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An overview on recent bird flu outbreak in India

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Abstract
Bird flu has spread across ten states, and over thousands of birds found dead across India. Maharashtra, Delhi, Kerala, Rajasthan, Madhya Pradesh, Himachal Pradesh, Haryana, Gujarat Uttar Pradesh and Uttarakhand are the states where it has been confirmed till 18.01.20. It is a highly contagious viral disease caused by Influenza viruses which generally affects poultry birds such as chickens and turkeys.
Wild aquatic birds such as ducks and geese are the natural reservoir of Influenza viruses and the central players in the ecology of these viruses. From water birds, many of whom migrate and travel long distances, the viruses are thus further spread to poultry and terrestrial birds. Among poultry birds, vaccination strategies can curtail the virus attack, massive culling is done to prevent spread of the disease.
The CZA (Central Zoo Authority) issued a memorandum saying avian influenza is a scheduled disease under the Prevention and Control of Infectious and Contagious Diseases in Animals Act 2009. The review paper focuses on the scare of the avian influenza and prevention strategies to curtail the spread of the diseases. It is hoped that this paper will provoke constructive bioethical deliberations, on how to ensure that the obligations towards health are fulfilled ethically and more effectively.

Keywords: bird flu, vaccination, aquatic birds, antiviral drugs and strategies

Introduction
Bird flu outbreaks have been affecting poultry around the globe for decades, and culling of infected birds has been a common measure to contain the spread. But it was in 1997 when humans are first known to have contracted bird flu following an outbreak in a live bird market of Hong Kong. It was contained, but re-emerged a few years later in various other parts of the globe and caused hundreds of human deaths, particularly in Southeast Asia. Movement of infected poultry and migratory birds, and an illegal bird trade are believed to be the causes of the spread.
Subsequently, several other strains of the virus such as H5N2 and H9N2 spread from animals to humans, thus becoming a global public health concern. If the virus mutates and becomes easily transmissible from person to person, say by altering its shape to grab human cells much more effectively, it can potentially cause a pandemic. Also, flu viruses are more prone to mutation because they have a segmented genome.
Notable contributions have been made in the field of avian influenza by Abadia and Hars 2006 [1], Brydak 2009 [2]., Chakraborti 2007 [3]., Clem and Galwankar 2006 [4]., Iwami *et al* 2009 [5]., Jan 2007 [6]., Juckett 2007 [7]., Kleinman *et al* 2008 [8]., Lahariya *et al* 2006 [9]., Lewis 2006 [10]., Ligon 2006 [11]., Liu 2006 [12]., Pandit 2013 [13]., Prakash 2006 [14]., Sorrell *et al* 2007 [15]., Stephenson 2006 [16] and WHO 2006 [17].

Bird flu scenario in India
In India, bird flu outbreaks have occurred on eleven occasions since 2006. Though there has been no human death reported, the pandemic has significantly hit the poultry industry and has generated serious concerns within India. The latest outbreak of bird flu virus was reported early January 2009 in West Bengal. West Bengal officials confirmed that they had begun culling about 60,000 poultry. This was the fourth outbreak of the deadly virus in the State since 2007. The third outbreak which resulted in the culling of 17,000 poultry was done barely a fortnight ago in December 2008. In November and December 2008, H5N1 a virulent strain of bird flu was detected in backyard and commercial poultry in several districts of Assam. To combat the spread of bird flu infection, nearly 4.3 lakh birds were culled. (Fig1)

Fig 1: Massive Culling Operation in India

Earlier, in April 2008, the deadly H5N1 strains infected backyard poultry in Tripura that led to the death of 3000 domestic birds and at the same time several dogs and jackals which consumed the affected birds were also found dead. Around 20,000 birds were culled as part of the operation. In July 2007, the highly pathogenic Qinghai strains of bird flu, capable of infecting humans, were detected in Manipur.
The frequent outbreak of bird flu pandemic in Asia and India is alarming. Poultry is a vital source of food and

income security in Asia, which is demonstrated by the fact that the region has 200 million small farmers, who have Between 10 to 100 birds each in their farms. In India, the poultry population is very large (about 150 million). Many people have been subject to economic insecurity because of the culling operations undertaken to contain the spread of the virus.

In India, no case of bird flu in humans has been detected so far, according to the Union health ministry. The department of animal husbandry has reported 25 episodes of H5N1 bird flu in poultry in 15 states from 2006 (when the first outbreak occurred in Maharashtra and Gujarat) till 2015. It has also been detected in crows. Bird flu has spread across 10 states, over 1,200 birds found dead across India till 18.01.20. Kerala, Rajasthan, Madhya Pradesh, Himachal Pradesh, Haryana, Gujarat, Delhi, Uttar Pradesh, Maharashtra and Uttarakhand are the states where it has caused severe outbreak. Unlike in birds, where it generally infects the gut, the avian influenza attacks the respiratory tract of humans and may cause severe respiratory illnesses such as pneumonia or Acute Respiratory Distress Syndrome (ARDS). Its early symptoms include fever, cough, sore throat, and sometimes abdominal pain and diarrhoea.

Antiviral drugs, especially oseltamivir, improve the prospects of survival in humans, according to the Union health ministry. The ministry advises people working with poultry to use PPEs and follow hand hygiene.

Among poultry birds, vaccination strategies advised by the World Organisation for Animal Health can be used to prevent the flu, and the Organisation recommends eradicating the highly pathogenic avian influenza (HPAI) at its source to decrease the disease in avian species and further human infections. Avian influenza (AI) is an infectious viral disease of birds, commonly known as bird flu. Wild water fowl such as ducks and geese are mostly affected by AI, but often show no apparent signs of illness. Poultry birds are also susceptible to AI infection that can cause large outbreaks and epidemics in poultry. (Fig 2)

Fig 2: Geese the natural reservoirs

Biology of Influenza A Virus

Influenza viruses are RNA viruses in the family Orthomyxoviridae, which includes four genera: Influenza A, B and C viruses and Thogotovirus, as recently proposed by the International Committee on Taxonomy of Viruses (ICTV). They are enveloped negative-stranded RNA viruses that can be distinguished on the basis of antigenic differences in nucleocapsid (N) and matrix (M) proteins.

Influenza A viruses are roughly spherical (120 nM) with glycoprotein spikes on the surface and genome consisting of eight RNA fragments that encode 10 proteins. The haemagglutinin (HA), neuraminidase (NA) and matrix (M2) proteins are embedded in the envelope lipid bilayer derived from the host cell (Figure 3). The M1 protein underlying the envelope is the major determinant of virion morphology. The nucleoprotein (NP) associates with each RNA segment to form the ribonucleoprotein (RNP) complex, which also contains small amounts of the three polymerase subunits. The nonstructural proteins NS1 and NS2 are found only in infected cells.

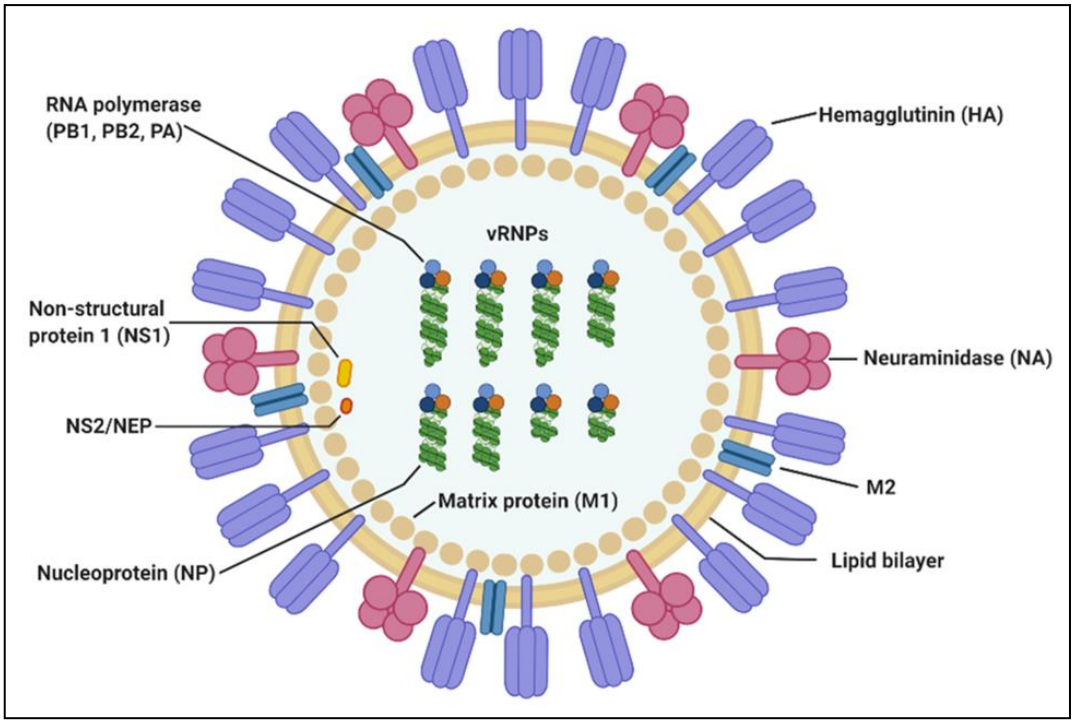

Fig 3: Structure of influenza virus

The surface glycoproteins HA and NA are critical for the biology of influenza virus. HA is responsible for the virus attachment to the cell surface, binding to sialic acid residues in cell membrane glycoproteins, thus triggering viral fusion and entry. The proteolytic cleavage of HA by serine proteases present in the infected tissue exposes hydrophobic fusion domains that mediate membrane fusion. This is an important molecular determinant of host range and tissue pathology. Some HA types can be cleaved by different serine proteases, what enables the virus to spread more efficiently in vivo. The RNA-dependent RNA polymerase and the NS1 proteins of influenza virus also are determinants of viral pathogenicity and host range.

NA cleaves terminal sialic acid from glycoconjugates present on respiratory mucins, cells, and progeny virions. This action is of key importance for the release of the virus from infected cells and, consequently, for the spreading of infection throughout the respiratory tract.

The antigenic diversity of HA and NA provides for influenza A virus subtyping. Sixteen HA and nine NA subtypes are currently recognized, with amino acid sequences differing by 30% or more. Six HA (H1, H2, H3, H5, H7 and H9) and three NA (N1, N2 and N7) subtypes have been identified in strains of influenza virus causing human infection, but only viruses of three HA (H1, H2 and H3) and two NA (N1 and N2) subtypes have remained in sustained circulation in the human population after causing pandemics.

Prospects of an H5N1 Pandemic: Current Situation

The World Health Organization has defined six stages of a global plan for influenza pandemic preparedness, including recommendations for control measures to be adopted before and during an overt pandemic period. The so called interpandemic period comprises the first two stages, when no new influenza virus subtypes are detected in humans, but a circulating animal influenza virus subtype poses a substantial risk of inducing human disease. The period called pandemic alert includes three phases: phase three, the one we are at as of this writing, is defined by the presence of detectable human cases of influenza caused by a new influenza virus subtype, but with limited human-to-human spread. In phase four human-to-human transmissions occurs, but only in small clusters, whereas in phase five such transmission occurs in larger clusters. Phase six is defined by a sustained transmission of a new flu subtype worldwide.

Signs and symptoms of Avian influenza A virus infections in humans

In Infection caused by low pathogenic avian influenza (LPAI) A virus, sign and symptoms ranged from conjunctivitis to influenza-like illness like fever, cough, sore throat, muscle aches to lower respiratory disease (pneumonia) requiring hospitalization.

Highly pathogenic avian influenza (HPAI) a virus infections in people have been associated with high grade fever with influenza like symptoms as cough with sputum (sometimes bloody) and sore throat. Some patients may show symptoms of lower respiratory tract involvement early in the illness.

Incubation period for A (H5N1) is ranging from two to eight days and may be as long as 17 days and for A (H7N9) it is between two to eight days, with an average of five days. The case fatality rate for A (H5N1) and A (H7N9) virus infections in people is much higher as compared to seasonal influenza infections.

Infection of avian populations with certain subtypes of avian influenza A virus poses continuing global public health risks because of two reasons, first- occurrence of sporadic human infections and second- emergence of a pandemic influenza strain (disease occurring over a wide geographic area and affecting an exceptionally high proportion of the population).

Disease is caused by avian influenza virus belongs to the Influenza A genus of the orthomyxoviridae family.AI viruses are divided in to two groups according to severity of the disease: high pathogenic viruses and low pathogenic viruses.

High pathogenic viruses are responsible for high death rates (up to 100% mortality within 48 hours) in some poultry species. Low pathogenic viruses, which are not, associated with severe disease but cause outbreak in poultry species.

Highly pathogenic avian influenza (HPAI) viruses are mainly restricted to H5, and H7 subtypes which are in circulation in poultry. These viruses have potential to cause serious disease in people and have the potential to change into a form that is more transmissible among humans. Following direct close or prolonged contact with sick or dead infected poultry, viruses enter into a person's eyes, nose or mouth, or are inhaled.

Risk factors for human infection

Direct or indirect exposure to Infected live or dead poultry or contaminated environments, such as live bird markets are the primary risk factors for getting the infection. Consumption of dishes made of raw, contaminated poultry blood can cause infection.

Slaughter, defeathering, handling carcasses of infected poultry, and preparing poultry for consumption, especially in household settings, are likely to be risk factors. Properly prepared poultry or eggs usually do not transmit the disease.

Presenting signs and symptoms of AI illness are non-specific therefore a detailed exposure history should be taken including any close/direct contact with sick or dead poultry, wild birds, other severely ill persons, travel to an area with AI activity, or work in laboratory handling samples possibly containing AI virus.

In India National Institute of Virology (NIV), Pune and National Centre for Disease Control (NCDC), Delhi are performing tests for diagnosis of AI in humanss. National Institute of High Security Animal Diseases (NIHSAD), Bhopal, Madhya Pradesh is an apex laboratory for testing AI in animals. Four bio-safety level lll (BSL lll) laboratories in Jalandhar, Kolkata, Bangalore, and Bareilly and a mobile BSL lll lab at Guwahati have been performing the test. Central/State diagnostic laboratories with bio-safety level II (BSL II) in 21 states are doing diagnosis for AI in animal populationb.

Diagnosis of Bird Flu

Avian influenza a virus infection is usually diagnosed by collecting a swab from the nose or throat of the sick person during the first few days of illness.

Following tests may be used to detect avian influenza in human samples-

Viral RNA detection by reverse transcriptase polymerase chain reaction (RT-PCR) and real time RT- PCR assay-PCR detects viral RNA present in either clinical specimens or

virus cultures. RT-PCR assay takes six to eight hours whereas Real time RT-PCR methods provide results in three to four hours and are more sensitive.

Virus culture- Because of the bio-safety concern, isolation of highly pathogenic viruses is usually performed only in specially qualified and equipped laboratories.

Rapid antigen detection- Viral antigen detection may be carried out by immunofluorescence or enzyme immunoassay (EIA) methods. Serological identification of antibodies against avian influenza A viruses-Serological tests available for the measurement of influenza A-specific antibody include the haemagglutination inhibition test (HI), enzyme immunoassay (EIA), and virus neutralization tests (VN)..

Prevention

Persons who work with poultry or who respond to avian influenza outbreaks are advised to use appropriate personal protective equipment (PPE) and follow proper hand hygiene.

Surveillance with Inter-sectoral coordination- Surveillance committees may be constituted at state and district level comprising experts from health, animal husbandry and other sectors for regular outbreak surveillance (early warning system) in domestic poultry, domestic birds and piggeries.

Travellers should also wash their hands often with soap and water. Travellers should follow good food safety and good food hygiene practices. Infection with an avian influenza virus should be considered in persons who develop influenza like illness during their travel or soon after returning from area where avian influenza is in transmission. Post-exposure antiviral chemoprophylaxis of close contacts of a patient with confirmed AI virus infection and/or high risk poultry/environmental exposures is advised.

Control measures in birds

When outbreak of AI occurs in birds, the immediate priority should be to contain the disease and eliminate the disease by destroying the infected or exposed birds (culling or stamping out), proper disposal of carcasses (burial), decontamination of the affected premises, movement controls, restocking of the bird after a safe period of destocking.

Vaccination strategies. And eradication of highly pathogenic avian influenza (HPAI) at its poultry source to decrease the disease in avian species and further human infections.

Conclusion

Avian influenza is a deadly virus that can pose serious health concerns. It can swap genetic materials and merge, thereby resulting in a new subtype different from the parent viruses. These highly pathogenic viruses crossbred with human influenza, would be transmissible from humans to humans by airborne droplets, driven by coughs and sneezes resulting in a human pandemic. At present, no vaccines have been developed to combat HPAI. Even if vaccines were developed, it would take months to produce sufficient doses to protect the entire population of India.

Several lines of evidence indicate that the threat of an H5N1 pandemic is real and that careful planning should be done in order for effective measures to be implemented to reduce the public health impact of H5N1. Monitoring and rapid detection of H5N1 is necessary to combat the spread of this virus.

The task of eradicating H5N1 virus is a difficult and an expensive task. However, avian flu can be contained if the poultry industry is adequately overhauled and new surveillance systems are placed to detect bird flu outbreaks. Constant alert and hard work could play a vital role in combating avian influenza. This is one battle that India cannot afford to lose.

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