Review Article

Epidemiological and Diagnostic Studies for the Surveillance of *Entamoeba moshkovskii*

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Abstract

Entamoeba moshkovskii is species of the big genus *Entamoeba*. This type of parasite rarely causes disease in humans. However, this has been more changed recently. The purpose of the current study was to review all obtainable published data regarding *E. moshkovskii* infections around the world and provides essential information on the epidemiology, incidence, diagnosis and microbiological information of *E. moshkovskii* at present, trying to understand if it can be considered as important risk diarrhoeal pathogen. Only studies that depending on polymerase chain reaction as a definitive diagnosis of *E. moshkovskii* have been included because *E. moshkovskii* is undistinguished from *E. histolytica* and *E. depress* morphologically, so very little information is available concerning the epidemiology and prevalence of *E. moshkovskii* because few searches have been used molecular diagnostic techniques to identify it. The ability of *E. moshkovskii* to grow and adapt to the various environmental hard conditions may make its risk of infection higher than the risk of *E. histolytica*. Reasons beyond *E. moshkovskii* differentiation from other *Entamoeba* complexes for stopping dispensable medications in patients infected with nonpathogenic amoebiasis. All *E. moshkovskii* infections were gastrointestinal tract diseases associated with infectious diarrhea, From available data in this review, *E. moshkovskii* considered an important and potential risk pathogen with a high rate of residence and prevalence worldwide.

Keywords: *Entamoeba*, *Entamoeba* complex, *Entamoeba moshkovskii*, epidemiological studies

Submission: 11-Oct-2019; **Accepted:** 29-Dec-2019; **Published:** 09-May-2020

Introduction

Enteric protozoa persist to be implicated to the burden from preventable infectious diseases affecting human health in the industrialised setting, and the WHO regarded amoebiasis in developing countries as one of the major health problems.[1] Amoebiasis is disseminated in places where improper sanitation allows the contamination of drinking water and food with faeces; in these regions, more than 40% of individuals with diarrhoea may be infected with amoebic dysentery.[2]

Molecular-based methods for the diagnosis of amoebiasis and other several infectious diseases have acquired heaviness in the past few decades because of many problems associated with conventional techniques to improve specificity, sensitivity and increasing simplicity.[3] There is a challenge to distinguish *Entamoeba moshkovskii* from other *Entamoeba* species as *Entamoeba histolytica* and *Entamoeba dispar* because it is morphologically indistinguishable. In the past, *E. moshkovskii* regards as a free-living parasite, but recently, it demonstrated that *E. moshkovskii* can cause infectious disease in humans with high predominance value.[4] For epidemiological searches and infection management, the exact differentiation of pathogenic *Entamoeba* spp. from non-pathogenic, especially in amoebiasis outbreaks, molecular diagnostic methods have been approved to satisfy this purpose to be the gold slandered diagnostic method.[3]

Conventional microscopic methods have been used for the conclusive differentiation of *E. moshkovskii* among another intestinal amoebiasis may be confused, while molecular diagnoses such as real-time polymerase chain reaction (PCR) and nested multiplex PCR have accurate diagnosis result.[5]

Few searches have been used molecular diagnostic techniques to identify it.[6] In the present time, there are considerable

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Quick Response Code:

Website: www.hamdanjournal.org

DOI: 10.4103/HMJ.HMJ_78_19

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How to cite this article: AL-Khikani FH. Epidemiological and diagnostic studies for the surveillance of *Entamoeba moshkovskii*. Hamdan Med J 2020;13:78-81.

gaps in the information of epidemiology and prevalence of *E. histolytica*, *E. dispar* and *E. moshkovskii* of the world, so we need specific diagnosis methods to be performed, especially in endemic countries, on the other hand, some *Entamoeba* spp. are detected mostly when molecular method is used as *E. moshkovskii*.[7] Epidemiological and clinical searches are needed to learn more about *E. moshkovskii* and its association with diarrhoeal disorders in various countries because many studies considered *E. moshkovskii* as non-pathogenic.[4]

This study aimed to record and evaluate all available evidence regarding human infections by *E. moshkovskii* globally and highlight on the epidemiology, incidence, diagnosis and microbiological information.

Microbiological Characteristics and History of *Entamoeba moshkovskii*

E. moshkovskii previously has been isolated from water and human specimens, and it is indistinguishable by conventional microscope from other parasitic *Entamoeba* spp. such as *E. histolytica* and *E. dispar*.[4]

Tshalaia in 1941 was the first person who discovered *E. moshkovskii* in the wastewater management system in the city of Moscow; this new strain had the same morphology of *E. histolytica* as excystation phase.[4]

The study that done by Entner and Most in 1965 revealed tow strains clinically isolated from the human body, and these strains were amoebicide resistance and have the ability to grow at room temperature; the authors recommended that these strains are new parasitic species.[8]

The first evidence of the possibility of *E. moshkovskii* as a human pathogen was mentioned in 1969 by Goldman that showed *E. moshkovskii* shared many features with *E. histolytica* as antigenic, biochemical as well as growth profile and morphology.[9]

The capacity of *E. moshkovskii* to grow in the various environmental conditions and to adapt to hard conditions suggested that the risk of infection may be higher than the risk of *E. histolytica* or *E. dispar* infections; also, evidence mentioned that risk factors to get *E. moshkovskii* infections are similar to *E. histolytica*/*E. dispar*.[9,10]

Despite *E. moshkovskii* is considered free-living organisms, it became so important in the past few decades. Many studies showed that *E. moshkovskii* can infect humans, and also, pathogenic potential has been recorded.[11,12]

Epidemiology of *Entamoeba moshkovskii*

For this review, PubMed was searched, and 5125 human specimens were collected; from them, 285 samples were positive to *E. moshkovskii*, and all these samples were diagnosed by PCR, resulting from 17 studies covering 9 countries around the world, which enables us to judge reliably the prevalence and molecular epidemiology of *E. moshkovskii* at the world level.

The current study revealed the high predominance of *E. moshkovskii* in India, Malaysia and Bangladesh[13-20] due to certain conditions such as poor living, poverty, crowded places, improved sanitation, socioeconomic conditions and malnutrition; these conditions are considered major factors in epidemiological prevalence risk factors.[21-23] Most studies in this review were conducted in rural areas.[11,14] There are two causes beyond the persisting predominance of amoebiasis globally. First, migration from endemic regions to the developed countries is increased. Second, asymptomatic carrier persons represent a challenge to the clinicians with persistence disease prevalence.[23] In children, amoebiasis infection persists to be one of the major problems, particularly in the developing world.[11] Three studies included in this article have been applied in children: Malaysia in 2013, Bangladesh in 2012 and other studies in Bangladesh in 2003[15,17,18] [Table 1].

The high predominance of *E. moshkovskii* in persons infected with HIV has been noted in two studies in this systemic review, Tanzania, Africa (2009), and Assam, India (2014); in these studies, the percentage of *E. moshkovskii* foundation was 13% and 40.98%, respectively.[19,25] This result concurs with some studies that mentioned amoebiasis is more prevalent in immunocompromised patients or mentally retarded persons and is considered one of the major health problems in these individuals;[32-36] this explained by suppression in their immune responses and unable to persist adequate personal hygiene.[37] Microscopic examination of acquired immune deficiency syndrome revealed that patients often appeared high percentages to *Entamoeba* cysts.[7]

Epidemiological and clinical searches are needed to learn more about *E. moshkovskii* and its association with diarrhoeal disorders in various countries, as well as detection groups with a high risk of infection, because many studies considered *E. moshkovskii* as a free-living parasitic pathogen.[4] As most common previous information were acquired using traditional diagnostic methods that incapable of differentiation among *Entamoeba* species, the exact epidemiology of *E. moshkovskii* and other *Entamoeba* species is not clear yet.[6]

Diagnosis of *Entamoeba moshkovskii*

E. moshkovskii is undistinguished from *E. histolytica* and *E. depress* morphologically, so very little information is available regarding the epidemiology and prevalence of *E. moshkovskii* because few searches have been used molecular diagnostic techniques to identify it. It is found in areas with poor clean water sources and is prevalent in some regions such as India, Malaysia and Bangladesh, but more recently, it has made its way to Australia, America and other developed countries.

The major disadvantage in traditional microscopic examination to *E. moshkovskii* is low sensitivity and accuracy as <60%.[4,38]

Table 1: *Entamoeba moshkovskii* prevalence information

Reference numbers	Type of diagnosis	Years	Region or country	Patients group	Total samples	Infected	Percentage
[13]	Multiplex PCR	2007	Puducherry, India	General population	202	18	0.1
[14]	Nested PCR	2012	Rural communities in Malaysia	General population	52	3	5.8
[15]	Real-time PCR	2013	Asli settlements in Malaysia	1-18 years	56	1	1.8
[24]	Multiplex real-time PCR	2010	Thailand	General population	36	1	0.02
[16]	Single-round PCR	2013	Orang Asli communities in Malaysia	General population	500	5	1.0
[17]	PCR	2003	Bangladesh	Children	109	23	21.1
[18]	PCR	2012	Bangladesh	Infants	1426	42	2.95
[25]	PCR	2009	Tanzania, Africa	HIV patients	136	18	13
[19]	Multiplex PCR assay	2014	Barak Valley, Assam, India	HIV patients	61	25	40.98
[20]	PCR assay	2015	North East Indian Population	General population	122	28	23
[26]	PCR assay	2015	Rural Area in Central Colombia	General population	181	46	25.4
[27]	PCR	2007	Sydney, Australia	General population	89	22	24.7
[28]	PCR	2017	Tehran Province, Iran	General population	561	1	0.2
[29]	Nested multiplex PCR	2019	west of Iran	General population	1383	1	0.07
[30]	PCR	2008	Tunisia	General population	27	24	88.8
[31]	PCR	2012	Pakistan	General population	129	24	19
[11]	PCR	2008	Sydney, Australia	General population	55	3	5.5
Total					5125	285	

PCR: Polymerase chain reaction

The sample should be examined within 1 h of collection to search for motile trophozoites which may contain red blood cells (RBCs). However, in patients who do not present with acute dysentery, trophozoites will not contain RBCs. Patients with asymptomatic carriage generally have only cysts in the faecal sample. Although the concentration technique helps to demonstrate cysts, the use of permanently stained smears (trichrome or iron haematoxylin) is an important method for the recovery and identification of *Entamoeba* species. Culture techniques for the isolation of *Entamoeba* species have been available for over 80 years.[39]

A new branch in amoebiasis diagnosis has been developed based on DNA detection as well as differentiation among *Entamoeba* species that have the same morphology, especially in regions with high endemic.[6] DNA-based methods are considered easy applied, high sensitivity and very accurate in differentiation among genetically related *Entamoeba*,[3] and also, this method has been used in intra-species genetic diversity,[7] so just this method for the diagnosis has been adopted in this study.

Stool microscopy examination revealed that cysts and trophozoites can be detected by a naked experienced eye and also by haemophagocytosis. Fresh stools revealed both trophozoites and cysts and can be performed as either wet mounts or stained preparations. Mature cysts have four nuclei measuring about 12–15 μm in diameter, while trophozoites have a single nucleus larger than a cyst. However, microscopy should not be utilised when other diagnostic methods are accessible.[38]

As serology tests considered as a useful adjunct to stool studies, many EIA kits for antibody detection are available today commercially, including indirect fluorescence, immunoelectrophoresis and immunosorbent assays. Antibodies stay detectable for many years after recovery by successful management, so it is difficult to distinguish between the recent and past infection.[38]

Real-time PCR is a modern and attractive methodology for laboratory diagnosis of infectious diseases, because of its characteristics that eliminate post-PCR analysis, leading to shorter turnaround time. Furthermore, the closed reaction tube minimises the chances of cross-contamination, and the assay output is quantitative rather than qualitative. Therefore, the main advantage of this technique is that it can monitor the parasite load.[5]

Conclusion

This review describes parasitic infections by *E. moshkovskii* around the world and provides information on the epidemiology, incidence, diagnosis and microbiological information. Over long decades, gastrointestinal parasitic unicellular disease regarded as a true public health issue that causes infectious diseases in millions of persons in all countries of the world. *E. moshkovskii* is responsible for diarrhoea; at the same duration; the severity of diarrhoea is caused by pathogenic *E. histolytica*. The ability of *E. moshkovskii* to grow and adapt to the various environmental hard conditions may make its risk of infection higher than the risk of *E. histolytica*. There are two reasons beyond *E. moshkovskii* differentiation from other *Entamoeba* complexes: the first is stopping dispensable medications in patients infected with non-pathogenic amoebiasis and the second comprehends the predominance of these species, worldwide. New important branches in amoebiasis diagnosis have been developed based on DNA molecular detection in stool specimens, as well as differentiation among *Entamoeba* species that exactly have the

same morphology, especially in regions with high endemic. *E. moshkovskii* is responsible for diarrhoea; at the same duration, the severity of diarrhoea is caused by pathogenic *E. histolytica*. From the available data in this systemic review, *E. moshkovskii* is considered an important and potential risk pathogen with a high rate of resident and prevalence worldwide.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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