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REVIEW

Amoebic dysentery: challenges and influencing factors

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Parasites are biological pathogens whose effects are not limited to bacteria, viruses, and fungi. They infect various living organs of the body, and intestinal parasites, in particular, are widespread worldwide. Among the newly discovered parasites are the Entamoeba genus and the infestation of amoebas. However, the result is useless colonization of the intestine, invasion of the colonic lining, or destruction of stratified tissues, such as the colon and liver, causing amoebiasis. Therefore, amoeba colonies develop as commensal parasites in the intestinal lumen and do not infect humans. Early diagnosis is achieved in a small number of individuals by laboratory examination under a light microscope, but this technique is ineffective at distinguishing between three phenotypically similar amoeba species: *E. histolytica*, *E. dispar*, and *E. moshicoviskii,* due to their close morphological similarity. The most common amoeba species are transmitted by ingesting contaminated food or drinking contaminated, untreated water. Recent human transmission confirms the presence of a special invisibility mechanism for infection. This invisibility has the ability to survive and occur monthly for several days, weeks, or months when moisture is available. The importance of this study is to define the disease and shed light on the history of amoebic dysentery and the factors that have long been determinants of the disease's spread. The current study sheds light on some of the historical and biological aspects related to amoebic dysentery. It highlights the most important parasitic species causing the disease, the parasite's life cycle leading to the development of symptoms, and some factors related to virulence.

Keywords: *E. histolytica*, biological pathogens, amoebiasis, diarrhea, dysentery

Introduction

Diseases resulting from intestinal parasitic infections are among the most common diseases, especially in developing countries, negatively impacting the lives of the population in these areas. The spread of parasitic animals among humans depends primarily on their lifestyle and their biological and physical environment (1). Humans play a major role in controlling this trend. Among the most important physical factors that directly affect the spread of parasites are temperature, humidity, aquatic environment, and soil. The biological factors that influence their spread are suitable vectors, such as intermediate hosts and final hosts (2). Parasites infect large numbers of people in all countries of the world, especially in Asia, Africa, and South America, due to the availability of suitable conditions for completing their life cycle and the presence of a host. They have been a cause of the death of large numbers of humans for long periods, and they remain pathogens that cause great suffering to the population (3). Intestinal protozoa are transmitted through contaminated hands or contaminated food and water. These parasites tend to exhibit similar life cycles, and the disease usually occurs after eating food containing mature cysts (4). They are the cause of approximately 70% of diarrheal cases in developing countries, due to food contamination with intestinal parasites, resulting from a lack of health awareness or poor hygiene and the resulting bad habits.

Crises, tribulations, and calamities have afflicted humanity throughout its long history, and various types of affliction have befallen people, such as plagues, famines, floods, earthquakes, droughts, and more. Of course, Muslims have suffered greatly from these calamities and pandemics, and their history has recorded their events, incidents, and effects. Perhaps the most devastating of these was the plague, which spread more than once in Egypt, the Levant, Morocco, Iraq, and Andalusia, killing thousands of their inhabitants. Historians who witnessed these events have provided diverse accounts of these epidemics, their effects, and their consequences throughout the world, such as al-Maqrizi, Ibn Taghri Bardi, Ibn Kathir, Ibn Iyas, Ibn Battuta, and Ibn Adhari al-Marrakushi. This has also been explored in the jurisprudential books of al-Wansharisi, Ibn Rushd, and others. Given the impact these epidemics have had on Islamic history, reflecting on the social, economic, political, and moral conditions of Islamic society and humanity as a whole, it is imperative to address them and study them. As for the Maghreb, its history has witnessed many epidemics, famines, and droughts during the Almoravid, Almohad, and Marinid eras, and even during the modern period. Perhaps the most significant of these was the plague of 571 AH, which spread throughout the Maghreb and Andalusia and is considered the most significant plague known to the Almohad era. It had disastrous consequences, and no one was spared. Four princes, brothers of Caliph Yusuf ibn Yaqub, died from it, while between 100 and 190 ordinary people died from it per day (5). The plague of 1798 AD also occurred in Morocco, transmitted by traders who carried it from Alexandria to Tunis, Algeria, and Morocco. The plague spread through Fez and Meknes and reached Rabat, claiming 130 victims per day (6). Ibn Adhari al-Marrakushi, in his chronicle of epidemics in Andalusia in the late fifth century AH/eleventh century AD, stated that in 498 AH/1105 AD, the famine in Andalusia and the Adwa region reached such an extent that people were certain of doom. There is no doubt that the demographic and economic repercussions that followed the famine in Morocco and Andalusia were the threatening spark of a series of successive natural disasters. Whenever a climatic disturbance occurred, it indicated, in the minds of the people of that period, more difficult living, psychological, and health conditions. During the same period, Morocco and Andalusia were afflicted by a series of famines and droughts in the first quarter of the sixth century AH/twelfth century AD, as a severe drought swept through the cities of Fez and Granada in 524 AH/1130 AD. In 526 AH/1132 AD, famine and epidemics intensified in Cordoba, and deaths increased, with the amount of wheat reaching fifteen dinars. Waves of natural disasters continued in the two hostile countries (Andalusia and Morocco), especially during periods of military confrontation, occuring in constant alternation (7).

Entamoeba spp.

Parasites are biological pathogens that are as effective as bacteria, viruses, and fungi, infecting various organs of the body. Intestinal parasites, in particular, are widespread worldwide (8). Among the pathogenic protozoan parasites are those belonging to the genus Entamoeba. Infection with amoeba species results in the formation of harmless colonies in the intestine, invasion of the colon walls, or destruction of host tissues, such as the lungs, liver, and brain, causing amoebiasis. It is worth noting that most amoeba species are commensal parasites in the intestinal lumen and do not cause disease in humans (9). Amoebiasis is most often diagnosed by examining laboratory specimens under a light microscope. However, this technique is unable to distinguish between three phenotypically similar amoeba species: *Entamoeba histolytica*, *E. dispar*, and *E. moshicoviskii*, due to their close morphological similarity (10). Although these species are phenotypically similar, they differ in their chemical and genetic makeup (9). *E. histolytica* is known for its clear pathogenicity, while the pathogenicity of the other two species remains unclear (11, 12).

E. dispar was initially considered a commensal parasite in the human intestine (9), while *E. moshicoviskii* initially appeared to be a free-living parasite (13). Infection with amoeba species occurs orally by eating food contaminated with mature cysts or drinking contaminated, untreated water. Human feces are considered a source of infectious cysts. These cysts have the ability to remain alive and cause infection for several days, weeks, or months when moisture is available (14). Most studies have focused on the spread of both *E. histolytica* and *E. dispar* without taking into account the type *E. moshicoviskii* due to the lack of necessary techniques to diagnose it, especially in cases of mixed infection (15). Due to the great similarity between these three species, many questions have been raised about the accuracy of diagnostic and epidemiological studies of amoebic dysentery, which made the estimation of the infection rate in the results of previous studies very misleading if we assert that the pathogen It is the species *E. histolytica* (16). The following is a definition of the three species:

E. histolytica

This species is the main cause of amoebiasis, amoebic dysentery, and extraintestinal amoebiasis. This disease has been mentioned since ancient times, with reference to it in ancient Greek books, such as Hippocrates' book (Corpus Hippocarticum), in which he described the symptoms of amoebic dysentery, calling it an epidemic (17). Roos and Quinck discovered the encysted stage of the parasite in 1898, while the infectious stage was discovered by Schaudinn in 1903. This scientist was the one who named the parasite

Entamoeba after it was previously called Amoeba. It was first named by the scientist Iedor Losch when he first described it (18). Studies continued until Sellards and Walke indicated in 1913 that the encysted stage is the infectious stage (19, 20). Amoebiasis is caused by ingesting food or drink contaminated with the encysted stage of the parasite. The encysted stage develops into the active stage, which invades the intestinal epithelium and destroys host tissues, causing severe illness (21). Intestinal amoebiasis is a public health concern due to its high incidence. An estimated 500 million people are infected annually with the parasite, whether or not they develop symptoms. Approximately 40,000 people die annually from the disease (22). Although the clinical manifestations of patients infected with *E. histolytica* are diverse, most are asymptomatic. An estimated 10% of the world's population is infected with both *E. histolytica* and *E. dispar*, but 90% of them are asymptomatic (21, 23).

E. dispar

E. dispar and *E. histolytica* are phenotypically very similar, so they cannot be distinguished by examining stool samples under a microscope. However, they can be distinguished based on certain genetic characteristics (24). This species has been considered a commensal parasite, although several studies have deemed it non-pathogenic (15, 25).

Studies several years ago conclusively established that *E. dispar* and *E. moshicoviskii* are not pathogenic at all, but rather commensal (15, 25). However, subsequent studies have established whether *E. dispar* is pathogenic or not, as in the study by Fotedar et al. (26), which demonstrated the ability of the feeding stage of this parasite to cause focal lesions in laboratory animals and that it has epithelial cell-lytic activity in culture. Dolabella et al. (27) also demonstrated the ability of the feeding stage of this parasite to cause amoebic liver abscesses in laboratory mice. Infection with this parasite was accompanied by various clinical signs, ranging in some individuals from amoebic liver abscesses to non-diarrheic colitis, sometimes accompanied by diarrhea. Some studies have identified specific symptoms of this infection, as in the study by Gonin and Trudel (28), when they studied samples of 96 patients in Canada infected with the parasite *E. dispar*, who showed symptoms such as chronic diarrhea for a period of 3 weeks. Other symptoms, including a small amount of blood, a 1-day fever, abdominal cramps, and nausea, were reported by Pestehchian et al. (29). Pestehchian et al. (29) reported symptoms of diarrhea, fever, and cramps in some body parts among those infected with this parasite in Iran. The distinction between *E. histolytica* and *E. dispar* is very important because infection with *E. dispar* does not necessarily require treatment (30), while infection with *E. histolytica* requires treatment because it causes amoebic dysentery, which, if neglected and treatment is delayed, can lead to death. This is consistent with what Pestehchian et al. (29) indicated regarding the lack of urgent need for treatment in cases of *E. dispar* infection with colitis. This species is widespread in areas with poor sanitation (29). Human infection occurs as a result of eating vegetables contaminated with the encysted stage of the parasite or drinking contaminated water. The feeding stage, *E. histolytica*, is characterized by its ability to digest red blood cells, resulting in bloody diarrhea (31). *E. dispar*, on the other hand, is capable of digesting red blood cells when cultured in laboratory media outside the body, but it is unable to do so in the colon. Even if blood is present in diarrhea in a single *E. dispar* infection, the cause is due to the presence of other secondary infections, such as Shigella infection (18).

Numerous studies have investigated the distinction between *E. dispar* and *E. histolytica*. *E. histolytica* and *E. dispar* as in the study of Troll et al. (32) which aimed to investigate the two species and differentiate between them using the concentration method and the conventional polymerase chain reaction (PCR) technique, and the study of Pillai et al. (33) in Canada to differentiate between the two species using the enzyme-linked immunosorbent assay (ELISA) technique, and the study of Pinheiro et al. (34) using the conventional PCR technique in Brazil, and the study of Nesbitt et al. (35) using the PCR technique in Tanzania, while El Sobky et al. (36) in Egypt, using the Multiplex PCR technique, and Pestehchian et al. (29) in Iran, using the traditional PCR technique, and Nasser (37) in Iraq, also in Tikrit, using the traditional PCR technique for diagnosis. In addition to Al-Kahfaji (38) in Diwaniyah Governorate in Iraq, using the single round PCR technique, and other studies that took it upon themselves to distinguish between these two types using molecular methods.

E. moshkoviskii

This species was known at the beginning of its appearance to be free-living, having been first recorded in 1941 in Tshalaia (11). It is found in various environments, ranging from clean river sediments to the shores of shallow ponds (39). It has also been found in sewage water in Russia, England, Central Asia, North America, and Brazil. The parasite then appears in the stool of patients with amoebic dysentery. Due to the great morphological similarity between the feeding and encysted stages of this parasite with *E. histoyltica*, it was difficult to diagnose. However, thanks to the development of diagnostic methods and the emergence of precise and highly sensitive techniques, it has become possible to detect the presence of the parasite in stool samples of infected patients (15, 40). Many studies have recorded infection rates that show that humans are the appropriate and true host for this parasite, not a transient host. The presence of this species in humans has been recorded in many countries, starting with North America, Italy, South Africa, and Bangladesh. It has not been reported that it is related to pathological

disorders (13, 41). Given that previous studies have not proven that *E. moshicoviskii* is capable of causing disease, careful attention must be paid to the diagnosis between it and similar species in order to avoid administering treatment for non-pathogenic species (42).

For the purpose of accurate diagnostic and epidemiological studies, research and studies continued with the advancement of diagnostic methods. The appearance of the species *E. moshicoviskii* was recorded for the first time in Bangladesh in 1998 among children by Haque et al. (41). It was also recorded in humans in India (25). Fotedar et al. (26) conducted the first molecular study of its kind to diagnose the three species in Sydney, Australia, and also recorded its presence in infected people in Turkey (43). In Iraq, Nasser (37) recorded the species *E. moshkoviskii* using the traditional PCR technique in Tikrit Governorate, followed by Al-Kahfaji (38) in Diwaniyah Governorate using the single-round PCR technique. Some studies have confirmed that the species *E. moshkoviskii* is not pathogenic (44), but there are studies at the same time that recorded the appearance of some pathological symptoms in those infected with this parasite, such as diarrhea and intestinal disorders (42). While a study conducted by Fotedar et al. (26) stated that the pathogenicity of this parasite is unclear, and they did not confirm that it is not pathogenic. Upon closer examination of the results of research and studies that focused on this type, it was noted in a study conducted by Tanyuksel et al. (45), during which 100 samples of people infected with the amoeba parasite were examined, that there were two cases of people infected with the type *E. moshkoviskii*; the first was a 2-year-old girl, and the second was a 36-year-old woman, and in both cases symptoms of diarrhea, weight loss, and fatigue appeared, and the stool samples were pale yellow in color.

This study indicated the possibility that the type *E. moshkoviskii* is a pathogenic type, and the study recommended conducting more accurate studies on the pathogenicity of this parasite. A study conducted in Sydney, Australia, gave a high probability about the ability of this parasite to The disease was caused by the parasite being isolated from people suffering from intestinal disorders, diarrhea, and abdominal pain. The same parasite was also investigated in stool samples from healthy people, and the absence of the parasite was confirmed, suggesting that the parasite is pathogenic. The study indicated the need to prove the cause of the disease, whether it is due to the parasite or the presence of other secondary infections. A study conducted by researchers (46) showed that the *E. moshkoviski* parasite has the ability to cause diarrhea, weight loss, and colitis when it infects mice. It was also found that this species is able to decompose the red blood cells of rats as a model of mammals, while human red blood cells were highly resistant to decomposition. Some studies indicated that this parasite is considered a causative agent of the disease and is used in the diagnosis of amoebiasis due to its high presence in areas where amoebiasis is widespread, accompanied by the presence of the *E. histolytica* parasite. It is worth noting that some studies indicated the emergence of intestinal disorders in cases that recorded mixed infections with the parasites *E. dispar* and *E. histolytica* (15, 25).

Classification

Kingdom: Protista

Subkingdom: Protozoa

Phylum: Sarcomastigophora

Subphylum: Sarcodina

Superclass: Rhizopoda

Class: Lobosea

Order: Amoebida

Family: Entamoebidae

Genus: Entamoeba

Species: *E. histolytica*, *E. dispar*, *E. moshkoviskii* (47).

Morphology and life cycle

The amoeba parasite has four distinct forms in its life cycle: the trophozoite stage, the precyst stage, the cyst stage, and the metacyst stage (48). **Figure 1** illustrates the life cycle of amoeba species.

Some factors affecting the amoeba parasite

Protozoan parasites and soil-transmitted helminths are major public health problems (49). Amoebiasis, caused by the parasite *E. histolytica*, is responsible for approximately 40,000–100,000 deaths annually. Therefore, this disease is considered a real health problem, especially in developing countries (50). The prevalence of amebiasis varies among individuals, as well as between countries and regions, depending on economic and social conditions. Its prevalence sometimes reaches 50% of the population in affected areas with poor health conditions. It is believed that amebiasis directly affects more than 50 million people, causing human losses and resulting in economic damage (20). Infection rates also vary between countries, environments, and health and population conditions in the region (51). As is well known, the cysts of histolytic amoebas are the sole cause of transmission. In most cases, infection occurs primarily in asymptomatic individuals carrying the parasite who pass the cysts in their feces, depending on the surrounding

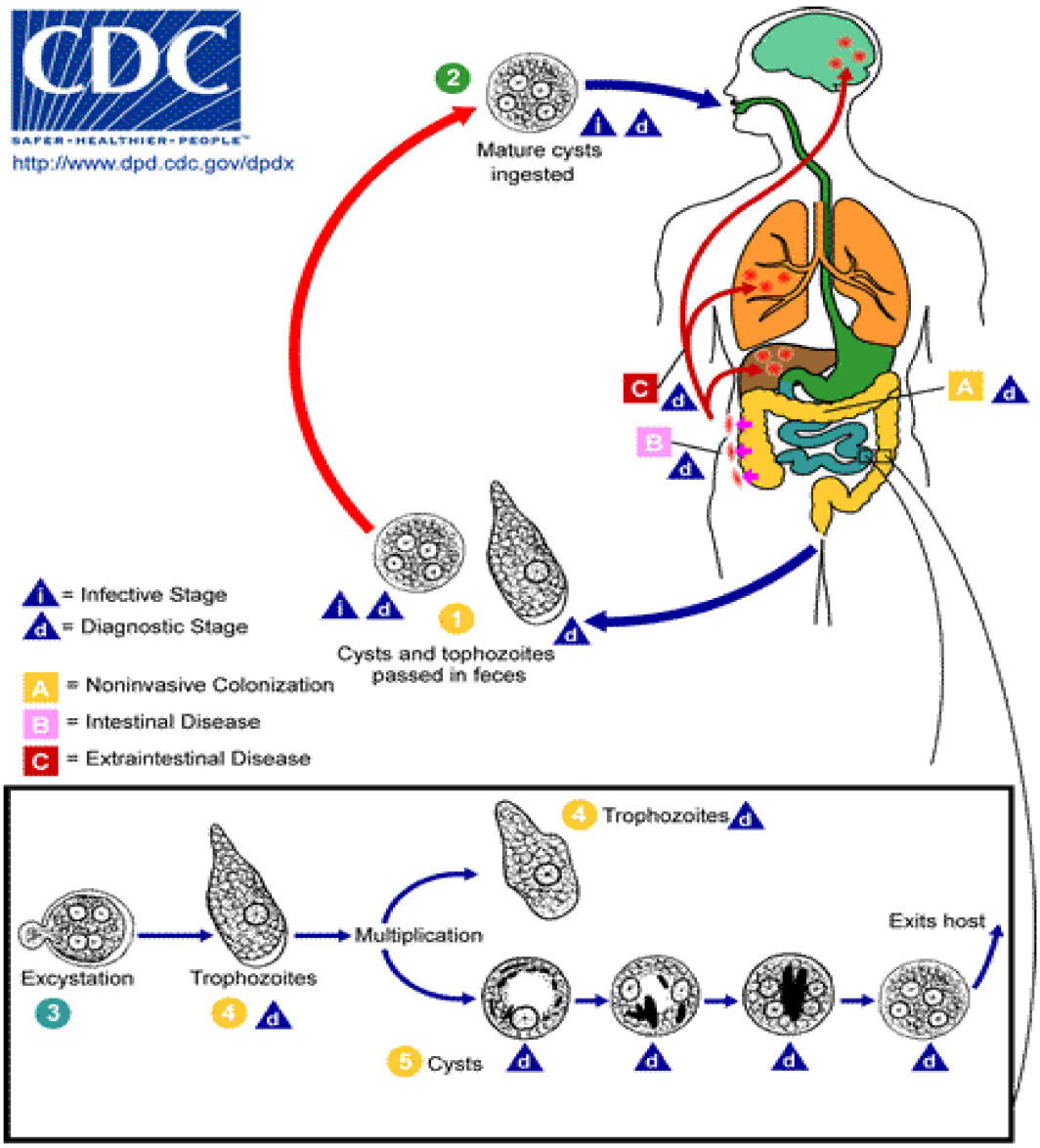

FIGURE 1 | Life cycle of amoeba species. From: CDC (52).

environmental conditions. These cysts are resistant to acidification, chlorination, and desiccation and can survive in humid environments for several weeks (53). Amoeba species are highly endemic in tropical and subtropical regions, especially in economically poor areas, where the incidence of the disease is linked to the demographic and health situation (54). Wastewater and feces of infected humans and animals are used as fertilizers for various agricultural crops in large areas, as they increase crop productivity by 10–30%.

This use is common in China and Southeast Asia, as well as various regions of the African continent. Irrigation water sources vary, as in Vietnam, as it depends on fresh water, wastewater, and groundwater. This shows that contaminated water is part of irrigation water, and about 85% of farmers in Vietnam use wastewater and feces of humans and animals in agriculture. Because of this, there is a definite risk of acquiring infection with amoebiasis when traveling to tropical regions where the disease is endemic (55). The high prevalence of the parasite in tropical regions is also attributed to low levels of sanitation, which leads to the cysts retaining their vitality and ability to infect. Infection also depends heavily on contaminated food and contaminated water, in which the housefly (Musca domestica) and cockroaches play an important role, as they are important mechanical vectors of the parasite's cysts from fresh feces to water, exposed food, and eating utensils. Other reservoir hosts besides humans, such as dogs, pigs, and monkeys, can also have a major role in disease transmission (48). Consuming water or food contaminated with feces containing amoeba cysts, as well as fecal-oral contact via contaminated hands, are the main methods of infection. Transmission of tissue-lytic amoeba through water is common in developing countries, as most

drinking water supplies are untreated, and the use of human waste as a soil fertilizer is also a significant source of infection (56, 57).

It is worth noting that there is a relationship between ABO blood groups and the incidence of amebic dysentery. A study by Hussein (58) showed that males and females with blood type O are most susceptible to amebic dysentery, followed by blood types AB, B, and A. Haque et al. (59) also reported that children in Bangladesh with blood types O and AB are more susceptible to amebic dysentery than children with blood types A and B. The relationship between blood types A, B, and O and the incidence of parasitic diseases may be due to one of the genes responsible for the inheritance of blood groups, which may help increase the susceptibility of pathogens to adhesion and thus cause disease.

Conclusion

Recent human transmission confirms the presence of a special invisibility mechanism for infection. This invisibility has the ability to survive and occur monthly for several days, weeks, or months when moisture is available. The importance of this study is to define the disease and shed light on the history of amoebic dysentery and the factors that have long been determinants of the disease's spread.

Author contributions

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Conflicts of interest

There is no conflicts of interest.

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