CD Alert

National Centre for Disease Control,
Directorate General of Health Services, Government of India

October 2024

AVIAN INFLUENZA (H5N1)

INTRODUCTION

Avian influenza (AI), also known as bird flu, is a zoonotic viral disease that primarily affects poultry and may occasionally spillover to mammals, including humans and swine. Influenza type A viruses are classified into subtypes based on Hemagglutinin and Neuraminidase proteins. Notable examples include H1N1, H3N2, H5N1, etc. All known subtypes of influenza A viruses can infect birds, except subtypes A(H17N10) and A(H18N11), which have only been found in bats. Further, Highly Pathogenic Avian Influenza (HPAI) subtypes like H5 and H7 are known to cause greater than 75% mortality in chicken farms. However, classification of viral strains as High PAI or Low PAI does not indicate disease severity in humans.

Avian influenza (AI), subtype H5N1 has zoonotic significance, posing major risks to public health and poultry worldwide. It is known to undergo rapid mutations and acquire genes from viruses that infect other animal species.

GEOGRAPHIC DISTRIBUTION

In 1996, the HPAI H5N1 virus was identified in geese in China. In 1997, first human infections were reported from Hong Kong, China. Since 2003, this virus has spread in bird populations across Asia, Europe, Africa, and the Americas. It is now endemic in poultry populations in many countries. Outbreaks have resulted in millions of poultry infections, several hundred human cases, and many human deaths. In April 2024, avian influenza was confirmed in dairy herds across USA with at least one human case presenting with eye inflammation.

EPIDEMIOLOGY

Human infections with avian and other zoonotic influenza viruses, though rare, have been reported sporadically. Current zoonotic influenza viruses have not demonstrated sustained person-to-person transmission. Birds that survive infection can excrete the virus through oral and faecal routes for at least 10 days. The typical incubation period in humans ranges from 3 to 5 days (can extend 7 to 10 days).

For avian influenza viruses, the primary risk factor for human infection appears to be exposure to infected birds and contaminated environments, such as workers in live/wet markets, handlers of fighting cocks, poultry cullers without PPE, feather pluckers, consumption of undercooked poultry products. There is no evidence to suggest that A(H5), A(H7N9) or other avian influenza viruses can be transmitted to humans through properly prepared and cooked poultry or eggs. A few influenza A(H5N1) human cases have been linked to consumption of dishes made with raw contaminated poultry blood. All influenza A subtypes are naturally found in wild aquatic birds. Viruses of avian influenza A are often transmitted from wild birds to domestic poultry and from domestic poultry to pigs. The influenza A virus can reassort in pigs from avian, swine, and human sources, and pigs are frequently exposed to human

and domestic poultry virus strains. Humans might be affected by influenza A viruses from pigs which act as mixing vessels for the transmission of these viruses.

SURVEILLANCE CASE DEFINITIONS

Suspect case

A person with all the following three conditions:

1. Fever (body temperature >38° C)
2. Any symptom from the following – muscle ache, cough, abnormal breathing (unusual breathing difficulty); or suspected of pneumonia/influenza by a physician
3. History of direct contact with infected/dead birds in the past 7 days; or occurrence of unusual death of birds in the community within the past 14 days; or contact with a pneumonia patient or another patient suspected of avian influenza

Probable case

A suspect case with any one of the following:

1. Preliminary positive test for influenza group A virus
2. Respiratory failure
3. Death

Confirmed case

A suspect or probable case with positive PCR test for H5N1 or isolation of H5 strain of influenza group A virus.

***Note**: Suspect and probable cases confirmed for any other illness should be excluded from line list.*

Influenza Like Illness (ILI)

Any person with acute respiratory infection (sudden cough and sore throat) with measured fever ≥ 38°C or ≥ 100.4°F along with onset within last 10 days

Severe Acute Respiratory Illness

Any person with Influenza Like Illness (ILI) who requires hospitalization.

CLINICAL MANAGEMENT

Management of a case with avian influenza is like that of influenza due to a primary human influenza virus. Any person presenting with flu- like symptoms should be screened for Avian Influenza and managed as per the categories A, B and C defined as follows.

Category-A
[mild uncomplicated]

- Symptoms: Patients with mild fever and cough/sore throat and any of the following; body ache, headache, diarrhea, or vomiting.
- Management:
  - No testing for Influenza required
  - Symptomatic treatment without Oseltamivir
  - Supportive care including fluid management and monitoring for complications
  - Reassessment at 24 to 48 hours by a healthcare provider for progression of disease
  - Isolation at home and avoid contact with the public and high-risk family members

Category-B
[Severe symptoms / high-risk groups without complications]

- Symptoms:
  - B1: Category A symptoms + High-grade fever (≥102 F) and severe sore throat.
  - B2: Category A + Individuals with high-risk conditions given in Box 1.
- **Management**:
  - No testing for Influenza required.
  - Treatment with Oseltamivir and symptomatic treatment, including fluid management and monitoring for complications given in Box 2.
  - Oseltamivir Regimen: 75 mg orally twice daily for five days.
  - Isolation: At home and avoid contact with the public and high-risk family members.

Category-C
[Complicated]

- Symptoms: Category-A symptoms + Category-B symptoms + with any of the signs and symptoms given in Box 2.
- Management:
  - Testing for Influenza recommended.
  - Immediate hospitalization and treatment with Oseltamivir. Do not wait for laboratory results.
  - Oseltamivir Regimen: 75 mg orally twice daily for five days. Use of modified regimens of oseltamivir treatment, including two-fold higher dosage, longer duration and possibly combination therapy with amantadine or rimantadine may be considered on a case-by-case basis.
  - Polymerase inhibitors like Baloxavir, Pimodivir and Favipiravir may also be considered for reducing the viral load.
  - Implement supportive therapy for Influenza A (H5N1) associated acute respiratory distress syndrome (ARDS), specifically including lung-protective mechanical ventilation.

Persistent symptoms: Evaluate for bacterial infections. Send for anti-viral sensitivity testing, if possible.

Note: As per the WHO Guidelines for the Clinical Management of Severe Illness from Influenza Virus Infections 2021

- Inhaled zanamivir not recommended
- Inhaled laninamivir not recommended
- Intravenous peramivir not recommended
- Plasma therapy not recommended
- Corticosteroids not recommended. May be considered for septic shock and adrenal insufficiency.

SPECIMEN COLLECTION

Clinical specimens (human):

- Throat swabs (oropharyngeal swab), nasal swabs, nasopharyngeal swabs
- Bronchoalveolar lavage or tracheal aspirates (3-5 mL in a sterile screw capped container) for intubated patients
- Alternatively, the sample collected in mucus extractor can also be sent
- In view of the recent cases in USA, conjunctival swabs should also be collected from symptomatic persons who are at high risk (bird vaccinators, cullers, farm workers etc.)

Note: All specimens should be collected <48 hours of symptom onset.
Note: Sputum is not a preferred sample for influenza testing.

Box 1: High risk population for complicated Influenza

1. Age ≥ 65 years
2. Extreme obesity (BMI ≥ 40 kg/m2)
3. Pregnancy (including up to two weeks post-partum)
4. Infants and Children aged ≤ 5 years (especially <2 years of age)
5. People <19 years on long-term aspirin – or salicylate-containing medications
6. People with following co-morbidities:
   - Chronic respiratory disease (asthma, COPD etc.)
   - Chronic heart, kidney, liver disease
   - Neurologic and neurodevelopmental disorders
   - Endocrine disorders (such as Diabetes Mellitus)
   - Blood disorders (including haemoglobinopathies)
   - Persons with immunosuppression (including HIV/ AIDS & use of long-term (≥ 2 weeks) corticosteroids, Post-transplant patients)
   - Malignancy

Box 2: Signs and symptoms of complicated Influenza

- Breathlessness
- Hemoptysis
- Altered mental status
- Somnolence and poor feeding in children
- Seizures
- Persistence or worsening of initial symptoms (>72 hours)
- Worsening of chronic illness like Diabetes, CKD, etc.
- Tachypnoea
- SpO2 <90%
- Hypotension
- Reduced urine output
- Cyanosis

Specimen collection from birds:

- Recently died or the birds showing acute signs after sacrificial culling.
- Cloacal and oro-pharyngeal swabs collected from healthy birds.
- Fecal material immersed in virus transport medium (PBS or tissue culture medium).
- Serum samples from birds showing acute signs of disease.

Note: Necropsy of birds suspected of having avian influenza should be avoided. It must be performed with proper precautions within a biosafety level 3 (BSL-3) facility.

Bio-safety measures for sample collection:

- Appropriate PPE should be worn by the sample collector
- Masks (N-95)/ triple layered surgical masks
- Gloves
- Protective eye wear (goggles)

Protective clothing (gown or apron)

Labelling of specimen:

- Should be done with pre-printed barcoded labels.
- Use permanent marker/ ball point pen only (don't use ink/gel pen)

SPECIMEN STORAGE AND TRANSPORT

Storage and transport of samples:

- Sample should be sent to the laboratory as soon as possible, at 4–8°C preferably within 24 hours.

In case of delay beyond 48 hours, the specimens must be stored at -70 °C

- Wrap samples in leak-proof plastic bags and place them in a disinfected polystyrene box with ice packs.

Include an appropriate form with the samples.

For intramural transport:

- Tightly closed and appropriately labelled VTM vial containing the sample should be transported to lab in a closed box (preferably vaccine carrier)
- Adequate absorbent material (cotton /tissue paper) should be wrapped around the vial immediately after collection

For extramural transport:

- All samples should be transported after proper packaging using the standard triple packaging system. https://idsp.mohfw.gov.in/WriteReadData/l892s/29900297861565252769.pdf
- Absorbent cotton, tissue paper, waste newspaper for wrapping primary container
- Secondary container to hold primary container i.e. bigger tube or sealed plastic bag. Triple packaging system to be followed all times and the sample proforma should be fastened on the tertiary container.

Note: The specimen should never be exposed to temperatures exceeding 25°C. Transportation should be done under strict cold chain.

SPECIMEN TESTING

- Preliminary testing on human involves real-time PCR testing for Influenza A group detection
- Confirmatory testing involves real time PCR testing for Influenza A subtyping and detection of H5N1.
- Serological investigations include enzyme-linked immunosorbent assay (ELISA) and hemagglutination inhibition tests but Serologic (antibody detection) testing is not advised for routine patient diagnosis and does not aid in clinical management. Collecting a single serum sample during the acute phase of illness is not useful for interpretation and should be avoided. While serological testing for antibodies against seasonal influenza viruses can be valuable in research settings, it requires the collection of both acute and convalescent serum specimens, which must be tested in specialized research laboratories
- Additionally, pathogenicity testing of virus isolates is crucial to determine whether the virus is classified as highly pathogenic avian influenza (HPAI) or low pathogenic avian influenza (LPAI).

VACCINATION

Vaccines designed for human use against the A(H5N1) virus have been developed and approved in multiple countries, following WHO guidelines. However, their availability remains limited, with decisions on usage dependent on infection risk assessments.

Influenza A (H5N1) Monovalent Vaccine, Adjuvanted (AUDENZ, manufactured by Sequirus, Inc) is an inactivated vaccine indicated for active immunization for the prevention of disease caused by the Influenza A virus H5N1 sub type and is FDA approved for use in persons 6 months of age and older at increased risk of exposure to the Influenza A virus H5N1 subtype. The dosage schedule comprises of the administration of 2 vaccine doses (0.5 ml each) intramuscularly 3-weeks apart.

Standard seasonal flu vaccines do not safeguard against A(H5N1) infections. However, in areas affected by A(H5N1), to minimize the risk of simultaneous human infection by both avian and human influenza viruses, targeted seasonal flu vaccination is recommended for

- First responders to A(H5N1) outbreaks
- Healthcare workers in facilities managing suspected or confirmed cases. However, vaccination is not recommended for the general population or individuals potentially exposed to infected animals in areas where A(H5N1) is endemic.

PREVENTIVE MEASURES

Guidelines for screening centers, isolation facility, critical care units and mortuaries

All hospitals identified to screen and admit patients with avian influenza should conform to these guidelines. Identified hospitals would have a separate screening area to screen outdoor patients and an isolation facility to admit those requiring indoor treatment.

I. Generic guidance

- Standard precautions to be followed at all patient care areas: hand hygiene, Gloves and use of personal protective equipment (PPE) to avoid direct contact with patient's blood, body fluids, secretions and non-intact skin, prevention of needle stick/sharp injury and cleaning and disinfection of the environment and equipment.
- Droplet precautions to be followed when caring for patients with avian

influenza (masks, respirators and eye shield) in isolation facilities.

- Airborne and Contact Precautions should complement Standard Precautions while managing case of avian influenza in critical care facilities.
- Hospitals should follow the hospital waste management protocols as per the biomedical waste management rules.
- Dead body should be handled using full cover of PPE.
- All visitors to wear masks, observe cough etiquettes and limit in person visitations to the hospitals and limit touching any surfaces. All visitors to be screened for flu like symptoms before entering the hospital. The movement of visitors within the hospital to be restricted.

II. Guidelines for pre-hospital care

All identified hospitals to have advanced life support ambulance.

- Designated paramedic and driver for the ambulance.
- The ambulance staff should follow standard precautions while handling the patient and airborne precautions if aerosol generating procedures are done.
- Triple layer surgical masks should be available and worn during transport.
- As far as possible the movements should be restricted.
- During transport, optimize the vehicle's ventilation to increase the volume of air exchange (e.g. opening the windows). When possible, use vehicles that have separate driver and patient compartments.
- Aerosol generating procedures to be avoided to the extent possible.
- Disinfect the ambulance after shifting patient.
- Notify the receiving facility as soon as possible.

Guidelines for setting up screening center

Purpose of the Screening Centre is to:

- Attend to patients of influenza like illness in a separate area so as to avoid these patients further infecting other patients in Out Patient Department.
- Facilitate implementing standard and droplet precautions.
- Triage the patients.
- Collect samples.
- Provide counselling and treatment (including medicines) to patients with influenza like illness in case they need home isolation

The screening area should have:

- A waiting area of about 2000 sq. feet to accommodate 50-100 patients.
- Preferably standalone building with separate entry.
- Well-ventilated to ensure frequent air changes. If airconditioned, then independent from central air conditioning. Exhaust air to be filtered through HEPA filter (desirable).
- Patient's seating to have at least one-meter clearance on all sides. Avoid overcrowding of patients.
- Will have cabins for registration, clinical examination chambers, sample collection rooms and drug distribution center.
- Facility for stretchers and wheelchairs in case patients collapse inside screening facility.
- Dedicated staff for screening centres and they should not be posted in other units.
- The waiting area should be adequately cleaned and disinfected.
- Source control (e.g. use of tissues, handkerchiefs, piece of cloth or triple layer surgical masks to cover nose and mouth) of the patient in the waiting room when coughing or sneezing, and hand hygiene after contact with respiratory secretions.
- Facility for hand wash, washrooms etc.

IV. Guidelines for setting up isolation facility/ ward

Patients should be housed in single rooms, whenever possible.

- However, if sufficient single rooms are not available, beds could be put with a spatial separation of at least 1 meter (3 feet) from one another.
- To create a 10-bedded facility, a minimum space of 2000 sq. feet area clearly segregated from other patient care areas is required.
- There should be double door entry with changing room and nursing station. Enough PPE should be available in the changing room with waste disposal bins to collect used PPEs.
- Place a puncture-proof container for sharps disposal inside the isolation room/area.
- Keep the patient's personal belongings to a minimum. Keep water pitchers and cups, tissue wipes, and all items necessary for attending to personal hygiene within the patient's reach.
- Non-critical patient-care equipment (e.g. stethoscope, thermometer, blood pressure cuff, and sphygmomanometer) should be dedicated to the patient, if possible. Any patient-care equipment that is required for use by other patients should be thoroughly cleaned and disinfected before use.
- Dedicated hand washes and washroom facilities.
- If room is air-conditioned, ensure 12 air changes/ hour and filtering of exhaust air. A negative pressure in isolation rooms is desirable for patients requiring aerosolization procedures (intubation, suction nebulization). These rooms may have standalone air-conditioning. These areas should not be a part of the central air-conditioning.
- If air-conditioning is not available negative pressure could also be created through putting up 3-4 exhaust fans driving air out of the room.

  In district hospital, where there is sufficient space, natural ventilation may be followed. Such isolation facility should have large windows on opposite walls of the room allowing a natural unidirectional flow and air changes. The principle of natural ventilation is to allow and enhance the flow of outdoor air by natural forces such as wind and thermal buoyancy forces from one opening to another to achieve the desirable air change per hour.
- Avoid sharing of equipment, but if unavoidable, ensure that reusable equipment is appropriately disinfected between patients.
- Ensure regular cleaning and proper disinfection of common areas, and adequate hand hygiene by patients, visitors and care givers.
- Visitors to the isolation facility should be restricted. For unavoidable entries, they should use PPE according to the hospital guidance, and should be instructed on its proper use and in hand hygiene practices prior to entry into the isolation room/area.
- Doctors, nurses and paramedics posted to isolation facility need to be dedicated and not allowed to work in other patient-care areas.
- Consider having designated portable X-ray equipment.
- Corridors with frequent patient transport should be well-ventilated.

  All health staff involved in patient care should be well trained in the use of PPE.
- A telephone or other method of communication should be set up in the isolation room/area to enable patients

or family members/visitors to communicate with nurses.

V. Guidelines for Critical Care facility

- At least one identified hospital may have a 10-bedded dedicated intensive care facility at state capital.
- The critical care facility is required to follow all the guidelines as mentioned above for infection control.
- Also, more than or equal to 12 air changes and maintain negative pressure of 40 psi.
- Should have dedicated equipment's, should also have additional equipment's to ventilate at least 10 patients manually.
- A telephone or other method of communication should be set up in the isolation room/area to enable patients or family members/visitors to communicate with nurses inside the facility.
- Would have an information board outside to update relatives on the clinical status.

VI. Mortuary care

- Mortuary staff should apply standard precautions i.e. perform proper hand hygiene and use appropriate PPE (use of gown, gloves, facial protection if there is a risk of splashes from patient's body fluids/ secretions onto staff's body and face).

  Embalming, if required should be conducted according to usual procedures, subject to local regulations/legislation.
- Hygienic preparation of the deceased (e.g. cleaning of body, tidying of hair, etc) also may be done using standard precautions.

Note: Chemoprophylaxis of close contacts of birds or poultry infected with avian influenza (H5N1 subtype) should be done with Oseltamivir 75 mg once daily for 5 days. Post-exposure prophylaxis of close contacts of a person with HPAI A (H5N1) virus infection is recommended with Oseltamivir twice daily treatment dosing instead of the once daily pre-exposure dosing.

CONTAINMENT STRATEGY

Once the occurrence of Highly Pathogenic Avian Influenza (HPAI) is confirmed through the laboratory tests; all contingency procedures for the containment and eradication of HPAI should be implemented with the following:

- Cross-sectoral notification to health and health related sectors, industry and farmers
- Restricted access to infected premises and alert zone
- Restrictions on movement and trade of poultry and its products
- Depopulation procedures for infected birds
- Strict compliance to biosafety and biosecurity protocols
- Vaccination of at-risk human populations
- Strengthen public awareness strategies

KEY MESSAGES

- Avian influenza (AI), also known as bird flu, is a zoonotic viral disease that primarily affects poultry and may occasionally spillover to mammals, including humans and swine. Influenza type A viruses are classified into subtypes based on Hemagglutinin and Neuraminidase proteins. Notable eg. include H1N1, H3N2, H5N1, etc.
- The typical incubation period in humans ranges from 3 to 5 days (can extend 7 to 10 days).
- For avian influenza viruses, the primary risk factor for human infection appears to be exposure to infected birds and contaminated environments, such as workers in live/wet markets, handlers of fighting cocks, poultry cullers without PPE, feather pluckers, consumption of undercooked poultry products. There is no evidence to suggest that A(H5), A(H7N9) or other avian influenza viruses can be transmitted to humans through properly prepared and cooked poultry or eggs.
- Management of a case with avian influenza is like that of influenza due to a primary human influenza virus.
- Vaccines designed for human use against the A(H5N1) virus have been developed and approved in multiple countries, following WHO guidelines. However, their availability remains limited, with decisions on usage dependent on infection risk assessments.
- Targeted seasonal flu vaccination is recommended for First responders to A(H5N1) outbreaks and Healthcare workers in facilities managing suspected or confirmed cases. However, vaccination is not recommended for the general population or individuals potentially exposed to infected animals in areas where A(H5N1) is endemic.
- Guidelines for screening centers, isolation facility, critical care units and mortuaries should be strictly adhered to.
- For containment, once the occurrence of Highly Pathogenic Avian Influenza (HPAI) is confirmed through the laboratory tests; all contingency procedures for the containment and eradication of HPAI should be implemented.