



# Primary Amebic Meningoencephalitis (PAM)

**Dias Rima Sutiono, Siti Aisyah**

Indonesia International Institute for Life Sciences (i3L), Jakarta, Indonesia

## ABSTRACT

*Naegleria fowleri* is one of free-living amoeba that can be found around the world. It is also known as the causative agent of Primary Amebic Meningoencephalitis (PAM). PAM is a rare Central Nervous System (CNS) infection and can lead to fatal outcome. Since the first discovery, it becomes the problem worldwide. Misdiagnoses are common in PAM patient. The causative agent of PAM is living in the warm freshwater. Thus, the occurrence of this infection is high in summer and warmest season through the year. Due to its life characteristics, this amoeba has the potential to live in the Indonesia waters. The purpose of this review is to describe the difference between PAM and bacterial meningitis, epidemiology, diagnosis, and prevention of PAM.

**Keywords:** *Naegleria fowleri*, Primary Amebic Meningoencephalitis (PAM)

## ABSTRAK

*Naegleria fowleri* adalah salah satu amuba yang hidup bebas dan dapat ditemukan di seluruh dunia. *N. fowleri* dikenal sebagai agen penyebab *Primary Amebic Meningoencephalitis* (PAM). PAM merupakan infeksi langka yang menyerang sistem saraf pusat (SSP) dan dapat berakibat fatal. Sejak ditemukan, PAM telah menjadi masalah global. PAM sering salah didiagnosis. Agen penyebab PAM hidup di air tawar hangat, oleh karena itu kejadian infeksi tertinggi saat cuaca terpanas. Karakteristik tersebut sesuai dengan iklim di Indonesia. Kajian ini diharapkan mampu menggambarkan perbedaan antara PAM dan meningitis yang disebabkan bakteri, epidemiologi, diagnosis, dan pencegahan PAM. **Dias Rima Sutiono, Siti Aisyah. *Primary Amebic Meningoencephalitis* (PAM)**

**Kata kunci:** *Naegleria fowleri*, Primary Amebic Meningoencephalitis (PAM)

## INTRODUCTION

Primary Amebic Meningoencephalitis (PAM) was first appeared in Australia in 1965.<sup>1</sup> Since the first case was identified, PAM has become serious problem worldwide. It is one of rare disease caused by infection of *Naegleria fowleri* in the Central Nervous System (CNS), but has relatively high Case Fatality Rate (CFR) which is more than 95%.<sup>2</sup> The high CFR is due to the short incubation period of only 1 – 16 days;<sup>3</sup> thus, patient usually shows symptoms in 1- 2 weeks after exposure. Death can occur in day 3-7.<sup>4</sup>

*N. fowleri* itself is a thermophilic amoeba which can be found throughout the world. The habitats of this amoeba are in lakes, bottom sediment, soil, ponds, rivers, contaminated tap water, low maintenance pools such as minimally chlorinated pool and hot spring. In nature, *N. fowleri* consumed smaller microorganism to fulfill their nutrition intake such as Gram-negative bacteria. However, once they enter the human body it will go to

the brain and eat the erythrocytes and nerve cells, causing brain inflammation and damage.

Depending on the condition, this free-living amoeba has 3 stages; cyst, flagellate and trophozoite. Under low nutrient surrounding, it will transform into flagellate. Cysts were formed under unfavorable condition such as cold temperature until the condition is getting better. When the nutrition and temperature are favorable, amoeba will transform into trophozoite which will infect the body.

*N. fowleri* is a heat-loving amoeba which optimally grows at 25°C – 42°C environment.<sup>5,6</sup> Thus, the organism has the ability to grow optimally in summer season. The range of water temperature in Indonesia is approximately 27°C-31°C;<sup>6</sup> it means that Indonesia might be one of the proper growing places for the amoeba.

## Epidemiology and Risk Factors

PAM cases were generally found in male

compared to female with 3:1 ratio. Of 440 cases reported worldwide in 2008,<sup>7</sup> most were occurred in America and Australia. There has been at least 39 cases reported in Asia, most cases were from Southern Asia including India and Thailand. Of 12 cases reported in Thailand, the gender ratio was 2:1, 2 cases were neonati.<sup>8</sup>

PAM might not be a familiar disease in Indonesia. However, the risk of having PAM may higher due to the life characteristics of the infectious agent. As shown in the figure, the water temperature in Indonesia in January 2016<sup>6</sup> has the potential to be the habitat of *N. fowleri*. In Indonesia, we commonly see kids, or young adults swim in the river or lakes or even the flood water which might have been contaminated with potentially harmful microorganisms. In 2001, Hidayat reported the presence of amoeba from *Naegleria* genus in the water sources basins from Cibural village, Bandung.<sup>22</sup> The basin water is the water source for fish pond and some are chemically treated and used as water supply in Bandung.



However, there is neither case reported nor journal that publish PAM in Indonesia yet.

There are several factors that may increase the risk of infection such as during summer time or warmest season;<sup>3,9</sup> *N. fowleri* is a thermophilic amoeba which can grow optimally in the warm freshwater. Therefore, amoeba has a higher chance to infect human especially during summer time in four-season-country.

Another factor is when the water level is low as kids commonly play in the sediment and the soil around lakes or rivers; this activity might accidentally make amoeba enter the body. When the sediment is digged in water-

related activities in shallow, warm freshwater areas, the amoeba can travel up the nose and into the brain. Once a person contact with amoeba via nasal mucosa, it will cross to the cribriform plate then move along to basilar olfactory bulbs; go to the cortex then move to periventricular system and causing meningoencephalitis with rapid cerebral edema that may result in intracranial pressure increase and cerebral herniation. However, infection will not occur when a person accidentally drink the contaminated water.<sup>1</sup>

**Clinical Manifestation**

The symptoms of PAM are mimicking symptoms of bacterial meningitis. Some cases

were reported misdiagnosed as bacterial meningitis.<sup>4</sup> In early stage the patient will show aspecific symptoms such as severe headache, high fever, nausea, and vomiting. Later the symptoms will develop into stiff neck, seizure, cranial nerve dysfunction such as vision loss, inability to smell and taste, anisocoria, altered mental status, hallucinations and coma.<sup>3</sup>

**Diagnosis and Treatment**

The diagnosis can be made by specific laboratory test. Due to its difficulty in initial detection, 75% are postmortem diagnosis.<sup>12</sup> Samples can be derived from brain tissue biopsy or cerebrospinal fluid (CSF) obtained from lumbar puncture (LP). The methods are direct visualization of the rapid move of amoeba in CSF sample under microscope.<sup>12,13</sup> Antigen detection can also detect the presence of *N. fowleri* in the specimen using immunohistochemistry and indirect immunofluorescence to stain the amebic antigen.<sup>12,13</sup> Polymerase chain reaction (PCR) and amoeba culture can also detect the amoeba.<sup>14-17</sup> Imaging tests such as CT scan and MRI are also be performed to detect edema and increased intracranial pressure.

Treatments can be administered through intravenous (IV) and intrathecal (IT) using specific antifungal such as amphotericin B 25 mg/kg/day, every 24 hours (daily 0.25 mg/kg increasing dosage up to 1 mg/kg/day), azoles: fluconazole, itraconazole, miconazole 10 mg/kg/day, every 24 h, synergistic antibiotics (rifampin) 10 mg/kg/day, every 24 hours; amoebas incubated with chlorpromazine (100 to 50 g/mL) showed a cell mortality rate of about 98%.<sup>23,24</sup>

**Comparison Study**

The clinical features of bacterial meningitis and Primary Amebic Meningoencephalitis are very similar. Hence, it is difficult to diagnose PAM initially.<sup>18</sup> Table shows the main differences of characteristics between bacterial meningitis and PAM.

**Prevention**

Considering the living environment of infectious agent and its transmission mode, several actions can be made, such as:

- Avoid to swim when the water level is low and during warmest season, during periods of high water temperatures and low water levels

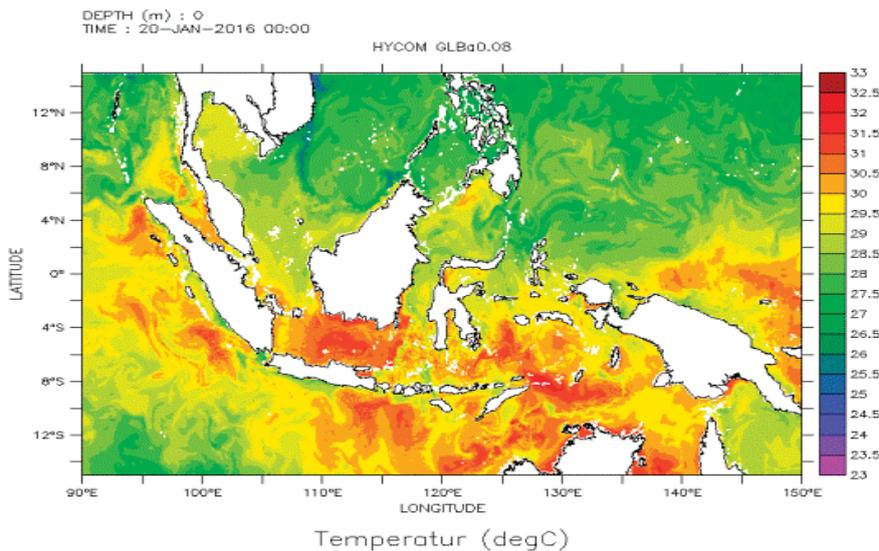


Figure. The water temperature in Indonesia in January 2016

	Bacterial Meningitis	PAM
<b>Infectious Agent</b>	Vary among age; <b>newborns:</b> Group B <i>Streptococcus</i> , <i>Escherichia coli</i> , <i>Listeria monocytogenes</i> <b>Infant and children:</b> <i>Streptococcus pneumoniae</i> , <i>Neisseria meningitidis</i> , <i>Haemophilus influenzae</i> type b <b>Adolescents and young adults:</b> <i>Neisseria meningitidis</i> , <i>Streptococcus pneumonia</i> <b>Older adult:</b> <i>Streptococcus pneumoniae</i> , <i>Neisseria meningitidis</i> , <i>Listeria monocytogenes</i>	<i>Naegleria fowleri</i>
<b>Transmission</b>	Some bacteria are not spread from person to person. Through respiratory and throat secretion (saliva or mucus). <i>Listeria monocytogenes</i> can be transmitted via contaminated food	Through swimming in contaminated water, usually warm freshwater in lakes and river. Drinking contaminated water cannot cause PAM. Cannot spread from person to person
<b>Case Fatality Rate (CFR)</b>	10-20%	>95%
<b>Diagnosis</b>	Blood cultures, CT scan and MRI, Cerebrospinal fluid (CSF)	PCR, Cerebrospinal fluid (CSF), CT scan, MRI
<b>Treatment</b>	Intravenous (IV) Antibiotics : ampicillin, cefotaxime, penicillin G, vancomycin	Intrathecal (IT) & IV amphotericin B, azoles : fluconazole, itraconazole. Synergistic antibiotics : azithromycin po, rifampin

Table. The main differences of characteristics between bacterial meningitis and PAM



- Close or use the nose coverage before jump to the lakes or any recreational water place
- Avoid digging the sediment or soil activity nearby warm freshwater area.

### CONCLUSION

Primary Amebic Meningoencephalitis (PAM) is one of rare disease that can cause fatal outcome. This infection is caused by free-living amoeba called *N. fowleri* which live in

the warm freshwater. The clinical feature of PAM is similar to bacterial meningitis infection. Thus, misdiagnoses are commonly happened. Better understanding and early treatment of PAM can increase the survival rate.

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