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Current status of Avian Influenza

CHANDEL B S*, CHAUHAN H C, RAJGOR MANISH
Department of Microbiology and Animal Biotechnology
CoVSc & AH, SDAU, Sardarkrushinagar
***Corresponding Author:** bschandel13@gmail.com

ABSTRACT

Avian Influenza (also known as **Bird flu, avian flu, Influenza virus A flu, type A flu or genus A flu)** is a highly contagious disease of viral etiology that ranges from a mild or even asymptomatic infection to an acute, fatal disease characterized by high morbidity and mortality rate with respiratory and nervous signs. A disease causing extremely high mortality in fowl was first defined in 1878 in Italy and was known as fowl plague. The disease is now known to exist word wide. The causative organism of this disease was shown to be an ultra filtrable agent *i.e.*, virus as early as 1901. However, it took almost six more decades to identify the causative agent as a member of Influenza A group of Orthomyxovirus. All the species of birds are considered to be susceptible to infection with avian influenza viruses, though some are more resistant to infection than others. The persistence of H5N1 subtype in many Asian countries and their ability to cause fatal infection in humans have raised serious concern and public health importance.

INTRODUCTION

Among the influenza viruses (A, B, C), influenza A viruses are the only orthomyxoviruses known to affect birds. These avian influenza viruses have antigenically related nucleocapsid and Matrixprotein, but are classified in to subtypes on the basis of their haemagglutinnin (HA) and neuraminidase (NA) proteins. As of now 16 HA (H1 to H16) and 9 NA (N1 to N9) subtypes are known to circulate among birds with various combinations. The frequency of antigenic variations among influenza A viruses is high due to antigenic drift and antigenic shift. Antigenic drift involves point mutation in the genes

***Corresponding Author:**
Dr. B.S. Chandel
Department of Microbiology and Animal Biotechnology
CoVSc & AH, SDAU, Sardarkrushinagar India
E.Mail: bschandel13@gmail.com
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coding for HA and/or NA proteins, whereas antigenic shift is due to reassortment of genes of two different viruses. Avian influenza viruses affect all the species of birds with variable susceptibility. These viruses usually (with exceptions) do not make wild birds sick, but some of them make domestic birds (chicken and turkeys) sick and kill them. The overwhelming majority of AIV isolates are non-pathogenic or mild pathogenic to chicken and turkeys, hence go unnoticed without any consequences. However, infection with some viruses causes wide spectrum of symptoms in birds, ranging from mild illness to a highly contagious and rapidly fatal disease resulting in epidemics. The latter is known as 'Highly Pathogenic Avian Influenza (HPAI)' and notifiable. Although all the HPAI viruses isolated to date have been H5 or H7 subtypes, at least two isolates both of H10 subtypes (H10N4 and H10N5) have fulfilled the definition of HPAI. Many viruses if not all, belonging to H5 and H7 subtypes isolated from birds have been of low virulence for poultry. In 1991, one of the two isolates of H5N1 isolated from a turkey was characterized as non-pathogenic. Due to the risk of H5 or H7 virus of low virulence becoming virulent by mutation, all H5 and H7 viruses have been categorized as notifiable avian influenza (NAI) virus. During the past two decades, research has shown that viruses of low pathogenicity can, after circulation for some time in a poultry population, mutate into highly pathogenic virus. During 1983-84 epidemics in the USA, the H5N2 virus initially caused low mortality, but within six months became highly pathogenic, with a mortality approaching 90 %. In an epidemic in Italy (1999-2001), the H7N1 virus initially considered as low pathogenic turned out to be highly pathogenic within a period of 9 months. Similar was the situation in Canada with H7N3 during2003-2004.

Avian influenza A viruses are enveloped viruses and thus are relatively sensitive to inactivation by lipid solvents, such as detergents. Infectivity is also rapidly destroyed by formalin, bet-propiolactone, oxidizing agents, dilute acids, ether, sodium deoxycholate, hydroxylamine, and sodium dodecylsulphate and ammonium ions. Avian influenza viruses are not endowed with unusual stability so inactivation of the viruses themselves is not difficult. They are inactivated by heat, extreme of pH, nonisotonic conditions and dryness.

Host range

Most avian species appear to be susceptible to at least some of the AI viruses. Migratory water fowls, most notably wild ducks and gulls are natural reservoirs of AIV. A particular isolate may produce severe disease in turkeys but not in chickens or any other avian species. Therefore, it would be impossible to generalize on the host range for HPAI, for it will likely vary with the isolate. This

assumption is supported by reports of farm outbreaks where only a single avian species of several species present on the farm became infected. Swine appear to be important in the epidemiology of infection of turkeys with swine influenza virus when they are in close proximity. Other mammals do not appear to be involved in the epidemiology of HPAI. Ample evidences suggest that all influenza viruses in mammals were probably derived from those in wild waterfowl at some time. In addition to those already established in mammals, the viruses have been transmitted to both mammals and to poultry from wild waterfowl and caused outbreaks in recent years.The infection of humans with an H5 avian influenza virus in Hong Kong in 1997 has resulted in reconsideration of the role of the avian species in the epidemiology of human influenza.

Influenza A viruses have been isolated from a variety of animals, including pigs, horses, minks, seals, whales and birds as well as humans. Interspecies transmission of influenza viruses, although rare, has been detected. Influenza A viruses normally seen in one species sometimes can cross over and cause illness in another species. For example, until 1997, only H1N1 viruses circulated widely in the U.S. pig population. However, in 1997, H3N2 viruses from humans were introduced in to the pig population and caused widespread disease among pigs. Recently, H3N8 viruses from horses have crossed over and caused outbreaks in dogs. Swine H1N1 viruses have been transmitted to humans and avian viruses to horses, seals, whales and mink. Experimentally, avian influenza viruses do not replicate efficiently in humans and other primates (more than 100-fold decrease). Similarly, human viruses do not replicate efficiently in water fowl when introduced by natural routes. However avian influenza viruses can be directly transmitted to humans as indicated by the incident in Hong Kong, but the probability that they will establish themselves in human populations is low, thereby limiting opportunities for the generation of human-avian reassortment viruses. Pigs may serve as “mixing vessels” for the production of reassortment influenza viruses. Indeed, a variety of avian and human influenza viruses replicate efficiently in pigs on experimental infection. Phylogenetic and epidemiologic analysis indicates that avian and human viruses have been transmitted to pigs in nature and that they have reassorted in pigs and been transmitted to humans.

Geographical distribution

Highly pathogenic avian influenza viruses have periodically occurred in recent years in Australia (H7), England (H7), South Africa (H5), Scotland (H5), Ireland (H5), Mexico (H5), Pakistan (H7) and United States (H5). Because laboratory facilities are not available in some parts of the world to differentiate Newcastle disease and HPAI, the actual incidence of HPAI in the world’s poultry flocks is difficult to

define (OIE, 2004). It can occur in any country, regardless of disease control measures probably because of its prevalence in wild migratory waterfowl, sea birds and shore birds.

Outbreaks of less virulent AI have frequently been described in domestic ducks in many areas of the world. The viruses are often recovered from apparently healthy migratory water fowl, shore birds and sea birds worldwide. The epidemiologic significance of these isolations relative to outbreaks in domestic poultry has led to the generally accepted belief that waterfowl serves as the reservoir of influenza viruses.

In humans, it is feared that avian influenza virus to which humans have not been previously exposed undergoes antigenic shift to the point where it can cross the species barrier from birds to humans, the new subtype created could be both highly contagious and highly lethal in humans. If a human infected with influenza virus also acquires H5N1, a mutant strain of bird flu that can be transmitted from human to human. Such a subtype could cause a global pandemic similar to the Spanish flu that killed up to 50 million people in 1918.

A variant of H1N1 was responsible for the Spanish flu pandemic that killed some 50 million to 100 million people worldwide over about a year in 1918 and 1919. The most recent cause of alarm occurred since December, 2003 involving 20 countries. In East-Asian countries where avian influenza virus has been encountered in birds due to H5N1 subtype as many as 62 people have died. The most affected countries are Vietnam, Thailand, Indonesia and Cambodia, in terms of human deaths. This occurred in three waves, January-March, 2004, August-October, 2004 and December-2004-October 2005. Besides H5N1 subtype of the virus, H9N2 and H7N7 caused illness in humans in Hong Kong (1999 and 2003), and the Netherlands in February-2003. In the Netherlands H7N7 virus caused illness in 90 people and the death of Veterinarian. Some 500 more people were infected directly from their relatives or colleagues during the outbreak.

India was fortunate up till January 2006, in not having highly pathogenic avian influenza as observed during continued attempts on surveillance for the last five years (2001-2005). However, on screening of more than 17823 serum samples and 772tissue samples at High Security Animal Disease Laboratory, Bhopal, antibodies to H9N2 were detected and 27 isolations (H9N2) were made. Analysis of the surveillance data indicated moderate incidence of AIV infection in 2003 (33.4%), which declined to 8.66 % in 2004 and 2.4 % in 2005. Moreover, viruses (H9N2) could be isolated in 2003 and 2004, but not in 2005, indicating clearing of the virus from majority of the poultry population. Besides identification of the virus by conventional methods genetic analysis was completed for HA,

NP and Matrix genes. These viruses had not more than one basic amino acid at the cleavage site of HA gene, which is considered to be the benchmark for assessing the pathogenicity. They also did not produce cytopathic effect (CPE) without trypsin. Of the characterized viruses, 7 isolates were tested by IVPI test which gave '0' index value, hence characterized as nonpathogenic. In a specific study on the pathogenic potentials of 5 isolates no gross or microscopic lesions could be observed in any organs, but 3 viruses had the properties of invasiveness while other 2 had no such property. There was also good correlation between the invasiveness and the reisolation of the virus. (Table 1 indicates the situation in 2015).

Situation in India

Up till January, 2006, India was said to be lucky that only LPAI was detected in India. But, on 19th February, 2006 Government officials in Maharashtra confirmed the country's first outbreak of the deadly H5N1 bird flu virus in chickens. The outbreak was reported at a chicken farm containing 2, 00,000 birds at Nandurbar near the border with Gujarat State, where fifty thousand birds died. The dead birds were sent to the High Security Animal Disease Laboratory (HSADL), Bhopal for diagnosis. They confirmed H5N1 bird flu in chickens. India has just under 500 million heads of poultry, according to the most recent livestock census. On the other hand all 95 samples collected from people suspected of carrying bird flu in India have tested negative, easing fears that the infection may have spread to humans here. Animal health officials in Maharashtra said they must still find and kill backyard chickens in 70 villages before completing the slaughter of all birds around India's first H5N1 outbreak in Navapur. (Table:2 shows latest status in India)

India (Gujarat): H5N1 strain confirmed at poultry farm; no confirmed human cases

At least 2 chickens found dead at a poultry farm in Gujarat state were infected with the H5N1 strain of bird flu, officials said on 25 Feb 2006. The birds were discovered at the National Poultry Farm in the Utchal area. The bird flu infections had been confirmed by tests in a federal laboratory. State government formed 4-member panel to prevent bird flu cases in Gujarat. Gujarat is located next to North West of Maharashtra, where an outbreak of bird flu previous week prompted the culling of over 200 000 chickens and domestic birds. Also, on 24 Feb 2006, the Health Ministry said tests on 9 people suspected of having bird flu in Maharashtra's Navapur region showed no signs of the disease.

Two samples of chicken were found positive for H5N1 bird flu in Kadaiya village in Daman district, following which the administration has prohibited import, sale and storage of poultry products, and banned restaurants from serving chicken and egg products for a month.

AHMEDABAD: The only place in Gujarat to have witnessed cases of bird flu is Ahmedabad. The National National Institute for High Security Animal Diseases (NISHAD) has in its recent report claimed that the serum samples sent from Surat, Bharuch and Jamnagar, which reported carcass of crows and pigeon were found negative for the dreaded virus. In Ahmedabad, guinea fowls and turkey brought from Crawford Market in Mumbai were tested positive. These birds were kept at the premises of an NGO in Hathijan area

SURAT: Three hens in the coop of a house at Digas village of Kamrej taluka in Surat district died of suspected bird flu on Sunday. The authorities are conducting tests on the infected hens and expect the reports to come by Monday evening. This incident has occurred soon after three ducks were found to be infected with bird flu in the Union Territory of Daman . Jan 9, 2017,

Transmission

There are considerable bodies of circumstantial evidence to support the hyposis that migratory waterfowl, sea birds, shore birds are generally responsible for introducing the virus in to poultry. When influenza viruses do move from feral birds to poultry, they may spread from flock to flock and farm to farm by a number of methods. Primarily, these consist of the mechanical transfer of infective faeces from infected to susceptible birds and inevitably there is human involvement in this transfer. The virus is spread from flock to flock by usual methods involving the movement of infected birds, contaminated equipments, egg flats, feed trucks and service crew. Preliminary trapping evidence indicates that garbage flies in the Pennsylvania outbreak were sources of virus on the premises of the diseased flock. Virus may readily be isolated in large quantities from the faeces and respiratory secretions of infected birds. It is logical to assume, therefore, that because virus is present in body secretions, transmissions of the disease can take place through shared and contaminated drinking water. Air borne transmission may occur if birds are in close proximity and with appropriate air movement. Birds are readily infected via instillation of virus in to the conjunctival sac, nares, or the trachea. Preliminary field and laboratory evidences indicate that the virus can be recovered from the yolk and albumin of eggs laid by hens at the height of the disease. The possibilities of vertical transmission are unresolved, however it is unlikely infected embryos could survive and hatch. Attempts to hatch eggs in a disease isolation cabinet from a broiler breeder flock at the height of disease failed to result in any AI infected chickens. This does not mean that broken contaminated eggs could not be source of virus to infect the chicks after they hatch in the same incubator. The hatching of eggs from a diseased flock would likely be associated with considerable risk. There is no evidence that virus can survive in well cooked meat.

Vaccination of birds can develop asymptomatic infections that allow virus to spread, mutate and recombine. Intensive surveillance is required to detect these “silent epidemics” in time to curtail them. In Mexico, for example, mass vaccination of chickens against epidemic H5N2 influenza in 1995 has had to continue in order to control a persistent and evolving virus.

Clinical signs

The incubation period is usually 3-7 days depending upon the isolate, dose of inoculum, the species and age of the bird. The prognosis for flocks infected with HPAI is poor. Morbidity and mortality rates may be near 100 percent within 2 to 12 days after the first signs of illness. Birds that survive are usually in poor condition and resume laying only after a period of several weeks.

Infections of HPAI viruses result in marked depression with ruffled feathers, in appetence, excessive thirst, cessation of egg production and watery diarrhoea. Mature chickens frequently have swollen combs, wattles and edema surrounding the eyes. The combs are often cyanotic at the tips and may have plasma or blood vesicles on the surface with dark areas of ecchymotic hemorrhage and necrotic foci. The last eggs laid, after the onset of illness, are frequently without shells. The diarrhea begins as watery bright green and progresses to almost totally white. Edema of the head, if present, is often accompanied by edema of the neck. The conjunctivae are congested and swollen with occasional hemorrhage. The legs, between the hocks and feet, may have areas of diffuse hemorrhage. Respiratory signs can be a significant feature of the disease, depending on the extent of tracheal involvement. Mucus accumulation can vary. It is not unusual in caged layers for the disease to begin in a localized area of the house and severely affect birds in only a few cages before it spreads to neighbouring cages. Death may occur within 24 hours of first signs of disease, frequently within 48 hours, or be delayed for as long as a week. Some severely affected hens may occasionally recover.

In broilers, the signs of disease are frequently less obvious with severe depression, inappetence and a marked increase in mortality being the first abnormalities observed. Edema of the face and neck and neurological signs such as torticolis and ataxia may also be seen.

The disease in turkeys is similar to that seen in layers, but it lasts 2 or 3 days longer and is occasionally accompanied by swollen sinuses.

In domestic ducks and geese, the signs of depression, inappetence and diarrhea are similar to those in layers, though frequently with swollen sinuses. Younger birds may exhibit neurological signs.

In humans, avian flu viruses cause similar symptoms to other types of flu. These include fever, cough, sore throat, muscle aches, conjunctivitis and, in severe cases, severe breathing problems and

pneumonia that may be fatal. The severity of the infection will depend on a large part on the state of the infected person's immune status. If the victim has been exposed to the strain before he is partially immune. In one case, a boy with H5N1 infection experienced diarrhoea followed rapidly by a comma without developing reparatory or flu-like symptoms, suggesting non-standard symptoms.

Gross lesions

Birds that die with the per-acute disease and young birds may not have significant gross lesions other than severe congestion of the musculature and dehydration. In the less acute form, and in mature birds, significant gross lesions are frequently observed. They may consist of subcutaneous edema of the head and neck area, which is evident as the skin is reflected. Fluid may exit the nares and oral cavity as the bird is positioned for postmortem examination. The conjunctivae are severely congested occasionally with petechiation. The trachea may appear relatively normal except that the lumen contains excessive mucous exudate. It may also be severely involved with hemorrhagic tracheitis similar to that seen with infectious laryngotracheitis. When the bird is opened, pinpoint petechial hemorrhages are frequently observed on the inside of the keel as it is bent back. Very small petechiae may cover the abdominal fat, serosal surfaces, and peritoneum, which appears as if it were finely splattered with red paint. Kidneys are severely congested and may occasionally be grossly plugged with white urate deposits in the tubules.

In layers, the ovary may be hemorrhagic or degenerated with darkened areas of necrosis. The peritoneal cavity is frequently filled with yolk from ruptured ova, causing severe airsacculitis and peritonitis in birds that survive for 7 to 10 days. Hemorrhages may be present on the mucosal surface of the proventriculus particularly at the juncture with the gizzard. The lining of the gizzard peels easily and frequently reveals hemorrhages and erosions underneath. The intestinal muscosa may have hemorrhagic areas especially in the lymphoid foci such as the caecal tonsils. The gross lesions are not distinctly different from those observed with velogenicviscerotropic Newcastle disease (VVND). The lesions in turkeys and domestic ducks are similar to those in chickens but may not be as marked.

Diagnosis

Field Diagnosis

Highly pathogenic avian influenza is suspected with any flock where sudden deaths follow severe depression, inappetence and a drastic decline in egg production. The presence of facial edema, swollen and cyanotic combs and wattles, and petechial hemorrhages on internal membrane surfaces increases

the likelihood that the disease is HPAI. However, an absolute diagnosis is dependent upon the isolation and identification of the causative virus.

Laboratory Diagnosis:

Specimens sent to the laboratory should be accompanied by a history of clinical and gross lesions, including any information on recent additions to the flock. Diagnosis depends upon the isolation and identification of the virus from tracheal or cloacal swabs, feces, or from internal organs. Trachea, lung, spleen, cloaca, and brain should be sampled. If large numbers of dead or live birds are to be sampled, cloacal swabs from up to five birds can be pooled in the same tube of broth. An alternative technique is to place 0.5 cm^3 of each tissue into the broth. Blood for serum should be collected from several birds. If the specimens can be delivered to a laboratory within 24 hours, they should be placed on ice. If delivery will take longer, quickly freeze the specimens and do not allow them to thaw during transit.

Isolation

1) Nine to 11-day-old embryonated chicken eggs are inoculated by allantoic route. After 72 hours or at death, the egg should be removed from the incubator, chilled and allantoic fluids collected. Viral replication is demonstrated by haemagglutination test.
2) Cell culture – chick embryo cells or MDCK is generally used to determine the pathogenicity of the virus. Most of the cell culture support the growth of HPAI viruses or those of low pathogenicity in the presence of trypsin.If these cell cultures support the growth of virus with cytopathic effect or plaque formation in the absence of trypsin, the isolate is considered to be a HPAI isolate.

Serological tests

a) **AGPT:** The presence of influenza A virus can be confirmed in agar gel immunodiffusion (AGID) tests by demonstrating the presence of the nucleocapsid or matrix antigens, both of which are common to all influenza A viruses. The antigens may be prepared by concentrating the virus from infective allantoic fluid or extracting the infected chorioallantoic membranes; these are tested against known positive antisera.
b) **Haemagglutination inhibition test:** (HI): HI titres may be regarded as being positive if there is inhibition at a serum dilution of 1/16 (24 or log24 when expressed as the reciprocal) or more against 4HAU of antigen, some laboratories prefer to use 8HAU in HI test. While this is permissible, it affects the interpretation of results so that a positive titre is 1/8 or more.

c) **ELISA:** Various ELISAs are also available. There is a sensitive and specific ELISA that demonstrates nucleoprotein of type A influenza virus using a monoclonal antibody against Influenza nucleoprotein. Commercially available type A influenza antigen-capture ELISA kits designed for use in human influenza have recently shown promise as a possible rapid diagnostic test for poultry.

Molecular Diagnosis:

RT-PCR: The presence of influenza virus can be confirmed by the use of RT-PCR using nucleoprotein specific conserved primers. Though the presence of subtype H5 or H7 influenza virus can be confirmed by using H5 or H7 specific primers,standardized procedure for these methods have yet to be established and agreed internationally.

*Differential Diagnosis***:**Highly pathogenic avian influenza is easily confused with VVND, because the clinical signs and postmortem lesions of the disease are similar, and may also be confused with infectious laryngotracheitis and acute bacterial diseases such as fowl cholera and *Escherichia coli.* However, in an area where AI is prevalent, such as during an outbreak, sound presumptive diagnosis can be made by flock history, signs, and gross lesions.

Prevention & control:

Treatment**:** Four different influenza antiviral medications (amantadine, rimantadine, oseltamivir, and zanamivir) are approved by the U.S. Food and Drug Administration (FDA) for the treatment and/or prevention of influenza. All four usually work against influenza A viruses. However, the drugs may not always work, because influenza virus strains can become resistant to one or more of these medications. For example, the influenza A (H5N1) viruses identified in human in Asia in 2004 and 2005 have been resistant to amantadine and rimantadine.

Vaccination**:** Inactivated oil-emulsion vaccines, although fairly expensive have been demonstrated to be effective in reducing mortality, preventing disease or both, in chickens and turkeys. These vaccines may not, however, prevent infection in some individual birds, which go on to shed virulent virus. More economical viable vaccines prepared using naturally avirulent or attenuated strains have the disadvantage of the possible creation of reassortant influenza viruses with unpredictable characteristics. These reassortants could result when a single host bird is simultaneously infected with both the vaccine and another AI virus. Owing to the segmented nature of the influenza virus genome, a reassortments of genetic material can readily occur, creating new influenza viruses. The basic drawback to any vaccine approach for the control of HPAI is the large number of HA subtypes that

cause the disease. Because there is no cross-protection among the 16 known HA subtypes, either a multivalent vaccine will be needed or vaccination postponed until the prevalent disease-causing subtype in the area is identified. A recombinant fowl pox virus vaccine containing the gene that codes for the production of the H5 antigen has recently been licensed. The use of a recombinant insect virus containing the gene for either the H5 or H7 antigen has been used to make these vaccine proteins in insect cell cultures.

Bio-security

The practice of accepted sanitation and bio-security procedures in the rearing of poultry is of utmost importance. In areas where waterfowl, shore birds, or sea birds are prevalent, the rearing of poultry on open range is incompatible with a sound AI prevention program. Appropriate bio-security practices should be applied, including the control of human traffic and introduction of birds of unknown disease status into the flock. Cleaning and disinfection procedures should be followed strictly.

Recently introduction of virus/disease into many countries has been observed through migratory birds like the black-headed gulls, the bar-headed geese and the large cormorants. All these birds come to various habitats in India during the winter season; hence there is a need to test samples from these birds. This will help in developing strategies to control infection/ disease in indigenous birds and to circumvent epidemics of avian influenza in the country.

Table 1.

Country	Date of outbreak	Human cases	Poultry cases/ environmental samples	Wild bird cases/ others
Bhutan	16/04/2015	N	Y	N
Burkina Faso	09/05/2015	N	Y	N
Canada	01/05/2015	Y	Y	Y
Cote D'Ivoire	01/09/2015	N	Y	N
Egypt	17/07/2015	Y	Endemic	N
Germany	27/07/2015	N	Y	N
Ghana	14/08/2015	N	Y	N
Hong Kong	05/05/2015	Y	N	Y
India	19/05/2015	N	Y	Y
Indonesia	31/03/2015	Y	Endemic	N
Iran	15/06/2015	N	Y	N
Israel	20/06/2015	N	Y	N
Kazakhstan	22/05/2015	N	N	Y
Anhui	12/06/2015	Y	N	N
Beijing	12/06/2015	Y	N	N
Fujian	12/06/2015	Y	N	N
Guangdong	14/08/2015	Y	Y	N
Guizhou	19/06/2015	Y	Y	N
Hubei	26/04/2015	Y	N	N
Inner Mongolia	22/07/2015	N	N	Y
Jiangsu	14/08/2015	Y	Y	N
Jiangxi	02/05/2015	Y	N	N
Qinghai	17/07/2015	N	N	Y
Shandong	10/04/2015	Y	N	N
Shanghai	11/06/2015	Y	N	N
Tibet Autonomous Region	22/07/2015	N	N	Y
Yunnan	11/07/2015	Y	N	N
Zhejiang	12/06/2015	Y	N	N
Mexico	08/04/2015	N	Y	N
Myanmar	15/05/2015	N	Y	N
Niger	21/04/2015	N	Y	N
Nigeria	06/10/2015	N	Y	N
Palestinian Autonomous Territories	13/04/2015	N	Y	N
Republic of Korea	19/09/2015	N	N	N
Russia	21/08/2015	N	Y	Y
Taiwan	02/10/2015	N	Y	Y
Turkey	18/05/2015	N	Y	N
United States	26/06/2015	N	Y	Y
United Kingdom	13/07/2015	N	Y	N
Vietnam	03/10/2015	N	Y	Y

Table.2.

State	District	Outbreak	Date	Species	Susceptible	Case	Death	Test
CHANDIGARH	Chandigarh	1	18/12/14	Birds	100	22	22	Real time RT-PCR
Kerala	Alappuzha and Kottayam	5	20/11/14	Birds	398441	20182	20182	Real time RT
U.P	Amethi and sultanpura	3	4/3/15	Birds and House Crow	1031	190	190	Real time RT
Manipur	Imphal	1	6/4/15		21814	940	940	Real time RT
A.P.	Rangareddy	1	12/4/15		201264	41040	41040	Real time RT
Orissa	Keonjhar	1	31/1/2014	House Crow		2	2	Real time RT

Table 3: Confirmed human cases of avian influenza A (H5N1) (# Affected areas with reports of human cases in the past 6 months)

Country	2003 cases	2003 deaths	2004 cases	2004 deaths	2005 cases	2005 deaths	2006 cases	2006 deaths	2007 cases	2007 deaths	2008 cases	2008 deaths	2009 cases	2009 deaths	2010 cases	2010 deaths	2011 cases	2011 deaths	2012 cases	2012 deaths	2013 cases	2013 deaths	2014 cases	2014 deaths	2015 cases	2015 deaths	Total cases	Total deaths
Azerbaijan	0	0	0	0	0	0	8	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	8	5
Bangladesh	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	2	0	3	0	1	1	0	0	0	0	7	1
Cambodia	0	0	0	0	4	4	2	2	1	1	1	0	1	0	1	1	8	8	3	3	26	14	9	4	0	0	56	37
Canada	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	1	1
China #	1	1	0	0	8	5	13	8	5	3	4	4	7	4	2	1	1	1	2	1	2	2	2	0	5	1	52	31
Djibouti	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Egypt #	0	0	0	0	0	0	18	10	25	9	8	4	39	4	29	13	39	15	11	5	4	3	37	14	136	39	346	116
Indonesia	0	0	0	0	20	13	55	45	42	37	24	20	21	19	9	7	12	10	9	9	3	3	2	2	2	2	199	167
Iraq	0	0	0	0	0	0	3	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	2

Laos	0	0	0	0	0	0	0	0	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	2
Myanmar	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Nigeria	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Pakistan	0	0	0	0	0	0	0	0	3	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	1
Thailand	0	0	17	12	5	2	3	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	25	17
Turkey	0	0	0	0	0	0	12	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	12	4
Vietnam	3	3	29	20	61	19	0	0	8	5	6	5	5	5	7	2	0	0	4	2	2	1	2	2	0	0	127	64
Total	4	4	46	32	98	43	115	79	88	59	44	33	73	32	48	24	62	34	32	20	39	25	52	22	143	42	844	449