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Zoonotic Amebiasis: A Journey from Epidemiology to Treatment Strategy

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Abstract

The protozoan parasite *Entamoeba histolytica* is the cause of the disease known as amebiasis, which typically manifests as acute diarrhea, dysentery, amebic colitis, and amebic liver abscesses. *E. histolytica* is the fourth leading parasitic cause of human death. It mostly infects children in developing nations and is spread through contamination of food and water. *Entamoeba sp*. is present in the majority of infected individuals. Asymptomatically colonizes the large intestine and resolves on its own, whereas in others, the parasite can spread to soft organs and cause abscesses by breaching the mucosal epithelial barrier and causing amebic colitis. The treatment for invasive amebiasis that is both recommended and most commonly used is metronidazole (MTZ). Despite the fact that no amebiasis vaccine has yet been approved for human clinical trials, numerous recent vaccine development studies offer promise. For the counteraction and control of amebiasis, improvement of water cleansing frameworks and cleanliness practices could diminish illness frequency. The epidemiology, transmission, clinical signs, pathogenesis, diagnosis, treatment, prevention, and control of zoonotic amebiasis are the primary topics of this review.

Keywords: Amebiasis; Dysentery; Amebic colitis; Liver abscess; Zoonotic amebiasis

Introduction

The protozoan parasite *Entamoeba histolytica* is the cause of the disease amebiasis. In 1875, Fedor Lösch was the first person to identify the single-celled amoeba *E. histolytica* as the cause of human dysentery. *Entamoeba histolytica* is predominantly communicated through food water pollution, and is the fourth driving parasitic reason for kids' mortality in agricultural nation's .The symptoms of amebiasis range from acute diarrhea to dysentery to amebic colitis to amebic liver abscesses. The US National Institute of Allergy and Infectious Diseases have designated *E. histolytica* as a category B priority biodefense pathogen due to its serious impact.

Entamoeba histolytica is found all over the world, but it is most common in tropical and subtropical areas where amebic cyst contaminated food and water are consumed. The areas with low sanitation, poor dietary habits, and poverty have seen outbreaks of amebiasis. However, travelers and immigrants returning from exposed regions in developed nations have also been associated with *E. histolytica* infections [1-5].

Not only will gaining knowledge of the parasite's epidemiology, pathology, and molecular biology enable the development of more effective and safe vaccines for the disease's control, but it will also improve diagnostic and treatment options. *Entamoeba spp*. transmission and epidemiology, clinical signs, and pathogenesis are the primary areas of focus in this review to show how zoonotic amebiasis is diagnosed, treated, prevented, and controlled [6-10].

Epidemiology

Cycle of life

E. histolytica's life cycle is fairly straightforward and consists of two stages: the dormant cyst stage and the vegetative trophozoite stage. Stool typically contains the mature cysts, the parasite's infective form; the trophozoites, the parasite's invasive form, are typically found in the host's intestine and occasionally in diarrheal stool. After ingestion through contaminated water and food, *E. histolytica* cysts travel through the stomach to excyst in the terminal ileum, where they mature into trophozoites that colonize the large intestine by adhering to colonic mucins and feeding on intestinal microbiota. Upon becoming invasive, commensal trophozoites begin to destroy the muco epithelial barrier, resulting in an overproduction of mucus, the death of host cells, inflammation, and dysentery. Trophozoite populations may aggregate and reach high densities. This is expected to initiate the transition from exponential growth to encystation. Occasionally, in immune compromised patients, the parasites travel through the portal vein into the liver, causing the primary extraintestinal infection known as an amoebic liver abscess, or to the lungs and brain [11-14].

Host variability

According to numerous reports, humans are the primary host for *E. histolytica*, which causes severe intestinal and extraintestinal amebiasis. Other Entamoeba species, including *E. dispar*, *E. moshkovskii*, *E. coli*, *E. hartmanni*, *E. polecki*, and *E. bangladeshi*, are found in human intestines in addition to *E. histolytica*. Among these species, the nonpathogenic *E. dispar* is the most predominant species (49.4%), followed by pathogenic *E. histolytica* (32.3%), *E. moshkovskii* (10.2%), *E. gingivalis* (4.6%), *E. coli* (2.0%), *E. hartmanni* (1.0%), *E. polecki* (0.04%), and *E. nuttalli* (0.02%) in people. *Entamoeba gingivalis* is the principally species tracked down in human oral hole, and viewed as a likely microbial driver for damaging periodontitis in people, however it has likewise been tracked down in the genitourinary lot of intrauterine contraceptive gadget clients . Globally, the *E. dispar* infection is significantly more prevalent than the *E. histolytica* infection, despite significant variation in local prevalence [9]. The Entamoeba species *E. chattoni*, *E. coli*, *E. dispar*, *E. hartmanni, E. nuttalli*, and *E. polecki* that have been identified in Nonhuman Primates (NHPs) . As of late, another Entamoeba clade, to be specific Contingent Heredity 8 (CL8) alongside high paces of *E. coli*, *E. dispar*, and *E. polecki* diseases (up to 80%) have been accounted for in howler monkeys in Mexico . *E. histolytica* human derived cysts

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can also be experimentally infected in NHPs. numerous studies have been conducted to expand the host range of *Entamoeba spp.* As a result, *Entamoeba spp*. have been found in a number of other domestic and wild animal species, including elephants, pigs, cattle, sheep, goats, horses, deer, rodents, and reptiles[11].

Epidemiology

Infections caused by *Entamoeba histolytica* can also occur in developed nations in North America and Europe, where returning travelers or immigrants frequently become infected. According to Nagaraja and Ankri, amebiasis is now the third most common cause of gastrointestinal diseases among international travelers returning home (after giardiasis and campylobacteriosis). Communities can remain susceptible despite modernized infrastructure, as evidenced by a significant outbreak in Georgia from July to September 1998 caused by contaminated municipal water supplies. Worldwide outbreaks of amebiasis caused by water have been documented, making this disease a persistent public health issue that necessitates the attention of health authorities.

It is estimated that amebiasis was a global disease that was responsible for 55,500 deaths and 2.237 million disability-adjusted life years. It school aged children and adolescents appear to have a higher risk of developing amebiasis than the general population in some nations. Farming occupations and poor hygiene practices are major risk factors for *E. histolytica* infections in children. In countries where it is not endemic, *Entamoeba histolytica* has also been identified as an emerging pathogen among homosexual populations, primarily men, in Australia, Japan, Spain, Taiwan (China), and the Republic of Korea . It is common for HIV-positive individuals to receive positive serological results for the *E. histolytica* infection, which was also supported by molecular detection.

Active zoonotic transmission

Despite the widespread consensus that *E. dispar* and *E. coli* are not pathogenic to humans, they have frequently been found in humans and a phylogenetic analysis revealed that *E. dispar* isolates were most closely related to *E. histolytica*, a pathogen that can cause disease in humans. Some *E. histolytica* contaminations have additionally been accounted for in NHPs all through the world, including Belgium, Netherlands.

Pathogenesis

While *E. dispar* is a harmless commensal, *E. histolytica* is a species of Entamoeba that can cause diseases in humans. It has yet to be established whether *E. bangladeshi* and *E. moshkovskii* are pathogenic. *Entamoeba histolytica* is able to adapt to changing gut environments and manipulate the host immune surveillance system thanks to a unique set of virulence related characteristics. The binding of trophozoites to the colon's mucus layer, which is composed of secreted MUC2 mucin, is the first step in pathogenesis. According to Faust and Guillen , trophozoite populations may aggregate to high densities, which is thought to initiate the transition from exponential growth to encystation and virulence. It has been demonstrated that the Gal lectin adhesion, the most well characterized protein of *E. histolytica* related to pathogenesis, can trigger pro inflammatory immune responses. According to the expression and functional evaluation of a set of virulence factors in hamster or gerbil animal models, the virulence of *E. histolytica* is typically attributed to its capacity to destroy tissues through adherence, host cell killing, and extracellular matrix proteolysis. Extraintestinal amebiasis occurs when the parasite enters the bloodstream and travels to the liver, causing liver abscess that can be fatal and extensive tissue damage. In addition to the parasite's genotype and phenotype, each individual's immune status and environmental factors influence the outcome of *E. histolytica* infections. Disease sequelae, such as self-limiting and invasive colitis, have been observed in addition to the direct pathological changes brought on by the *E. histolytica* infection. These clinical manifestations may show up years after the infection was asymptomatic.

Diagnosis methodology

Amebicides, which are prescribed based on the severity of the infection, are typically used to treat amebiasis. According to their site of action, these medications are categorized as luminal amebicides (such as paro- momycin, diloxanide furoate, iodoquinol, and nitazoxanide) or tissue amebicides (such as chloroquine, emetine, tinidazole, and Metronidazole (MTZ)).

Metronidazole (MTZ), the most commonly prescribed and recommended treatment for invasive amebiasis. The parasite's thioredoxin reductase and possibly ferredoxin reduce MTZ to a nitroradical anion or, if further reduced, a reactive nitroimidazole, both of which are toxic to the parasite. However, MTZ treatment is associated with serious side effects such as anorexia, ataxia, skin rashes/itching, headaches, and a metallic or bitter taste in the mouth by Marie and Petri Jr. Despite the fact that as the most usually utilized medication to treat amebiasis, amebicidal fixations of MTZ were found to prompt parasite opposition under lab conditions. It was demonstrated that an increased expression of iron-containing superoxide dismutase and peroxiredoxin may have contributed to drug resistance. Additionally, some clinical strains of *E. histolytica* have been found to exhibit partial resistance to MTZ, pointing to the emergence of MTZ-resistant strains.

Preventive measures

There are both specific and non specific ways to prevent and manage amobiasis. Specific measures include vaccines against amobiasis, which are cost effective, safe, long-lasting, and have fewer adverse effects. Inoculations utilizing local and recombinant structures of the parasite Lady/GalNAc lectin were shown to have the option to safeguard creatures against digestive amebiasis and amebic liver cancer.

Conclusion

Amebiasis remains a significant threat to public health worldwide, particularly for children living in developing nations. The majority of the documented waterborne outbreaks of amebiasis were brought on by contamination of the water supply.

In order to improve our understanding of Entamoeba, further research into its epidemiology, pathogenesis, diagnosis, and treatment is required. This will ultimately assist in the prompt detection and control of amebiasis. Despite the fact that nitroimidazoles remain the primary treatment for amebiasis, new therapies are still required due to their toxicity and potential concerns regarding the emergence of resistant strains. Drug rediscovery, drug targeting of essential *E. histolytica* components, drug targeting of existing amebicides, and the utilization of probiotics and bioactive natural products ought to be purposefully designed and evaluated for their efficacy. In addition to drug design, efforts are required to create safe, cost effective vaccines against *E. histolytica* infections. With the distinguishing proof of proteins which assume focal part in infection pathogenesis, ongoing examinations present promising outcomes for the advancement of immunizations. To reduce Entamoeba infection, effective parasite control is even more important. However, it takes a significant amount of time, modifications to government policies, and financial investments to improve water

purification systems and hygiene practices, which can significantly reduce disease incidence. Thus, the improvement of antibodies what's more, the presentation of immunization programs in non-industrial nations address appealing other options.

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