

Review Article

Epidemiology Of Naegleria Fowleri-Caused Meningoencephalitis Across And The Globe And India: A Review Of An Emerging Infectious Disease.

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Abstract

Naegleria fowleri, a deadly organism that causes Primary amoebic meningoencephalitis (PAM), has a worldwide distribution. This disease has claimed around 300 lives globally, and survivors of this infection are rare. The organism thrives in warm environments, can withstand high temperatures, and multiplies in hotter months of the year. It is mainly found in aquatic habitats and soil. Over four hundred cases of PAM have been reported across the world. In India, there have been twenty reported cases from several parts of the country, and the infection has shown a growing trend. The majority of the cases identified in India were fatal, and the disease mostly affected children and young adults. *Naegleria fowleri* can be detected through Cerebro-Spinal Fluid (CSF) culture and Polymerase chain techniques. Control measures include chlorination, identification of the source, controlling pollution, and global warming.

Keywords : *Naegleria fowleri*, Primary amoebic meningoencephalitis (PAM), Global, India, Infectious, Disease.

INTRODUCTION

Naegleria fowleri is a type of free living amoeba that can be found in soil and water all around the world. This pathogen can cause a severe and often deadly infection of the central nervous system called primary amoebic meningoencephalitis (PAM). The disease progresses rapidly and can be fatal in a short amount of time. The amoeba was named after Malcolm Fowler, who first identified it in a patient with PAM.¹

Healthy children and young adults often contract illness after exposure to contaminated water sources from recreation, domestic use, or the environment.²⁻³ Exposure to a contaminated water source can cause PAM, which can be fatal within 1-2 weeks of being admitted to the hospital. Due to the rapid onset of the infection and delayed diagnosis, very few people survive it. Only around 10 cases of survivors have been reported in the literature for *Naegleria fowleri* PAM.⁴

Naegleria fowleri is an organism that thrives in warm environments and can withstand high temperatures, up to

45°C. Therefore, these amoebae grow in number during the hotter months of the year when the temperature rises.⁵ *Naegleria fowleri* has been discovered in various aquatic habitats, such as swimming pools, lakes, rivers, hot springs, and tap water.¹

It is possible that climate change is causing an increase in *Naegleria fowleri* infections. While most cases in the United States have historically occurred in southern states, recent reports show infections in northern areas. Rising air and water temperatures, along with lower water levels, provide an ideal environment for the amoeba to thrive. Heat waves, which can cause higher than usual temperatures in air and water, may also contribute to the amoeba's growth.¹

One more possibility which has come into India, a tropical country with warm climates, provides an excellent environment for parasites to grow. The high fatality rate of Primary Amoebic Encephalitis makes it a significant public health concern that requires review.

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EPIDEMIOLOGY ACROSS THE GLOBE

Australia

The first case of *Naegleria fowleri* was detected in Australia in the year 1965.⁶ In total the Australian region has 19 cases reported till now while New Zealand has reported around 9 cases. The North Australian region reported thirteen cases of *Naegleria fowleri* from 1965 to 2023 due to insufficient water chlorination.⁷

In South Australia, the organism was historically detected in mains water sourced from the River Murray, which was delivered through lengthy overland pipes. This resulted in increased water temperature and a lack of chlorine residual. From the 1980s to the 2000s, no cases were reported in Southern Australia. However, four cases were reported from 2000 to 2017.⁸

The North Australian region reported thirteen cases of *Naegleria fowleri* from 1965 to 2023 due to insufficient water chlorination.⁹

United States of America

The Centers for Disease Control and Prevention (CDC) reported 146 cases of illness in the United States in the year 2022. Of these cases, 86 people were exposed to harmful sources found in lakes, ponds, and reservoirs. Other sources of exposure included rivers, streams, canals, ditches, puddles, geothermal heated water, tap water, and other unknown sources. Most of these cases were reported during July and August.⁹

Canada

Canada is experiencing significant changes in its climate, and it is expected to continue in the future. The rise in temperatures is a cause of concern, but this presents an opportunity for people to work together to address the issue. With awareness and collective action, steps should be taken to mitigate the effects of climate change. Doing so can help ensure a sustainable future for generations to come. Additionally, the temperature rise could lead to the growth of thermotolerant pathogens in water, which could be prevented through proactive measures.^{10,11}

There have been no findings of *Naegleria fowleri* in Canadian soil. However, during a survey conducted by Rafik dey¹² on famous recreational lakes in Alberta, Canada, the presence or absence of *Naegleria* species was determined during the summer bathing period. While *Naegleria fowleri* was not isolated in this study, other thermotolerant species, including *Naegleria pagei*, *Naegleria gruberi*, *Naegleria jejuensis*, and *Naegleria fultoni* were identified using culture-based methods, indicating the potential conditions to support *Naegleria fowleri*. Therefore, ongoing monitoring and examination of water for pathogenic amoebae is recommended to assist in the public health management of water sources.

Africa and African Countries

Multiple instances of infection by *Naegleria fowleri* have been reported in different African countries. In Nigeria, four cases have been reported, including one of a farmer who sniffed water up his nose and three in children. Although no direct contact with water was noted in the children, it is believed that the dust in the air may have introduced the amoeba. *Naegleria fowleri* was subsequently identified in the nasal passages of the infected children, as well as in dust and water samples. In Namibia, one case was reported where a child was infected by *Naegleria fowleri* after swimming in stagnant pools that originated from hot springs. In Madagascar, one person died after swimming in a warm freshwater lake. In Egypt, two *Naegleria* species (*Gruberi* and *fowleri*) were identified in various water sources in Lower and Upper Egypt. The researchers examined samples from different water sources in Alexandria and the nasal passages of 500 healthy children living near these sources for the presence of free-living amoebae. The same two species were found in the water of canals and drains. *N. Gruberi* was also found in the nasal passages of six healthy children living near the contaminated canals. The authors noted that no amoebae were found in the drinking water, swimming pools, sea, or lake water that was included in their study.¹³

Asia and India

There was a reported case of *Naegleria fowleri* infection in Taiwan in 2011. Later, a thermal spring was found to be contaminated by *Naegleria fowleri*. In the Chinese mainland, there were three suspected cases of PAM due to the presence of amoebic trophozoites found in the cerebrospinal fluid (CSF) or brain tissue after death. However, a precise diagnosis of *Naegleria fowleri* infection couldn't be made due to a lack of other evidence. In August 2016, a 42-year-old male in the Chinese mainland was diagnosed with PAM due to *Naegleria fowleri* infection. Unfortunately, he passed away 14 days after showing symptoms. In 2022, the Chinese mainland reported its first pediatric case of *Naegleria fowleri* infection, which had a highly acute disease course.¹⁴

According to a study, Pakistan has the second-highest incidence of *Naegleria* infections globally. The first recorded case of PAM in Pakistan occurred in Karachi in October 2008.¹⁵ According to a review done by Nadeem et al¹⁶, she found out that the reported cases of PAM from the year 2008 and 2023 were one hundred fifty-four.

In Thailand, cases of *Naegleria fowleri* has emerged over the years. Retrospective literature search of PAM cases in Thailand from 1982 through April 2021 was performed after that 17th PAM case was reported in 2021.¹⁷

Epidemiology across India

India is a tropical country with a hot and humid climate that provides excellent conditions for the growth of various

organisms. A search was conducted in West Bengal, India, to find *Naegleria fowleri* in the environment. In May 1989, one pathogenic strain was isolated from pond water with a temperature of 35-38°C. To isolate pathogenic *Naegleria*, water samples of 250 ml were filtered through 1.2 µm cellulose acetate membranes and inoculated onto Bacto Agar seeded with living *Escherichia coli*. The mixture was then incubated at 45°C for the selective outgrowth of pathogenic *Naegleria*.¹⁸ Panda et al.¹⁹ conducted a study on the distribution of free-living amoebae (FLA) in selected water bodies in Rohtak and Jhajjar of the Haryana state in India. The study focused on *Naegleria fowleri*, and the two sites were chosen because most of the clinical cases in North India were reported from these areas.

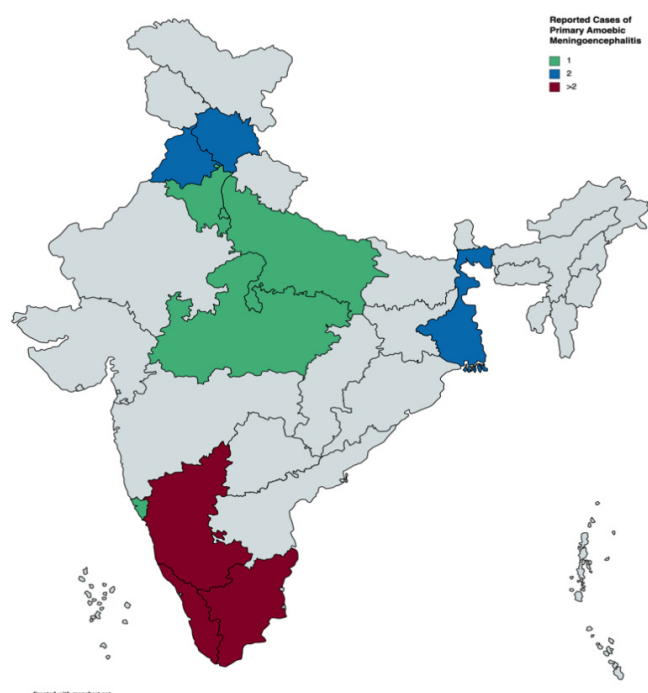
A warming trend was observed in India's annual mean surface air temperature from 1901-2010, based on IMD's gridded monthly station data.²⁰

Surveys suggest that microorganisms contaminate more than a third of rural groundwater sources in India, while geogenic factors like arsenic and fluoride, as well as anthropogenic factors like nitrate and organic contamination, also affect water quality.²¹ Till date India has reported twenty scientific case reports of PAM caused by *Naegleria fowleri* as given in **Table 1** and demographic distribution is given **Figure 1**.

Table 1. Reported Cases of Primary Amoebic Meningoencephalitis Caused by *Naegleria fowleri*(N=20).

S. No	Age	Gender	Place	Exposure	Fatality	Author, Year
1	3yrs	Male	Kolkata, WB	Puddles of water	No	Pan and Ghosh et al, 197121
2	6Months	Male	Kolkata, WB	Refugee Camp(Unknown)	No	Pan and Ghosh et al, 197121
3	8 yrs	Male	-	-	No	Singh et al, 199822
4	5months	Male	Mangalore, Karnataka	Well Water	Yes	Shalini Shenoy et al, 200223
5	26yrs	Female	Chandigarh	Unknown	Yes	Jain et al, 200224
6	6months	Male	Mangalore, Karnataka	Unknown	Yes	ShrikiranHebbbar et al, 200525
7	40yrs	Male	-	Unknown	Yes	P. Singh et al, 200626
8	8months	Male	Allahabad, UP	-	No	Ruchi Rai et al, 200827
9	20yrs	Male	Rohtak, Punjab	Unknown	Yes	Naveen Gupta et al, 2009 18
10	85yrs	Male	Kangra, HP	Pond water in Goa	Yes	A. Angrup et al, 201028
11	5Months	Male	Manipal, Karnataka	-	Yes	Vinay et al, 2011 29
12	73yrs	Male	Ludhiana, Punjab	Unknown	No	Gautam et al, 201230
13	6yrs	Male	Kangra HP	Kuhl Water	No	Sood et al, 201431
14	15yrs	Male	New Delhi	Uncleaned Pond water	Yes	Ravinder K et al, 201532
15	40yrs	Male	Jabalpur, Madhya Pradesh	Well Water	No	Gupta R et al, 201533
16	8months	Female	Haryana	Unknown	Yes	Mittal N et al, 202034
17	62yrs	Male	Thrissur, Kerala	Unknown	Yes	Suseela et al, 202135
18	47yrs	Male	Madurai, Tamil Nadu	River Water	No	Perumalsamy et al, 202136
19	14yrs	Male	Alappuzha	-	Yes	Joseph R et al, 202237
20	11 yrs	Male	Calicut	Pool Water	Yes	Joseph R et al, 202237

The case reports had varied age groups from three months to Eighty-five years, although most of the cases are found in children and young adults, the most commonly affected gender are males, and most of them had exposure to water, However, we cannot establish the fact that the source can only be water. As the cases are found across many states in India, but due to lack of information regarding the weather condition, we are unable to comment on the temperatures or season at which the disease was most commonly found.

Figure 1. Distribution of reported cases across India.

DETECTION

Direct wet-mount microscopy

To test for the presence of *Naegleria fowleri*, a small amount of cerebrospinal fluid (CSF) is mixed with 1 mL of distilled water. After an hour, the mixture is observed for flagellated forms, which are characteristic of the organism. If the enflagellation test result is positive, it indicates the presence of trophozoites of *Naegleria fowleri*. These trophozoites typically measure between 10-25 µm and exhibit limacine/eruptive amoeboid movement.^{38,39}

Examination of a stained cerebrospinal fluid (CSF) smear

Direct fluorescent antibody staining of CSF smears is useful for detecting *Naegleria fowleri* in the CSF.

Culture

To grow *Naegleria* species, one can use non-nutrient agar or a low-nutrient agar that contains a small amount of nutrients such as peptone (0.05%), yeast extract (0.05%), and glucose (0.1%), along with either living or killed bacteria. It can also be grown in defined axenic media. The plate should be incubated at 42°C because this temperature facilitates the growth of thermophilic amoebae while killing other free-living amoebae. A non-nutrient/low-nutrient agar is chosen to prevent bacterial overgrowth. The bacteria of choice include nonmucoid strains of *Klebsiella pneumoniae*, *Enterobacter aerogenes*, *Enterobacter cloacae*, and *Escherichia coli*. After several days, the plate should be microscopically inspected,

and *Naegleria* cysts can be identified by trails left by migrating amoebae in the lawn of the bacteria.^{38,39}

In 2017, a modified liquid encystment medium was discovered to be effective in isolating pure *Naegleria fowleri* cysts. The medium was developed from Page's amoeba saline.^{38,39}

Polymerase Chain Technique

PCR is used to amplify DNA sequences and is available at some research sites. A DNA probe specific to *Naegleria fowleri* is available to identify the pathogen in environmental samples. A rapid and sensitive assay for detecting *Naegleria fowleri* using the Mp2C15 probe has been developed in the US. A nested PCR assay has been applied to detect the parasite in domestic water sources.^{40,41}

THE PUBLIC HEALTH INTERVENTION

Chlorination of water

Chlorination and UV radiation are commonly used in recreational waters to remove *Naegleria fowleri*, however, viable cells can still appear in treated water despite chlorine doses being applied. In experimental testing conditions, the use of UV radiation in combination with similar doses of chlorine achieves complete removal of *Naegleria fowleri*.^{42,43}

The Indian states where *Naegleria fowleri* cases are detected should take the lead in instructing the village health and sanitation committees to strengthen their chlorination services. Besides chlorinating drinking water, it is also important to timely chlorinate wells, ponds, and other water reservoirs. This is the most cost-effective public health intervention that can be taken to prevent *Naegleria fowleri*-related diseases and deaths.

Regular Water or Soil Sample Detection

Due to the limited understanding of the ecology of *Naegleria fowleri* in India, it is crucial to take practical measures to prevent and control *Naegleria* infections. This involves increasing awareness of the disease within the medical community and educating the general public with the help of civic authorities.

Panda et al.¹⁹ conducted a study to identify the various species of *Naegleria fowleri* present in Northern India using the Polymerase chain reaction technique. This study can be replicated in other regions of India to aid in the easy detection of the organism in water bodies. Consequently, appropriate control measures can be implemented.

Other modalities

Individuals should avoid bathing or swimming in suspected contaminated water sources. Children must be closely supervised by their guardians while playing with sand, soil, or in outdoor fields and playgrounds.

CONCLUSION

Naegleria fowleri is a type of amoeba that causes Primary Amoebic Meningitis, which has a high fatality rate. In India, the cases reported are just twenty, However, the actual number of cases in India may be much higher than reported due to a lack of understanding of the organism, its ecology, and the best management methods. The disease has been on the rise globally over the years due to increasing pollution and rising global temperatures, which create a suitable environment for *Naegleria fowleri* to grow. As the disease is rare case control studies should be conducted in hospital set-up. In India to study the organism and develop early detection methods further researches should be considered. However, Polymerase Chain Reaction (PCR) testing can be costly, so the most cost-effective measures are either to avoid using contaminated water sources or to use chlorination. This review aims to help researchers, clinicians, and public health specialists understand the epidemiological pattern of *Naegleria fowleri* and take steps to prevent the emergence of this infectious disease in the future.

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Conflict of interest

There is no Conflict of interest.

Ethical Consideration

Not Applicable as it is a review article.

Author's Contribution

Concept RS, NA. Write up RS, DP. Review, RS, NA, GNK, DP. Figures and Table RS.

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