

# Recurring seasonal cases of *Naegleria fowleri* (Brain-Eating Amoeba) in Pakistan: A rapidly growing threat

Dear Editor,

*Naegleria fowleri* is a free-living amoeba commonly found in warm freshwater sources such as hot springs, rivers, and lakes. It is infamous for causing a rare but usually fatal infection of the brain, known as primary amoebic meningoencephalitis (PAM). The amoeba earns its nickname "brain-eating amoeba" due to its ability to invade the brain. The amoeba is known to enter the human brain through the nose, most likely during water-related activities or religious ablution.<sup>1</sup>

It primarily enters through the nasal passages and bypasses the blood-brain barrier via the olfactory nerve route, causing extensive tissue damage and triggering an inflammatory response leading to neurological symptoms. Additionally, it secretes cytolytic enzymes, induces hemolysis, and progresses rapidly, resulting in high mortality rates despite aggressive treatment.<sup>2</sup> Karachi, the largest city in Pakistan and a major metropolitan city and coastal area, is experiencing an alarming rise in *N. fowleri* cases, with three deaths reported in just 1 week of May 2023<sup>3</sup> and it has spread to the city of Lahore as reported at the start of July 2023.<sup>4</sup> This deadly amoeba poses a severe public health threat that requires urgent attention.

The incidence of PAM in Pakistan was first documented in 2008, and as of May 2022, Karachi had reported a total of 147 cases.<sup>5</sup> Pakistan has nearly the same number of PAM cases reported in the USA in just a decade, whereas it took the USA half a century to reach almost similar numbers. This is an alarming situation as Pakistan does not have as good a surveillance system as the USA does, meaning that there might be hundreds of more cases which go unreported in Pakistan.<sup>6</sup> It is also worth noting that the total number of cases reported in all countries other than Pakistan and the USA is up to only 195, recorded till 2018.<sup>7</sup> The reported data in this paragraph are visualized in Figure 1.

Unlike the USA, where PAM cases are typically reported in children under 14 years of age, in Pakistan most cases occur in adults aged 26–45 years.<sup>6</sup> The majority of cases are also reported during the summer months and before the onset of the monsoon season. The discovery of *N. fowleri* in Pakistan has raised concerns about the impact of climate change. The prolonged periods of hot and humid weather, attributed to climate change, have created conducive conditions for the growth and multiplication of amoebas in water bodies.<sup>6</sup>

One of the present challenges in dealing with *N. fowleri* in Karachi is the lack of awareness about the disease and its transmission. Most

of the population is unaware that *N. fowleri* can be found in warm freshwater sources and can enter the body through the nose during water activities or ablution for religious purposes. Not only is making an early diagnosis of *N. fowleri* infections difficult, but effective treatment of this organism is almost impossible at the moment, as the fatality rate of PAM is more than 98%.<sup>7</sup> The symptoms of PAM are initially very mild, including a headache, stiff neck, fever, and stomach pain. A person usually dies within five to 7 days after infection.<sup>6,8</sup>

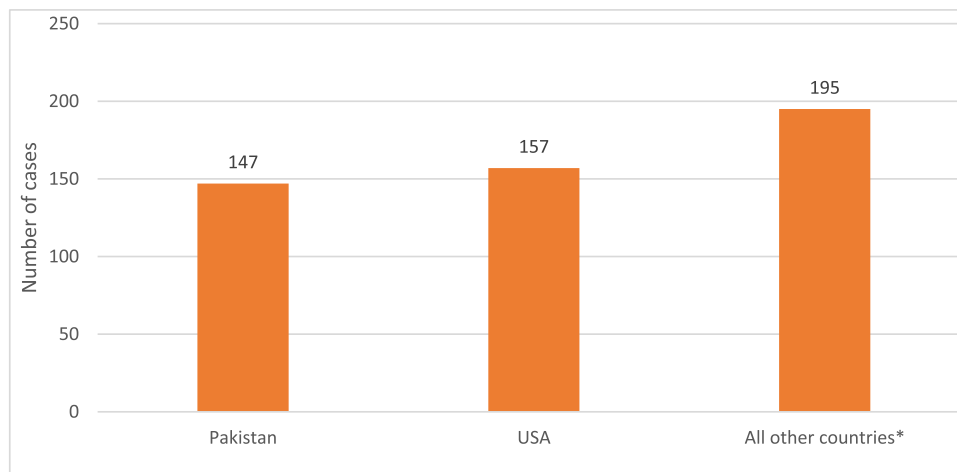
An important issue is the possibility of a genetically unique strain of *N. fowleri* in Pakistan. While most cases of PAM in the USA were reported in children younger than 14 years, in Pakistan, most cases are reported in adults aged 26–45 years, which suggests the possibility of a genetically unique strain in Pakistan.<sup>6</sup> Additionally, in Karachi, as most of the water supply used for cleansing and washing purposes has saline properties, the survival of *Naegleria* in such circumstances, where it usually cannot grow, makes it a different and resistant strain from what is found in other countries like the United States.<sup>6</sup> Also, Pakistan is one of the most heavily affected countries by global climate change, and this development has resulted in longer summers and increased humidity, creating favorable conditions for the growth and proliferation of amoebas in aquatic environments.<sup>9</sup>

In general, water sanitation is often poorly managed or not given enough attention in developing countries, which can lead to the contamination of water with sewage and other waste.<sup>7</sup> This can provide a breeding ground for *N. fowleri* and other harmful microorganisms. Additionally, many people do not have access to clean water, which means they may be more likely to come into contact with contaminated water, increasing their risk of infection. In developing countries, population densities are often high, making it more difficult to control the spread of diseases such as *N. fowleri*.

There is a need for increased research and understanding of *N. fowleri* and its pathogenesis, as there is not only a deficiency of effective mechanisms by which it can be diagnosed at early stages, but also there are no successful treatment options.<sup>10</sup> A genomic approach that investigates the whole genome of *N. fowleri* could identify examples of novel contents and provide an exciting research opportunity to elucidate the genome sequence of this newly emerging resistant strain in Pakistan that will be helpful in diagnosis, early disease prevention, and treatment.

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**FIGURE 1** Total *Naegleria fowleri* cases since the first-ever reported case till 2022. \*All other countries data are reported till 2018.

Genomic profiling techniques, especially those utilizing PCR, play a crucial role in the precise and prompt identification of *N. fowleri* infections. Methods like conventional PCR, nested PCR, multiplex PCR, and real-time PCR enhance sensitivity, specificity, and rapidity, rendering them essential for early detection and strain differentiation of *N. fowleri*.<sup>11</sup>

A recent study on genomic and transcriptomic analysis of *N. fowleri* characterized novel clinical and environmental *N. fowleri* genomandith transcriptomic data, identifying unique genes potentially linked to pathogenicity. Population structure analysis reveals ten populations within *Naegleria* species, with genomic data used to develop molecular assays and conduct future global genomic analysis, aiding in the understanding and monitoring of *N. fowleri* infections.<sup>12</sup>

Early diagnosis is critical for effective treatment, but it can be difficult to diagnose the infection as the symptoms are often similar to other diseases, such as meningitis or encephalitis. Doctors need to be aware of the possibility of *N. fowleri* infection and should order CSF analysis and MRI of the brain as soon as they suspect this infection. Currently, there are no effective treatments for the infection. The most common treatment is amphotericin B, but it is not always effective.<sup>10</sup>

One of the biggest concerns to address is the lack of awareness about the disease and its transmission. Public health campaigns can help to raise awareness about *N. fowleri* infection and its transmission. These campaigns can be conducted through a variety of media, including television, radio, print, and social media. They can also be conducted through government channels, such as health department websites and brochures. These campaigns can educate people about the risks of swimming in warm, freshwater, the importance of using nose clips, and guidance about performing religious activities like nose rinsing. They can also educate people about the symptoms of *N. fowleri* infection and the importance of seeking medical attention early. These campaigns can help people make informed decisions about their activities and protect themselves from infection.

Public health campaigns can share the following guidelines which can be helpful in the prevention of *N. fowleri* infections.

Avoid stirring up the sediment at the bottom of warm freshwater bodies.<sup>9</sup> *N. fowleri* can live in the sediment and can be released into the water when the sediment is disturbed. Boiling tap water for 1 min and letting it be cooled down before using it for drinking, cooking, or rinsing sinuses can kill any *N. fowleri* that may be present in the water. Using filters such as a carbon filter or a reverse osmosis filter can help remove any *N. fowleri* that may be present in the water.<sup>7,8</sup>

Due to *Naegleria*'s similar presentation with other bacterial and viral illnesses, difficult diagnosis, and lack of successful treatment, we are in dire need of scientific research to find ways for early diagnosis and effective treatment. Otherwise, the rapid spread of this deadly infection in this region would extend to other countries, especially the neighboring ones where similar underdeveloped circumstances exist. This way, *N. fowleri* can pose a serious threat to humanity if rapid measures are not taken to control and eventually eradicate this deadly infection.

#### AUTHOR CONTRIBUTIONS



**Rana Uzair Ahmad:** Conceptualization; investigation; writing–original draft; validation; methodology; visualization; writing–review and editing; project administration; data curation. **Muhammad Arslan Bilal:** Conceptualization; writing–original draft; investigation; visualization; validation; supervision. **Muhammad Fawad Ashraf:** writing–original draft; investigation; conceptualization; writing–review and editing; validation; visualization; data curation. **Safi Ur Rehman Daim:** Conceptualization; visualization; writing–original draft; funding acquisition; validation; methodology; formal analysis; writing–review and editing. **Malik Olatunde Oduoye:** Visualization; validation; funding acquisition; software. **Inibehe Ime Okon:** writing–original draft; funding acquisition; investigation; conceptualization; visualization; validation; methodology; project administration.

#### DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

## TRANSPARENCY STATEMENT

All the authors testify all writing materials and resources used for this study are unique and well-referenced.

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