Zoonotic Challenges of Avian Influenza Strain H_5N_1

Shamreza Aziz[1,*], Heyran Gasimova[2], Ayah Talal Zaidalkilani[3], Ammar AL-Farga[4] and Shahid Hussain Farooqi[5]

[1]Department of Epidemiology & Public Health, University of Veterinary & Animal Sciences, Lahore, Pakistan
[2]Nakhchivan State University, Faculty of Natural Sciences and Agriculture, Department of Veterinary Medicine, Nakhchivan, Azerbaijan
[3]Faculty of Pharmacy and Medical Sciences, Department of Nutrition, University of Petra, Amman, Jordan
[4]Department of Biological Sciences, College of Science, University of Jeddah, Jeddah, Saudi Arabia
[5]Department of Clinical Sciences, KBCMA College of Veterinary and Animal Sciences, Narowal, Sub-campus UVAS-Lahore, Pakistan
*Corresponding author: shamrezaaziz@gmail.com

Abstract

As an important zoonotic threat, Avian influenza viruses have gained a vital position as this virus is capable of infecting a large number of avian species including wild birds and poultry, animals, and also humans. Due to the zoonotic potential of avian influenza viruses especially H5N1, many epidemics and pandemics have occurred, especially flu outbreaks in human populations globally. The transmission of the virus in humans can occur through direct or indirect contact with the infected bird or animal. The major reservoir hosts for almost every subtype of influenza are domestic birds. The control strategies of the deadly virus include enhancement of the surveillance system for early detection of the virus that will help the policy makers to develop interventions according to the situation. The monitored use of vaccines and antivirals is another way to prevent the virus growth. This chapter will describe the zoonotic potential of avian influenza H5N1 virus and different ways through which this virus can be controlled.

Keywords: Avian influenza virus, H5N1, Wild birds, Poultry, Surveillance systems, Antivirals, Vaccines

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Introduction

Avian influenza virus (AIV) poses major threats worldwide to public health especially to humans and animals health over the past decade (Govindaraj et al., 2018; Szablewski et al., 2023). Thousands of cases of avian influenza virus outbreaks which include almost 34 subtypes of the virus were reported in the animals during the time span of 2013 to 2022. These outbreaks result in the loss of more than 325 million birds (Szablewski et al., 2023). The aftermath of a panzootic of 2020 to 2023 show that more than 48 different species of mammals were infected by H5N1 (avian influenza virus strain) naturally. The ability of the AIV to adapt to different animal hosts enhances the chances of zoonotic spread of AVI in humans (Morens et al., 2023; Plaza et al., 2024). Different AVI subtypes are more dangerous to humans and possess life threatening impacts on human health for instance H5N1 and H3N8 outbreaks in 2023. The overall disease burden of AIV is underrated which may be due to the unavailability and less efficiency of the diagnostic tools for the detection of AIV and another reason is the insufficient surveillance at the level of human and animals' interactions (Jimenez-Bluhm et al., 2023). The chemistry of AIV shows that it is a single stranded, negative sense RNA virus having eight gene segments. The gene segments consist of haemagglutinin and neuraminidase, while the other six are internal genes (Figure 1). The basic property of classification of AIV is the presence of surface proteins including haemagglutinin and neuraminidase (Dey et al., 2023). The emergence of pandemic strains of AIV is majorly due to the evolution of the virus which is ultimately the reason for the deaths of 50 million people around the world (Webster et al., 1993; Smith et al., 2009). Studies suspect that some strains of AIV including H5, H7, H9, and H10 may be the reason for specific spillover events resulting as a cause for major pandemics in future (CDC, 2023a; Lu et al., 2023). The H5N1 virus is a subtype of AIV which belongs to the viral family Orthomyxoviridae. The genomic structure of H5N1 consists of single stranded, negative sense RNA molecules having a length of approximately 13.5 kilobases. There are eight segments in the genome of the H5N1 virus, each segment encoded for distinct proteins which play different roles in the life cycle of the virus (Sautto et al., 2018). The main reason for the high spread rate of AIV is due to a new genotype of H5N1 which quickly spread in wildlife (Dhanasekaran et al., 2023). It was first confined to Asia only but now it is also present in Europe, Africa (Fusaro et al., 2019; Fusaro et al.,2024; Olawuyi et al., 2024), North America (Caliendo et al., 2022; Youk et al., 2023), South America (Jimenez-Bluhm et al., 2023; Leguia et al., 2023), and the Antarctic (Banyard et al., 2024).

Evolution of HPAI H5N1 Virus

Over the past six decades, H5N1 has shown distinguished advancements. The initial outbreak of H5N1 in poultry birds was in Scotland in 1959 and after that in Hong Kong, H5N1 virus took lives of six individuals among those 18 individuals who came in contact with the virus in 1997. This incident in Hong Kong highlights the identification of a strain of H5N1 virus in humans which prominent the importance of H5N1 in the world (Liu et al., 2023). After a temporary pause, in 2003, H5N1 resurged and persisted till date causing disease in avian populations in different continents including Europe, Asia, and Africa (Krammer & Schultz-Cherry, 2023). H5N1 expanded geographically and spread across not only East Asia but also in South and West Asia, and North Africa, affecting both wild and domestic avian populations in Europe (Verhagen et al., 2021). The increasing spread of H5N1 outbreaks in wild birds, poultry, and domestic avian populations indicate the potential transmission of virus in humans (Aznar et al., 2023; Lv et al., 2023).

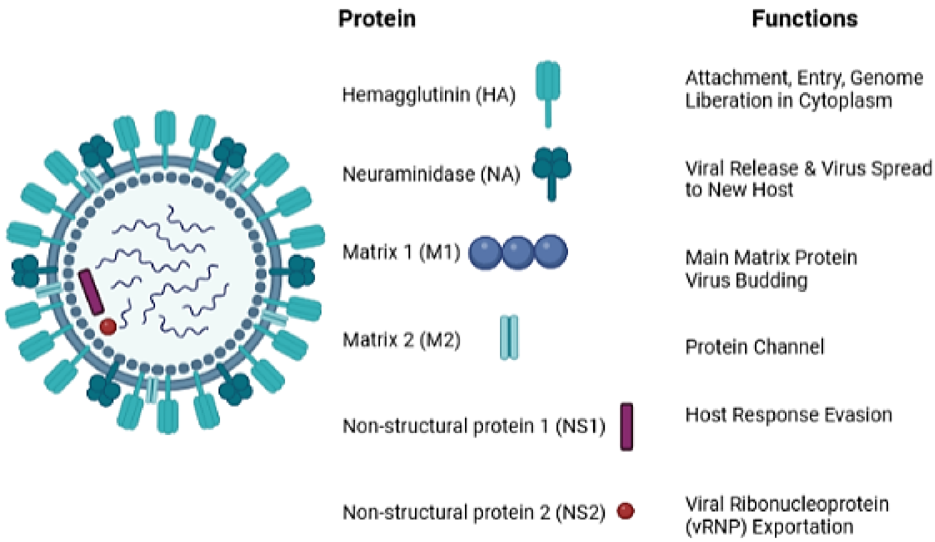

Fig. 1: Structure of Avian Influenza H5N1 Virus explaining important viral components and their functions.

Transmission and Reservoir of H5N1

The primary reservoir of AIVs, especially subtypes H1 to H16, are aquatic bird species as virus is naturally prevalent in them (De Marco et al., 2023). Before 2005, the transmission of H5N1 virus was less common from poultry to wild avian species. After that a shift has occurred, entering a new phase in the epidemiological dynamics of H5N1 virus in wild avian species (Charostad et al., 2023). Other than avian species, H5N1 has been naturally isolated from a large number of different animal species such as dogs, cats, seals, foxes, minks, otters, leopards, skunks, tigers, pikas, lions, polecats, raccoons, porpoises, pigs, bears, and fish, etc. (Abdelwhab & Mettenleiter, 2023). AIVs present in the intestinal tract of wild birds, shed by these birds through different routes including saliva, feces, and nasal secretions (Dey et al., 2023). H5N1 virus is transmitted to humans only when humans come in direct contact with infected birds. The H5N1 virus can travel within airborne particles for approximately 10 m. In macroscopic particles containing viral RNA, the virus can travel up to 80 m (Mehta et al., 2018). The factors which play a significant role in influencing the dynamics of viral spread of H5N1 virus include indirect contact with wild birds and efficient biosecurity measures (James et al., 2023). The detection of viral RNA of H5N1 from environmental specimens for example dust swabs increase the threat of potential airborne transmission of the virus through the inhalation process while the virus moves in the body of the host (Horm et al., 2012). The H5 subtypes of AIV do not affect humans majorly as the virus cannot grow in the upper respiratory tract which results in less human to human transmission of the deadly virus. But few strains of the virus have the ability to cross the barriers between species and cause a spectrum of infection in humans including mild flu-like symptoms to severe disease which may end up to death of the individual (Krammer & Schultz-Cherry, 2023; Scheibner et al., 2023). The H5N1 virus has the ability to cross the barrier of placenta and causes the infection of the fetus (Le et al., 2019). The transmission of virus from human to human is very rare but the transmission from birds to human is designated as uncommon (Figure 2) (Gandhi et al., 2022).

World Health Organization Plan for H5N1 Pandemic

Six stages of a global plan for the preparedness of pandemic influenza has been defined by the World Health Organization, this plan also includes suggestions for the prevention and control measures which should be adopted before and during the period of pandemic (WHO, 2011). The first two stages of this plan comprises an interpandemic period during which there are no new subtypes of influenza virus detected in humans but there is a chance of induction of human disease possessed by a circulating animal influenza virus subtype. The next three stages are called as period of pandemic alert, phase or stage three in which there are detectable cases of human infection caused by a new subtype of AIV but the spread is limited in human to human transmission. In the fourth stage, the human to human transmission occurred only in small clusters but in the fifth stage, the transmission among humans occurs in larger clusters. The stage six is coded by a sustained transmission of a novel flu subtype around the world (Proença-Módena et al., 2007).

Strategies for Prevention and Control

The mutations and recombinations of H5N1 virus show that this virus is a potential threat to public health which signifies the need of preparedness against the deadly virus. This situation emphasizes the need to focus on the development of tools and their application for example vaccines, therapeutics, and reagents used for diagnostic purposes. There is also a need for enhancement in the field of surveillance and early warning systems. The concept of "One Health" provides a way to develop a comprehensive strategy for the purpose of control of influenza virus while focusing on interconnectedness of animals, humans, and the environment (Wang et al., 2024).

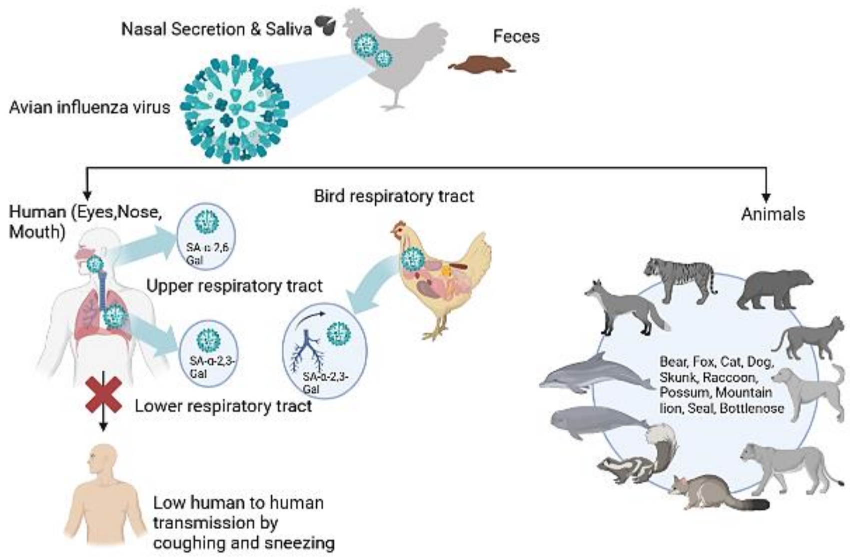

Fig. 2: Transmission of AIV from poultry to humans and other animals.

Improved Surveillance Systems

In areas where the detection of virus in animals has occurred, the surveillance of human influenza virus should be increased (Branda et al., 2024). The surveillance systems used for the detection of avian influenza in humans include Enhanced surveillance of severe avian influenza virus in hospitals and targeted surveillance, in Europe during the time period of 2023 to 2024 (EFSA, 2024). The surveillance program should cover all the domestic mammals (fur animal farms), wild birds, poultry birds, and captive birds. Furthermore, there is a need for well-organized surveillance systems that should be implemented in areas where there is a chance of an increase of H5N1 virus in mammal species as there is an incredible increase in cases in recent years (Enetwild Consortium, 2024). International guidelines should be developed and implemented to standardize surveillance systems for animals at high risk of developing influenza virus such as wild terrestrial and aquatic mammals. To thoroughly observe the evolution of H5N1 virus in different animal species, it is necessary to enhance and strengthen the international network of laboratories to confirm the rapid detection and analysis of virus and sharing the information globally. Data should be available to accessible platforms and interpretation of the data should be done as soon as possible after the detection of the first human case. This approach will help in advancement of knowledge on pandemic and zoonotic issues related to AIV (Alm et al., 2024).

Quarantine of Exposed Individuals

The term quarantine is described as the containment of live birds to secure holdings for a specific time period after they move across the countries, where the birds are observed closely to check for any sign of disease. Quarantine is one of the possible ways to control and prevent a disease from spreading in the surrounding area. But it is not considered as a viable way to prevent a disease as it is not practical to apply a quarantine approach during the movement of commercial poultry mainly because of the time period it requires (Capua & Cattoli, 2013). In the case of humans, one a person is exposed to the infection, self-isolation and testing is important during the first 10 to 14 days after the contact (Enkirch et al., 2005).

Production of Novel Vaccines

The vaccines available for the seasonal influenza do not prevent the spread of AIV in humans around the world. In case of emergency, several countries in the world have been preparing vaccines against H5N1 virus. In the United States, three vaccines have been prepared with or without adjuvant to be used against H5N, which can be used in any pandemic situation (CDC, 2023b). It has been shown that in adults (human) having three licensed adjuvanted vaccines against H5N1, they have produced cross-neutralizing antibodies against the H5N1 virus circulating in blood (Khurana et al., 2024). While individuals who only received two licensed vaccines, produced cross-reactive binding and cross-neutralizing antibodies against the virus. In addition to these licensed vaccines, a monovalent messenger RNA lipid nanoparticle vaccine has been developed and its use in animal models reveal the protective nature of the vaccine against the virus. The best advantage of this nanoparticle vaccine is that it can be produced rapidly (Furey et al., 2024). Vaccination in poultry against H5N1 is one of the best ways to enhance the process of control of viral spread (Thompson et al., 2024). The fact that vaccination in poultry can be a risk for transmission of virus in humans is still under discussion (Yamaji et al., 2020). If the vaccines are not administered properly it can be dangerous and may become a barrier in the control and eradication programs of the virus.

Prevention by Antivirals

As soon as symptoms appear in humans, treatment should be started with antivirals as AIVs are susceptible to antivirals. It has been described in many studies that even after the 48 hours of onset of symptoms, treatment with antivirals helps to lower the chances of mortality in patients with severe infection (Muthuri et al., 2013). Another technique used for the treatment after an individual has been exposed to infected animals is post exposure prophylaxis. The use of antivirals in poultry birds, farmed animals, and other mammalian species during an outbreak of this virus is not recommended as it raises various concerns such as development of different strains of virus which may be drug resistant. This situation may result in reducing the treatment potential in an individual and also the efficiency of the treatment options available may decline during the time of a pandemic (Parry, 2005).

Recommendations and Interventions

According to recent data the severity of the H5N1 virus pandemic in the future is not clear yet but the fatality of the virus is much lower in recent years as compared to outbreaks of the deadly virus in the past. Different areas need to be focused while planning the control and prevention of the virus. The surveillance systems should be strengthened for rapid identification of the cases of the virus and also monitored the emerging strains of virus which may or may not have zoonotic potential (Domańska-Blicharz et al., 2023). Continuous surveillance of wild birds is needed especially in the areas with high risk of emerging disease. This will help the policy makers to design policies and interventions related to control of the virus. The genomic study of the virus is very important which will help to understand the pathogenicity of the viral strains, their pattern of transmission and mutations in the genomic structures of the viruses subtypes (Fauci, 2006). The cross species transmission of the influenza virus is a major concern and there is a need to study the potential factors and events which are involved in the process of the development of cross species transmission of the virus. Vaccines are one of the vital weapons against the fatal virus, research should be done to enhance the efficiency of the vaccines to work against a larger number of strains of virus and protected delivery of the vaccines (Stokstad, 2022). There is a need for exploring and manufacturing broad spectrum antivirals to be used against different subtypes of influenza viruses. This may help in improving the health status of the individual and generate enhanced outcomes of the therapy.

Conclusion

Avian influenza strain H5N1 has a devastating effect on wild birds, farmed animals, domesticated birds and animals, mammals all around the world with its zoonotic spread in humans and globally. The virus has a variety of reservoir hosts to spread rapidly and cause a high mortality rate. As it was first confined to birds and animals only but in recent decades, the virus went through several mutations as many cases of infection have been seen in humans. Different techniques have been used to stop the spread of the virulent virus and many strategies of control have been used successfully such as vaccinations and proper use of antivirals. But antivirals may be save to use if only prescribed by a doctor and the course of treatment is complete as it can give rise to another potential risk of resistance against these antivirals in the viruses. Rapid action is needed to fully control the virus from causing more drastic impact on animal, birds, and human health.

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