ORIGINAL ARTICLE

Intestinal parasites and diabetes: A systematic review and meta-analysis

Mohammad Zibaei[a,b], Saeed Bahadory[a,c], Hassan Saadati[d], Kumars Pourrostami[e], Farzaneh Firoozeh[f] and Masoud Foroutan[g]

a *Department of Parasitology and Mycology, School of Medicine, Alborz University of Medical Sciences, Karaj, Iran,* b *Evidence-based Phytotherapy and Complementary Medicine Research Center, Alborz University of Medical Sciences, Karaj, Iran,* c *Department of Parasitology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran,* d *Department of Epidemiology and Biostatistics, School of Health, North Khorasan University of Medical Sciences, Bojnurd, Iran,* e *Department of Pediatrics, School of Medicine, Alborz University of Medical Sciences, Karaj, Iran,* f *Department of Microbiology, School of Medicine, Alborz University of Medical Sciences, Karaj, Iran and* g *Department of Basic Medical Sciences, Faculty of Medicine, Abadan University of Medical Sciences, Abadan, Iran*

Abstract

Background: Investigating the association between infectious agents and non-communicable diseases is an interesting emerging field of research. Intestinal parasites (IPs) are one of the causes of gastrointestinal complications, malnutrition, growth retardation and disturbances in host metabolism, which can play a potential role in metabolic diseases such as diabetes. The aim of the present study was to investigate the prevalence of IPs in diabetic patients and the association between IPs and diabetes.

Methods: A systematic literature search was conducted from January 2000 to November 2022in published records by using PubMed, Scopus, and Web of Science databases as well as Google scholar search engine; Out of a total of 29 included studies, fourteen cross-sectional studies (2676 diabetic subjects) and 15 case-control studies (5478 diabetic/non-diabetic subjects) were reviewed. The pooled prevalence of IPs in diabetics and the Odds Ratio (OR) were evaluated by CMA V2.

Results: In the current systematic review and meta-analysis, the pooled prevalence of IPs in diabetic patients was 26.5% (95% CI: 21.8–31.7%) with heterogeneity of I^2 = 93.24%; $P < 0.001$. The highest prevalence based on geographical area was in Region of the Americas (13.3% (95% CI: 9.6–18.0)).There was significant association between the prevalence of intestinal parasites in diabetic cases compared to controls (OR, 1.72; 95% CI: 1.06–2.78).

Conclusion: In line with the high prevalence of IPs in diabetic patients, significant association was found however, due to the limitations of the study, more studies should be conducted in developing countries and, the prevalence of IPs in diabetics should not be neglected.

Keywords: Intestinal parasites, Diabetes, Systematic review, Meta-analysis
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Corresponding author. Department of Parasitology and Mycology, School of Medicine, Alborz University of Medical Sciences, Karaj, Iran. Corresponding author. Evidence-based Phytotherapy and Complementary Medicine Research Center, Alborz University of Medical Sciences, Karaj, Iran.
E-mails: Zibaeim@sums.ac.ir **(M. Zibaei),** Saeed.Bahadory@yahoo.com **(S. Bahadory)**

Authors' contributions

MZ and SB were responsible for designing the study.All studies were screened by SB and FF. Studies data were extracted by SB and KP and double-checked by MF, all data analyzed by HS. The MZ and SB resolved disputes or controversial obstacles.

1. Introduction

It is estimated that around 3.5 billion people worldwide suffer from intestinal parasites (IPs), especially in developing countries where have poor water, sanitation, and hygiene (WASH) [1,2]. These non-aggressive and widespread infections are a health problem that inflicts significant economic losses in addition to significant mortality; the high prevalence of these infections is due to transmission through contaminated water and food sources in areas with poor hygiene [3]. The most widespread

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DeclarationsList of abbreviations

IPs	intestinal parasites
OR	odd ratio
DM	diabetes mellitus
PRISMA	preferred reporting items for systematic reviews and meta-analyses
NOS	Newcastle-Ottawa scale
NR	not reported

infections have been reported with medically important protozoa such as *cryptosporidium spp*., *Giardia* sp. and *Entamoeba histolytica*, hence the most isolated helminth species are *Strongyloides stercoralis*, *Trichuris trichiura, Ascaris lumbricoides,* and hookworms eggs [4,5]. Parasitic infections are contagious, but evidence shows that they can contribute to asthma and allergies, autoimmune diseases, metabolic non-communicable disorders such as obesity, diabetes, and so on [6–10].

Diabetes is a major chronic non-communicable metabolic disorder in which the body is unable to produce or use insulin and thereby, hyperglycemia occurs; insufficient insulin production or defect in insulin acquisition are known as type 1 and type 2 diabetes, respectively [11]. According to the diabetes facts and figures, nearly 463 million people live with diabetes, which is assessed to reach 700 million in 2045 [12]. Clinical complications can manifest as severe thirst, frequent urination, weight loss, fatigue, and sensation loss [13]. Many of the factors associated with diabetes are mentioned, some of which have been proven and others of which are debatable [14]. In the past, genetics, nutrition, overweight, family history, and pregnancy (gestational diabetes) could be implicated, and in recent cases, urbanization and stress, as well as infectious agents, have been discussed [15]. Diabetes can be considered as an underlying disease that may make a person vulnerable and prone to infections or other diseases [16,17].

In recent decades, numerous studies have investigated the association between infectious agents and allergies, metabolic diseases, and autoimmune diseases and they have concluded that some infectious agents, such as *Helicobacter pylori*, Hepatitis C virus, and *Toxoplasma gondii* are associated with diabetes [18–20]. On the other hand, it has been proven that infectious agents such as parasites are able to alter certain enzymes and metabolic factors in the infected host [21]. In the present meta-analysis, the results of studies that investigated the prevalence of IPs in diabetics were used to assess the association between the prevalence of IPs and diabetes. Despite the limited number of included studies, our findings can be considered in health decisions and diabetes prevention programs in underdeveloped and developing areas.

The main question is whether there is a significant relationship between diabetes and the prevalence of intestinal parasites? In other words, does diabetes act as an underlying factor and predispose the host to parasitic infections? Finding the answer to this question is the main goal of this study.

2. Methods

2.1. Preliminary research/idea validation and eligibility criteria

A preliminary search was conducted to ensure the validity of the proposed idea (association of intestinal parasites and diabetes), and to avoid duplication of the proposed topic, as well as to ensure that a sufficient number of studies were available for analysis.

Eligible studies in terms of abstract and title were screened by two independent researchers. In the next step, to remove duplicate records, all studies were imported into the Endnotes X8 software. Overall included studies met all of the four criteria: 1) Original studies and brief reports, all in English text or abstract with no restrictions regarding the geographical area, patients gender, age, and race were published up to November 30, 2022, 2) Case-control, cross-sectional, and hospital based studies with diabetes and intestinal parasites, 3) The populations studied for diabetes or intestinal parasites were comparable, 4) All full-text and/or abstracts that have a data about the only intestinal parasites examination in diabetic patients.

Studies that did not meet any of these conditions were excluded, including *in-vivo* and *in-vitro* studies, letters to the editor, reviews, thesis/dissertations, case report studies, as well as reports with confusing and/or unclear data, disproportionate population surveys, and reports that biasedly examined non-intestinal parasites (blood, tissue, etc.) in diabetic patients.

2.2. Search strategy

In this study, a systematic search was conducted for the association of diabetes and intestinal parasites in English published records in the Scopus, PubMed, and Web of Science databases as well as Google scholar search engine between Jan 01, 2000, and Nov 30, 2022, following PRISMA 'preferred reporting items for systematic reviews and meta-analyses' guidelines which developed by Moher et al. [22,23]. The following terms were used alone or in combination to search the databases: "Intestinal parasites' OR 'Parasitic infections' OR 'Parasite", AND "Prevalence' OR 'Epidemiology'" AND "Diabetes' OR 'Diabetes mellitus' OR 'Diabetic patients' ". In addition, references

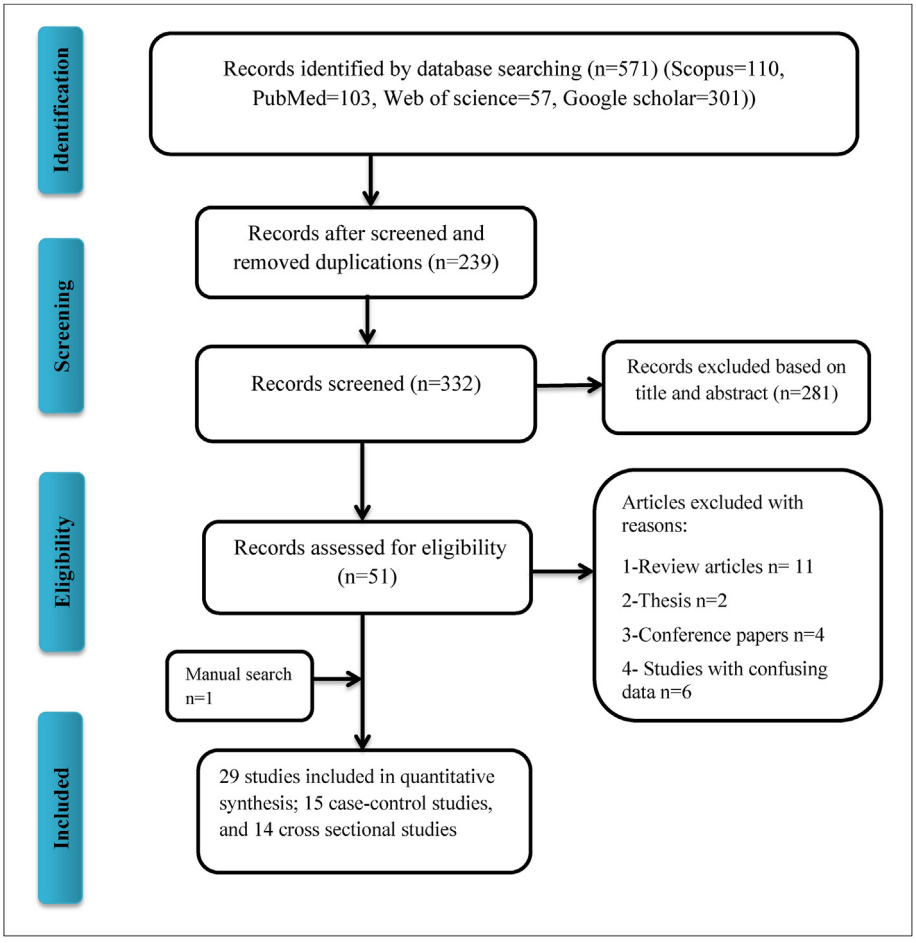

FIG. 1. Flow diagram of the literature search for studies included in the meta-analysis.

of all eligible articles were manually searched to find related studies that may have been missed during search process.

2.3. Study selection and data extraction

All studies entered with the mentioned eligibility criteria were screened by SB and FF. After the initial evaluation and ensuring the existence of extractable data, data were extracted by SB and double-checked and analyzed by HS. The MZ and FF resolved disputes or controversial obstacles. The extracted data included the authors, geographical area (including country and city), sample population, sample type, type of diagnostic method used for parasite detection, and positive cases of intestinal parasites in diabetic patients. In cross-sectional studies, the total sample was considered the general population, and in case-control studies, patients with diabetes were considered as the study population.

2.4. Quality assessment

The Newcastle-Ottawa Scale (NOS) and the Joanna Briggs Institute (JBI) checklist were used to assess the quality of the potential case-control and cross-sectional studies. NOS contains ten questions with four answering options include, yes, no, unknown, and not available. The maximum score a study can obtain is ten (one star for each item) [24]. Studies with a total score of 6 $\leq$ were acceptable and included our study. According to the JBI ten-question scale, each study can achieve a maximum of ten points (one point for each question) [25], in this study, any study whose total score is $\leq$ 3 is considered as a low-quality study and not included in the analysis.

2.5. Data synthesis and statistical analysis

We pooled the intestinal parasitic infections (IPIs) prevalence in diabetic patients using the random-effect model intended to perform the meta-analysis in comprehensive meta-analysis software (CMA V2.2, Bio stat). As well, we applied the random-effects meta-analysis framework as we expected variability in the prevalence estimates from different studies. Subgroup analysis was conducted based on study type, studies geographical area (WHO categorized regions and countries), and diagnostic methods. The heterogeneity of results between

TABLE 1. Summary of studies characteristics with IPs prevalence in diabetic patients based on cross-sectional studies.

Author name	Pub year	Research period	WHO regions	Country	City/State	sample type	Method	Total sample	Pos sample	Parasite type (N)
Alemu et al. [27]	2018	2017–2017	African region	Ethiopia	Arba Minch	Stool	direct wet mount	215	42	*Cryptosporidium* spp. (18), *Ascaris lumbricoides* (8), Hookworms(4),*Trichuris trichuria*(4),*Giardia lamblia*(6), *Teania* spp(2)
Ambachew et al. [28]	2020	2018–2018	African region	Ethiopia	Amhara	Stool	Formal-ether, microscopic	234	45	*Ascaris lumbricoides* (15), *Entamoeba histolytica/dispar* (9), Hookworms (9)
Engidaw and Feysa [29]	2020	2019–2019	African region	Ethiopia	Debre Tabo	NR	NR	265	69	IPs
Sisu et al. [30]	2021	2021–2021	African region	Ghana	Bolgatanga	Stool	Formal-ether, microscopic	152	19	*Giardia lamblia* (9), *E. histolytica* (4), *C. parvum* (3), *Entamoeba. coli* (3), *A. lumbricoides* (1) and hookworm (1)
Baqai et al. [31]	2005	2003–2003	Eastern Mediterranean	Pakistan	Karachi	Stool	Kinyoun method	20	5	*Cryptosporidium* spp.
Ali et al. [32]	2018	2017–2018	Eastern Mediterranean	Iraq	Kirkuk	Stool	Microscopic examination	419	62	*Blastocystis hominis*(22),*C. parvum*(8), *E. histolytica/dispar*(11),*G. lamblia*(16),*Iodamoeba butschlii*(1), *Strongyloides stercoralis*(1),*Hymenolepis nana*(3)
AL-Mousawi and Neamah [33]	2021	2020–2021	Eastern Mediterranean	Iraq	Najaf	Stool	sedimentation, modified Ziehl Neelsen stain	372	137	*E. histolytica* (47), *G. lamblia* (39), *A. lumbricoides* (19), *T.vaginalis* (12), *T.gondii* (11), *C.parvum* (9)
Nami et al. [34]	2022	2015–2019	Eastern Mediterranean	Libya	Benghazi	Stool	direct wet mount, Ziehl-Neelsen staining	200	80	*Blastocystis hominis*(1), *E.histolytica/dispar* (10), *G.lamblia* (10), *E.coli* (21), *C.parvum* (17), *E.hartmani* (9), *Isospora.belli* (5), *D.fragilis* (3), *A.lumbricoides* (0), *Enterobius.vermicularis* (1)
Machado et al. [4]	2018	2011–2012	Region of the Americas	Brazil	Taguatinga	Stool	Formal-ether, microscopic	156	102	*E. coli*(43), *Endolimax nana*(23), *Giardia lamblia*(16), *E. hartmanni*(10), *A. lumbricoides*(12), *Teania* spp.(3), Hookworms(2), *H. nana*(1), *S. stercoralis*(1), *E. vermicularis*(1), *Schistosoma mansoni*(1).
Calderon de la Barca et al. [35]	2020	2016–2018	Region of the Americas	Mexico	Sonora	Stool	PCR	37	28	*Cryptosporidium* spp., *Cyclospora* spp., *Blastocystis* spp.
Bora et al. [36]	2016	2015–2016	South-east Asia	India	India	Stool	Microscopic examination	17	3	*E. histolytica/E. dispar*, Hookworms, *S. stercoralis*, *Teania* spp., *G. lamblia*, *T. trichiura*
Chandi et al. [37]	2020	2019–2019	South-east Asia	India	Bhilai	Stool	Microscopic examination	110	15	*E. histolytica/dispar*(8),*C. parvum*(5), *A. lumbricoides*(2) *G. lamblia*(1)[a]
Popruk et al. [38]	2020	2019–2020	South-east Asia	Thailand	Phra Nakhon Si Ayutthaya	Stool	Nested-PCR	130	16	*Blastocystis* spp.
Htun et al. [39]	2018	2016–2016	Western pacific region	Laos	Four areas	Stool	Formal-ether, microscopic	349	100	*Opishorchis viverrini* (90), *Minute intestinal flukes* (18), *Paragonimus* spp. (1), Hookworms (14), *S. stercoralis* (6), *Teania* spp. (13)[a]

[a]In these studies, more than one parasite was detected in some participants, NR: Not Reported, DM: Diabetes Mellitus, T1, 2D; Type 1, 2 Diabete.

studies was checked using Cochran's Q statistic ($P < 0.10$) and was quantified using the I^2 and t^2 statistic. A combination of the visual inspection of funnel plots, and Egger's test [26] were performed to investigate the presence and the effect of publication bias. Two-tailed statistics and the significance level of less than 0.05 were considered for all analyses, except the heterogeneity test with a significance level of less than 0.1.

3. Results

The process of literature search and study selection based on the PRISMA flow chart is shown in Fig. 1. Overall, 571 potentially relevant articles were recognized from the initial search. Of these, 520 articles were excluded after removing duplicates, screening the titles and abstracts, and the full text of the remaining 51 articles was achieved from different sources. Lastly, 29 studies met the inclusion criteria and were included in the meta-analysis.

Cross sectional and case-control studies investigating the prevalence of IPs in diabetics as well as controls that were published between Jan 1, 2000, and Nov 30, 2022 included 29 records conducted in 4 different geographical areas; among them, seven studies were from African region, twelve reports from Eastern Mediterranean region, three studies were from Region of the Americas, similarly three papers related to the South-east Asia region and one study from European and Western pacific regions (Tables 1 and 2).

3.1. The pooled prevalence of IPs in diabetic patients

Based on the random-effects model, the pooled prevalence of IPs in diabetic patients was estimated to be 26.5% (95% CI: 21.8–31.7%). The sub-total prevalence of IPs in diabetic patients showed that based on studies WHO categorized regions, the highest and lowest prevalence were in Region of the Americas and South-east Asia region, respectively (13.3% (95% CI: 9.6–18.0) *vs.* 58.6 (95% CI: 34.0–79.5)). In the present study, 5278 subjects (2676 in cross-sectional and 5478 in case-control studies) were studied. (Summarized in Table 3).

Substantially high heterogeneity was observed between different studies ($I^2 = 93.24\%$; $t^2 = 0.44$, $P < 0.001$). Fig. 2 depicts the results in forest plot format.

TABLE 2. Summary of studies characteristics with IPs prevalence in diabetic patients based on case-control studies.

First author	Pub year	WHO regions	Country	Parasites detection method(s)	Total diabetic cases	IPs positive No	Total control	IPs positive No
Akhlaghi et al. [40]	2005	Eastern Mediterranean	Iran	Formalin-ether/acid-fast staining	250	39	250	25
Akinbo et al. [41]	2013	African region	Nigeria	Formalin-ether	150	28	30	0
Bafghi et al. [42]	2015	Eastern Mediterranean	Iran	Formalin-ether	250	61	250	58
Elnadi et al. [43]	2015	Eastern Mediterranean	Egypt	Modified Ziehl-Neelsen Acid	100	25	100	7
Mohtashamipour et al. [44]	2015	Eastern Mediterranean	Iran	Formalin-ether/acid-fast and trichrome staining	118	31	118	8
Poorkhosravani et al. [45]	2019	Eastern Mediterranean	Iran	Baermann and trichrome staining	254	32	247	46
Tangi et al. [46]	2016	African region	Cameroon	Formalin-ether/acid-fast staining	150	15	85	20
Nazligul et al. [47]	2001	European region	Turkey	Parasitology method	200	94	1024	724
Rady et al. [48]	2019	Eastern Mediterranean	Egypt	Parasitology method	413	86	260	52
Al-heety et al. [49]	2020	Eastern Mediterranean	Iraq	PCR	40	17	30	1
Waly et al. [50]	2021	Eastern Mediterranean	Egypt	Parasitology method	100	44	100	32
Almugadam et al. [51]	2021	Eastern Mediterranean	Sudan	Parasitology method	150	31	150	16
Maori et al. [52]	2021	African region	Nigeria	Parasitology method	138	70	46	4
de Melo et al. [53]	2021	Region of the Americas	Brazil	PCR	99	34	76	23
Bebia et al. [54]	2022	African region	Nigeria	Parasitology method	190	48	110	12

3.2. The overall odd ratio of IPs in diabetic patients based on case-control studies

As shown in Fig. 3, we found that despite the high prevalence of IPs in diabetic patients, according to case-control studies, there was statistically significant association between the case and control groups (OR, 1.72; 95% CI: 1.06–2.78) (I^2 = 89.01%; t^2 = 0.72).

3.2.1. Publication bias. A funnel plot was used to identify the potential publication bias. In present study, studies with cross-sectional (Fig. 4 A) and case-control (Fig. 4 B) design respectively. Also, according to Egger's regression test, significant and no significant publication bias was found in studies presenting results for case-control (P = 0.00) and cross-sectional (P = 0.50) design respectively.

TABLE 3. Pooled and subgroup prevalence results of IPs in diabetic patients based on geographic region and diagnostic method.

Variables	Studies NO	Samples NO	Pooled prevalence (95% CI)	Heterogeneity I^2	Heterogeneity t^2
WHO Regions					
African region	**9**	**1644**	**21.4 (15–29.6)**	**91.42**	**036**
Ethiopia	3	714	21.7 (17.5–26.5)	53.60	0.03
Ghana	1	152	12.5 (8.1–18.8)	0.00	0.00
Cameroon	1	150	10.0 (6.1–15.9)	0.00	0.00
Nigeria	3	478	30.2 (15.2–51.0)	94.56	0.57
Sudan	1	150	20.7 (14.9–27.9)	0.00	0.00
Eastern Mediterranean region	**12**	**2536**	**25.4 (19.9–31.8)**	**90.99**	**0.29**
Iran	4	872	19.1 (13.4–26.3)	82.49	0.15
Iraq	3	831	29.2 (14.0–51.2)	96.19	0.63
Pakistan	1	20	25.0 (10.8–47.8)	0.00	0.00
Libya	1	200	40.0 (33.4–46.9)	0.00	0.00
Egypt	3	613	28.9 (17.1–44.4)	90.79	0.32
European region	**1**	**200**	**47.0 (40.2–53.9)**	**0.00**	**0.00**
Turkey	1	200	47.0 (40.2–53.9)	0.00	0.00
Region of the Americas	**3**	**292**	**58.6 (34.0–79.5)**	**93.01**	**0.73**
Mexico	1	37	75.7 (59.5–86.8)	0.00	0.00
Brazil	2	255	50.0 (22.1–77.9)	95.56	0.78
South-east Asia	**3**	**257**	**13.3 (9.6–18.0)**	**0.00**	**0.00**
India	2	127	14.2 (9.1–21.5)	0.00	0.00
Thailand	1	130	12.3 (7.7–19.1)	0.00	0.00
Western pacific region	**1**	**349**	**28.7 (24.2–33.6)**	**1.00**	**0.00**
Laos	1	349	28.7 (24.2–33.6)	0.00	0.00
Diagnostic method[a]					
Microscopic	24	2411	24.9 (20.1–30.5)	93.67	0.44
Molecular	4	306	38.5 (17.1–65.4)	93.61	1.18
Pooled prevalence	**29**	**5278**	**26.5% (95% CI: 21.8–31.7%)**	**93.24**	0.44

[a]In one report, the diagnosis method was not reported.

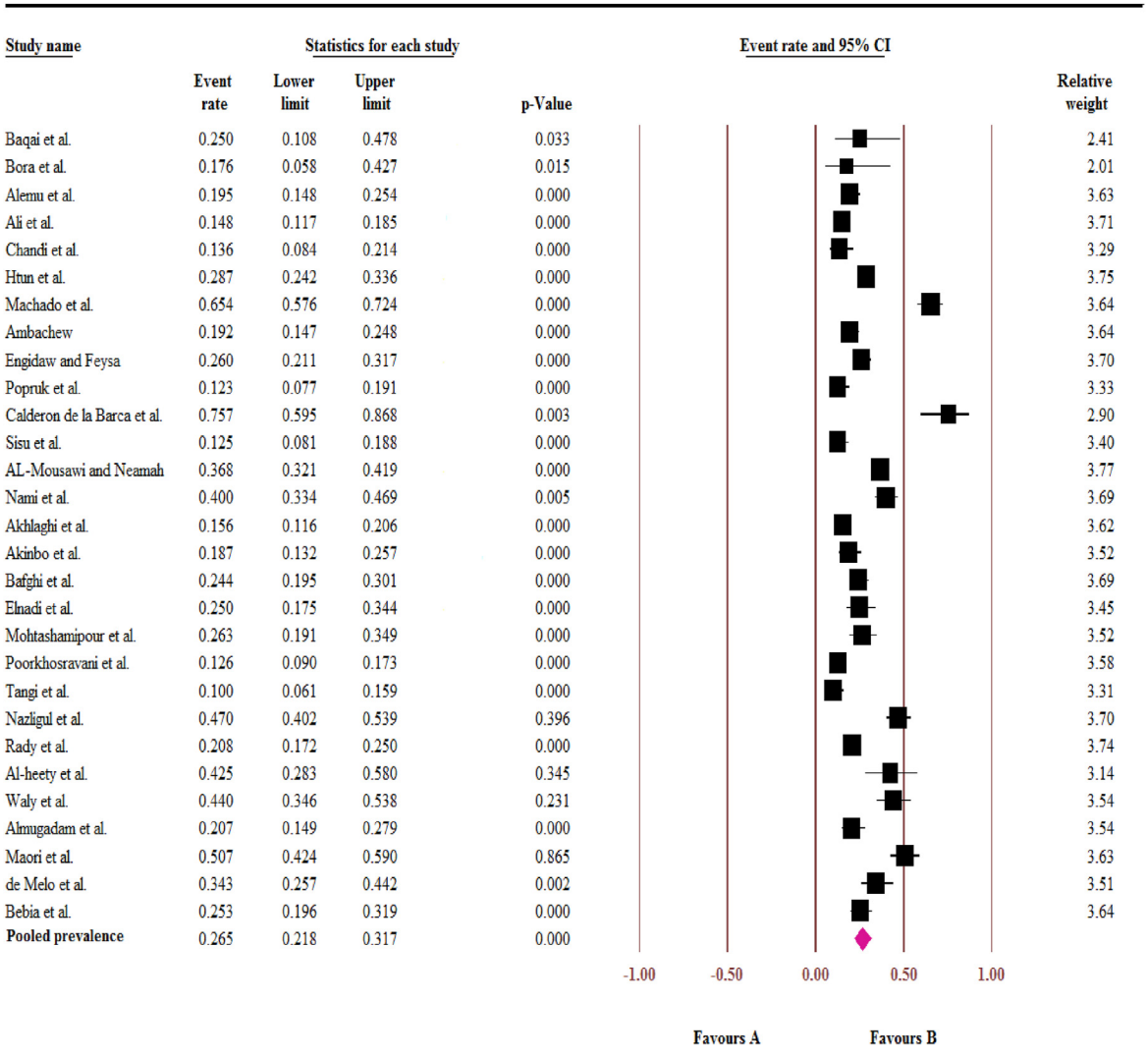

FIG. 2. Forest plot of intestinal parasites pooled prevalence in diabetic patients.

4. Discussion

In the last two decades, extensive studies have been conducted on the associations of infectious agents and diabetes. These studies were two-dimensional; some of them have evaluated the prevalence of infectious agents in diabetics while the rest of them have investigated the frequency of diabetes in people with infections. *Toxoplasma gondii* and *Strongyloides stercoralis* infections were among the parasitic diseases that have been studied in diabetics but none of the studies have provided a comprehensive summary of intestinal parasites in diabetic people. The present study is the first report in this field. According to our results, the overall pooled odds ratio of IPs was significant in diabetic patients compared to non-diabetic controls (OR, 1.72; 95% CI: 1.06–2.78).

IPs infections generally occur in poor hygiene and contamination of the water and food sources, which we see in underdeveloped and developing countries [55]. The included studies were also conducted in such areas that had a moderate to low human development index. It seems that the spread and transmission of many IPs infections have been controlled by improving the environment, sanitary disposal of human waste, mass treatment and providing safe drinking water in most of the developed regions of the world. Most of the included reports were from areas with lower sanitation and underdeveloped

Study name	Odds ratio	Lower limit	Upper limit	p-Value	Relative weight
Akhlaghi et al.	1.664	0.973	2.844	0.063	7.59
Akinbo et al.	14.192	0.843	239.050	0.066	2.16
Bafghi et al.	1.068	0.708	1.613	0.753	7.90
Elnadi et al.	4.429	1.816	10.801	0.001	6.51
Mohtashamipour et al.	4.899	2.144	11.197	0.000	6.72
Poorkhosravani et al.	0.630	0.386	1.028	0.064	7.71
Tangi et al.	0.361	0.174	0.751	0.006	7.02
Nazligul et al.	0.367	0.270	0.500	0.000	8.10
Rady et al.	1.052	0.715	1.547	0.797	7.95
Al-heety et al.	21.435	2.652	173.249	0.004	3.25
Waly et al.	1.670	0.938	2.972	0.081	7.48
Almugadam et al.	2.182	1.137	4.187	0.019	7.26
Maori et al.	10.809	3.676	31.781	0.000	5.90
de Melo et al.	1.205	0.635	2.289	0.568	7.29
Bebia et al.	2.761	1.394	5.465	0.004	7.17
Overall OR	1.719	1.063	2.781	0.027	

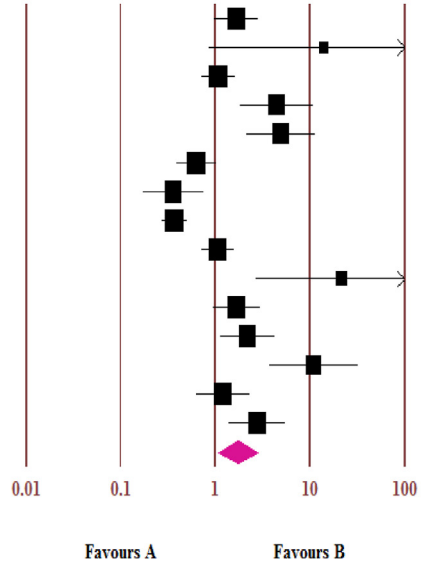

FIG. 3. Forest plot of odds ratios for the intestinal parasites in diabetic patients, based on case-control studies.

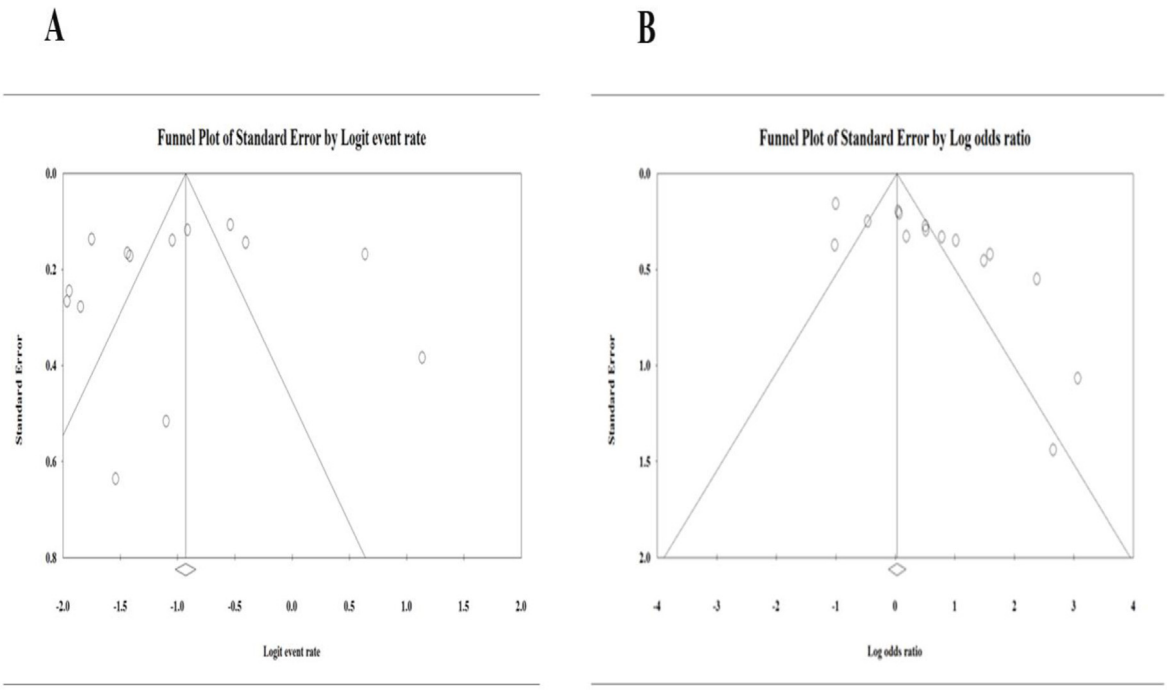

FIG. 4. Publication bias using funnel plots. (A) Publication bias in studies with cross-sectional design (B) Publication bias in studies with a case-control design.

countries. In this regard, the highest prevalence was related to the Region of the Americas and the Mexico country which is very remarkable. It is noteworthy that approximately 80% of people with diabetes living in low- and middle-income countries. Therefore, it is interesting to investigate the association of these two health problems in the mentioned area [56]. As we know, diabetes is classified into two main types. Type 1 diabetes is an autoimmune response in which the immune system attacks the insulin-producing cells in the pancreas; this type is also known as insulin-dependent diabetes mellitus. In type 2 diabetes, the body is unable to use the insulin produced and is not able to control blood sugar at normal levels. The incidence of type 1 and 2 diabetes rates are 5%–10% and 90%–95%, respectively [57]. Diabetes is thought to be a long-lasting, chronic complication that gradually causes dysfunction and malfunctions in the various organs as well as blood pressure; therefore, it makes a person susceptible to a wide range of diseases, especially infectious diseases [58].

IPs are responsible for disorders extending from self-limiting discomforts to serious danger condition like malnutrition, growth retardation, and anemia. As well, nearly 40 million worldwide disability-adjusted life years (DALYs) disabilities have been associated with diseases caused by IPs [51]. According to our search finding, the most isolated parasites were *Ascaris lumbercoides, Entamoeba species*, *Cryptosporidium* spp., *Giardia lamblia* and *Strongyloides stercoralis* in cross-sectional studies. The technique used to isolate parasites in most studies, was parasitological methods such as Formal-Ether sedimentation and staining methods. It should be noted that the sensitivity of microscopic detection is low and there is a possibility of missing parasites. Hence, the estimated prevalence represents the tip of the iceberg and the true prevalence may be much higher. In contrast to molecular methods, they have high sensitivity and specificity, in the four included studies, the prevalence was higher than the microscopic method (38.5% (95% CI: 17.1–65.4) *vs.* 24.9% (95% CI: 20.1–30.5). Several studies have examined a particular special parasite in diabetics. Majidiani et al. did not observe the significant association between *Toxoplasma gondii* and type 1 diabetes, but ex vivo studies are controversial [7]. However, the number of studies conducted on people with type 1 diabetes has been limited due to its nature and low prevalence. Nosaka et al. found a significant association between *Toxoplasma gondii* and type 2 diabetes (OR, 2.32; 95% CI 1.66–3.24, $P < 0.001$) they concluded that if *Toxoplasma gondii* was shown to be involved in chronic inflammation leading to diabetes, it should be considered as a factor in the early prognosis of diabetes [59] which was in line with the results of the present study. In accordance with the findings of the present study, this hypothesis can also be generalized to IPs; this means that IPs due to their high prevalence in diabetics can play a risk factor for diabetes. Significant heterogeneity can be due to differences in operators, the small number of studies, geographical areas as well as differences in applied methods sensitivity/specificity.

The limitations that this meta-analysis study has faced include 1) the small number of studies in this field, especially on a limited geographical scale, 2) Existence of different techniques for detecting parasites in diabetics who were not homogeneous in terms of sensitivity and specificity, 3) The orientation of some studies in the diagnosis of only one parasite and ignoring other parasitic organisms that were easily detectable, 4) The included studies had insignificant details of the demographic characteristics of the participants such as age, sex, type of diabetes status, etc.

Conclusion: The present meta-analysis study indicates a remarkable prevalence of IPs in diabetic individuals; the association between IPs and diabetes was found to be significant, therefore, the prevalence of IPs in diabetics should not be neglected. It is suggested that future studies with larger sample sizes and more details and Homogeneity of case and control group be designed.

Ethics approval and consent to participate

The study design including its ethical aspects was reviewed and approved by the Ethics Committee of Alborz University of Medical Sciences (IR.ABZUMS.REC.1399.230).

Consent to participate

Not applicable.

Consent to publish

All authors of this manuscript declare that we have seen and approved the submitted version of this manuscript.

Availability of data and materials

The data associated with this manuscript are included in the article.

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Declaration of competing interest

None.

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References

[1] Gizaw Z, et al. Childhood intestinal parasitic infection and sanitation predictors in rural Dembiya, northwest Ethiopia. Environ Health Prev Med 2018;23(1):26.

[2] Yemata G, et al. Prevalence of intestinal parasitic infections and associated factors among diarrheal outpatients in South gondar zone, Northwest, Ethiopia. 2020.

[3] Ramana K. Intestinal parasitic infections: an overview. Ann Trop Med Publ Health 2012;5(4):279.

[4] Machado ER, et al. Host-parasite interactions in individuals with type 1 and 2 diabetes result in higher frequency of Ascaris lumbricoides and Giardia lamblia in type 2 diabetic individuals. J Diabetes Res 2018;2018.

[5] De Ruiter K, et al. Helminths, hygiene hypothesis and type 2 diabetes. Parasite Immunol 2017;39(5):e12404.

[6] Zibaei M, et al. Human Toxocara infection: allergy and immune responses. Anti-Inflammatory Anti-Allergy Agents Med Chem 2019;18(2):82–90.

[7] Majidiani H, et al. Is chronic toxoplasmosis a risk factor for diabetes mellitus? A systematic review and meta-analysis of case-control studies. Braz J Infect Dis 2016;20(6):605–9.

[8] Zavala G, et al. Intestinal parasites: associations with intestinal and systemic inflammation. Parasite Immunol 2018;40(4):e12518.

[9] Hays R, et al. Does Strongyloides stercoralis infection protect against type 2 diabetes in humans? Evidence from Australian Aboriginal adults. Diabetes Res Clin Pract 2015;107(3):355–61.

[10] Khatami A, et al. Two rivals or colleagues in the liver? Hepatit B virus and Schistosoma mansoni co-infections: a systematic review and meta-analysis. Microb Pathog 2021;154:104828.

[11] Musselman DL, et al. Relationship of depression to diabetes types 1 and 2: epidemiology, biology, and treatment. Biol Psychiatr 2003;54(3):317–29.

[12] Federation I. IDF diabetes Atlas. eighth ed. 2017.

[13] Yagihashi S, Yamagishi S-I, Wada R. Pathology and pathogenetic mechanisms of diabetic neuropathy: correlation with clinical signs and symptoms. Diabetes Res Clin Pract 2007;77(3):S184–9.

[14] Petry CJ. Gestational diabetes: risk factors and recent advances in its genetics and treatment. Br J Nutr 2010;104(6):775–87.

[15] Group S-TDPS. Presence of diabetes risk factors in a large US eighth-grade cohort. Diabetes Care 2006;29(2):212–7.

[16] Vieira MN, Lima-Filho RA, De Felice FG. Connecting Alzheimer's disease to diabetes: underlying mechanisms and potential therapeutic targets. Neuropharmacology 2018;136:160–71.

[17] Casqueiro J, Casqueiro J, Alves C. Infections in patients with diabetes mellitus: a review of pathogenesis. Indian J Endocrinol Metabol 2012;16(Suppl1):S27.

[18] Jeon CY, et al. Helicobacter pylori infection is associated with an increased rate of diabetes. Diabetes Care 2012;35(3):520–5.

[19] Negro F, Alaei M. Hepatitis C virus and type 2 diabetes. World J Gastroenterol: WJG 2009;15(13):1537.

[20] Li Y-X, et al. Toxoplasma gondii infection in diabetes mellitus patients in China: seroprevalence, risk factors, and case-control studies. BioMed Res Int 2018;2018.

[21] Roth EJ, et al. The enzymes of the glycolytic pathway in erythrocytes infected with Plasmodium falciparum malaria parasites. 1988.

[22] Moher D, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev 2015;4(1):1.

[23] Tawfik GM, et al. A step by step guide for conducting a systematic review and meta-analysis with simulation data. Trop Med Health 2019;47(1):1–9.

[24] Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol 2010;25(9):603–5.

[25] Munn Z, et al. The development of software to support multiple systematic review types: the Joanna Briggs Institute system for the unified management, assessment and review of information (JBI SUMARI). JBI Evid Implement 2019;17(1):36–43.

[26] Egger M, Davey-Smith G, Altman D. Systematic reviews in health care: meta-analysis in context. John Wiley & Sons; 2008.

[27] Alemu G, Jemal A, Zerdo Z. Intestinal parasitosis and associated factors among diabetic patients attending Arba Minch Hospital, Southern Ethiopia. BMC Res Notes 2018;11(1):1–6.

[28] Ambachew S, et al. The prevalence of intestinal parasites and their associated factors among diabetes mellitus patients at the University of Gondar Referral Hospital, Northwest Ethiopia. J Parasitol Res 2020:2020.

[29] Engidaw MT, Feyisa MS. Prevalence of anemia and its associated factors among adult diabetes mellitus patients at Debre Tabor General Hospital, Northcentral Ethiopia. Diabetes, Metab Syndrome Obes Targets Ther 2020;13:5017.

[30] Sisu A, et al. Intestinal parasite infections in diabetes mellitus patients; A cross-sectional study of the Bolgatanga municipality, Ghana. Scientific African 2021;11:e00680.

[31] Baqai R, Anwar S, Kazmi S. Detection of Cryptosporidium in immunosuppressed patients. J Ayub Med Coll Abbottabad 2005;17(3).

[32] Ali OS, Mohammad SA, Salman YJ. Incidence of some intestinal parasites among diabetic patients suffering from gastroenteritis. Int J Curr Microbiol Appl Sci 2018;7(8):3695–708.

[33] hussein Al-Mousawi A, Neamah BAH. A study on intestinal parasites among diabetic patients in Najaf governorate of Iraq and its effect on some blood parameters. Iranian Journal of Ichthyology 2021;8:127–32.

[34] Younis E. Helicobacter pylori infections among patients with type 2 diabetes mellitus in Benghazi, Libya. J Gstro Hepato 2022;8:1–7.

[35] Calderón de la Barca AM, et al. Enteric parasitic infection disturbs bacterial structure in Mexican children with autoantibodies for type 1 diabetes and/or celiac disease. Gut Pathog 2020;12(1):1–9.

[36] Bora I, et al. Study of intestinal parasites among the immunosuppressed patients attending a tertiary-care center in Northeast India. Int J Med Sci Publ Health 2016;5(5):924–9.

[37] Chandi DH, Lakhani SJ. Prevalence of parasitic infestation in diabetic patients in tertiary care hospital. Int J Curr Microbiol Appl Sci 2020;9(2):1434–41.

[38] Popruk N, et al. Prevalence and subtype distribution of Blastocystis infection in patients with diabetes mellitus in Thailand. Int J Environ Res Publ Health 2020;17(23):8877.

[39] Htun NSN, et al. Association between helminth infections and diabetes mellitus in adults from the Lao People's Democratic Republic: a cross-sectional study. Infectious Dis Poverty 2018;7(1):1–11.

[40] Akhlaghi L, et al. Survey on the prevalence rates of intestinal parasites in diabetic patients in Karaj and Savodjbolagh cities. Razi J Med Sci 2005;12(45):23–9.

[41] Akinbo FO, et al. Intestinal parasitic infections among diabetes mellitus patients. Biomarkers Genom Med 2013;5(1–2):44–7.

[42] Fattahi Bafghi A, Afkhami-Ardekani M, Dehghani Tafti A. Frequency distribution of intestinal parasitic infections in diabetic patients–Yazd 2013. Iran J Diabetes Obes 2015;7(1):33–7.
[43] Elnadi NA, et al. Intestinal parasites in diabetic patients in Sohag University hospitals, Egypt. J Egypt Soc Parasitol 2015;45(2):443–9.
[44] Mohtashamipour M, et al. Intestinal parasitic infections in patients with diabetes mellitus: a case-control study. J Res Clin Med 2015;3(3): 157–63.
[45] Poorkhosravani Z, et al. Frequency of intestinal parasites in patients with diabetes mellitus compared with healthy controls in Fasa, Fars Province, Iran. 2018 Hormozgan Med J 2019;23(2). e91284-e91284.
[46] Tangi FB, et al. Intestinal parasites in diabetes mellitus patients in the Limbe and Buea municipalities, Cameroon. Diabetes Res Open J 2016;2(1):1–7.
[47] Nazligul Y, Sabuncu T, Ozbilge H. Is there a predisposition to intestinal parasitosis in diabetic patients? Diabetes Care 2001;24(8):1503–4.
[48] Rady HI, et al. Parasites and Helicobacter pylori in Egyptian children with or without diabetes with gastrointestinal manifestations and high calprotectin level. J Egypt Soc Parasitol 2019;49(1):243–8.
[49] Al-heety MS, Al-Ani SF, Jasem MA. Molecular and parasitological study on selected opportunistic intestinal parasites in immunocompromised patients. Indian J Forensic Med Toxicol 2020;14(4).
[50] Waly WR, et al. Intestinal parasitic infections and associated risk factors in diabetic patients: a case-control study. J Parasit Dis 2021;45(4): 1106–13.
[51] Almugadam BS, et al. Association of urogenital and intestinal parasitic infections with type 2 diabetes individuals: a comparative study. BMC Infect Dis 2021;21(1):1–9.
[52] Maori L, et al. Intestinal parasitic infections among diabetes mellitus patients attending murtala Muhammad specialist hospital (Mmsh), Kano, Kano state. South Asian J Parasitol 2021:6–14.
[53] Melo GBd, et al. Blastocystis subtypes in patients with diabetes mellitus from the Midwest region of Brazil, 63. Revista do Instituto de Medicina Tropical de São Paulo; 2021.
[54] Bebia GP, et al. Prevalence of malaria and intestinal parasitic Co-infection among diabetic patients in Calabar. Global J Pure Appl Sci 2022;28(2):193–200.
[55] Alum A, Rubino JR, Ijaz MK. The global war against intestinal parasites—should we use a holistic approach? Int J Infect Dis 2010;14(9): e732–8.
[56] Forouhi NG, Wareham NJ. Epidemiology of diabetes. Medicine 2010;38(11):602–6.
[57] de Ornelas Maia ACC, et al. Prevalence of psychiatric disorders in patients with diabetes types 1 and 2. Compr Psychiatr 2012;53(8): 1169–73.
[58] Lilliu MA, et al. Diabetes causes morphological changes in human submandibular gland: a morphometric study. J Oral Pathol Med 2015;44(4):291–5.
[59] Nosaka K, Hunter M, Wang W. The association between Toxoplasma gondii and type 2 diabetes mellitus: a systematic review and meta-analysis of human case-control studies. Bull Natl Res Cent 2020;44(1):1–9.