



Mini-Narrative Review

The recommendations and the way forward to fight human infections caused by influenza A (H1N1) in Brazil

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ABSTRACT

Many recent outbreaks of influenza A (H1N1) in the world, especially in Brazil, it has become clear that the severity of the disease is not known in the same form. On Wednesday, June 7, 2023, Brazil notified the WHO of a fatal case of human infection with a variant of the influenza A(H1N1) virus of swine origin, this case was confirmed in a laboratory in the region of the interior state of Paraná. This is the first human infection caused by an influenza A (H1N1) virus reported in 2023 nationwide in Brazil. To mitigate H1N1 flu in Brazil, we urge the Brazilian government through its Ministry of Health to improve on mass awareness about the signs and symptoms of H1N1 flu among the Brazilians. The Brazilian government should also implement the One Health approach towards the control of H1N1 flu in Brazil, as we believe that these recommendations would go a long way in preventing future cases and the spread of H1N1 flu in Brazil. This article aims to present the clinical presentations of the H1N1 flu and the implications, recommendations and the way forward to protect the Brazilian population against the H1N1 flu.

1. Introduction

Because of the many recent outbreaks of influenza A (H1N1) in the world, especially in Brazil, it has become clear that the severity of the disease is not known in the same form. In the early days of June 2023, Brazil recently notified the World Health Organization (WHO) about a fatal laboratory and confirmed case of human infection caused by Influenza A (H1N1) of the swine-origin variant (v) virus [1]. The influenza A virus is the most common infectious agent in humans, it infects about twenty per cent of the world's population while causing millions of hospitalizations each year and cases of death have also been recorded [2]. Influenza A (H1N1) is a pulmonary pathology of viral origin with very high human-to-human transmission, this virus belongs

to the family of type A Influenza viruses, they evolve regularly while modifying the protein membrane which constitutes their envelope [3]. co-morbidities and immunosuppression represent only a part of most cases and the complications they causes. However, this does not explain the differential severity among people who are healthy during periods of epidemics and pandemics of this disease [4]. During the period of the influenza A (H1N1) pandemic from 2009 to 2011, it affected millions of people and the vast majority were not serious, the emphasis was placed on a better understanding of the determinants and the pathogenesis of serious influenza infections [4,5]. Many Influenza A (H1) influenza viruses are enzootic in swine populations in most parts of the world, especially with the recent findings in Brazil.

When the influenza virus circulates in pigs is detected in a person, it

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is called a swine-origin influenza A (H1N1) virus (v) variant [1]. Although, generally, H1N1, H1N2 and H3N2 are the main swine influenza A virus subtypes that infect the human population [6]. Human infections with variants tend to result in mild clinical pathology. However, some cases have been hospitalized for a more severe form sometimes resulting in death. It was confirmed by the International Health Regulations (IHR) in 2005 that a human infection caused by a novel influenza A virus subtype has a high public health impact on the human race [2,6]. In place of the recent situation of H1N1 flu in Brazil, this present article thus aimed to present the clinical presentations of the H1N1 flu and the implications, recommendations and the way forward to protect the Brazilian population against the H1N1 flu.

2. Methods

Specific keywords (Animals; H1N1 Subtype; Humans; Influenza A Virus; Influenza Human Diagnosis) were subjected to list down and analyzed the literature from Pubmed – Medline, Google Scholar and official link of World Health Organization. Given the commentary character of the present report, all types of peer-reviewed records, including original research, systematic reviews, and meta-analysis, were considered. The focus was given on studies published between the year 2013–2023. The reference lists of the included studies were also hand-searched to identify additional relevant records. Out of all the articles, as per inclusion criteria, we selected 21 for further analysis and narrative to build.

3. Main text

3.1. Current situation of influenza A (H1N1) in Brazil

Recently, sporadic human infections caused by influenza virus variants A (H1N1) and A (H1N2) were recorded in Brazil but with no evidence of human-to-human transmission in the region [1]. On Wednesday, June 7, 2023, Brazil notified the World Health Organization of a fatal case of human infection with a variant of the influenza A (H1N1) virus of swine origin, this case was confirmed in a laboratory in the region of the interior state of Paraná [1]. This is the first human infection caused by an influenza A (H1N1) virus reported in 2023 nationwide in Brazil and the third human infection reported in the state of Paraná [1]. Despite the available information that the World Health Organization currently has, it considers this to be a sporadic case and with no observed human-to-human transmission [1]. This first case of Influenza A (H1N1) in Brazil was a 42-year-old woman with underlying conditions who lived near a pig farm [1]. She had developed a fever, headache, sore throat and abdominal pain since May 1, 2023 and she was hospitalized two days later, on May 3 of the same year for a severe acute lung infection, then admitted to the service. intensive care and unfortunately she died on May 5, 2023 [7].

3.2. Clinical manifestation of influenza A (H1N1)

The H1N1 flu is transmitted like other kinds of flu [4,15]. People transmit the disease to each other by sneezing, by spreading droplets of virus-infected saliva into the surrounding air [1]. People infected with the H1N1 virus are contagious within days of the onset of symptoms. Healthy people become contaminated by breathing or by eye or mouth contact with these droplets of saliva infected with the H1N1 virus from a sick person. But also surfaces infected with the flu virus remain active for a few minutes or even hours with about 2 h maximum [8,9].

Symptoms of the H1N1 flu are fever, body aches, cough, fatigue, sore throat, runny nose, nausea and vomiting or even diarrhea. The H1N1 flu is as deadly as most flus, especially in people who are weakened by other illnesses, with a weak immune system or by old age. Often in some cases, sick people show only mild symptoms and their recovery is quick and complete [8,10].

3.3. Implications and current efforts to fight influenza A (H1N1)

In Brazil, the national government as well as the Ministry of Health through national and international organizations working in public health and in the prevention of tropical and infectious diseases must be massively involved in the fight against the spread of the H1N1 flu both at the local, state, and the federal level. Otherwise, the spread of HINI flu in Brazil could cause epidemics which could cause high mortality and morbidity among the Brazilians. At the local level, the Brazilian government should strengthen epidemiological investigations as well as the follow-up of all contacts in the population and in health structures, especially in areas with overwhelmed healthcare settings [8]. At the state level, the Brazilian government should Strengthen the H1N1 influenza surveillance system by seeking to analyze the behavior and trends of the respiratory virus in the population. Since the virus is constantly evolving, but also the extent of the circulation of influenza viruses in animals is not well known with precision [11], epidemiological and virological surveillance should be systematically pursued at the federal level and follow-up of suspected human cases as well as surveillance must be put in place to detect any virological, epidemiological and clinical changes in H1N1 influenza. It is also important that the Brazilian health authorities should maintain vigilance in the face of the emergence of new influenza viruses that can give rise to a pandemic, which can be very fatal on a global level. Continuous surveillance is important in Brazil to detect infections in animals and humans. Collaboration between the animal and human health sectors, therefore a call to the One Health system is essential in the prevention and surveillance of this lung disease of the H1N1 virus [12–14].

3.4. Recommendations and the way forward

Currently, despite advances in medicine, there is no vaccine against influenza A(H1N1) virus infection in humans [4,15]. Vaccines against seasonal influenza and against human influenza viruses are generally not intended to protect humans against influenza viruses that are carried by swine, but sometimes they can reduce the likelihood of contracting both the human influenza and influenza virus variants [13,15]. For this reason, the prevention of the flu remains the simplest and is essentially based on frequent hand washing (avoiding touching your eyes, mouth or nose when your hands are not clean) [15,16].

For tourists traveling to Brazil during this period, they should avoid pig farms, contact with animals in live animal markets, entry into areas where animals may be slaughtered, or contact with surfaces that appear to be contaminated with animal feces. They must also respect hygiene measures (washing their hands regularly with clean water and soap) and sanitary and food hygiene measures. Travellers should strictly comply with barrier measures against all infectious diseases especially H1N1 such as; washing their hands often with soap and water or with hydroalcoholic solutions, covering their mouth and nose, and avoiding touching their eyes frequently [15]. They should also practice good food safety and personal hygiene measures. These measures would serve to preventing a future pandemic or even an epidemic of H1N1 flu in Brazil.

Another recommendation for the Brazilian government is for them to adopt the One Health approach in the mitigation of H1N1 flu in Brazil. One Health is a concept that involves a collaborative, multisectoral, and transdisciplinary approach [17]. One Health approach in mitigating H1N1 flu in Brazil would involves all the healthcare workers in Brazil to work together at the local, state, and the federal levels, including at the global level with the international communities to achieve optimal health outcomes that recognize the interconnection of influenza viruses among the Brazilian people, animals, plants, and their shared environment.

We urge the Brazilian government to therefore implement One Health policy control about H1N1 such as cleaning and disinfection of cages, bowls, and other fomites including hygiene measures and hand washing while farmers or any one is dealing with pigs in Brazil. Clothing

used during animal care should be cleaned by washing it with detergent at normal laundry temperatures [18]. We urge the Brazilian health authorities to work *pari-pasu* with the Centers for Disease Control and Prevention (CDC), including the WHO, the Food and Agriculture Organization (FAO) of the United Nations, the World Organization for Animal Health (OIE), which are commonly known as the Tripartite organizations [19] in conducting a risk assessment on the pandemic potential of H1N1 flu using the Influenza Risk Assessment Tool [18].

Controlling swine influenza flu in Brazil requires early detection before it becomes a major problem and consequently, more difficult to control in the country. While prevention is still the first line of defense against zoonoses and other infectious diseases [18], we strongly urge the Brazilian government to implement systematic and sentinel surveillance at the animal-human interface which could support the early detection of a new strain capable of infecting humans [20]. Surveillance system for zoonotic diseases like influenza virus in Brazil should then be coordinated through a data-driven One Health approach, which could be used to project the H1N1 flu progression and predict as accurately as possible the magnitude and time of a potential outbreak, based on a range of mathematical model assumptions and an understanding of pathogen transmission dynamics [21].

Overall, there is a need for more mass awareness campaigns by the health authorities in Brazil about influenza viruses among the Brazilian population especially on its early signs and symptoms, wide vaccination coverage against zoonotic diseases, especially for pet owners, local farmers, and hunters in the country. Veterinary doctors, physicians, nurses, pharmacists, including psychologists, social welfare officers, and other para-medical health workers, as well as the medical and para-medical students in Brazil and the world at large should work together in conducting more research about H1N1 flu, as well as holding more regional and international conferences about H1N1 for more updates and in finding a long-lasting solution for the disease. After due review of studies above a common comparison depicts that current reliance on sentinel surveillance, while valuable for early detection, is not very substantive in comparison to a comprehensive, data-driven system. The proposed One Health approach, with its focus on real-time data analysis and predictive modeling, offers a far more proactive approach. By anticipating potential outbreaks and their trajectory, authorities can be better prepared to implement targeted interventions and minimize the impact of future H1N1 flu waves.

3.5. Limitations

This study has limitations including a potentially limited generalizability beyond Brazil due to regional variations as compared to the rest of the world, a wide scope confined to 2013–2023, major reliance on data available from sources like PubMed and Google Scholar, the dynamic evolution of the H1N1 virus not fully captured in a snapshot, and a need for more interdisciplinary collaboration for a comprehensive One Health approach. Recognizing these limitations is essential for interpreting our findings and underscoring the significance of continued research efforts. Addressing these constraints will contribute to the advancement of our comprehension of Influenza A (H1N1) within the Brazilian context.

4. Conclusion

Human infections caused by swine influenza A (H1N1) flu in Brazil are one of the viruses of public health importance because of their propensity to cause epidemics and pandemics. Despite no definitive reports of human infections with H1N1 flu, there is a possibility of the Brazilians contracting the disease, which could cause significant health problems, economic, and financial including mental health problems to the Brazilian population. Thus, to mitigate H1N1 flu in Brazil, we urge the Brazilian government through its Ministry of health to improve on mass awareness about the signs and symptoms of H1N1 flu among the

Brazilians. The Brazilian government should also implement the One Health approach towards the control of H1N1 flu in Brazil, as we believe that these recommendations would go a long way in preventing future cases and the spread of H1N1 flu in Brazil.

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Declaration of competing interest

The authors declare that there no conflict of interest.

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References

- [1] WHO. Influenza A (H1N1) variant virus in Brazil. <https://www.who.int/emergencies/diseases-outbreak-news/item/2023-DON473>.
- [2] Pérez-Rubio G, Ponce-Gallegos MA, Domínguez-Mazzocco BA, Ponce-Gallegos J, García-Ramírez RA, Falfán-Valencia R. Role of the host genetic susceptibility to 2009 pandemic influenza A H1N1. *Viruses* 2021;13(2):344. <https://doi.org/10.3390/v13020344>.

- [3] Ventura CG, Roque FL, Sousa IQ, Lobo RD, Luders C. Influenza A (H1N1): outbreak management in a dialysis unit and clinical outcomes of infection in chronic hemodialysis patients. *J Bras Nefrol* 2020;42(2):182–90. <https://doi.org/10.1590/2175-8239-jbn-2019-0180>.
- [4] Akilimali A, Oduoye MO, Biamba C, Cakwira H, Onesime J, Lopez K, et al. The main recommendations to fight human infections caused by avian influenza A (H5) and the way forward in Ecuador. *IJS Global Health* 2023;6(2):e129. <https://doi.org/10.1097/GH9.0000000000000129>.
- [5] Pawlus B, Żukowska J, Nitsch-Osuch A. Influenza A (H1N1) and respiratory syncytial virus (RSV) Coinfection in a newborn child: a case report. *Adv Exp Med Biol* 2021;1324:29–34. https://doi.org/10.1007/5584_2020_602.
- [6] García-Ramírez RA, Ramírez-Venegas A, Quintana-Carrillo R, Camarena ÁE, Falfán-Valencia R, Mejía-Aranguré JM. TNF, IL6, and IL1B polymorphisms are associated with severe influenza A (H1N1) virus infection in the Mexican population. *PLoS One* 2015;10(12):e0144832. <https://doi.org/10.1371/journal.pone.0144832>.
- [7] Organisation mondiale de la Santé. Bulletin d'information sur les flambées épidémiques. Variant du virus de la grippe A(H1N1) – Brésil. Jun 16th. 2023. Available at: <https://www.who.int/fr/emergencies/disease-outbreak-news/item/2023-DON473>. [Accessed 24 June 2023].
- [8] Shahnoor S, Khan AW, Fatima A, Khan AM, Oduoye MO, Abdulrahman MO, et al. The use of trifluoromethyl tubercidin as a novel treatment of influenza in an overwhelmed health care setting: a correspondence. *Int J Surg: Glob Health* 6(3): e0140, <https://doi.org/10.1097/GH9.0000000000000140>.
- [9] Rodrigues Guimarães Alves V, Perosa AH, de Souza Luna LK, Cruz JS, Conte DD, Bellei N. Influenza A(H1N1) pdm09 infection and viral load analysis in patients with different clinical presentations. *Mem Inst Oswaldo Cruz* 2020;115:e200009. <https://doi.org/10.1590/0074-02760200009>.
- [10] Pawlus B, Żukowska J, Nitsch-Osuch A. Influenza A (H1N1) and respiratory syncytial virus (RSV) coinfection in a newborn child: a case report. *Adv Exp Med Biol* 2021;1324:29–34. https://doi.org/10.1007/5584_2020_602.
- [11] Alavi SM, Nashibi R, Moradpoor F. Prevalence and mortality of influenza A (H1N1) virus among patients with acute respiratory infection in Southwest Iran. *Jundishapur J Microbiol* 2014 Apr;7(4):e9263. <https://doi.org/10.5812/ijm.9263>.
- [12] Krishna S, Jayaram A, Shetty U, Varambali P, Mukhopadhyay C, Jagadesh A. Detection of H275Y oseltamivir resistance gene mutation among Influenza A (H1N1) pdm09 patients by allelic discrimination real-time RT-PCR. *J Med Virol* 2023;95(5):e28764. <https://doi.org/10.1002/jmv.28764>.
- [13] Kondratiuk K, Hallmann E, Łuniewska K, Szymański K, Brydak L. Influenza and influenza-like virus infection in Children under 14 Years of age: an investigation of 725 cases in the 2021/2022 influenza epidemic season in Poland. *Med Sci Mon Int Med J Exp Clin Res* 2023;29:e940368. <https://doi.org/10.12659/MSM.940368>.
- [14] Muthuri SG, Venkatesan S, Myles PR, Leonardi-Bee J, Al Khuwaitir TS, Al Mamun A, et al. Effectiveness of neuraminidase inhibitors in reducing mortality in patients admitted to hospital with influenza A H1N1pdm09 virus infection: a meta-analysis of individual participant data. *Lancet Respir Med* 2014;2(5):395–404. [https://doi.org/10.1016/S2213-2600\(14\)70041-4](https://doi.org/10.1016/S2213-2600(14)70041-4).
- [15] Oduoye MO, Akilimali A, Nazir A, Yusuf HA, Cakwira H, Zubairu AZ, et al. Highly pathogenic avian influenza (HPAI A H5N1) outbreak in Spain: its mitigation through the One Health approach - a short communication. *Ann Med Surg (Lond)*. 2023;85(4):1352–5. <https://doi.org/10.1097/MS9.0000000000000399>.
- [16] Keynan Y, Malik S, Fowke KR. The role of polymorphisms in host immune genes in determining the severity of respiratory illness caused by pandemic H1N1 influenza. *Public Health Genomics* 2013;16(1–2):9–16. <https://doi.org/10.1159/000345937>.
- [17] Ghai RR, Wallace RM, Kile JC, et al. A generalizable one health framework for the control of zoonotic diseases. *Sci Rep* 2022;12:1–11.
- [18] Oduoye MO, Wechuli PN, Abdulkareem HA, Javed B, Zubairu AZ, Gharaibeh RS. Re-emergence of canine influenza in the United States of America; a call for One Health approach; a letter to the editor. *IJS Global Health* 2023;6(4):e0191. Jul1.
- [19] Oduoye MO, Nazir A, Nazir A, Karim KA, Sakr SM, Bah TA, et al. First Marburg virus outbreak in Equatorial Guinea; what should we do to prevent future occurrence? *Int J Surg: Glob Health* 2023;6(5):e0322. <https://doi.org/10.1097/GH9.0000000000000322>.
- [20] Meseko COC. How a One Health approach can mitigate the social and economic burdens of zoonoses in Africa. *LSE Blogs* 2022:1–4.
- [21] Busayo IA, Roper K, Richardson ABA. One health approach: a data-driven priority for mitigating outbreaks of emerging and re-emerging zoonotic infectious diseases. *Trav Med Infect Dis* 2022;7:4.