Original Article

Arousal of a New, Life-Taking Threat to the World..... Naegleria Fowleri!!

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ABSTRACT

Objective: Since we are living in the city near the cost shore and we have got a marine life as well along with the humans living in Karachi, A newly introduced life threatening Marine amoeba 'Naegleria Fowleri' should be brought into special considerations. Health officials have disclosed the news that this about 144 lives has been claimed in different countries all over the world by this deadly water borne infection (Primary amoebic meningoencephalitis).
Method: The major object of this study was to know how many people actually know about this lethal protist and what amount of victims we have of this brutal organism. A general survey was conducted among 100 people belonging to various categories of our society in Karachi. The type of participants we got included Students, Teachers, working men and women, local citizens and old age people who watch news on a regular basis with great interest.
Results: Our results showed us that most of the people in Karachi have some kind of perception regarding Naegleria and the major source of information was found to be Media and television. But none of them knew about the symptoms that appear after inhalation of this amoeba which creates greater chances of death of our people.
Conclusion: Since Naegleria fowleri enters through the nose and invades the CNS where it starts Tissue necrosis, due to which it is known as 'the brain-eating amoeba'. This brute has been causing frequent deaths of people around the world since the year 1962 and its first victim belonged to Czechoslovakia. Since the organism is not so common worldwide that's why people do not pay much attention towards it but number of deaths associated with it is increasing day by day throughout the world which is becoming a major cause of concern for our safety and health. The report highlights the major causes and symptoms of PAM so that people should have awareness about the fatal outcomes, this organism causes.

Keywords: life-taking threat, Naegleria fowleri, Central nervous system.

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INTRODUCTION

The major rationale of this whole study and research is the rapidly increasing number of deaths in Pakistan which is caused by this brutal organism i.e. Naegleria Fowleri, and all of the information mentioned below was collected through various articles, research papers, ebooks, books etc. N. Fowleri, a new threat to the world, is an amoeba that is usually found in fresh water and soil[1]. The organism belongs to the group of Perocolozoa or Heterolobosea and is supposed to be a free-living, thermophilic i.e Temperature loving form of protist and is usually present in warmer environment of ponds, lakes, rivers etc. The organism is also supposed to be present in soil, warm water discharges which are produced from the industrial plants and may also be present in swimming pools in which chlorination is not done properly and has greater risks of contamination. It is popularly known as 'Brain-eating Amoeba'[2]. There is no evidence of this organism living in salt water[1].

The question arises that when and by whom this Ameoba was discovered. With the help of various historical reports we have reviewed, it has been revealed that the first discovery of this lethal disease which is Primary Ameobic Meningoencephalitis, caused by Naegleria was done by the famous physicians M. Fowler and R. F. Carter in Australia, in the year of 1965[3]. This amoebic protozoan complete its life cycle in two stages, in which one phase is completed in the environment they are living whilst the second phase is completed in a human body. The first time when this amoeba was discovered was when a death took place in the year of 1961 due to this infection. Soon after, a death was reported from U.S in the year of 1962 and the person got infected was a common dweller in Florida. Before that, tissue samples were autopsied in Virginia in the year of 1937 and positive results of this infection PAM were obtained[4]. The studies and researches we performed showed us that more than 144 cases have been confirmed in a variety of countries since the year of 1965. And finally, in 1966, Fowler termed the infection resulting from N. Fowleri primary amoebic meningoencephalitis (PAM) so that the disease can be distinguished from other Central Nervous System disorders which may be caused by other organisms such as Entamoeba Histolytica[1].

Almost all of the researchers, scientists and physicians working on this deadly brute, have supported the fact that the assassin invades and attacks the human nervous system. The infection and availability of this organism is not so common but if this amoeba gets inside the human body it always result to death of the victim. The case fatality rate is estimated at 98%[1].Usually, the major source of inhalation this organism is via swimming. If a person loves diving and he inadvertently aspirates water through his nostrils then the amoeba enters through the nose and travels to brain where it starts invading the brain cells by performing tissue necrosis and death of the individual may occur within a few days and sometimes even in few hours. It may also be present in well-waters so children have the greater tendency of attaining this infection during bathing as their immune system is not so strong which may fight against such type of organisms. [3] Also, the major source of entering of N. fowleri into our nose is through ritual ablutions (wuzoo) performed by our adults as a part of our religious practices[5].

Researchers have documented that the organism goes through three stages in its life cycle: amoeboid trophozite stage (in this phase the mode of nutrition for amoeba is bacteria and the mode of replication is via

promitosis which is a type of binary fission and the organism proliferates but its nuclear membrane remains intact), if the environmental conditions become unfavorable for the amoeba as the ionic concentrations or temperature gets low, then the trophozoites will be transformed into the flagellated stage and reverts back when the conditions become favorable for them. But if the environmental conditions become highly unfavorable for them then they encyst their selves. The pathogenic form of this amoeba which is usually found in the CSF is the trophozoite form. Just like other amoebas, Naegleria Fowleri's mode of locomotion is also via pseudopodia[6]. While their mode of nutrition is of two types, they may be feeding on bacteria if they are in trophozoidal and free-living state; whilst if the trophozoites are present inside the human body, they get their nutrition by engulfing RBCs and WBCs and performs destruction of tissues[3]. The feasible period for the growth of this organism is during summer months as it is thermophilic in nature. In the popular press, Naegleria fowleri is intermittently called the brain-eating amoeba, and meningoencephalitis is sometimes referred to as Naegleriasis[4].

Literature survey revealed the pathways of N. Fowleri through which it performs major destruction in our brain cells. If the individual is freshly been exposed to fresh water, swimming pools, lakes, ponds or contaminated tap water containing this brutal protist, then the first and major path of entering into human body is via nose. N. Fowleri majorly pathogenies the Central Nervous System. The olfactory mucosa and the cribriform plate present in the nasal tissues allows penetration of this organism which starts causing necrosis and hemorrhaging of the nasal tissues and cells and moves forward by causing destruction of the olfactory bulbs. From there, the amoeba climbs along the nerve fibers via the floor of cranium and finally enters into the brain via neuroepithelium, and there it extends a special and unique apparatus from its cell surface for the purpose of sucking, and begins to consume cells of the brain imperceptibly, turning into a real pathogenic organism leading to the infection Primary Ameobic Meningoencephalitis (PAM or PAME) [2]. After the patient got hit by this life-taking amoeba, the major symptoms that develops initially appears within 5 days of exposure or it may take a few weeks to be prominent enough to notice. In the beginning of this infection patient suffers through changes in smell or taste which then progress to nausea, fever, loss of appetite and headache and finally the major symptoms appears as confusions, semi consciousness or coma. Physical examination shows fever and a stiff neck (meningismus)[7]. As we have discussed above that it is a Central Nervous System disorder so for further examination spinal tap should be performed in which spinal fluid will be examined to check whether the amoeba is present or not. A patient may also go through some of the newer tests available which includes the PRC i.e. Polymerase Chain Reaction technology to detect amoebic DNA in the spinal fluid[1].Chutatip Siripanth revealed in his research journal Amphizoic amoebae: pathogenic free-living protozoa that the organism N. Fowleri can be easily detected with the help of its life cycle as the amoeba goes through three stages of its life cycle which firstly includes the flagellate stage, trophozoidal stage and the cystic stage. It has also been discovered that around 10% of Naegleria species were found to be of Naegleria Fowleri in the human environment[9]. This life-taking specie can also be analyzed experimentally. Literature shows that if one needs to perform experimental analysis on N. Fowleri then this organism can be artificially grown by preparing a medium which may consists

of 2% Bacto-Casitone (Difco) and 10% fresh horse serum dissolved in distilled water. [10]. As we have already discoursed that inflammatory reactions are produced in the brain thus, the host inflammatory response and polymorphonuclear cell lysis contribute to a great extent to the central nervous system tissue damage and in this way the amoeba invades our CNS[11].

Taking the treatment in consideration, best choice would be amphotericin B through intravenous administration[5]. For the achievement of better results, it has been seen that instillation of amphotericin B through I/V and then also through I/C i.e. intrathecally (directly into the brain) improves the condition of the patient rapidly[8].

After observing some of the case studies present in various research articles, it has been showed that, so far the best treatment of PAM was done of a 9-year-old girl whose disease was diagnosed in early stages, with the help of intravenous and intrathecal administration of amphotericin B, intravenous and intrathecal miconazole and oral rifampin, this treatment provided the patient a healthy recovery by having only some of the minor neurologic ramifications. [10]In another research journal, it was reported that a 25-year-old Indian boy survived by a successful treatment consisting of amphotericin B, rifampicin, and fluconazole for 4 weeks, along with ventriculoperitoneal shunt for obstructive hydrocephalous. The child was kept under treatment for about 8 months and finally he recovered from all the neurologic disorders which may occur as a consequence of PAM. [11]. Current research shows intranasal administration of Cry1Ac protoxin alone or in combination with amoebic lysates increases protection against Naegleria Fowleri meningoencephalitis in mice[2].

Another method comprising of indirect immunofluorescence techniques may also be used for the detection of N. Fowleri in CSF. Studies from the literature surveys have showed that so far, the most effective treatment for Primary Amoebic Meningoencephalitis (PAM) is through the administration of amphotericin B[12,13]. The results of another study supported previous finding that not only amphotericin B, but, one of its derivative i.e. methyl ester of amphotericin B is also proved to be a really effective agent against this organism. A lot of combinations have been administered in order to achieve the best results for treatment of this disease but amongst all of them amphotericin B along with minocyclines or amphotericin B plus tetracyclines showed synergism[14]. In Britain, two children were infected by PAM due to muddy, puddle soil and they also survived and recovered by the treatment of Amphotericin B[15]. One of the literature reports also showed a case of a Chinese whose CSF was taken and N. fowleri was detected positively in it and successful results were obtained when a regular 6-week course of amphotericin B was administered along with rifampicin and chloramphenicol and brain drainage was also performed[16]. But Amphotericin B was a toxic antibiotic which may cause harms to other organs of the body so a new exploration was performed in which Chlorpromazine, Amphotericin B and Miltefosine were administered together in mice and the survival rates increased up to 75%. Thus, Chlorpromazine had so far, much better therapeutic activity against PAM[17]. Additionally, a disquisition has proven that azithromycin has both *in vitro* and *in vivo* activity versus N. Fowleri[18]. When further investigations for the vaccination of N. fowleri were performed it was suggested by the researchers that nfa1 vaccination might prove to be an effective method for treatment of N. Fowleri infection[19]. Desferrioxamine B and

rhodotorulic acid are supposed to be iron-chelating agents of microbial origin, and it has been launched that they exert a pronounced inhibitory effect on pathogenic specie of Naegleria at microgram levels[20]. Dilemma is that, many of the doctors, pharmacists, pathologists and laboratorians are still unaware about this free living brutal organism and the symptoms that appear after inhalation of N. Fowleri[21]. In Thailand, around 5 cases of N. fowleri infections were reported and around 4 of the 5 cases were males and none of them were exposed to the common sources which proves that amoebas can travel from one source to another [22]. It was also noticed in a research work, that, in Thailand there was fortunately a non-lethal case, and the author emphasized in his article that a dose regimen comprising of short doses of amphotericin B for a prolong period of time is much more effective as compared to larger doses of the drug for a short period of time to achieve immediate recovery from PAM[2324].

The focus of this article is mainly allied on the fact, that people are utterly incognizant regarding to the mortal organism N. fowleri and unfortunately, 2 lives has been claimed in Karachi this year due to same reason, which is a very big and dangerous threat for the people of our country. So it is our responsibility to spread consciousness about this deadly slayer and keep our society aware about the life-threatening dangers that this organism can produce. The objective of this research paper would be succeeded if health officials will make some good efforts for the betterment of people's health. Likewise, from now on, the locals of Pakistan should get complete understanding of PAM disease and its causative agent, and they should start taking some precautionary measures by keeping in consideration their children's healthy and sound future. In fact, for the betterment of or people, doctors constantly advise to use freshly, boiled, sterilized or filtered water and sewerage water should be avoided for drinking purposes. Also during ritual ablutions (wuzoo) nasal area should be cleaned properly, thus, all of the actions through which there are chances of inhalation of water inside our body like brushing teeth, gargling etc. should be done with proper measures and cleanliness should be a major factor to be concerned about. Furthermore, children should be completely informed about this fatal organism so that they avoid swimming the contaminated pools and rain water, in order to spread awareness among the people, government should launch various campaigns by pharmacists, clinicians and doctors who may advice to people and make them aware about all the precautionary measures they must take to be safe from the consequences of Primary Amoebic Meningoencephalitis. The major purpose of this research work is to make the people aware about the outcomes of this deadly organism, and all of the studies and cases that are highlighted in this paper are taken from the authentic journals and articles.

METHODOLOGY

The survey was conducted among 100 people belonging to various categories of our society in Karachi including students, teachers, working men and women, local citizens of our society and old age people who watch news regularly with great interest. Mostly socially active people were selected for our survey as their general knowledge is comparatively higher than the simple house wives. Also, media has been covering quite a few times about N. Fowleri that is why people who watch news regularly gave a better and positive response than the people who are not updated. The study that we conducted is based on general questions regarding Naegleria Fowleri, which included what they know about this

organism and how do they know. A questionnaire containing common questions about N. Fowleri was distributed among the common people and also generalized interviews were taken from the people belonging to different age groups. The survey was scrutinized using common language. People were questioned in a manner that whether they like swimming during summers or not, do they take any precautions while doing so and also, their familiarity to any water borne disease or specifically N. Fowleri was inquired.

Statistical analysis

The survey results are expressed in percentages in order to compare ratios of the people who know about the deadly water borne infections that can cause serious threats to our lives. (See figure 1.)

The distribution of N. Fowleri infections throughout the world are described as shown in Fig 2. Results are investigated from authentic references and researches.

RESULTS

Survey reports have showed that most of the people like to swim during summers but they do not pay any attention towards the important precautions they should take. Familiarity to the waterborne diseases was not as low as expected, in fact, most of the people surveyed, already knew about N. fowleri infection, and media proved to be the major source of information for them, but dilemma has been inspected that people do not consult to doctors if any of the symptoms like headache, nausea, stiff neck appear after they have dived in water. We also came to know that people were really interested to cognize more about the infection and they wanted the government to start some campaigns so that alertness could be spread amongst them.

From the data of Fig 1, 100 common people were surveyed in a report, 65% of whom were taken from the age between 20-25 years, 10% of them was of 35 years and above, 15% were the old age people ranging in between 60-75 years whilst 10% of teenagers of 20 years and below were involved. It has been examined from our reports that mostly people had some perceptions of water borne infections and a major quantity were also familiar with N. fowleri but still if any symptoms appear related to the disease, they do not pay much attention towards it and do not consult to their doctors which could bring a very hazardous situation in their lives as the disease is completely fatal and survival rates are extremely low. Government should start organizing some awareness campaigns so that the common dwellers of our country would become more conscious and protective about their children's life and it might save some of the innocent lives.

In Fig 2, Total data for 112 people has been investigated for observing the epidemiology of N. fowleri throughout the world. Among them 16 cases were reported from Czechoslovakia, 8 people were proclaimed from New Zealand, 22 victims were of Pakistan, a girl was broadcasted from United Kingdom, major distribution of this disease was observed to be found in United States, 9 lives were taken from Virginia, 20 fatal cases were reported from India, 2 patient belonged to Louisiana while one of them were from Vietnam. The result shows that, greater number of victims was found to be habitants of United States and after that Pakistan is on the main target of this brutal organism. So our locals should get beware of it.

DISCUSSION

Naegleria Fowleri is an amoebic parasite usually found in fresh water. It is supposed to be most active during summer months as it has also been found near warm water discharges, swimming pools and even the accumulated rain water. The organism

does not live in the presence of salt. It is aspirated through the nasal cavity and travels to the brain where it starts tissue necrosis and hemorrhaging, so ultimately it is known as 'Brain-eating Amoeba'. It is one of the best examples of microbes that complete their life cycle in the environment as well as inside the human body. The parasite goes through three stages of its life cycle i.e. cyst, trophozoite and the flagellate stage. It is the trophozoite form that causes human diseases. It mainly attacks the human nervous system and produces lethal effects.

The disease produced by this deadly amoeba is known as 'Primary Ameba Meningoencephalitis'. M. Fowler and R.F Carter were the first discoverers of this organism in the year 1965 in Australia. Epidemiology of PAM was initiated from Czechoslovakia between the years of 1962 and 1965 because of bathing in indoor swimming pools. And after that, the slayer has taken so many lives of innocent people all over the world, finally, a girl got survival of this life-taking disease in 2013 in United States, when the doctors lowered her temperature to 93 F. The survival rates of this disease are extremely low as just 2 among 128 people have survived so far. Signs and symptoms produced by this brute initiates from severe headache, nausea, vomiting, neck stiffness and then it leads to the secondary symptoms including confusion, hallucinations, lack of attention, ataxia, and seizures. As soon as the symptoms starts appearing in a patient of PAM, immediate diagnosis could be performed in a lab, simply by preparing an artificial liquid axenic media in which agar solution is poured with no nutrients in it on a petri dish and it is coated with a layer of bacteria. A drop of the CSF sample to be analyzed is dropped over the plate. If the CSF is victimized by N. Fowleri then the agar will be cleared off in thin tracks as the organism in its trophozoite stage will be feeding over the bacteria. If god forbid, diagnosis proves to be positive for the infection, doctors used to prefer Amphotericin B as the first choice of treatment for them. Then some of the research findings showed that Amphotericin B along with other drugs can produce greater therapeutic effect. But Amphotericin B was a toxic antibiotic so researches testified that Chlorpromazine had also a great therapeutic activity with less adverse effects to other organs. Vaccine development for this disease is still on progress but by far, researches revealed that nfa-1 gene can be used as a vaccination for N. fowleri infection.

PAM has a greater prominence in males rather than females with a ratio of 3:1. The organism has no prominent attraction according to the sex of the individual, but the only reason we have found so far is that there is a greater chance of exposure of males to the contaminated water and environment rather than females. Also children are at a greater risk of being swindled by the organism because they are greatly exposed to the contaminated pools, rain water etc. One more factor is considered which depends on the porosity of cribriform plate i.e. the cribriform plate in children and young individuals in found to be more porous as compared to the adults that is the reason they are more likely to be victimized by this lethal organism. So, children and young individuals who have recently bathed in swimming pools or hot water must be tested completely to diagnose the presence of this organism. PAM has also been reported via tap and hot water domestically and some cases of PAM has also been documented via fresh water during summer months when the sources of sewage water are usually warm. Number of cases have been reported till now but the actual reason that why this amoeba attack some specific individual and others are not affected by it is still cannot be identified. But to take precautionary measures especially during summer months should be highly considered in order to keep yourself and your family safe

from any lethal hazards caused by this amoeba.

Since primary amebic meningoencephalitis is a rare disease, and people are not much informed about the disease and the signs and symptoms that appear after inhalation of N. Fowleri are not known by the people, so our health care providers and especially our pharmacists must be well informed about each and everything regarding PAM, its signs and symptoms and also the treatment so that they may answer the patient's queries. Furthermore, it is their responsibility to spread awareness amongst people, and for that, they should organize informative campaigns regarding the precautionary measures people must take to be safe from N. Fowleri[25].

CONCLUSION

Naegleria Fowleri is the only specie of its Genus Naegleria, which causes serious lethal infections to human brain. It is not really common worldwide, that is the reason people do not pay much attention in spreading knowledge and awareness about it. The result of our survey has reported an increase of N. Fowleri PAM cases in the world and especially in Pakistan. Also various cases have been reported till now. Most cases were associated with freshwater swimming while ritual ablution (wuzoo) has also been a major factor for acquiring this disease as N. fowleri enters through the nostrils by aspiration and this has been the major route of acquiring this infection. This shows that threat is increasing day by day and many of the karachiites are at greater risk of having this lethal disease. So our locals should become more concerned about it, and pay attention towards taking the precautionary measures they usually ignore. And also our government should take some powerful decisions about sewage water we use, and make it sure to be clearly purified and free from Naegleria. Otherwise, chances of occurrence of more deaths from this fatal slayer will increase gradually.

This report highlights basic information about the fatal N. fowleri and emergence of its infection in a megacity. One of the major reasons for sudden increasing death rates due to N. Fowleri are the climatic changes which have badly affected the environment and people are being more prone to this disease. A worldwide survey must be conducted to identify the reason of this rise in PAM cases. And also, the research work at a greater extent must be performed for its treatment and development of vaccination if we really want to save the world from hazards of this organism.

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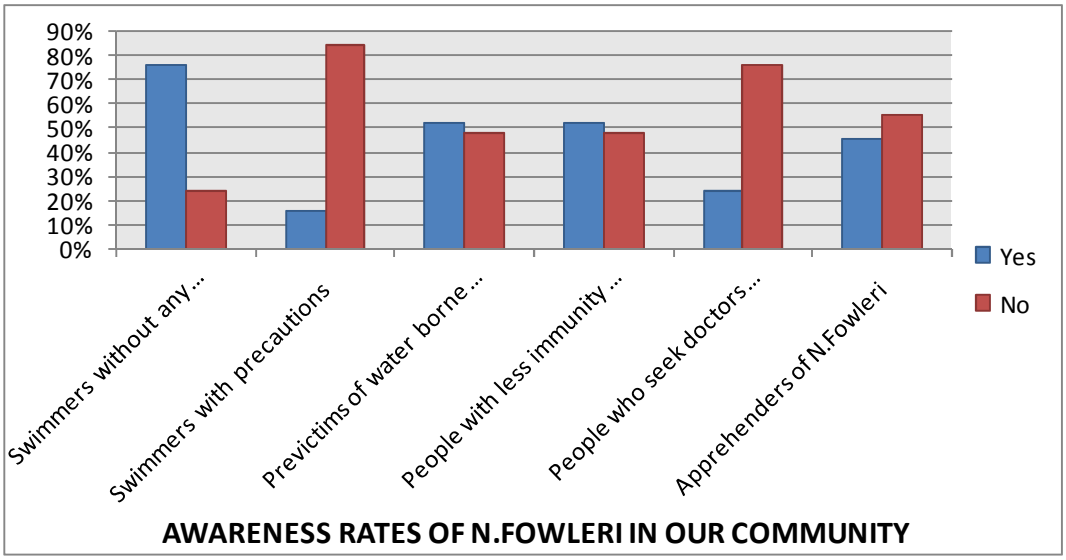

Figure 1. Survey reports of N. fowleri

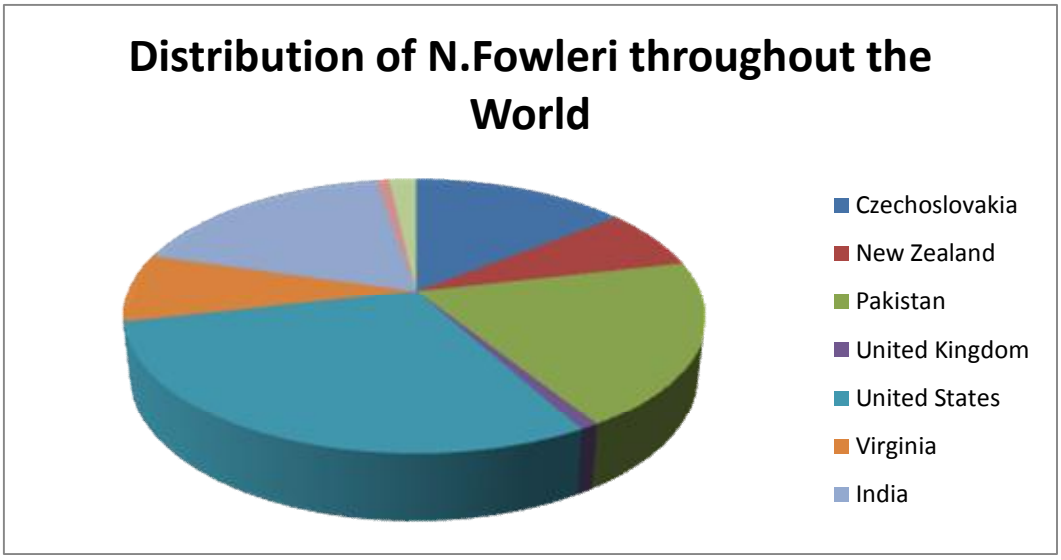

Figure 2. Epidemiology of N. Fowleri