Chapter

Prologue: Avian Influenza - An Overview from Endemic to Pandemic

Muhammad Abubakar, Abdullah Iqbal, Shumaila Manzoor and Kashif Saleemi

1. Introduction

Avian influenza also called as bird flu is an acute, contagious disease caused by Influenza A virus. Birds of order *Anseriformes* and *Charadriiformes are reservoir hosts of* influenza A viruses [1]. These viruses have the ability to infect many mammal species such as horses, pigs, cats, dogs, and humans. Influenza A viruses are negative-sense single-stranded RNA viruses with enveloped structure [2]. Influenza A viruses have shown high antigenic variability due to antigenic drift and shift phenomena. These mutation methods result in the emergence of new variants. These new variants can have different host ranges, mortality rates, morbidity rates, and patterns of infection [3].

Influenza A viruses are further divided into highly pathogenic avian influenza (HPAI) or low pathogenic avian influenza (LPAI). Up till now, only some H5 and H7 subtypes have been confirmed as HPAI viruses. However, it is reported that some LPAI H5 and H7 subtypes can mutate to HPAI due to antigenic shift and drift phenomena [4].

Some influenza A viruses have a zoonotic potential and can cause a pandemic hazard to human population. Outbreaks of HPAI in poultry have affected the poultry industry worldwide [5]. In 2002, due to HPAI outbreaks, Chile suffered a loss of almost $31 million USD. In 2003, the HPAI outbreak resulted in the loss of more than $3387 million USD in Indonesia and $55 million USD in Vietnam. Similarly, in 2012, Mexico suffered an economic loss of approximately $475 million USD due to HPAI outbreaks [1].

2. Influenza A virus

Influenza A viruses belong to family *Orthomyxoviridae*. Influenza A viruses are single-stranded negative-sense RNA viruses having genome with 8 segmentation that encode for 10 viral proteins: hemagglutinin (HA), neuraminidase (NA), matrix proteins (M1 and M2), nucleocapsid protein (NP), nonstructural proteins (NS1 and NS2), and polymerase proteins (PB1, PB2, and PA) [6].

Influenza viruses are further classified into subtypes on the basis of their hemagglutinin (HA) and neuraminidase (NA) genes [7]. A total of 18 HA and 11 NA types has been identified up till now. On the basis of phylogenetic analysis and sequence homology of the HA gene, these viruses are clustered into virus clades [4].

A nomenclature system for influenza viruses has been established by the World Health Organization (WHO) and FAO. This system contains the type of influenza, the first place of isolation of virus, strain, and year of isolation. For example, A/Hong Kong/156/97 would be interpreted as influenza type A, isolated in Hong Kong, strain 156, and isolated in 1997 [1].

Hemagglutinin mediates binding of the virus to sialic acid receptors at the cell surface. Neuraminidase plays its role in the detachment of the virus from the cell surface [8]. A specific type of hemagglutinin binds with a specific type of cell surface that further clarifies the difference host range for different influenza virus types [9]. Mutation of genes coding hemagglutinin and neuraminidase affects the transmission of the virus along with the alteration of the host range [10].

3. Avian influenza in birds

Healthy birds can become affected by the avian influenza virus by direct contact with an infected bird. Avian influenza virus has the capability to infect more than 100 species of birds worldwide [11]. Reservoir hosts of the virus include waterfowls and shorebirds. Low pathogenic avian influenza infection does not cause any clinical disease. But, the virus survives in the host and sometimes mutates to produce highly pathogenic avian influenza virus [12].

Some species of birds are more disease resistant than others. For example, domestic poultry is more susceptible to H5N1 HPAIV infection than wild ducks. Wild ducks spread the disease to other susceptible hosts [2].

HPAI infection in susceptible birds can cause systemic infection including damage to the nervous and circulatory system that ultimately leads to death. HPAI virus inhabits and multiplies in the respiratory and gastrointestinal tracts [13]. Clinical signs and symptoms of HPAI infection in birds include loss of appetite, diarrhea, nasal discharge, respiration problem, misshapen eggs, ataxia, and incoordination [10]. The maximum mortality rate in poultry due to HPAI infection can be up to 95%. Confirmatory diagnosis of HPAI can be done by performing PCR analysis of tracheal or fecal swabs of suspected birds [14].

4. Transmission of disease from birds

Waterfowls and shorebirds are natural reservoirs of the influenza virus, and these birds spread the virus to domestic poultry by contaminating the water source, feed, and housing of domestic poultry [15]. Influenza virus secreted in feces can survive up to 35 days at 4°C. Aerosol transmission of the virus is also possible. Indirect contamination via shoes, clothing, and contaminated feathers is also reported [2].

Interspecies transmissions of the avian influenza virus are also possible. In Europe and the United States, H1N1 and H3N2 are commonly prevalent in swine population, and outbreaks have been reported by the transmission of these viruses to susceptible turkeys and chickens [11]. In another case, an outbreak in turkey flock has been reported in Canada from a poultry worker having a respiratory problem [1].

5. Transmission of disease to humans

In most cases of human infection with the influenza virus, the previous contact with alive or dead bird was recorded. People who are involved with poultry at any

level are more prone to exposure than other people [16]. Meat workers, poultry farmworkers, and bird sellers are under constant threat. Veterinarians are also at higher risk due to their contact with different types of birds [17]. Direct human to human transmission is also possible at mass gatherings such as airports, concerts, and funeral ceremonies [18].

6. Prevention and control

For the control of avian influenza in commercial and rural poultry, risk management is the most important point [18]. Implementation of good agricultural practices such as strict biosecurity measures, training of poultry workers, availability of non-contaminated water, disinfection of equipment, and decontamination of farm premises before the introduction of the new flock can decrease the chance of an outbreak of AI [16].

In case of an outbreak, rapid culling and depopulation are recommended. Rapid culling can reduce the spread of the virus and minimize economic loss [19]. Poultry and their products infected with HPAI are banned to enter the food chain in developed countries [1], whereas in developing countries, HPAI-infected meat and products are consumed as feed after cooking at high temperatures. The use of effective vaccination can limit the H5N1 HPAI virus spread [18].

7. One health perspective

The first influenza A virus pandemic in humans was recorded almost a century ago, in 1918, which resulted in the death of around 20–50 million humans worldwide [20, 21]. So far, three other pandemics of influenza A virus in humans that have caused considerable loss include the 1957 H2N2 pandemic, the 1968 H3N2 pandemic, and the 2009 H1N1 pandemic [22]. From East Asia to Southeast Asia, sporadic human infection of H5N1 viruses was reported in 2003–2004 along with outbreaks in the poultry [21].

H5N1 viruses have been reported from domesticated poultry and wild birds in Asia, North Africa, Central Africa, and Europe [23]. The transmission of HPAI H5N1 viruses from poultry to humans was first documented in 1997 in Hong Kong. Some subtypes of avian influenza virus such as H5, H7, H9, and H10 have the capability of interspecies transmission [18]. According to the World Health Organization, the total confirmed human cases of H5N1 infection to date are 860 with 454 fatal cases [24]. In 2013, a LPAI H7N9 virus caused an outbreak in China with a 36% case fatality [25]. Influenza viruses are a permanent threat for humans as well as birds.

Author details

Muhammad Abubakar[1*], Abdullah Iqbal[2], Shumaila Manzoor[1] and Kashif Saleemi[3]

1 National Veterinary Laboratory, Islamabad, Pakistan

2 Department of Microbiology, Faculty of Biological Sciences, Quaid-i-Azam University, Islamabad, Pakistan

3 Department of Pathology, Faculty of Veterinary and Animal Sciences, University of Agriculture, Faisalabad, Pakistan

*Address all correspondence to: hayee42@yahoo.com

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