

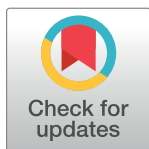
## OVERVIEW

# The association between the lack of safe drinking water and sanitation facilities with intestinal *Entamoeba spp* infection risk: A systematic review and meta-analysis

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## Abstract

Intestinal protozoa infections are responsible for considerable morbidity and mortality, especially where the exposed population suffers from a lack of drinking water and sanitation facilities. In this study, the association between the lack of safe drinking water and sanitation (toilet) facilities with intestinal *Entamoeba spp* infection in the children (5–11 years), adult (18–55 years), and all age (5–55 years) were assessed. For this purpose, some of the international databases such as Scopus, PubMed, Web of Science, and Embase were screened to up to 7 June 2019 in order to retrieve the related citations. Also, the pooled odds ratios (ORs) following 95% confidence intervals (CIs) were calculated using a random-effects model. Twenty-nine articles with 36 studies were included while the OR extracted or calculated by using 2 × 2 contingency tables. However, the ingestion of contaminated water insignificantly can increase the odds ratio (OR) of *Entamoeba spp* infection (OR 1.01, 95% confidence interval [CI] 0.58 to 1.43), no access to sanitation (toilet) facilities significantly can increase odds of *Entamoeba spp* infection (OR 1.18, 95% CI 1.05 to 1.32). The meta-regression analysis showed that over time, odds of intestinal *Entamoeba spp* infection increased in both lack of safe drinking water (Coefficient: 3.24, P-value < 0.01) and sanitation (toilet) facilities (Coefficient: 2.36, P-value < 0.05) subgroups. Considering the findings, lack of safe drinking water resulted in a further increase in intestinal *Entamoeba spp* infection among adult (OR: 2.76), children (OR = 0.57) and all age groups (OR: 1.50), and also

lack of sanitation (toilet) facilities resulted in further increase intestinal *Entamoeba spp* infection in children (OR: 1.06), adult (OR: 1.26) and all age (OR: 1.16). In this context, the lack of safe drinking water and sanitation facilities (toilet) was associated with a high risk of intestinal *Entamoeba spp* infection. Further attempts to providing public health facilities can control the prevalence of intestinal *Entamoeba spp*.

## 1. Introduction

While the intestinal protozoa infections with some types of *Entamoeba spp* such as *Entamoeba histolytica*, *Giardia intestinalis*, *Strongyloides stercoralis*, and *Cryptosporidium spp*, they can be considered as one of the serious human health threats due to the notable malnutrition, mortality and morbidity rates in the worldwide [1–6]. In this context, according to the World Health Organization (WHO), the endemic of schistosomiasis occurred in 78 countries, which resulted in further treatments for about 261 million people [7]. The prevalence of *Giardia intestinalis* among the developing and developed countries was estimated as 20–30% and 2–3%, respectively, which can be accounted for serious health risks [4, 8]. While the high prevalence of *Giardia intestinalis* among developing was highlighted, the higher prevalence of *Cryptosporidium spp* in the people infected with HIV (which mainly are found in developing countries particularly concentrated in African continent) highlighted the dangerous consequences of Intestinal protozoa infections [9, 10]. Moreover, amoebiasis due to *Entamoeba spp* can cause ~ 100,000 deaths annually, hence amoebiasis is one of the main global parasitic infections [2, 3]. However, the information regarding the burden of the disease caused by the intestinal parasitic is rare, probably due to the difficulty of accurate diagnosis [11]. Furthermore, due to amoebiasis and cryptosporidiosis 2.2 million and 8.4 million disability-adjusted life years (DALYs) were reported as in 2010 [12]. Also, DALYs related to both intestinal protozoa and schistosomiasis infections were estimated at about 26.1 million persons in 2015 [13].

While the environmental fecal contamination, poor hygienic standards, and lack of sanitation facilities are associated with intestinal parasitic infections (IPIs) [14, 15]. Also, socio-economic and ecological factors have a considerable effect on the burden of IPIs [16, 17]. For instance, the calculated risk of IPIs for children who are living in under developing countries (low and middle income) was recognized as high, mainly due to lack in providing safe drinking water and sanitation facilities [18–20]. In this regard, it was assumed that the health of more than 600 and 270 million children in preschool and school-age, respectively, can be threatened due to transmission intestinal parasites [21, 22]. In another hand, the IPIs are strongly associated with malnutrition, which contributes to one-third of all deaths of children under five age [23].

Since intestinal parasites can be transmitted through the oral-fecal route and contaminated water, the prevalence of intestinal infections countries that are facing the lack s in safe drinking water and suitable sanitation facilities like low and middle-income countries and rural areas is relatively high [24, 25]. Based on the reports, about 2.5 million and 780 million people have no access to sanitation facilities and safe drinking water, respectively [26]. Additionally, considerable geographical heterogeneity in the safe drinking water supply and sanitation facilities was observed in developing countries [27].

Since several contradictory studies have been conducted on the risk of intestinal *Entamoeba spp* infection in the communities with the lack of safe drinking water and sanitation facilities [28–40], a systematic review and meta-analysis can help us to elucidate the association of

contaminated drinking water consumption and live in poor sanitation with the risk of intestinal *Entamoeba spp* infection.

Therefore, the current systematic review and meta-analysis were performed to determine the risk of intestinal *Entamoeba spp* infection based on the ingestion of the contaminated drinking water as well as poor sanitation facilities based on the age population (children, adults, and all age), besides the evaluation of studies quality. Also, a meta-regression analysis was approached to determine the associated risk of intestinal *Entamoeba Spp* infection over time.

## 2. Materials and methods

### 2.1. Protocol and search strategy

A systematic review and meta-analysis were conducted according to the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines [41] and Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) [42]. In this regard, the main international databases, including Scopus, Web of Science, PubMed, and Embase, were screened to retrieve the related citations between up to 7 June 2019. Keywords and MeSH terms of “water” OR “toilet facilities,” OR “sanitation,” AND “risk factor, AND “odds ratio” OR “relative risk” AND “Intestinal Protozoa,” OR “*Entamoeba histolytica*,” OR “*Entamoeba dispar*,” OR “*Entamoeba moshkovskii*.” were used. It is noteworthy, in this study *Entamoeba histolytica*, *Entamoeba dispar* and *Entamoeba moshkovski* considered as *Entamoeba spp*.

The title, abstract and full texts of obtained articles were screened for eligibility. Also, according to performed systematic review studies [43–47], the references list of articles were screened to collect more citations.

### 2.2. Inclusion and exclusion criteria

An article was included when it met the proposed inclusion criteria [48–51], including a) Full-text of the article in the English language published; b) prevalence of *Entamoeba histolytica*, *Entamoeba dispar*, and *Entamoeba moshkovskii* in stool, c) cross-sectional (c-s) and case-control (c-c) studies; d) reporting the lack of sanitation facilities (toilets); e) investigation regarding the lack of safe drinking water. In this regard, the ecological, animal studies, genetic, theses, case reports, books, and review articles, and original studies with other languages (except English) were excluded. Studies that reported the risk factors after an outbreak and epidemic also were excluded. As chlorination cannot be considered as an efficient way to reduce and control of intestinal protozoa, studies that have described chlorination as water treatment have been excluded [52, 53].

### 2.3. Data extraction and quality assessment

The extracted data can be summarized as the study design, lacks safe drinking water and sanitation facilities, odds ratio (OR) following confidence interval (CI), country, study year, age group. Also, while the OR was presented among results of a study, same OR was included in the current, however, in the case of no reported OR, or presentation of results as text format and/or  $2 \times 2$  contingency tables, further calculations by the following equation were performed to obtain the OR [54]:

$$OR = \frac{a \times d}{b \times c} \quad (1)$$

Where, a is the number of infected cases in the bad group; b, number uninfected cases in the

bad group; c, number infected cases in good group and d, number uninfected cases in the good group [54].

Moreover, if a study contains both forms of OR (unadjusted and adjusted), the former one was employed to have an overview regarding the comparison between the cross-studies [4].

The quality of the studies was assessed according to the development and evaluation method [4, 55], Grading of Recommendations Assessment [56, 57], and diagnostic method to identify protozoa, assess the sanitation facilities and safe drinking water and finally strengths and limitations of the study. Studies with a total score of 4–6, 2–3, and lower 0–2 points were considered to be of high, moderate, and low qualities, respectively, while no studies were excluded according to performed quality assessment [56, 57].

## 2.4. Meta-analysis of data

A meta-analysis of ORs was conducted by STATA 14.0 (2015; STATA 14.0 Statistical Software, College Station, TX, USA). P-value < 0.05 was selected as statistical significant. Heterogeneity of studies was detected using Cochrane's Q-test and  $I^2$  index as when  $I^2 > 50\%$ , heterogeneity is significant [58, 59]. When  $I^2$  index < 50% fixed effect model (FEM) but if  $I^2$  index > 50% random effect model (REM) was used [58]. In the current study, OR > 1 indicates an increasing effect of the lack of safe drinking water and sanitation facilities on the odds of infection with intestinal parasites. The Egger test was used to detect publication bias [58, 60]. A meta-analysis of data was performed based on lack of safe drinking water and sanitation facilities, age groups of the exposed population including children (5–11 years), adult (18–55 years), and all age (5–55 years), and quality of study subgroups. Also, meta-regression between ORs of safe drinking water lack and sanitation facilities with a year of publishing was performed in the non-linear model [50, 61].

## 3. Results

### 3.1. Study characteristics

In the initial step, 834 citations out of 1,164 collected articles were excluded due to duplication by the aid of EndNote X7<sup>®</sup> software (Thomson Reuters, Toronto, Canada). Based on the assessment of the abstracts and titles, 456 articles were identified as suitable and were screened separately. Two hundred and sixty articles were excluded due to irrelevant content of title (n = 204) and abstract (n = 56). Full text of 70 articles was downloaded and considered, while 39 articles were removed due to no data about searched risk factors, different toilet types, and other reasons. Finally, 29 articles with 36 studies were included in the current study (Fig 1).

The rank order of countries based on number of published studies were Brazil (7) > India (6) > Ethiopia (3) > Cote d'Ivoire (2) ~ Kenya (2) ~ Lesotho (2) ~ Mexico (2) > Vietnam (2) ~ Colombia(1) ~ Ecuador (1) ~ Cuba (1) ~ Chile(1) ~ Cambodia(1) ~ Iraq (1) ~ Nigeria (1) ~ South Africa (1) ~ Uganda (1) ~ Yemen(1). Overall, 36 studies, 25 studies were related to the risk of *Entamoeba spp* infection with lack of sanitation facilities, and 11 studies were associated with the issues raised by consuming contaminated drinking water. Also, among all studies, 34 and 2 studies were cross-sectional and case-control studies, respectively (S1 Table).

### 3.2. Meta-analysis of findings

The meta-analysis result regarding the association between the intestinal *Entamoeba spp* infections and safe drinking water lack was presented in Fig 2. While a marginally insignificant positive correlation with high heterogeneity ( $I^2 = 52.50\%$ ,  $P = 0.021$ ) was noted (OR, 1.01; 95%CI 0.58 to 1.43) (Fig 2). The meta-analysis of the association between intestinal *Entamoeba spp*

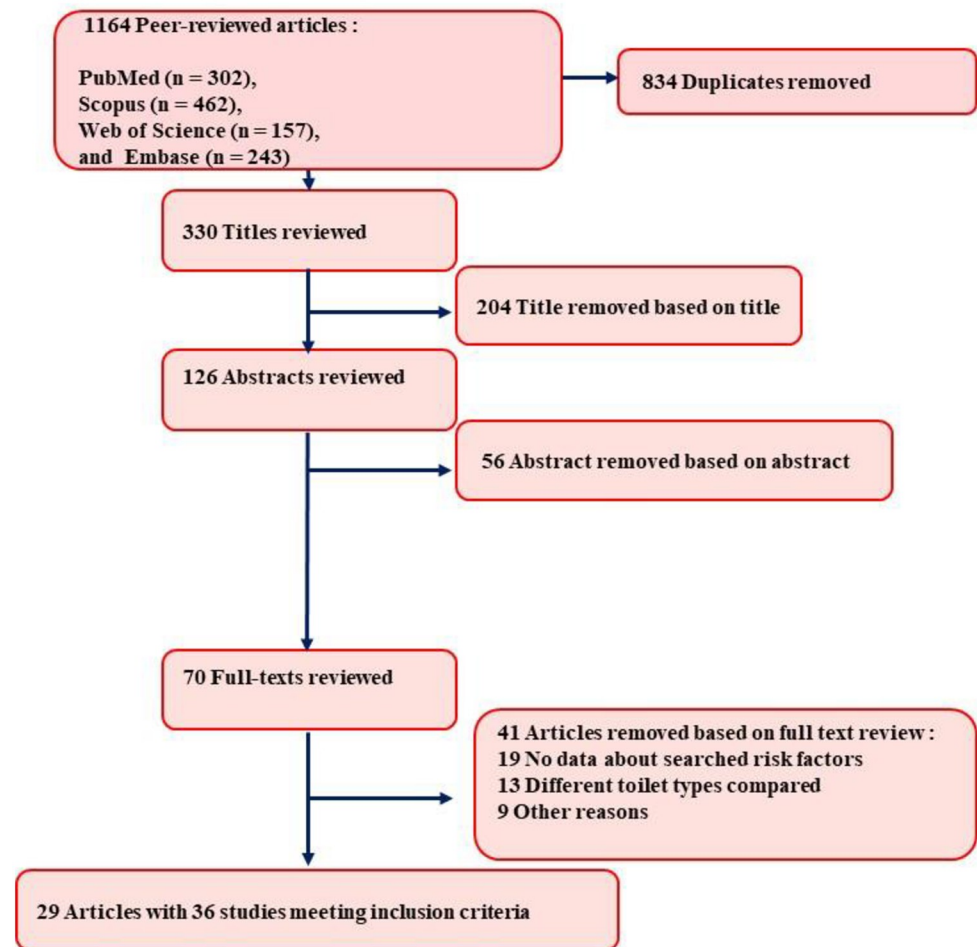


Fig 1. Schematic protocol for the selection and extraction of relevant studies.

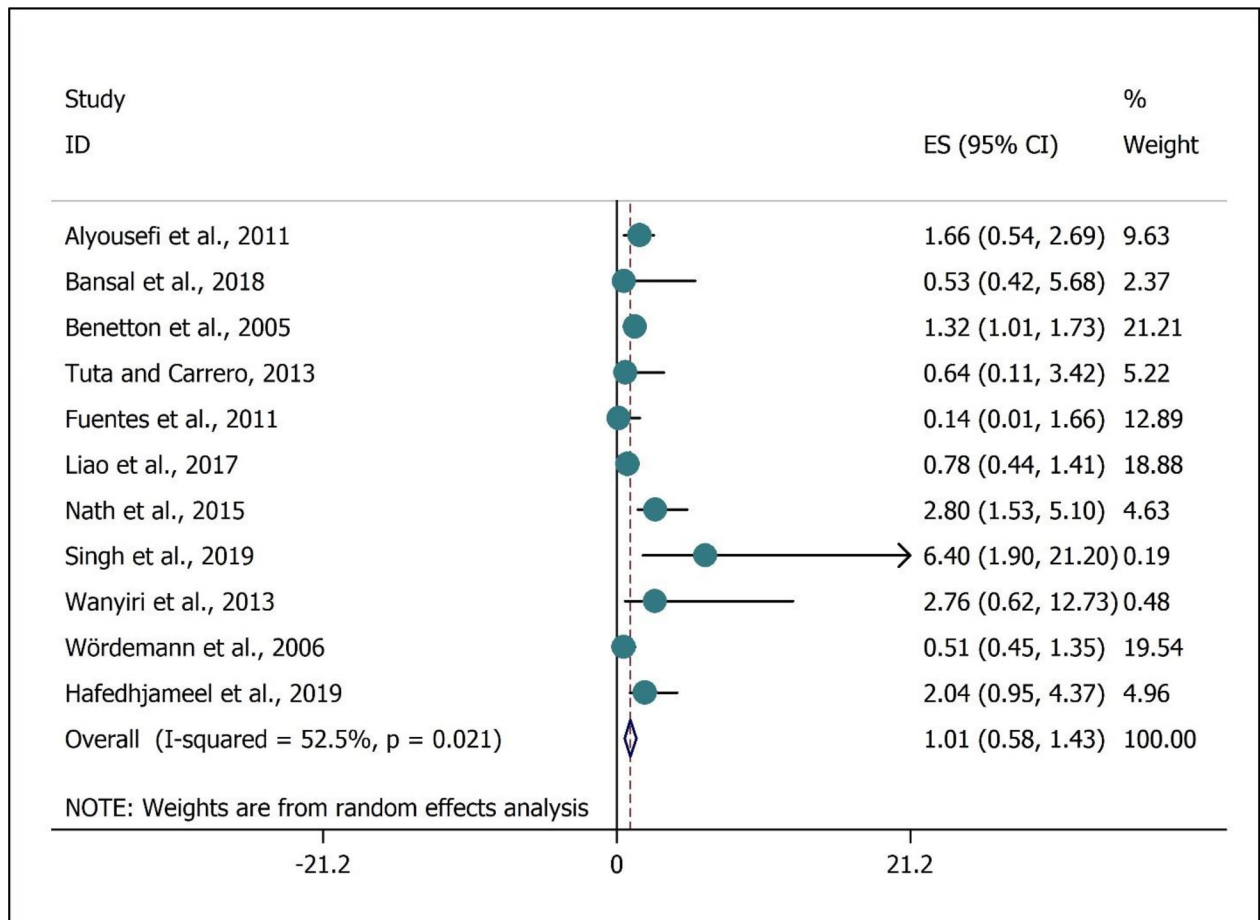
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infections with a lack of sanitation facilities (toilet) was presented in Fig 3. While a significant positive correlation with low heterogeneity ( $I^2 = 39.1\%$ ,  $P = 0.025$ ) was determined (OR, 1.18; 95%CI 1.05 to 1.32) (Fig 3).

However, a negative insignificant association between the intestinal *Entamoeba spp* infection and lack safe drinking water in low-quality studies was observed (OR, 0.68; 95%CI 0.25 to 1.11), in moderate quality studies, a positive insignificant was observed (OR, 1.31; 95%CI 0.68 to 1.99) (S1 Fig). A positive insignificant association between the intestinal *Entamoeba spp* infection and lack sanitation facilities (toilet) in low-quality studies was noted (OR, 1.15; 95%CI 0.74 to 1.56). While in moderate quality studies, a positive significant association between the intestinal *Entamoeba spp* infection and lack sanitation facilities (toilet) was observed (OR, 1.19; 95%CI 1.04 to 1.36) (S2 Fig).

Although a negative significant association between the intestinal *Entamoeba spp* infection and the lack safe drinking water in children (OR, 0.57; 95%CI 0.27 to 0.87) was observed, a positive insignificant association among adult and all-age population (OR, 2.76; 95%CI 0.62 to 12.73), (OR, 1.50; 95%CI 1.08 to 1.93), respectively, was observed (S3 Fig). Additionally, a positive insignificant association between the intestinal *Entamoeba spp* infection and lack sanitation facilities (toilet) in children (OR, 1.06; 95%CI 0.71 to 1.40), positive significant in adult (OR, 1.26; 95%CI 1.05 to 1.48), and positive insignificant all age (OR, 1.16; 95%CI 0.95 to 1.37)





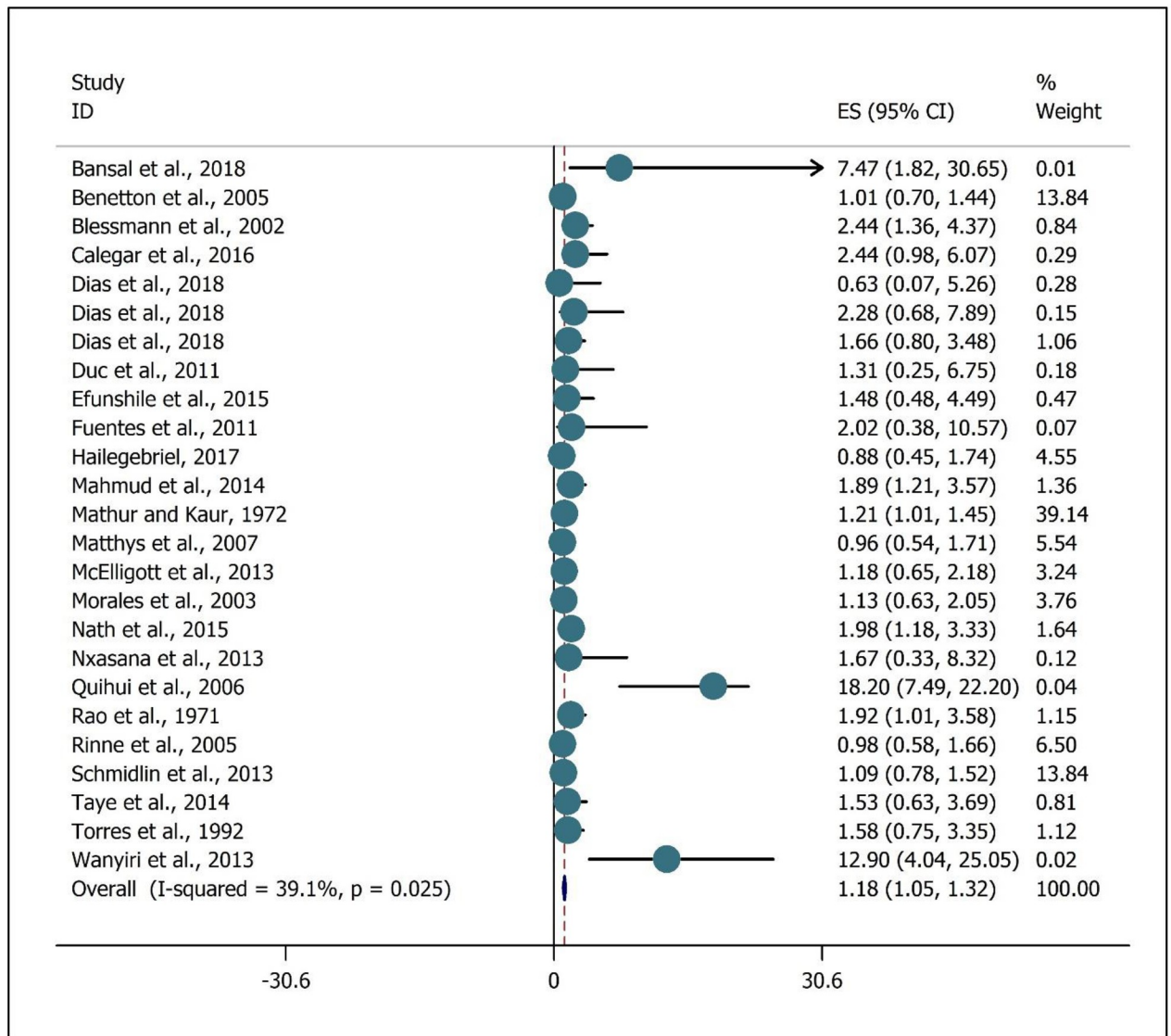
**Fig 2. Meta-analysis of the association intestinal *Entamoeba spp* infection with lack safe drinking water.** ES is Effect size.

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was observed (S4 Fig). According to meta-regression analysis, a significant positive regression between *Entamoeba spp* infection and year of study in the safe drinking water lack subgroup was observed (Coefficient: 3.24, P-value < 0.01) (Fig 4A) and also regarding the lack sanitation (toilet) facilities subgroup (Coefficient: 2.36, P-value < 0.05) same observation was noted (Fig 4B). No significant publication bias regarding the lack of safe drinking water (P-value = 0.91) and lack of sanitation (toilet) facilities (P-value = 0.08) subgroups was reported based on the findings of publication bias test.

#### 4. Discussion

In recent decades, the *Entamoeba spp*, due to the presence of invasive parasites within their species, particularly *Entamoeba histolytica*, has been investigated by several researchers [62]. In this context, the Amoebiasis as a threatening disease caused by mainly *Entamoeba histolytica* attracted notable attention [63]. However, in addition to *Entamoeba histolytica*, in many studies, other species like *Entamoeba dispar* have an effective role in the prevalence of intestinal diseases in humans as well as other animals [37, 64, 65]. In this context in most of the countries [63, 65, 66], except some countries around the Pacific Rim, the higher frequency of *Entamoeba dispar* rather than *Entamoeba histolytica* was noted. Moreover, a recent report published by Costa et al. (2018), in the city of Belo Horizonte located in southeastern Brazil, by



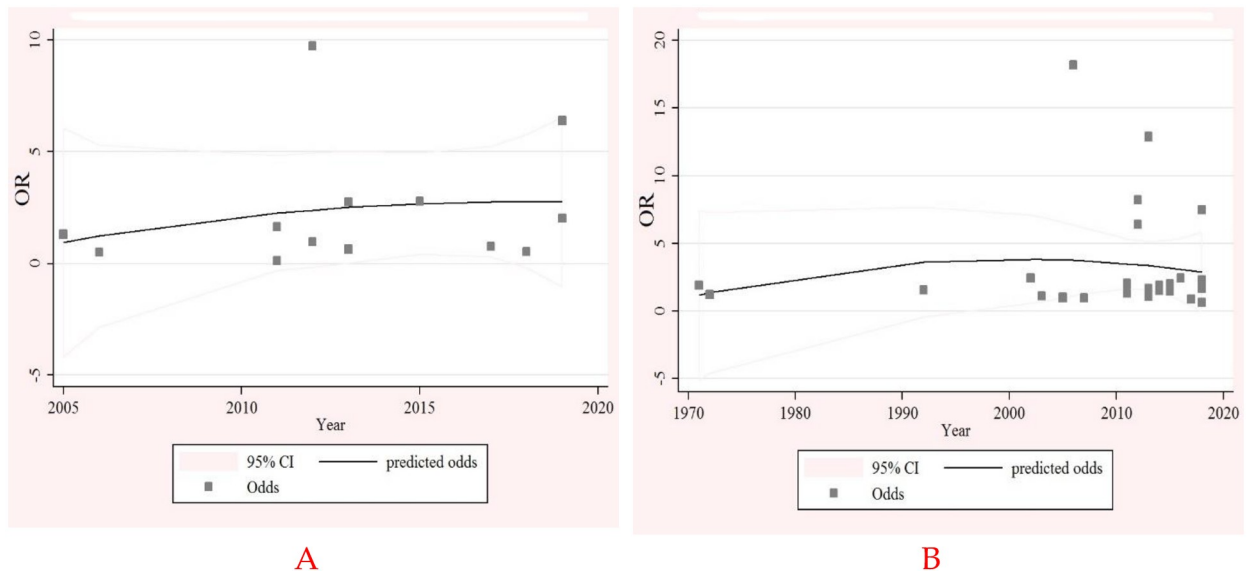
**Fig 3. Meta-analysis of the association intestinal *Entamoeba spp* infection with lack sanitation facilities (toilet).** ES is Effect size.

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applying the polymerase chain reaction, pointed out that the prevalence of *Entamoeba histolytica* is less than *Entamoeba dispar* [67].

The identified *Entamoeba* spp by using microscopic tools, are including *Entamoeba histolytica* and *Entamoeba dispar*, (pathogenic and non-pathogenic respectively) [68, 69]. However, other *Entamoeba* spp like *Entamoeba moshkovski* and *Entamoeba bangladeshi* were identified by some molecular methods [70]. Among the different *Entamoeba* spp, the distinction of *Entamoeba histolytica*, *Entamoeba dispar*, and *Entamoeba moshkovskii* by former method (microscope due to similar morphological) is difficult [67, 71]. Therefore, in the current systematic review, the association between the access to safe water and sanitation practices and infection of *Entamoeba* was assessed, without considering their species.

The ingestion of food/water contaminated with the cyst or through direct fecal-oral transmission can be considered as the main transmission route of the genus *Entamoeba* into the humans' and animals' bodies [72]. Indeed, *Entamoeba* spp. can distribute through the fecal-



**Fig 4. Meta-regression regarding the association of intestinal *Entamoeba spp* infection with year of publication study in the lack of safe drinking water (A) and lack sanitation (toilet) facilities (B) subgroups.**

<https://doi.org/10.1371/journal.pone.0237102.g004>

oral route with contaminated food and water [73]. In the current investigation, a marginally insignificant positive association between the intestinal *Entamoeba spp* infection and safe drinking water lack was observed (Fig 2). However, according to a previously published article, no association between the microbial water quality and infection of intestinal parasites was noted while this contrary results were attributed to the intervention of various factors [66]. As noted earlier, in addition to *E.hstolitica*, *Entamoeba dispar*, and *Entamoeba moshkovskii* can also play a remarkable role in the prevalence of intestinal parasites infection. Moreover, several factors are intervening on the transmission of protozoa into the body through contaminated water and food, which could influence the observed association between the contaminated drinking water and *Entamoeba spp* infection.

Maintaining water resources from microbial contaminants plays an important role in the control of transmitting diseases. In this regard, the parasitological quality of water collected from five different sources in rural areas of Tunisia was investigated, and the high level of intestinal parasite prevalence of (about 97%) mainly was correlated with protozoan [74]. Based on their findings, cleaning in the underground reservoirs and surface of rainwater collectors, changing the cover of reservoirs, and preventing run-off entrance to the reservoirs were proposed. In another study [75] in rural and urban areas of Jiroft, Iran, the quality of water and personal hygiene were recognized as the most important factors on the prevalence of parasites. Also, with applying of humans and animal feces as fertilizer or during food preparation with polluted hands and even by polluted water, this issue can be stimulated [76, 77]. Washing of hands before eating and after toilet, nail trimming [17, 78], consumption of well cleaned raw vegetables [37], and safe disposal of feces (toilet using) are the main sanitation practices that could reduce direct fecal-oral transmission. In most communities, the probable transmission of parasitic infections was increased by the lack of sanitation facilities, including not access toilets [79]. Sungkar et al. [80] conducted a cross-sectional study in Kalena Rongo village, Indonesia, where access to safe water and sanitary toilets was rare. This condition resulted in a lack of handwashing and taking a shower just once per week. After investigation, they found that about half of the residents were infected by protozoan diseases.



According to the findings of Nath et al. (2015a) who investigated the *Entamoeba spp.* in stool samples [81], the unhygienic toilet had a significant role in protozoan distribution. Moreover, discharged feces to open drains have a higher risk for infection [79]. As mentioned earlier, there are several factors that could affect sanitation, as classified into three levels of individual/family, social, and environmental. However, they have an inter-association within and between the levels.

#### 4.1. Individual/family level

Based on the extracted data from literature, income [82], animal contact [83], family size [37], nutritional status [24, 84], age [85], gender [86], occupation status [81], and some other cases, such as sexual act [87], genetic and immunity system of host [67, 74] were considered as the most effective factors.

Among the above-mentioned factors, poverty is usually caused by unemployment, and families by low-income are deprived of many primary life health standards such as insurance, education, safe water, and food, etc. [88, 89]. Most marginalized populations have low incomes, and because of low health services, zoonotic diseases are prevalent among their societies [90]. Due to the scavenging activities and the consumption of water and food with unknown sources, animals easily infected with parasitic infections. Therefore, direct contact with infected animals can increase the risk of animal-to-human transmission [30]. According to Liao et al. [91], based on 308 questionnaires collected from primary schools in Battambang, Cambodia, 95.1% of infected children kept animals at their homes. Also, Hemmati et al. [83] stated that direct contact with animals besides the drinking water quality is among the most important factors on the intestinal infection. However, in a report conducted in Kisumu, Kenya, only direct contact with a domestic animal was correlated by the distribution and diversity of intestinal parasites [82].

Additionally, the number of family members have a primary role in intestinal parasitic infection. In this regard, 5 times more risk was reported for the families with a population of more than 5 members, due to increase in people's activity among the family, the risk can be increased [37].

Diet is an important factor against invasive pathogens. Hence, the deficiency in vital body elements leads to malnutrition, which results in the susceptibility of the body against various diseases [92]. Raja and Karthick [93] demonstrated that due to nutritional deficiency, alcoholics are more susceptible to *Entamoeba histolytica* infection. However, since iron is a vital element for *Entamoeba histolytica*, iron deficiency in women who have regular menstrual blood loss could prevent the risk of *Entamoeba histolytica* infection [94].

In most of the studies, a factor of age usually was related to the occupation type. Indeed, with an increase in age, especially since childhood, human activity, and communication due to attending school and work have increased [17]. In another investigation, age, unlike sex, statistically had a significant association with the prevalence of *Entamoeba histolytica* and *Entamoeba dispar*. In a study published in southern Brazil, a higher risk of intestinal protozoa (60%) was reported for the male while compared with a female which attributed to their occupation [95]. Based on the findings of Al-Mekhlafi et al. [17], the risk of infection in males was about 1.5 times higher than females.

#### 4.2. Social level

Some factors such as economic development [17], culture [77], water/wastewater infrastructures [96], waste disposal [82], education [97], and governor policies [98] were considered. In this regard, among developed countries due to the availability of appropriate water treatment

technologies and educated citizens a better condition for control and decrease of pathogenic infection can be expected. Although, occasionally, there are issues with the entrance of other country infected citizens [98]. Also, the economic development resulted in further improvements in the sanitation conditions such as infrastructures, education, incomes, water and food quality, vector control, and sewage and waste disposal [84, 99]. In this regard, due to the strong association between the high level of education and modern culture, better sanitation behaviors are expected [100, 101]. Proper education about sanitary and routes of infection can have a remarkable controlling role in disease prevalence [102]. According to Ben Ayed et al. (2018), the education of hygiene behaviors such as regular handwashing, safe storage, and consumption of water is crucial for keeping safe water resources in rural areas [99]. However, the larger communities need to have better management for water supply and sanitary disposal of wastes and wastewater [45, 74]. These goals require appropriate infrastructure, which is largely related to government policy and economics [63, 85, 98, 99].

### 4.3. Environmental level

Desertification, deforestation, and modification in regions besides long and short term climate changes are among the environmental variables that affect the distribution of parasites [76, 101]. Prolonged drought besides hot weather leads to the consumption of water from inappropriate sources which results in higher prevalence risk [103]. Accordingly, the summer had the highest, and winter had the lowest positive effect on the prevalence of protozoan infections. While according to another investigation, the prevalence of *Entamoeba dispar* and *Entamoeba histolytica* is increased in rainy seasons. Early precipitation through roof cleaning and submergence of drains can lead to water supply pollution [66]. Nath et al. after comparing the *Entamoeba histolytica* prevalence in pre-monsoon, monsoon, and post-monsoon seasons, concluded that monsoon season has the greatest role in the *Entamoeba histolytica* prevalence [65]. As argued above, in recent decades, climate change has become a concerning phenomenon. In some regions of the world, the phenomenon causes prolonged drought. On the other regions, heavy rain, and subsequently, a flood can result in a higher prevalence of these issues [104]. Although cold and heat stress due to their influences on the endocrine and immune systems, can change the survival status of parasites in the body of hosts [105].

Concerning the mentioned factors, it can be concluded that the prevalence of *Entamoeba spp.* is varied from country to country. However, based on the findings of the current investigation, the intestinal *Entamoeba spp* infection due to safe drinking water lack in Malaysia, Kenia and Iraq was higher than other countries and also due to lack of sanitation (toilet) facilities in Malaysia, Kenia and Mexico were higher than other countries. Food and water-related diseases, particularly, protozoan infections known as the main health problems in Peninsular Malaysia [106]. After investigating the intestinal parasitism among two indigenous groups in Malaysia, given that many indigenous peoples had farming activities, Chin et al. attributed the infection in these two indigenous peoples to the use of "night soil" as fertilizer [89]. Also, poverty and lack of appropriate water network systems were considered as intervention factors. In the case of Kenya which has not yet reached the Millennium Development Goals specified by the United Nations, using of safe drinking water in an urban and rural area of Kenya, were 82% and 57%, respectively [107]. Iraq, one of the Middle East and North African countries (MENA), considered as an arid or semi-arid region. Concerning the reports, this country had improved sanitation of 98% for urban areas and 82% for rural areas. While wastewater management infrastructures in Iraq were weak, and most wastewater treatment systems did not have the proper efficiency resulting in untreated wastewater discharged to the environment. In another word, about 70% of wastewater is discharged to the rivers without any treatment

which can be resulted in a low microbial quality of water resources [108–110]. Parasitic infections are among the top 20 diseases in Mexico, and about 53% of peoples are affected by these problems. In a study carried out in states of Sonora and Oaxaca in Mexico, the results indicated that parasitic infection had a prevalence of 47.2% among children. Lack of education, poverty, highly populated families, direct animal contact, and malnutrition can be listed among the most important causes [111, 112]. At a glance, it can be said that all of the mentioned countries are among the developing countries.

## Conclusion

In this work for the first time, the risk of *Entamoeba spp* infection due to encounter public health parameters consist of lacks safe drinking water and sanitation facilities based on defined subgroups were meta-analyzed. The risk of *Entamoeba spp* infection due to the lack of safe drinking water increased, insignificantly; however, the risk of *Entamoeba spp* infection due to the lack of sanitation facilities increased significantly. The risk *Entamoeba spp* infection with the lack of sanitation facilities in the children's age groups was insignificantly decreased, therefore, in order to obtain more accurate results, it needs to be conducted more studies on the children's age group in the future. Overall, the current study showed that public health could have the main role in increasing the risk of *Entamoeba spp* infection. Therefore, it is recommended to be performed plans to increase public health in communities.

## Supporting information

**S1 Checklist. PRISMA 2009 checklist.**

(DOCX)

**S1 Table. Main characteristic of the included studies.**

(DOCX)

**S1 Text.**

(DOCX)

**S1 Fig. Meta-analysis of the association intestinal *Entamoeba spp* infection with lack safe drinking water based on quality of studies.** ES is Effect size.

(DOCX)

**S2 Fig. Meta-analysis of the association intestinal *Entamoeba spp* infection with lack sanitation facilities (toilet) based on quality of studies.** ES is Effect size.

(DOCX)

**S3 Fig. Meta-analysis of the association intestinal *Entamoeba spp* infection with lack safe drinking water based on age groups subgroup.** ES is Effect size.

(DOCX)

**S4 Fig. Meta-analysis of the association intestinal *Entamoeba spp* infection with lack sanitation facilities (toilet) based on age group subgroup.** ES is Effect size.

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