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Brain Eating Amoeba: A Critical Analysis

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Abstract: ***Primary amoebic meningoencephalitis (PAM) is an uncommon yet deadly brain infection caused by a eukaryotic organism known as Naegleria fowleri (N. fowleri). The objective of this review is to consolidate recently published case reports of N. fowleri infections by detailing its epidemiology and clinical features, with the aim of disseminating this information to healthcare professionals. A critical analysis was done by using different available databases until August 31, 2023. All studies from 2013 onwards were extracted, and rigorous quality assessments were performed prior to their inclusion in the final analysis. The cases were geographically diverse, with 72.7% of cases resulting in mortality. The youngest case involved an 11-day-old infant, while the oldest was a 75-year-old individual. Substantial exposure to brackish water, either through recreational activities or the habit of nasal flushing, preceded the onset of symptoms. Early symptoms included fever, headache, and vomiting, while later stages exhibited neurological manifestations. Accurate diagnosis remains challenging due to symptom overlap with bacterial meningitis. Confirmatory tests involve visualizing the amoeba directly or using polymerase chain reaction (PCR) techniques. Infection with N. fowleri is rare but leads to PAM, a condition with global presence and significant fatality risk. A suggested clinical case profile, based on the findings, involves the sudden onset of fever, headache, vomiting, and meningeal symptoms after exposure to freshwater within the past 14 days. Continuous health promotion and public education about freshwater activities can enhance awareness and knowledge before engaging in such activities involving brackish water.***
Keywords: brain-eating amoeba; Naegleria fowleri; primary meningoencephalitis; encephalitis; amoebic encephalitis; free-living amoeba.

I. INTRODUCTION

In a tragic turn of events, India has reported its first recorded death caused by brain-eating amoeba on 6 July 2023. This incident has brought attention to the potentially fatal consequences of such infections and highlights the need for increased awareness, prevention, and research in tackling this rare but deadly infection. The victim, a 15 years old male, was admitted to Government Medical College Hospital (MCH), Alappuzha, India, with severe symptoms such as, which progressively worsened over a short span of time. Medical investigations and tests confirmed the presence of *Naegleria fowleri*, a free-living amoeba found in warm freshwater environments, which had caused a rare but severe infection known as primary amebic meningoencephalitis (PAM). Despite the medical team's efforts, the patient's condition rapidly deteriorated, and unfortunately, the infection proved fatal [1].

A. Brain-Eating Amoeba And Infection Mechanism

Naegleria fowleri is responsible for causing primary amebic meningoencephalitis, a rare but devastating infection of the brain and its surrounding tissues. The amoeba enters the body through the nasal passages, typically when an individual engages in activities such as swimming or diving in warm freshwater bodies, or by using contaminated water for nasal irrigation [2]. Once inside, the amoeba travels to the brain, leading to inflammation and tissue destruction. Amoebic encephalitis, a rare and often fatal infection of the central nervous system, has two main types: primary amoebic meningoencephalitis (PAM) and granulomatous amoebic encephalitis. These conditions are caused by free-living amoebae (FLA), microorganisms commonly found in freshwater environments like lakes and rivers, without requiring a specific host to survive [7]. Four primary genera of amoebae—*Naegleria*, *Acanthamoeba*, *Sappinia*, and *Balamuthia*—can transmit the disease to humans, with *Naegleria* causing PAM. *Naegleria fowleri*, nicknamed the brain-eating amoeba, is responsible for PAM and typically enters the body as the trophozoite form. It has a lifecycle with three stages and thrives in warm, soil-contaminated freshwater. Onset of the disease after infection can be rapid, with vague initial symptoms like fever and headache, progressing to more severe neurological signs as brain tissue is affected. Diagnosis is challenging as it mimics bacterial meningitis, but a history of freshwater exposure and cerebrospinal fluid analysis can help. Neuroimaging techniques like MRI and CT scans aid in visualizing affected brain regions, especially in later disease stages [8].

While infections caused by *Naegleria fowleri* remain extremely rare, the consequences can be dire [3]. The amoeba thrives in warm waters, particularly during the summer months, making warm freshwater bodies like lakes, hot springs, and poorly chlorinated swimming pools potential breeding grounds [4]. People engaging in activities that involve water contact with the nose are at risk, especially if the water is untreated or contaminated.

The potential reservoirs of *N. fowleri* are widespread [13]. According to a recent meta-analysis, *Naegleria* spp. prevalence in water sources from 35 countries is estimated at 26.42% [14]. Despite Malaysia's equatorial location, it hasn't reported *N. fowleri* cases. However, local studies reveal a significant presence of *Naegleria* spp., raising concerns due to existing waterborne parasitic infections [15] affecting parts of the country [16]. Over 70% of water samples from 11 states contain *Naegleria* spp. A brain-eating amoeba case linked to travel to Southeast Asia recently reported in South Korea has renewed attention [5]. This systematic review aims to consolidate *N. fowleri* knowledge from the past decade, offering insights for clinicians and public health specialists to plan interventions and stay updated on infections.

II. METHODS

The systematic review involved utilizing various databases including government sites. The selection of these databases was based on the authors' familiarity, institutional subscription coverage, and their recognized extensive collections. The search process followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

A. Operational Definition

Naegleria fowleri infection is commonly referred to as the brain-eating amoeba. In this study, articles were selected based on strict criteria, focusing on confirmed cases of *N. fowleri* infection, along with cases where other diseases were present simultaneously. This inclusion aimed to address the challenges healthcare facilities encounter when diagnosing *N. fowleri* infection. The diagnostic approach for *Naegleria* infection encompassed various methods, including but not limited to CSF, blood, and biopsy samples.

B. Data Extraction Tool

Each article's information was independently extracted by researchers onto an Excel sheet. The extracted data encompassed details such as year of publication, country, case count, gender, patient age, ethnicity, comorbidities, risk factors, exposure, symptoms, time to onset, elicited signs, full blood count, other blood results, CSF result, PCR result, culture result, imaging result, initial diagnosis, treatment, and survival outcome [9].

III. RESULTS

Regarding blood work, leucocytosis and raised CRP were common. Some cases had unique findings, like microcytic hypochromic anemia and raised ESR. Most studies reported CSF results, showing low glucose and high protein levels, with turbid fluid and elevated white cells. PCR tests were performed in most studies, often using CSF samples. Culture tests were mostly unsuccessful. Imaging techniques like CT and MRI were used widely. Finally, cases with confirmed or probable *N. fowleri* infection were treated with antifungal medications. One case was diagnosed postmortem using immunohistochemistry.

A. Discussion

This study provides an updated summary of knowledge about brain-eating amoebae. *N. fowleri* infections are rare but have resulted in a few case reports over the past decade. Earlier reports from the USA spanning 1978 to 2018 indicated 0 to 6 cases of PAM associated with water activities per year (total of 85 cases). However, some regions, like Pakistan, showed slightly higher transmission risks, with four cases in 2022. It's challenging to gauge the true infection burden due to underreporting, partly caused by diagnostic difficulties [8]. Diagnosing PAM is complicated by its vague initial symptoms and resemblance to bacterial meningitis, often leading to delays. Limited diagnostic tools exacerbate the issue [10]. While proposing key diagnostic features, it's emphasized that clinicians must remain highly suspicious and consider exposure history. *N. fowleri* is found worldwide, excluding Antarctica, in various water sources. Rapid diagnosis is crucial since PAM progresses swiftly, causing death within days. The amoeba's rapid entry into the brain via the nasal cavity leads to brain swelling and artery herniation.

Two models explain its pathogenesis: contact-dependent mechanisms involving adhesion and phagocytosis, and those linked to cytolytic molecules secreted by *N. fowleri*. Symptoms are linked to immune responses and affected brain areas [11]. Constitutional symptoms like fever arise due to reactive oxygen species, while specific brain regions exhibit distinct signs. Neuroimaging aids in pinpointing the involved areas.

The CSF sample findings can assist in ruling out viral causes of CNS involvement. Typically, a lumbar puncture is done for neurological symptoms and low opening pressure. Low CSF glucose with high protein levels excludes viral causes. If expertise is available, motile amoebae can be observed under a microscope. Accurate diagnosis is crucial; molecular techniques are recommended by the US CDC. Public health measures are vital due to *N. fowleri*'s high fatality. Public education and health promotions are needed for freshwater safety. Messages should include avoiding stagnant water, using nose protection, and more. Seeking treatment for symptoms post-water activities is emphasized. Proper maintenance of pools and using safe water for nasal irrigation is advised. The study has limitations in diagnosing PAM and language coverage. Some full texts were inaccessible due to subscription issues.

B. Prevention and Awareness

To minimize the risk of infection, individuals are advised to take several precautions:

1) Avoid water-related activities that could lead to water entering the nasal passages.
2) Use nose clips or hold the nose shut when participating in activities like swimming in freshwater bodies.
3) Ensure proper maintenance and chlorination of swimming pools and other water facilities.
4) Use only sterile or treated water for nasal irrigation or other similar activities.

S.No.	Country	Age	Sex	Exposure
1.	China	43 years	Male	Waterpark activities; traveller
2.	Turkey	11 days old	Male	History of bathing with unchlorinated well water
3.	India	15 years	Male	Bathing in unclean village pond
4.	Zambia	24 years	Male	Swimming in river; police recruit at training camp
5.	Bangladesh	15 years	Male	Bathing and contact with untreated ground water and river; irrigating nostrils

Table 1. Epidemiological data of some PAM cases reviewed [5,7 & 9].

IV. CONCLUSIONS

The first recorded death due to brain-eating amoeba in India serves as a grim reminder of the potential dangers lurking in warm freshwater environments. While the risk of infection remains low, it is crucial for individuals to be aware of the preventive measures that can be taken to safeguard themselves and their loved ones. Furthermore, continued research into understanding the infection's mechanisms and potential treatments is essential to address this rare yet life-threatening condition [12]. *N. fowleri* infection, while rare, results in PAM and is a global occurrence with a significant fatality risk. The proposed likely case description, based on findings, involves the rapid onset of fever, headache, and vomiting along with meningeal symptoms after exposure to freshwater in the past 14 days [17]. Opting for a broad clinical definition ensures quick suspicion in medical consultations, enabling timely diagnostic investigations. Ultimately, an early and accurate diagnosis is crucial for initiating aggressive treatment.

A. Contributions

Dr. Ravikant Singh design the review, Sanskriti Singh, Priya Kushwaha, Bhavya Shukla, Devraj Singh, Aniket Dubey, Ritika Kaushal and Preeti Singh collect the data and rewrite the work.

Conflict of interest: No conflict of interest.

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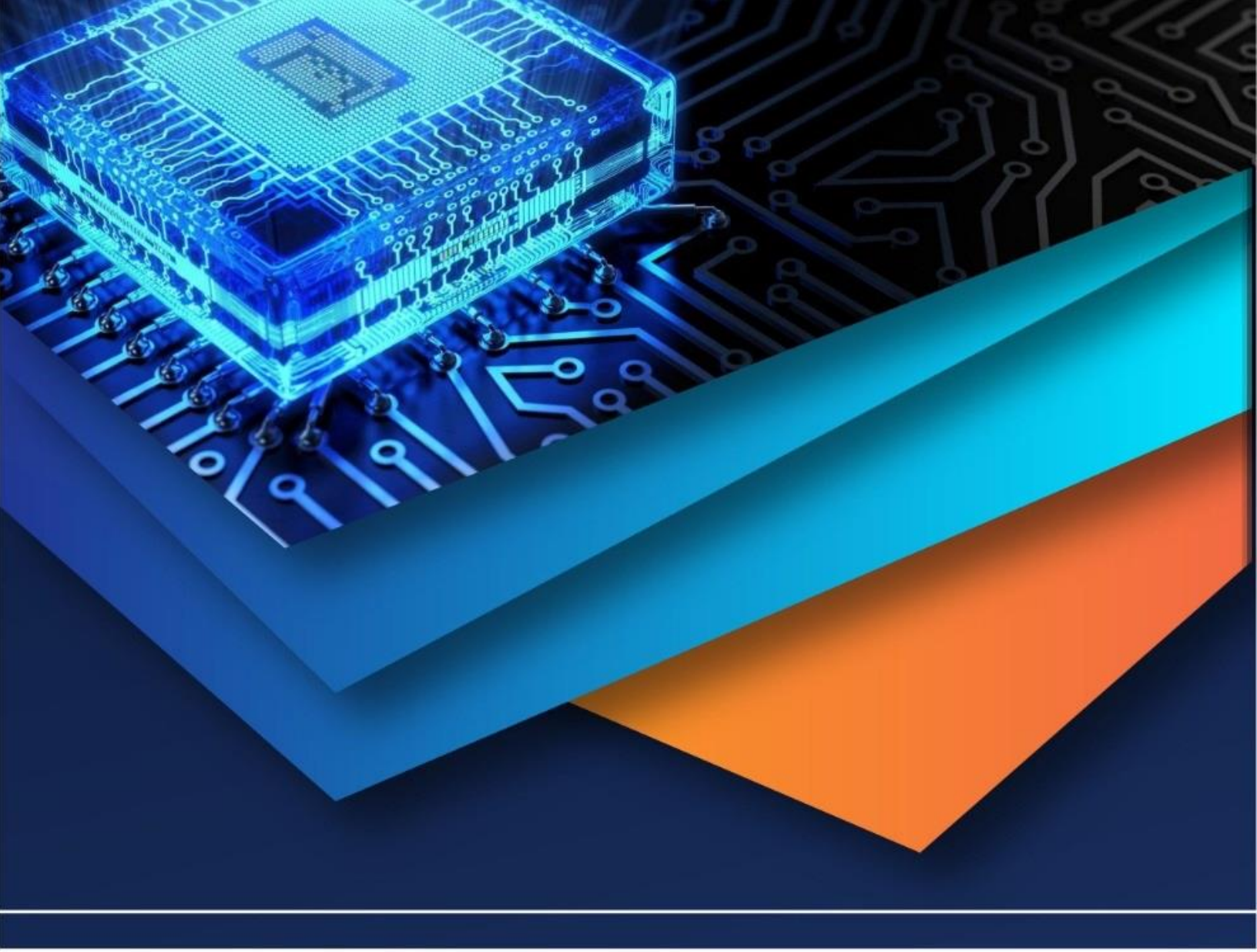

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