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# Avian Influenza A (H5N1) Outbreak 2024 in Cambodia: Worries Over the Possible Spread of the Virus to Other Asian Nations and the Strategic Outlook for its Control

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**ABSTRACT:** Asia has been alarmed by the resurgence of avian influenza A (H5N1) in Cambodia in 2024. H5N1 could be swiftly transmitted by wild birds to poultry populations along their migration route via infection. Circulation of endemic H5N1 in Asian poultry facilitates recurrent human transmission. Cambodia's role as a reservoir heightens the potential dangers of uncoordinated containment and surveillance across Southeast Asia. This correspondence addresses the risk factors, seasonal patterns, transmission dynamics, and potential pathways for the global dissemination of H5N1. This underscores the criticality of supervising regional initiatives aimed at eliminating the virus from poultry and humans, before its potential escalation into a deadly influenza pandemic across Asia.

**KEYWORDS:** Avian influenza, seasonal flu, viral infection, H5N1, public health

Dear Editor,

The 2024 avian influenza A (H5N1) outbreak in Cambodia raises concerns about its potential spread across Asian countries. This highly pathogenic strain primarily affects birds but can also infect humans.<sup>1</sup>

Cambodia's history of sporadic outbreaks makes it a focal point for monitoring and containment efforts in Southeast Asia. We focus on the possibilities of the potential spread of H5N1 from Cambodia to neighboring Asian countries, aiming to understand the likelihood, pathways, and risk factors linked to virus transmission across the region.

In 1996, H5N1 avian influenza was first detected in domestic waterfowl in Southern China.<sup>2</sup> Cambodia experienced its initial outbreak of HPAI H5N1 in December 2003, affecting wild birds. Sporadic cases of human infection via poultry-to-human transmission were reported until 2014. Two cases each in February, October, and November of 2023 brought the total number of new cases to 6 after a brief hiatus. H5N1 infection in humans leads to severe illness, high mortality, and falls under International Health Regulations (2005) notification requirements.<sup>1</sup>

Human infections with H5N1 avian influenza have occurred sporadically through direct contact with sick or dead poultry.<sup>3</sup> Wild birds can contract the virus from domestic poultry and spread it when they migrate to other countries, potentially infecting poultry populations there.<sup>4</sup> Changes in cluster epidemiology, such as larger and more frequent clusters, increased cases among unrelated individuals, and milder clinical cases, may indicate the adaptation of a novel influenza A virus for human transmission.<sup>5</sup> A study highlights that in Southeast Asia, H5N1 outbreaks in poultry and human cases mostly

occur during cooler months, particularly from January to March. Additionally, H5N1 cases coincide with seasonal flu outbreaks, raising concerns about co-infections and potential reassortment of viruses, leading to novel strains capable of human-to-human transmission.<sup>6</sup> Highly pathogenic avian influenza strains, such as H5N1, cause severe mortality in unvaccinated chicken flocks, while low-pathogenic strains may show mild or no symptoms. H5N1 strains, characterized by unique features in the hemagglutinin cleavage site, are now common in wild birds and poultry. Although highly pathogenic in chickens, their impact varies in ducks and mammals.<sup>7</sup>

In the depicted timeline from 2003 to 2023, the cumulative number of cases and deaths are shown in Figure 1 in which a peak in prevalence was noticed between 2003 and 2009 in Asia countries. Fewer cases were detected after 2009.

A recent WAHIS: World Animal Health Information System report updates on highly pathogenic avian influenza outbreaks in Southeast Asia from January 6 to January 26, 2024, detailing newly reported outbreaks in the Asian regions for both poultry (Cambodia and Korea) and non-poultry (Japan) animals.

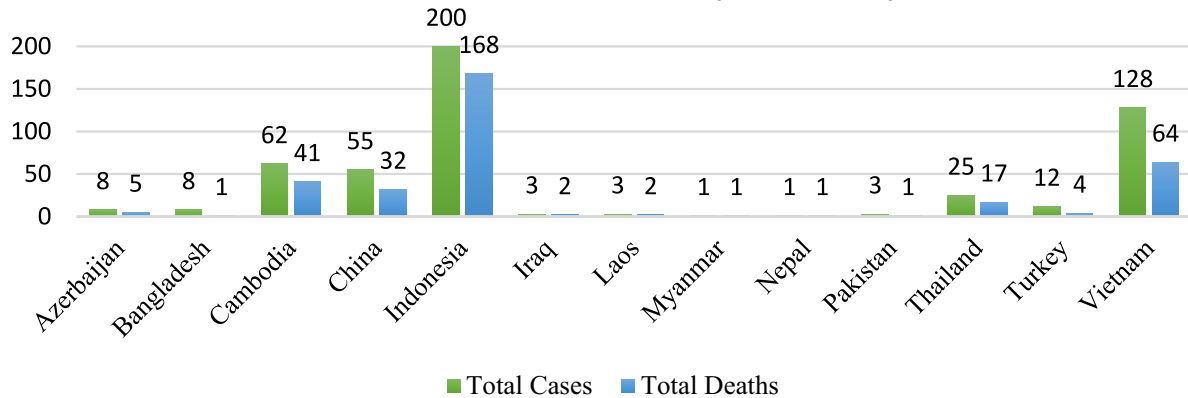
Avian influenza comes with numerous challenges. It presents challenges for healthcare facilities, including limited testing capacity, shortages of medical supplies, staffing constraints, and a surge in patient load. Additionally, in countries like Bangladesh, Myanmar, and Cambodia where poultry is a primary protein source, the economic impact could be significant. Just as the arrival of COVID-19 caught us unprepared,<sup>8</sup> an outbreak of avian influenza could strain healthcare and economic recovery efforts, underscoring the need for proactive measures.

Though there is no direct vaccination for H5N1, emergency vaccinations of other strains were tested. Commercially available inactivated vaccines A, B, and C based on influenza virus strains H5N2, H5N9, and H5N3 respectively were

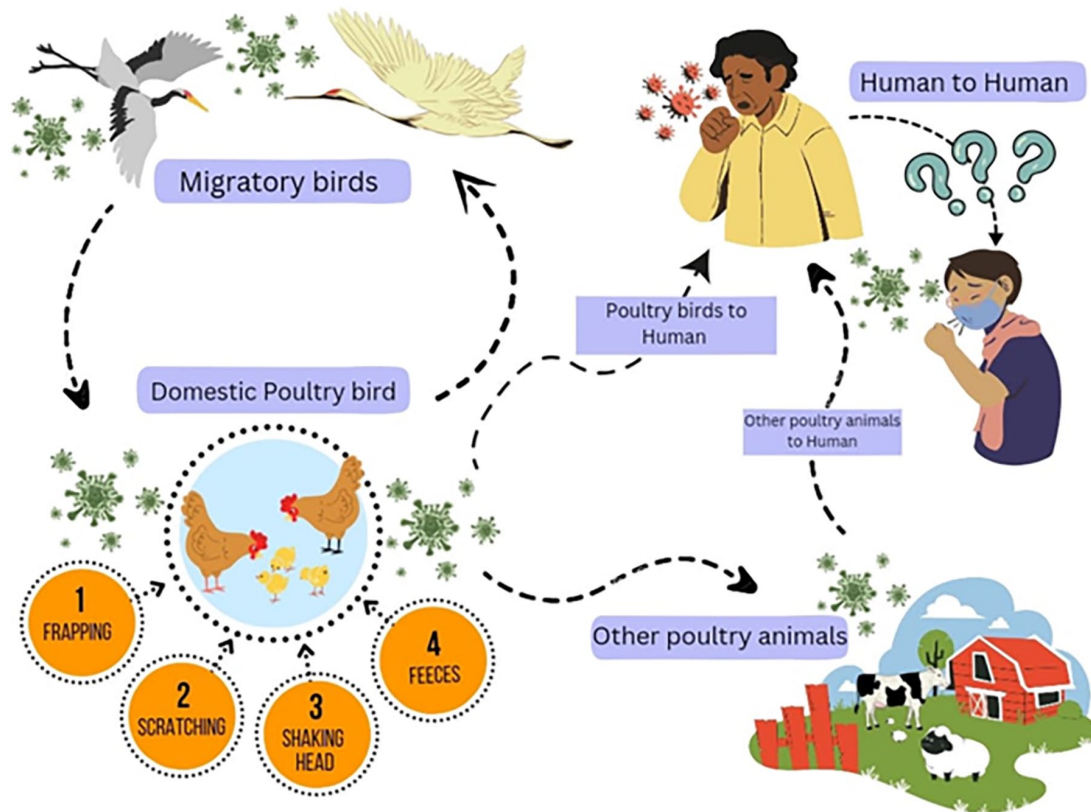
\*These authors contributed equally to this work.



## Total cases and deaths by Influenza A (H5N1) from 2003 to 2023 by country



**Figure 1.** Confirmed human cases of avian influenza A(H5N1) reported to the World Health Organization (WHO), 2003 to 2023 by country (data collected from <https://tinyurl.com/bdhtdeyj> on March 16, 2024).



**Figure 2.** Possible transmission ways of avian influenza A (H5N1).

tested against H5N1 in chickens. Despite the recommended doublevaccination for vaccines B and C, a single immunization was administered to assess their potential as emergency vaccines. Three weeks post-immunization, vaccine A was the most effective with limited shedding of infectious virus followed by B and C.<sup>9</sup> In case of humans there is no mention of many available vaccines except the FDA-approved AUDENZ by Seqirus, the first adjuvanted, cell-based vaccine for potential H5N1 flu pandemics, also believed to boost the immune

response by generating antibodies against mutated virus strains.<sup>10</sup>

The migratory birds play a significant role in spreading the H5N1 virus from poultry to various countries (Figure 2). Mammals and humans can also become infected through contact with poultry, further contributing to the spread. While human-to-human transmission has not been confirmed, there was a reported case that suggests otherwise.<sup>5</sup> The index patient fell ill shortly after contact with infected

chickens. Despite no recognized exposure to poultry, the mother, who provided care, succumbed to pneumonia. Another person (the patient's aunt), also providing care, later fell ill with similar symptoms. Testing confirmed influenza A (H5N1) in both cases, with no further transmission chains identified. Analysis of viral genes indicated a close resemblance to recent avian H5N1 sequences from Thailand.<sup>5</sup> It is likely that the mother and aunt caught the disease from the index patient, suggesting person-to-person transmission of the lethal avian influenza virus during their close, unprotected contact. However, the pathways of human-to-human transmission remain unknown, indicating that vigorous research could potentially lead to the dissemination of the virus on a large scale. Equally important is the development of a vaccine with 100% effectiveness to prevent severe disease resulting from virus infection, which also requires clinical trials. These proactive steps are vital for readiness against potential pandemics like COVID-19, aiming to reduce the necessity for extended quarantines and ensure prompt preventive measures. Given that influenza is transmitted through the air, it is imperative to adopt preventive measures. This entails adhering to COVID-19 protocols<sup>11</sup> such as frequent handwashing, sanitization, mask-wearing, and maintaining physical distance, particularly during colder seasons. It is crucial to raise awareness through various channels like news, print media, social media, workshops, and seminars, not only for avian influenza but for any other viral infections.

In conclusion, the presence of H5N1 in humans underscores our vulnerability to future pandemics. Immediate action is crucial to halt outbreaks in poultry and minimize human exposure. Healthcare providers must remain vigilant, promptly diagnosing and treating H5N1 cases to protect patients and staff. Addressing the H5N1 outbreak urgently is imperative to prevent a potential pandemic.

### Author Contributions

FYN and MBM conceptualized and wrote the manuscript draft. SMRD conceptualized, reviewed, and revised the

manuscript, and supervised the project. All the authors agreed to submit the manuscript in its current form.

### Data Availability

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

### Ethic Statement

Not applicable.

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