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Amoebic meningoencephalitis: we need to be more evidence based

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Abstract

Amoebic meningoencephalitis (AME) in India is on the rise each year, presenting a growing concern for public health. Despite its rarity, the high fatality rate associated with this amoeba poses a significant challenge. With India's abundant freshwater reservoirs, there is a potential risk of AME spreading to a larger population, as evidenced by a few reported deaths in various states, prompting concern among public health experts and healthcare professionals. Given the sporadic nature of AME cases and the lack of a robust treatment landscape and infrastructure, along with a shortage of well-trained healthcare personnel, patients are often diagnosed in advanced stages and face fatal outcomes. It is imperative to enhance our public health system and operational strategies to effectively address such emerging health threats. By implementing advanced diagnostic techniques, efficient treatment plans, and evidence-based practices to strengthen the healthcare workforce, we can better prepare ourselves to combat unforeseen and challenging healthcare scenarios. The current editorial delves into India's readiness to manage AME, focusing on epidemiology, diagnostic capabilities, treatment protocols, public health strategies, and research endeavors. It identifies existing gaps and offers recommendations to bolster the country's capacity to tackle this emerging health crisis.

Keywords: *Amoebic meningoencephalitis, communicable diseases, emerging tropical illnesses, brain disease, India*

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Evidence in Context

- AME is a rare, yet fatal emerging illness in India.
- The delay in diagnosis of AME poses challenges in the treatment and better patient outcomes.
- We need to equip our diagnostic centres and hospitals with advanced technology and updated information to handle the clinical situation of AME successfully.
- Public health policy and infrastructure should focus more on program implementation and its effectiveness in curbing the outbreaks of AME in our country.

To view Article

Editorial

India has been identified by the World Health Organization (WHO) as a country with a notable number of AME cases globally. In 2020, it was estimated that there are approximately 1,000-2,000 cases reported annually in India. This year, the unexpected emergence of a flu-like illness among certain individuals has captured the attention of public health professionals, following the COVID-19 pandemic. Despite previous cases of Naegleriasis, also known as brain-eating amoeba, the recent news has sparked concern within the public health community [1]. The rising incidence of cases, prolonged time to diagnose AME, and uncertainty surrounding the efficacy of established AME in India is on the rise each year, presenting a growing concern for public health. Despite its rarity, the high fatality rate associated with this amoeba poses a significant challenge. With India's abundant freshwater reservoirs, there is a potential risk of AME spreading to a larger population, as evidenced by a few reported deaths in various states, prompting concern among public health experts and healthcare professionals. Given the sporadic nature of AME cases and the lack of a robust treatment landscape and infrastructure, along with a shortage of well-trained healthcare personnel, patients are often diagnosed in advanced stages and face fatal outcomes. It is imperative to enhance our public health system and

Operational strategies to effectively address such emerging health threats. By implementing advanced diagnostic techniques, efficient treatment plans, and evidence-based practices to strengthen the healthcare workforce, we can better prepare ourselves to combat unforeseen and challenging healthcare scenarios. The current editorial in The Evidence Journal delves into India's readiness to manage AME, focusing on epidemiology, diagnostic capabilities, treatment protocols, public health strategies, and research endeavors. It identifies existing gaps and offers recommendations to bolster the country's capacity to tackle this emerging health crisis. treatment methods create a challenging situation for healthcare providers [1, 2].

The free-living amoebae, *Naegleria fowleri*, *(N. Fowleri*) is a facultative parasite, which does not depend on humans to reproduce and multiply. It is found in freshwater bodies and soil and causes AME, a rare and threatening central nervous system infection. Though this microbe, doesn’t need a definite host, it enters the brain via olfactory nerve [3] while swimming, and it destroys the brain tissues, mimicking the symptoms of meningitis. Poorly chlorinated swimming pools, water parks, lakes, and ponds are the source of this single-celled microbe, and it is less frequently reported from tap water at home [4]. They are larger than bacteria and well tolerate temperatures up to 115 degrees Fahrenheit. AME is identified into two types, caused by two different bacteria. *N. fowleri* does not spread through oral route, droplets or water vapour [5]. Transmission between humans and transmission caused by organ transplantation also have not been confirmed [6]. Primary meningoencephalitis (PAME) mimics bacterial meningitis and the other type is granulomatous amoebic encephalitis (GAE) which has symptoms of brain abscess, meningitis, or encephalitis. In many cases, the accurate diagnosis will be delayed because of the features mentioned above, and the mortality of the victims is exponentially higher even in hospitalized cases [2].

U.S Centres for Disease Control and Prevention (CDC) highlights that patients affected with PAME show symptoms within three to seven days but not later than two weeks after the infection. Initially, the patients experience headaches, fever, severe nausea, and vomiting. Later it worsens to a stiff neck, photophobia, behavioral abnormalities, confusion, seizures, hallucinations, coma, and eventually death. Death usually occurs after the onset of initial symptoms in the first stage. PAME is considered to be extremely fatal. Detection of protists by the immune system poses a greater challenge compared to bacterial and viral infections due to the similarity in cellular structure between the eukaryotic pathogen cells and host cells. This resemblance often leads to the pathogen being perceived as non-foreign by the immune system's pattern recognition mechanisms [7]. Animal studies have demonstrated that Tumor Necrosis Factor Alpha (TNFα) is essential in regulating the disease and the progression of PAM. Administration of TNFα to animals prevented the development of PAM, even when administered after the disease had already begun [8]. This throws light to the research in the treatment aspect of *N. fowleri* infection. PAME manifests in the brain through the occurrence of extensive hemorrhages and the subsequent necrosis of brain tissue [9].

There are a total of more than 20 cases reported in India as of May 2024. The cases are primarily reported from rural areas, particularly in states with a high number of water bodies, compromised sanitation, and poor drainage systems which can contaminate the water sources, particularly in monsoon. The role of social factors like urbanization, inadequate healthcare infrastructure, and climate change, in the contribution to the outbreak of AME cannot be neglected [10].

Although cases of AME are rare, the gigantic threat the disease poses to medical science is a challenging aspect. In most of the hospitals, an adequate measure to detect this illness is still in the pipeline. Besides, as it is uncommon for the frontline healthcare workforce to handle the cases, they will not be well prepared to handle, or frustrated to manage such situations. A lack of treatment algorithms in the cases of emerging tropical illnesses adds catastrophe to the emotional chaos of the medical team and other auxiliary staff despite the critical necessity of early diagnosis. Standard diagnostic tests including cerebrospinal fluid (CSF) analysis, microscopic tests of fluid from the patient’s nose and histological examination of tissues from Bulbus olfactorius may help to identify the infection with *N. fowleri*. Elevated white blood cell counts , increased protein levels, and low glucose levels. Even though Microscopic examination of CSF can reveal trophozoites, but this method is often unreliable. Recent advancements in molecular diagnostics offer more sensitive and specific options. Polymerase chain reaction (PCR) assays and next-generation sequencing can detect amoebic DNA in CSF or biopsy samples, facilitating early diagnosis. Additionally, metagenomic approaches have shown promise in identifying the presence of amoebae in clinical specimens, potentially revolutionizing the diagnostic setting for AME [11]. A distinguishing trait that

Can be utilized in the detection of *N. fowleri* is its capability to differentiate cells. When exposed to hypotonic water, *N. fowleri* transforms into its flagellate form within two hours. This distinctive feature facilitates the accurate diagnosis of *N. fowleri*, as other pathogens lack this specific ability [12].

The current treatment landscape with traditional prescriptions with medications including amphotericin B, rifampin, fluconazole, azithromycin, and miltefosine has evidenced the survival of a very small number of PAM cases and a combination of antibiotics (sulfadiazine, trimethoprim-sulfamethoxazole), antifungals (fluconazole, itraconazole), and miltefosine in GAE cases also has not shown a very promising outcome. More clinical and microbiological research into the host immune response to amoebic infections might bring out some positive outcomes shortly regarding definitive treatment regimens [13].

A recent case report of a 43 year old male in China, who was presented to the hospital with a high fever. There was no tracing in his medical history which indicated a possibility of contracting a communicable disease. His vital signs other than the temperature were normal, non-contrast CT scan of the brain did not show any significant abnormalities. Cardiac support and symptomatic treatment with piperacillin-tazobactam empirical antibiotic therapy was started. Four hours later, he suffered from seizures and fell into a coma. His Glasgow Coma Score was 3, and he showed signs of meningeal irritation. He was intubated, put on a mechanical ventilator, and admitted to the intensive care unit. A lumbar puncture was performed, revealing an opening pressure of 39 cmH2O (normal, 8–18 cmH2O). The CSF appeared yellow and cloudy, with a white blood cell count of 1081 cells/μL (89% neutrophils). Rapidly moving amoeba trophozoites were observed in the CSF. Staining of the CSF with Giemsa confirmed the presence of amoeba. The individual received meropenem (2000 mg every 8 hours), metronidazole (500 mg every 8 hours), and fluconazole (800 mg daily), as well as mannitol to decrease intracranial pressure and norepinephrine (16–24 μg/min) to sustain blood pressure. Nevertheless, by the second day of hospitalization, despite an escalation in vasopressor dosage, the patient's blood pressure continued to be low, ultimately leading to his demise, which was caused by *N. Fowleri* [14].

As our country, especially many states has a widespread presence of natural ponds, rivers, and other water bodies, the natural presence of amoeba poses a public health threat, especially among the people who engage in water-related activities such as swimming and other leisure entertainments. The socioeconomic and other ecological elements of our country, and the status of being a highly populated country, we are at high risk of an outbreak of illness and it transforms into a disaster in no time. We experienced the bitterness of COVID-19 a few years ago to the maximum extent in all the aspects to which the pandemic could lash the country. The lessons we have learned from the brunt of such a calamity certainly inspire us to rethink and re-question our public health policies and infrastructure, in terms of its scope to protect the populations of our nation [15]. The baton of public health expertise must be fuelling the decision makers to strengthen the basic concepts that would make us capable of being the number one country in the world, or at least among the Southeast Asian countries. A robust public health strengthening response paves the way for mitigating the emerging communicable diseases in our land. We need to cement the following components to fortify ourselves in the public health perspective. WHO stresses the necessity of advanced surveillance programs, elevated diagnostic practices, and advanced treatment strategies, especially in the regions where there is an outbreak of AME. Additionally, WHO recommends the need for early detection of the cases and effective therapy, so that it can bring out better patient outcomes and effective control measures with collaborative public health interventions [16, 17].

N. fowleri is classified under neglected tropical disease (NTD) due to financial constraints and a lack of trained medical professionals, and many NTDs play a significant role in the public health system of the south-east Asian countries [18, 19]. In line with WHO strategies to curb the magnitude and burden of AME, we need to focus on the following determinants, which are effective in mitigating this deadly disease [20].

Epidemiology

We lack true and clear updated data on the cases of AME. Our geographical terrain with its diverse climate and abundant freshwater resources is conducive for the growth of amoebae. The data on the incidence and prevalence of AME is limited as some cases may not get accurately diagnosed, or others may not be notified to government registries.

Recent Case Reports and Studies

Recently various cases have been reported from many states and sporadically in the past years, from other regions in the country. We need to develop a database for comprehensive reporting of AME or PAM cases, without underestimating the rarity nature of it.

Diagnostic Capabilities

The challenges in the early diagnosis are caused by the non-specific clinical presentations and the uncommon nature of the outbreak. Although these challenges are overlooked, early diagnosis and prompt treatment are critical in improved patient outcomes and reduction of fatality.

Laboratory Infrastructure

As AME is not a common communicable disease in India, (yet the number is increasing), we still rely on traditional laboratory methods to diagnose the cases. We need to have a kick-start in the development of advanced infrastructure for molecular diagnostic techniques and next-generation sequencing.

Training and Awareness

The need for training healthcare professionals in recognizing, diagnosing, and treating AME is reiterated by the increasing number of cases reported recently from many states. Dedicated and strategic awareness programs and training sessions focussing on clinicians, microbiologists, pathologists, and nursing staff, can improve the quality of care and standardization of the treatment protocol across the country.

Treatment Protocols

The treatment of AME in India follows international guidelines, with a combination of drugs such as amphotericin B, rifampin, fluconazole, azithromycin, and miltefosine. However, the availability and accessibility of these medications pose a challenge in many states of our country. More data need to be recorded and analyzed to develop a unique treatment protocol, considering the social, racial, geographical, and other parameters that affect the treatment outcome [21, 22].

Accessibility and Affordability

Treatment and management of AME is a challenge in many parts of India due to the unavailability of medications and problems with supply chain management, especially in some of the rural areas. Efforts are required to make available these drugs to the most needed rural areas for the effective management of AME. However, the accessibility and affordability of the treatment cost and facilities may not be a burden to the economy, as we have very few numbers of cases reported.

Public Health Strategies

Multifaceted public health campaigns and awareness programs must be launched by healthcare authorities, focusing on environmental management and regulatory measures. These campaigns should focus on safe recreational water practices, including avoiding swimming in warm freshwater bodies and using nose clips. Collaboration between health departments, environmental agencies, and local authorities is essential to ensure compliance and effectiveness.

Environmental Monitoring and Control

Monitoring and managing water quality in public swimming areas and water supplies are critical. Implementing guidelines for chlorination and regular testing of water bodies can help reduce the risk of amoebic contamination.

Epidemiological Studies

Large-scale epidemiological studies by the government and other private organizations are needed to determine the true burden of AME in India. People should be trained in the use of research materials to assess the facts and figures. These studies can provide valuable insights into risk factors, geographic distribution, and seasonal patterns.

Conclusion

India faces significant challenges in addressing the threat of amoebic meningoencephalitis, but with targeted efforts, the country can enhance its preparedness. Strengthening diagnostic capabilities, ensuring access to effective treatments, implementing robust public health strategies, and fostering research are key components of a comprehensive response. By addressing these areas, India can improve its ability to prevent, diagnose, and treat AME, ultimately safeguarding public health. Amoebic meningoencephalitis, though rare, poses a significant public health threat due to its high mortality rate and the increasing number of reported cases. Addressing this challenge requires a multifaceted approach encompassing early diagnosis, effective treatment, and robust prevention strategies. Continued research and public health vigilance are paramount in combating this devastating disease and safeguarding public health.

Abbreviations

AME: Amoebic meningoencephalitis

CSF: Cerebrospinal fluid

GAE: Granulomatous amoebic encephalitis

PAME: Primary meningoencephalitis

NTD: Neglected tropical disease

N. Fowleri: Naegleria fowleri

TNFα: Tumor Necrosis Factor Alpha

WHO: World Health Organization

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