

Review: Facts Concerning *Entamoeba histolytica* Induced Amoebiasis

Nida Tabassum Khan*

Department of Biotechnology, Faculty of Life Sciences and Informatics, Balochistan University of Information Technology Engineering and Management Sciences, Quetta, Pakistan

***Corresponding author:** Nida Tabassum Khan, Department of Biotechnology, Faculty of Life Sciences and Informatics, Balochistan University of Information Technology Engineering and Management Sciences, (BUIITEMS), Quetta, Pakistan, Tel: +92 81111717111; E-mail: nidatabassumkhan@yahoo.com

Received: April 20, 2017; **Accepted:** May 04, 2017; **Published:** May 08, 2017

Abstract

Amoebiasis poses a serious health threat in tropical and subtropical developing areas of South and West Africa, Central and South America, India, Pakistan and Mexico caused by *Entamoeba histolytica*, a parasitic protozoan which invades the large intestine of the young ones and infants producing either asymptomatic conditions or dysentery with blood. All the data and valuable information obtained from previous researches and surveys indicating different prevalence rates of intestinal parasitic infections in different parts of the world. And its association with different parameters responsible for its distribution were also mentioned.

Keywords: Amoebiasis; *Entamoeba histolytica*; Dysentery; Prevalence

Introduction

Amoebiasis is the harboring of the protozoan parasite "*Entamoeba histolytica*" with or without clinical signs. It predominately infects the large intestine of humans and other primates [1]. This infection is quite common in children and adults, with widespread distribution in the tropical and subtropical areas [2]. It is documented that about 450 million individuals were suffered every year, with a frequency of 50 million deaths in total [3]. However, about 90% of these infections do not manifest any clinical symptoms while the remaining 10% shows a series of medical conditions such as inflammation of the intestine, presence of blood and mucus (dysentery) and liver abscess [4].

Prevalence of Amoebiasis

Amoebiasis as a potential health risk caused by *Entamoeba histolytica* [5], which enters the host tissues and causes acute amoebic dysentery followed with blood, mucus and tenesmus. Occurrence of intestinal infections were reported to be high among children less than five years [6,7] suggesting that screening tests for this age group may be useful revealing that *Entamoeba histolytica* was the most common protozoal infection as compared to Helminths [8]. *Entamoeba histolytica* induced infections were reported to be high in suburban communities [9] with an incidence rate of 1.4% in Islamabad [10], 8% in northern areas of Pakistan [11] and 48.86% in Konkor, Gadap, District East, and Karachi [12]. However, a low

prevalence of Ameobisis as 5.9% in children in Muzaffarabad city was reported [13]. Thus, amoebiasis is predominant in the developing countries, leading to deaths behind malaria and schistosomiasis [14,15]. However, distribution of *E. histolytica* infection varies from one place to another with different degree of infection severity [16] depending on a country socioeconomic condition. Approximately 50% of the population is affected in regions with poor sanitary conditions [17]. Rate of amoebiasis incidence in developed countries is low but has high occurrence rate in the developing countries such as Central and South America, India, tropical and sub-tropical countries of South and West Africa, Pakistan and Mexico [15]. According to a survey conducted in 2005, it was reported that prevalence of *Entamoeba histolytica* in childhood dysentery was high stating that it is a protruding aetiology of childhood dysentery [18]. Likewise, in 2008, intestinal amoebiasis in infants and junior school children was reported to be 11%. However improved sanitary conditions, good hygiene and deliberate government health policies will certainly alleviate its incidence rate by reducing the transmission of this intestinal parasite [19].

***E. histolytica*, the Amoebic Parasite**

Dysentery is caused by either *Shigella*, a bacterium or *Entamoeba histolytica*, an amoeba. *Shigella* induced dysentery is severe but can easily be treated. In contrast dysentery caused by amoeba is milder but respond slowly to medical treatment and often becomes chronic. Genus *Entamoeba* contains many species, six of which (*Entamoeba histolytica*, *E. dispar*, *E. moshkovskii*, *E. polecki*, *E. coli*, and *E. hartmanni*) harbor human intestinal lumen [20]. Among these, *E. histolytica* is regarded as the most hostile type due to its tissue dissolving carnivorous potential [21]. However initially *E. histolytica* was thought to be a single species, but molecular based diagnostic tests such as PCR or ELISA revealed two genetically distinct but morphologically identical species: the pathogenic *E. histolytica* that causes amebic by dysentery and liver abscess and the non-pathogenic *E. dispar* [22-25]. Multiplex PCR is more sensitive and reliable than conventional microscopy in the differential detection of *E. histolytica* and/or *E. dispar* in case of asymptomatic individuals in which *E. dispar* is more prevalent than *E. histolytica* and during mixed infection which is more common than single *E. histolytica* infection. Hence an accurate differential diagnostic tool for identification of *E. histolytica* and *E. dispar* is needed for appropriate chemotherapy and epidemiological purposes [26-28]. Due to recent redefinition of the two species, there felt a need for a new treatment approach for the individuals carrying these parasites because limited number of drugs are available to treat amoebiasis [29-32].

Mode of Transmission

E. histolytica is commonly transmitted through contaminated fresh food or water or by means of oral-anal sexual contact [33].

Life Cycle of *E. histolytica*

Life cycle of *E. histolytica* consists of two stages; cyst (infective stage) and the invasive trophozoites (vegetative stage). Cysts can survive outside the host for several months but intolerant to extremely low and high temperatures i.e. below -5°C and 40°C [34]. Infection occurs via ingestion of the infective cysts (only one is sufficient to cause disease), finding its way from the stomach to the terminal ileum, where they excyst to form daughter trophozoites. Approximately in 90% of cases, trophozoites re-encyst to produce asymptomatic infections which subsides within 12 months. However, in the remaining 10%, symptomatic amoebiasis develops. Trophozoites are motile and extend cytoplasmic projections, called pseudopodia to

engulf food particles and red blood cells. They invade intestinal epithelial cells, causing tissue destruction and enhanced intestinal secretion, leading to bloody diarrhea. They can also spread through the bloodstream, causing extra-intestinal lesions, mainly liver abscesses. The incubation period can last from two days to four months. *E. histolytica* trophozoites can convert back into a cyst during precyst stage in the large intestine. The cyst is then excreted in stools, thereby restarting the cycle [33].

Pathogenicity

The pathogenicity of amoebic trophozoites is related to their binding capability to the epithelial cells of the intestinal lining by a specific lectin (the galactose/N acetylgalactosamine lectin) and lysis of the target cells through a variety of molecules, including proteases, adhesins and amoeba pores [33]. During the invasive phase, mucosal IgA antibodies are produced against lectin to provide protection against invasion. Lymphocytes such as interferon- γ is produced in response to antigen-antibody interaction which mediates the macrophages against the trophozoites. Cell mediated immune response limits the spread of the disease and provide protection against recurrences. Although asymptomatic *E. histolytica* associated infection is able to invoke an antibody response but infections with *E. dispar* is not [31].

Sign and Symptoms of Amoebiasis

Clinical manifestation of amoebiasis may include abdominal distress, physical weakness, sickness, constipation with episodes of diarrhea, dysentery with blood and mucus [21,23,24]. Majority of *E. histolytica* infections are either asymptomatic or associated with very mild symptoms [34]. Risk factors for development of severe disease and increased mortality include young age (especially neonates), pregnancy, malignancy, corticosteroid use, malnutrition, and alcoholism [30,31]. Symptomatic amoebiasis is manifested by symptoms such as mild diarrhea, severe dysentery (proctocolitis), abdominal discomfort, bloody diarrhea and colic pain. Although one-fifth of the patients also experience weight loss [34] and 8% to 38% had fever [30]. These conditions can easily distinguish bacterial induced diarrhea where patients frequently suffers from fever, anxieties, headache, anorexia, nausea and vomiting [33]. Characteristic colonic features vary from mucosa thickening to ulcers which predominantly occur in the cecum. Less commonly, localized chronic colonic infection can result in a mass of granulation tissue called an amoeboma, which can be mistaken for colon cancer. Other rare intestinal complications include perianal cutaneous lesions, rectovaginal fistulae, and toxic mega colon. Although it occurs in only 0.5% of cases, fulminant colitis with necrosis, perforation, and peritonitis carries a mortality rate of about 40% to 50%. The most prominent extra intestinal exhibition of amoebiasis is liver abscess. Liver abscess occurs ten times more frequently in adults and males compared to children and females, respectively. With regards to laboratory investigations, leukocytosis can happen, but eosinophilia is not seen. ESR is usually elevated. In 80% of cases, elevated levels of alkaline phosphatase (ALP) and transaminases is seen with reduced levels of albumin. Stool analysis in the acute state commonly shows presence of Charcot-Leyden crystals and blood, absence of leukocytes in feces [33].

Diagnosis

Methods such as stool examination for the presence of cysts or trophozoites, serological testing, colonoscopy and biopsy of intestinal lesions could be used to diagnose invasive amoebiasis [33,34]. However, antigen and DNA detection enzyme immunoassays (EIA) and PCR could be employed for specie identification. Some consider EIA to be the best clinical test for diagnosing *E. histolytica*. Several antigen detection assays to differentiate *E. histolytica* from *E. dispar* are now commercially

available. Serological tests are also useful, as antibodies can be detectable in 75% to 85% of patients with symptomatic infection within five to seven days. Although indirect hemagglutination (IHA) is a sensitive assay to detect antibodies not accurate when differentiating between acute and previous infection, since antibodies can persist for years after resolution of disease. Although some consider stool microscopy to be less sensitive than antigen testing [35,36]. Sigmoidoscopy and especially colonoscopy are valuable tools for visualizing mucosal inflammation and typical ulcers covered with yellowish exudates, as well as obtaining scrapings and biopsy specimens. Ultrasound and CT are employed in cases of amoebic liver abscess and cerebral amoebiasis, respectively. It is recommended that individuals who are asymptomatic carriers of *E. histolytica* must be treated, as cyst carriers can be infectious and may develop disease after some time.

Treatment

Antibiotics such as metronidazole could be employed for intestinal amoebiasis treatment to eliminate the multiplying trophozoites and paromomycin for non-invasive type. Metronidazole treatment has cure rates of approximately 90% with no reports of resistance development. Other drugs such as tinidazole, ornidazole, chloroquine, and dehydroemetine is recommended for in-patient use. Treatment of peritonitis generally includes broad spectrum antibiotics. While surgery is indicated if significant bowel perforation is present, or if non-responsiveness to antibiotics with development of abscess following perforation develops. The one absolute indication for surgery is toxic mega colon, which is treated with total colectomy [30,31]. Work on vaccine development is currently in progress. Besides preventative measures like avoiding raw or uncooked food, unboiled water, contaminated fruits and vegetables etc. [37,38].

Conclusion

Thus “Amoebic dysentery” is recognized to have a global prevalence though precise incidence of its invasive dysenteric form in the tropics and subtropics where it is apparently pervasive is still unidentified. Regrettably, there is scarcity of data with respect to the dominance of intestinal amoebiasis in children inspite the number of affected ones is elevating.

REFERENCES

1. Lebbad M, Svard SG. PCR differentiation of *Entamoeba histolytica* and *Entamoeba dispar* from patients with amoeba infection initially diagnosed by microscopy. Scand J Infect Dis. 2005;37:680-5.
2. Ohnishi K, Kato Y, Imamura A, et al. Present characteristics of symptomatic *Entamoeba histolytica* infection in the big cities of Japan. Epidemiol Inf. 2004;132:57-60.
3. Ravdin JL, Petri WA. *Entamoeba histolytica* (Amoebiasis). Principles and practice of infectious disease 4th edition, 1995.
4. Trivediv VP, Nesamany S, Shara Vk. A clinical study of effects of Bilwa Majja Churna on intestinal parasites. J Res Indian Med yoga homeopathy. 1978;13:28-35.
5. Santos FLN, Goncalves Mde S, Soares NM. Validation and utilization of PCR for differential diagnosis and prevalence determination of *Entamoeba histolytica/Entamoeba dispar* in Salvador City, Brazil. Braz J Infect Dis. 2011;15(2):119-25.
6. Abdul-Aziz Kadir M, Mohammad-Al SM. Nutritional status of children infected with *Giardia lamblia* and *Entamoeba histolytica* infections in Kalar town, Iraq. Tikrit J Pharm Sci. 2011;7(2):1-10.
7. Mumtaz S, Siddiqui H, Ashfaq T. Frequency and risk factors for intestinal parasitic infection in children under five years

- age at a tertiary care hospital in Karachi, JPMA, 2009.
8. Mehmood K, Khan Sherwani MI, Ahmed M, et al. Parasitic infestation in children of district Vehari: An underdeveloped area of Pakistan. *Pak J Med Res.* 2009;48.
 9. Chacin-Bonilla L, Bonilla E, Parra AM, et al. Prevalence of *Entamoeba histolytica* and other intestinal parasites in a community from Maracaibo, in Venezuela. *Ann Trop Med Parasitol.* 1992;86:373-80.
 10. Ashok KT, Shamim AQ, Koji H, et al. Intestinal parasites in stool samples from children at the Children's Hospital Laboratory, Islamabad. *Pak. Pediatr J.* 1995;19:61-4.
 11. Hussain SM, Raza MI, Naseem S. Prevalence of intestinal parasites in Northern areas of Pakistan (Baltistan Division-Skardu). *Biomedica.* 1997;13:60-4.
 12. Siddiqui MI, Bilquees FM, Iliyas M, et al. Prevalence of parasitic infections in a rural area of Karachi, Pakistan. *J Pak Med Assoc.* 2002;52:315-20.
 13. Chaudhry OA, Petri WA. Vaccine prospects for amoebiasis. *Expert Rev Vaccines.* 2005;4:657-68.
 14. Wanke C, Butler T, Islam M. Epidemiologic and clinical features of invasive amoebiasis in Bangladesh: A case-control comparison with other diarrheal diseases and postmortem findings. *Am J Trop Med Hyg.* 1988;38:335-41.
 15. Farthing MS, Cavellos AM, Kelly P, et al. Intestinal Protozoa; In Manson's Tropical Disease. 20th edition, London W.B. Saunder Company. 1996;1255-67.
 16. Roche J, Benito A. Prevalence of intestinal parasite infections with special reference to *Entamoeba histolytica* on the island of Bioko (Equatorial Guinea). *Am J Trop Med Hyg.* 1999;60:257-62.
 17. Al-Harhi SA, Jamjoom MB. Diagnosis and differentiation of *Entamoeba* infection in Makkah Al Mukarramah using microscopy and stool Antigen Detection Kits. *W J Med Sci.* 2007;2:15-20.
 18. Ogunlesi T, Okeniyi J, Oyedeki O, et al. Childhood dysentery In Ilesa, Nigeria: The unusual role of *Entamoeba histolytica*. *Inter J Trop Med.* 2005.
 19. Nyenke C, Chukwujekwu DC, Stanley HO, et al. Prevalence of intestinal amoebiasis in infant and junior school children in Degema general hospital and environs. *J Appl Sci Environ Manage.* 2008;12(3):83-7.
 20. Fotedar R, Stark D, Beebe N, et al. PCR detection of *Entamoeba histolytica*, *Entamoeba dispar*, and *Entamoeba moshkovskii* in stool samples from Sydney, Australia. *J Clin Microbiol.* 2007;45:1035-7.
 21. Harold WB. *Entamoeba histolytica* in basic clinical parasitology. 4, Appleton-Century-Croft/New York. 1975:23-7.
 22. Gathiram V, Jackson TFHG. Frequency distribution of *Entamoeba histolytica* in a rural South African population. *Lancet I.* 1985:719-21.
 23. Haque R, Neville LM, Hahn P, et al. Rapid diagnosis of *Entamoeba histolytica* Infection by using *Entamoeba histolytica* stool antigen detection kits. *J Clin Microbiol.* 1995;33:2558-61.
 24. Haque R, Ali IKM, Petri WA. Prevalence and immune response of *E. histolytica* infection in preschool children in Bangladesh. *Am J Trop Med Hyg.* 1999;60:1031-4.
 25. Huston CD, Petri WA. Amoebiasis: Clinical implications of the recognition of *Entamoeba dispar*. *Curr Infect Dis Rep.* 1999;1:441-7.
 26. El Sobky MM, El Melegi MA, Abo-Khalil NA. Use of multiplex PCR in the differential detection of *Entamoeba histolytica* and/or *Entamoeba dispar* in comparison to microscopic examination. *PUJ.* 2011;4.
 27. Haque R, Faruque ASG, Hahn P, et al. *Entamoeba histolytica* and *Entamoeba dispar* infection in children in Bangladesh. *J Infect Dis.* 1997;175:734-6.

28. Rivera WI, Tachibana H, Kanbara H. Field study on the distribution of *Entamoeba histolytica* and *Entamoeba dispar* in the northern Philippines as detected by PCR. *Am J Trop Med Hyg.* 1998;59:916-21.
29. Lucas R, Upcroft JA. Clinical significance of the redefinition of the agent of amoebiasis. *Rev Latinoam Microbiol.* 2001;43:183-7.
30. Leder K, Weller PF. Intestinal amoebiasis. [monograph on the Internet]. Waltham, MA: UpToDate; 2005.
31. Horga MA, Naparst TR, Dhawan VK. Amoebiasis. [monograph on the Internet]. New York: eMedicine; 2006.
32. Stark D, Fotedar R, van Hal S, et al. Prevalence of enteric protozoa in human immunodeficiency virus (HIV)-positive and HIV-negative men who have sex with men from Sydney, Australia, 2007.
33. Espinosa-Cantellano M, Martinez-Palomo A. Pathogenesis of intestinal amoebiasis: From molecules to disease. *Clin Microbiol Rev.* 2000;13(2):318-31.
34. Tanyuksel M, Petri WA. Laboratory diagnosis of amoebiasis. *Clin Microbiol Rev.* 2003;16(4):713-29.
35. Abd-Alla MD, Ravdin JI. Diagnosis of amoebic colitis by antigen captures ELISA in patients presenting with acute diarrhoea in Cairo, Egypt. *Trop Med Int Health.* 2002;7:365-70.
36. Barbosa-Sabanero G, Avila E. Recognition of *Entamoeba histolytica* IIS, KDA surface protein by human secretory immunoglobulin from asymptomatic carriers. *Journal of Parasitology Institute De Investidcion En Biologia Experimental Facultad De Quimica Unersida De Guanajuato, Mexico PMID: 15165062, 2004.*
37. Knight R. Intestinal parasites and host susceptibility in children. In: Hendrickse RG, editor. *Pediatrics in the Tropics. Current Review.* 1st edition. ELBS/Oxford University Press, Oxford. 1985: 326-7.
38. Phuc Pham Duc, Hung Nguyen-Viet, Jan Hattendorf, et al. Risk factors for *Entamoeba histolytica* infection in an agricultural community in Hanam province, Vietnam. *Parasit Vectors.* 2011;4:102.