

Avian Influenza (Bird Flu) in Humans: Recent Scenario

¹Prajapati Hetal Ritesh, ²Brahmkshatriya Pathik Subhashchandra
³Vaidya Hitesh Bharatbhai and ⁴V. Thakkar Dinesh

¹A.R. College of College of Pharmacy, Sardar Patel University, Vallabh Vidyanagar, Gujarat, India

²L.M. College of Pharmacy, Gujarat University, Ahmedabad, Gujarat, India

³Institute of Pharmacy, Nirma University of Science and Technology, Ahmedabad, Gujarat, India

⁴Atmiya Institute of Pharmacy, Kalawada Road, Rajkot, Gujarat, India

Abstract: There are four major types of influenza viruses: A, B, C and Thogotovirus. Only influenza A viruses are further classified into subtypes on the basis of the two main surface glycoproteins hemagglutinin (HA) and neuraminidase (NA). Influenza A subtypes and B viruses are further classified by strains. Avian influenza virus can be distinguished as Low Pathogenic Avian Influenza (LPAI) and Highly Pathogenic Avian Influenza (HPAI) forms based on genetic features of the virus and the severity of the illness they cause in poultry. Influenza virus A is usually responsible for bird flu (Avian influenza) but same time also responsible for pandemics of influenza in humans. Out of hundreds of strains of avian influenza A viruses, only four are capable to produce infection in humans: H5N1, H7N3, H7N7 and H9N2. Out of these, highly pathogenic avian influenza, H5N1 strain is of greatest concern for human infection. This virus has affected poultry flocks and other birds in more than 50 countries. Total 309 laboratory-confirmed cases of avian influenza infection in humans have been reported to the World Health Organization between end of December 2003 to end of May 2007; out of which 187 deaths were confirmed. While human cases remain relatively rare and are largely the result of direct virus transmission from infected birds, a few cases of human-to-human transmission have been reported. But still there is a matter of great assurance that, H5N1 strain does not easily cross from birds to infect humans. Oseltamivir is the first orally active antiviral drug used in the treatment and prophylaxis of influenza A and B viruses provided that the treatment is started within 48 hours of onset of symptoms. The severity of disease and the potential for human-to-human spread has provided an urgent need to develop a human vaccine for avian influenza. Efforts to produce vaccines are under way.

Key words: Birds • Influenza • Avian influenza • H5N1 strain Highly Pathogenic Avian Influenza (HPAI) • World Health Organization • Prophylaxis • Pandemics

INTRODUCTION

Avian influenza is an infectious disease of birds caused by Influenza virus A genus of the Orthomyxoviridae family. Certain birds, particularly water birds, act as hosts for influenza viruses. Infected birds shed viruses in saliva, nasal secretions and feces. Fecal-to-oral transmission is the most common mode of spread between birds. Ducks have been reported to be asymptomatic carriers and duck products could be contaminated with virus. Other bird species, including domestic poultry, develop disease when infected with avian influenza viruses [1]. These viruses rarely affects humans and do not normally infect species other than

birds and pigs. However severe disease in human has now been reported with bird flue virus [2].

Types, subtypes and strains: Avian influenza viruses belong to the Orthomyxoviridae family of RNA viruses and are constituted of four types, Influenza virus A, B, C and Thogotovirus. Influenza A viruses are further divided into hemagglutinin (HA) and neuraminidase (NA) subtypes depending upon the cell surface antigens. There are 16 known HA and 9 NA subtypes. Many different combinations of HA and NA proteins are possible. For example, an H5N1 virus designates influenza A subtype that has a HA 5 protein and a NA 1 protein [3-5].

Influenza A viruses are further divided into two distinct groups on the basis of their ability to cause disease; Highly Pathogenic Avian Influenza (HPAI) and Low Pathogenic Avian Influenza (LPAI). Infection of HPAI viruses may result in 100% mortality in poultry as well as in humans while LPAI infections cause mild respiratory disease, depression and egg production problems in laying birds and very mild symptoms (e.g. conjunctivitis to influenza like illness) in humans [6, 7]. Infection due to influenza A H5 viruses have been documented among humans, sometimes causing severe illness and death. While H7 infection in humans is rare, but can occur among persons who have direct contact with infected birds. A few influenza A H9 infections in humans have also been reported. Influenza B and C are exclusively human viruses and able to produce epidemics and inapparent infections [8].

Mechanism of transmission of influenza viruses to humans: Influenza viruses are dynamic and are continuously evolving. They can change in two different ways, antigenic drift and antigenic shift. These viruses change by antigenic drift all the time, but antigenic shift happens only occasionally.

Antigenic drift occurs through point mutations in two genes that contain the genetic material to produce the main surface proteins, hemagglutinin and neuraminidase.

By this way antigenic drift produces new virus strains that may not be recognized by human antibodies to earlier influenza strains and infection with a new strain can occur.

Antigenic shift produces a novel influenza A virus subtypes in humans that was not currently circulation among people. Antigenic shift can occur either directly through animal-to-human transmission or through mixing of human influenza A and animal influenza A virus genes to create a new human influenza A subtype virus through genetic reassortment process. Thus influenza A viruses may responsible for a pandemics of influenza in humans [9, 10].

Threat of H5N1 in humans: Avian influenza viruses are normally highly species specific so that after infection to an individual species i.e. humans, birds, pigs, horses, seals; they stay to that species only and rarely spill over to cause infection in other species. Although avian influenza viruses usually do not infect humans, rare cases of human infection with these viruses have been reported since 1997 [11].

Of hundreds of strains of avian influenza A viruses, only four are known to caused human infections: H5N1, H7N3, H7N7 and H9N2. Out of these four strains, H5N1 has caused the largest number of detected cases of severe diseases and death in humans [5, 12].

Table 1: Cumulative number of confirmed human cases of avian influenza A/(H5N1) reported to WHO up to 31st May 2007 [13]

Country	2003		2004		2005		2006		2007		Total	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
Azerbaijan	0	0	0	0	0	0	8	5	0	0	8	5
Cambodia	0	0	0	0	4	4	2	2	1	1	7	7
China	1	1	0	0	8	5	13	8	3	1	25	15
Djibouti	0	0	0	0	0	0	1	0	0	0	1	0
Egypt	0	0	0	0	0	0	18	10	16	4	34	14
Indonesia	0	0	0	0	20	13	55	45	23	20	98	78
Iraq	0	0	0	0	0	0	3	2	0	0	3	2
Lao people's												
Democratic Republic	0	0	0	0	0	0	0	0	2	2	2	2
Nigeria	0	0	0	0	0	0	0	0	1	1	1	1
Thailand	0	0	17	12	5	2	3	3	0	0	25	17
Turkey	0	0	0	0	0	0	12	4	0	0	12	4
Viet Nam	3	3	29	20	61	19	0	0	0	0	93	42
Total	4	4	46	32	98	43	115	79	46	29	309	187

H5N1 type influenza A virus is of greatest concern for human infection because of following reasons [14]:

1. It can cause severe diseases in human.
2. The birds that survive infection excrete virus for at least 10 days, orally and through faeces, helping spread of the virus at poultry markets and also by migratory birds.
3. It mutates rapidly and seems to acquire genes from virus infecting other animal species.
4. The more humans get infection, the people can become infected both human and bird flu strains.

Of the human cases associated with the ongoing H5N1 outbreaks in poultry and wild birds in Asia and parts of Europe, the near east and Africa, more than half of those people reported infected with the virus have died. Total 309 cases of avian influenza infection in humans have been reported between end of December 2003 to end of May 2007; out of which 187 deaths were confirmed. But it is a matter of great assurance that, H5N1 avian influenza virus does not easily cross from birds to infect humans [13].

Mode of transmission: Investigations of all the most recently confirmed cases, in China, Turkey and Indonesia have identified that the most likely source of exposure is close contact with infected or dead poultry or their faeces. According to World Health Organization (WHO), almost all human sufferers caught the disease directly from birds and only tiny number of infected person has infected another. Other sources are flesh (even refrigerated/frozen carcasses), eggs from infected birds which can harbor the virus both outside and within the cell. Indirect transmission is also possible through contaminated clothing, footwear, vehicles and equipments. Contaminated feed, water, insects, rodents, cats, dogs can also act as vectors and transmit the disease [15, 16].

Route of transmission: Route of transmission is mainly respiratory tract. Conjunctiva may be affected directly. The incubation period for H5N1 avian influenza ranges from 2 to 8 days and possibly as long as 17 days. WHO recommends that an incubation period of 7 days be used for field investigations and monitoring of patients' contacts [17-19].

Clinical diagnosis:

- Initial symptoms include a high fever, usually with a temperature higher than 38°C and influenza like symptoms.
- In some patients, diarrhoea, vomiting, abdominal pain, chest pain and bleeding from the nose and gums have also been reported as early symptoms. Watery diarrhoea without blood appears to be more common in H5N1 avian influenza than in normal seasonal influenza.
- Respiratory distress (in few cases respiratory failure); a hoarse voice, a crackling sound when inhaling are commonly seen.
- Sputum production is variable and sometimes bloody.
- Viral pneumonia which doesn't respond to antibiotics can also be seen.
- Common laboratory abnormalities include lymphopenia, leucopenia, elevated aminotransferases and mild to moderate thrombocytopenia with some instances of disseminated intravascular coagulation.
- Another common feature is multi-organ dysfunction, notably involving the kidney and the heart [20-23].

Precautionary measures to prevent spread of disease:

The following precautionary measures must be taken during the period of epidemics of bird flu in an area [24].

1. Live poultry marketing directly to consumers should be discouraged.
2. Close contact with poultry or even wild ducks should be avoided.
3. Poultry meat, eggs, duck products, pig meats should not be taken.
4. As flesh and eggs of affected birds contains viruses, so these should not be exposed to persons without protective gloves, masks, goggles etc.
5. Cooking methods of flesh and eggs should be such that the center of the product reaches a minimum temperature of 70°C.
6. Sick bird should never be slaughtered for consumption and their eggs should not be marketed for human or animal consumption.
7. All persons who have been in close contact with infected animals should wash their hands frequently with soap and water.
8. All concerned should be vaccinated with the current WHO recommended influenza vaccine as soon as possible prior to anticipate risk exposure.

9. Concern cullers and transporters should be provided with personal protective equipments e.g. impermeable apron, rubber boots, goggles etc.
10. Serological surveillance of exposed animal workers and veterinarians is encouraged.

Medical prophylaxis: Vaccination is the only approach for controlling the infection caused by H5N1 strain, avian influenza. Influenza vaccine must be both subtype and strain specific. Research studies to test a vaccine to protect humans against H5N1 virus began in April 2005 but effective vaccine against H5N1 virus is not yet available. Live attenuated cold adapted H5N1 vaccine development is under trial. The first human trial of a DNA vaccine designed to prevent H5N1 avian influenza infection began in December 2006. It contains only portions of the influenza virus' genetic material. Once inside the body, the DNA instructs human cells to make proteins that act as a vaccine against the virus [25-27].

Treatment: The H5N1 virus that causes human illness and death is resistant to amantadine and rimantadine, two antiviral medications commonly used for influenza. Oseltamivir (Tamiflu) is a medication that decreases the spread of influenza A and B viruses. It is a neuraminidase inhibitor. Neuraminidase is an enzyme that enables influenza virus to spread from infected cells to healthy cells. By blocking the action of this enzyme, it prevents the spread of virus from cell to cell and thus reduces the symptoms and duration of influenza if treatment is started within 48 hours of onset of symptoms. Zanamavir, being a neuraminidase inhibitor would also work to treat influenza [28, 29].

CONCLUSION

Avian influenza or bird flu is a highly contagious disease of birds, caused by avian influenza A (H5N1) virus. This virus has affected poultry flocks and other birds in more than 50 countries. In humans, the first case was documented in Hong Kong in 1997, when 18 people infected with H5N1 virus strain, 6 of them died. Till dated 309 people have caught the infection out of which 187 people died. The source of infection in most cases was close and direct contact with infected birds. Oseltamivir is the first orally active antiviral drug. Being a neuraminidase inhibitor, it is used in the treatment and prophylaxis of influenza A and B viruses provided that the treatment is started within 48 hours of onset of symptoms. As

vaccination is the only approach for controlling the infection caused by H5N1 strain, the development of vaccines is under trial. At present, H5N1 remains a very rare disease in people and it doesn't infect human easily and if a person is infected, it is very difficult for the virus to spread to another person, but there are chances that it may develop this ability or may create a new virus by merging with human flu viruses. If happens so, it may give rise to the fear of a new human flu pandemic. Knowledge of epidemiology, natural history and management of influenza A (H5N1) disease in humans is still incomplete and more coordination in clinical and epidemiologic research among institutions in countries with cases of influenza A (H5N1) and internationally.

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