



CLINICAL ASPECTS OF CONFIRMED CASES OF INFLUENZA A (H1N1) PDM09 DURING THE PANDEMIC IN BRAZIL

ASPECTOS CLÍNICOS DOS CASOS CONFIRMADOS DE INFLUENZA A (H1N1) PDM09 POR REGIÃO DURANTE A PANDEMIA NO BRASIL

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Abstract

Objective: To describe the clinical aspects of Influenza A (H1N1) pdm09 in Brazil by geographic region, during the pandemic that occurred between 2009 and 2010. **Method:** This is an observational epidemiological study, with an analytical ecological design. Data were collected from information from the Notifiable Diseases Information System (SINAN), using the Tabnet web tab on the DATASUS website. As inclusion criteria, data recorded during the period 2009 and 2010 were considered; only confirmed cases; and data available for the five Brazilian regions. **Results:** The region of Brazil with the highest number of confirmed cases of influenza A (H1N1) pdm09 during the pandemic period was the South. The most affected age group varied between regions, but in general, it was predominant in young people and adults. In all locations, the sex with the most confirmed cases was female. The South was also the one with the highest percentage of evolution to SRAG, however, it was the Southeast that had the highest number of SRAG requiring hospital admissions. Despite having the highest number of cases, the South region also had the highest percentage of cure. **Conclusion:** Brazil suffered great impacts from the influenza A (H1N1) pandemic. Thousands of people were affected. In general, unlike other common flu viruses, the influenza A virus affects younger people and female individuals in all Brazilian regions.

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Keywords: Virus H1N1; Severe Acute Respiratory Syndrome; Epidemiology.

Resumo

Objetivo: Descrever os aspectos clínicos da Influenza A (H1N1) pdm09 no Brasil por região geográfica, durante a pandemia que ocorreu entre os anos de 2009 e 2010. **Método:** Trata-se de um estudo epidemiológico observacional, analítico de delineamento ecológico. Os dados foram coletados a partir de informações do Sistema de Informação de Agravos de Notificação (SINAN), utilizando o tabulador web Tabnet no site do DATASUS. Como critérios de inclusão, foram considerados dados registrados durante o período de 2009 e 2010; apenas casos confirmados; e dados disponíveis para as cinco regiões brasileiras. **Resultados:** A região do Brasil com o maior número de casos confirmados de influenza A (H1N1) pdm09 durante o período pandêmico foi o Sul. A faixa etária mais acometida variou entre as regiões, mas em geral, predominou-se em jovens e adultos. Em todas as localidades o sexo que mais apresentou casos confirmados foi o sexo feminino. O Sul também foi o que apresentou maior percentual de evolução para SRAG, entretanto, foi o Sudeste que teve o maior número de SRAG que demandaram internações hospitalares. Apesar de apresentar o maior número de casos, a região Sul também apresentou o maior percentual de cura. **Conclusão:** O Brasil sofreu grandes impactos com a pandemia de influenza A (H1N1). Milhares de pessoas foram afetadas. Em geral, ao contrário de outros vírus da gripe comum, o vírus da influenza A acomete pessoas mais jovens e indivíduos do sexo feminino em todas as regiões brasileiras.

Palavras-chave: Vírus H1N1; Síndrome Respiratória Aguda Grave; Epidemiologia.

INTRODUCTION

In March 2009, the first records of cases of complaints caused by a new variant of the influenza A (H1N1) virus began in the Americas¹. The disease quickly spread to other continents and, in June of the same year, the World Health Organization declared a pandemic state¹. At the time, scientists verified that the virus had different molecular properties from human, avian and swine influenza until then, later identifying that it was a new influenza A (H1N1) virus of swine origin (S-OIV)².

The flu caused by the Influenza A (H1N1) pdm09 virus is characterized by symptoms similar to seasonal flu, such as sudden fever, headache, cough, dyspnea, runny nose and muscle and joint pain³. This disease is highly contagious and mutable, transmitted through the airways and through contact with secretions³. It can also affect the respiratory system acutely, with the possibility of severe pulmonary involvement³, leading to a condition called severe acute respiratory infection – SARI⁴. The proportion of fatalities varied significantly between countries.



However, in general, deaths occurred in much younger people compared to seasonal flu cases⁵.

In Brazil, the first case was confirmed on May 7, 2009⁶. In July of the same year, the new pandemic influenza A (H1N1) infection was considered widespread in the country⁷, reaching its peak in the first week of August of the year in question, with subsequent continuous reduction⁴. After confirmation of the spread throughout the national territory, the notification and investigation of SARI cases began to be prioritized by the guidelines for the surveillance of influenza⁸. Thus, despite being a predominantly tropical country, Brazil was considered one of the most affected by the H1N1 flu⁹.

Until the influenza A pandemic in 2009, the knowledge of the dynamics of the disease in Brazil came mainly from studies in temperate regions. Thus, the pandemic was an opportunity for the health sciences to study its clinical aspects in tropical countries. Furthermore, it was possible to compare epidemics that occur simultaneously in various latitudes, which until then had not been possible, considering that this virus has always been more prevalent in temperate countries⁴. In view of this, the objective of this study was to describe, through data available at the Department of Informatics of the Ministry of Health (DATASUS), the clinical aspects of Influenza A (H1N1) pdm09 in Brazil by geographic region, during the pandemic that occurred between the years 2009 and 2010.

METHODOLOGY

The present work is an observational, analytical, epidemiological study of ecological design carried out from data recorded on cases of influenza A (H1N1) pdm09 in the five Brazilian regions during the pandemic that took place in 2009 and 2010. The inclusion criteria were: i) data recorded during the period 2009 and 2010; ii) confirmed cases; and iii) data available for the five Brazilian regions (South, Southeast, Midwest, North and Northeast). Underreported cases, unconfirmed cases and the number of admissions were excluded.



The source of information used to obtain data was the Notifiable Diseases Information System (*Sistema de Informação de Agravos de Notificação - SINAN*), using the Tabnet web tab on the DATASUS website, in the “pandemic influenza” module. Microsoft Office Excel 2016 was used to compile all collected data. Database duplications and inconsistencies have been fixed. The database for 2009 was closed on 02/08/2010 and the database for 2010 was closed on 21/01/2011. As definitions, were used: i) Severe Acute Respiratory Syndrome (SARS) - Individual with acute respiratory disease characterized by fever, cough and dyspnea; and ii) Severe Acute Respiratory Syndrome with Hospitalization - Individual with an acute respiratory disease characterized by fever, cough and dyspnea and requiring hospitalization.

The clinical aspects searched were: i) most affected region; ii) age group most affected by region; iii) sex most affected by region; iii) evolution tables for SARS by region; iv) evolution for hospitalization by region. Based on this information, a more accurate analysis of confirmed cases was done in each of the five Brazilian regions.

The present study did not need to be submitted to the Research Ethics Committee as it was based on the use of public character Committee data.

RESULTS

During the period 2009 to 2010, 105,227 cases of influenza A (H1N1) pm09 were registered in DATASUS, of which 54,171 were confirmed. Of these, the North, Northeast and Midwest regions had 2% of cases each, the Southeast comprised 25% of records, while the South had 68% of confirmed cases.

The age group most affected by the disease in the North region was 10 to 19 years old, with 29% of cases, followed by 23% between 20 and 29 years old, while the lowest incidences were reported in people over 60 years old (3%) and between 50 and 59 years (5%). In the Northeast, 26% of cases occurred in individuals aged 20 to 29 years, followed by 24% in people aged 10 to 19 years, 5% in those aged 50 to 59 years and 4% in those aged over 60. In the Southeast, 24% of cases were in people between 20 and 29 years, 17% from 10 to 19 years, 7% from 50 to



59 and 4% in over 60 years. In the South, 25% of cases occurred in individuals aged between 20 and 29 years, 18% between 10 and 19 years, 7% between 50 and 59 years and 5% in individuals over 60 years. In the Midwest, 29% of the records were in young people aged 20 to 29 years, followed by 18% in those aged 10 to 19 and 5% in those aged 50 to 59 and 3% in those aged over 60 years.

The sex most affected by influenza A, in the North region, was female, with a total of 62%, with males accounting for 38%. In the Northeast, 58% of women were affected and 42% of men. In the Southeast, it was 56% women and 44% men. In the South 57% of cases were in female patients and 43% in male patients. In the Midwest region, 58% of women were affected, and 42% of men.

The cases of disease progression to SARS were higher in the South, with 96% of diagnosed patients. The Midwest was the second region that most reported developments to SARS, with 93% of cases, followed by the Southeast, with 89%. The Northeast and North were the ones with the least complications, with 72% and 71%, respectively. However, when the SARS cases that required hospitalization of patients were evaluated, the region with the most complications, the Southeast (79%) and Midwest (78%) were the most affected, followed by the North (75%), Northeast (62%) and, with much lower values, the South (28%). Thus, although the South region has presented a predominance in cases of SARS compared to other regions, with 35,426 patients, only 10,438 needed hospitalizations.

Regarding the outcome of the cases, in the North, 88% of patients recovered from influenza A, 8% died and the other 5% did not present any record of cure or death. There were also no records of deaths from secondary causes of patients with influenza A. Patients in the Northeast had 72% recovery, 7% deaths, 20% without records and 0.5% deaths caused by secondary causes. In the Southeast 72% of patients recovered, 8% died, 20% were not registered and 0.3% died from other causes. In the South, 95% of affected patients were cured, 2% died, 3% were not registered and 0.02% died from secondary causes. In the Midwest, there were 83% recovery, 12% deaths and 5% with final classification not registered. There were also no deaths from secondary causes.



In terms of patient evolution, the South, despite having the highest number of cases, also had the highest percentage of recovered patients, with 95% of patients who beat influenza A (H1N1) and 2% who died because of the disease, with 3% of cases not being registered. On the other hand, the Southeast, even registering a lower total number of cases than the South, had a greater total number of deaths, with 1,026, while in the South, 824 died. It is also important to highlight that the Southeast did not confirm the recovery status of 2,679 patients, while in the South, 984 were not registered, therefore, these results can be underestimated. In other states, the number of deaths from influenza was lower, however, for the percentage of cure within each region, they were close to or even higher than in the South and Southeast.

For better comparison of results, all values obtained in DATASUS were organized in Table 1, below:

Table 1: Indicators obtained from DataSUS records in percentage of cases between 2009 and 2010.

INDICATORS	NOTIFICATION REGION				
	North	Northeast	Southeast	South	Midwest
Confirmed	2%	2%	25%	68%	2%
> 2 years	6%	5%	11%	7%	9%
2 to 4 years	6%	4%	6%	5%	5%
5 to 9 years	10%	7%	8%	6%	7%
10 to 19 years	29%	24%	17%	18%	18%
20 to 29 years	23%	26%	24%	25%	29%
Age Group					
30 to 39 years	12%	17%	14%	16%	14%
40 to 49 years	6%	7%	9%	11%	10%
50 to 59 years	5%	5%	7%	7%	5%
< 60 years	3%	4%	4%	5%	3%
No data	0	0	0,01%	0,01%	0
Sex					
Female	62%	58%	56%	57%	58%
Male	38%	42%	44%	43%	42%
SARS					
Yes	71%	72%	89%	96%	93%
No	29%	28%	11%	4%	7%
SARSHOSP					
Yes	75%	62%	79%	28%	78%
No	25%	38%	21%	72%	22%
Outcome					
Heal	88%	72%	72%	95%	83%
Influenza's Deaths	8%	7%	8%	2%	12%
Other Deaths	0	0,51%	0,39%	0,03%	0
Unregistered	5%	20%	20%	3%	5%

Source: DATASUS (2021).



DISCUSSION

The region of Brazil with the highest number of reported cases of influenza A (H1N1) pdm09 during the pandemic period between 2009 and 2010 was the South. The most affected age group varied between regions, while in all of them the sex that most affected presented confirmed cases was female. Regarding the severity of the cases, the South was also the one with the highest percentage of evolution to SARS. However, in cases of SARS, the region with the greatest need for hospitalization was the Southeast. Regarding the conclusion of cases, the South also had the highest percentage of recovered patients, while the Southeast had the highest number of deaths caused by the disease.

Of the 54,171 confirmed cases of influenza A, 36,829 (68%) occurred in the South region, while in the Southeast, almost a third fewer cases were reported (13,585 –25%). The other locations, together, did not reach 10% of the total cases registered in Brazil. Thus, although the Southeast region encompasses one of the largest urban centers in the country with the highest population concentrations, it had much lower numbers than the region most affected by the disease, the South. This result was possibly due to the epidemiological aspects of influenza A (H1N1) pdm09, since, when compared to temperate regions, its seasonality is highly dynamic in the tropics¹⁰. In the winter, the virus is transmitted more efficiently, since, with lower temperatures, there is a lower vapor pressure, stimulating the formation of aerosols for a longer period¹¹. Therefore, climatic variables have been suggested and analyzed as factors that cause such variability. Therefore, in subtropical areas of Brazil, influenza epidemics are associated with low temperatures, as in temperate countries¹⁰.

From the analysis of regions, young people were mostly more affected by influenza A (H1N1) pdm09. On the other hand, the elderly group was the one with the least confirmed cases of the disease. In this context, statistics in several countries showed that the prevalence of H1N1 infection was higher among younger adults during the pandemic^{12,13,14}. Admission data from different parts of the world also suggest that a third of patients with severe disease were healthy adults. The elderly, as well as the results shown in this study, comprise the least affected



group¹⁴. The H1N1 virus has mutated since 1918, so elderly people who had already acquired immunity through previous exposure were less affected in this pandemic¹¹. However, they are more likely to have bad hospitalizations outcomes¹⁵.

In all regions evaluated, the sex predominantly affected by influenza A (H1N1) pdm09 was female. As sexual disparities in infection have not been extensively studied¹⁶, however, they may exist due to differences in hormonal and immunological responses to infection^{16,17,18,19}. Most reports on gender differences refer to pandemic A (H1N1). One of them, issued by the WHO, using data from the first wave of the 2009 H1N1 pandemic, gender differentiation, concluding that the outcome was preferentially worse for women¹. Despite the greater adherence of females to hygiene measures, the number of cases in this group was higher, including in studies carried out in India and Australia, suggesting the involvement of a humoral factor²⁰. Wong et al. (2019) noted that they exist of age, as women may be more susceptible to certain subtypes of the flu virus. These experiences obtained that there is an interaction between age and sex in the susceptibility to influenza infection, which varies according to the virus subtype²¹.

The lack of studies on climatic variables and the disparities in the number of cases between the sexes became a limitation of the work, as well as the data underreported by the system. Despite the limitations, the present study was able to analyze in detail several variables in the Brazilian territory, which may be useful for a greater epidemiological understanding of the pandemic caused by the H1N1 virus.

CONCLUSION

Influenza A (H1N1) pdm09 impacted the entire planet as the first major pandemic of the 21st century. In Brazil it was no different. Thousands of people were affected and, considering that the records obtained come from DATASUS, the values may have been underestimated. However, they are enough to understand a little about the clinical aspects of the disease in each of the regions of the country. In general, this virus, unlike other common flu viruses, has been found to affect younger people, a typical feature of pandemic diseases. The southern region was the most affected, with the highest cases of evolution to SRAG, but with the



highest percentage of cure. In contrast, the Southeast had a higher rate of hospitalization and deaths. Women were the most affected in all locations, but more studies are needed to explain this correlation. Furthermore, although most cases in all regions have evolved to SARS, the percentage of patients who were cured was high. Despite the data found, further studies are needed to further clarify the epidemiological profile and pathophysiology of the virus.

Declaration of Conflict of Interest: Nothing to declare.

REFERENCES

1. WHO. World Health Organization. Pandemic (H1N1) 2009 - update 82. 2010. Disponível em: https://www.who.int/csr/don/2010_01_08/en/. Acesso em: 01 fev. 2021.
2. Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team, 2009. Emergence of a Novel Swine-Origin Influenza A (H1N1) Virus in Humans. *N Engl J Med* 2009; 360:2605-2615.
3. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância Epidemiológica. Influenza. Influenza. Caderno 1. Guia de Vigilância Epidemiológica. 7a ed. Brasília, (DF): Ministério da Saúde; 2009. p. 1-23 [série A normais e manuais técnicos].
4. Codeço CT, Cordeiro JS, Lima AWS, Colpo RA, Cruz OG, Coelho FC et al. The epidemic wave of influenza A (H1N1) in Brazil, 2009. *Cad. Saúde Pública*. 2012;28(7):1325-1336.
5. Perez-Padilla R, de la Rosa-Zamboni D, Ponce de Leon S, Hernandez M, Quinones-Falconi F, Bautista E, et al. Pneumonia and respiratory failure from swine-origin influenza A (H1N1) in Mexico. *N Engl J Med* 2009 [Epub ahead of print].
6. Pires Neto RJ, Lemos DRQ, Cavalcanti LPG, Ramos Junior AN, Alencar CH, Façanha MC, et al. Pandemic influenza A (H1N1) 2009: Epidemiological analysis of cases in a tropical/semi-arid region of Brazil. *Rev Soc Bras Med Trop*. 2013;46(2):141-6.
7. Schout D, Hajjar LA, Galas FRBG, Uip DE, Levin ASS, Caiaffa Filho HH et al. Epidemiology of human infection with the novel virus influenza A (H1H1) in the Hospital das Clínicas, São Paulo, Brazil - june-september 2009. *Clinics*. 2009; 64(10):1025-30.



8. Ribeiro AF, Pellini ACG, Kitagawa BY, Marques D, Madalosso G, de Cassia Nogueira Figueira G, et al. (2015) Risk Factors for Death from Influenza A(H1N1)pdm09, State of São Paulo, Brazil, 2009. PLoS ONE 10(3): e0118772. <https://doi.org/10.1371/journal.pone.0118772>
9. Oliveira W, Carmo E, Penna G, Kuchenbecker R, Santos H, Araujo W, Malaguti R, Duncan B, Schmidt M; Surveillance Team for the pandemic influenza A(H1N1) 2009 in the Ministry of Health. Pandemic H1N1 influenza in Brazil: Analysis of the first 34,506 notified cases of influenza-like illness with severe acute respiratory infection (SARI). Euro Surveill 2009;14(42):pii=19362.
10. Moura, Fernanda EA. Influenza in the tropics, Current Opinion in Infectious Diseases. 2010; 23(5):415-420 doi: 10.1097/QCO.0b013e32833cc955
11. Golynski K S, Marques C M, Avaliação epidemiológica dos casos de influenza a (H1N1) e o impacto da vacinação em indivíduos que residem em Curitiba-PR. Caderno da Escola de Saúde. 2017; 14:32-51.
12. Kelly HA, Grant KA, Williams S, Fielding J, Smith D. Epidemiological characteristics of pandemic influenza H1N1 2009 and seasonal influenza infection. MJA. 2009;191(3):146-149.
13. Khandaker G, Dierig A, Rashid H, King C, Heron L, Booy R: Systematic review of clinical and epidemiological features of the pandemic influenza A (H1N1) 2009. Influenza Other Respir Viruses. 2011, 5:148-156.
14. Punpanich W, Chotpitayasunondh T: A review on the clinical spectrum and natural history of human influenza. Int J Infect Dis. 2012, 16:714-723.
15. Dhandapani NSPSK. Evaluation of Pregnancy, Younger Age, and Old Age as Independent Risk Factors for Poor Hospitalization Outcomes in Influenza A (H1N1) pdm09 Virus a Decade After the Pandemic. Cureus. 2020;12(11): e11762.
16. Wang XL, et al. Age and sex differences in rates of influenza-associated hospitalizations in Hong Kong. Am J Epidemiol. 2015;182(4):335–44.
17. Klein SL, Hodgson A, Robinson DP. Mechanisms of sex disparities in influenza pathogenesis. J Leukoc Biol. 2012;92(1):67–73.
18. Giefing-Kroll C, et al. How sex and age affect immune responses, susceptibility to infections, and response to vaccination. Aging Cell. 2015;14(3):309–21.
19. Peretz J, Hall OJ, Klein SL. Sex differences in influenza virus infection, vaccination, and therapies., in Sex and Gender Differences in Infection and Treatments for Infectious Diseases. Springer International Publishing. 2015, 183–210.



20. Milanesi, Rafaela, Caregnato, Rita Catalina Aquino e Wachholz, Neiva Isabel Raffenato. Pandemia de Influenza A (H1N1): mudança nos hábitos de saúde da população, Cachoeira do Sul, Rio Grande do Sul, Brasil, 2010. *Cadernos de Saúde Pública*. 2011, 27(4):723-732. Disponível em: <<https://doi.org/10.1590/S0102-311X2011000400011>>. Epub 09 Maio 2011. ISSN 1678-4464. <https://doi.org/10.1590/S0102-311X2011000400011>.

21. Wong K, Luscomb GM, Hawke C. Influenza infections in Australia 2009–2015: is there a combined effect of age and sex on susceptibility to virus subtypes? *BMC Infect Dis*. 2019, 19(42).