Current status and future challenges of avian influenza – a literature review

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Abstract

An infectious agent affecting both domestic and wild birds may cause avian influenza. All of them can be transmitted by coming into contact with tainted food, drink, or bird emissions, particularly feces. Numerous clades of H5N1 infections have been circulating since 2003, including one introduced to the United States in 2014 by wild birds, which persisted until 2016. There were 2,240 wild birds found in 45 states and 519 counties in the United States alone by September 14, 2022. According to the World Organization for Animal Health (WOAH), the predominant Highly Pathogenic Avian Influenza (HPAI) A (H5) virus subtype causing poultry outbreaks worldwide from late 2021 to early 2022 is A (H5N1). Most notifications from wild birds across multiple countries and regions suggest that the virus may have been introduced and spread via uncontrolled bird migration. The primary instance of a goose/Guangdong/1/96-lineage H5 HPAI infection inside the Americas since June 2015 was checked by the later disclosure of an H5N1 HPAI outbreak in Newfoundland, Canada. The avian flu Type A viruses, or bird flu viruses, rarely cause human infection; some bird flu viruses have done so in the past. The HPAI (H5) virus has been persistent in wild bird populations in Europe since the 2020-21 epidemic wave, according to the paper titled "Avian Influenza Overview: March-June 2022." Even regions like Antarctica had avian influenza cases in 2023-24. Prevention and control can be done by monitoring and reporting outbreaks, preventing avian influenza at its source in animals, banning chicken farms, controlling methodologies, remuneration for ranchers, and vaccination.

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Key words: Influenza A Virus, H5N1 subtype, disease outbreaks, vaccination, poultry, humans, remuneration.

Conflict of interest: the author declares no potential conflict of interest.

Funding: none.

Availability of data and materials: all data generated or analyzed during this study are included in this published article.

Ethics approval and consent to participate: this evaluation does not require ethical approval because no patient data will be collected. Plagiarism, confidentiality, malfeasance, data falsification and falsification, double publishing and submission, and duplication are the ethical problems examined in this study.

Acknowledgments: the author thanks all the faculty members, paramedical staff, colleagues, friends, and family for their guidance and support in conducting this study.

Acknowledgements:

Received: 25 January 2024.
Accepted: 23 March 2024.

Infectious Diseases and Herbal Medicine 2024; 5:386
doi:10.4081/idhm.2024.386

Introduction

An infectious agent affecting both domestic and wild birds may cause Avian Influenza (AI). Though less frequently, AI viruses have been isolated from mammals, including humans. Multiple virus subtypes (H5N1, H5N3, H5N8, *etc*.) are responsible for this complicated illness with genetic characteristics that are rapidly changing. Although there are distinct subtypes that are more prevalent in some regions than others, the condition can be found anywhere on the planet.[1]

The various avian influenza virus strains can be split into two groups based on how seriously they affect poultry.

Low-Pathogenic Avian Influenza (LPAI) has a low mortality rate and ability to infect, causing little to no disease in birds, because they can only replicate in tracheal tissues and the small intestine.[2] Low-pathogenic avian influenza viruses do not cause ruffled feathers or decreased egg production in chickens or poultry. The vast majority of avian influenza A viruses that infect wild birds are low pathogenic and have only minor effects on their victims. In some chickens, high-pathogenic Avian influenza viruses can mutate into common pathogenic viruses.[3]

High-Pathogenic Avian Influenza (HPAI) is a stress of the virus that can motivate extreme scientific symptoms and an excessive mortality price. An excessive mortality price and extreme infection are caused by infected poultry's exceedingly virulent avian flu infections. The HPAI virus can cross respiratory and intestinal barriers, diffuse to the blood, and damage all tissues of the bird.[4] HPAI refers to strains with an "Intravenous Pathogenicity Index" (IVPI) greater than 1.2 or a mortality rate equal to or higher than 75% of the total number of poultry over a period of 10 days.[4] The HPAI pathogenic strains of avian influenza belong to the H5 and H7 subtypes, with bird mortality that

exceeds 90-100% during the 48 h after disease onset.[5] To date, subtypes H5 and H7 have been recognized as HPAI viruses capable of generating acute and considerable diseases in chickens, turkeys, and other economically significant birds. Moreover, H9 has been included as another subtype with pandemic risk because their high mutability could favor the evolution of viruses that allow sustained transmission in the human species, and H9 can cause zoonotic infections.[5]

Transmission and spread

A few things that will help AI infections spread include the following: i) global trade and globalization, ii) cultivating and dealing (live feathered creature markets), iii) migratory paths and wild birds. AI infections are seen in the feces and respiratory secretions of avian creatures. All of them can be transmitted by coming into contact with tainted food, drink, or bird emissions, particularly feces. AI infections are easily conveyed on cultivation equipment and spread from cultivation to cultivation due to their resistance, which includes the ability to endure prolonged cold periods.[1] On 18,620 HPAI, WOAH data were gathered after carrying out a Seasonal and Trend decomposition using Loess (STL) analysis to determine the seasonal pattern of the disease as in Figure 1. Between 2005 and 2019, 76 countries and territories impacted by the virus reported outbreaks in poultry (Figure 2). Typically, a bird virus peaks in February, rises in October, and reaches its lowest point in September.[1-5]

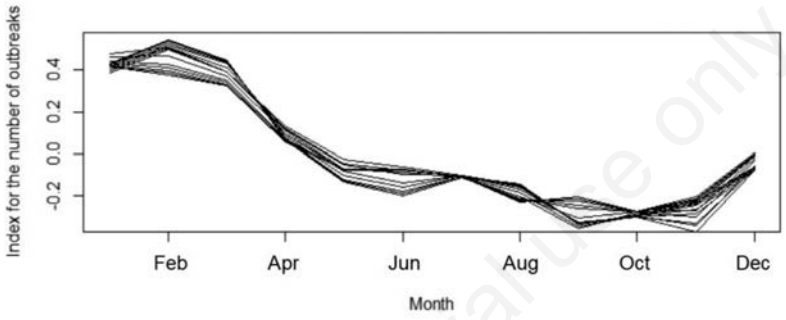

Figure 1. Seasonal trends in global Highly Pathogenic Avian Influenza (HPAI) index in poultry.

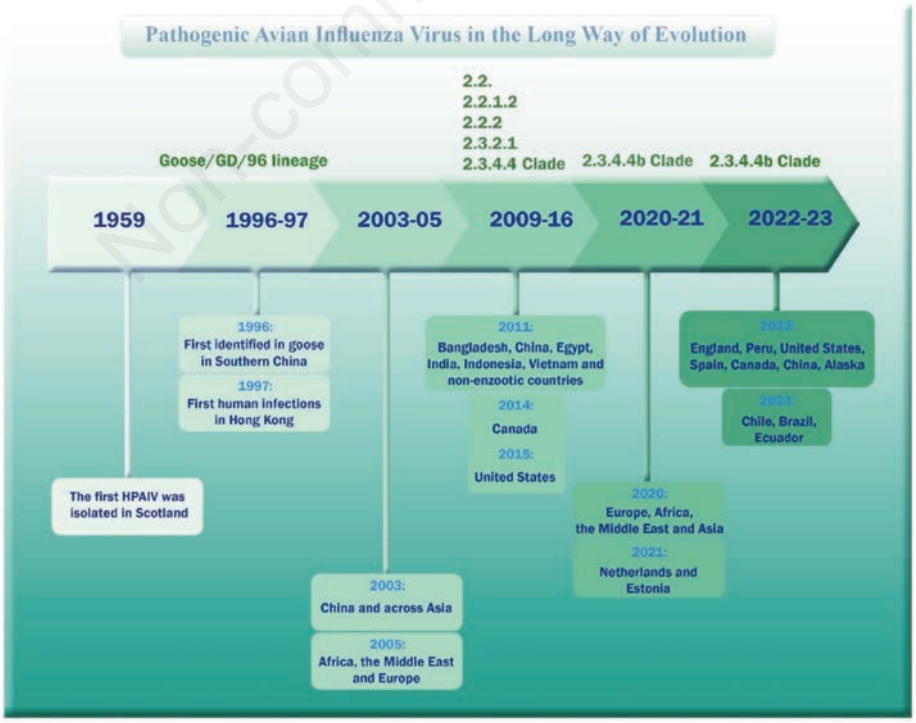

Figure 2. Timeline of Highly Pathogenic Avian Influenza (HPAI) H5N1 evolution (1959–2023). The timeline showcases significant events and outbreaks associated with the virus, along with the corresponding countries and clades involved.

The global impact of Avian Influenza

Due to the growing number of affected nations and circulating subtypes, HPAI are a global concern. Dr. Keith Hamilton, in charge of the Readiness and Strength Office at WOAH, claims that "avian flu can kill huge herds of winged creatures, generating destructive disasters for the cultivating segment".[3] Emergencies of avian influenza can disrupt international trade, the health of wild birds, the livelihoods of farmers, and the poultry industry. Additionally, the biodiversity of our ecosystems could be irreparably damaged due to AI's effects on wildlife.[6-9]

Moreover, by crossing the species obstruction, avian flu can contaminate rodents, mice, weasels, ferrets, pigs, cats, tigers, mutts, and steeds. It is usually uncommon, and avian influenza is only transmitted from birds to humans in rare cases. Frequent interaction with infected birds or living in a contaminated area increases their risk of avian flu. As a result, avian influenza outbreaks remain a worldwide public health concern.[6-9]

H5N1 bird flu detections globally

Wild birds

The number of contaminations of feathered creatures, their geographic spread, the number of subtypes of the virus that have contaminated them, and the species of feathered creatures that these infections have infected have all increased over the previous ten years. The number of HPAI A (H5N1) infection episodes in wild birds and poultry increased noticeably between 2004 and 2006. A variety of H5 and H7 infection subtypes, as well as H3, H5, H6, H7, and H9 infection subtypes, were kept an eye out for animal events between 2013 and 2021.[9]

Since 2020, HPAI A (H5) flare-ups in wild birds of prey and poultry have become more widespread. More assaults were reported in 2020-2021 than combined in the previous four years. In 2020, several H5N8 flare-ups were documented in Europe, Africa, and Southeast Asia. HPAI occurrences began in 2021.

In addition, poultry HPAI A (H5N2) infection outbreaks were documented in Southeast China concurrently with H5N6 infection outbreaks in Asia, namely in China and Vietnam. Numerous clades of A H5N1 infections have been in circulation since 2003, including one that was introduced to the United States in 2014 by wild birds and persisted there until 2016. [9]

There will be 2,240 wild birds found in 45 states and 519 counties in the United States alone by September 14, 2022. In addition, in the United States, highly pathogenic avian influenza A viruses were found in backyard and hobbyist flocks, commercial poultry, and wild aquatic birds in January 2022. Since 2016, the H5 virus has not been detected in the United States. Some virus specimens have been subjected to preliminary genetic sequencing and RT-PCR testing, both of which have revealed that these viruses are HPAI A (H5N1) viruses that are members of clade 2.3.4.4b.[9]

Poultry

According to WOAH, the predominant HPAI A (H5) virus subtype causing poultry outbreaks worldwide from late 2021 to early 2022 is A (H5N1). New HPAI A (H5N1) virus poultry outbreaks were reported in Africa (Niger), Europe (Germany, Russia, Sweden, Denmark, and Portugal), and Asia in December 2021 (Israel, Japan, Korea, and Vietnam). Most notifications in wild birds across multiple countries and regions suggest that the virus may have been introduced and spread via uncontrolled bird migration.[6-8,10]

The primary instance of a goose/Guangdong/1/96-lineage H5 HPAI infection inside the Americas since June 2015 was checked by the later disclosure of an H5N1 HPAI outbreak in Newfoundland, Canada. This demonstrates that wild birds are the disease's primary global transmission source. Concern for the well-being of wild birds has been sparked by an unprecedented number of outbreaks that have resulted in thousands of deaths in Israel and the United Kingdom. The increased number of notifications reflects the seasonal pattern in HPAI cases over the year. The spread of HPAI is predicted to increase in several regions over the next few months based on this established pattern.[6-8]

Since June 2015, the later discovery of an H5N1 HPAI infection in Newfoundland, Canada, has been the primary instance of a goose/Guangdong/1/96-lineage H5 HPAI infection in the Americas. This demonstrates that wild birds are the disease's primary global transmission source. Concern for the well-being of wild birds has been sparked by an unprecedented number of outbreaks that have resulted in thousands of deaths in Israel and the United Kingdom. Over 246 million poultry were slaughtered by HPAI A viruses between 2005 and 2020, with peaks in 2006 and 2016. According to WOAH, between the peak years of 2006 and 2016, there was an HPAI A virus outbreak in about a quarter of the world's nations.[6-8]

Warning sirens are sounding across the continent about an unstoppable avian flu outbreak, which farmers fear will result in poultry farm bans in vulnerable wetland areas. In the Netherlands, the most severe attack in history has resulted in the culling of over 3.7 million chickens, ducks, and turkeys.[10] In France, where duck breeding is widespread, the government reported that 16 million farmed birds had been destroyed, with farmers' livelihoods collapsing "like a house of cards". Henk Staghouwer, the Dutch environment minister, admitted earlier this year that bird flu was now "unavoidable" in a country where water covers 19% of the surface area. Since October 2021, there have been 66 outbreaks, with a total of 77 by August 2022.[6-9]

Humans

The avian flu Type A viruses, or bird flu viruses, rarely cause human infection; some bird flu viruses have done so in the past. The severity of human illnesses brought on by bird flu virus infections has ranged from no symptoms to minor fatal ailments (such as eye infections and upper respiratory symptoms). Most human infections with bird flu viruses have happened following close or extended unprotected contact (*i.e.*, not donning gloves, respiratory protection, or eye protection) with sick birds or places touched by their saliva, mucous, or feces.[11]

Bird flu viruses can infect people when they come into contact with their eyes, nose, mouth, or inhale. Flu can occur if a person breathes in a virus in the air (in droplets or dust) or touches their mouth, eyes, or nose after touching something with a virus. Rarely do bird flu viruses spread from one infected person to close contact, and they do not cause other human infections. Human respiratory illnesses have been caused by five subtypes of bird flu viruses (H5, H6, H7, H9, and H10).[11]

Europe: the largest epidemic of bird flu

The European Commission claims that this season's HPAI outbreak is the biggest in the continent's history. During the 2021/2 season, there were 2,398 outbreaks in 36 European nations, result-

ing in the culling of 46 million birds from affected establishments. In addition, 168 instances of highly pathogenic avian flu in confined birds and 2,733 cases in wild birds were reported. According to reports from 28 EU/EEA countries and the United Kingdom, 750 highly pathogenic cases of avian influenza virus were detected in poultry, 410 in the wild, and 22 in captive birds between March 16 and June 10, 2022.[12]

The worst affected country is France. France has experienced the worst poultry outbreaks, accounting for 68% of all cases recently, while Hungary accounted for 24%. No other EU nation achieved more than 2%. The Netherlands - 98, the UK - 48, and Germany - 158, however, had the highest number of wild bird detections among 410 in total. The HPAI (H5) virus has been persistent in wild bird populations in Europe since the 2020-21 epidemic wave, according to the paper titled "Avian Influenza Overview – March-June 2022." Hence, poultry farmers can anticipate it to be present throughout the year, with the highest risk in the autumn and winter months.[12,13]

Antarctica and beyond - recent updates

On Thursday, 11th Jan 2024, it was proven for the first time that mammals in the sub-Antarctic were infected with HPAI. Specialists from the world-famous Animal Plant Health Agency (APHA) in the UK discovered the disease in elephants and fur seals on the island of South Georgia. In October 2023, following the deaths of multiple brown skuas, HPAI was initially suspected on Bird Island, off the northwest coast of South Georgia. It is most likely migrating birds from South America that have carried the virus, according to sequence analysis of affected birds' tissue.[14-16]

Recently, in November 2023, the Scientific Committee on Antarctic Research (SCAR) discovered that gentoo penguins, a species that is indigenous to sub-Antarctic islands, may have had 35 possible instances of H5N1 avian influenza virus. Of those cases, 14 have been confirmed using PCR testing. As it got ready "for a large-scale outbreak," the Falkland Islands government reportedly discovered "over 200 dead chicks alongside a handful of adults" and was awaiting test results from rockhopper penguins.[14-16]

Recently, Alaska reported the first-ever example of a polar bear (*Ursus maritimus*) passing away from HPAI. After the body was discovered in the farthest northern town of Utqiagvik in October 2023, officials with the state's Division of Environmental Health verified the death in December 2023. According to experts, the bear scavenged on infected birds and then got the illness. An additional setback to polar bear populations already threatened by climate change could come from bird flu. It is possible that polar bears contract bird flu after consuming bird carcasses contaminated with the lethal H5N1 strain. The case was not surprising because the fatal virus has previously been discovered in black bears (*Ursus americanus*) and brown bears (*Ursus arctos*).[14-16]

The environment in which polar bears reside makes it challenging to monitor for the virus in them. Because polar bears are solitary animals, experts say there is little chance of bear-to-bear transmission. However, the fact that melting sea ice has forced some subpopulations of bears to eat more seabirds raises serious concerns about increased virus exposure. Polar bears may be more susceptible to avian flu as a result of pollution. Because anthropogenic chemicals build up in the high-fat diets of the animals, they have a significant effect on the species.[14-16]

Human infection with Avian Influenza A (H5) viruses – latest updates

Two new instances of avian influenza A (H5N1) virus infection in humans were reported to WHO in the Western Pacific Region between February 02 and February 08, 2024. A three-year-old boy from the province of Prey Veng was the first instance. He went to the hospital on January 16 after exhibiting symptoms on January 1. A 69-year-old man from the province of Siem Reap was the second instance. He went to the hospital on January 23 after exhibiting symptoms on January 21. There was exposure to diseased poultry in both cases. There isn't any proof that the two occurrences are related epidemiologically. Since then, both situations have improved.

Prevention and control

Monitoring and reporting outbreaks

The first line of protection against the avian flu is early disease detection and declaration, which enables quick action. However, accurate warning systems must be implemented first to control and prevent the disease. Due to the rapid spread of avian influenza across regions, countries must promptly report cases to anticipate and prepare for new outbreaks.

It is a disease on the WOAH list. National veterinary authorities are, therefore, obligated to report the following: i) regardless of subtype (domestic or wild), any high-pathogenic avian influenza viruses found in birds; ii) all viruses with low pathogenicity have shown natural transmission to humans with severe consequences in domestic or captive wild birds.

Using voluntary reports on wildlife diseases not on the WOAH list, nations can report LPAI viruses found in wild birds. In addition, nations may voluntarily declare that high-pathogenic avian influenza does not exist on their territory.[1]

Preventing avian influenza at its source in animals

Robust biosecurity procedures and exceptional cleaning standards are necessary to prevent bird flu outbreaks due to the virus's inherent resilience and highly contagious nature. A few crucial precautions include: i) separating poultry from wild bird life; ii) cleaning poultry housing and equipment, iii) notifying the Veterinary Administrations of illnesses and deaths in the flock.[1]

Control methodologies and remuneration for ranchers

When a poultry disease is discovered, it is often contained, controlled, and eradicated as quickly as possible through a plan to separate affected animals and close relatives.

Movement restrictions, improved hygiene and biosecurity, selective eradication of infected poultry, improved biosecurity, and effective surveillance should all significantly reduce environmental viral contamination. Whether or not vaccination is a component of the overall plan, these safety measures must be followed. Additionally, several financial compensation schemes are available worldwide for farmers and manufacturers who have lost animals due to the necessary animal separation demanded by national veterinary specialists; regrettably, they are yet to be available in some countries. The WOAH motivates its members to develop and abandon compensation schemes as a crucial driving force.

The WOAH motivates its members to establish remuneration plans as a crucial means of supporting the early detection and public disclosure of instances of animal diseases such as the avian flu.

Banning chicken farms

Last year, a complete ban on farms in "water-rich" areas was one solution, but it was met with skepticism.

Derk Boswijk, MP and spokesman for the Christian Democratic Appeal on agriculture, said: "You can't just draw a line through businesses full of people trying their best to protect poultry", and "Vaccinations and the culling of poultry are the most crucial methods of defense against bird flu". The poultry industry can only be protected from the "invisible enemy" by a vaccine.[10]

Vaccination

It may be advised to vaccinate poultry in certain circumstances. However, this action should not be viewed as a long-term answer to the problem of avian influenza control. Instead, it must be combined with other health measures as part of an all-encompassing disease control plan. Its goal is to support infection management until the infection may be eliminated using different techniques.

Immunization has its benefits, but it can also hide contaminants that haven't been around for a while and make it more challenging to monitor circulating strains. It must be based on territorial and national hazard assessments that evaluate the global context, potential financial repercussions of recent occurrences, and the Veterinary Services' capacity to properly manage immunizations. The Veterinary Specialist for each country determines vaccine schedules.[17,18]

Future challenges and recommendations

The HPAI H5N1 virus continues to pose a serious worldwide threat because of its extensive distribution and high fatality rates. The known human instances of HPAI H5N1 infection and the current outbreaks in a number of animal species highlight the continued worries about transmission and possible human infections. The genomic differences found in HPAI H5N1 strains highlight the necessity for ongoing study and attention in order to comprehend the virus's changing nature. Future trends must be addressed with a proactive strategy because of the persistent issues presented by HPAI H5N1. To properly control the virus's transmission and effects, a number of crucial areas need concentrated attention and study.

Monitoring and early detection to quickly detect and track newly emerging strains of avian influenza, particularly those with zoonotic potential, it is imperative to fortify worldwide monitoring networks. Ongoing observation of wild bird populations, domestic poultry, and high-risk regions can offer early indicators of viral transmission and enable prompt remedial actions.

Genetic variants and viral evolution: the fact that HPAI H5N1 strains exhibit genetic variants emphasizes the necessity of continuing genetic surveillance and investigation. Understanding the virus's reassortment events and mutations can shed light on its pathogenicity, dynamics of transmission, and capacity for evolution.

Cross-species transmission and reservoirs, concerns regarding the creation of viral reservoirs, and enduring hazards to both people and animals have been raised by the cross-species transmission between mammalian species and bird populations that has been reported. Future studies should examine the processes and elements that promote cross-species transmission, focusing especially on locating possible reservoir species and comprehending the dynamics of transmission in these populations.

Vaccines and preventive measures: it is crucial to develop and implement efficient vaccinations against HPAI H5N1. The main goals of the research should be to enhance vaccination effectiveness, extend protection against a wider range of virus strains, and streamline vaccine delivery methods.

Antiviral medicines and treatment techniques, in order to control HPAI H5N1 infections, more research into antiviral medicines and treatment techniques is necessary. The development of new antiviral drugs with broad-spectrum protection against avian influenza viruses needs to be the main goal of research. Furthermore, lowering the severity of illness and enhancing patient outcomes can be achieved by researching host immunological responses and creating immunomodulatory treatments.

International cooperation and preparedness, in order to confront the worldwide issues brought on by HPAI H5N1, it is imperative that nations strengthen their international collaboration and information exchange. Robust communication networks, surveillance data exchange, and coordinated response activities will help enable prompt reaction, early containment, and efficient management of epidemics.

Conclusions

Although the COVID-19 pandemic and the "post-pandemic fatigue" that followed have mainly diverted attention from other infectious disease dangers, we still need to exercise caution to prevent the emergence of an even more severe avian influenza pandemic. For a considerable amount of time to come, H5N1 is probably going to pose a major risk to both human and animal health. It is obvious that efforts to contain the present H5N1 pandemic are warranted. If not, public health will still be faced with challenges because of the accompanying pandemic danger posed by H5N1.

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