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The risk factors for intestinal *Giardia spp* infection: Global systematic review and meta-analysis and meta-regression

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ABSTRACT

Parasitic infections are a public health concern as they can cause aggression, growth retardation, weight loss, anemia, and other health problems. In this study, a systematic review and meta-analysis were performed to find an association between the probable social-environmental risk factors including lack of safe drinking water, no hand washing, sex, age, no access to education, no access to toilet, and *Giardia spp* infection. We conducted literature research among international databases including Scopus, PubMed, Web of Science and Cochrane from1 January 1995 to March 15, 2020, including 23 articles with 102 studies while the odds ratio (OR) was calculated using 2 × 2 tables or extracted. The pooled effect size with 95% confidence intervals (CIs) was estimated using a random or fixed-effects model. The results show a significant association between intestinal *Giardia spp* infection risk and lack of safe drinking water (OR: 1.14; 95%CI: 1.02-1.25); no access to toilet (OR: 1.22; 95%CI: 1.07-1.37); and age (2-10 vs 10-30 year) (OR: 1.42; 95%CI: 1.09-1.78). An insignificant association was observed between intestinal *Giardia spp* infection risk and age (<2 vs 2-10 year) (OR: 0.89; 95%CI: 0.75-1.02); no access to education (OR: 1.10; 95%CI: 0.80-1.40); Sex (male vs female) (OR: 1.04; 95%CI: 0.74-1.34); and no handwashing (OR: 1.18; 95%CI: 0.87-1.49). The results of meta-regression also indicate that intestinal *Giardia spp* infection has decreased over time (C= -0.024, p-value = 0.03) significantly, and also by growth of human development index (HDI) (C= - 0.42, p-value = 0.29) insignificantly. Improvement of personal hygiene, sanitation and raising public awareness can be effective in reducing *Giardia spp* infections.

1. Introduction

Intestinal parasitic disease (IPD) is the most common public health problem around the world which imposes economic and mortality burdens. WHO declared that about one-third of the world's population are infected with IPD, the majority of whom are children. Helminth (*T. trichiura, A. lumbricoides, S. stercoralis and Taenia species*), protozoan genus (*E. histolytica, D. fragilis, B. coli*), *cryptosporidium spp* and *giardia spp* are the most important intestinal parasites (Gholipoor et al., 2019; Gyang et al., 2019; Xiao et al., 2018).

Flagellated protozoa of the genus *Giardia* has six species including *Giardia duodenalis (lamblia and intestinalis), Giardia agilis, Giardia muris, Giardia microti, Giardia ardeae* and *Giardia psittaci. Duodenalis* species can infect a wide range of mammalian, leading to one of the most frequently parasitic enteric diseases known as giardiasis (Aw et al., 2019b; Ligda et al., 2020; Masangkay et al., 2020; Robertson, 2013). Four characteristics of *G. duodenalis* that boost its prevalence are as follows: a) the low infective dose of 10 to 100 cysts in humans; b) rapid spread among mammals after stool excretion; c) cysts can survive for weeks to months and; consequently d) presence in drinking water and food (Anuar et al.,

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2014). Fecal-oral and polluted water/food are direct and indirect transmission routes of giardiasis from person to person. Nevertheless, pets (cats and dogs) are also the major zoonotic transmission routes to humans (Aw et al., 2019b).

The global estimation reported that more than 200 million people of all age groups have giardiasis related diarrhea yearly, whereas children, especially those who live in poor sanitation areas, are at higher risk. In this respect, the infection ranges of 10-50% and 0.1-5% were dedicated to giardia in developing and developed countries, respectively (Al-Mekhlafi, 2017; Beale et al., 2013; Boontanom et al., 2011; Masangkay et al., 2020). The infection appears as acute diarrhea and if left untreated it can become chronic and asymptomatic over time. On the other hand, chronic infection is associated with malabsorption which causes growth retardation, weight loss, iron deficiency, anemia, and sometimes cognitive impairment in children. There is also reliable evidence that giardiasis may have a co-infecting role with bacteria, viruses, and other parasites (Manko-Prykhoda et al., 2020; Samie et al., 2020; Tembo et al., 2020). Although the pathogenic process of *Giardia spp* is not obvious, yet it includes disruption on the gastrointestinal epithelium and covering mucus layer with considerably changeable symptoms such as abdominal pain, diarrhea, and dehydration (Júlio et al., 2012). However, diagnosis and treatment of giardiasis are simple to implement by direct microscopy of faeces and oral consumption of antiparasitic drugs like secnidazole and tinidazole, respectively (Bello et al., 2011b; Moore et al., 2016b).

According to previous studies, various risk factors affect *G. duodenalis* prevalence which allows it to vary across countries (Samie et al., 2020). Factors like education (Al-Mekhlafi, 2017; Naz et al., 2018a), access to treated drinking water (Puebla et al., 2017b; Waqar et al., 2014), water storage (Bello et al., 2011b; CIFUENTES et al., 2004b), hand washing (Cifuentes et al., 2004a; Yahaya and Dogara, 2018), toilet, poor sanitary conditions (Bello et al., 2011a; Júlio et al., 2012), rural residency (Naz et al., 2018b), poverty, number of children in the family, poor food hygiene (Bello et al., 2011b; Pereira et al., 2007), and overcrowding (Younas et al., 2008)in developing countries and institutionalization, homosexuality, international travel and immigration (EKDAHL and ANDERSSON, 2005; Samie et al., 2020) in developed countries are considered as prevalence risk factors. However, independent factors like sex (Aw et al., 2019a; Waqar et al., 2014), age (Caron et al., 2018; Saaed and Ongerth, 2019), and seasons (Cifuentes et al., 2004a; Mohammed Mahdy et al., 2008a) have also been taken into consideration.

In several studies, different risk factors of giardiasis have been identified, such as consumption of drinking piped water and raw vegetables(Mohammed Mahdy et al., 2008b), while in another study, unsafe water resources and keeping dogs was identified as significant risk factors(Puebla et al., 2017a). Since there are no comprehensive results on determining the most important risk factors of *Giardia spp* infection, this study is innovatively aimed to introduce probable social-environmental risk factors including lack of safe drinking water, no handwashing, sex, age, no access to education and no access to toilet through a meta-analysis and meta-regression.

2. Method

2.1. Protocol and search strategy

In this study, the databases of Web of Science, PubMed, Scopus, and Cochrane were searched to retrieve included articles in agreement based on PRISMA guideline from 1 January 1995 to March 15, 2020 (Atamaleki et al., 2019; Moher et al., 2009; Stroup et al., 2000). The search syntax of "water" OR "toilet facilities" OR "sanitation" AND "risk factor" AND "relative risk" OR "odds ratio" OR AND "Intestinal Protozoa" OR "*Giardia spp*" OR "*Giardia duodenalis*" OR "*Giardia lamblia*" OR "*Giardia intestinalis*" was applied up to March 15, 2020. Disagreement between the two authors about select and/or exclude one article was resolved with the final opinion of the corresponding author.

2.2. Inclusion and exclusion criteria

Four criteria for articles inclusion were determined as follows: 1) access to full text in the English language, 2) prevalence of *G. duodenalis spp. (lamblia and intestinalis*), 3) risk factors related to *G. duodenalis,* and 4) cross-sectional and case-control studies. Studies conducted on intestinal parasite without separating the types of parasites and also, animal studies, theses, books, and review articles were excluded.

2.3. Data extraction and quality assessment

The extracted data were considered according to country, year of study, odds ratio (OR), confidence interval (CI) of OR, positive and total number of cases, and subgroups including sex, age, education, seasons, toilet, drinking water access, hand washing. 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 × 2 contingency tables, further calculations were performed to obtain the OR by following equation (Morris and Gardner, 1988):

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

Where a is the number of infected cases in the bad group; b is number of uninfected cases in the bad group; c is number of infected cases in the good group and d is number of uninfected cases in the good group (Morris and Gardner, 1988). In the studies with both the unadjusted and adjusted OR, unadjusted OR was applied to have an overview regarding the comparison between the cross-studies.

2.4. Meta-analysis of data

STATA software Ver.14.0 was used for meta-analysis of ORs. In addition, Cochrane's Q-test and I^2 index were used for determining heterogeneity. $I^2 > 50\%$ and P-value < 0.05 considered significant heterogeneity and statistically significant test result, respectively (Fakhri et al., 2019; Higgins. and Thompson, 2002; Kuroki et al., 2017). When I^2 index was lower than 50%, the fixed effect model was used and if I^2 index was higher than 50%, the random effect model was utilized (Fakhri et al., 2018; Foroutan et al., 2019; Kuroki et al., 2017; Rostami et al., 2017; Rostami et al., 2019). Within this regard, for detection of publication bias, the Egger test was also used (Egger et al., 1997; Kuroki et al., 2017). A meta-analysis of data was performed based on lack of safe drinking water, no hand-washing, sex, age, no access to education and no access to toilet subgroups. Also, meta-regression between *Giardia spp* infection ORs and year of study and HDI score was performed (Foroutan et al., 2019; Rahmani et al., 2018).

Fig. 1

3. Results

3.1. Meta–analysis

This study obtained 23 articles with 102 data-reports for the meta-analysis (n = 854) as shown in Tables 1s. The association between intestinal *Giardia spp* infection and lack of safe drinking water risk factor was presented in **Fig. 2**. The results show a significant positive association between intestinal *Giardia spp* infection risk and lack of safe drinking water risk factor (OR: 1.14; 95%CI: 1.02-1.25) with low heterogeneity ($I^2 = 35.4\%$) (**Fig. 2**).

The association between intestinal *Giardia spp* infection and no handwashing was presented in **Fig. 3A**. The results show an insignificant positive association between intestinal *Giardia spp* infection risk and no

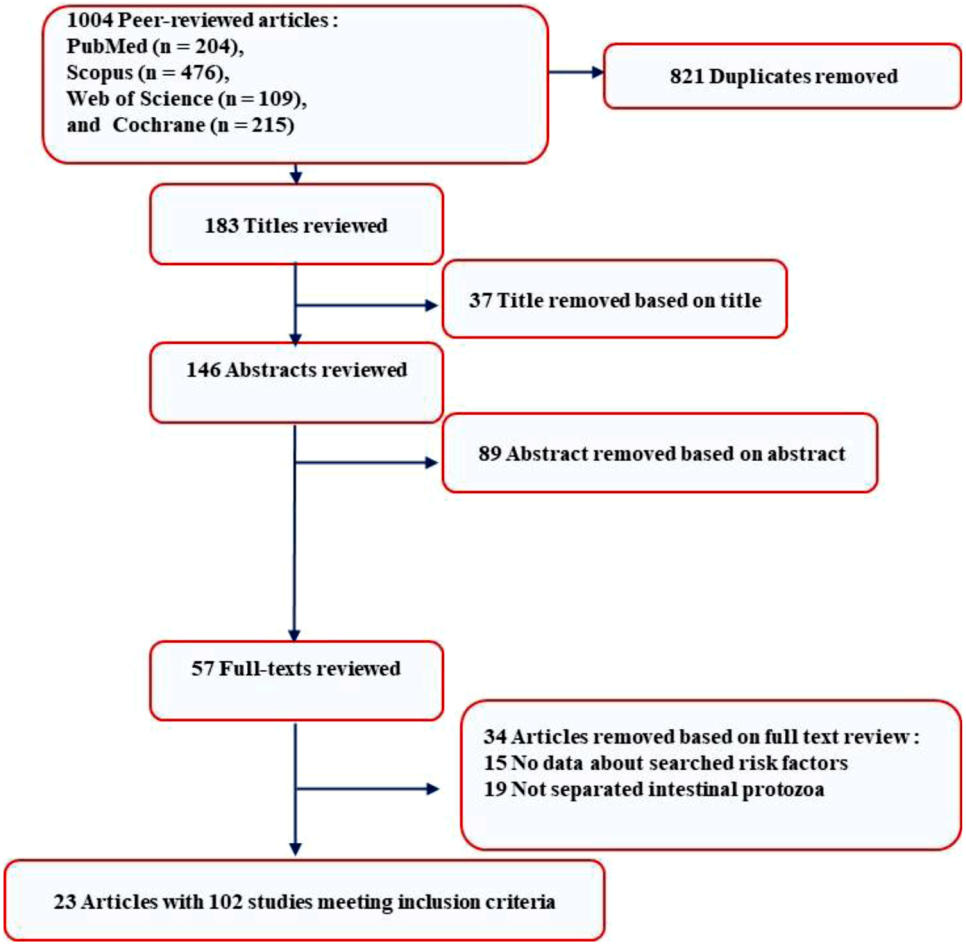


Fig. 1. Selection of studies process.

hand-wash risk factor (OR: 1.18; 95%CI: 0.87-1.49), with high heterogeneity ($I^2 = 61.4\%$) **(Fig. 3A)**.

The association between intestinal *Giardia spp* infection and sex differences was presented in **Fig. 3B**. The results show an insignificant positive association between intestinal *Giardia spp* infection risk with sex differences (male vs female) risk factor (OR: 1.04; 95%CI: 0.74-1.34), with high heterogeneity ($I^2 = 88.6\%$) **(Fig. 3B)**.

The association between intestinal *Giardia spp* infection and education risk factor was presented in **Fig. 4A**. The results show an insignificant positive association between intestinal *Giardia spp* infection risk and no access to education risk factor (OR: 1.10; 95%CI: 0.80-1.40), with high heterogeneity ($I^2 = 73.70\%$) **(Fig. 4A)**.

The association between intestinal *Giardia spp* infection and no access to toilet risk factor was presented in **Fig. 4B**. The results show a significant positive association between intestinal *Giardia spp* infection risk and no access to toilet risk factor (OR: 1.22; 95%CI: 1.07-1.37), with low heterogeneity ($I^2 = 11.40\%$) **(Fig. 4B)**.

The association between intestinal *Giardia spp* infection and age risk factor (2-10 vs 10-30 year) was presented in **Fig. 5A**. The results show a significant positive association between intestinal *Giardia spp* infection risk and age risk factor (2-10 vs 10-30 year) (OR: 1.42; 95%CI: 1.09-1.78), with low heterogeneity ($I^2 = 0.00\%$) **(Fig. 5A)**.

The association between intestinal *Giardia spp* infection and age risk factor (<2 vs 2-10 year) was presented in **Fig. 5B**. The results show an insignificant negative association between intestinal *Giardia spp* infection risk and age risk factor (<2 vs 2-10 year) (OR: 0.89; 95%CI: 0.75-1.02), with low heterogeneity ($I^2 = 42.90\%$) **(Fig. 5B)**.

3.2. Meta-regression

The results of meta-regression show that intestinal *Giardia* spp infection risk has decreased significantly over time (C=-0.024, p-value = 0.03) (**Fig. 6 A**). Also, intestinal *Giardia* spp infection risk has decreased insignificantly with HDI score increment (C=-0.42, p-value = 0.29) (**Fig. 6 B**).

4. Discussion

Lack of access to safe drinking water significantly increases the chance of Giardia infection by 14 percent. Drinking water is one of the most important necessities of life and it is a potential cause of many bacterial and parasitic infections diseases if be contaminated (Naz et al., 2018a). In the previous studies, unsafe drinking water has been recognized as one of the causes of parasitic infections among individuals (Daryani et al., 2017; Júlio et al., 2012; Utami et al., 2020) and one of the main rout of Giardia transmission is to ingest adult cysts living in drinking water. The risk of Giardia transmission is mostly reported in rural areas that suffer from drinking water shortages and use un-piped drinking water such as streams, wells, reservoirs, and springs (Al-Mekhlafi, 2017). The consumption of untreated/unfiltered drinking water can increase the risk of infection to Giardia lamblia in children by 4 folds compared to purified/filtered drinking water (Naz et al., 2018a).

The association between drinking water and the risk of giardiasis infection can also be due to contaminated hands and containers for water retention. Previous studies have pointed to the critical importance of water hygiene in the control of parasitic infections (Al-Mekhlafi, 2017).

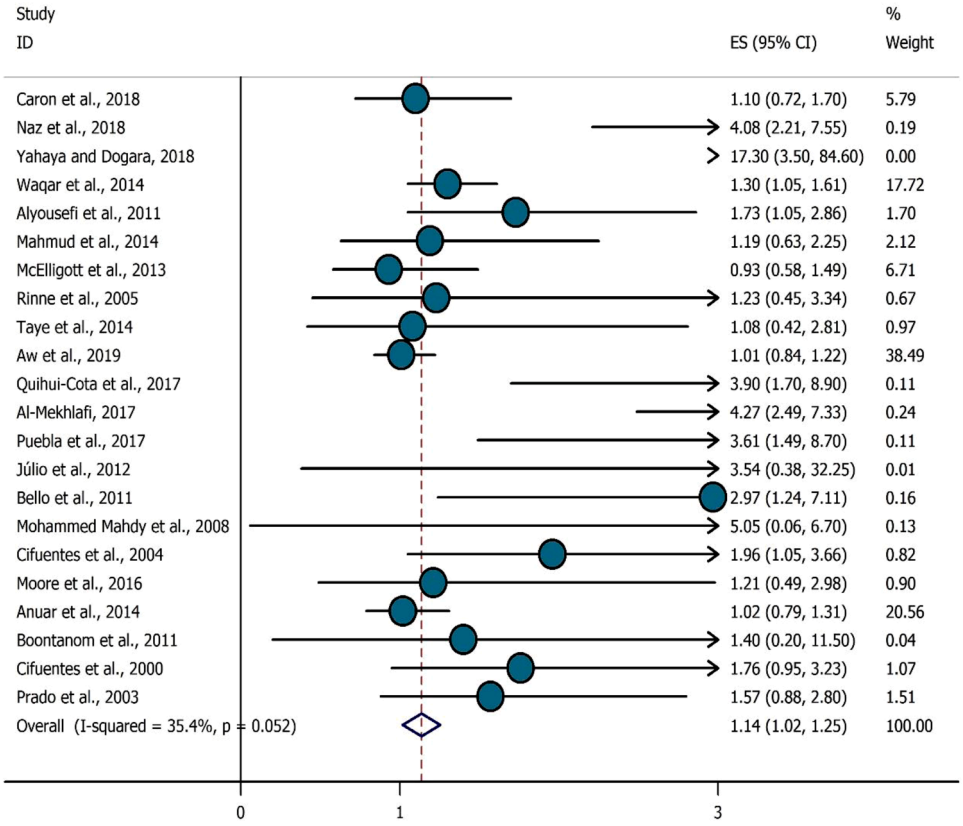


Fig. 2. Meta-analysis of the association intestinal *Giardia spp* infection with lack safe drinking water based on HDI score. ES is Effect size.

Access to water also affects the frequency of handwashing. It has been shown that mothers need 20 liters of water to wash their hands after using the toilet, before preparing meals, before eating, before feeding the baby, and before preparing food or drinking water containers. Unavailability of water in addition to mother's infection will cause infection of other family members, especially children (Alyousefi et al., 2011).

Unsafe drinking water can directly transmit Giardia cysts. In addition, in areas with unhealthy drinking water, personal and social health levels is also low which exacerbates the risk of infection. Studies have reported that access to safe drinking water along with personal hygiene, especially hand washing, can reduce the risk of giardiasis infection by up to 90 percent (Al-Mekhlafi, 2017).

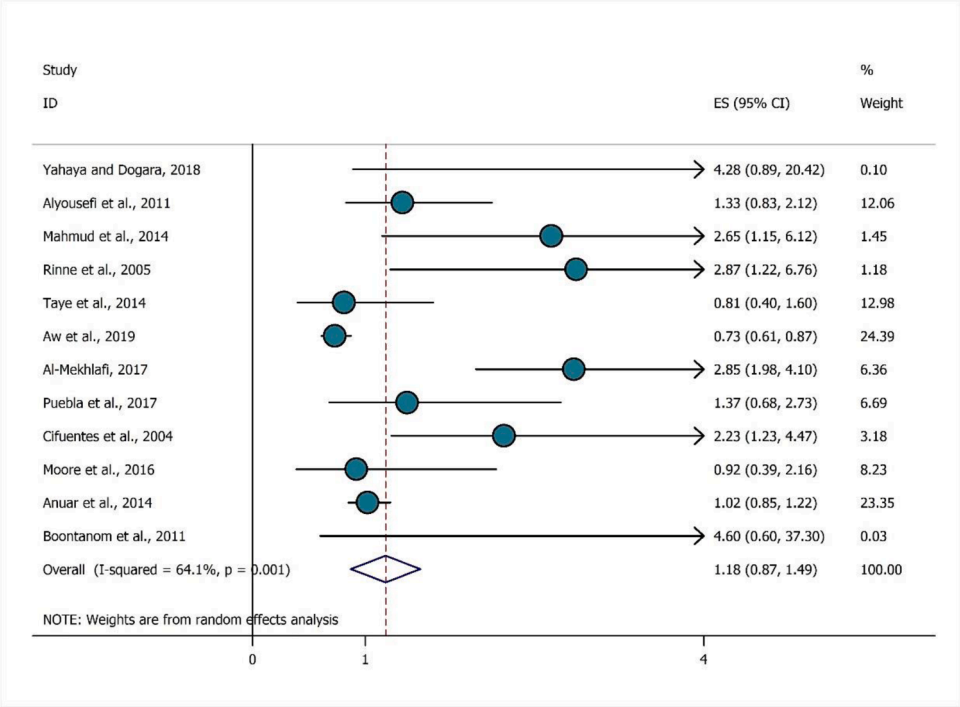
Failure to hand wash was found to be positively associated with giardiasis infection. It is well established that handwashing is the most essential health measure to control pathogen transmission including bacterial, viral, fungal and parasitic agents. Failure to hands wash, especially after defecation, has been reported as one of the main causes of the Giardia outbreak (Al-Mekhlafi, 2017).

The fecal-oral route is the most common method of giardia transmission through contaminated hands and fingers (Mahmud et al., 2014). Risk of up to three-fold giardiasis infection has been reported due to failure to hand wash after defection. Unlike some intestinal nematodes and trematodes that require soil or intermediate hosts to form an infectious form, Giardia cysts are infectious immediately after defection or shortly thereafter. Thus, cysts on unwashed hands can be transmitted from person to person, or contaminate the surroundings, such as door handles and bells, which itself is a source of infection for other people (Al-Mekhlafi, 2017).

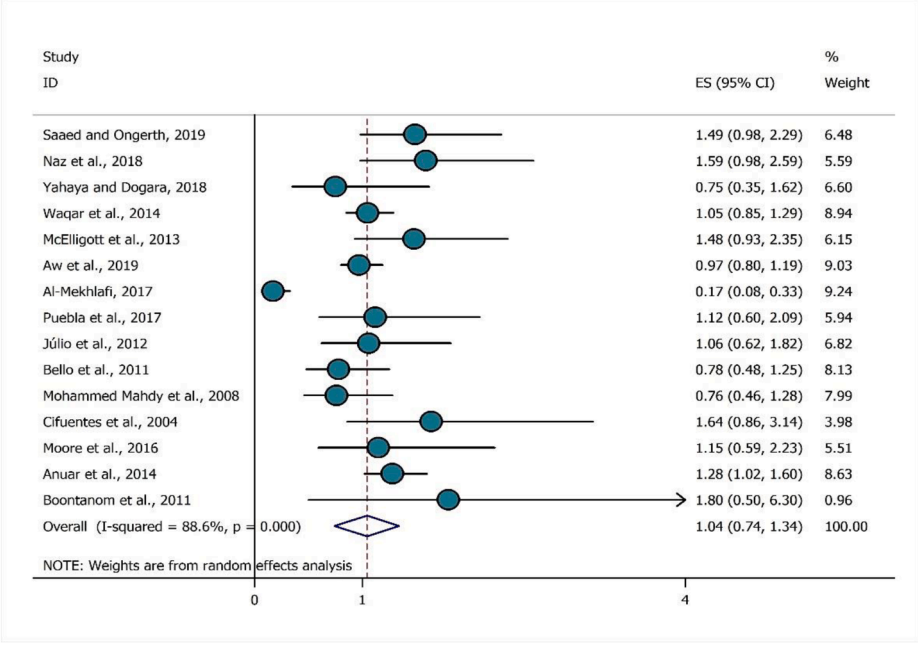
In addition, not washing hands after contact with animals such as dogs, cats, goat, cow, sheep, and donkeys (Yahaya and Dogara, 2018) and before handling food, and before and after eating (Moore et al., 2016a; Yahaya and Dogara, 2018) can be effective in transmitting Giardia cysts (Al-Mekhlafi, 2017). It is also noted that most of giardiasis infections in children compared to adults are due to children not washing their hands before and after eating and touching their mouths more (Mohammed Mahdy et al., 2008a).

No difference was found between males and females in terms of infection to giardia. There are inconsistencies in the association between gender and the prevalence of giardiasis in different studies. This contradiction can be due to the dissimilar behavioral patterns of men and women and the different roles they play in managing of life in various communities. In communities where women have the task of collecting potable water, because of exposure to contaminated water, their risk of giardiasis infection is high (Daryani et al., 2017; Yahaya and Dogara, 2018). Cooking vegetables and consumption of raw vegetables during cleaning it and women's more desire for raw salads are other causes of higher prevalence of giardia among females than males (Daryani et al., 2017). Nursing children in societies with a high incidence of infection can also increase the risk of giardiasis infection in females compared to males (Júlio et al., 2012). Inadequate personal hygiene, playing on the ground, biting nails, not washing hands before meals, more mobility and more outdoor activities in boys and adult males compared to girls and adult females in some societies, cause more prevalence of Giardia infection in males than in females (Daryani et al., 2017).

Lack of education increases the risk of giardia infection, though the association is not statistically significant. It has also noted that highly educated mothers and fathers reduce the risk of giardia infection. The reason may be that higher levels of education for parents, especially fathers, reflect better socioeconomic status (Júlio et al., 2012; Naz et al., 2018a; Prado et al., 2003; Waqar et al., 2014). On the other hand, the low level of education is also associated with low levels of health, poor housing conditions, crowding and lack of health facilities (Júlio et al., 2012; Naz et al., 2018a; Waqar et al., 2014). Education is also associated with other risk factors such as how to dispose of waste and contact with



A



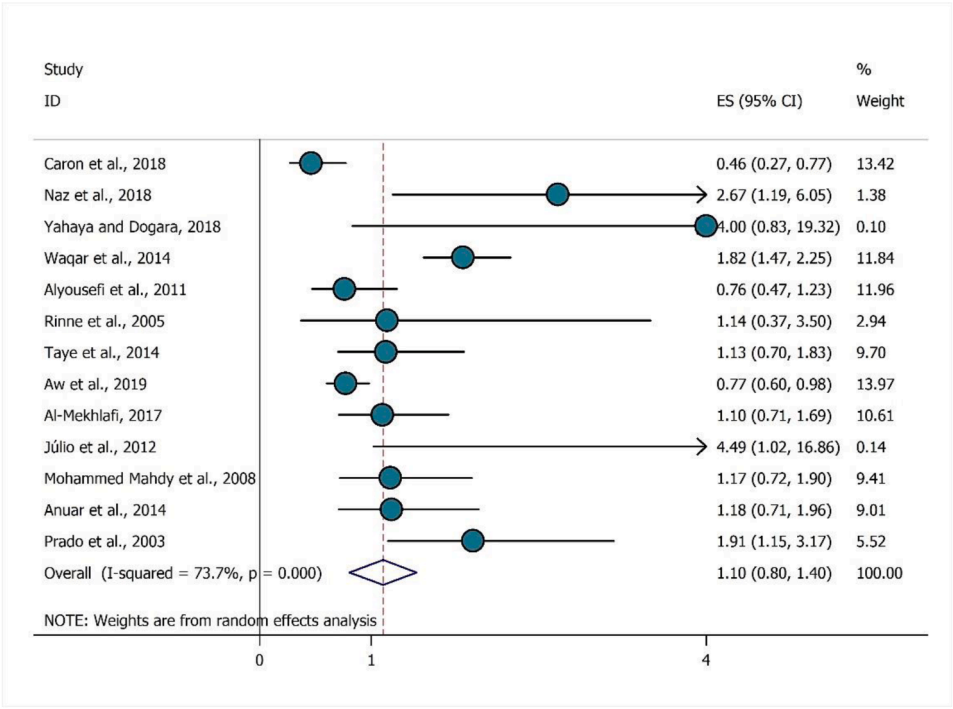
B

Fig. 3. Meta-analysis of the association intestinal *Giardia spp* infection with no hand-wash (A) and sex (male vs female) (B) based on HDI score. ES is Effect size.

animals which can influence the giardia transmission (Yahaya and Dogara, 2018). In addition to school and college education, training mothers and fathers regarding the principles of personal and public health have an important role in reducing parasitic infections and having a healthy community (Al-Mekhlafi, 2017; Daryani et al., 2017). Health education on food hygiene and personal hygiene (especially handwashing) is highly recommended to reduce the risk of infection to Giardia (Bello et al., 2011a).

No access to proper toilet was found to increase the risk of giardia infection. It is well established that the risk of giardia infection is higher in people living in homes without proper toilets than in persons with hygienic toilets (Bello et al., 2011a; Mohammed Mahdy et al., 2008a; Saaed and Ongerth, 2019; Yahaya and Dogara, 2018). The lack of sanitary toilets causes contamination of water resources and transmission of Giardia through contaminated water (Waqar et al., 2014). Soil contamination and, as a result, contamination of crops by human feces can also increase the risk of infection with Giardia in populations that do not use toilets. In addition, the lack of sanitary toilets indicates a low level of socioeconomic status and education which plays an important role in the high prevalence of giardia infection.

In terms of age dependency of Giardia infection, children aged from 2 to 10 years old were at risk more than those from 0-2 and older than 10 years old. Therefore, age is known to be an effective factor in the prevalence of parasitic infections (Quihui-Cota et al., 2017). School



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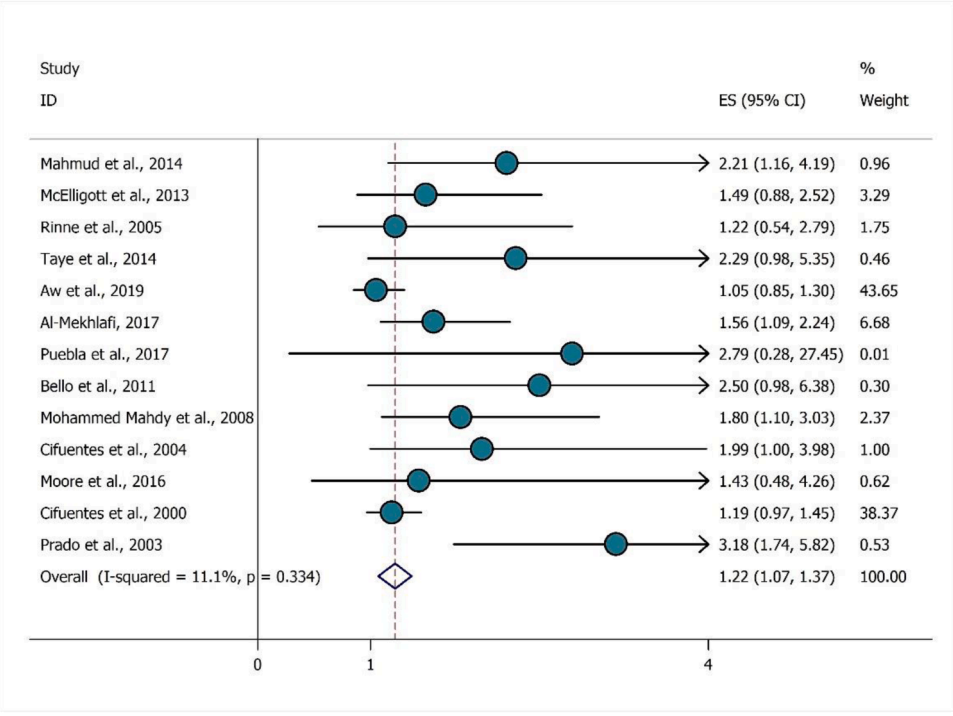
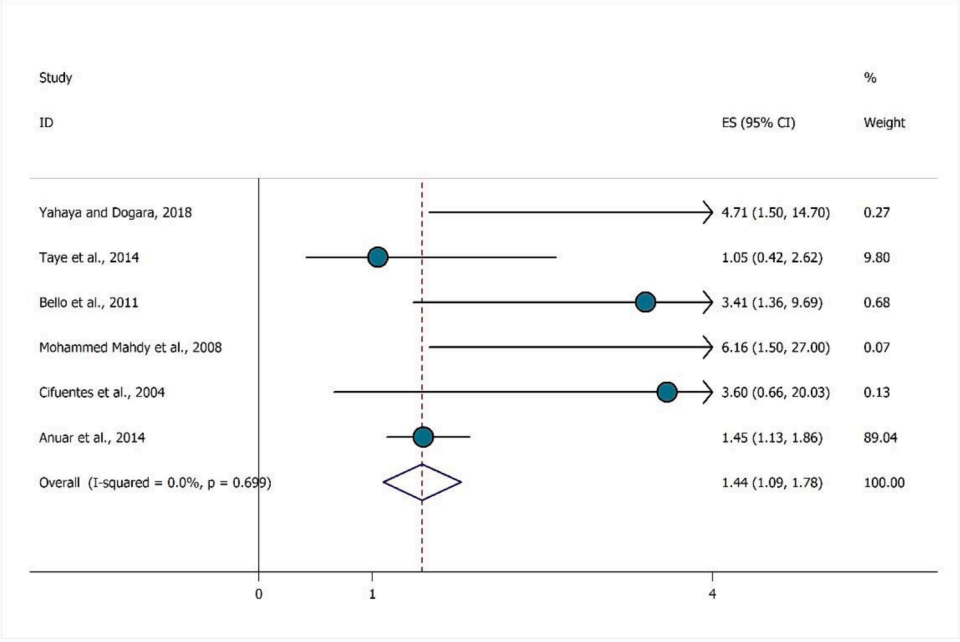


B

Fig. 4. Meta-analysis of the association intestinal Giardia spp infection with not access education (A) and not access toilet (B) based on HDI score. ES is Effect size.

children showed a higher rate of Giardia infection compared to pre-school children. This may be due to poor environmental health, poor school health, and more outdoor activities for school children than for pre-school children (Daryani et al., 2017). Also young children have been shown to be more susceptible to Giardia infection than other age groups, and this may be due to low personal hygiene standards and their health behaviors compared to older adults and children (Al-Mekhlafi, 2017).

Prevalence increment with age has been reported to be related to the personal independence acquired with the increase in age. While children aged 1-2 years old are monitored more often, children from 3 to 5 years old become more independent and less supervised, which may mean a decline in good health practices. As a result, older children are more likely to be at risk more than their younger peers (Caron et al., 2018). Also the more prevalence among children aged 0–9 years is probably related to poor health hygiene, poor toilet training, overcrowding, low socioeconomic status, close contact with other potentially infected children in child-care settings, and a lack of previous exposure to



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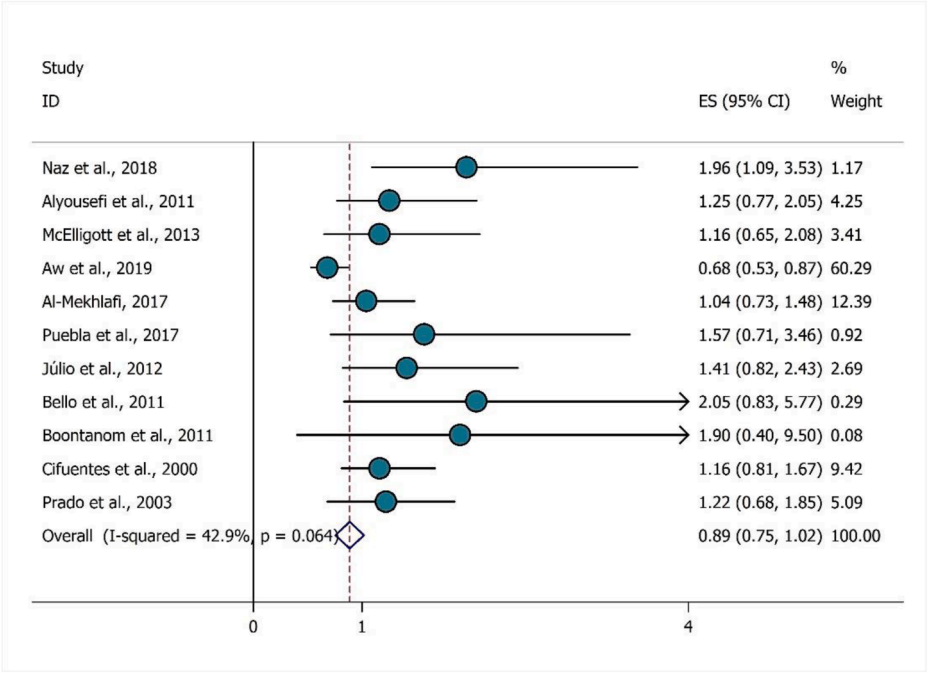

B

Fig. 5. Meta-analysis of the association intestinal Giardia spp infection with 2-10 year vs 10-30 year (A) and <2 year vs 2-10 year (B) based on HDI score. ES is Effect size.

Giardia, which could render them more susceptible to infection and illness (Rodríguez-Morales et al., 2016).

An increase in the human development index (HDI) score reduces the risk of Giardia infection insignificantly. The human development index (HDI) is a composite index of life expectancy, education, and per capita income, and is a measure of countries' development based on these three parameters (Sagar and Najam, 1998). As mentioned previously, higher household incomes lead to improved health housing indicators such as having health facilities such as toilets, kitchens, and bathrooms. Higher household incomes also lead families to access larger housing and reduce family crowding. Also promoting educational indicators, especially parent education, influences other indicators responsible for Giardia infection, such as food and personal hygiene.

5. Conclusion

In this study, it was tried to find an association between the social-environmental risk factors including lack of safe drinking water, no hand-wash, sex, age, no access to education and no access to toilet, and *Giardia spp* infection. The results of current study show that drinking water supply, access to sanitation facilities and education can considerably reduce the risk of *Giardia spp* infection. On the other hand, since children are more susceptible to *Giardia spp* infection hence more attention should be paid to them.

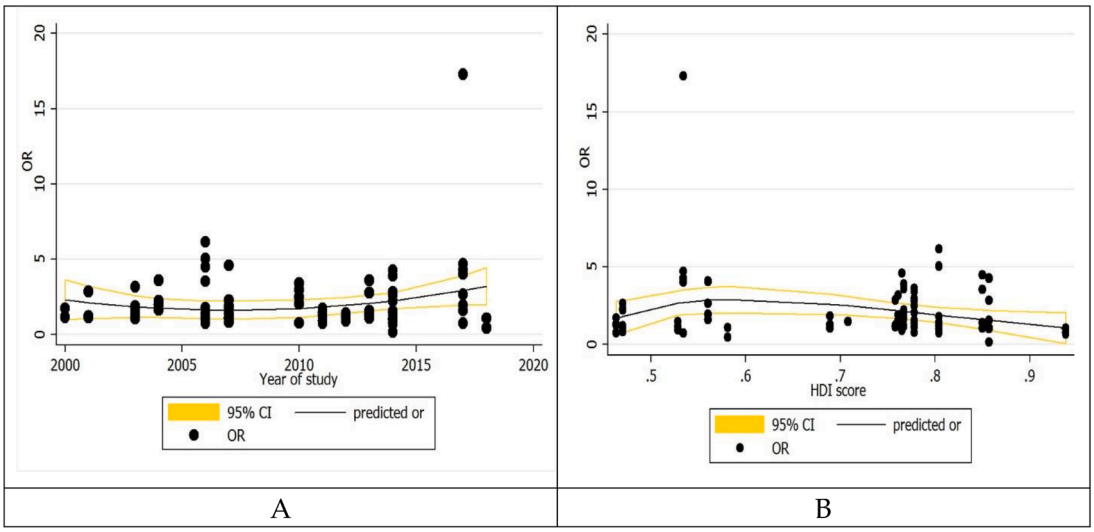

Fig. 6. Meta-regression of intestinal *Giardia spp* infection with year of publish study (A) and HDI score (B).

Declaration of Competing Interest

There is no conflict of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.actatropica.2021.105968.

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