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Endemic Free-Living Amoebic Meningoencephalitis - A Public Health Headache & Breakthrough in Kerala, India?

Suresh Kishanrao*

*Family Physician & Public Health Consultant Bengaluru, India.

***Correspondence:**
Suresh Kishanrao, Family Physician & Public Health Consultant Bengaluru, India.

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Abstract: Brain infections are a major public health challenge in India as; there are an estimated 650,000 cases of encephalitis and 560,000 cases of meningitis annually nationally. Primary Causes of Meningitis include Streptococcus pneumoniae, Haemophilus influenzae type b (Hib), mostly in children and Neisseria meningitidis, Listeria monocytogenes and Tuberculous meningitis (TBM) contribute to vulnerable or older population's infections. Viral encephalitis due to Japanese Encephalitis (JE) are the leading aetiologies, a serious mosquito-borne condition contributing up to 40% of paediatric cases, and Herpes simplex virus (HSV), Enteroviruses, Dengue, and Chikungunya are other viruses causing encephalitis. Parasitic meningoencephalitis in India primarily refers to rare but highly lethal Primary Amoebic Meningoencephalitis (PAM) caused by free-living amoebae (FLA) like Naegleria fowleri often called the "brain-eating amoeba.

The first ever case of amoebic meningoencephalitis in India was documented in 1971 in two children in Kolkata, West Bengal. For decades, cases were rarely diagnosed and often lumped into the broader, poorly defined category of Acute Encephalitis Syndrome (AES). Between 2024 and 2025, the state of Kerala experienced its largest-ever documented outbreaks of amoebic meningoencephalitis.

Materials and Methods: This review integrates current understanding of their biology, epidemiology, clinical features, diagnostics, and treatment strategies, learning from Kerala outbreaks in 2024–2025. Rising water temperatures, high-risk behaviours like swimming in untreated freshwater and nasal irrigation with non-sterile water contribute to pathogen proliferation. People's practices of defecating and ablution near water sources leading to coliform contamination on one hand, and inadequate chlorination of most sources, increase exposure to contaminated water. Better diagnosis through PCR and metagenomic sequencing, have improved detection of infection and early Treatment, resulted in lower mortalities (24%) compared to the global rate of 90%.

Outcomes: The first reported case of PAM in 2024 was on May 21, involving a five-year-old girl. Official figures indicate a breakdown of the year-wise confirmed cases and reported fatalities 336 confirmed cases with 81 fatalities since the first case. Kerala has seen a surge in reported cases of amoebic meningoencephalitis due to stricter mandatory testing of all clinically suspected cases and statewide tracking. Given the fulminant course of Primary amoebic meningoencephalitis, aggressive empiric early therapy strategy on clinical suspicion without waiting for confirmation of diagnosis, with a combination of different classes of drugs, including amphotericin B and miltefosine, has been shown to improve survival.

Key words & Abbreviations: Primary Amoebic Meningoencephalitis (PAM), Amoebic liver abscess (ALA), Japanese Encephalitis (JE), Tubercular Meningitis (TBM), Naegleria fowleri, Acanthamoeba, CSF wet mount examination, Gram stain, Calcofluor stain, Giemsa stain, culture for bacteria as well as free-living amoebae & PCR testing, Amphotericin B, Nitroxoline, Public health alerts

Introduction

Brain infections are a major public health challenge in India. Nationwide, there are an estimated 650,000 cases of encephalitis and 560,000 cases of meningitis annually. Bacterial and viral pathogens cause most of these cases, with higher incidence rates and seasonal outbreaks disproportionately affecting children. Primary Causes of Meningitis include Streptococcus pneumoniae, Haemophilus influenzae type b (Hib), mostly in children and Neisseria meningitidis, Listeria monocytogenes and Tuberculous meningitis (TBM) contribute to vulnerable or older population's infections. Viral encephalitis due to Herpes simplex virus (HSV), Enteroviruses, Dengue, and Chikungunya and Japanese Encephalitis (JE) are the leading aetiologies in which JE, a serious

mosquito-borne condition contributes up to 40% of paediatric cases, particularly during seasonal outbreaks in states like Uttar Pradesh & Bihar.

Parasitic meningoencephalitis in India primarily refers to rare but highly lethal Primary Amoebic Meningoencephalitis (PAM) caused by free-living amoebae like Naegleria fowleri (often called the "brain-eating amoeba"), Balamuthia Mandrillaris and Eosinophilic meningitis (EM) a chronic aseptic meningitis often caused by helminthic infestation. EM is defined as eosinophils >10 per mm3 in CSF or >10% of total CSF leukocyte.[2] The most common infectious cause of EM worldwide are Angiostrongylus cantonenis, Gnathostoma spinigerum and Basyliascaris procyonis. Non-infectious causes include malignancy like non-Hodgkin lymphoma, multiple sclerosis, hyper eosinophilic syndromes, malfunctioning ventriculo-peritoneal shunt and adverse drug reactions.[2]

The first ever case of amoebic meningoencephalitis in India was documented in 1971 in two children. For decades, cases were rarely diagnosed and often lumped into the broader, poorly defined category of Acute Encephalitis Syndrome (AES). Between 2024 and 2025, India particularly the state of Kerala experienced its largest-ever documented outbreaks of amoebic meningoencephalitis. Amoebic liver abscess (ALA) is a leading cause of morbidity in India. While overall prevalence and demographic profiles have remained largely unchanged over the past 60 years. Modern advances in medicine have dramatically reduced mortality. While approximately 10% of the global population is infected with Entamoeba histolytica, with the highest prevalence concentrated in developing tropical countries, and nearly 20% of the Indian population carries the parasite, making India one of the highest-incidence regions in the world for liver abscesses.

This review integrates current understanding of their biology, epidemiology, clinical features, diagnostics, and treatment strategies, with a focus on the recent Kerala outbreaks in 2024-2025. Rising water temperatures, high-risk behaviours like swimming in untreated freshwater and nasal irrigation with non-sterile water contribute to pathogen proliferation and practices of inadequate chlorination, coliform contamination on one hand and better diagnosis through PCR and metagenomic sequencing, have improved detection.[3]

Outbreak & Case Reports:

Kerala PAM outbreak details: Amoebic Meningoencephalitis cases are predominantly associated with Kerala's clusters, sporadically documented across West Bengal, Tamil Nadu, Maharashtra, Uttar Pradesh, and Rajasthan.

Amoebic Meningoencephalitis in India remained dormant, after first two cases were documented in 1971 in two children in Kolkata. For decades, cases were rarely diagnosed and often lumped into the broader, poorly defined category of Acute Encephalitis Syndrome (AES). Between 2024 and 2025, the state of Kerala experienced its largest-ever documented outbreaks of amoebic meningoencephalitis. In 2016, Kerala (India) reported its first death from amoebic meningoencephalitis, a rare but almost always fatal disease, after which the state recorded a sharp rise in cases. The first reported case of PAM in 2024 was on May 21, involving a five-year-old girl. The second case, reported on June 25, involved a 13-year-old girl. Two additional cases were reported in July. All four children affected by the disease died.[1,3] The five-year-old girl bathed in a local river four days prior with four other children. Kerala has seen a surge in reported cases of amoebic meningoencephalitis due to stricter mandatory testing protocols and statewide tracking. Official figures indicate a breakdown of the year-wise confirmed cases and reported fatalities as 2024: 39 confirmed cases with 9 fatalities.2025: 201 confirmed cases, resulting in approximately 55 fatalities and 2026 (Jan–April): 96 confirmed cases and 17 fatalities.[4,5]

Enhanced surveillance and mandatory reporting under Kerala's One Health Action Plan, now are providing a closer reflection of true incidence. Earlier amoebic meningoencephalitis outbreaks could be traced to an individual source and season; however, cases in 2025 & 2026 appeared in scattered areas across Kerala, possibly enhanced by particularly warm weather and long monsoons. 2026 year's outbreak spans a wide age range, from young children to older adults, with age-related vulnerabilities likely contributing to higher case numbers. Consumption of water from contaminated wells or ponds and the practice of ritual nasal cleansing with unsterile water increase the risk for infection.

Kerala's One Health Action Plan (KOHA): KOHA is a multi-sectoral framework designed to manage infectious diseases, zoonotic outbreaks, and antimicrobial resistance (AMR). It is coordinated by the Centre for One Health-Kerala (COH-K) and integrates the Health, Animal Husbandry, Forest, and Local Self-Government departments. Following an initial implementation in the four districts of Pathanamthitta, Alappuzha, Kottayam, and Idukki, under the Rebuild Kerala Initiative, the program is now expanded statewide. KOHA prioritised active surveillance for amoebic meningoencephalitis, in 2025 which identified more cases than in 2024, with many lacking clear exposures, highlighting the need for ongoing detection. The government utilizes hundreds of thousands of local volunteers and elected representatives to track and report animal-to-human disease risks like leptospirosis, rabies in forest fringe and high-density settlements.

Discussions:

Globally, the first confirmed cases of Primary Amoebic Meningoencephalitis (PAM) were documented in 1965 in Adelaide, Australia, after four children died. The etiological agent, Naegleria fowleri, was identified by physicians Fowler and Carter. The first ever case of amoebic meningoencephalitis in India was documented in 1971 in two children in Kolkata. While cases were historically rare and sporadic, recent years have seen a surge, with large outbreaks and clusters centred in Kerala. Until 1970, amoebic meningoencephalitis was rarely diagnosed and often lumped into the broader, poorly defined category of Acute Encephalitis Syndrome (AES). Between 2024, 2025 & 2026 till date, state of Kerala, India experienced its largest-ever documented outbreaks of amoebic meningoencephalitis.

Historically, encephalitis tracking in India was dominated by the Japanese Encephalitis virus (JEV) first recorded in Vellore in 1955. While mortality rates have improved over time due to widespread immunization and better critical care, brain infections remain a severe concern. In India, Tubercular (TB) and bacterial meningitis present case-fatality rates exceeding 12% and up to 14% of survivors suffer from permanent neurological disabilities, such as hearing loss or cognitive deficits. Persistent challenges include underreporting, lack of standardized surveillance, limited rapid diagnostics, and absence of specific anti-amoebic agents. While JEV cases have declined in some regions following widespread immunization, amoebic and other zoonotic aetiologies (scrub typhus) have emerged as critical public health concerns.

Two types of amoebic meningoencephalitis exist: primary amoebic meningoencephalitis and granulomatous amoebic encephalitis. Primary amoebic meningoencephalitis is caused by Naegleria fowleri infection acquired within 14 days of exposure. The amoeba enters through the nose, travels along the olfactory nerve to the brain, and triggers severe inflammation, necrosis, and haemorrhage. Granulomatous amoebic encephalitis is caused by other free-living amoebae, such as Acanthamoeba, Balamuthia mandrillas, and Vermamoeba vermicularis, which can invade the brain and trigger devastating illness like N fowleri. The outbreaks occurring in Kerala since 2023, are mainly caused by N fowleri, Acanthamoeba, and Vermamoeba vermicularis.

Amoebiasis remains a significant public health issue in India, driven by E. histolytica as observed by this author since mid-1967. Prevalence ranges from 3-23% in asymptomatic populations and 0.64-11% in symptomatic patients. While overall intestinal cases have declined since the 1960s due to improved sanitation, severe extra-intestinal complications like amoebic liver abscesses remain highly endemic, particularly in regions like Tamil Nadu, the Northeast, and Andaman & Nicobar Islands.

Free-living amoebic meningoencephalitis (FLAM) is a rare but often fatal central nervous system infection caused by Naegleria fowleri, Acanthamoeba spp, Balamuthia Mandrillaris, with mortality exceeding 90 % globally.[3]

Epidemiology: The recent surge in Kerala has been linked to climate change, rising water temperatures, and poor chlorination or coliform contamination of recreational water bodies. The infection disproportionately affects children and young adults who participate in swimming or diving in untreated, warm water without nose clip. Clinical diagnosis of amoebic meningoencephalitis is challenging due to its non-specific presentation and resemblance to other CNS infections.

Patho-parasitology: The easiest route for Amoeba to reach brain is through nose. The nose harbours a cavity with multiple connected passages and chambers located deep in the skull. Cribriform plate a thin bone about half the size of our fingernail, separates the brain from nasal cavity. Amoeba must burrow a short distance to enter the brain. Once Amoeba reaches the brain it feeds on the brain tissue and multiplies. Sometimes Amoeba carries with it other organisms like bacteria and fungi which worsens the impact, as disease progresses rapidly, starting from headache & fever to seizures & coma and is almost always fatal.

Free living amoebae viz. Naegleria fowleri, Acanthamoeba genotypes T1-T23, Balamuthia mandrillaris and various other genera, are ubiquitous organisms that live in fresh or warm brackish water, lakes, ponds, irrigation canals, soil, etc. All the species rare central nervous system infections, Acanthamoeba is also associated with vision-threatening keratitis and disseminated disease. More than 20 genotypes (T1–T23) of Acanthamoeba have been described, of which a subset, genotypes T1, T2, T3, T4, T5, T10, T12, and T18, are implicated in human disease. Many patients have some comorbid conditions, like hypertension, diabetes, chronic liver disease, etc., additional risk factors warranting further investigations. Among these, the T4 genotype is the most isolated from both clinical and environmental samples and is considered the predominant pathogenic genotype worldwide.

N. fowleri, the only pathogenic species of genus Naegleria, causes an acute fulminant Primary amoebic meningoencephalitis (PAM) that is associated with high mortality. N. fowleri trophozoites especially thrive in warmer water temperatures between 30°C and 46°C. Acanthamoeba and Balamuthia lead to subacute to chronic infection (Granulomatous amoebic encephalitis) with relatively better survival. The infections are clinically indistinguishable from bacterial or viral meningitis or encephalitis. Naegleria trophozoites enter the brain mainly through the Naso-olfactory route and can affect healthy individuals. Acanthamoeba or Balamuthia infection is primarily acquired through breaks in the skin and spread via a hematogenous route, or via Naso-olfactory route or inhalation and mainly affects immune compromised individuals. Therefore, swimming in natural water & nasal irrigation practices are considered risk factors for free-living amoebae infections.

Symptoms: Symptoms of PAM include Headache, Fever, Nausea, Vomiting, trembling initially and develop later into Stiff neck, Confusion, Lack of attention to people & surroundings, Loss of balance, Seizures, Hallucinations, photophobia, Confusion and Coma.

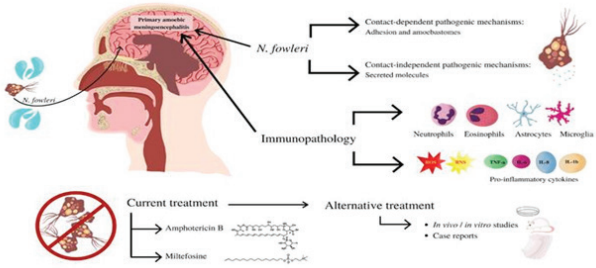

Fig 1. Immunopathology & Treatment of N Fowleri

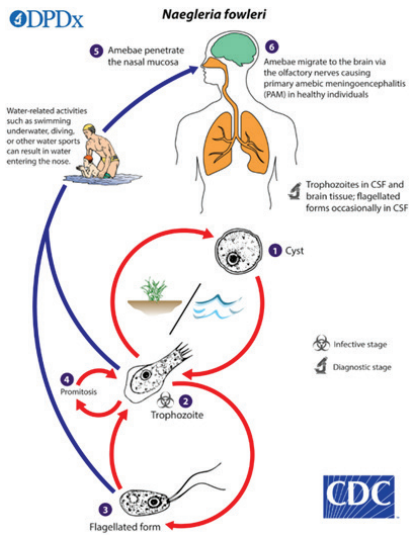

Fig 2. Life Cycle of N Fowleri

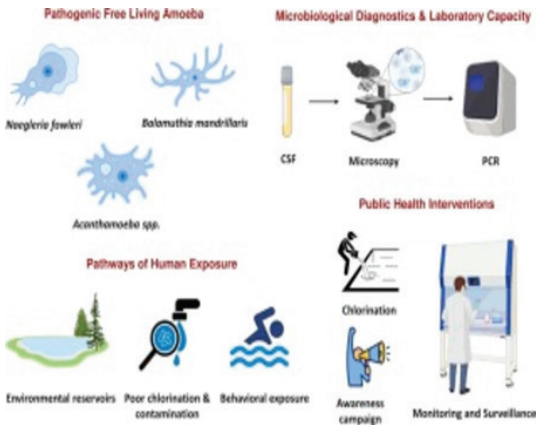

Fig 3. Free living Amoeba, Lab diagnostics, Pathways of human exposure and Public Health Interventions.
Sources: CDC Atlanta

Diagnosis: Routine culture methods do not detect these pathogens, making rapid microscopic examination of cerebrospinal fluid essential for identification; however, poor clinical familiarity with the organisms often contributes to missed diagnoses. Infection is confirmed by PCR and sequencing. Current guidelines in Kerala encourage a parallel search for multiple pathogens, to rule out concurrent infections as even when a bacterial or fungal cause is found, free-living amoebae can act as Trojan horses, in refractory or unusual cases".

Treatment: There are very few effective therapies for rare CNS infections caused by Acanthamoeba, Balamuthia, and Naegleria. Most available options involve off-label use of repurposed drugs, for example, a) for Acanthamoeba pentamidine (IV), sulfadiazine, flucytosine, miltefosine, and nitroxoline and for Naegleria-Amphotericin B, Azithromycin, Posaconazole, Rifampicin, dexamethasone, nitroxoline. Recently, Nitroxoline has emerged as a promising candidate, offering a safer, better antibiotic for neglected infections. Given the fulminant course of Primary amoebic meningoencephalitis, empiric aggressive early therapy is the strategy on clinical suspicion is high, and not wait for confirmation of diagnosis, as even a delay of a few hours worsens the prognosis. A combination of different classes of drugs, including amphotericin B and miltefosine, has been shown to improve survival.

Favourable Environment of Kerala: Kerala has an abundant, intricate network of low-lying freshwater and brackish water systems, mainly lakes, ponds, backwaters, etc. The temperature is warm and conducive to the proliferation of free-living amoebae. Intermittent chlorination, open reservoirs and informal water storage increase the risk of free-living amoebae proliferation and subsequent contact with humans in peri-urban and rural settings. Global warming has extended the ecological range of these free-living amoebae and is especially reported in unusually hot summers. Moreover, increased droughts and enhanced evaporation reduce water levels creating warm, shallow stagnant pools in which free-living amoebae flourish. In India, sporadic cases of free-living amoebae CNS infections are reported from all parts of India, but are increasingly reported from Kolkata and Kerala, and both these States have similar geography and climate. In these regions, close human-water interaction is common due to cultural and occupational practices such as recreation, bathing, swimming, religious rituals, irrigation, fishing, etc. Thus, there are multiple opportunities for exposure to the pathogenic free-living amoebae that may increase the risk of infection and disease. Most of the reported cases from Kerala have a history of swimming or nasal irrigation. It is, important to mention that Kerala's geographical landscape comprises of 40% water and it is next to impossible to treat each pond or well in the State and this may also lead to killing of fishes in ponds which is a source of livelihood.

Diagnostic vigilance of Kerala: It is documented that approx. 30-80 per cent cases of meningoencephalitis remain undiagnosed in developing countries. Kerala is known for its well-developed health infrastructure and was quick to respond to initial cases of PAM or Granulomatous amoebic encephalitis. Any patient with meningoencephalitis, especially with a history of exposure to recreational freshwater or non-treated water, are tested for free-living amoebae. It promptly improved diagnostic vigilance, built in-state capacity for PCR diagnostics of free-living amoebae, and sent the samples to referral laboratories outside the State to Postgraduate Institute of Medical Education and Research, Chandigarh, which detected Acanthamoeba with a few cases of N. fowleri and even one case of non-fowleri Naegleria. Most of the samples sent to the reference laboratories are responsible for recent rise in cases heightened clinical suspicion & early diagnostic workup for free-living amoebae. Early lumbar puncture, CSF wet mount examination, Gram stain, Calcofluor stain, Giemsa stain, along with culture for bacteria as well as free-living amoebae & PCR testing for multiple pathogens, including free-living amoebae are important. Brain biopsy remains the last resort for indeterminate progressive cases.

Kerala's success in improving survival: Kerala has been successful in improving the survival outcome of these patients in comparison to global mortality rates of >90 per cent, especially for Primary amoebic meningoencephalitis, due to early diagnosis and institution of an aggressive antimicrobial therapy with the addition of amphotericin B and miltefosine.

Concomitant Infections: Many of the reported cases in Kerala have documented the concomitant isolation of other pathogens from CSF in addition to free-living amoebae viz. Pneumococcus, Mycobacterium tuberculosis and Staphylococcus. This observation raises the possibility that free-living amoebae may act as a 'trojan horse' and harbour pathogens intracellularly and transport these to the CNS.

Public health messaging, alerts: Kerala outbreak management has strengthened public health understanding of the need to clearly alert public about the risk of infections while swimming in untreated waters. Keeping head above water or use nose clips while swimming or bathing, & avoiding nasal irrigation with untreated water, staying away from garden sprinklers, etc. are other individual actions.

Way Forwards: Research must focus on improved diagnostics, especially point of care tests, epidemiology, molecular epidemiology, pathogenesis & environmental surveillance. Non-invasive diagnostic approaches targeting free-living amoebae using small RNA detection in clinical specimens such as urine, blood and CSF have been recently described. These assays exploit parasite-derived small RNA or extracellular vesicle-associated nucleic acid identified by qPCR. Such biomarkers hold promise and exploration/validation in the Indian context could improve timely case detection, management and surveillance.

A clinical registry must be made to capture details of each case to learn about clinical features, risk factors and treatments that work better than others. There is a pressing need for comprehensive epidemiological, clinical and environmental tracking of free-living amoebae in India. Establishing an integrated surveillance framework that links clinical data and environmental sampling will allow identification of high-risk ecological niches. Real time reporting system and geospatial mapping tools can facilitate early detection of clusters, trace potential exposure sites and monitor environmental conditions conducive to free-living amoebae proliferation.

Environmental surveillance and management: High risk water bodies or hot spots (recreational lakes, pools, holy ponds, suspect sources implicated in case histories) should be tested using standardised sampling and concentration methods for further needful action if required. Longitudinal tracking of water sources, climate parameters, microbial co-association provide insights into transmission patterns, such multidisciplinary, data-driven approaches are essential for guiding public health strategies and mitigating future outbreaks.

Conclusion:

The vast majority of E. histolytica infections (≈ 90%) are asymptomatic. When clinical symptoms do manifest, present either as a) Intestinal Amoebiasis with symptoms typically emerging 1-3 weeks post-infection and include mild to moderate diarrhoea, severe abdominal cramping, and dysentery or b) Extraintestinal Amoebiasis- the most common being the Amoebic Liver Abscess, characterized by a high fever, hepatomegaly and intense pain in the right upper quadrant of the abdomen. Other complications associated with amoebiasis reported include colonic perforation, and ameboma. Rare but highly risky condition is Free-living amoebic meningoencephalitis (FLAM). High-Risk Groups include Immunocompromised individuals, notably HIV-positive populations. Kerala outbreak of amoebic meningoencephalitis serves as a reminder of how pathogens can exploit ecological niches and human behaviour. It also underscores the critical importance of strengthened diagnostics, timely clinical suspicion, & a swift public health response in reducing PAM morbidity & mortality. To minimize the risk of infection when handling local water sources in people must be advised a) not to swim, dive, or bathe in unclean, warm, or stagnant fresh water sources. b) use nose clips if swimming or diving in natural water bodies c) when performing ritual nasal cleansing always use boiled, cooled, or distilled water and avoid using untreated tap or well water d) Ensure that swimming pools and water theme parks are actively and properly chlorinated.

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