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The 1918–1920 influenza pandemic in Peru

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Abstract

Background—Increasing our knowledge of past influenza pandemic patterns in different regions of the world is crucial to guide preparedness plans against future influenza pandemics. Here, we undertook extensive archival collection efforts from 3 representative cities of Peru (Lima in the central coast, Iquitos in the northeastern Amazon region, Ica in the southern coast) to characterize the age and geographic patterns of the 1918–1920 influenza pandemic in this country.

Materials and Methods—We analyzed historical documents describing the 1918–1920 influenza pandemic in Peru and retrieved individual mortality records from local provincial archives for quantitative analysis. We applied seasonal excess mortality models to daily and monthly respiratory mortality rates for 1917–1920 and quantified transmissibility estimates based on the daily growth rate in respiratory deaths.

Results—A total of 52,739 individual mortality records were inspected from local provincial archives. We found evidence for an initial mild pandemic wave during July-September 1918 in Lima, identified a synchronized severe pandemic wave of respiratory mortality in all three locations in Peru during November 1918-February 1919, and a severe pandemic wave during January 1920- March 1920 in Lima and July-October 1920 in Ica. There was no recrudescent pandemic wave in 1920 in Iquitos. Remarkably, Lima experienced the brunt of the 1918–20 excess mortality impact during the 1920 recrudescent wave, with all age groups experiencing an increase in all cause excess mortality from 1918–19 to 1920. Middle age groups experienced the highest excess mortality impact, relative to baseline levels, in the 1918–19 and 1920 pandemic waves. Cumulative excess mortality rates for the 1918–20 pandemic period were higher in Iquitos

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(2.9%) than Lima (1.6%). The mean reproduction number for Lima was estimated in the range 1.3–1.5.

Conclusions—We identified synchronized pandemic waves of intense excess respiratory mortality during November 1918-February 1919 in Lima, Iquitos, Ica, followed by asynchronous recrudescent waves in 1920. Cumulative data from quantitative studies of the 1918 influenza pandemic in Latin American settings have confirmed the high mortality impact associated with this pandemic. Further historical studies in lesser-studied regions of Latin America, Africa, and Asia are warranted for a full understanding of the global impact of the 1918 pandemic virus.

Keywords

1918 influenza pandemic; Peru; Lima; Iquitos; transmissibility; age-specific mortality

INTRODUCTION

The 1918–1920 influenza pandemic represents a unique epidemiological phenomenon of recent history. During the last few years, there has been increasing interest among the scientific community in elucidating the signature epidemiological patterns associated with this pandemic, especially with respect to variation with age, geography and transmissibility [1–3]. A better understanding of these patterns is essential to better prepare for future influenza pandemics.

Quantitative analyses in North America (US [4, 5], Canada [6, 7], Mexico [8]), Europe (Denmark [9], Spain [10], France [10]) and Asia (Japan [11], Singapore [12] Taiwan [13]) have revealed characteristic features of the 1918–20 influenza pandemic, including increased mortality rates in young adults, relative to seasonal epidemics, and the occurrence of multiple pandemic waves over short periods of time [1] . In addition, available data suggest that senior populations in the US and Europe experienced little or no excess mortality during the pandemic. This phenomenon of “senior sparing” was likely associated with exposure to related influenza viruses in the 19th Century, a concept known as “original antigenic sin” which was described by Francis [14]. Despite recent interest in historical studies, pandemic mortality patterns remain poorly described in many areas of the world, particularly in Latin America, Africa and Asia.

Recent epidemiological surveillance efforts have shed light on the contemporary patterns of influenza circulation in Peru [15–17], but the impact of historical influenza pandemics remains poorly understood. Here, we undertook a detailed historical study of the 1918–20 influenza pandemic in Peru, a geographically diverse country with a wide variety of ecological systems including desert coastal areas, temperate highlands, and rainforest, to characterize the age and geographic patterns of the pandemic in this region.

MATERIAL AND METHODS

Localities studied

To obtain detailed data about the temporal dynamics of pandemic waves in Peru, we carried out intense data collection efforts in 3 representative cities of Peru: Lima, Iquitos, and Ica. Lima, capital of the Republic of Peru, is located on the central coast of the country, with an estimated population size of 194,640 in 1917. Iquitos is located in the Northeast of Peru in the Amazonian jungle and is the capital of the Loreto department. Iquitos is surrounded by three rivers, and is the most populous city in the world that cannot be reached by road. By 1880 Iquitos had become a major center of the rubber industry and its population was

estimated at 11,466 in 1917. The city of Ica was founded in 1563 and is located about 300km South of Lima along the desert coast of southern Peru.

Data sources

We manually retrieved a total of 52,739 mortality records from local Public Benevolent Institutions or Regional Archives (Table 1). For each death record, we compiled the age, gender, cause and exact date of death from the original documents.

Lima had reliable historical records; however, cause of death and age were either missing or not legible for the great majority of records in the other two cities. Analysis of the archival data from Ica suggested a substantial under-reporting of deaths, as baseline total death rates in pre-pandemic years were more than an order of magnitude lower than in Iquitos or Lima. This could be explained by the presence of a substantial number of informal cemeteries in rural areas at that time. In consequence, we only used the Ica data to illustrate the timing of the 1918 pandemic, rather than to quantify its mortality impact.

Estimation of excess mortality attributable to influenza

To estimate the mortality attributable to the influenza pandemic during 1918–20, we calculated excess mortality for each city, pandemic wave, age group, and mortality outcome (respiratory deaths and all-cause), using a combination of previous approaches [9, 18, 19] [8, 20]. First, we identified influenza pandemic periods by fitting a cyclical seasonal linear regression model to respiratory mortality after excluding months with increased respiratory mortality (above 75 percentile of mortality) [9, 18, 19]. Influenza pandemic periods were defined as the months when mortality exceeded the upper limit of the 95% confidence interval on the model baseline. This approach produced a period of significant excess respiratory mortality during Nov 1918 – Jan 1919 in all 3 cities, and a recrudescent period of pandemic activity during year 1920 in Lima and Ica.

In the second step, we calculated excess mortality as the observed mortality during pandemic months minus the average mortality observed in corresponding non-pandemic months of surrounding years, 1915–1921. We summed the excess deaths above the model baseline during each pandemic period identified during 1918–20 to estimate the mortality burden of the pandemic. Similar “empirical” methods have been used in past research [8, 20] and are particularly well-suited to mortality data with weak seasonality, as in Peru (Figure 1). Finally, we also calculated the relative risk of pandemic death, defined as the ratio of excess mortality during pandemic periods to the expected mortality in the absence of influenza virus activity, given by the model baseline. The relative risk measure has been shown to facilitate comparison between age groups and locations, which have different baseline risks of death [19, 21].

Estimation of transmission potential

The basic reproduction number (R_0) measures the potential for an infectious disease to spread in a theoretical setting in terms of the average number of secondary cases generated by a primary case during the initial epidemic period in an entirely susceptible population [22, 23]. A related quantity is the effective reproduction number, R, which gives the average number of secondary cases per primary case in the presence of pre-existing immunity and/or public health interventions [3]. In the case of influenza pandemics, we can expect little or no residual immunity and hence R is a good approximation of R_0 (assuming no intervention). We estimated the reproduction number, R, using a simple method that relies on the growth rate during the initial exponential phase of the pandemic, as in [3, 8, 24]. We estimated the growth rate “r” by fitting an exponential function to the initial increase in the daily number of respiratory deaths [8, 25]. The reproduction number was calculated by using our estimates

of the growth rate and assuming exponentially distributed latent and infectious periods or a fixed generation interval (delta distribution) [24].

We also evaluated the sensitivity of R estimates to the choice of mortality indicator and compared estimates derived from crude respiratory deaths and excess respiratory deaths above baseline.

Because of the uncertainty associated with the generation interval for influenza, we considered two extreme values of the generation interval used in past research: a short interval of 3 days (where the latent and infectious periods were both set to 1.5 days [24, 26, 27] and a longer interval of 6 days (latent period=1.9 days and infectious period=4.1 days [5, 28]. We have used the same approach in prior studies of the 1918 influenza pandemic in Copenhagen [9] and two Mexican cities [8].

Results

We found evidence of multiple pandemic waves of respiratory mortality in Lima from records of respiratory deaths during 1918–1920 (Figure 1). According to reports of the Lima Provincial Council, a mild wave of pandemic activity hit Lima during winter months of July-September 1918, with a peak of mortality in August [29]. This mild wave could be identified in August of 1918 from the daily time series of respiratory mortality (Figure S1). A similar increase in respiratory mortality was reported among the military who suffered an average mortality rate increase of 13% in 1918 relative to years 1916–1917 according to the statistical abstract of Peru [30].

Lima, Iquitos and Ica experienced a well-synchronized severe pandemic wave of mortality spanning November 1918-January 1919 as indicated by a significant elevation in all-cause and respiratory mortality time series (Figure 1). This finding was consistent with an increase in the mortality rate among the military by 46% in 1919 relative to the average mortality rate during 1916–1917 as displayed in Figure S2. In Lima and Iquitos, where excess mortality rates could be estimated, we found important variation in the burden of the 1918–19 pandemic wave, with 10-fold higher rates in Iquitos (288 per 10,000) than Lima (29 per 10,000; Table 2). We note that respiratory and all-cause mortality outcomes produced very similar estimates of excess mortality rates for the 1918–19 pandemic wave in Lima, but this was not the case in Iquitos.

Approximately one year later during January 1920-March 1920, the population of Lima experienced a recrudescent wave of respiratory mortality in excess of baseline levels (Figure 1 and Figure S1). This mortality wave was confirmed to have been associated with the influenza pandemic from newspaper reports highlighting the dramatic impact of the influenza pandemic on the population [31]. Since cause of death was widely underreported in Lima during this third pandemic wave, we rely on all-cause excess mortality estimates. These estimates suggest that the third wave in Jan-Mar 1920 had a ~4-fold higher mortality impact than the second wave in Nov 1918 – Jan 1919 (Table 2). Ica also experienced a subsequent wave of excess mortality in July – October 1920 (Figure 1), and the number of recorded deaths suggests that it was milder than the earlier wave (not shown). Iquitos did not experience a recrudescent wave in 1920.

Next, we explored the age patterns of all-cause excess deaths associated with the pandemic in Lima, where age information was available (Figure 2). Given the lack of age-specific population estimates for this period, we report age patterns using the relative risk of deaths over baseline (ratio of excess deaths over baseline), which allows standardization for different background risks of deaths, and in our case, population sizes. The relative risk of death was highest among 25–44 years old during the pandemic wave in Nov 1918-Jan 1919

with a 5-fold increase over baseline respiratory deaths and 20% increase over baseline all-cause deaths. By contrast, the relative risk of death was highest among 15–24 years in the subsequent wave in Jan-Mar 1920 (Table 3). All age groups experienced an increase in all cause excess mortality from the second pandemic wave in Nov 1918-Jan 1919 to the third pandemic wave in Jan-Mar 1920, confirming the severity of the 1920 recrudescent wave in Lima.

Reproduction number

The initial growth phase and corresponding exponential growth model fits are shown in Figure S3 and the summary estimates of R in Lima assuming a short and long duration of the mean generation interval (3 and 6 days) are given in Table S1. Additionally, we also estimated R using all respiratory deaths and excess respiratory deaths over a baseline. Overall, the mean R estimates were found to lie in the range 1.3–1.4 based on a 3-day generation interval and 1.6–2.0 assuming a generation interval of 6 days.

Discussion

Quantitative analyses on the impact of the pandemic in the Americas, Africa and Asia are still scarce. In order to increase our understanding of the impact and characteristic features of the 1918–1920 influenza pandemic in South America, we undertook intensive data collection efforts across 3 cities of Peru, which comprise a variety of ecological zones. We quantified mortality burden and transmissibility as well as the temporal and age mortality patterns of the pandemic. The Peruvian cities of Lima (central coast), Ica (south central coast) and Iquitos (northeastern Amazon region) experienced substantial increases in mortality above baseline levels during several months of 1918–20, which we associate with influenza pandemic activity based on contemporaneous newspaper and archival reports.

The archival mortality data presented here are subject to limitations, including underreporting and relatively scarce information about cause of death, so that our most reliable estimates of excess mortality rates are based on total mortality. Considering the cumulative mortality impact of the pandemic during 1918–20, we note that Iquitos experienced a substantially higher mortality impact than Lima, with cumulative excess death rates estimated at 2.9%, occurring during a single pandemic wave in 1918–19. The 1918–20 pandemic appeared milder in Lima, with cumulative excess death rates estimated at 1.6%, and a mortality impact spread over a 2-year period. The higher mortality rate in Iquitos could be explained by the limited access to quality health care in this relatively isolated area compared to Lima. These estimates from Peru are in the high range of 1918–20 pandemic mortality estimates available from various locations around the world, with lowest cumulative excess mortality rate reported in Denmark at 0.4% [9], and highest rate reported in India at 4.9% [20]. Our estimates for Lima and Iquitos are also relatively high as compared with those reported for Mexican cities, ranging from 0.7% in Mexico City to 1.9% in Toluca [8], or with the average European excess mortality rate estimated at 1.1% [32].

The first official publication that raised concerns about an increase in respiratory disease in Lima was issued on 19 September 1918 as an Editorial in the newspaper “La Prensa.” Subsequent news reports published on 19 October 1918 highlighted the benign character of the early pandemic wave, e.g., there was a significant increase in the number of respiratory cases, but only a few cases succumbed to the disease. Nevertheless, several days later (28-October-1918), news reports alerted about a “worsening epidemic of respiratory disease” in Lima with a significant reduction in school attendance. As a result, influenza notification was made mandatory in Peru. Furthermore, to mitigate the effects of a secondary severe pandemic wave, the Hygiene Council announced the implementation of a series of public

health measures including the closing of schools for 15 days and prohibition of gatherings in cemeteries during the celebration of the Dead during November 1–2, 1918.

The presence of an initial mild wave of respiratory mortality in Lima is in line with reports of this and other pandemics from the last century [33]. In the Americas, New York City [4], Mexico City and Toluca, Mexico [8] exhibited early herald pandemic waves during the Spring-Summer of 1918. Early waves of respiratory mortality in young adults were also observed prior to the main wave of the 1918 influenza pandemic in Copenhagen [9], UK [3], Geneva [34], Madrid and Basque Country, Spain [10] and Singapore [12].

As in other locations in Latin America and elsewhere [4, 8–10], young adults in Lima were the hardest hit during the main pandemic wave, relative to baseline levels of deaths in comparable non-pandemic periods. Given the lack of age-specific population data, it is difficult to tell whether seniors were spared in Lima, as in New York City or Copenhagen, or whether they experienced high excess mortality, as in Mexico [8]. The high relative risk of respiratory death observed during Nov 1918-Jan 1919 in seniors from Lima, as compared with baseline mortality, suggests substantial excess mortality in this population, reminiscent of the Mexican patterns. Further studies from Latin America are warranted for a clear understanding of senior excess mortality patterns in this region. Such information would be particularly useful to gain insight into the pre-existing immunity profiles and circulation of historical influenza viruses in the 19th Century.

Lima and Ica experienced severe recrudescent waves of pandemic excess mortality in 1920 as indicated by all-cause mortality data. Most remarkably, our data suggest that Lima experienced the brunt of the 1918–20 pandemic mortality impact in the second year of influenza virus circulation. Substantial 1920 pandemic waves have also been reported for New York City [4], Mexico City [8] and Taiwan [13]. The relative impact of a post-1918 pandemic wave could be associated with the effects of control interventions put in place during the main pandemic wave in 1918, which contributed to maintain important levels of susceptibility in the population the following influenza season. For instance, in Taiwan, the age groups with the highest mortality impact during the 1918 pandemic wave experienced reduced excess mortality rates during the 1920 pandemic wave and vice versa [13]. However, the possibility that the novel virus changed into a different strain the following season cannot be ruled out.

Influenza pandemic waves tend to occur outside of the typical activity periods for seasonal influenza [1]. The pandemic wave in Iquitos occurred during Nov 1918-Feb 1919 where influenza incidence is weakly seasonal with higher activity in Feb-May [17]. Similarly, the largest impact of the pandemic in Lima during the summer periods of 1918–1919 and 1919–1920, occurred outside of typical activity periods for seasonal influenza in Peru [15], which is consistent with the 2009 pandemic patterns [16].

A comparison of different locations in the Americas indicates that the reproduction number of the main pandemic wave was highest in Toluca, Mexico [8], intermediate in US cities on average [5, 24], and lowest in Mexico City [8], and Lima (this study).

In conclusion, recent quantitative reports on the 1918–1920 influenza pandemic in Peru and central Mexico [8] have revealed substantial excess mortality impact associated with this pandemic. Age-specific profiles of mortality, overall excess mortality burden, timing of pandemic waves, and transmissibility estimates, varied greatly across locations. For instance, Central Mexico and Lima experienced a mild herald pandemic wave in 1918 similar to the US and Europe, while the available evidence suggests that Iquitos and Ica did not. Overall, this analysis suggests important geographical variation in the epidemiology of the 1918 pandemic between Europe, the US, and Latin American countries. Further

historical studies in lesser-studied regions of Latin America, Africa and Asia are essential for a full understanding of the global health impact of the 1918–1920 pandemic virus and to inform scenarios predicting the potential impact of future pandemics.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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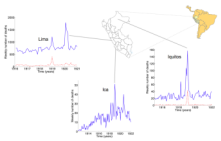

Figure 1.
Monthly time series of all-cause (blue solid line) and respiratory (red dashed line) deaths from 3 representative cities of Peru, 1916–1920, where extensive data collections efforts were carried out.

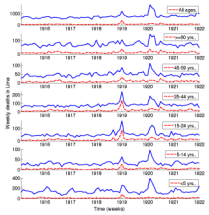

Figure 2.
Age-specific weekly time series of respiratory and all-cause mortality in the city of Lima, Peru, 1915–1921.

Table 1

Distribution of individual all-cause mortality records retrieved from three representative cities of Peru.

Location	Population size estimate in 1917	Years	Total mortality records	Source
Lima	194,640	1916–1920	46,711	Public Benevolent Institution of Lima
Iquitos	11,466	1915–1921	2,576	Public Benevolent Institution of Iquitos
Ica	70,439	1912–1922	1,749	Public Benevolent Institution of Ica

Table 2

Comparison of the mortality impact of successive pandemic waves in Lima and Iquitos, Peru, 1918–20. Excess mortality estimates are calculated by subtracting observed mortality during epidemic months from mortality in corresponding months of surrounding years. Estimates are given as excess rates per 10,000 and as relative risk (RR) over baseline.

	1918–1919 pandemic wave		1920 pandemic wave	
Location	**Excess P&I Mortality per 10,000 (RR)**	**Excess all-cause Mortality per 10,000 (RR)**	**Excess P&I Mortality per 10,000 (RR)**	**Excess all-cause Mortality per 10,000 (RR)**
Lima	27 (3.4)	29 (0.2)	*	129 (1.2)
Iquitos	64 (28)	288 (3.2)	No wave	No wave

* Deemed unreliable due to under-reporting of cause of death during the third pandemic wave

Table 3

Age-specific excess mortality impact associated with the November 1918-January 1919 and January-March 1920 influenza pandemic waves in Lima, Peru. Excess mortality estimates are based on subtracting the observed mortality during pandemic months from mortality in corresponding months of surrounding years. Estimates are presented as a relative risk (RR) of death, calculated as the ratio of excess mortality to baseline mortality, facilitating comparisons across age groups which have different background risk of death and population sizes. The highest estimates for each pandemic wave and mortality outcomes are highlighted in bold.

	Nov 1918 – Jan 1919 Pandemic Wave		Recrudescent Pandemic Wave Jan – Mar 1920	
Age Group	**RR of excess P&I mortality over baseline**	**RR of excess all-cause mortality over baseline**	**RR of excess P&I mortality over baseline**	**RR of excess all-cause mortality over baseline**
All ages	3.4	0.2	1.9	1.2
Under 5 yrs	3.2	0.2	1.3	0.9
5 to 14 yrs	3.0	0.5	2.2	1.3
15 to 24 yrs	4.8	1.2	**2.4**	**1.3**
25 to 44 yrs	**5.1**	**1.2**	2.0	1.2
45 to 59 yrs	2.5	0.7	1.4	1.2
Over 60 yrs	1.5	0.3	1.9	1.2

P&I: Pneumonia and Influenza