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Prevalence of *Naegleria fowleri* in Pakistan

Abdul Raheem[1], Muhammad Zaid Khalil[1*] and Warda Qamar[2]

1. **Faculty of Veterinary Science, University of Agriculture Faisalabad, Pakistan.**
2. **Department of Parasitology, University of Agriculture Faisalabad, Pakistan.**

*Corresponding Author: **muhammadzaidkhalil@gmail.com**

ABSTRACT

Naegleria fowleri is a free-living parasite known as a "brain-eating amoeba." It causes "primary amoebic meningoencephalitis" (PAM). It has low morbidity but high mortality. It is an increasing threat to Pakistan, as several cases are reported in different regions this year. Three people died within a week in May in Karachi in 2023. It is difficult to diagnose as it causes the death of a patient within days after initial exposure. Improperly chlorinated pools and poor water supply are its main dissemination sources. A combination of drugs that limit amoebic growth is used to treat PAM.

Introduction:

Naegleria fowleri is a "brain-eating amoeba" that lives in warm freshwater, like rivers, hot springs, and lakes. It causes a brain infection as the water enters through the nose that contains amoeba. It is responsible for "primary amoebic meningoencephalitis" (PAM), a fulminating and acute condition that can cause death within 2 weeks after the entrance of an amoeba into the body. Young adults and immunocompetent children are susceptible to this infection. Because of low morbidity, there is an insufficiency of knowledge and awareness of this disease and its pathogenesis. It is an extremely rare disease but has a high mortality rate of about 98% [1]. Its symptoms are generally non-specific, so PAM is commonly unrecognized, unreported, or mistaken for viral and bacterial infections [2].

Prevalence in Pakistan

Naegleria fowleri is an emanating issue in Karachi, which is a coastal site and metropolitan city of Pakistan. The first case of the disease was reported in 2008. From 2008 to October 2019, the number of reported cases increased to 146. In the USA, only 142 cases were reported between 1968 and 2019. The maximum number of cases were reported in children under 14 years of age in the USA [3], while in Pakistan, most of the cases are reported in persons aged 26-45 years which highlights the possibility of the genetically modified strain in Pakistan [4].

Most of the cases are reported before the monsoon or summer season. The appearance of *N. fowleri* in Pakistan is riveting the attention of scientists toward climate change. *N. fowleri* prevails in domestic water provision of Karachi, and ablution is the major cause of infection [5], which is unanticipated as water is saline in Karachi, and amoebas do not survive in a saline environment. It suggests that the strain of *N. fowleri* in Pakistan has resistance against saline environments, or it is different from the strains reported in other countries. The first case of *N. fowleri* was reported in 2023 by health officials in Lahore, Pakistan. A 30-year-old patient was admitted to the Services Hospital Lahore (SHL). MS of SHL, Dr. Ehtisham Haque, stated that the patient had different symptoms, including fever and headache for the last four days. It is the 4th case of the lethal PAM reported this year in Pakistan; the other three cases are reported in Karachi [6]. A 32 years old woman who was a citizen of the Qayyumabad area died because of PAM on 24th May; later on, on 26th May, a 45 years old man in Surjani Town and a 19-year-old boy on 28th May died due to this disease [7].

Pathogenesis

N. fowleri is amphizoic in nature. It is a free-living organism and can occupy the central nervous system of humans. Recreational activities like diving, water skiing, and swimming are the major causes of infection in adults and children. When water enters the nasal cavity, then *N. fowleri* infects the host by gaining entry from the nose. At first, it attaches to the nasal mucosa and then moves through the cribriform plate beside the olfactory nerve to gain access to olfactory bulbs inside the CNS. When it reaches the desired site, it evokes a remarkable immune response by the activation of the innate immune system, which includes neutrophils and macrophages. It has three forms cysts, trophozoites, and flagellated forms, and it enters the human body in trophozoite form. There are special structures on the surface called food cups which enable it to ingest fungi, human tissue, and bacteria [8].

As the food cups destroy the tissue, the *N. fowleri* also releases the cytolytic molecules, which include the phospholipolytic enzymes, phospholipases, neuraminidases, and hydrolases that can cause the destruction of nerves in the host. Severe immune response and the pathogenicity of the organism results in CNS tissue damage and nerve damage, which often leads to death [9]. The life cycle of *N. fowleri* is given below (Fig. 1).

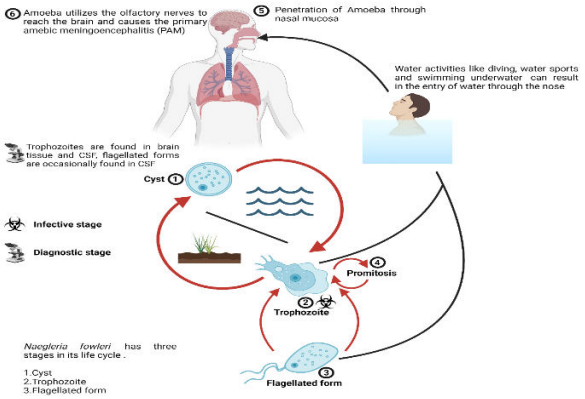

Fig.1: Life cycle of *Naegleria*

Clinical Manifestations

The initial signs and symptoms appear after two weeks of exposure to *N. fowleri* infection. Early symptoms show mild clinical signs, including headache, fever, vomiting, and nausea. Later symptoms include disorientation, lethargy, hallucination, neck stiffness, photophobia, cranial nerve abnormality, and seizures. After the onset of initial symptoms, PAM progresses rapidly within a few days and leads to coma. During this period, it causes cranial edema by destroying the brain tissues, ultimately leading to the death of the infected patient. PAM is difficult to diagnose because these symptoms can mimic other bacterial meningitis, and the infection proliferates so fast that the diagnosis often occurs after a patient dies [10]. Computerized tomography (CT) scan and magnetic resonance imaging (MRI) can be performed to monitor the affected area of the brain. Molecular diagnostic techniques like enzyme-linked immunosorbent assay (ELISA) and reverse transcription polymerase chain reaction (RT-PCR) are more sensitive and specific methods to detect this pathogen [11].

Treatment and Management

A few people survive the Naegleria illness. However, this disease is treatable if it is diagnosed early. Primary amoebic meningoencephalitis (PAM) can be treated by using a combination of drugs to limit amoebic growth. Miltefosine drug is used against living amoebae like *N. fowleri* and has successfully been proven to treat this disease [12].

N. fowleri mostly grows in water bodies. A person does not get this infection by drinking infected water but does illness when contaminated water enters the nose. It can be managed by preventing the water from entering the nose during ablution, swimming, and diving. Considering the situation, experts have warned the public to abstain from swimming in improperly chlorinated pools [13].

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