Study of the relationship between socio-demographic characteristics and new influenza A (H1N1)

ABSTRACT

Objective: The pandemic of new influenza A (H1N1) has spread rapidly throughout the world, characterized by high transmissibility, but low pathogenicity and virulence. The aim of this study was to understand the pandemic event and available technologies for disease surveillance, prevention, control and management. **Methods:** In this retrospective study, we used data from patients in the State of Paraná who had been diagnosed with the disease during the 2009 pandemic. Data were collected from the disease notification form and the study only included patients with confirmed laboratory diagnosis by RT-PCR. **Results:** We present the epidemiological profile of 4,740 patients that met the inclusion criteria. The variables age, level of schooling and gestational age were shown to be associated with mortality due to the infection. Gender and race/ethnicity were not associated with the outcome of the infection. **Conclusion:** These results underscore the importance of knowing the variables associated with unfavorable outcomes of pandemic influenza infection in order to minimize the health related consequences. Attention should be given to its forms of transmission and to the frailty of certain age groups that have no cross-immunity.

Keywords: influenza A virus, H1N1 subtype; disease outbreaks; causality.

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INTRODUCTION

In March 2009, an outbreak of respiratory illness was recorded in Mexico, which quickly spread to the United States and then to the rest of the world.[1] In early April of that year, the etiologic agent was identified as an influenza A virus (H1N1), from a triple recombination between the swine, avian and human influenza viruses. It was concluded that the pig was probably the host that allowed the new genetic recombination, thanks to its capacity to express receptors for human influenza virus, as well as for the avian and swine influenza viruses.[2]

Influenza viruses have a genetic material comprising a segmented, single stranded, negative RNA. Owing to this characteristic, they have high variability and instability and can cause outbreaks, epidemics and pandemics.[3,4] It is worth remembering that the same viral strain, influenza A (H1N1) was the cause of the Spanish flu in 1918, known for its severity and high lethality rates.[5]

As for the clinical aspects, the most common symptoms of influenza are characterized by fever, chills, headache, dry cough, sore throat, nasal congestion, runny nose, myalgia, anorexia and fatigue. Less often reported are nausea, abdominal pain, diarrhea and vomiting.[5,6] In general, evolution is benign and self-limited. However, the impact on the elderly, children, pregnant women or individuals with chronic diseases considered to be risk groups for this pathology may be more severe and can lead to death.[7,8]

During the pandemic of the new influenza A (H1N1) in 2009, the population of the State of Paraná, Brazil, was heavily affected. Despite the low lethality rates, there was panic due to the rapid spread of the disease. As in other parts of the country, schools were closed and gatherings were discouraged. Considering that the severity of the disease can change across different geographical areas, seasonal conditions and because the virus can adapt or not to its new host, the aim of this study was to understand the pandemic event and the available technologies for disease surveillance, prevention, control and management, allowing the organization of measures to limit its spread, especially in individuals at risk of death due to the disease.

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We declare no conflict of interest

METHODS

This is a descriptive and retrospective study carried out with data obtained from disease notification forms of patients from the state of Paraná that had a diagnosis of influenza A (H1N1) during the year of 2009, provided by the Health Secretary of the State of Paraná - SESA-PR/CIEVS. The criterion established for inclusion of patients was laboratory confirmation of the pandemic strain of influenza A (H1N1) by RT-PCR. Information about sex, age, ethnicity/race, level of schooling, pregnancy and clinical evolution (outcomes) were abstracted from the forms. Patients were grouped according to disease outcome as having progressed for cure or death.

The data were analyzed using the SPSS Statistics for Windows software, version 17.0. Univariate analysis assessing the correlation between epidemiological variables and disease outcome was tested using the chi-square test. A p-value < 0.05 was considered statistically significant. This project was approved by the Ethics Committee in Research of the Division of Health Sciences, Universidade Federal do Paraná, under registration number 938.063.10.06: and CAAE: 0038.0.091.000-10, according to Resolution 196/96 of CNS.

RESULTS

According to inclusion criterion, 4,740 patients that acquired influenza A (H1N1) pandemic strain during 2009 with laboratory confirmed diagnosis were selected. Epidemiological data observed can be seen in Table 1, as well as p-values obtained in the correlations with outcomes. Due to the severity of the clinical presentation, 1,911 (40.3%) patients were hospitalized and 273 (5.8%) patients died.

Of the patients included in the study, 53.3% were females. The overall mean age was 23.5 (± 15.7) years. The mean age of patients who were cured was 22.7 (± 15.2) years and 37.7 (± 15.8) years in the group who died. The predominant age-range of patients who acquired the infection was 20 to 29 years, totaling 25.8% of patients, whereas only 2.0% were 60 years or more, as shown in Table 1. Patients aged between 30 and 39 years had the highest death toll.

Most patients were Caucasians (81.8%). Race/ethnicity was not significantly associated with disease outcome. Among women who acquired the pandemic influenza A (H1N1), 1,803 (71.3%) were of childbearing age (10 and 49 years).[9] Of these women, 352 (19.5%) were pregnant, of whom 20.4% were in the first trimester, 42.6% in the second trimester and 34.7% in the third gestational trimester. Of the pregnant women who were in the third trimester, 7.4% died, comprising 56.3% of the total deaths observed among pregnant women in this patient population.

Although pregnancy and gestational period were not significantly associated with disease outcomes the highest proportion of deaths occurred in the subgroup of pregnant women in the third trimester. Table 2 shows the relation between pregnancy and age. The highest frequency of deaths occurred in patients who were in the third trimester of pregnancy (Figure 1).

Regarding education, 13.9% of the patients were children not of school age, and only 11.8% had graduated from high school. Level of schooling was also significantly associated with disease. Most patients who died were illiterate or had unknown level of schooling. In contrast, higher cure rates were observed in patients who had completed high school, or college/university, both complete and incomplete, as well as in children who were not yet of school age.

DISCUSSION

Disease outcomes were not significantly different among men and women.

In relation to age range, it was also observed that 92.0% of patients were younger than 50 years, confirming previous reports,[10,11] showing that the highest incidence of the disease occurred in young adults. In contrast, this information assumes the presence of cross-immunity by the older population, which can be attributed to the antigenic similarities of this virus with the circulating viruses. The seasonal influenza vaccine administered to this population annually is comprised by viruses that share similar antigen detrminants. Age was significantly associated with disease outcomes indicating that age is a risk factor.

In contrast, race/ethnicity does not seem to play a role in disease outcome.

In the present study we could not show any significant association between pregnancy and higher risk of dying. Similar results were observed in another study by Saraceni.[12] However, as most of the pregnant women and the majority of infected patients were in the age range of 20 to 29 years, age might have confounded the association of pregnancy and unfavorable outcome, as detailed in another study.[12]

Pregnant women in the third trimester had the highest percentage of deaths, suggesting this period to be the most likely to result in disease severity and death during infection. Factors that may be related to death in this group during the infection are mainly due to the physiological changes of pregnancy, such as (I) reduced pulmonary functional capacity caused by compression of visceral structures by the pregnant uterus; (II) hypervolemia, which would decrease the capacity of hemodynamic adaptation in case of sepsis; and (III) immunological impairment of cell-mediated immunity attributed to

Table 1. Epidemiological characteristics of the population and analysis of factors associated with disease outcome

Epidemiological characteristics	Number of patients	% Σ	Correlation (p-value)
Outcomes			
Cure	4,467	---	---
Death	273		
Sex			
Female	2,527	---	0.291
Male	2,213		
Age range			
Mean	23.5	---	
Standard deviation (SD)	23.5	---	
≤ 2 years	322	6.8	
3 a 10 years	760	22.8	
11 a 19 years	999	43.9	0.000[a]
20 a 29 years	1,223	69.7	
30 a 39 years	666	83.8	
40 a 49 years	392	92.0	
50 a 59 years	285	98.0	
≥ 60 years	93	100	
Race/Ethnicity			
Caucasian	3,878	---	
Black	90		
Asian	62		0.123
Brazilian Mulatto	435		
Native Brazilian	53		
Not informed	222		
Pregnant women	352	---	0.304
Gestational period			
First trimester	72	---	
Second trimester	150		0.127
Third trimester	122		
Not informed	8		
Level of schooling			
Illiterate	26		
Incomplete primary school[b]	414	---	
Complete primary school[b]	148		
Incomplete junior high[c]	518		
Complete junior high[c]	188		
Incomplete high school	374		0.000[a]
Complete high school	557		
Incomplete college/university	224		
Complete college/university	386		
Does not apply[d]	660		
Not informed	1,245		

[a]Variables that had correlation with outcome; level of significance < 0.05.
[b]Primary school: 1st to 5th grades (in Brazil).
[c]Junior high: 6th to 9th grades (in Brazil).
[d]Does not apply: children not of school age.

Table 2. Pregnant women divided according to gestational period and age range

Age ranges	1st Trimester	2nd Trimester	3rd Trimester	NI	n
10 to 19	15	30	24	2	71
20 to 29	42	91	82	3	218
30 to 39	15	27	15	3	60
40 to 49	0	2	1	0	3
Total	72	150	122	8	352

NI, gestational period not informed; n, frequency of pregnant women in each age range.

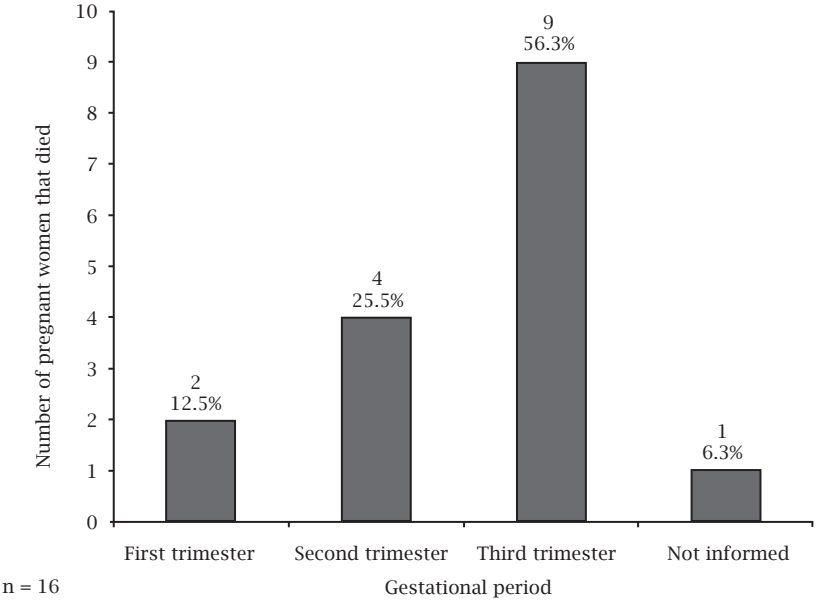

Figure 1: Percentage of deaths among pregnant women, according to the gestational trimester.

immune tolerance to paternal antigens of the fetus, which would limit the immunity against the flu virus.[13,14]

Schooling level was shown to be a factor related to disease outcome, not only for acquiring the infection, but also predisposing the individual to death from the disease. It is believed that patients with higher educational level probably had a higher cure rate because they have better understanding regarding the disease and the need to seek medical attention when perceiving the first infection-related symptoms. In turn, children not of school age have an important characteristic for cure of the infection, that could be attributed to the care and attention received from parents and relatives, as well as the fact that they are not subject to gatherings in the schools. These data highlight that the knowledge about the disease and its modes of transmission was extremely important to prevent and fight this pandemic.

Moreover, it is known that the level of schooling has a direct association with the socioeconomic level of the individual. It is believed that individuals from lower social classes would be more prone to contract the infection, as they use public transportation, live in and attend places with larger number of individuals, and have less access to medical resources. Among other factors, they would have fewer resources to adopt preventive measures such as the use of gel alcohol for hand sanitizing as well as therapeutic measures, such as the use of palliative drugs, thus predisposing these individuals to death by infection.

CONCLUSION

In spite of the initial panic due to the history of influenza pandemics with high mortality rates that occurred in the last century, the new influenza A (H1N1) pandemic that occurred in 2009 showed high transmissibility, but low pathogenicity and virulence.

The most important characteristic of this pandemic was its rapid dissemination throughout the world, and not its severity, as it was expected due to its similarity to the viral strain that caused the Spanish flu. The results confirm that individuals under the age of 50 years had a higher prevalence of infection by the new influenza A (H1N1). This fact is probably due to the lack of immunity of younger individuals caused by the lack of previous contact with virus strains antigenically similar to that of the current pandemic, resulting in a higher susceptibility to the disease. The large number of cases was further intensified by seasonality, resulting in the record of about 180 cases per day in periods of colder weather in the state of Paraná.

Considering the modes of disease transmission, level of schooling was directly related with the outcome, as the individual's knowledge about ways of preventing the disease can contribute to the defense against infection. This result contributes to the conclusion that educating the individual regarding self-care is an important tool in the prevention and control of a pandemic.

This study allowed the identification of the association between some epidemiological characteristics and the possible outcomes, based on events during the 2009 pandemic. Knowing the age range and schooling level were factors related to this pandemic event, both for contracting the infection and predisposing to death from the disease. Educational campaigns and containment measures were useful in the management of new influenza A (H1N1). This information can be used for establishing strategic measures for the prevention and control of possible future pandemics.

Moreover, it was observed that pregnant women have higher mortality as gestational age progresses, and pregnant women in the third trimester had a higher proportion of deaths when compared to the other pregnant women in other gestational periods, with this characteristic being attributed to the physiological changes of pregnancy.

It is noteworthy that, in this study, cases of the new influenza A (H1N1) were considered positive only after laboratory confirmation by RT-PCR, as established by the Ministry of Health. However, the sample could be higher, if cases considered positive according to the clinical-epidemiological diagnosis were also taken into account.

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REFERENCES

1. Carmo E, Oliveira W. Risco de uma pandemia de influenza pelo vírus A (H1N1). In: Secretaria de vigilância em Saúde - Ministério da Saúde. Cad. Saúde Pública 2009; 1192-3.
2. Neumann G, Noda T, Kawaoka Y. Emergence and pandemic potential of swine-origin H1N1 influenza virus. Nature 2009; 459(7249):931-9.
3. Ho TS, Wang SM, Liu CC. Historical review of pandemic influenza A in Taiwan. Pediatr Neonatol 2009; 51(2):83-8.
4. Palese P, Shaw ML. Orthomyxoviridae: the viruses and their replication. In: D.M. Knipe, P.M. Howley (Eds.), Fields virology, Williams & Wilkins, 2007.
5. Bouvier NM, Palese P. The biology of influenza viruses, Vaccine 2008; 26(Suppl 4):D49-D53.
6. Tumpey TM, Belser JA. Resurrected pandemic influenza viruses. Annu Rev Microbiol 2009; 63:79-98.
7. Dutkowski R. Oseltamivir in seasonal influenza: cumulative experience in low- and high-risk patients. J Antimicrob Chemother 2010; 65(Suppl 2):ii11-ii24.
8. Chang LY, Shih SR, Shao PL, Huang DT, Huang LM. Novel swine-origin influenza virus A (H1N1): the first pandemic of the 21st century. J Formos Med Assoc 2009; 108(7):526-32.
9. Centro Brasileiro de Classificação de Doenças. Boletim do Centro Colaborador da OMS para a classificação de doenças em português [internet]. 2002 [cited on Nov 3 2009];23(2). Available at: http://hygeia.fsp.usp.br/~cbcd/.
10. Hui DS, Lee N, Chan PK. Clinical management of pandemic 2009 influenza A(H1N1) infection. Chest 2010; 137(4):916-25.
11. Khazeni N, Bravata DM, Holty JE et al. Systematic review: safety and efficacy of extended-duration antiviral chemoprophylaxis against pandemic and seasonal influenza. Ann Intern Med 2009; 151(7):464-73.
12. Saraceni V. Outcomes of pandemic influenza (H1N1) 2009 in women of childbearing age, in the city of Rio de Janeiro. Epidemiol. Serv. Saúde Brasília 2010; 19(4):339-346.
13. Duarte P, Venazzi A, Youssef N et al. Pacientes com infecção por vírus A (H1N1) admitidos em unidades de terapia intensiva do Estado do Paraná, Brasil. Rev Bras Ter Intensiva 2009; 21(3):231-6.
14. Montane E, Lecumberri J, Pedro-Botet ML. Influenza A, pregnancy and neuraminidase inhibitors. Med Clin (Barc) 2011; 136(15):688-93.