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National Focal Point for International Health Regulations

No: F.1-22/Advisory/CDC/2022

Islamabad, 9th June 2023

Subject: **Advisory for the Prevention and Control of Primary Ameobic Meningo-encephalitis (PAM) / Naegleriasis**

Purpose of the Advisory:

Naegleria Fowleri is an amoebic infection transmitted through warm freshwater (for example, lakes, pools, rivers, and hot springs) and soil. Deaths related to PAM have been regularly reported from Karachi and some other parts of country since 2008. With 03 recently reported case in 2023, the total count of cases has climbed up to 150 in country during last 14 years.

The purpose of this advisory is to provide public health information for mitigating the risks associated with the disease spread. It is imperative to undertake immediate and long term preventive measures in mega cities particularly Karachi. Vigilant surveillance is also imperative to pick the suspected cases for early disease confirmation and ensuring aggressive measures to interrupt further transmission.

Another objective of this advisory is to alert the public health authorities, water and sanitation agencies and other relevant stakeholders to undertake necessary steps for prevention and control of PAM across Pakistan especially Karachi.

Basic Information:

N. fowleri (also known as brain eating amoeba) is a single-celled, thermophilic, free-living pathogen found widely in freshwater environments i.e. warm bodies of fresh water, such as lakes, rivers, hot springs and even in soil. Despite lower incidence, the PAM disease is also widely distributed in tropical areas and mostly occurs during hot summer months. Most cases of PAM arise from freshwater sources (lakes, pools) but an increasing number are now linked to drinking water systems.

The acute infection in the human body is developed when water containing N. fowleri is forcefully inhaled into the upper nasal passages during bathing, swimming, or other recreational activities, followed by migration of the amoebae to the brain via the olfactory nerve. Within the brain, N. fowleri causes extensive inflammation, hemorrhage, and necrosis, leading to death in 3 to 7 days.

Clinical presentation:

Incubation period ranges from 2 to 15 days with median 7 days, Clinical features of PAM are quite similar to meningitis with initial presentation of sudden onset of frontal or temporal headache, high fever, nuchal rigidity, anorexia, vomiting, irritability and restlessness. Other symptoms such as photophobia, neurological abnormalities, including altered mental status, ataxia, cranial nerve palsy, hallucinations, delirium and coma usually occur late in the clinical course leading to death in 3-8 days. The fatality rate is over 97%.

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Diagnosis:

The diagnosis is based on history, clinical examination, signs and symptoms. CSF sample may be collected for microscopy and advanced referral testing. Because of the rarity of the infection and difficulty in initial detection, about 75% of case diagnoses are made after death of the patient.

Laboratory confirmation:

PAM infection can be confirmed the through below mentioned laboratory procedures:

Laboratory test	Findings
Direct Visualization	The motile amoeba can often be seen moving under a microscope in a fresh sample of CSF. The amoeba can also be stained with a variety of stains, such as Giemsa-Wright or a modified trichrome stain, for identification.
Antigen Detection	A specific antibody to *N. fowleri* can be used in conjunction with another antibody that deposits a chemical (immunohistochemistry [IHC]) or glows under specific types of light (indirect immunofluorescence [IIF]) to directly stain the amoebic antigens in tissue.
Polymerase Chain Reaction (PCR)	Specific molecular tools can amplify DNA from the amoeba in CSF or tissue.
Amoeba Culture	The amoeba can be grown in culture to increase the likelihood of detecting the amoeba by direct visualization or PCR
Environmental detection	Water samples can be collected, concentrated, and put into culture to grow and select for *N. fowleri*

Medical Treatment: Early diagnosis and treatment are crucial for survival.

- Suspected cases should immediately be reported to health authorities for corrective measures.
- Rapid diagnosis and intensive supportive care may provide the likelihood of survival. In few such documented cases, the combination of 3 drugs; Amphotericin B (IV/intrathecal), Rifampicin (Oral 10 mg/ Kg/day) and Fluconazole (IV/ oral 10 mg/ kg/ day) is used along with steroids.
- Azithromycin has both in vitro and in vivo efficacy against N. fowleri and may be tried as an adjunct to Amphotericin B. Miltefosine has also shown some in vitro amoeba- killing activity against free-living amoebae, including N. fowleri.

Prevention and Control measures:

- N. fowleri cannot survive in clean, cool and chlorinated water. Chlorine kills N. fowleri and is the most effective way to disinfect swimming pools and reticulated water supplies. Maintain the chlorine level in the water, as almost all the PAM cases are linked with the use of inadequately chlorinated water.

- Community education and awareness raising assumes significance in known endemic areas. Key recommended messages may include:
  - During recreational activities like swimming, avoid diving and getting water up in the nose. Try to avoid water-related activities when the water is not chlorinated.
  - Empty and clean small collapsible bathing pools daily.
  - Ensure swimming pools and spas are adequately chlorinated and well maintained.
  - Avoid jumping or diving into bodies of warm fresh water, avoid putting head under water in hot springs and other untreated geothermal waters.
  - If using un-chlorinated water, don't allow water to go up in nose when bathing, showering or washing the face.

- Potentially contaminated water should not be used for any form of nasal irrigation or nasal lavage.

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Advise for water utilities:

- Water supplies at risk include; reticulated raw and drinking water, lakes, dams, bores, tanks, reservoirs, pipelines, and swimming pools that are poorly maintained, under or un-chlorinated.
- Proper design, management and cleaning of assets (e.g. pipes and storage tanks) is required to minimize the sediment (which may harbor *Naegleria* cysts) and reduce water stagnation (which may lead to loss of disinfectant residual).

Chlorination:

- Water supplies at risk of *N. fowleri* must ensure adequate primary disinfection and maintain a chlorine residual of at least 0.5 mg/L at all times, in all parts of the distribution system. According to the World Health Organization (WHO), free chlorine having residual concentration equal or more than 0.5 mg/L, at pH less than 8.0 and at 20°C, after a contact time of at least 30 minutes is effective for chlorine disinfection.
- Regularly monitor the water temperature and chlorine residual throughout the distribution system. Periodic testing for *N. fowleri* can be carried out for risk systems.

Risk Communications:

Symptoms of *N. fowleri* infection are clinically similar to viral and bacterial meningitis and these conditions are much more common than amoebic meningoencephalitis. Making doctors aware about the disease may therefore, improve case detection and provide insight into human or environmental determinants of infection and allow improved assessment of treatment effectiveness.

Health Education:

Awareness and education in the affected areas must also be undertaken to educate people on requisite preventive measures. Households should also be warned of the potential risk, if adequate disinfection cannot be maintained throughout the distribution system.

Disease Surveillance and Notification:

Surveillance and notification of PAM infection should be enhanced with the dissemination of standard case definitions and diagnostics options to areas of transmission and areas at risk. The guidelines for standard case definitions is available at NIH website: https://www.nih.org.pk/guidelines (Surveillance Case Definitions of Epidemic-prone and Priority Communicable/ Infectious Diseases in Pakistan (2019))

The situation may please be continuously monitored and updates along with the actions taken be kindly communicated to the NIH regularly on phone no. +92-51-9255237, Fax: +92-51-9255099, E-mail: fedsd@nih.org.pk

The above 'Advisory' may please be circulated widely to all concerned.

(Dr. Muhammad Salman)
Chief Executive Officer, NIH

Distribution Overleaf

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46. Medical Superintendent, Railway Hospital, Rawalpindi
47. In-charge, Federal Disease Surveillance Unit (FDSRU), NIH Islamabad
48. Officer In-charge, Provincial Disease Surveillance Unit (PDSRU) at Provincial Health Directorates, Lahore, Hyderabad, Peshawar, Quetta, Gilgit and Muzaffarabad
49. Deputy Commissioners with the request to direct all concerned departments at district level

Copies to:

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2. Surgeon General Pakistan Army, GHQ Rawalpindi
3. Chief Commissioner, ICT Administration Islamabad
4. WHO Country Representative, Islamabad
5. SPS to Federal Minister of Health, M/o NHSR&C, Islamabad
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