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Entamoeba histolytica Infection in the Philippines: A Review

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Authors' contributions

This work was carried out in collaboration among all authors. The work was supervised by author RVP Jr. Literature survey, screening of articles, and writing of the manuscript and revisions were done by all authors. All authors read and approved the final manuscript.

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ABSTRACT

Entamoeba histolytica, an intestinal protozoan parasite, is the primary causative agent of both intestinal and extraintestinal amoebiasis. While six species of *Entamoeba* have been identified in the human gut, only *E. histolytica* is well recognized as a pathogenic amoeba associated with intestinal and extraintestinal infections. In many cases of *E. histolytica* infection, symptoms are either absent or mild, whereas the most frequent clinical manifestations are colitis and liver abscess due to amoebic infection. Diagnosis typically relies on microscopic and serological methods. Metronidazole is the standard therapy for treating children and adults with invasive amoebiasis. However, the absence of an effective vaccine poses a significant challenge to controlling the transmission and progression of the parasite into an active, invasive disease. Notably, in

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developing tropical countries like the Philippines, significant cases of *E. histolytica* infections have been documented in communities with inadequate sanitation and hygiene practices. The development of pragmatic and cost-effective diagnostic methods is therefore crucial for the clinical care of amoebiasis patients. Drawing from a limited pool of published articles (2010 to date) on cases of *E. histolytica* infections and parasitological surveys in the Philippines, the current review underscores the critical knowledge gap on the prevalence of amoebiasis as well as the disease pathology and treatment of this zoonotic parasitic disease.

Keywords: Entamoeba histolytica; amoebiasis; prevalence; epidemiology; Philippines.

1. INTRODUCTION

Entamoeba histolytica is an invasive protozoan parasite responsible for the intestinal infection known as amoebiasis or amoebic dysentery. *Entamoeba* spp. with morphologically similar cysts and trophozoites can reside in the human intestine, including *E. histolytica, E. dispar, E. moshkovskii,* and the recently described *E. bangladeshi* [1–3]. The taxonomic identification of *E. dispar* and *E. moshkovskii* could only be ascertained by molecular-based methods because these non-pathogenic and non-invasive protozoa defy morphological differentiation from *E. histolytica*. Thus, in line with the recommendations of the World Health Organization [4] and Uslu *et al*. [5], appropriate treatment of the *E. histolytica* infection is strongly advised. Amoebiasis can be asymptomatic or may lead to the development of a severe infection. Invasive intestinal disease can manifest over several weeks, presenting symptoms such as cramping, abdominal pain, and both watery and bloody diarrhea, accompanied by notable weight loss [6]. Furthermore, this condition has the potential to extend beyond the confines of the intestine, giving rise to infections of various organs located outside the gastrointestinal tract. The predominant organ affected in extraintestinal amoebiasis is the liver, culminating in the formation of amoebic liver abscesses (ALA) and consequential hepatic damage. Subsequently, other organs such as the lungs, skin, and brain may also be involved in the disease progression. This condition is endemic to regions including Central and South America, Asia, and Africa, exhibiting a staggering prevalence that can reach up to 40%. The gravity of its impact is underscored by an estimated 55,000 annual fatalities attributed to extraintestinal amoebiasis [7,8].

Amoebiasis caused by *E. histolytica* can be acquired through the intake of contaminated food and water containing infective stages of the parasite. Direct contact with contaminated water, feces, soil, and vegetation is the most common way to contract infections [9]. The significant widespreadity of this infection is more common in developing countries of the tropics and subtropics, including the Philippines, where sanitation and proper hygiene are poor or deficient. The World Health Organization reported a threat of parasitic infections among 7 million Filipinos in the country after a series of food and waterborne disease outbreaks in the last five years [4,9]. Water, sanitation, and hygiene (WASH) predictors are important in preventing the transmission of parasitic diseases; hence, a lack of clean drinking water and inadequate sanitation and hygiene standards can readily spread parasitic diseases [10]. Gaining further knowledge about *E. histolytica* is essential for the creation of therapies and prophylactics in the future. A thorough understanding of the parasite's origin, modes of transmission, and interactions with the host will enable focused therapies, enhance control, and reduce the disease's adverse impacts on human health. Further understanding of parasite biology and pathogenesis will advance future targeted therapeutic and preventative strategies [8].

The diagnosis of intestinal and extraintestinal amoebiasis caused by *E. histolytica* infection is usually carried out by microscopic examination of stool samples and pus aspirated from the wall of liver abscesses. Other methods and kits with higher sensitivities that are being used in the Philippines for the epidemiologic detection of *E. histolytica* and *E. dispar* infections include PCR using DNA extracted from the formalin-fixed stools [11], loop-mediated isothermal amplification (LAMP) assay [12], stool enzyme-linked immunosorbent assay (ELISA) [13], and more advanced technologies such as dotLab™ methods [14]. Several studies have shifted their focus to diagnosing *E. histolytica* infection by detecting antibodies present in saliva samples from infected individuals. Notably, there is a rapid and accurate detection kit designed specifically for amoebiasis patients, utilizing salivary IgA as a diagnostic marker [15]. Additionally, advancements include the formulation of an

ELISA-based method for detecting anti-*E. histolytica* IgA in saliva samples [7]. These innovations in non-invasive diagnostic approaches present promising avenues for more accessible and efficient identification of *E. histolytica* infections. These developments in diagnostic techniques in the Philippines have apparently improved our understanding of the rapid, safe, and accurate diagnosis of *E. histolytica* infection, i.e., through the identification and separation of *E. histolytica* from other nonpathogenic *Entamoeba* species such as *E. dispar* and *E. moshkovskii* [2,16]. Therefore, timely identification and distinction between the pathogenic *E. histolytica* and nonpathogenic/commensal *Entamoeba* species, such as *E. dispar, E. moshkovskii*, and *E. bangladeshi*, are pivotal for effective clinical management of patients with amoebiasis [2].

This review primarily aims to provide updated knowledge and information on *E. histolytica* infection in the Philippines through an assessment of the published papers from 2010 to date delving into parasitological surveys conducted by various researchers across the country, thereby presenting a clear overview of the current epidemiologic approach to studying the distribution, diagnosis, and control of this invasive intestinal parasite.

2. THE EPIDEMIOLOGY OF AMOEBIASIS IN THE PHILIPPINES

Amoebiasis is a worldwide problem; individuals living in developing countries are at greatest risk given the poor sanitation and socioeconomic conditions [6]. *E. histolytica* is estimated to infect about 50 million people worldwide and is responsible for up to 100,000 deaths per year, placing it second only in mortality to malaria [17]. Parasitological surveys have been conducted in recent years by several researchers throughout the Philippines in an attempt to determine and update the distribution and prevalence of *E. histolytica* infections among rural populations. Rivera et al. [11], for instance, showed the prevalence of *E. histolytica* and *E. dispar* in the BASECO compound, a slum area adjacent to Manila Harbor. However, there is still limited information regarding the prevalence and incidence rate of amoebiasis in the Philippines, i.e., despite recommendations aimed at investigating the epidemiology of amoebiasis within the location of choice for the study or epidemiological studies being carried out in other parts of the country. Thus, investigations incorporating variables such as livelihood, settlement types, and sanitation practices are strongly advocated. This recommendation will undoubtedly enhance the generation of comprehensive documentation pertinent to the epidemiology of *Entamoeba* infections, particularly in the urban slum areas of the country [11]. In 2023, Valenciano et al. [10] reviewed the presence, prevalence, and trend of soil-transmitted helminths and *Entamoeba* spp. in Southeast Asia. Only 3 of the 101 studies that this study reviewed provided adequate data on the prevalence of *E. histolytica* in the Philippines. In that review, there was a lack of availability for high-quality epidemiological data on STH infections and *Entamoeba* species in Southeast Asia. There were also discrepancies in the study design of the reviewed selected studies, sampling strategies, and the number of sample sizes, which restricted the reviewers from identifying and understanding the true prevalence of various soil-transmitted helminthes along with *E. histolytica* and *E. dispar* [10].

Rivera et al. [11] investigated the prevalence of *E. histolytica* and *E. dispar* infections among residents of the BASECO compound using polymerase chain reaction (PCR). Their study also explored whether age and sex influenced the occurrence of *E. histolytica*. Among the 2,232 residents sampled, 38 tested positive for *E. histolytica* and *E. dispar*, resulting in a prevalence rate of 1.7%. PCR analysis revealed eight cases of *E. histolytica* and 23 cases of *E. dispar*, with one sample positive for both species. *E. histol*ytica was found in two age groups, 5–14 and 35–44 years, with prevalence rates of 0.771% and 2.857%, respectively. Sex-specific prevalence rates showed no statistically significant difference between males (0.279%) and females (0.433%) for *E. histolytica* [11].

A more recent study by Rivera *et al.* [13] investigated the prevalence of *E. histolytica* in the same location previously mentioned, i.e., the BASECO compound, using stool ELISA. Among the 627 stool samples (493 males and 134 females) examined, 55 individuals were positive for *E. histolytica* and *E. dispar*, resulting in a prevalence rate of 8.77%. Specifically using *E. histolytica* II kits, the prevalence rate was 9.09% (5/55), indicating a higher occurrence of the nonpathogenic species. Among different age groups, there were no statistically significant differences regarding the prevalence of *E. histolytica*. Individuals aged 0–10 years had a prevalence rate of 0.62%, while those aged 31–40 and 41-50 had prevalence rates of 2.56% and

6.67%, respectively. Notably, the prevalence rate of *E. histolytica* was lower in males (0.61%) compared to females (1.49%) [13].

Manahan-Suyom et al. [14] assessed the prevalence of *E. histolytica* infections in a community of relocated individuals in San Isidro, Rodriguez, Rizal, Philippines, using a rapid immunoassay, the dotLab™ system. One hundred nineteen (119) stool samples were collected from volunteers in the relocation area in Rodriguez, Rizal. The study population consisted of 45 (37.8%) males and 74 (62.2%) females, with ages ranging from less than 1 to 68 years old (median of 12 and mean of 20). Of the 119 samples, 31 were positive for *E. histolytica* infections. Nineteen (19) of the positive samples came from females (64.5%) and eleven (11) from males (35.5%) [14].

3. DIAGNOSTIC METHODS FOR AMOEBIASIS

Numerous diagnostic techniques, such as molecular testing, serology, microscopy, and antigen detection, are available to achieve an accurate diagnosis. To establish an accurate diagnosis, multiple tests are frequently needed, as well as a combination of diagnostic methods. Traditionally, microscopy has been the most widely used but has limited diagnostic utility and is no longer recommended as a reliable way to diagnose amoebiasis [8]. This method cannot distinguish between *E. histolytica* and its non-invasive relative, *E. dispar*, or other *Entamoeba* species [7,16]. The management of patients and epidemiological investigations of amoebiasis outbreaks rely on the accurate identification of pathogenic *E. histolytica* from nonpathogenic *Entamoeba* spp. Molecular-based techniques have been proven adequate to satisfy these needs and hence have emerged as the gold standard for diagnostic tests in the current era [2,5]. Parija *et al.* [2] mentioned that serological tests may be useful in the diagnosis of amoebiasis in developed countries since *E. histolytica* infection is uncommon, whereas in developing countries, infection due to *E. histolytica* remains endemic. Due to the challenge of distinguishing the current infection from a previous one, amoebiasis is difficult to accurately diagnose by antibody detection. ELISA, however, remains an important diagnostic tool in patients with invasive amoebiasis and has no cross-reactions with other nonpathogenic *Entamoeba* species, contributing to its high specificity [2]. ELISA has become a widely used technique for studying amoebiasis compared to other antibody detection assays. In the Philippines, the practice of these techniques has been implemented in numerous studies, and new diagnostic methods have been developed. With the benefits of greater sensitivity, specificity, and ease of use, molecular biology-based diagnostic tests and antibody detection assays have become more significant in the past few years for diagnosis. The World Health Organization [4] recommended that *E. histolytica* be identified and, if present, treated. Several techniques, including antigen detection and PCR analyses, have by far become indispensable tools for the accurate diagnosis of invasive *Entamoeba* species [1]. More so, with the adoption of real-time PCR (qPCR), the diagnostic sensitivity and accuracy of diagnostic cases of *E. histolytica* infections has been greatly realized [1]. While the utilization of PCR-based diagnostic tests have been increasingly observed in developed countries [1,18], many diagnostic laboratories in the Philippines still rely on microscopic examination for the detection of *E. histolytica* in fecal samples [19].

Microscopic examination of stool/pus specimen in a saline wet mount is a less sensitive technique (sensitivity < 10%) even when viewed by an expert microscopist and needs to be examined within a short period of collection time (usually within half an hour) for motile trophozoites [2]. However, it is still the preferred method for diagnosing *E. histolytica* because it is relatively inexpensive, suitable for resource-limited laboratories, and provides rapid results for the timeliness of treatment. In addition, it is usually combined with other diagnostic techniques to obtain a more comprehensive and accurate assessment. In the recent studies conducted by Rivera *et al*. [11, 13] to determine the prevalence of *E. histolytica* infection in slum communities, collected stool samples were analyzed using microscopic examination for the initial identification of parasitic worm eggs and protozoan cysts. Using light microscopy, the samples were then viewed, and the different parasites observed were identified and noted. The samples were also subjected to other methods, such as stool ELISA and PCR, to further distinguish between pathogenic *E. histolytica* and non-pathogenic *E. dispar.* By using stool ELISA, the study estimated the prevalence of *E. histolytica* infections in an urban slum community in the Philippines to be 0.797%. It was discovered to be slightly higher than the prevalence estimate reported in a previous study

by Rivera *et al*. [11] in the same community (0.358%) using polymerase chain reaction (PCR). Warren *et al*. [20] examined the association between adult patients in the Philippines who had endoscopic or histopathologically confirmed colitis and *C. difficile* or *E. histolytica* infection. Two hundred and ten patients undergoing colonoscopy were enrolled, and stool specimens underwent microscopy before they were assayed for *C. difficile* and *E. histolytica* by stool ELISA. *C. difficile*, *E. histolytica,* and intestinal parasites were seen in 17 (43.6%), 10 (25.6%), and 11 (28.2%), respectively, of patients with colitis, compared with 36 (21.7%), 13 (7.8%), and 56 (33.7%), respectively, of those without colitis. Twenty-three specimens, of which 10 came from patients with colitis, were positive for *E. histolytica* antigen but negative by routine direct fecal smear [20].

Adao *et al*. [7] developed a salivary IgA detection method for *E. histolytica* using ELISA. The results of the method these authors utilized were compared with current diagnostic methods such as microscopy and PCR results from stool DNA extracts. The presence of *E. histolytica* and *E. dispar* in stool samples was determined using the PCR primer pairs P11/P12 and P13/P14, respectively [7]. The results of the study showed that the salivary anti-*E. histolytica* IgA detection method produced relatively accurate results comparable to the results obtained by PCR using stool samples for the diagnosis of *E. histolytica* infection. The developed method has an accuracy of 85.5–90%. It also performed much better than microscopy, which could not properly distinguish between *E. histolytica* and *E. dispar* due to their identical morphology [7]. When compared to stool samples needed for stool antigen detection kits and PCR, saliva samples from patients are much simpler to obtain and recollect. Moreover, the antigen plates for the salivary IgA detection method can be stored for up to a year at −4°C without any changes in the method's results [7].

In a similar study conducted by Rivera *et al.* [15], a kit was designed to utilize IgA concentrations in saliva as the basis for the detection of *E. histolytica*. The kit was self-contained, and the results could be visualized in about 3.5 hours. It has a sensitivity of 94.1% and specificity of 97.6%, with an overall diagnostic accuracy of 98% when compared with a polymerase chain reaction. The detection kit made it possible to carry out extensive epidemiological studies that could quickly determine the prevalence and geographic distribution of amoebiasis in the country and could enable prompt disease management and prevention measures. Thus, this detection kit could allow large-scale epidemiological studies to be conducted, studies that would speedily determine the prevalence and distribution of amoebiasis in the country, as well as allow immediate action to be taken for disease prevention and management [15].

Loop-mediated isothermal amplification (LAMP) technology was introduced in the year 2000 with the aim of improving nucleic acid amplification efficacy in terms of sensitivity and specificity [21]. It is a newly developed, sensitive technique that provides a method of nucleic acid amplification that works rapidly and precisely and is a cost-effective and economical method of diagnosing infections and illnesses. It has been developed for widespread clinical use, particularly in genetic testing. This is especially true in the diagnosis of infectious diseases such as hepatitis, tuberculosis, and hereditary diseases [22]. Thus, considering its advantages, Rivera and Ong [12] developed LAMP for the rapid and cost-effective identification of *E. histolytica*. The mechanism of LAMP revolves around the amplification of DNA, such as primers designed from *E. histolytica*, and a positive LAMP reaction corresponds to an increase in the turbidity of the reaction mixture. Based on the results of the study, positive LAMP reactions turned turbid, while negative ones remained clear. Under ambient light, all positive reactions turned green upon the addition of a fluorescent dye, while the negative control remained orange. Judging the absence or presence of this white precipitate allows easy and rapid visual identification that the target DNA was amplified by LAMP [12]. Therefore, loop-mediated isothermal amplification (LAMP) makes it possible to amplify DNA under isothermal conditions rapidly and precisely, and it eliminates the need for complex thermal cycling equipment. Due to its affordability, simplicity, and sensitivity, LAMP may be considered an invaluable tool for rapid molecular diagnostics that can be utilized by developing countries, including the Philippines. Due to its ease of use, a LAMP assay that is highly specific and sensitive for *E. histolytica* will undoubtedly facilitate the identification of the protozoan parasite with the utmost rapidity and efficiency. This feat may be of great advantage to the clinical community, particularly in the laboratory and field diagnosis of amoebiasis [12].

Table 1. Comparison of various diagnostic methods employed in the surveillance studies for the detection of *E. histolytica* in the Philippines

Diagnostic Method	Purpose and Findings	Reference
Detection kit through salivary IgA	• Utilized IgA concentrations in saliva as the basis for the detection of *E. histolytica.* • The kit shows results in about 3.5 hours and is more accurate than the polymerase chain reaction, with 94.1% sensitivity, 97.6% specificity, and 98% overall diagnostic accuracy.	[15]
Loop mediated isothermal amplification (LAMP)	• Developed a loop-mediated isothermal amplification (LAMP) assay. • The newly developed LAMP assay enables fast and simple detection of *E. histolytica*, suitable for both laboratory and field diagnosis of amoebiasis.	[12]
Polymerase chain reaction (PCR)	• Assessed the prevalence of *E. histolytica* and *E. dispar* infections using PCR on stool samples. • Among 2,232 residents, 1.703% tested positive for *E. histolytica/E. dispar* microscopically, with PCR analysis indicating 0.358% *E. histolytica* and 1.030% *E. dispar* infections, showcasing the efficacy of PCR for epidemiological detection, while age group and area distribution showed statistically significant differences, but not sex distribution.	[11]
ELISA-based anti-*E. histolytica* IgA detection in saliva samples	• Developed a novel amoebiasis detection method aimed at identifying anti-*E. histolytica* IgA in saliva. • The enzyme-linked immunosorbent assay (ELISA) demonstrated a 90% accuracy, 88.89% sensitivity, and 90.22% specificity when compared to polymerase chain reaction (PCR), offering a convenient and accurate alternative for diagnosing amoebiasis using saliva samples instead of stool or blood samples, with potential applications in both diagnosis and epidemiological studies.	[7]
Stool enzyme linked immunosorbent assay (ELISA)	• Stool specimens were assayed for *C. difficile* and *E. histolytica* by ELISA. This study indicates that *C. difficile* infection is common and may go unnoticed in areas where intestinal parasites and amoebiasis are predominant. • This study in the urban slum community of BASECO, Manila, Philippines, utilized stool enzyme-linked immunosorbent assay (ELISA) to determine a prevalence of 0.797% for *E. histolytica,* with no significant differences found in age, sex, or geographic location. The study suggests a lower prevalence compared to previous estimates using different techniques.	[20] [13]
dotLab™ immunoassay	• Used dotLab™ method on stool samples from relocated families of San Isidro, Rodriguez, Rizal, Philippines to directly detect *E. histolytica* infections. The assay's results were compared to those acquired through the use of real-time PCR. • The dotLab™ method demonstrated faster completion, with a 66-minute process compared to the 1.5-hour PCR run (excluding DNA extraction time), exhibiting increased sensitivity by detecting as low as 5.45 cells/mL of *E. histolytica* and identifying 1.6 times more positive stool samples than real-time PCR.	[14]

Due to the challenge of identifying and distinguishing *E. histolytica* infections using traditional techniques, more cutting-edge technologies are being developed to improve specificity and distinguish between various species. Manahan-Suyom *et al*. [14] utilized a novel technology called the dotLab™ system, created by Axela Biosensors, Inc., which allowed for the development of a quick immunoassay that could identify cells/mL of *E. histolytica* in stool samples rapidly and precisely. Their study applied this technology for the detection of *E. histolytica* infections directly using stool samples and combined the principles of grating-based light diffraction and immobilized capture surfaces. Additionally, they compared it with the real-time PCR method. The occurrence of *E. histolytica* infections using real-time PCR was 15.97%, while 26.05% used the developed dotLab™-based assay. The dotLab™ method has a sensitivity of 94.74% and a specificity of 74.79% with reference to real-time PCR. Axela's dotLabTM was discovered to be a potential diagnostic tool in the ongoing hunt for an improved method for the identification of *E. histolytica* and a reliable substitute for PCR [14]. The identification and separation of *E. histolytica* from other non-invasive *Entamoeba* species, as well as the safe, quick, and precise diagnosis of *E. histolytica* infection, have all been made possible by these advancements in diagnostic techniques in the Philippines. A summary of the diagnostic methods, purposes, and major findings used in various published studies in the Philippines is presented in Table 1.

4. PATHOGENESIS AND TRANSMISSION

The pool of information delving into the pathogenesis and transmission of *E. histolytica* in the Philippines is scarce. It is assumed that there are no new updates or findings on the pathogenesis and clinical features related to amoebiasis. There is also insufficient data concerning the causes of transmission among Filipino residents, as there may be vulnerabilities or factors affecting susceptibility that could be potentially minimized or eliminated. Rivera *et al.* [23] reported the first molecular detection of *E. histolytica* and *E. dispar* among macaques in the Philippines. The role of non-human primates in the transmission of amoebiasis is yet to be elucidated. This study complements the sparse collection of information available on the animal hosts of *E. histolytica* in the Philippines [23].

5. TREATMENT AND VACCINE

Generally, there are no commercially available vaccines for the prevention of amoebiasis to date, and currently, work is in progress to develop a vaccine. Recent experimental studies seem promising [8, 24, 25]. Currently, models, including rodents and nonhuman primates, are being used to investigate vaccines. Using both native and recombinant forms of the amoebic Gal/GalNAc lectin, protection against intestinal and liver infection has been demonstrated [25]. Drug therapies such as metronidazole and other nitroimidazole-derived compounds are effective for treating invasive parasites. However, these drugs display adverse side effects, are expensive, and not easily available in certain countries and areas [25, 26]. Further research and testing are therefore urgently needed for the development of a successful vaccine as well as a comprehensive understanding of parasite biology and pathogenesis to advance future targeted therapeutic and preventative strategies. Vaccination against *E. histolytica* is currently unavailable in the Philippines; therefore, prevention focuses on sanitation and access to clean water. Upon data analysis gathered by Valenciano *et al.* [10], a common factor among these infections is poor sanitation and hygiene predictors, accompanied by warm and humid tropical climates in Southeast Asian countries, including the Philippines.

6. RECOMMENDATIONS AND CONCLUSION

It is prudent to enhance the depth of epidemiological investigations on *E. histolytica* infection across diverse regions in the Philippines to establish a more comprehensive and consistent dataset regarding its prevalence and infection rate. This approach will significantly contribute to forming well-supported conclusions about the extent of *E. histolytica* infection in the country. Moreover, comparing the outcomes of these studies with historical data can reveal trends and variations in amoebiasis cases over time. Consequently, conducting extensive studies is imperative, employing reliable diagnostic methods to ensure the reliability and coherence of results, aligning with the methodologies employed in previous research. Additionally, there is a need for exploration into novel diagnostic and detection methods to further advance our understanding of *E. histolytica* infection.

In conclusion, a comprehensive understanding of the pathogenesis, clinical features, and transmission of *E. histolytica*, particularly within the context of the Philippines, is imperative. This knowledge is crucial in determining whether there are distinctive characteristics of amoebiasis in the Philippines compared to other countries. By elucidating the causes of transmission and identifying factors that increase susceptibility to *E. histolytica* infection, we can proactively address the challenges and work towards reducing the prevalence of amoebiasis in the Philippines. Moreover, this information serves as a foundation for advancing our comprehension of the parasite, paving the way for future breakthroughs in treatment and prevention strategies. To enhance the likelihood of developing a viable human vaccine, concerted efforts and investigations into potential strategies for protection should be prioritized in the Philippines. Regardless of experimental outcomes, these studies can contribute to an enriched understanding of the parasite, refinement of experimental methods, and an expanded knowledge base, setting the stage for more informed and successful future research endeavors. Ultimately, the results of these endeavors will not only benefit the local context but also contribute to global initiatives aimed at combating *E. histolytica* infection, potentially leading to a significant medical breakthrough.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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