Rapid communications

Epidemiological and transmissibility analysis of influenza A(H1N1)v in a southern hemisphere setting: Peru

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We present a preliminary analysis of 1,771 confirmed cases of influenza A(H1N1)v reported in Peru by 17 July 2009 including the frequency of the clinical characteristics, the spatial and age distribution of the cases and the estimate of the transmission potential. Age-specific frequency of cases was highest among school age children and young adults, with the lowest frequency of cases among seniors, a pattern that is consistent with reports from other countries. Estimates of the reproduction number lie in the range of 1.2 to 1.7, which is broadly consistent with previous estimates for this pandemic in other regions. Validation of these estimates will be possible as additional data become available.

Introduction

On 24 April 2009, the World Health Organization (WHO) informed about an epidemic caused by new swine-origin influenza A(H1N1)v virus originating from Mexico, and declared a public health emergency of international importance. The level of influenza pandemic alert was raised sequentially up to phase 6 on 11 June 2009 after global spread of the pandemic virus was confirmed [1].

In this study we present an analysis of 1,771 confirmed cases of influenza A(H1N1)v who developed the disease by 17 July 2009 and were reported to the National Surveillance Network in Peru, which since 2006 has conducted virological surveillance of influenza and other respiratory viruses by establishing sentinel sites throughout the country [2]. The patients' age distribution, their clinical characteristics as well as their spatial distribution were studied. Estimates of transmission potential from the initial epidemic phase were also derived and compared with published estimates from other regions of the world.

Methods
Surveillance system

On 24 April 2009, the public health authorities of Peru implemented new regulations for epidemiological surveillance and outbreak control of influenza A(H1N1)v defining the procedures of

Geographical distribution of confirmed cases of influenza A(H1N1)v in Peru, as of 17 July 2009 (n=1,771)

detection, notification, investigation, follow-up and epidemiological control of A(H1N1)v cases in Peru.

An active surveillance system was established at all airports (especially in travellers returning from affected areas) and healthcare facilities, including private clinics. Also a telephone hotline (INFOSALUD) was made available by the Ministry of Health for citizens reporting influenza-like illness. A suspected case was defined as a person with a sudden onset of fever (>=38°C) and respiratory symptoms. Suspected cases and their contacts were visited in their homes for clinical evaluation and nasal or pharyngeal specimens were taken from symptomatic persons and submitted to the National Institute of Health or the United States Naval Medical Research Center Detachment for RT-PCR as described by the Centers for Disease Control and Prevention (CDC). Suspected cases were informed about control measures to limit spread (voluntary isolation, use of face masks, and increased hygiene). Contacts of cases were monitored daily via phone calls or home visits. Symptomatic contacts were subjected to the same procedure as suspected cases. Clinical and epidemiological data were collected utilising a case report form (CRF) from all patients who met the case definition. Antivirals were given to all suspected cases until early July when the containment strategy was replaced by mitigation approach and treatment began to be administered only to high-risk groups.

Descriptive epidemiology

Based on the clinical and epidemiological data of the National Surveillance Network, we characterised the descriptive epidemiological features of influenza A(H1N1)v infection in Peru. First, we described the distribution of cases as a function of space, age and gender. Time-dependent characteristics were more analytically examined to estimate the transmission potential (see below). We also examined travel history of cases returning from countries with ongoing epidemics of A(H1N1)v infection, and the age-distributions between imported and indigenous cases were compared by means of non-parametric Mann-Whitney test. Second, we characterised frequency of symptoms reported for confirmed cases. The clinical-epidemiological forms were entered into a database created in Microsoft (MS) Office Access 2003, and data were analysed using MATLAB (The Mathworks, Inc.).

Estimation of transmission potential

A key epidemiological quantity which informs the expected magnitude of an epidemic is the basic reproduction number (denoted by R_0), defined as the average number of secondary cases generated by a primary case in an entirely susceptible population [3,4]. When $R_0>1$ an epidemic can occur while $R_0<1$ cannot support an epidemic. The reproduction number, R was estimated exploring time-evolution of confirmed cases. Statistical methods were based on pure birth process (to estimate the intrinsic growth rate r) and renewal process (to estimate R using r), and were identical to those given elsewhere [5]. Whereas we analysed the temporal distribution including all possible primary cases (i.e. including imported cases) as the number of imported cases was in a negligible order, we also examined the estimate excluding imported cases (as it can then exclude imported cases from the category of secondary cases).

Age distribution of confirmed cases of influenza A(H1N1)v reported in Peru as of 17 July 2009 (n=1,765*)
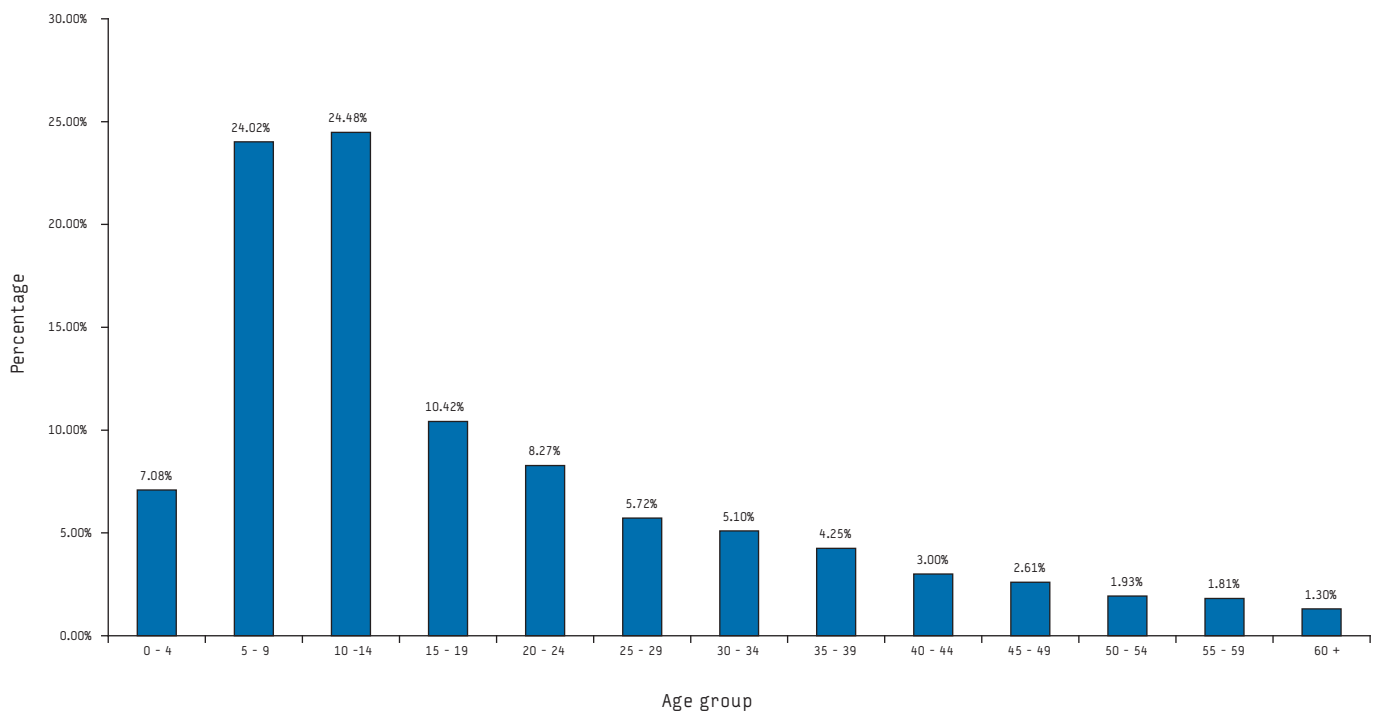

*Number of cases with available data on age

Results

The first influenza A(H1N1)v confirmed case in Peru was a Peruvian citizen returning from New York on 9 May with a respiratory disease. Since then the pandemic has quickly spread throughout the country. As of 17 July 2009, a total of 1,771 cases, involving eight deaths, have been confirmed. This yields a crude case fatality ratio of 0.33 % (95% confidence interval: 0.14, 0.65). Of the 1,771 cases, 1,420 (80.1%) were from Lima, the capital city, 84 (4.7%) from Piura and 81 (4.6%) from La Libertad. Figure 1 shows the geographic distribution of confirmed cases of influenza A(H1N1)v in Peru.
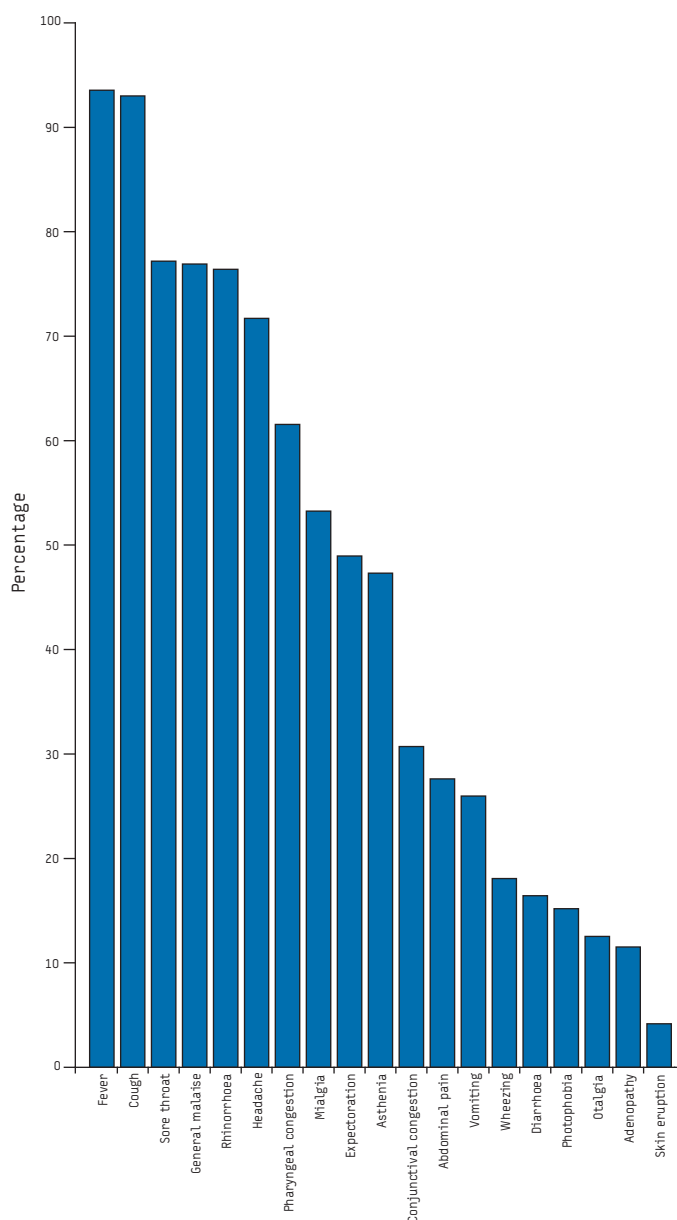
A total of 78 (4.4%) confirmed cases had a history of recent travel to the United States, Dominican Republic or Argentina. Imported cases generated clusters of different sizes that established indigenous transmission in Peru. For example, between 8 and 30 May, 600 private high school students travelled to Punta Cana in the Dominican Republic for vacations. One student presented influenza-like illness before returning and other 11 students developed symptoms upon returning to Peru.

Females (52%) were slightly more affected than males (48%). The most affected age group was that of 5-14 years (Figure 2). The age of the cases ranged from 0 to 87 years with a mean of 18.5 years and a median of 13 years. The mean age of the imported cases was 28 years while indigenous cases had a mean age of 18 years (Mann-Whitney test, P<0.001).

Figure 3 summarises the clinical characteristics of the confirmed cases of influenza A(H1N1)v infection. The most frequent symptoms were fever (94%), cough (93%), sore throat (77%), general malaise (77%) and rhinorrhoea (76%). Gastrointestinal symptoms including abdominal pain (28%), vomiting (26%) and diarrhoea (16%) were not uncommon.

Epidemic curve and transmissibility

Figure 4A shows the temporal distribution of confirmed cases as a function of the date of onset. The number of cases greatly increased from mid-June to mid-July. It should be noted that cases in mid-July are likely underestimated due to reporting delay, and the temporal dynamics are also influenced by spatial spread from Lima to the rest of the country in the subsequent time periods. Based on the epidemic curve, the first three weeks (from 6 to 29 May) were considered as "random phase". Informed by deviation of our simple model from the observed data (i.e. Akaike Information Criterion obtained from negative loglikelihood and a single parameter to be estimated), 30 May was assumed to be the starting time point of exponential growth (and called Day 1). We also assumed that the exponential growth phase continued up to 20 June (for three weeks which should capture the dynamics of the first 6-10 generations), while allowing plus/minus two days. Including all imported cases, the intrinsic growth rate, r was estimated at 0.117 (95% CI: 0.106, 0.128) per day. Excluding all imported cases, r was estimated at 0.135 (95% CI: 0.122, 0.149) per day. Assuming that the mean generation time = 2.8 days, and coefficient of variation (CV) = 47.1%, R for these settings was estimated at 1.37 (95% CI: 1.33, 1.41) and 1.44 (95% CI: 1.39, 1.49), respectively. Figure 4B compares observed and predicted epidemic curves. We also examined the sensitivity of R for different lengths of mean generation time (ranging from 1.6 to 4.0 days) (Figure 4C), and the maximum likelihood estimate of R ranged from 1.2 to 1.6. When we use different windows (18 June to 22 June as the latest time points of exponential growth), R appeared to range from 1.3 to 1.4 (Figure 4D).

Discussion

The current pattern of spread of influenza A(H1N1)v in Peru is dominated by a wave that emanates from the capital city, Lima, the early dynamics of which may most likely be associated with high frequency of international travel, thereby increasing the chances of a major epidemic in the capital city.

Our early findings indicate that public health interventions need to be in accord with the epidemiological behaviours (e.g. temporal and spatial increase) and moderate severity of the disease. For

Figure 3

Clinical characteristics of confirmed cases of influenza A(H1N1)v reported in Peru as of 17 July 2009 (n=1,771)

instance, while in some countries radical control measures aimed at rapid containment, such as contact tracing and complete proactive school closures, were conducted during the early phase of this pandemic, the epidemic in Peru without obvious school clusters during the early phase did not offer an opportunity to implement similar countermeasures. In such settings it may be more realistic to focus interventions on minimising mortality at the population level (e.g. early diagnosis and treatment of severe cases).

Despite the lack of obvious large clusters, the great majority of cases were documented among school age children and young adults, with the lowest frequency of cases among seniors, a pattern that is consistent with reports form other countries [5-8]. It should be noted that the age-distribution of cases could change as the epidemic develops. Also, it should be noted that the impact of high school and university students (i.e. those aged from 15 to 19 years) on the transmission dynamics is presumably smaller

A) Epidemic curve of confirmed cases of influenza A(H1N1)v in Peru by date of symptoms onset, 8 May 2009 to 17 July 2009; B) Exponential growth fit to the early epidemic phase of influenza A(H1N1)v in Peru. Data are the black dots, the solid line is the exponential fit to the data, and dashed lines correspond to uncertainty bounds of the expectation based on the confidence limits of the intrinsic growth phase; C) The reproduction number estimates from the early epidemic phase of the epidemic curve of influenza A(H1N1)v cases in Peru as a function of plausible mean generation times and D) using different end dates of the initial growth phase.
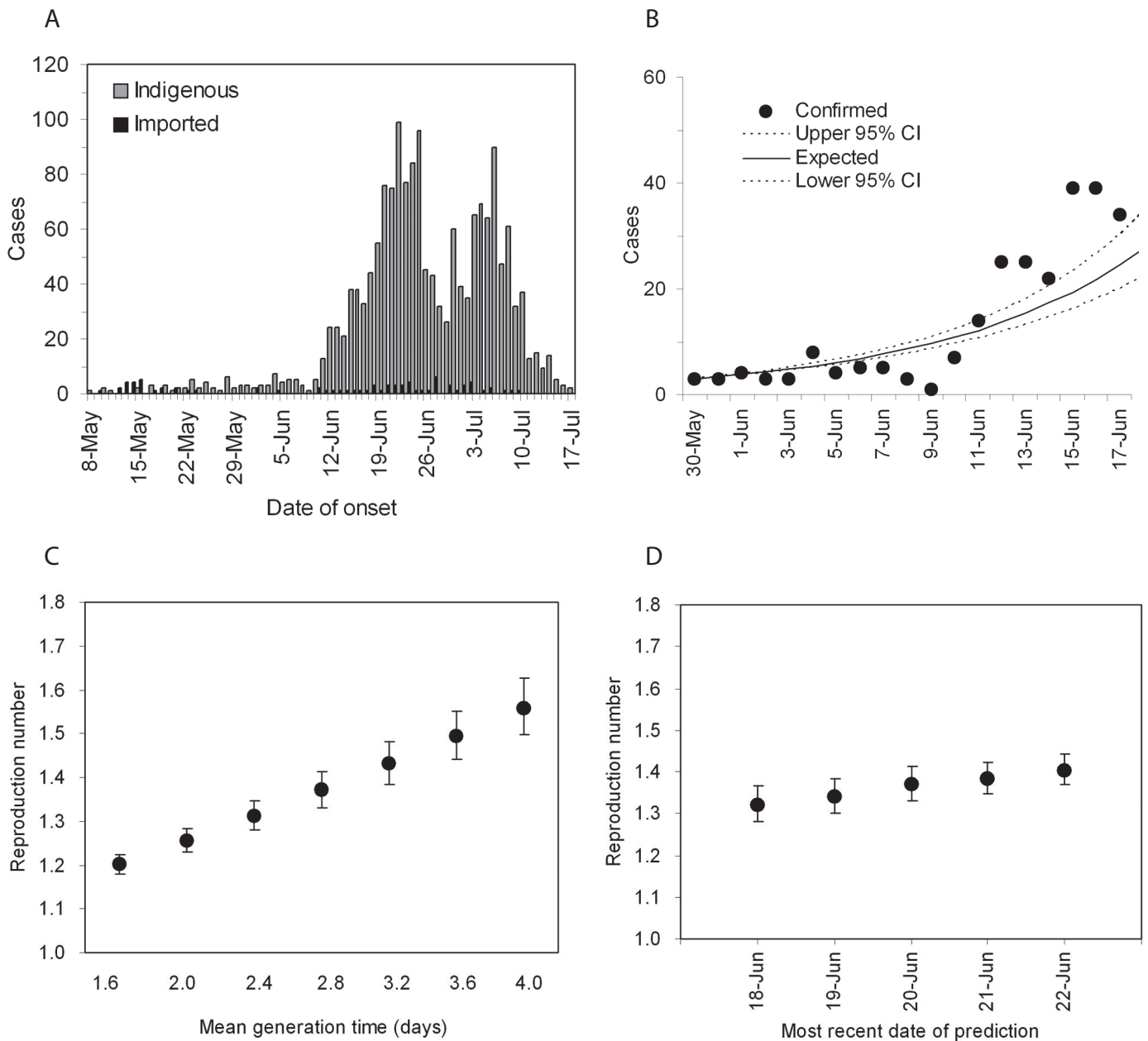
than that observed in Japan [5]. While this age group, especially the presence of high-school clusters, may have contributed more significantly to generating a higher estimate of R in Japan [5], our estimate of R is probably less affected by such school clusters and therefore not so likely to be an overestimate.

The frequency of respiratory symptoms recorded for A(H1N1)v cases in Peru is in line with those reported for other influenza-like infections in Peru [8], but the gastrointestinal symptoms that included abdominal pain, vomiting and diarrhoea were remarkably more common among cases infected with the pandemic virus. Similar observations were made in other countries including Mexico [6] and Japan [9].

R was estimated at 1.37 in our setting in Peru. Sensitivity analysis revealed that the estimates lied in the range of 1.2 to 1.7, which is broadly consistent with previous estimates for this pandemic in other regions [10-12] and in line with estimates for seasonal influenza in temperate countries [13]. Nevertheless, it must be remembered that due to antiviral treatment which was administered to a substantial fraction of confirmed cases in early June our R calculation might be slightly underestimated. In addition, there is significant uncertainty associated with estimation of R in a setting where the reporting biases are likely to be changing on a daily basis. Validation of these estimates will be possible as additional data become available on population-based sero-surveys and growth patterns observed in individual community-level outbreaks.

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