

# ***Entamoeba histolytica* Neglected Tropical Diseases (NTDs) Agents that Infect Humans and Some Other Mammals: A Review**

Junaidi Junaidi<sup>1\*</sup>, Umi Cahyaningsih<sup>1</sup>, Trioso Purnawarman<sup>1</sup>, Hadri Latif<sup>1</sup>, Etih Sudarnika<sup>1</sup>, Zinatul Hayati<sup>2</sup>, and Muslina Muslina<sup>3</sup>

<sup>1</sup> Department of Animal Diseases and Veterinary Health, Faculty of Veterinary Medicine, IPB University, Bogor, Indonesia

<sup>2</sup> Department of Microbiology, Faculty of Medicine, Syiah Kuala University, Banda Aceh, Indonesia

<sup>3</sup> Technical Unit for Implementation of Artificial Insemination and Incubator Livestock of Aceh Province, Jantho, Indonesia

**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*, amoebiasis, zoonotic potential.

## **1 Introduction**

*Entamoeba histolytica* is a pathogenic intestinal protozoan that is transmitted through water and food [1] [8]. 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 [2,5]. In some cases (4-10%), parasites can invade other organs, especially the liver, lungs, kidneys, and brain [1,8,48]. *E. histolytica* infection causes amoebiasis, and based on the location of the infection, amoebiasis is divided into two types namely intestinal amoebiasis and extraintestinal amoebiasis [4,16]. Extraintestinal amoebiasis is an advanced stage of infection and if it does not get proper therapy it can be fatal [5,6,7].

Amoebiasis is now rarely reported, even though the disease is still ranked third most deaths originating from parasitic agents after malaria and schistosomiasis [9,17]. 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 amoebiasis which often results in fatality [3]. 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 [7,18,37].

Besides humans, *E. histolytica* also infects Non-human primates (NHPs), cats, and dogs [38,39,41,42], 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.

## **2 Materials and Methods**

Our article search strategy uses the help of four search engines namely Google Scholar, PubMed, Science Direct, and Springer. The eligibility criteria are carried out by collecting all article titles and abstracts containing *E. histolytica* words or sentences, infections in humans or residents or groups of people, infections in Non-human primates (NHPs), infections in cats, and infections in dogs.

## **3 Results and Discussion**

### **3.1 Results**

We have scanned 317 titles and abstracts of scientific articles that contain the main words or sentences in the search engine, we found 119 article titles that match the aspects of our study. After reading one by one the abstract from the title, we picked 51 articles that were worthy of review.

\* Corresponding author: [junaidi\\_akljg@apps.ipb.ac.id](mailto:junaidi_akljg@apps.ipb.ac.id)

### 3.2 Discussion

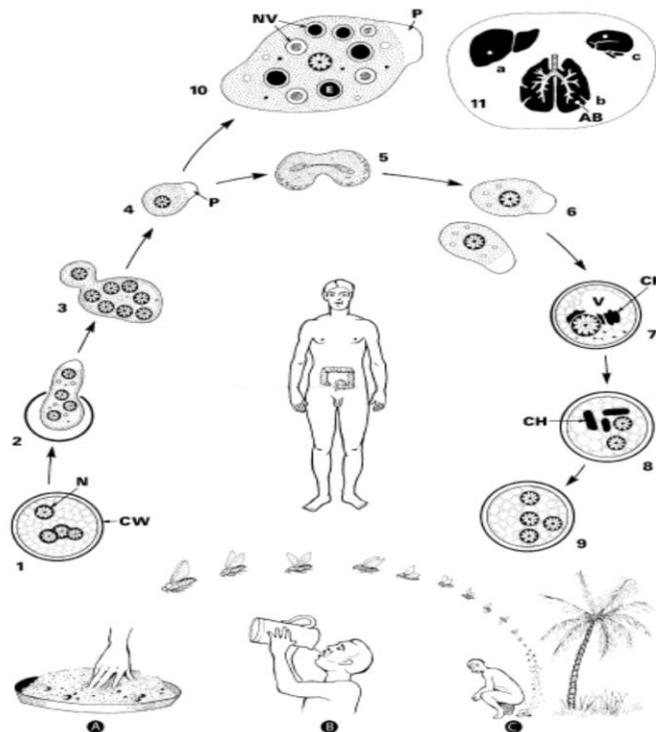
#### 3.2.1 *Entamoeba histolytica* is the causative agent for amebiasis

*Entamoeba histolytica* is an intestinal parasite that causes amebiasis originating from the Sarcomastigophora phylum, the Lobosea class, the Endamoebidae family, the Amoebida order and the genus *Entamoeba* [43]. 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 [19,20]. Only around 1875, a doctor from Russia, Dr. 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 [10]. And of the three, only *E. histolytica* is pathogenic while the others are only commensal organisms [21].

*Entamoeba histolytica* and other intestinal amoebas can be detected microscopically, antigenic and antibody

reactions, culture, and Polymerase chain reaction (PCR) [22]. 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 [23]. 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 [22,24]. However, since the widespread introduction of isoenzyme molecular identification methods, the method for identifying identical *Entamoeba* has not become an obstacle anymore [19,26].

The life cycle of *E. histolytica* includes trophozoite stages, precysts, cysts, metacysts, and metacystic trophozoites (Figure 1) [14,25]. 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 trophozoites 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 trophozoites which have the potential to infect new hosts [27].



**Figure 1.** Life cycle of *E. histolytica*. 1) Cyst with 4 nuclei (metacyst) from contaminated food or drinking water (A-C). 2-4) Once in the small intestine, the cytoplasm and nucleus are divided into 8 small amoebulae (metacystic to trophozoites). 5, 6) adult trophozoites (*minuta* form) reproduce by binary fission 7) Non-nucleated cysts (precursors) containing large chromatoid objects and glycogen vacuoles. 8) Cyst with 2 nuclei and body chromatoid. 9) Metacyst is excreted with the patient's stool and transmits another host. 10-11) Some forms of *minuta* can grow into histolytic (*magna*) forms, penetrate the intestinal wall and through the bloodstream, to other organs such as the liver, lungs, and brain (11 ac), parasites cause abscesses (amoebomae). Live amoebas are only found at the edge of this amoeboma. AB, abscess; CH, body chromatoid; CW, cyst wall; E, erythrocytes; P, singular, pale pseudopodium; N, Nucleolus (karyosome); NV, food vacuoles; V, young glycogen vacuoles of young cysts [13].

### 3.2.2 Pathogenicity and clinical symptoms

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 [11]. 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 [3]. In addition, several other specific enzymes such as proteinase, phospholipase, and hemolysin also act as synergistic factors, cell adhesion and cell damage [12,28].

The incubation period for *E. histolytica* can be several days to several months. Symptomatic sufferers often experience diarrhea and abdominal pain. In

advanced infections, patients can experience diarrhea with feces mixed with blood, mucus, and pus [29] [30]. 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 [14,15,36].

*Entamoeba histolytica* is one of the water-borne zoonotic agents [14,40]. Besides humans, some mammals that can be infected by *E. histolytica* are Non-human primates (NHPs), cats, and dogs [1,38,39,41] (Table 1). Other animals such as mice and pigs can also be infected with this parasite, but only act as a transit host [42]. *E. histolytica* infections in humans originating from animals almost never occur [35]. This may be related to the characteristics of parasites which very rarely encysts in the intestinal lumen of animals [42].

**Table. 1** Prevalence of *E. histolytica* infections in humans and some mammals

Research Title	Examination Methods (%)			References
	Number and type of sample	Microscopic	ELISA PCR	
Entamoeba infections in different populations of dogs in an endemic area of Lahore, Pakistan	600 dog faeces samples	55,7	11	Alam <i>et al.</i> 2015
Factors Associated with High Prevalence of Intestinal Protozoan Infections among Patients in Sana'a City, Yemen	503 man clinical stool samples	17,1		Alyousefi <i>et al.</i> 2011
Prevalence of <i>Entamoeba histolytica</i> among Primary School children in Ukwa West Local Government Area, Abia State, South East, Nigeria.	300 stool samples from children aged 0-14	16		Amaechi <i>et al.</i> 2014
Different Clinical Outcomes of Entamoeba histolytica in Malaysia: Does Genetic Diversity Exist?	500 stool samples population	18,60	5,6	Anuar <i>et al.</i> 2013
<i>Entamoeba dispar</i> , <i>Entamoeba moshkovskii</i> , and <i>Entamoeba hartmanni</i> in the context of water scarcity in northeastern Brazil	213 stool samples population	10,30		Calegar <i>et al.</i> 2016
Prevalence of <i>Entamoeba histolytica</i> , <i>Giardia lamblia</i> , and <i>Cryptosporidium</i> spp. in Libya: 2000-2015	-	19,90		Ghenghesh <i>et al.</i> 2016
Molecular identification of <i>Entamoeba</i> spp. in captive nonhuman primates.	520 sampel feses population		36,0	Leveck <i>et al.</i> 2018
Prevalence of <i>Entamoeba</i> species in captive primates in zoological gardens in the UK	37 in captive primates		16,2	Regan <i>et al.</i> 2014
Prevalence of intestinal parasites among expatriate workers in Al-Khobar, Saudi Arabia	1,019 medical files from expatriate workers	9,2		Abahussain and Abahussai. 2005
Intestinal parasitic infections in Campalagian district, south Sulawesi, Indonesia	380 samples population stool	10,9		Mangali <i>et al.</i> 1993
Status of gastrointestinal parasites in Red Panda of Nepal	272 samples Red Panda stool	7,41		Bista <i>et al.</i> 2017
A Survey of Intestinal Parasites of Domestic Dogs in Central Queensland	300 samples dog's stool	< 1		Gillespie <i>et al.</i> 2017
Intestinal parasitic infestations and anemia among urban female school children in Kancheepuram district, Tamil Nadu	360 samples of adolescent student stool	23.2		Gopalakrishnan <i>et al.</i> 2018

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) borne transmission vector [32,33,45]. Other factors that can also increase the risk of disease transmission are malnutrition, poverty, low education, population density, inadequate water supply, and poor sanitation [44,15]. 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 [31,47]. 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 [34,45,36].

## 4 Conclusion

*Entamoeba histolytica* is a parasite that causes amebiasis, a disease caused by this parasite as the third leading cause of death after malaria and schistosomiasis. Besides humans, *E. histolytica* also infects non-human primates, dogs, cats, and red pandas with very varied proportions. Although this parasite can infect several types of mammals. However, so far we have not found reports of human amebiasis 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 amebiasis in humans acts as the dominant host for transmission of this parasite either from human to human or from human to animal.

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