Jurnal Epidemiologi Kesehatan Komunitas
11 (4), 2026, 402-414

JEKK



Avian Influenza Outbreaks Worldwide from 2020 to 2025: How Subtype and Pathogenicity Shaped Mortality

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Article Information : Received 23 July 2026 ; Last Revised 02 November 2026 ; Accepted 09 November 2026 ; Available Online 13 November 2026 ; Published 13 November 2026



ABSTRACT

Background: Avian influenza subtypes differ widely in behavior: some spread silently through poultry with little harm, whereas others cause rare but severe human illness. Tracking this difference informs the allocation of resources for surveillance and pandemic preparedness.
Methods: Outbreak events from January 2020 to June 2025 were downloaded from FAO EMPRES-i Plus Global Animal Disease Information System and analyzed descriptively by region, subtype, reporting source, and numbers of human infections and deaths, with cross-tabulations of subtypes by region and country.
Results: Of 212 outbreak events (202 in Asia), low-pathogenic avian influenza (LPAI) H9N2 was the most frequent (42,5%), followed highly pathogenic avian influenza (HPAI) H5N6 (31,6%) and H5N1 (18,9%). The events reported 220 human infections and 35 deaths (crude case fatality 15,9%). Infections peaked in 2021 (n = 53) and deaths in 2023 (n = 8). Asia accounted for 92,3% of infections and 97,1% of deaths; China and Cambodia together accounted for 88,6% of infections and 94,3% of deaths. H9N2 caused 40,9% of infections but one death (case fatality 1,1%), whereas H5N6 (67 infections) and H5N1 (42 infections) caused 31 of the 35 deaths (case fatality 25,4% and 33,3%).
Conclusion: H9N2 accounted for most reported human infections but few deaths, whereas H5N1 and H5N6 caused fewer infections but more deaths. Cases were concentrated in Asia, while differences in reporting systems limited regional comparisons. Coordinated One Health surveillance is essential to improve case detection and interpretation.

Keywords: Avian Influenza ; Disease Outbreaks ; Zoonoses ; One Health ; Public Health Surveillance

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DOI : https://doi.org/10.14710/jekk.v11i4.33838

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Introduction

Avian influenza viruses remain among the most serious zoonotic threats to global health, with recurrent outbreaks affecting both avian and mammalian hosts. Highly pathogenic avian influenza (HPAI) strains, such as H5N1 and H5N6, have been associated with severe disease and high case fatality rates in humans. In contrast, low-pathogenic strains such as H9N2 circulate on a much wider scale, causing lower mortality but higher prevalence. Since the earliest reported human outbreak (H5N1: 18 cases, 6 deaths in 1997), the virus has continued to cross the avian-human barrier and raise concerns about its potential to cause a pandemic.[1] Since then, the World Health Organization (WHO) has documented hundreds of laboratory-confirmed H5N1 infections with mortality rates greater than 50%, confirming its serious position as a global health problem.[2] The epidemiology of avian influenza has become more challenging over the past 20 years, with the emergence of diverse viral clades and reassortant subtypes. Clade 2.3.4.4b H5N1 viruses, for instance, have migrated into new continents, generating novel variants such as H5N2, H5N5, H5N6, and H5N8, and are now associated with cross-species transmission in mammals, with new outbreaks occurring in mink farms and marine mammals.[3]

Human infections with avian influenza viruses were already concentrated in Asia before 2020. Between 2003 and 2019, the World Health Organization (WHO) recorded 861 laboratory-confirmed human A(H5N1) infections, including 455 deaths (crude case fatality 52,8%), from 17 countries.[4] Asian countries (including Azerbaijan, Iraq, and Turkey) accounted for 499 of these infections (58,0%) and 333 of the deaths (73,2%), led by Indonesia (200 infections, 168 deaths), Viet Nam (127 and 64), Cambodia (56 and 37), and China (53 and 31), whereas Egypt reported most of the remaining infections (359 infections, 120 deaths).[4] Other subtypes added to this burden. By the end of 2019, 1,568 human A(H7N9) infections with 615 deaths (case fatality 39%) had been reported globally since 2013, together with 54 A(H9N2) infections (one death) and 24 A(H5N6) infections, all of the latter from China.[5]

Such versatility poses a risk of viral evolution towards long-term human-to-human transmission. Conversely, H9N2 is considered a low-pathogenic strain and has contributed significantly to zoonotic infections through widespread poultry dissemination and frequent human detection, notably in Asia.[2] The human clinical burden of avian influenza differs by subtype. Although H9N2 disease is generally mild to moderate, both H5N1 and H5N6 are linked to severe respiratory illness, multi-organ involvement, and markedly increased morbidity/mortality.[1,3] Histopathological studies have demonstrated that H5N1 causes diffuse alveolar damage, disseminates into the systemic circulation, and dysregulates cytokine response, thus contributing to the high virulence of this virus.[1]

Three subtypes (H9N2, H5N1, and H5N6) account for most recent human reports, but for different reasons. H9N2 is a low-pathogenic virus that is widespread in poultry in Asia and the Middle East, which gives people repeated opportunities for exposure; most human infections are mild and occur in children, and only one death had been recorded among the 54 infections reported worldwide by the end of 2019, and two among 181 infections reported to WHO in the Western Pacific Region since 2015.[5–8] In contrast, H5N1 and H5N6 are highly pathogenic viruses that circulate in poultry and wild birds; human infections are fewer but severe and usually follow direct contact with infected poultry or visits to live-poultry markets.[9,10] WHO has recorded 997 human H5N1 infections with 478 deaths (47,9%) from 2003 to March 2026,[4] and 93 human H5N6 infections with 58 deaths (62,4%) in the Western Pacific Region since 2014.[6] H5N6 viruses of clade 2.3.4.4 can bind both avian-type and human-type receptors and have become a dominant highly pathogenic subtype in poultry in southern China, gradually replacing H5N1.[10] Other subtypes have contributed fewer reports. A(H7N9) caused 1,568 infections in 2013–2019 but almost disappeared from human surveillance after China began nationwide poultry vaccination in 2017,[5,11] and most other

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subtypes (for example H3N8, H10N3, and H10N5) have been reported only as sporadic cases.[6]

The continued presence of these extremely pathogenic strains in avian reservoirs and their spillover events into humans underscores the persistent risk of mortality and the importance of vigilant surveillance of "Avian Influenza death" patterns globally. Considering these dynamics, a thorough understanding of the distribution of avian influenza outbreaks, the pathogenicity of the given subtype, and the health outcomes in humans is a prerequisite for pandemic preparedness. Surveillance data not only inform risk assessment but also One Health strategies intended to break the chain of transmission at the interface between the animals and humans. The current study aims to summarize the worldwide distribution, heterogeneity of populations of avian influenza, and temporal trends of avian influenza outbreaks from 2020 until mid-2025 (including an examination of human infections and mortality). Based on recent outbreak data, we hope to provide valuable insights into the patterns of "Avian Influenza death" and their implications for public health response.

Methods

A. Study design and data source

The current study was a descriptive analysis of global avian influenza outbreak reports from January 1, 2020, to June 30, 2025. Data were collected from the EMPRES-i Plus Global Animal Disease Information System, a publicly available surveillance system established and managed by the Food and Agriculture Organization (FAO). Data download The dataset was downloaded in Microsoft® Excel® format from the EMPRES-i Plus website (https://empres-i.apps.fao.org/) on July 21, 2025. The dataset contained, for each incident, the event ID number, virus subtype, date of observation and reporting, host category, country, geographical region, reporting authority, diagnostic status, and whether the case was attributed to a human.

B. Data preprocessing and data analysis

The dataset was curated and prepared for analysis using Microsoft® Excel® for Microsoft 365 MSO (Version 2506 Build 16.0.18925.20076). Records were restricted to infection occurrences during the outbreak events observed through the study period (Jan. 1, 2020–Jun. 30, 2025). The data were grouped by virus pathotype, subtype, publication source, region, country, number of cases and number of deaths. To summarize the distribution of outbreaks, descriptive statistics, such as frequencies and percentages, were computed. Crosstabulations were performed to characterize the behavior of virus subtypes across regions, linkages with human infections and deaths, and differences in human infections and deaths across regions. Table 1 counts outbreak events, whereas Tables 2 and 3 count the human infections and deaths reported within those events, so the totals differ (212 events versus 220 human infections). The cross-tabulation of human infections and deaths by pathotype, subtype, and region (Table 2) was derived by combining the regional subtype counts of outbreak events (Table 1) with the country totals (Table 3) and the subtype totals of the dataset. Crude case fatality was calculated as the number of deaths divided by the number of reported human infections.

C. Data presentation

The findings were summarized with tables and charts using Microsoft Word for Microsoft 365 (Version 2506 Build 16.0.18925.20076) from the cleaned dataset.

D. Ethics Approval and Consent to Participate

This study utilized exclusively publicly available, open-access datasets obtained from established online repositories. No human participants were directly recruited, no interventions were conducted, and no identifiable personal information was accessed. Consequently, this study did not necessitate approval from an institutional ethics committee or informed consent from participants, in accordance with the relevant institutional and international ethical

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guidelines governing secondary analyses of publicly available anonymized data.

Result

A. Reporting sources

The dataset contained 212 outbreak events, which reported 220 human infections and 35 deaths. National authorities supplied 58% of the records and WHO was the second-largest source, whereas FAO officers, the World Organization for Animal Health (WOAH), and FAO field officers together contributed only a small fraction (Figure 1).

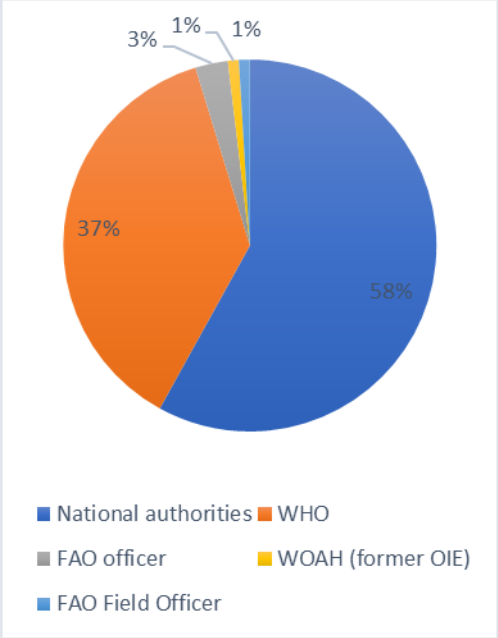


Figure 1. Distribution of reporting sources for avian influenza outbreaks, 2020–June 2025.

B. Geographical and subtype distribution

Asia accounted for 202 of the 212 outbreak events (95,3%); the other ten were reported from the Americas (n = 6), Europe (n = 2), Africa (n = 1), and Oceania (n = 1). LPAI H9N2 (n = 90; 42,5%), HPAI H5N6 (n = 67; 31,6%), and HPAI H5N1 (n = 40; 18,9%) together made up 92,9% of events, and HPAI viruses accounted for 112 events (52,8%) compared with 100 (47,2%) for LPAI. H5N6 occurred only in Asia and H9N2 in Asia except for one event in Africa, whereas H5N1 was recorded in four of the five regions (Table 1, Figure 2).

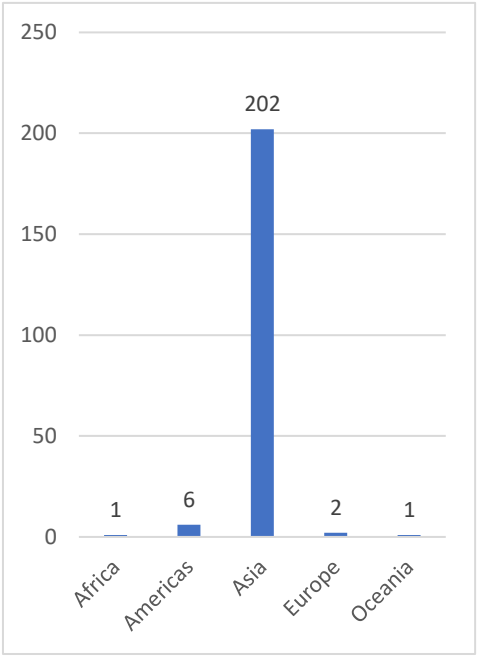


Figure 2. Regional distribution of avian influenza outbreaks, 2020–June 2025.

Table 1. Outbreak events (n = 212) by pathotype, subtype, and region, 2020–June 2025

Pathotype	Subtype	Africa	Americas	Asia	Europe	Oceania	Total	%
HPAI	H3N8	0	0	1	0	0	1	0,5
	H5	0	1	0	0	0	1	0,5
	H5N1	0	3	35	1	1	40	18,9
	H5N2	0	1	0	0	0	1	0,5
	H5N6	0	0	67	0	0	67	31,6
	H5N8	0	0	0	1	0	1	0,5
	HPAI	0	1	0	0	0	1	0,5
LPAI	H3N8	0	0	2	0	0	2	0,9
	H9	0	0	1	0	0	1	0,5

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Continued Table 1. Outbreak events (n = 212) by pathotype, subtype, and region, 2020–June 2025

Pathotype	Subtype	Africa	Americas	Asia	Europe	Oceania	Total	%
LPAI	H9N2	1	0	89	0	0	90	42,5
	H10N3	0	0	6	0	0	6	2,8
	H10N5	0	0	1	0	0	1	0,5

Percentages are shares of all 212 outbreak events. HPAI in the Subtype column denotes events in which only the pathotype was recorded.

C. Temporal trends in human cases and deaths

Human infections peaked in 2021 (n = 53) and deaths in 2023 (n = 8); annual deaths were otherwise 6–7 from 2021 onward, after a single death in 2020. The 39 infections and seven deaths recorded in the first half of 2025 cover only six months and are not comparable with full-year totals (Figure 3).

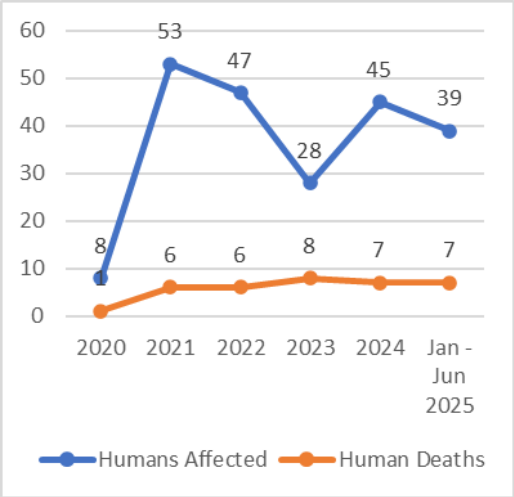


Figure 3. Annual human avian influenza infections and deaths, 2020–June 2025. Line chart showing the number of confirmed human infections (blue line) and deaths (red line) per year. Data for 2025 represent January–June only.

D. Human infections and deaths by subtype and region

The 220 human infections caused 35 deaths (crude case fatality 15,9%). HPAI viruses accounted for 120 infections (54,5%) but 33 deaths (94,3%; case fatality 27,5%), compared with 100 infections and two deaths (case fatality 2,0%) for LPAI. H9N2 caused the most infections (n = 90; 40,9%) but one death (case fatality 1,1%), whereas H5N6 (67 infections, 17 deaths; 25,4%) and H5N1 (42 infections, 14 deaths; 33,3%) together caused 31 of the 35 deaths. Asia accounted for 203 infections (92,3%) and 34 deaths (97,1%). H5N6 was reported only from Asia, H5N1 was the only subtype reported from four regions, and the only death outside Asia was an H5N2 infection in Mexico (Table 2).

Table 2. Human infections (n = 220) and deaths (n = 35), with crude case fatality, by pathotype, subtype, and region, 2020–June 2025

Pathotype	Subtype	Asia	Outside Asia	Infections, n (%)	Deaths, n (%)	CFR (%)
HPAI	H3N8	1 (1)	–	1 (0,5)	1 (2,9)	–
	H5	–	1 (0)	1 (0,5)	0 (0,0)	–
	H5N1	36 (14)	6 (0)	42 (19,1)	14 (40,0)	33,3
	H5N2	–	1 (1)	1 (0,5)	1 (2,9)	–
	H5N6	67 (17)	–	67 (30,5)	17 (48,6)	25,4
	H5N8	–	7 (0)	7 (3,2)	0 (0,0)	–
	Unspecified	–	1 (0)	1 (0,5)	0 (0,0)	–
HPAI subtotal		**104 (32)**	**16 (1)**	**120 (54,5)**	**33 (94,3)**	**27,5**
LPAI	H3N8	2 (0)	–	2 (0,9)	0 (0,0)	–
	H9	1 (0)	–	1 (0,5)	0 (0,0)	–
	H9N2	89 (1)	1 (0)	90 (40,9)	1 (2,9)	1,1
	H10N3	6 (0)	–	6 (2,7)	0 (0,0)	–
	H10N5	1 (1)	–	1 (0,5)	1 (2,9)	–
LPAI subtotal		**99 (2)**	**1 (0)**	**100 (45,5)**	**2 (5,7)**	**2,0**
Total		**203 (34)**	**17 (1)**	**220 (100)**	**35 (100)**	**15,9**

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Cells show human infections (deaths); a dash indicates none reported. Percentages are shares of all 220 infections and 35 deaths. CFR, crude case fatality (deaths/infections), is shown only for groups with at least 10 infections. Outside Asia: H5N1, Americas 3, Europe 2 (United Kingdom), and Oceania 1 (Australia); H5N8, Europe 7 (Russian Federation); H9N2, Africa 1 (Ghana); H5, H5N2 (Mexico, the only death), and unspecified HPAI, Americas 1 each. Region-level counts were derived from Tables 1 and 3.

E. Human infections and deaths by country, with emphasis on Asia

Human infections were concentrated in two Asian countries: China (166 infections, 75,5%; 21 deaths, 60,0%) and Cambodia (29 infections, 13,2%; 12 deaths, 34,3%), which together accounted for 88,6% of infections and 94,3% of deaths. Crude case fatality was 12,7% in China, 41,4% in Cambodia, and 8,0% (2 of 25) in all other countries combined. All 67 H5N6 infections and 17 H5N6 deaths were reported from China, equivalent to 40,4% of Chinese infections and 81,0% of Chinese deaths. The remaining Asian countries (Bangladesh, Hong Kong SAR, India, and the Lao People's Democratic Republic) reported eight infections and one death, and all other regions together reported 17 infections and one death (Table 3).

Table 3. Human infections and deaths by region and country, with crude case fatality, 2020–June 2025.

Region / country	Infections, n (%)	Deaths, n (%)	CFR (%)
Africa	**1 (0,5)**	**0 (0,0)**	**–**
Ghana	1 (0,5)	0 (0,0)	–
Americas	**6 (2,7)**	**1 (2,9)**	**–**
Canada	1 (0,5)	0 (0,0)	–
Chile	1 (0,5)	0 (0,0)	–
Ecuador	1 (0,5)	0 (0,0)	–
Mexico	1 (0,5)	1 (2,9)	–
United States of America	2 (0,9)	0 (0,0)	–
Asia	**203 (92,3)**	**34 (97,1)**	**16,7**
Bangladesh	2 (0,9)	0 (0,0)	–
Cambodia	29 (13,2)	12 (34,3)	41,4
China	166 (75,5)	21 (60,0)	12,7
Hong Kong, SAR	2 (0,9)	0 (0,0)	–
India	2 (0,9)	1 (2,9)	–
Lao People's Democratic Republic	2 (0,9)	0 (0,0)	–
Europe	**9 (4,1)**	**0 (0,0)**	**–**
Russian Federation	7 (3,2)	0 (0,0)	–
United Kingdom	2 (0,9)	0 (0,0)	–
Oceania	**1 (0,5)**	**0 (0,0)**	**–**
Australia	1 (0,5)	0 (0,0)	–
Total	**220 (100)**	**35 (100)**	**15,9**

Percentages are shares of all 220 infections and 35 deaths. CFR, crude case fatality (deaths/infections), is shown only for regions and countries with at least 10 infections.

Discussion

A. Geographic Distribution and Epidemiology

In the analysis of reported outbreaks, a total of 212 incidents were identified, with 202 occurring in Asia and the remaining 10 dispersed across other global regions. This distribution exacerbates the epidemiological burden within Asia, where China accounted for 75,5% of human infections and 60,0% of fatalities. Cambodia followed as a distant second, contributing 13,2% of cases, yet accounting for 34,3% of deaths. The biological dynamics involved are relatively straightforward: migratory flyways across Asia facilitate the seasonal movement of H5N1 among wild waterfowl. Furthermore, decades of regional exposure to the virus have fostered a patchwork surveillance system characterized by inconsistencies.[12,13] The resurgence of the virus in Cambodia in 2024 serves as a pertinent illustration of the inherent

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risks, as a reservoir-based population along active migratory corridors poses a potential threat for outbreaks extending beyond national borders should containment measures prove ineffective.[14]

In contrast, Europe and North America present distinct epidemiological landscapes. Although their surveillance systems are ostensibly more uniform, the disease patterns in these regions primarily reflect the migratory patterns of wild birds rather than endemic poultry flows. Consequently, systems designed to monitor one epidemiological profile may overlook cases associated with another, thus rendering sporadic human infections in these regions potentially undetected, notwithstanding the allocation of additional resources.[15] The alarming absence of reported cases from Africa, the Americas, and Oceania warrants further scrutiny. Surveillance capabilities in these regions are often limited, and there exists a tangible economic incentive to underreport cases due to trade implications contingent on outbreak status. Additionally, detection systems are frequently designed to identify severe cases rather than mild or asymptomatic infections.[16–18] Collectively, these factors suggest significant undercounting rather than a mere absence of disease, an important consideration for pandemic preparedness, as underreporting artificially inflates the apparent case-fatality rate and may misleadingly reassure risk assessments.

The disproportionate case count observed in Asia also underscores the region's poultry retention practices. Factors such as high population density, extensive human populations, backyard farming with inadequate waste management, frequent close contact with birds, and the cultural practice of transporting live poultry during festivals contribute to elevated exposure levels—conditions that industrialized poultry systems typically mitigate.[19,20] Enhanced biosecurity practices further highlight this disparity; for instance, U.S. operations routinely implement vehicle disinfection protocols and controlled access to facilities. Fieldwork in Cambodia corroborates this perspective, revealing high rates of human-poultry contact among men aged 16 to 40 years, indicative of occupational and cultural exposure patterns rather than incidental encounters.[9,21]

Within Asia, the data show two distinct epidemiological profiles. China reported 166 infections and 21 deaths (crude case fatality 12,7%), a mixture of H5N6 (67 infections, 17 deaths) and low-pathogenic infections. Because LPAI viruses caused 100 infections in total, and at most 38 of these could have occurred outside China (one in Ghana and, at most, 37 in the other five Asian countries), at least 62 of the 99 non-H5N6 infections in China involved low-pathogenic subtypes. This mixture is consistent with the comparatively low case fatality in China and with the detection of mild H9N2 infections, mostly in children, by national surveillance.[8] Cambodia, in contrast, reported 29 infections and 12 deaths (case fatality 41,4%); because only two of the 35 deaths in the dataset were associated with LPAI subtypes (H9N2 and H10N5), at least ten of the 12 Cambodian deaths involved HPAI subtypes. WHO data indicate that this pattern reflects a geographic shift in human H5N1 infections. Before 2020, Indonesia, Viet Nam, and Thailand accounted for 352 of the 499 H5N1 infections reported from Asian countries (70,5%), whereas in 2020–2024 none was reported from Indonesia or Thailand and only two from Viet Nam, and Cambodia reported 16 of the 23 Asian infections.[4] Because case fatality is calculated among reported infections only, differences between countries may also reflect differences in the detection of mild infections, as discussed below.

B. Influence of Avian Influenza Subtypes and Pathogenicity on Case Fatality

The dataset under review reveals the presence of two distinct subtypes that function as polar opposites in terms of epidemiological behavior. H9N2 accounted for 42,5% of outbreaks and 40,9% of human infections but was responsible for only 2,9% of deaths, resulting in an approximate case-fatality rate of 1,1%. The underlying mechanism is clear: H9N2 preferentially binds to α-2,3 sialic acid receptors in the lower respiratory tract and rarely disseminates systemically, enabling widespread transmission with minimal

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detriment to individual hosts. Conversely, H5N6 and H5N1 lie at opposite ends of the spectrum, with case-fatality rates of 25,4% and 33,3%, respectively, despite contributing relatively fewer cases overall. Factors such as cytokine storms, multi-organ spread, and polybasic cleavage sites—allowing the virus to exploit proteases beyond the respiratory tract—provide insight into the increased lethality of these subtypes.[22,23]

The case fatality estimates in this dataset agree with previous reports for H9N2 but are lower than those reported for H5N1 and H5N6. For H9N2, the case fatality of 1,1% is the same as that of the two deaths among 181 infections (1,1%) reported to WHO in the Western Pacific Region since 2015 and close to the single death among 54 infections reported worldwide by the end of 2019; these infections are predominantly mild and occur mostly in children.[5–8] For H5N1, however, the case fatality of 33,3% is below the 47,9% reported cumulatively by WHO for 2003 to March 2026 (478 deaths among 997 infections) and the 52,8% for 2003–2019,[4] and for H5N6 the 25,4% found here is well below the 55,4% reported for 65 infections in China up to 2021 and the 62,4% reported to WHO.[6,10] Several explanations are plausible. The WHO tables include detections in asymptomatic people,[4] so the recent H5N1 series may contain milder infections; outcome information in a passively collected dataset may be incomplete, particularly for patients who died after a report was filed; and EMPRES-i Plus holds fewer human records than WHO for some countries, as WHO lists 71 human infections from the United States (67 of them in 2024, including cases reported as A(H5)), compared with two in the present dataset.[4] The contrast between H9N2 and the highly pathogenic subtypes is nevertheless consistent with earlier comparative analyses of fatal human infections with high-pathogenicity (H5N1 and H5N6) and low-pathogenicity (H7N9 and H9N2) avian influenza viruses.[24]

This divergence can be interpreted as a manifestation of competing evolutionary strategies, with H9N2 sacrificing severity for increased reach. Its genetic flexibility and propensity for frequent reassortment facilitate cross-species transmission while maintaining a mild phenotype that precludes triggering culling and containment responses.[25,26] In contrast, H5N1 and H5N6 maximize the severity of each outbreak, inflicting rapid and significant host mortality, thereby limiting the extent of viral dissemination even in the context of rapid event proliferation.[27,28] The distribution patterns substantiate this interpretation: H9N2 displays widespread prevalence across numerous countries, aligning with its subclinical transmission capabilities.[29,30] In contrast, H5N6 has remained confined to China in this dataset, with all 67 reported cases occurring within its borders. H5N1 has emerged sporadically across continents, likely facilitated by migratory bird movements, and its lethality may serve as a self-limiting factor, curtailing transmission chains before they can extend significantly.[24,31]

The distribution of subtypes in this dataset is also consistent with earlier descriptions of their ecology. H9N2 is widespread in poultry in Asia and the Middle East and is regarded as endemic in China, Viet Nam, and South Korea,[7] and reported human H9N2 infections in China have increased since 2013, reaching 25 in 2021, mostly in children,[8] which fits the large number of mild infections recorded here. H5N6 clade 2.3.4.4 viruses have been endemic in birds in China and Southeast Asia, four new genotypes drove the rise in human infections in 2021, and 93,8% of patients reported poultry exposure, with more than 60% having visited a live-poultry market,[10] which explains why all 67 H5N6 infections in this dataset arose in China. A(H7N9), which caused the largest number of human infections before 2020 (1,568 infections, 615 deaths),[5] is absent from the dataset, in keeping with the near-disappearance of human H7N9 infections after poultry vaccination began in China in 2017.[11] Differences in the numbers of reported infections and deaths between subtypes therefore depend on the exposure opportunities created by their circulation in poultry and on animal-health control measures, as well as on pathogenicity itself.

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C. Temporal and Evolutionary Trends

The incidence of human cases peaked in 2021, while the number of deaths was highest in 2023. This temporal gap should be interpreted cautiously: annual deaths varied only narrowly (6–8) from 2021 onwards, and the dataset cannot separate changes in the virus from changes in detection or reporting. The surge in 2021 coincided with the global emergence of HPAI (H5N1) clade 2.3.4.4b, which facilitated extensive spillover as the virus disseminated to new regions via migratory pathways.[32,33] Deaths in 2023 (n = 8) exceeded those in neighboring years (6–7) by only one or two, so they do not by themselves indicate a clear upward trend. More than half of all circulating H5N1 viruses in 2023 displayed molecular markers indicative of mammalian adaptation, and the emergence of newer reassortant variants has demonstrated heightened lethality compared to earlier strains, which raises the possibility of increased virulence; however, the aggregated counts analyzed here cannot confirm such a trend.[34,35]

Migratory patterns continue to shape seasonal transmission dynamics, with peaks in spring and autumn when waterfowl from various flyways converge, facilitating viral transmission. Cooler temperatures prolong viral survival in aquatic environments, while seasonal fluctuations in poultry farming and market activities increase human-bird interactions.[32,33] Selection pressures during colder months may favor virulent strains, coupled with seasonal declines in respiratory immune defenses, although the present data cannot show whether these factors contributed to the slightly higher number of deaths in 2023.[36] The first half of 2025 recorded 39 infections and 7 deaths, before the typical autumn migration season, which historically corresponds with heightened transmission rates. These counts cover only six months and cannot be used to project the 2025 total; whether they reflect enhanced viral fitness, broader exposure, or improved detection capabilities cannot be determined from these data.[27,34]

The broader implications of these trends reflect genuine viral evolution. Genetic reassortment led to the emergence of new H5N8 genotypes during the 2020-2021 outbreaks, and the transition from H5N8 to H5N1 in 2022 indicates increased pathogenicity and a wider host range.[28,37] Mutations in the polymerase gene have facilitated H5N1's adaptation to mammalian cells, with such traits increasingly manifesting in diverse species, including dairy cattle, seals, minks, and dolphins. Ongoing migratory bird movements and environmental conditions remain critical determinants of spillover outcomes, while the wild-domestic bird interface continues to play an essential role in transmission dynamics[38,39]

D. Public Health Implications and Suggestions for Policy Reforms

The most pressing concern for pandemic preparedness lies in the pathogen clusters H5N1 and H5N6, which exhibit case fatality rates of 33,3% and 25,4%, respectively, and evidence of molecular adaptations that heighten the potential for human transmission. H5N1 clade 2.3.4.4b, which has been circulating since late 2020, has broadened its host range across a remarkable diversity of mammalian species. Approximately half of the newly identified H5N1 viruses exhibit molecular signatures indicative of mammalian adaptation, with mutations in the polymerase gene facilitating enhanced replication in mammalian cells.[32,34] Given the documented capacity for reliable reassortment and the potential for H5N6 to recombine, particularly with H9N2—there is a tangible risk that viral traits may converge in a manner that facilitates human-to-human transmission.[27,35]

The stark disparity in case counts between Asia and other regions constitutes a significant surveillance failure with far-reaching global implications. Inadequate diagnostic capacity, insufficient healthcare infrastructure, and weak linkages between animal and human health monitoring in underprivileged areas likely obscure the actual transmission dynamics in these regions. The dispersion of H5N1 clade 2.3.4.4b across continents via

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migratory pathways renders this oversight a global concern rather than a localized one.[17,40] Bangladesh exemplifies a model for improved surveillance, having successfully enhanced detection through integrated monitoring of poultry flocks and live-bird markets. This approach has proven effective in bolstering biosecurity at the source of spillover.[41,42] Expanding such efforts to other regions necessitates genuine integration of veterinary medicine, public health, environmental science, and policy, grounded in shared data rather than operating through parallel, disconnected institutions. Achieving this integration is fraught with challenges: geopolitical tensions can inhibit information sharing, cross-sector and cross-border coordination is inherently complex, and surveillance systems frequently lag behind rapidly evolving viral strains.[43]

Advancements in vaccine technologies, encompassing recombinant and mRNA platforms that can be rapidly deployed for emerging strains, complement the available response toolkit. However, translating these advancements into effective practice will require enhanced laboratory capacity, better-trained healthcare professionals, and comprehensive strategies that account for the multifaceted dimensions of H5N1 transmission, particularly in underrepresented areas where coordinated surveillance can offer crucial early warnings for global pandemic preparedness.[44,45]

Conclusions

Between 2020 and mid-2025, reported avian influenza outbreaks and human deaths were concentrated in Asia, with China and Cambodia accounting for 88,6% of human infections and 94,3% of deaths. H9N2 accounted for the largest share of human infections (40,9%) but a single death, whereas H5N1 and H5N6 accounted for fewer infections but 31 of the 35 deaths. Strengthening biosecurity in live-bird markets and smallholder farms, together with integrated One Health surveillance linking animal, environmental, and human health, is a plausible priority in Asia.

These findings should be interpreted with caution. The data are aggregated and passively collected, and the few reports from Africa, the Americas, and Oceania probably reflect limited surveillance rather than a low disease burden. Only infections that were tested and reported are counted, and detection favors severe cases, so the case-fatality figures are crude proportions among reported cases and probably overestimate the risk of death after infection, to a degree that may differ between subtypes, countries, and years. As a descriptive analysis, the study cannot establish differences in transmissibility or virulence between subtypes.

Acknowledgement

The authors express their sincere gratitude to the Food and Agriculture Organization (FAO) for maintaining and providing public access to the EMPRES-i Plus Global Animal Disease Information System, which served as the foundational data source for this study.

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