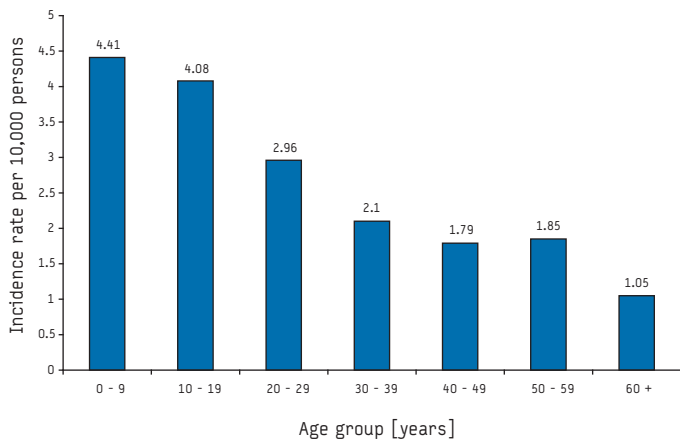
Sentinel surveillance has been implemented in 50 health centres in the country. Nasal or pharyngeal swabs were processed at the Instituto Nacional de Salud (National Institute of Health, INS) and the Naval Medical Research Center Detachment (NMRCD) as previously described [3].

Case and cluster investigation

On 9 May 2009, after the WHO issued a global pandemic alert, a surveillance system based on the case definition for pandemic H1N1 influenza was established by the MoH to define the procedures of

FIGURE 1

Incidence of confirmed cases of pandemic H1N1 influenza, by age group, Peru, 9 May-27 September 2009



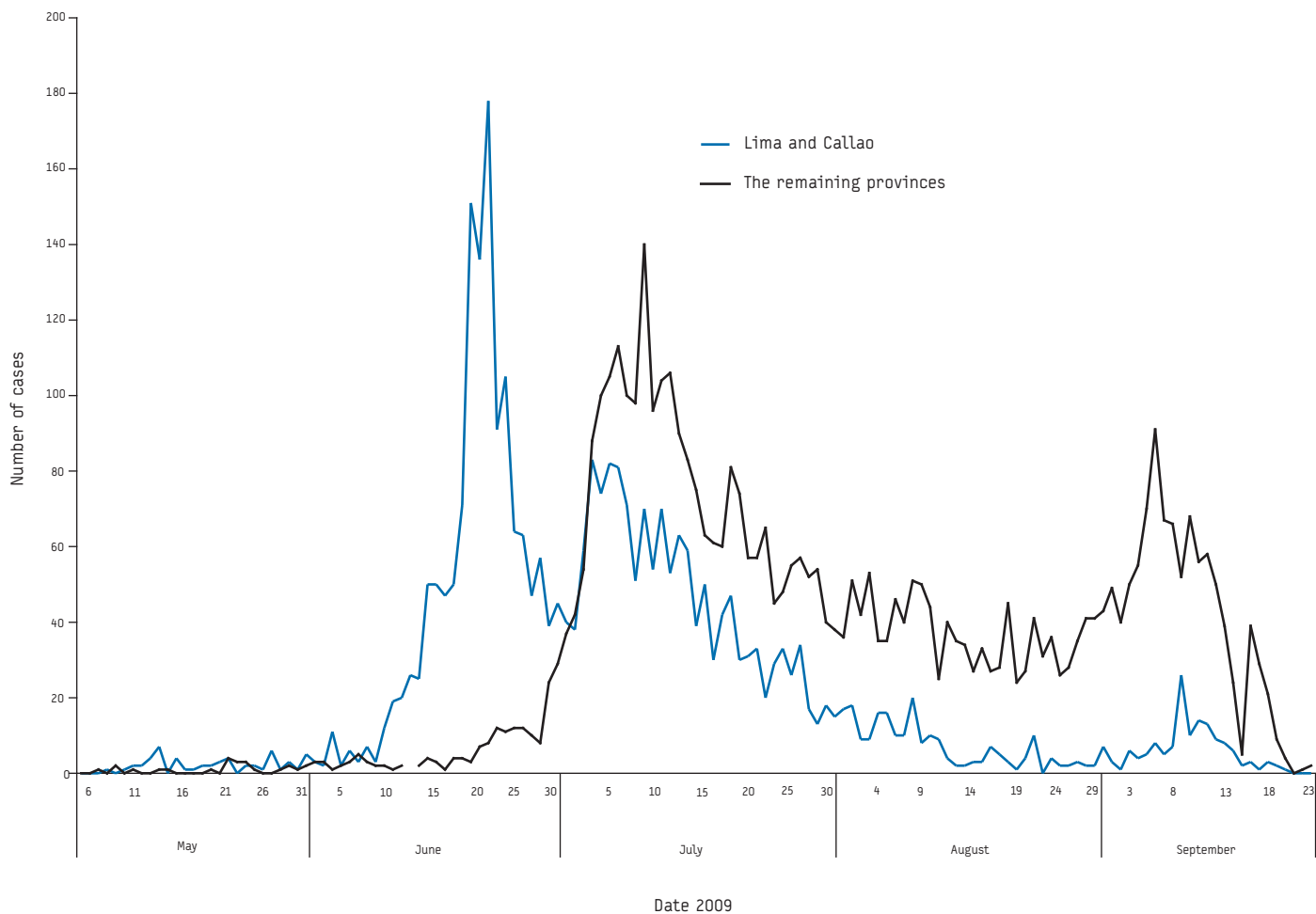
detection, notification, investigation, follow-up and epidemiological control of the H1N1 influenza in Peru [5,6]. A suspected case was defined as any person with a sudden onset of fever ($>38^{\circ}\text{C}$) and at least one of the following symptoms: cough or sore throat within seven days of symptoms onset, in an area where confirmed pandemic H1N1 influenza cases were reported or epidemiologically linked to a close contact of a confirmed case. A confirmed case was defined as any person with a positive result in the RT-PCR for influenza A(H1N1)v virus. This system was stopped on 7 July with the change to the mitigation phase.

Surveillance for severe acute respiratory infections and associated deaths

In July 2009, when community transmission of influenza was identified, the MoH of Peru intensified surveillance efforts to reinforce the sentinel surveillance of SARI [7]. SARI was defined as any patient, with sudden fever $>38^{\circ}\text{C}$, together with cough or sore throat and respiratory distress who needed medical care in a hospital. Hospitalisation was defined as a patient spending at least one night in a hospital or healthcare center. An online platform with

FIGURE 2

Confirmed pandemic H1N1 influenza cases by onset of symptoms, Peru, 6 May-25 September 2009 (n=7,886)



* for whom date of onset was available.

information of hospitalisation, comorbidities, outcomes, treatment and other variables was established.

Acute respiratory infections, pneumonia and pneumonia deaths surveillance

This system was optimised to follow up the spread of the pandemic. ARI included all children under the age of five years, while pneumonia cases and deaths were reported for all age groups.

Laboratory analysis

From nasal and/or oropharyngeal swabs, RT-PCR assays for the detection of influenza A(H1N1)v virus were performed at the INS and NMRCD as described by United States Centers for Disease Control and Prevention [8]. At NMRCD in Lima, the specimens were stored at -70°C, and later inoculated for virus isolation and identification [3]. An online official system (NETLAB-INS) was established to access the results.

FIGURE 3
Cases of severe acute respiratory infections, Peru, EW22-EW37, 2009 (n=1,458)

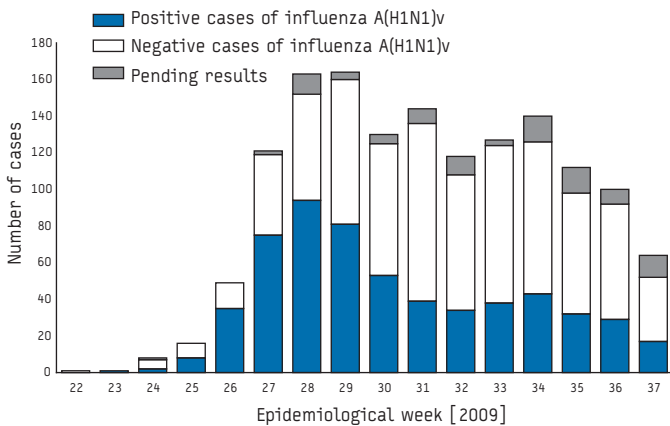
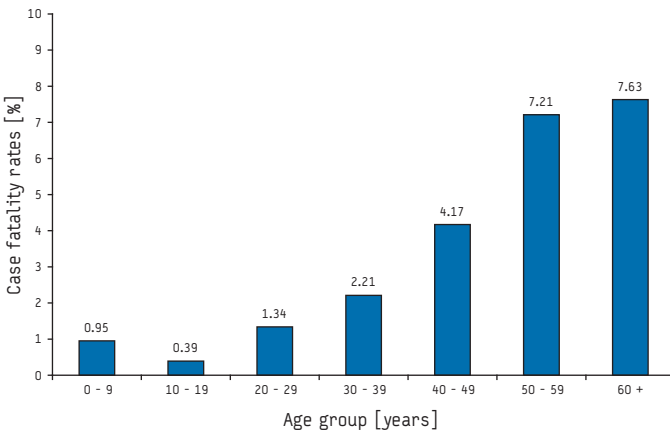


FIGURE 4
Case fatality rate per 100 cases by age group among patients infected during the influenza pandemic, Peru 2009, 9 May-19 September 2009 (n=143)



Control measures

When the active surveillance system was in place, case clusters were identified by sampling symptomatic cases. Control measures included the use of respiratory masks, increased hygiene (hand washing) and administration of antiviral drugs (oseltamivir) to all suspected and confirmed cases and their contacts during this containment phase [4]. Following the WHO pandemic alert, travel restrictions to Mexico were put in place on 30 April and measures were taken to increase awareness of travellers of the new influenza virus. Furthermore, active surveillance of febrile patients was established in all airports, and a telephone hotline was established to receive reports from the population on respiratory disease and house identification of cases and contacts [4]. During the subsequent mitigation phase, antiviral treatment was established on 21 July and it was focused on the high-risk group (pregnant women, cases under five years or over 60 years of age, or patients with SARI or a risk comorbidity) [4].

The clinical-epidemiological forms of the cases were entered into a database (NMRCD) or directly into an online platform on a website of the Dirección General de Epidemiología (General Directorate of Epidemiology, DGE).

Results

Sentinel surveillance of influenza-like illness cases and virological surveillance

We have previously reported the results of the sentinel surveillance system in Peru from June 2006 to May 2008 [3]. Until 27 September, approximately 1,122 cases of pandemic H1N1 influenza (13.4% of the confirmed cases) were identified by this system. During the pandemic, the implementation of this surveillance system allowed us to identify the first outbreak of community transmission (18 May) with 11 confirmed cases in one of the surveillance sites (Huanuco province) located in the highland region of Peru.

TABLE

Comorbidities and/or risk conditions detected in pandemic H1N1 influenza cases with fatal outcome, Peru, 9 May-19 September 2009 (n=143*)

Comorbidity and/or risk condition (N=143)	n (%)
No comorbidity or risk condition	35 (24.5)
Comorbidity and/or risk condition	108 (75.5)
Metabolic	36 (25.2)
Cardiovascular	30 (21.0)
Respiratory	16 (11.2)
Neurological	14 (9.8)
Renal	13 (9.1)
Genetic	13 (9.1)
Other	10 (7.0)
Pregnancy and puerperium	6 (4.2)
Rheumatologic	6 (4.2)
Infectious	5 (3.5)
Digestive	4 (2.8)
Cancer	3 (2.1)

* Multiple answers were possible

Case and cluster investigation

Description of cases

Until 27 September 2009, a total of 8,381 cases of pandemic H1N1 influenza have been confirmed, including 143 deaths. A total of 4,263 confirmed cases (52%) were males. The subjects' age ranged from ≤ 1 year to 80 years, with a median age of 19 years. Seventy-five percent of the cases were under 30 years-old and only 3.15% were older than 60 years. ILI cases were notified in all departments (administrative regions) of Peru, but Lima and Callao together notified almost 40% of the cases.

The risk of infection was greater in those younger than 20 years, probably associated with sustained transmission within schools. The incidence rates per 10,000 persons were 4.4 and 4.1 among the 0-9 year-olds and the 10-19 year-olds, respectively (Figure 1). During the containment phase, the large number of suspected cases that were detected (close to 400 per day) led to a delay in the generation of laboratory results by INS and NMRCDC. When the containment phase ceased on 7 July, laboratory testing was focused on SARI patients.

After 13 June (epidemiological week EW 23), an increase in the daily number of ILI cases was identified with a peak on 22 June (EW 25), as shown in Figure 2. This was followed by a consistent decrease in the number of cases especially in Lima and Callao.

Further, the percentage of positive samples increased from 10% (EW23) to 70% (EW 25) and then started to decrease.

While the first epidemic peak occurred in Lima and Callao, secondary peaks in the epidemic curve correspond to the epidemic wave in the rest of Peru. The aggregated epidemic curve is multimodal due to the sum of local epidemics at different spatial locations where the novel influenza virus arrived at different times.

Description of clusters

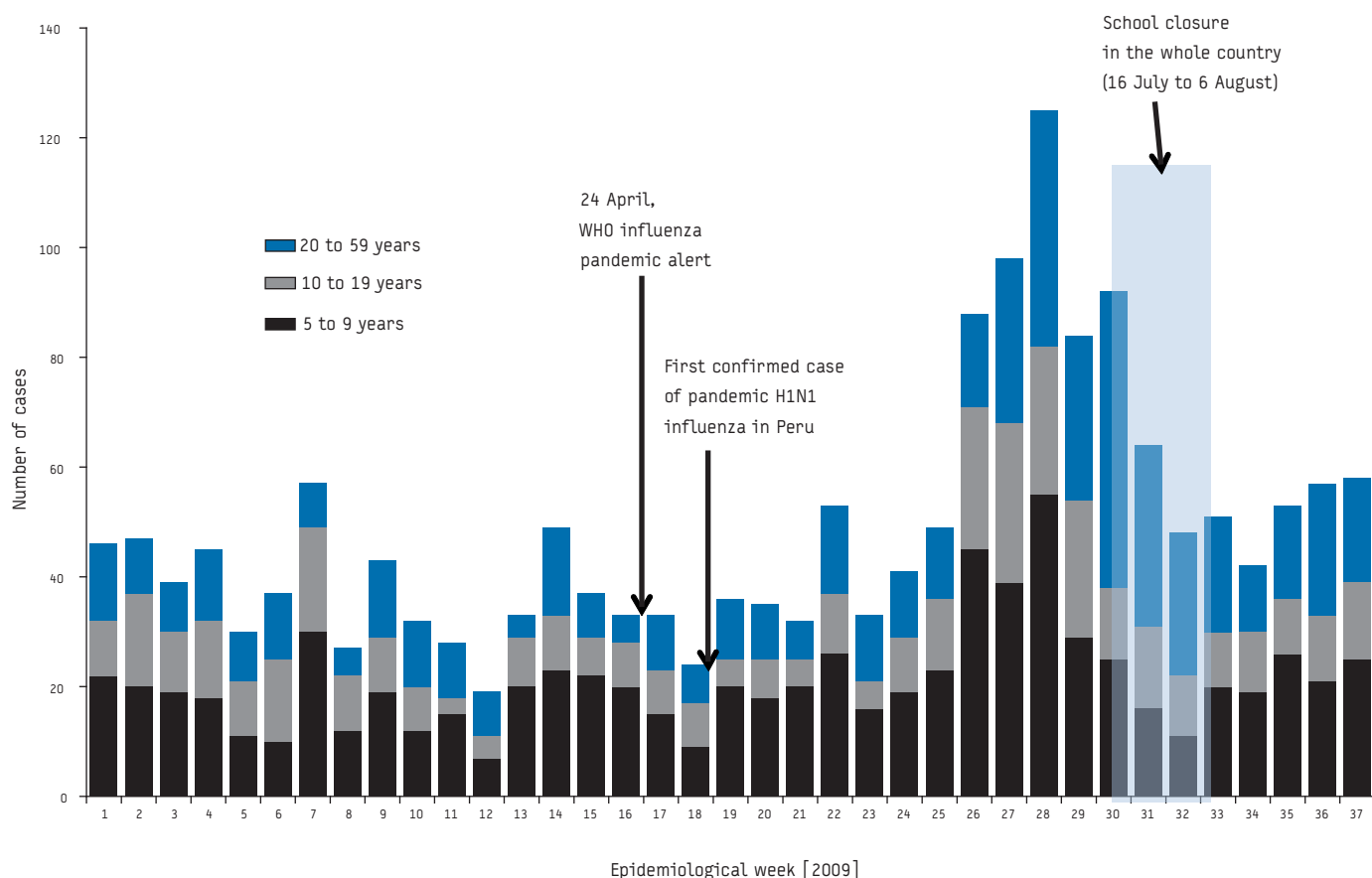
The onset of symptoms of the first case was on 9 May 2009. Following the index case, our surveillance system detected many isolated imported cases that generated clusters of different size. We detected and investigated six clusters associated with persons returning from countries with or without demonstrated transmission at the time. These countries included the Dominican Republic, Mexico, Argentina and the US. Two of these clusters led to community transmission in Peru. These clusters will be described in depth elsewhere.

Surveillance for severe acute respiratory infections and associated deaths surveillance

After the switch of the surveillance strategy from the containment to the mitigation phase (7 July) as described above, the epidemic trend was monitored through the detection of SARI cases. At the time of writing this report, the trend of SARI cases for the whole

FIGURE 5

Cases of pneumonia among 5-59 year-old patients from Lima and Callao, 2009 (n=1,798)



of Peru is slowly decreasing. In Peru, the peak was reached during EW 28, followed by a decrease in SARI cases (Figure 3). In the northern regions of the country, the peak was reached during EW 34, and in the southern regions a bimodal curve was observed with two peaks at EWs 28 and 34 (data not shown).

SARI deaths

During EWs 26-37, a total of 143 deaths associated with SARI were notified in 14 out of the 24 departments comprising Peru, a case fatality percentage of 1.63%, based on confirmed cases. Almost half of the deaths were recorded in the city of Lima and the port of Callao. The maximum peak was reached at EW 30 with 37 deaths. After that, the number of fatalities decreased to two cases in EW 37.

The median age of deaths was 39 years (range: 0-85 years) and 54% were women. The fatality rate was greater (7.63%) in persons over the age of 59 years, whereas the rate in the younger age groups (under 19 years of age) was lower than 1 (Figure 4).

In 32 of the deaths (24%), there were no recorded underlying conditions. Six of the deaths (4.5%) were in pregnant women or women in puerperium; six deaths were in cases with Down syndrome; 23 in cases with obesity; nine in cases with diabetes mellitus type 2 (three of them associated with obesity) (Table).

Acute respiratory infections, pneumonia and pneumonia fatalities surveillance

The epidemic curve of pneumonia cases among 5-59 year-olds in Lima and Callao increased in EW 26, reached the peak in EW 28 when schools were temporarily closed for three weeks. Following this measure, the number of cases decreased as shown in Figure 5.

Control measures

Between 24 April and 4 July 2009, no cases were identified in nearly 500,000 screened travellers, and hence the screening system at airports was deemed ineffective and was suspended. The first imported cases in travellers were identified who reported to the telephone hotline centre implemented by the MoH.

Discussion

Surveillance of pandemic H1N1 influenza in Peru provided valuable information about the behaviour of the pandemic in a developing southern hemisphere country. Lessons can be learned regarding the public health impact, prevention and control, impact on health services, and effective surveillance.

Public health impact of the pandemic

Lima, the largest city with a population of eight million, has the main international airport and was the first city in Peru affected by the new influenza virus. In addition, all laboratory testing for the country is centralised in this city. These factors could explain the fact that almost 30% of the initial confirmed cases of pandemic H1N1 influenza were located in Lima.

Until September 2009, Peru identified over 8,000 confirmed cases, but this is only the tip of the iceberg. The pattern of dissemination of this pandemic in Peru is associated with people's mobility and population density, and more populated areas tend to be affected earlier than smaller populations. Access to laboratory resources across Peru is not uniform and could have affected this transmission pattern. Moreover, distant and geographically isolated

locations may have not reported cases before the appearance of severe cases who require mechanical ventilation in hospital settings.

We observed that while a great number of people under the age of 24 years were infected, this group had a lower probability of dying from influenza. The lower frequency of pandemic H1N1 influenza cases among those over 59 years of age supports the hypothesis that people who were exposed to influenza A(H1N1) during childhood before the 1957 have a certain extent of immunological protection to the influenza A(H1N1)v virus [9]. Such a consistent pattern has been reported in other regions including Mexico, the US, Europe, Australia and New Zealand [10-11]. When infected, however, these older patients had a high risk of fatality, in our country as reported in other regions [12].

Cases of pandemic H1N1 influenza in Peru presented predominantly mild and self-limiting illness, and although fever and cough were the most common clinical manifestations, many subclinical or asymptomatic cases should have circulated in the country. The majority deaths related to pandemic H1N1 influenza (75.5%) had a reported underlying medical condition. In fact, almost half of the deaths had conditions classified as high risk in other countries [13]. The fact that 25% of the cases did not have high risk conditions suggest that additional factors such as immunological status or access to healthcare could have contributed to the fatal outcome.

Our case definitions were very specific, but allowed us to develop interventions and to sample suspected cases to help us identify clusters and follow virus dissemination patterns throughout the country.

Control measures and limitations of the study

Initial control measures established by the MoH of Peru included travel restrictions and quarantine of suspected travellers following WHO recommendations [14]. However, these actions were not effective and did not significantly delay the spread of the virus into other nations including Peru. Also, many travellers could have entered the country during the incubation period, as detected in other countries [15]. The telephone hotline was found to be useful in identifying case clusters of suspected and confirmed cases and following the dissemination of the virus throughout the country [16]. House identification of cases and contacts and follow-up procedures involved a great deal of human resources. As a result, those activities were discontinued.

We believe that the epidemiological surveillance system recommended by WHO, i.e. early case detection and investigation, comprehensive assessment and pandemic monitoring [17], was essential for the development of adequate control measures. At the beginning of the pandemic, it is possible that our surveillance systems failed to detect many cases, especially those with mild disease. Many patients may not have visited a health centre or may not have had access to laboratory services. ARI surveillance was not as helpful as we expected, due to the limitations in detecting cases among outpatients. The SARI surveillance system, however, was useful because it allowed us to monitor the pandemic trends in all age groups and among the more severe cases. It also allowed us to evaluate the impact of the pandemic.

Conclusion

It is well known that previous pandemics have presented a second or third wave of morbidity and mortality. These multiple wave profiles could be associated with spatial, seasonal, hemispheric (north, south, tropics) or climatic (humidity, temperature) factors [18,19]. Currently, the impact of the pandemic in the Peruvian population has not been severe, and fortunately healthcare centres have not been overwhelmed. However, the future of this pandemic is uncertain and despite the fact that our country has not been seriously affected, we should be prepared for upcoming pandemic waves.

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Disclaimers

The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Ministry of Health of Peru and the Department of the Navy, Department of Defense, nor the U.S. Government.

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*Editor's note: Weeks in this article are numbered as epidemiological weeks as defined by the Pan American Health Organization (PAHO) and the World Health Organization (WHO): <http://amro.who.int/english/sha/be993calend.htm>

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