



Human death due to H5N1 amid the COVID-19 pandemic and Mpox outbreak: A call for action

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Dear Editor,

The family *Orthomyxoviridae* includes viruses that cause influenza. They have contributed to numerous respiratory illness outbreaks and pandemics and are one of the main causes of morbidity and mortality. The three influenza virus genera are influenza A, influenza B, and influenza C. Multiple (–ve) sense single-stranded RNA segments make up viral RNA. Each segment encodes a distinct viral protein that serves a distinct purpose. Influenza A and B viruses have eight RNA segments each, but influenza C virus has seven segments. RNA replication occurs typically in the nucleus^[1].

Avian influenza (bird flu) is a condition brought on by infection with avian influenza A viruses. These viruses can infect domestic poultry, bird, and mammal species, and are naturally circulated among wild aquatic birds globally. In general, humans are not infected, but occasionally human infections with bird flu have occurred. The most prevalent strain of avian flu is avian influenza virus (AIV) H5N1. There are other bird flu virus strains, but H5N1 was the first to infect people. H5N1 can persist for a prolonged period of time. For up to 10 days, H5N1-infected birds continue to release the virus in their feces and saliva. The disease can spread from the source of infection in open-air marketplaces where eggs and birds are sold in cramped, unhygienic settings. Contact with sick birds or surfaces contaminated by their

HIGHLIGHTS

- Highly pathogenic avian influenza has been reported around the world in the year 2022.
- In October 2022, a human case of avian influenza A (H5N1) was reported from Hong Kong, China.
- H5N1 has high mortality in humans and has the potential to cause an outbreak

droppings, saliva, or feathers appears to be the biggest risk factor for contracting bird flu. The disease's human transmission is still a mystery. Bird flu has rarely been spread from one person to another by humans. However, the greatest risk comes from sick birds, not from people. Avian flu in birds occurs in two types, one mild and the other highly virulent and infectious (fowl plague). AIV is further categorized as highly pathogenic avian influenza (HPAI) variant and low pathogenicity avian influenza (LPAI) variant. To better understand the pandemic potential of H5N1, scientists have genetically altered H5N1 to make it contagious. However, the possibility of its transmission to man raised concern about its use as a potential biological warfare agent^[2].

The disease can easily transmit from region to region by migratory birds and through international trade in live poultry. Humans who are in close contact with sick birds like poultry farmers and slaughterhouse workers are at a high risk of infection. This year many HPAI has been reported around the world (Fig. 1a). Despite confined examples of person-to-person, transmission occurring since 1997, constant transmission has not been observed. However, after a hasty evolution and mutation called antigenic shift, two viral subtypes, for example, one bird flu virus (H5N1) and the other a human influenza virus can assort parts of their gene pool to give rise to novel viral subtypes. The majority of individuals are either asymptomatic or develop minor upper respiratory symptoms which include dry cough, headache, chills, muscle aches, high-grade fever, and anorexia, which appear after an incubation period of about 18–72 h. It is a self-limiting condition, indistinguishable from the infections caused by other upper respiratory tract pathogens. High-risk groups include patients with underlying chronic cardiac, renal, pulmonary or hepatic disease, any central nervous system conditions, and people with low immunity like people living with HIV/AIDS, etc^[3].

According to WHO, AIV H5N1 was first discovered in humans in 1997 in Hong Kong and has killed nearly 60% of those infected. More than 800 people were infected with H5N1 during the span of 13 years, that is between 2003 and 2016 with mortality rate being more than 50%. The majority of human

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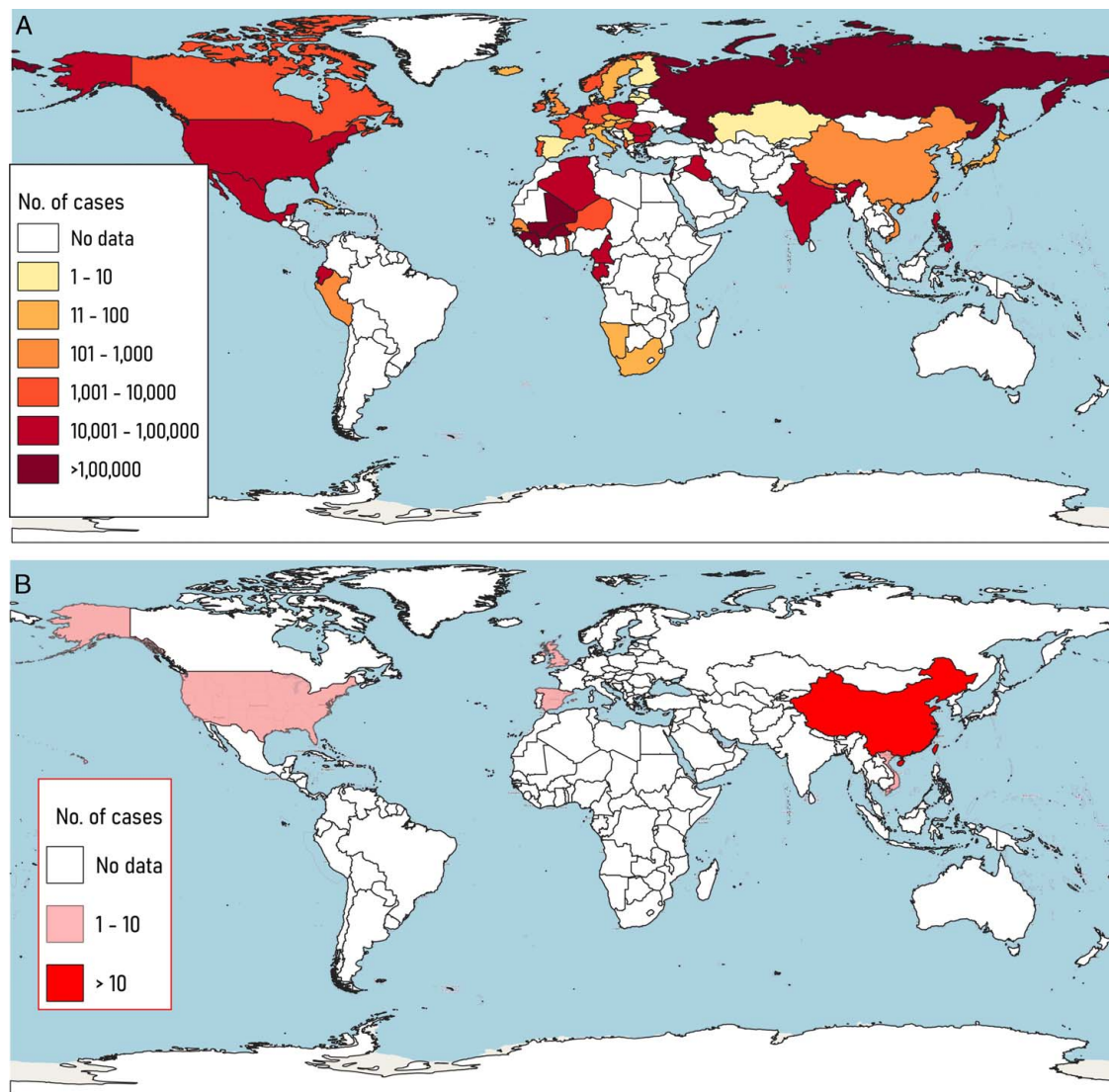


Figure 1. Choropleth map showing the global outbreaks of avian influenza (H5N1) animal (a) and human (b) cases between 1 January 2022 and 2 December 2022 as reported at ProMed news (<https://isid.org>). The map was created using QGIS 3.28.0. The base layer map was used from ArcGIS Hub.

H5N1 infections and deaths occurred in Egypt, Vietnam, and Indonesia^[4].

Recently, in October 2022, a human case of avian influenza A (H5N1) was reported from Hong Kong, China (Fig. 1b). Earlier, two human cases were reported from Spain in September 2022 and one from the United States of America in April 2022. On 20 September, in Spain, two poultry workers on a single farm contracted the infection, following an outbreak in poultry. The detection of the virus in these individuals was linked to exposure to infected poultry and its contaminated surroundings. No evidence of person-to-person transmission was identified at the time of the outbreak^[5]. In April 2022, WHO documented a human case of avian influenza A virus in Colorado State, USA, on 29 April 2022. The patient was isolated and managed with antivirals, and the patient recovered^[6].

In Mainland, China, a woman of reproductive age group, a resident of Qinzhou, Guangxi, who was working closely with domestic poultry, developed symptoms on 22 September and

succumbed to fatal pneumonia on 18 October. Since the year 2005, 54 human cases of H5N1(32 deaths) have been documented in Mainland, China. In the current year 2022, this case is the fourth human case and the first death reported globally because of avian influenza^[7]. As of November 2022, 240 cases of human avian influenza A (H5N1) virus have been confirmed from the Western Pacific Region since 2003 with a case fatality rate of 56%. Worldwide, from 2003 to 05 October 2022, 865 cases were reported from 21 countries with a case fatality rate of 53%^[8].

The Centre for Health Protection, the Department of Health, China, and the WHO is closely monitoring avian influenza A cases, and citizens were instructed to preserve strict personal and environmental hygiene at home or while traveling outside. All those traveling to the Mainland were warned against going to wet or poultry markets and farms. Also, a high alert was issued for those having backyard poultry. Cautious purchase of live or

freshly slaughtered poultry was advised and residents were instructed to avoid touching birds or their droppings.

Travelers returning from the disease-affected area were asked to consult a healthcare professional if symptoms develop; for prompt diagnosis and appropriate management. It was mandatory to disclose travel history or history of close contact with live poultry, which makes one exposed to a contaminated environment. All these precautions were of paramount significance for timely isolation, diagnosis, and treatment of any potential case. A public advisory was issued regarding handling poultry at the time of the outbreak. The advisory mentioned avoiding buying live chickens and touching them, eggs had to be washed suitably if soiled with fecal material and immediate cooking and consumption cook were advocated, eggs were to be cooked thoroughly. One should avoid eating raw eggs or using any sauce with raw eggs. Proper hand hygiene was to be carried before touching the nose, mouth, or eyes, before handling food or eating anything, after using washrooms, touching public services such as escalators, elevator panels or door handles and knobs, or when hands are contaminated after sneezing and coughing^[9]. The best way to prevent infection is to avoid sources of exposure; infected birds shed the bird flu virus in their saliva, mucous, and feces. Close, prolonged and unprotected contact with infected birds should be avoided at any cost^[2].

Influenza viruses are constantly mutating and evolving segmented viruses, there is a need for global surveillance to track and monitor genetic and epidemiological changes associated with the novel, or circulating influenza viruses that may affect man and poultry. If there is any suspicion of a human case by a novel influenza virus with pandemic potential, an exhaustive epidemiologic investigation should be carried out. History of exposure to animals and birds and travel to the affected area should be taken.

When avian influenza cases are prevalent in an area, workers involved in sampling sick avian population, disposing infected birds/eggs, and cleaning contaminated surroundings should be trained on the proper use of appropriate personal protective equipment. All these people should be kept under close observation in local healthcare facilities for a minimum period of 1 week after the last contact with the poultry or their surroundings. Travelers should follow proper food hygiene practices. All human infections caused by a novel influenza subtype must be notified under the International Health Regulations and State Parties to the International Health Regulations are required to promptly notify WHO of any confirmed case of influenza A virus with the potential to cause a pandemic^[5].

As a huge number of HPAI has been reported around the world and now we also have a human case demised due to H5N1, the world is at risk of the outbreak. An influenza pandemic if happens, it adds to the already burdened public healthcare systems and essential community services due to the coronavirus disease 2019 pandemic and the monkeypox outbreak. Surveillance and monitoring, development of new vaccines, antivirals, diagnostic tests, personal protective equipment, and other non-pharmaceutical interventions are fundamental constituents of outbreak planning and response.

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References

- [1] Arbeitskreis Blut. Untergruppe. Arbeitskreis Blut, Untergruppe «Bewertung Blutassoziiierter Krankheitserreger». *Influenza Virus. Transfus Med Hemother* 2009;36:32–9. doi:10.1159/000197314 PMID: 21048819; PMCID: PMC2928832.
- [2] Avian Influenza in Birds. Accessed December 2, 2022. <https://www.cdc.gov/flu/avianflu/avian-in-birds.htm>
- [3] World Health Organization. Influenza (Avian and other zoonotic). Accessed 15, November 2022. [https://www.who.int/news-room/fact-sheets/detail/influenza-\(avian-and-other-zoonotic\)](https://www.who.int/news-room/fact-sheets/detail/influenza-(avian-and-other-zoonotic)).
- [4] Tam JS. Influenza A (H5N1) in Hong Kong: an overview. *Vaccine* 2002;20 (Suppl 2):S77–81.
- [5] World Health Organization. Disease Outbreak News; Avian Influenza A (H5N1) – Spain (3 November 2022). Accessed 1, December 2022. <https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON420>
- [6] Avian Influenza A (H5N1) – United States of America. Accessed 2, December 2022. <https://www.who.int/emergencies/disease-outbreak-news/item/2022-E000111>
- [7] China: Human H5N1 avian influenza case/death reported in Guangxi. Accessed 30, November 2022. <https://outbreaknewstoday.com/china-human-h5n1-avian-influenza-case-death-reported-in-guangxi-40381/>
- [8] Avian Influenza Weekly Update Number 872. Accessed 1, December 2022. https://www.who.int/docs/default-source/wpro---documents/emergency/surveillance/avian-influenza/ai_20221125.pdf?sfvrsn=5f006f99_107
- [9] CHP closely monitors human case of avian influenza A(H5N1) in Mainland. Accessed 1, December 2022. <https://www.info.gov.hk/gia/general/202211/30/P2022113000354.htm>