GOVERNMENT OF KERALA

Abstract

Health & Family Welfare Department - "Kerala State Technical Guidelines and SOP with regard to Highly Pathogenic Avian Influenza A [H5N1] Virus Infection" - Orders issued.

HEALTH & FAMILY WELFARE (F) DEPARTMENT

G.O.(Rt)No.1451/2024/H&FWD Dated,Thiruvananthapuram, 15-06-2024

Read:- Proposal dated 13.06.2024 from the Chairperson, State Medical Board.

ORDER

Highly Pathogenic Avian Influenza HPAI A(H5N1) clade 2.3.4.4b viruses have spread widely among wild birds worldwide since 2020–2021, resulting in outbreaks in poultry and other animals. Based on available evidence, human health risk to the public from HPAI A(H5N1) viruses is low. However, people with close or prolonged, unprotected exposures to infected birds or environments contaminated by infected birds are at greater risk of infection.

In response to recent Avian Influenza outbreaks in the State, Government are pleased to issue **"Kerala State Technical Guidelines and SOP with regard to Highly Pathogenic Avian Influenza A [H5N1] Virus Infection: Interim Recommendations on Prevention, Monitoring and Public Health Investigations"**, as annexed to this order.

(By order of the Governor)
SHIJA C G
JOINT SECRETARY

To:
The Secretary, Animal Husbandry Department.
The State Mission Director - National Health Mission, Thiruvananthapuram.
The Director of Health Services, Thiruvananthapuram.
The Director of Medical Education, Thiruvananthapuram.
The Director of Animal Husbandry, Thiruvananthapuram.
The Chairperson, State Medical Board
All District Animal Husbandry Officers.
All District Medical Officers.

Principal Accountant General (A&E/Audit), Kerala, Thiruvananthapuram.
Information & Public Relations (Web & New Media) Department.
Stock File/ Office Copy (to file F2/180/2024-HEALTH).

Forwarded /By order

Signed by
Vilasini K V
Section Officer
Date: 18-06-2024 16:05:41

Annexure

KERALA STATE TECHNICAL GUIDELINES AND SOP WITH REGARD TO HIGHLY PATHOGENIC AVIAN INFLUENZA A [H5N1] VIRUS INFECTION: INTERIM RECOMMENDATIONS ON PREVENTION, MONITORING AND PUBLIC HEALTH INVESTIGATIONS

Background

Sporadic human infections with Highly Pathogenic Avian Influenza (HPAI) A(H5N1) virus, with a wide spectrum of clinical severity and a cumulative case fatality of more than 50%, have been reported in 23 countries over more than 20 years. HPAI A(H5N1) clade 2.3.4.4b viruses have spread widely among wild birds worldwide since 2020–2021, resulting in outbreaks in poultry and other animals. Recently, HPAI A(H5N1) clade 2.3.4.4b viruses were identified in dairy cows, and in unpasteurized milk samples, in several U.S. states. Three cases of HPAI A(H5N1) virus infection in dairy farm workers were recently reported from the USA. Although human infections with HPAI A(H5N1) virus are rare, having unprotected exposure to any infected animal or to an environment in which infected birds or other animals are or have been present can pose a risk of infection. Most human infections with H5N1 virus have occurred after unprotected exposures to sick or dead infected poultry. There is no evidence of sustained human-to-human H5N1 virus transmission. Therefore, people with work or recreational exposures to H5N1 virus-infected animals may be at increased risk of infection and should follow recommended precautions. In Kerala, to date, H5N1 has been reported only in birds. Spillover of H5N1 to mammals has not been reported from Kerala.
Influenza A viruses infect the respiratory and gastrointestinal tracts of birds causing birds to shed the virus in their saliva, mucous, and faeces. Influenza A viruses can also infect the respiratory tract of mammals and cause systemic infection in other organ tissues. Human infections with avian influenza A viruses can happen when enough virus gets into a person's eyes, nose, or mouth or is inhaled. People with close or prolonged unprotected contact with infected birds or animals or their contaminated environments are at greater risk of infection. HPAI A(H5N1) virus human infections have ranged from mild (e.g., upper respiratory symptoms) to severe illness (e.g., pneumonia, multi-organ failure) resulting in death.

A wide range of terrestrial and marine mammals have been reported with HPAI A(H5N1) virus infection in multiple countries, typically resulting in neurologic signs of disease and death. HPAI A(H5N1) virus infection has been reported in wild mammals such as foxes, bears, seals, and sea lions, and domesticated animals, including pets such as cats and dogs, farmed mink and foxes, and livestock such as goats and cows.

Based on available evidence, human health risk to the public from HPAI A(H5N1) viruses is low. However, people with close or prolonged, unprotected exposures to infected birds or environments contaminated by infected birds are at greater risk of infection.

Transmissibility and transmission Routes

HPAI A(H5N1) viruses preferentially bind to α2, 3-linked sialic acid receptors that are prevalent in the respiratory and intestinal tracts of waterfowl and poultry, and in the human lower respiratory tract but do not currently have the ability to easily infect cells and bind efficiently to α2,

6-linked sialic acid receptors that are predominant in the human upper respiratory tract. The ability to bind efficiently to α2, 6-linked sialic acid receptors would be needed to increase the risk of transmission to people. Using recombinantly expressed hemagglutinin, analysis of receptor binding of the HPAI A(H5N1) virus identified in the dairy farm worker from Texas (A/Texas/37/2024) revealed binding only to avian-type α2, 3-linked sialic acid receptors.

There are different ways that avian influenza A(H5N1) can be transmitted to humans. According to the source of infection, transmission can be divided into:

Animal to human:

Individuals can be exposed to the virus through contact with infected birds, dead birds, or birds' secretions (mucus, saliva), blood and faeces (as birds shed the virus in their secretions and faeces). Transmission of the virus occurs via inhalation or contact with mucus membranes (e.g., eyes, nose, mouth).

Human infection has been reported after de-feathering of influenza A(H5N1) infected dead swans, and it has been determined that the influenza A(H5N1) virus can survive in feathers for several weeks in moderate temperatures, and over 5 months in cooler temperatures.

The ability of infected wild mammals to transmit avian influenza A(H5N1) to humans has not yet been determined. Although theoretically possible, there has never been a documented case of mammal-to-human influenza A(H5N1) transmission. Nonetheless, avian influenza detections in mammals and evidence of mutation or mammalian adaptation in the viral genome sequences from infected animals are important areas to monitor.

Mutations found within some of the Eurasian/North American reassortant influenza A(H5N1) strains circulating in North American birds and mammals in 2022 have been shown to enhance polymerase activity and replication in mammalian cells, help evade the immune response, and increase virulence in mice experimentally. Recent preliminary findings from pathogenicity and transmissibility studies indicate that the reassortant influenza A(H5N1) strains cause more severe illness in ferrets, increasing concerns about the potential for transmission to humans.

Food-borne transmission:

There have been rare reports of human cases of avian influenza A(H5N1) possibly associated with the consumption of raw or undercooked contaminated poultry products, such as raw duck organs and duck blood.

It is important to note that there is no evidence to suggest that the consumption of fully cooked poultry, game meat or eggs could transmit the influenza A(H5N1) virus to humans. All evidence to date indicates that thorough cooking will kill the virus.

Environmental exposure:

The majority of influenza A(H5N1) human cases have occurred after contact with infected poultry; however, some cases have been associated with exposure to contaminated environments, such as live bird markets and poultry farms.

Theoretically, humans could get infected with influenza A(H5N1) by exposure to contaminated water (i.e., inhalation, ingestion, conjunctival or intranasal inoculation), however, the evidence to support this is limited. Environmental exposure through contaminated water (for example, bathing or swimming in household ponds, or lacking an indoor water source) has been suggested as a possible risk factor for human infection in a small number of influenza A(H5N1) studies.

Human to human:

Evidence of limited human-to-human transmission of influenza A(H5N1) (via close physical contact, for example within a household) has been suggested in previous outbreaks. Sustained human-to-human transmission of avian influenza A(H5N1) has never been observed.

Clinical manifestations

Avian influenza A(H5N1) in humans mainly affects the respiratory tract. However, it can manifest with gastrointestinal or central nervous system symptoms (e.g., encephalopathy). Most human cases have reported a history of exposure to dead or ill poultry, and the incubation period after exposure is usually 1 to 5 days and up to 9 days.

Recommendations for the Public

1. People should avoid unprotected (not using respiratory or eye protection) exposures to sick or dead birds including wild birds, poultry, other domesticated birds, and other wild or domesticated animals, as well as with faeces, litter, or materials contaminated by birds suspected or confirmed HPAI A(H5N1) virus infection.

2. Personal protective equipment (PPE) should be worn when in direct or close contact (within about six feet) with sick birds including poultry, wild birds, backyard bird flocks, or faeces, litter, or materials potentially contaminated with HPAI A(H5N1) viruses.
    - PPE includes properly fitted unvented or indirectly vented safety goggles, disposable gloves, boots or boot covers, N-95 mask (ideally fit-tested), disposable fluid-resistant coveralls, and disposable head cover or hair cover.
3. People exposed to HPAI A(H5N1)-virus-infected birds (including people wearing recommended PPE) should monitor themselves for new respiratory illness symptoms, including conjunctivitis (eye redness), beginning after their first exposure and for 10 days after their last exposure. They should remain in home quarantine for 10 days from the last day of exposure.
4. Influenza antiviral post-exposure prophylaxis with Oseltamivir should be considered to prevent infection, particularly in those who had unprotected exposure to HPAI A(H5N1)-virus-infected birds.

5. Persons who develop any illness symptoms after exposure to HPAI A(H5N1) virus-infected birds should seek prompt medical evaluation, molecular testing and antiviral treatment by their clinician or from the public health department. Symptomatic persons should isolate away from others, including household members, until it is determined that they do not have HPAI A(H5N1) virus infection.

Recommendations for Protecting Farmers and Poultry, Backyard Bird Flock Owners

1. To reduce the risk of HPAI A(H5N1) virus infection, poultry farmers and poultry workers, backyard bird flock owners, livestock farmers and workers, veterinarians and veterinary staff, and emergency responders should avoid unprotected direct physical contact or close exposure with the following birds, animals and materials potentially infected or confirmed to be infected with HPAI A(H5N1) virus:

    - Sick birds, or sick livestock in a 10 km radius around epicenter.
    - Carcasses of birds, livestock, or other animals in a 10 km radius around the epicenter.
    - Faeces or litter
    - Raw milk of sick animals.
    - Surfaces and water (e.g., ponds, buckets, pans, troughs) that might be contaminated with bird and animal excretions.
2. Farmers, workers, and emergency responders should wear appropriate PPE when in direct or close physical contact with sick birds, livestock, or other animals, carcasses, faeces, litter, raw milk or surfaces and water that might be contaminated with animal excretions from potentially or confirmed infected birds, livestock, or other animals, and when going into not yet disinfected buildings where these animals or materials are or were housed.

Recommendations for Clinicians

Clinicians should consider the possibility of HPAI A(H5N1) virus infection in persons showing signs or symptoms of acute respiratory illness who have relevant exposure history. This includes persons who have had contact with potentially infected sick or dead birds within 9 days before symptom onset (e.g., handling, slaughtering, de-feathering, butchering, culling, preparing for consumption or consuming uncooked or undercooked food of potentially infected birds); and persons who have had prolonged exposure to potentially infected birds in a confined space. Clinicians should admit and isolate the patient, contact the state public health department to arrange testing for the influenza A(H5N1) virus, collect recommended respiratory specimens using PPE and start empiric oseltamivir. Testing for other potential causes of acute respiratory illness should also be considered depending upon the local epidemiology of circulating respiratory viruses, including SARS-CoV-2.

Recommendations for Surveillance and Testing

People exposed to HPAI A(H5N1)-infected birds (including people wearing recommended PPE) should be monitored for signs and symptoms of acute respiratory illness beginning after their first exposure and for 10 days after their last exposure.

Criteria for Avian Influenza A Virus Testing

Testing should be performed on persons who meet Epidemiologic criteria AND either Clinical OR Public Health Response criteria and should be tested for HPAI A(H5N1) virus infection by reverse-transcription polymerase chain reaction (RT-PCR) assay using H5-specific primers and probes.

Epidemiological Criteria

Persons with recent exposure (within 10 days) to HPAI A(H5N1) virus through one of the following:

◆ Exposure to HPAI A(H5N1) virus-infected birds defined as follows;

- Close exposure (within six feet) to birds or other animals, with confirmed avian influenza A(H5N1) virus infection. Bird or other animal exposures can include, but are not limited to handling, slaughtering, de-feathering, butchering, culling, or preparing birds or other animals for consumption, or consuming uncooked or undercooked food or related uncooked food products,

OR

- Direct contact with surfaces contaminated with faeces, unpasteurized (raw) milk or other unpasteurized dairy products, or bird or animal parts (e.g., carcasses, internal organs) from infected birds or other animals,

OR

- Visiting a live bird market with confirmed bird infections or associated with a case of human infection with the HPAI A(H5N1) virus.

◆ Exposure to an infected person – Close (within six feet) unprotected (without the use of respiratory and eye protection) exposure to a person who is a confirmed, probable, or symptomatic suspected case of human infection with HPAI A(H5N1) virus (e.g., in a household or health care facility).

◆ Laboratory exposure (unprotected exposure to HPAI A(H5N1) virus in a laboratory)

Clinical Criteria

Persons with signs and symptoms consistent with acute upper or lower respiratory tract infection, or complications of acute respiratory illness without an identified cause. In addition, gastrointestinal symptoms such as diarrhoea are often reported with HPAI A(H5N1) virus infection. Examples include but are not limited to:

- Mild illness (e.g., cough, sore throat, eye redness or eye discharge such as conjunctivitis, fever or feeling feverish, rhinorrhea, fatigue, myalgia, arthralgia, headache)
- Moderate to severe illness: (e.g., shortness of breath or difficulty in breathing, altered mental status, seizures)
- Complications: pneumonia, respiratory failure, acute respiratory distress syndrome, multi-organ failure (respiratory and kidney failure), sepsis, meningoencephalitis

Public Health Response Criteria

1) Symptomatic persons who are residing within the designated Alert Zone (10 km radius from the epi-centre) should be thoroughly screened for direct physical contact or close exposure with birds,animals and materials potentially infected or confirmed to be infected with HPAI A(H5N1) virus. If there is no potential exposure testing should be undertaken as per the existing ILI/SARI protocol.
2) Testing of asymptomatic persons for HPAI A(H5N1) virus infection is not routinely recommended. As part of public health investigations, asymptomatic persons, such as close contacts of a confirmed case of HPAI A(H5N1) virus infection, might be tested after consultation with State RRT.

Preferred Clinical Specimens

For persons with suspected HPAI A(H5N1) virus infection, the following specimens should be collected as soon as possible after illness onset or when deemed necessary: a nasopharyngeal swab and a nasal swab combined with an oropharyngeal swab (e.g., two swabs combined into one viral transport media vial). The nasopharyngeal swab and the combined nasal-throat swabs should be tested separately. If these specimens cannot be collected, a single nasal or oropharyngeal swab is acceptable**.** If the person has conjunctivitis (with or without respiratory symptoms), both a conjunctival swab and a nasopharyngeal swab should be collected. Patients with severe respiratory disease also should have lower respiratory tract specimens (e.g., an endotracheal aspirate or bronchoalveolar lavage fluid) collected, if possible. For severely ill persons, multiple respiratory tract specimens from different sites should be obtained to increase the potential for HPAI A(H5N1) virus detection.

Recommendations for Infection Prevention and Control

Standard, contact and airborne precautions are to be adopted while caring for patients presenting for medical care or evaluation who have illness consistent with influenza and recent exposure to birds or other animals potentially infected with HPAI A(H5N1) virus.

Recommendations for Influenza Antiviral Treatment and Chemoprophylaxis

There are no data from randomized clinical trials of antiviral treatment of outpatients or hospitalized patients with H5N1 virus infection. Among patients hospitalized with seasonal influenza A or B, pandemic 2009 influenza A (H1N1), or highly pathogenic avian influenza A(H5N1) virus infections, observational studies suggest that early treatment [within 48 hours of symptom onset] reduces disease severity and mortality. Although earlier antiviral treatment results in greater clinical benefit, observational studies support the use of antiviral treatment in hospitalized patients with seasonal influenza even when started after 48 hours of illness, including in critically ill patients. Neuraminidase inhibitor treatment with oseltamivir, peramivir, or zanamivir has been used for severely ill persons infected with A(H7N9) viruses, but their effectiveness for treatment of severe disease caused by avian influenza A virus infections has not been determined. Most avian influenza A(H7N9), A(H5N1), and A(H5N6) viruses are susceptible to the neuraminidase inhibitors (oseltamivir, peramivir and zanamivir) and baloxavir, but are often resistant to the adamantanes (amantadine and rimantadine).

Treating Symptomatic Persons with Bird or Other Animal Exposures

Outpatients meeting epidemiologic exposure criteria who develop signs and symptoms compatible with influenza should be referred for prompt medical evaluation, testing and empiric initiation of antiviral treatment with oseltamivir as soon as possible. Clinical benefit is greatest when antiviral treatment is administered early, especially within 48 hours of illness onset.
Hospitalized patients who are confirmed, probable or suspected cases of human infection with the HPAI A(H5N1) virus, regardless of time since illness onset are recommended to initiate antiviral treatment with oseltamivir as soon as possible. Antiviral treatment should not be delayed while waiting for laboratory testing results.

- The standard dose of oseltamivir is 75 mg twice daily for 5 days. However, the optimal duration and dosing are uncertain for patients with severe disease. Avian influenza A(H5N1) and A(H7N9) viruses have been shown to be associated with higher virus levels and longer duration of viral replication (particularly in the lower respiratory tract) in hospitalized patients than with seasonal influenza A or B virus infection. Pending further data, longer courses of treatment (e.g., 10 days) should be considered for severely ill hospitalized patients with novel influenza A virus infections.

Antiviral treatment recommendations according to case definition category for human infection with novel influenza A viruses associated with severe disease.

Case Category	Definition	Antiviral Treatment
Confirmed Case	Avian influenza A virus infection in a person that is confirmed by CDC's Influenza Division Laboratory or a CDC designated laboratory using methods mutually agreed upon by CDC and the Council of State and Territorial Epidemiologists (CSTE).	Recommended for all (hospitalized patients and outpatients)
Suspected Case (also called Case under investigation)	A person meeting criteria for avian influenza A virus infection below and for whom confirmatory laboratory test results are unknown or pending.	
Probable Case	A person meeting criteria for avian influenza A virus infection below and **for whom laboratory test results do not provide a sufficient level of detail to confirm HPAI A H5 virus infection.**	Recommended for all (hospitalized patients and outpatients)

*Criteria for Avian Influenza A Virus Testing are given above.

Chemoprophylaxis of Persons with Exposure to HPAI A(H5N1) Virus: Chemoprophylaxis with influenza antiviral medications can be considered for any person meeting epidemiologic exposure criteria. Decisions to initiate post-exposure antiviral chemoprophylaxis should be based on clinical judgment, with consideration given to the type of exposure, duration of exposure, time since exposure and known infection status of the birds or animals the person was exposed to.

Antiviral chemoprophylaxis is not routinely recommended for personnel who used proper PPE and experienced no breaches while handling sick or potentially infected birds or other animals or decontaminating infected environments (including animal disposal).
If antiviral chemoprophylaxis is initiated, oseltamivir treatment dosing (one dose twice daily) is recommended instead of the antiviral chemoprophylaxis regimen for seasonal influenza.

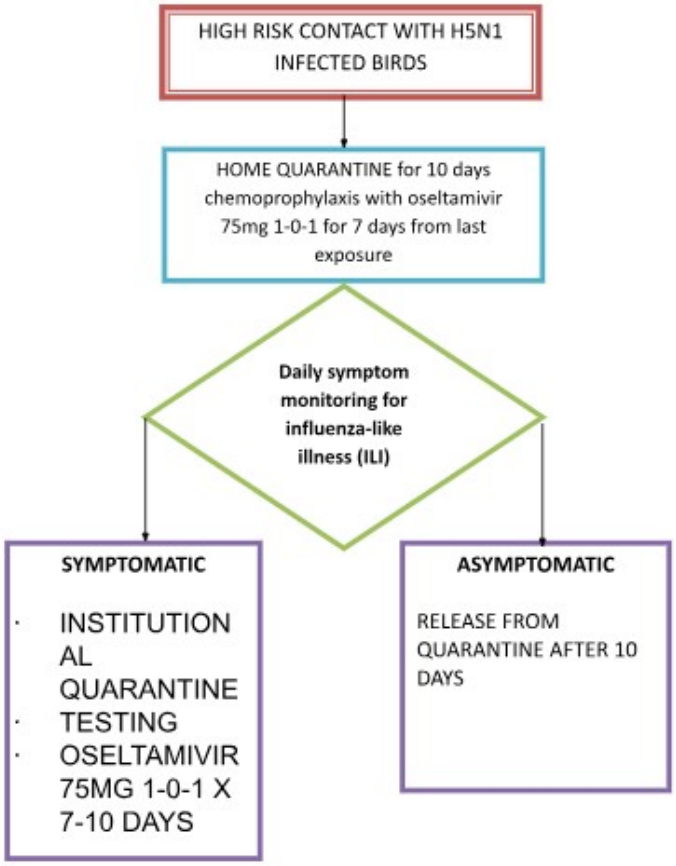
Treatment and Chemoprophylactic dose of oseltamivir for H5N1

If younger than 1 yr old: 3 mg/kg/dose twice daily. If 1 yr or older, the dose varies by child's weight: 15 kg or less, the dose is 30 mg twice a day: >15 to 23 kg, the dose is 45 mg twice a day : >23 to 40 kg, the dose is 60 mg twice a day: >40 kg, the dose is 75 mg twice a day.

Renal dose Modification of Oseltamivir

	Creatinine Clearance	Recommended Treatment Regimen
Oral Oseltamivir	Creatinine Clearance 61 to 90 ml/ min	75 mg twice a day
	Creatinine Clearance 31 to 60 ml/ min	30 mg twice a day
	Creatinine Clearance 11 to 30 ml/ min	30 mg once daily
	ESRD patients on hemodialysis Creatinine Clearance ≤ 10 ml/min	30 mg after every hemodialysis cycle. Treatment duration not to exceed 5 days
	ESRD patients on Continuous Ambulatory Peritoneal Dialysis Creatinine Clearance ≤ 10 ml/min	A single 30 mg dose administered immediately after a dialysis exchange

SOP FOR HIGH-RISK CONTACTS OF H5N1 INFECTED BIRDS



Conclusions

A small number of sporadic human cases of highly pathogenic avian influenza (HPAI) A(H5N1) have been identified worldwide since 2022, amidst a panzootic of these viruses in wild birds and poultry. Nearly all human cases reported globally since 2022 were associated with poultry exposures, and no cases of human-to-human transmission of the HPAI A(H5N1) virus have been identified. Three human cases of HPAI A(H5N1) virus infection in dairy farm workers were reported during April and May 2024 in the United States and were attributed to exposures to dairy cattle. One previous human case was detected in the United States in 2022 during poultry culling work. In a few cases, the source of exposure to the HPAI A(H5N1) virus was unknown. To date, HPAI A(H5N1) viruses currently circulating most commonly in birds and poultry, with spillover to mammals and humans, do not have the ability to efficiently bind to receptors that predominate in the human upper respiratory tract. This is a major reason why the current risk to the public from HPAI A(H5N1) viruses remains low. However, because of the potential for influenza viruses to rapidly evolve and the wide global prevalence of HPAI A(H5N1) viruses in wild birds and poultry outbreaks and following the identification and spread among dairy cattle in the United States, additional sporadic human infections are anticipated. Continued comprehensive surveillance of these viruses in wild birds, poultry, mammals, and people worldwide and frequent reassessments are critical to determine the public health risk, along with ongoing preparedness efforts.

References

1. Interim Guidance on the Use of Antiviral Medications for Treatment of Human Infections with Novel Influenza A Viruses Associated with Severe Human Disease –CDC
2. Highly Pathogenic Avian Influenza A(H5N1) Virus Infection in a Dairy Farm Worker Published May 3, 2024**:**DOI: 10.1056/NEJMc2405371
3. H5N1 Technical Report: CDC