

Brief Communication

Occurrence of influenza among patients hospitalized for suspicion of influenza A (H1N1) infection in 2010 at a sentinel hospital in São Paulo, Brazil*, **

Ocorrência de influenza em pacientes hospitalizados com suspeita de infecção por influenza A (H1N1) em 2010 em um hospital sentinela na cidade de São Paulo

Thaís Boim Melchior, Sandra Baltazar Guatura, Clarice Neves Camargo, Aripuanã Sakurada Aranha Watanabe, Celso Granato, Nancy Bellei

Abstract

In 2010, 96 patients suspected of being infected with the influenza A (H1N1) virus were hospitalized at the *Hospital São Paulo*, located in the city of São Paulo, Brazil. Of those 96 patients, 4 (4.2%) were found to be infected with influenza A virus—3 with influenza A (H1N1) and 1 with seasonal influenza A—and 2 patients (2.1%) were found to be infected with influenza B virus. Most (63.5%) of the suspected cases occurred in children, as did half of the positive cases. The second wave of influenza A (H1N1) infection was weaker in São Paulo. The decrease in the number of hospitalizations for H1N1 infection in 2010 might be attributable to vaccination.

Keywords: Influenza A virus, H1N1 subtype; Influenza, human; Pneumonia; Pandemics.

Resumo

Em 2010, 96 pacientes com suspeita de infecção por influenza A (H1N1) foram hospitalizados no Hospital São Paulo, na cidade de São Paulo (SP). Desses, 4 pacientes (4,2%) foram diagnosticados com influenza A – 3 com influenza A (H1N1) e 1 com influenza sazonal – e 2 pacientes (2,1%) foram diagnosticados com influenza B. A maioria dos casos suspeitos (63,5%) e metade dos casos positivos ocorreram em crianças. A segunda onda de influenza A (H1N1) foi mais fraca em São Paulo. A vacinação pode ter contribuído para a redução das internações devido a essa infecção em 2010.

Descritores: Vírus da influenza A subtipo H1N1; Influenza humana; Pneumonia; Pandemias.

Influenza virus infections are a major cause of respiratory disease worldwide. In early 2009, a new subtype of influenza A virus emerged and spread rapidly around the world. In May of 2009, the first case of the novel influenza A (H1N1) virus was confirmed in Brazil, and the virus affected thousands of people during the first pandemic wave, mostly in the south and southeast of the country.⁽¹⁾ Presentations varied from mild flu to severe pneumonia and death, and the first wave of the influenza A (H1N1) outbreak led to a great number of hospitalizations for suspected infection.⁽²⁾ At the *Hospital São Paulo*, a sentinel

hospital located in the city of São Paulo, Brazil, over 4,000 patients with influenza-like symptoms were treated in 2009, during the first wave of influenza A (H1N1) infection,⁽³⁾ and 159 of those patients were hospitalized. Among the 159 hospitalized patients, infection with the influenza A (H1N1) virus was confirmed in 31 (19.5%).⁽⁴⁾ Between March and June of 2010, a national H1N1 immunization program was implemented for various risk groups.⁽⁵⁾ The objective of the present study was to describe the types of influenza viruses affecting patients who were hospitalized at the *Hospital São Paulo*

* Study carried out in the Virology Laboratory, Infections Diseases Branch, Medicine Department, Federal University of São Paulo, São Paulo, Brazil.

Correspondence to: Nancy Cristina Junqueira Bellei. Rua Pedro de Toledo, 781, 15º andar frente, Vila Clementino, CEP 04039-032, São Paulo, SP, Brasil.

Tel./Fax: 55 11 5081-5394. E-mail: nbellei@uol.com.br

Financial support: None.

Submitted: 22 March 2011. Accepted, after review: 6 June 2011.

** A versão completa em português deste artigo está disponível em www.jornaldepneumologia.com.br

for suspected influenza A (H1N1) infection in 2010.

Nasal swabs were collected from 96 patients (median age, 3.0 years; range, 0-85 years) hospitalized between January and December of 2010. The study was approved by the local research ethics committee, and all participating patients gave written informed consent.

From the samples collected, viral genomic RNA was extracted using an extraction kit (QIAamp Viral RNA; QIAGEN, Hilden, Germany). Influenza A and B tests were performed by RT-PCR,⁽⁶⁾ and the products were submitted to electrophoresis on 1.5% agarose gels. The diagnosis of influenza A (H1N1) was based on real-time RT-PCR results.⁽⁷⁾

Of the 96 admissions evaluated, 11 (11.5%) occurred during epidemiological week 23 (June 6-12), more than in any other epidemiological week. Most of the patients (55.2%) were hospitalized before the end of the H1N1 influenza vaccination program. Of the samples collected, only 4 (4.2%) tested positive for influenza A, and 2 (2.1%) tested positive for influenza B.

Among the hospitalized patients studied, the male/female ratio was 1.34. Of the suspected cases, 61 (63.5%) were in children under 12 years of age (median age, 2.0 years; range, 0-7 years), as were 3 (50.0%) of the 6 positive cases (Figure 1).

As can be seen in Figure 2, the samples testing positive for influenza A had been collected during epidemiological weeks 16, 17, and 18 (April 18-24, April 25-May 1, and May 2-8, respectively)—all being confirmed as infected

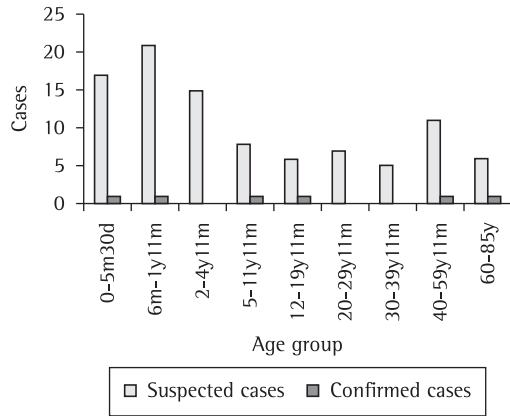


Figure 1 - Hospitalization rate for suspected and confirmed cases of influenza in 2010, by age group. d: days; m: months; and y: years.

with the influenza A/California/04/2009 (H1N1) virus—and one had been collected during epidemiological week 45 (November 7-13), being confirmed as infected with the seasonal influenza virus. The samples testing positive for influenza B had been collected during epidemiological weeks 23 and 33 (June 6-12 and August 8-14, respectively).

The first three patients with confirmed influenza A (H1N1) infection, all of whom were male, were 9 months, 54 years, and 3 months of age, respectively. The two patients with influenza B infection, both of whom were female, were 5 and 19 years of age, respectively, and another, 62-year-old, female patient was infected with the seasonal influenza A (H3N2) virus.

All six patients infected with the influenza virus required oxygen therapy, three (50%)

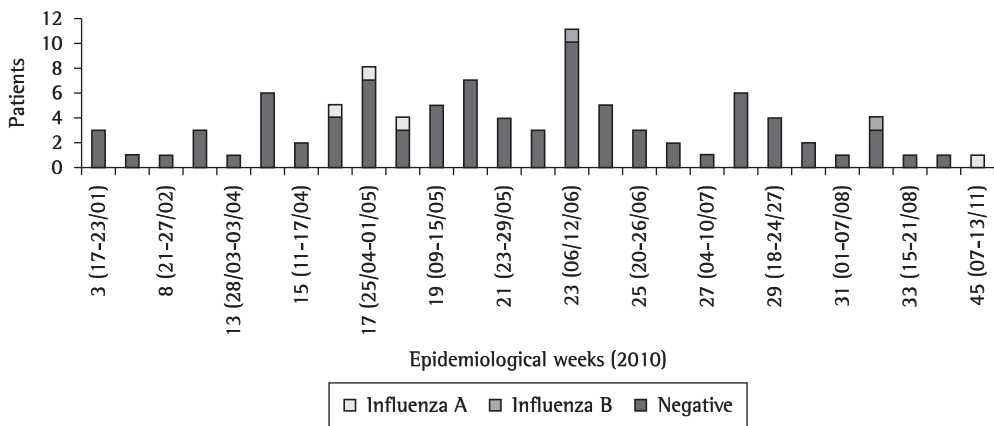


Figure 2 - Influenza infection in hospitalized patients in 2010, by epidemiological week.

requiring mechanical ventilation. Two (33.3%) of the six patients had an underlying disease. The 9-month-old male infant had received one dose of the vaccine less than 14 days before symptom onset and was co-infected with adenovirus, as confirmed during hospitalization. That child required mechanical ventilation and developed nosocomial bacterial pneumonia. The 54-year-old male patient had chronic kidney disease and had been unaware of the immunization program. The 3-month-old child, who was admitted with wheezing and cyanosis, required oxygen therapy. That child was found to have no bacterial infection and was discharged after a few days. The 62-year-old female patient had chronic heart failure and had not been vaccinated against influenza. She presented with bacterial pneumonia due to *Staphylococcus aureus* and required mechanical ventilation. The 5-year-old girl infected with the influenza B virus had not been vaccinated against influenza and showed no signs of underlying disease but required oxygen therapy. In the 19-year-old female patient infected with the influenza B virus, with no preexisting risk factors, the outcome was unfavorable, the patient being admitted to the ICU and requiring mechanical ventilation. Antiviral drugs were administered to all six patients. Although antiviral therapy was started more than 48 hours after the onset of illness, all six of those patients survived.

In 2009 and 2010, the prevalence of confirmed infection with influenza A (H1N1) virus among patients hospitalized at our sentinel hospital was 19.5% (31/159)⁽⁴⁾ and 4.2% (4/96), respectively. In 2010, the Brazilian National Pandemic Influenza A (H1N1) Immunization Program exceeded the goal of vaccinating 80% of the target population, vaccinating over 87 million people, mainly those with chronic diseases, children under 2 years of age, pregnant women, adults in the 20-39 age bracket, health care workers, and indigenous people.⁽⁸⁾ Over 45% of the national population was vaccinated, making this program the largest campaign of its kind in the world. The United States, for example, vaccinated 24% of its population, whereas Mexico, France, and Germany vaccinated 20%, 8%, and 6%, respectively.⁽⁹⁾ Influenza A (H1N1) vaccination programs might be credited with the decrease in the number of hospitalizations at our hospital in 2010, although the levels of

influenza A (H1N1) circulating in the population cannot be estimated.

Worldwide, the rate of influenza A (H1N1) infection decreased in 2010, even in European countries, where the coverage of vaccination programs has been low.⁽¹⁰⁾ Possible explanations for this decrease include the use of preventive measures, such as frequent hand washing with soap, water, and alcohol, by the population,⁽¹¹⁾ as well as the fact that the seroprevalence rates for individuals previously infected with the influenza A (H1N1) virus remain unknown.

The influenza vaccination strategy developed by the Brazilian National Ministry of Health targets people with chronic comorbidities, such as patients with heart disease or renal disease. Unfortunately, two of our adult patients with influenza had not been immunized. One of those patients had also forgone the seasonal vaccine recommended for the elderly in late April.⁽¹²⁾

On August 10, 2010, the World Health Organization announced that H1N1 was in the post-pandemic phase.⁽¹³⁾ The influenza A (H1N1) virus is still circulating in the city of São Paulo, albeit at lower levels. By epidemiological week 35 of 2010, only 9.2% of the cases reported to the Department of Health Surveillance of the Brazilian National Ministry of Health had been confirmed as cases of infection with the influenza A (H1N1) virus.⁽¹⁴⁾

The great number of negative suspected cases might suggest the circulation of other respiratory viruses and of bacterial infections in the same period. One limitation of the present study was that negative samples were not tested for other viruses.

The future of influenza A (H1N1) as a seasonal virus is uncertain. However, a considerable number of cases have recently been reported, during winter in the northern hemisphere.⁽¹⁵⁾ Surveillance for influenza remains essential due to the diversity of influenza strains circulating worldwide.

References

1. Portal da Saúde [homepage on the Internet]. Brasília: Ministério da Saúde [cited 2010 Apr 13]. Boletim Eletrônico Epidemiológico. Influenza Pandêmica (H1N1) 2009 - Análise da situação epidemiológica e da resposta no ano de 2009. [Adobe Acrobat document, 21p.] Available from: http://portal.saude.gov.br/portal/arquivos/pdf/ano10_n01_influenza_pandh1n1_br.pdf
2. Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team, Dawood FS, Jain S, Finelli L, Shaw

- MW, Lindstrom S, et al. Emergence of a novel swine-origin influenza A (H1N1) virus in humans. *N Engl J Med.* 2009;360(25):2605-15. Erratum in: *N Engl J Med.* 2009;361(1):102.
3. Cabeça TK, Carraro E, Goto JM, Cuba GT, Hidalgo S, Granato CF, et al. Clinical characteristics of 2009 H1N1 patients at a tertiary hospital in Sao Paulo, Brazil. 7th Congresso Paulista de Infectologia; 2010 Jun 3-6; São Paulo, Brazil. São Paulo: Elsevier; 2010.
 4. Watanabe AS, Carraro E, Moreira L, Camargo C, Sinohara J, Puerari D, et al. Respiratory virus infections among hospitalized patients with suspected influenza A H1N1 2009 virus during the first pandemic wave in Brazil. *Braz J Infect Dis.* 2011;15(3):220-4.
 5. Prefeitura de São Paulo [homepage on the internet]. São Paulo: Prefeitura de São Paulo. [updated 2010 Jun 02; cited 2010 Oct 05]. Secretaria Municipal da Saúde - Vacinação Influenza A/H1N1. Available from: http://www.prefeitura.sp.gov.br/cidade/secretarias/saude/vigilancia_em_saude/doencas_e_agravos/index.php?p=16476
 6. Carraro E, Neto DF, Benfca D, SittaPerosa AH, Granato CF, Bellei NC. Applications of a duplex reverse transcription polymerase chain reaction and direct immunofluorescence assay in comparison with virus isolation for detection of influenza A and B. *Diagn Microbiol Infect Dis.* 2007;57(1):53-7.
 7. World Health Organization [homepage on the internet]. Geneva: World Health Organization. [updated 2009 Oct 06; cited 2010 Apr 13]. CDC protocol of realtime RTPCR for influenza A (H1N1). [Adobe Acrobat document, 8p.] Available from: http://www.who.int/csr/resources/publications/swineflu/CDCRealtimeRTPCR_SwineH1Assay-2009_20090430.pdf
 8. Portal da Saúde [homepage on the Internet]. Brasília: Ministério da Saúde [cited 2010 Apr 13]. Informe Técnico Quinzenal de Influenza. Influenza Pandêmica (H1N1) 2009 - Monitoramento da Síndrome Respiratória Aguda Grave (SRAG) em Hospitalizados. [Adobe Acrobat document, 7p.] Available from: http://portal.saude.gov.br/portal/arquivos/pdf/informe_influenza_8_agosto19_8_10.pdf
 9. Portal da Saúde [homepage on the internet]. Brasília: Ministério da Saúde. [updated 2010 Jun 02; cited 2010 Dec 17]. Notícias - Mobilização nacional chega ao fim, mas vacinação contra H1N1 em municípios continua. Available from: http://portal.saude.gov.br/portal/aplicacoes/noticias/default.cfm?pg=dspDetalleNoticia&tid_area=124&CO_NOTICIA=11359
 10. Centers for Disease Control and Preventions. [homepage on the internet]. Atlanta: Centers for Disease Control and Preventions. [updated 2011 Apr 1; cited 2011 Apr 1]. Seasonal Flu: International Situation Update. Global Flu Activity Update. Available from: <http://www.cdc.gov/flu/international/activity.htm>.
 11. Machado AA. How to prevent, recognize and diagnose infection with the swine-origin Influenza A (H1N1) virus in humans. *J Bras Pneumol.* 2009;35(5):464-9.
 12. Ministério da saúde. Secretaria de vigilância em saúde. Departamento de vigilância epidemiológica. Programa nacional de imunizações. Informe Técnico Operacional - Estratégia Nacional de Vacinação Contra o Vírus Influenza Pandêmico (H1N1) 2009. Brasília: Ministério da Saúde; 2010.
 13. World Health Organization [homepage on the Internet]. Geneva: World Health Organization. [updated 2010 Aug 10; cited 2010 Nov 26]. H1N1 in post-pandemic period. Available from: http://www.who.int/mediacentre/news/statements/2010/h1n1_vpc_20100810/en/index.html
 14. Portal da Saúde [homepage on the Internet]. Brasília: Ministério da Saúde [cited 2010 Apr 13]. Informe Técnico Quinzenal de Influenza. Influenza Pandêmica (H1N1) 2009 - Monitoramento da Síndrome Respiratória Aguda Grave (SRAG) em Hospitalizados. [Adobe Acrobat document, 6p.] Available from: http://portal.saude.gov.br/portal/arquivos/pdf/informe_influenza_setembro_2010.pdf
 15. Centers for Disease Control and Preventions. [homepage on the internet]. Atlanta: Centers for Disease Control and Preventions. [updated 2011 Feb 19; cited 2011 Feb 22]. FluView: 2010-2011 Influenza Season - Week 7 ending February 19, 2011. Available from: <http://www.cdc.gov/flu/weekly>

About the authors

Thais Boim Melchior

Master's Student in Biological Science. Federal University of São Paulo, São Paulo, Brazil.

Sandra Baltazar Guatura

Laboratory Supervisor. Virology Laboratory, Infections Diseases Branch, Medicine Department, Federal University of São Paulo, São Paulo, Brazil.

Clarice Neves Camargo

Doctoral Student. Federal University of São Paulo, São Paulo, Brazil.

Aripuanã Sakurada Aranha Watanabe

Postdoctoral Student. Federal University of São Paulo, São Paulo, Brazil.

Celso Granato

Head. Virology Laboratory, Infections Diseases Branch, Medicine Department, Federal University of São Paulo, São Paulo, Brazil.

Nancy Bellei

Head. Virology Laboratory, Infections Diseases Branch, Medicine Department, Federal University of São Paulo, São Paulo, Brazil.