A Review on *E. histolytica* Agents That Can Infect Humans

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***Abstract*: Amoebiasis caused by *Entamoeba histolytica* is an important issue in world public health because it is associated with high morbidity and mortality. *Entamoeba histolytica* is the only species of its genus that commonly causes mild irritation, injury, to inflammation of the walls of the colon and cecum. In some cases, parasites also invade other organs, especially the liver, lungs, kidneys, and brain.**
Methods: Our article search uses the help of four search engines namely Google Scholar, PubMed, Science Direct, and Springer. Results: *Entamoeba histolytica* is not easily transmitted from animals to humans, due to the fact that this parasite rarely encysts in the intestinal lumen of animals which is an important factor in the transmission of this parasite, and conversely, subclinical amoebiasis in humans acts as the dominant host for transmission of this parasite either from human to human or from human to animal.

***Keywords*: Entamoeba Histolytica, Zoonotic Potential, Amoebiasis.**

1. Introduction

Entamoeba histolytica is a pathogenic intestinal protozoan that is transmitted through water and food [1] [2]. This parasite is the only species of its genus that can cause mild irritation, injury, to inflammation of the walls of the colon and cecum [3,4]. In some cases (4-10%), parasites can invade other organs, especially the liver, lungs, kidneys, and brain [1,2,5]. *E. histolytica* infection causes amebiasis, and based on the location of the, amoebiasis is divided into two types namely intestinal amoebiasis and extra intestinal amoebiasis [6,7]. Extraintestinal amoebiasis is infection an advanced stage of infection and if it does not get proper therapy it can be fatal [4,8,9].
Amoebiasis is now rarely reported, even though the disease is still ranked third most deaths originating from parasitic agents after malaria and schistosomiasis [10-12], and the second leading cause of intestinal parasitosis behind cryptosporidiosis [12]. Case reports do not compare to the proportion of population deaths correlated with subclinical amoebiasis patients who are undetected and without treatment. Patients with subclinical amoebiasis for a long time are likely to become extraintestinal amoebiation which often results in fatality [13]. In addition, their sufferers also act as carriers of infective cyst transmission to other hosts. These phenomena of amoebiasis are often overlooked and difficult to eliminate in a community or state [9,14,15].
Besides humans, *E. histolytica* also infects Non-human primates (NHPs), cats, and dogs[16-19], and scientific studies have been widely reported. However, there are no reports of cases of amoebiasis transmitted from humans or vice versa, causing a lack of scientific studies that can answer the phenomenon of the transmission of this parasite across species. This review literature, we try to provide a scientific view of *E. histolytica* infection in humans and some mammals.

Methods:
Using combinations of keywords such as "*Entamoeba histolytica*" "amoebiasis" "zoonotic potential" etc. a search was performed on different search engines for articles on the topic related to *E. histolytica*. The search was limited to English language articles published previously. Resulting abstracts were reviewed and articles were excluded if the focus was not on the present topic in hand. Articles representing a developing body of literature were limited to the most recent date.

Results:
A total of 268 articles were retrieved through various search engines such as Science Direct, Google Scholar, Springer and Elsevier. We found 125 article titels that match the aspects of our study. Abstracts of 82 were reviewed 48 of which were selected and reviewed here.

Discussion:
1. Definition of parasite
The definition of parasite (literally para-beside, sitos-food) is any organism that derives benefits from living in or on another organism (the host) at a cost to the host[20].
2. Classification of Parasite:
Parasites of humans are classified in six major divisions. These include the protozoa (amebae, Flagelletes, ciliates, sporozoans and coccidia, microsporidia), the Nematoda or roundworms, the Platyhelminthes or flatworms (cestodes, trematodes), the pentastomids or tongue worms (may be grouped with the arthropods), the Acanthocephala or thorny-headed worms, the Arthropoda (e.g. insects, spiders, mites, ticks and so on). Although these categories appear to be clearly defined, there may be confusion in attempting to classify parasites, often due to the lack of known species or the presence of strains or races of the same species with slightly different characteristics [21].

3. *Entamoeba histolytica:*

Entamoeba histolytica is a pseudopod forming non-flagellated intesinal protozoan parasite [22,23].That causes amoebiasis originating from the Sarcomastigophora phylum, the Lobosea class, the Endamoebidae family, the Amoebida order and the genus Entamoeba[24,25]. National institute of Allergy and Infectious Disease (NI-AID) has characterized *Entamoeba histolytica* as a class B priority biodefence organism due to its minimal Infectious dose, ability to show resistance to chlorine, and natural steadiness which can represent a danger of simple dispersal through pollution of food and water supplies [22]. Amoebiasis is considered globally as a leading parasitic cause of human mortality and morbidity. However individuals living in developing countries, affecting both the young and the old, malnourished individuals and pregnant women are at greatest risk given poor sanitation and socio-economic conditions.[22,26]. In developed countries, such as in North America, amoebiasis is most common in travelers and rescent immigrants from endemic areas, and less common in men who have sex with men and immunosuppressed individuals [23,26]. Areas with highest rate of infection include India, Africa, and Central and South America particularly Mexico [22,26]. Worldwide it has been estimated that up to 50 million people are affected by *Entamoeba* histolytica and responsible for 40,000 to 100,000 deaths per year [22,23]. The rate of infection in amoebic colitis is almost identical between males and females. Amoebic liver abscess (ALA) is ten times more common males than in females and affects on those individuals of age between 18 and 50 years [26].

3.1 Life history:

Symptoms of the disease are identical agents that cause amebiasis has long been mentioned by Hippocrates (460-377 BC) as a disease of fever and deadly dysentery [25,27,28]. Only around 1875, a doctor from Russia, Losch managed to isolate the invasive organisms originating from the feces of chronic dysentery patients, then through long research in 1903 Schaudinn named the organism as *E. histolytica*. In the last two decades, the taxonomy of *E. histolytica* has changed significantly because there are two more species namely *E. dispar*, and *E. moshkovskii* which are very identical to them but are very different from the structure of DNA and biochemical molecules [29]. And of the three, only *E. histolytica* is pathogenic while the others are only commensal organisms [30]. *Entamoeba histolytica* and other intestinal amoebas can be detected microscopically, antigenic and antibody reactions, culture, and Polymerase chain reaction (PCR) [31]. Of these methods, microscopic methods are the Gold Standard for diagnosing diseases caused by this parasite. Besides being inexpensive, microscopic methods can also observe cell characteristics which are then used as species markers [32]. By distinguishing three species of identical morphological *Entamoeba* based on differences in genetic and biochemical structures, causing microscopic methods can not be used as the primary choice to distinguish these identical morphological species [31,33]. However, since the widespread introduction of isoenzyme molecular identification methods, the method for identifying identical *Entamoeba* has not become an obstacle anymore [27,34].

3.2 Life Cycle and Transmission:

life cycle of E. histolytica includes trophozoite stages, precysts, cysts, metacysts, and metacystic trophozoites [35,36]. Stage *E. histolytica* transition is strongly influenced by factors of food availability and environmental stress. Favorable environmental conditions, this parasite is in the excitation phase, namely the release of tropozoites from cysts that have the potential to invade tissue. Whereas, in a less conducive environmental condition, the parasite is in an enistation phase, namely the formation of cysts from tropozoites which have the potential to infect new hosts [37]. Estimated that 10-20 *E. histolytica* cyst cells that are ingested can cause disease especially in susceptible hosts. One infective cyst cell that is swallowed, will divide into eight young trophozoites and do not have the ability to invade tissue [38]. Under ideal environmental conditions, trophozoites quickly reach maturity. Mature trophozoites adhere easily and cause damage to tissue structures mediated by galactose or N-acetyl-D-galactosamine (GalNAc) and N-acetyl-D-glucosamine (GlcNAc) polymers [13]. In addition, several other specific enzymes such as proteinase, phospholipase, and hemolysin also act as synergistic factors, cell adhesion and cell damage [39,40]. The incubation period for *E. histolytica* can be several days to several months.

3.3 Pathogenicity and Clinical Symptoms:

Symptomatic sufferers often experience diarrhea and abdominal pain. In advanced infections, patients can experience diarrhea with feces mixed with blood, mucus, and pus [41,42]. Biologically, *E. histolytica* has the ability to be able to invade and migrate. The form of *E. histolytica* cyst can never be formed in tissue, and tissue invasion is a dead-end form in its life cycle. This also shows that *E. histolytica* is an opportunistic pathogen and invasion occurred accidentally [35,43,44]. *Entamoeba histolytica* is one of the water-borne zoonotic agents [35,45]. Besides humans, some mammals that can be infected by E. histolytica are Non-human primates (NHPs), cats, and dogs [1,16-18,25]. Other animals such as mice and pigs can also be infected with this parasite, but only act as a transit host [18,25]. *E. histolytica* infections in humans originating from animals almost never occur [25,38]. This may be related to the characteristics of parasites which very rarely encysts in the intestinal lumen of animals [18]. Three important pathways that contribute to the spread and spread of *E. histolytica* are 1) person to person transmission; 2) water and foodborne transmission and 3) vectorborne transmission [25,39-41]. Other factors that can also increase the risk of disease transmission are malnutrition, poverty, low education, jb density, inadequate water supply, and poor sanitation [42,36]. Fruits and vegetables that are eaten raw are not peeled and not washed properly as a medium for entry of various parasites into the digestive system [43,44]. Parasitic cysts do not die by water chlorination and detergents. However, washing with detergent and running water can dissolve attached parasites and carry water. Cysts can also be damaged with 5% acetic acid or low heating for 15 minutes [46,41,37]. Although this parasite can infect several types of mammals. However, so far we have not found reports of human amoebiasis from animals. We argue that *E. histolytica* is not easily transmitted from animals to humans, which is due to the fact that this parasite rarely encysts in the intestinal lumen of animals which is an important factor in the transmission of this parasite. And conversely, subclinical amoebiasis in humans acts as the dominant host for transmission of this parasite either from human to human or from human to animal.

Approximately 90% of *Entamoeba* infections are asymptomatic. Amoebic colitis generally has a acute onset with symptoms that can range from mild diarrhea to severe dysentery with abdominal pain and watery bloody diarrhea [26]. Amoebic liver abscess is the most common extra intestinal manifestation of amoebiasis. Approximately 50-80% of individuals with ALA will present with symptoms within 2 to 4 weeks, with fever and constant aching right upper quadrant pain. The lungs are the second most common extraintestinal organ affected. Pulmonary amoebiasis generally occurs by direct extension of an ALA but can also occur by direct hematogenous spread from intestinal lesions or by lymphatic spread[26].

Treatment:

Specific diagnosis and treatment is warranted in all infections caused by *Entamoeba* histolytica, even in asymptomatic carriers, not only because of the potential of developing invasive disease, but also to diminish the spread of disease.

Non-invasive colitis may be treated with only luminal agent such as Paromycin to eliminate intraluminal cysts. For invasive amoebiasis and extra intestinal disease, nitroimidazoles (e.g., metronidazole) are the mainstay therapy but are only active against the trophozoite stage. Fulminant amoebic colitis develops, broad-spectrum antibiotics should be added to the treatment due to risk of bacterial translocation. Surgical intervention is rarely necessary and reserved for those patients with signs of acute abdomen or those with toxic megacolon. In certain instances, aspiration of ALA is required, particularly when there is no clinical response after five to seven days of antiamoebic therapy. Patients with high risk of abscess rupture (cavity diameter of ≥ 5 cm and left lobe abscesses) or large amoebic plural effusions should also be considered for drainage. Imaging-guided percutaneous needle aspiration are catheter drainage is the procedure of choice.[26].

Education regarding the importance of hand washing and hygiene is the single most important measure in preventing the spread of amoebiasis, as well as other infectious diseases. It is estimated that washing hands with soap and water could reduce diarrheal diseases-associated mortality by up to 50%, particularly after using the toilet, changing diapers, and before handling or preparing food [26]. However, practicing personal hygiene may be difficult in many areas of the world due to lack of resources such as clean water and soap [26].

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