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THERAPEUTIC ADVANCES in
Infectious Disease

Original Research

The global prevalence of human fascioliasis: a systematic review and meta-analysis

Ther Adv Infect Dis

2023, Vol. 10: 1–18

DOI: 10.1177/20499361231185413

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Abstract

Background: Fascioliasis is a parasitic zoonosis that can infect humans and be a source of significant morbidity. The World Health Organization lists human fascioliasis as a neglected tropical disease, but the worldwide prevalence of fascioliasis data is unknown.

Objective: We aimed to estimate the global prevalence of human fascioliasis.

Data sources and methods: We performed a systematic review and prevalence meta-analysis. We used the following inclusion criteria: articles published in the English, Portuguese, or Spanish languages from December 1985 to October 2022 and studies assessing the prevalence of *Fasciola* in the general population with an appropriate diagnostic methodology, including longitudinal studies, prospective and retrospective cohorts, case series, and randomized clinical trials (RCTs). We excluded animal studies. Two reviewers independently reviewed the selected studies for methodological quality, performing critical standard measures from JBI SUMARI. A random-effects model was conducted of the summary extracted data on the prevalence proportions. We reported the estimates according to the GATHER statement.

Results: In all, 5617 studies were screened for eligibility. Fifty-five studies from 15 countries were selected, including 154,697 patients and 3987 cases. The meta-analysis revealed a pooled prevalence of 4.5% [95% confidence interval (CI): 3.1–6.1; $I^2 = 99.4\%$; $T^2 = 0.07$]. The prevalence in South America, Africa, and Asia was 9.0%, 4.8%, and 2.0%, respectively. The highest prevalence was found in Bolivia (21%), Peru (11%), and Egypt (6%). Subgroup analysis showed higher prevalence estimates in children, in studies from South America, and when Fas2-enzyme-linked immunosorbent assay (ELISA) was used as a diagnostic method. A larger study sample size ($p = 0.027$) and an increase in female percentage ($p = 0.043$) correlated with a decrease in prevalence. Multiple meta-regression showed a higher prevalence for hyperendemic than hypoendemic ($p = 0.002$) or mesoendemic ($p = 0.013$) regions.

Conclusion: The estimated prevalence and projected disease burden of human fascioliasis are high. Study findings support that fascioliasis continues to be a globally neglected tropical disease. Strengthening epidemiological surveillance and implementing measures to control and treat fascioliasis is imperative in the most affected areas.

Keywords: epidemiology, *F. gigantica*, *F. hepatica*, human fascioliasis, meta-analysis, neglected tropical disease, prevalence, systematic review

Received: 6 March 2023; revised manuscript accepted: 14 June 2023.

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Introduction

Fascioliasis is an emerging global parasitic disease caused by *Fasciola hepatica* and *F. gigantica*. *Fasciola* spp. have a complex life cycle that involves intermediate aquatic gastropod hosts and definitive mammalian hosts such as humans.[1] Eating habits are the most significant risk factor of infection by *Fasciola* spp., with the consumption of wild watercress contaminated with infective metacercariae being the most reported source of infection. Likewise, studies in the highlands of Peru indicate that drinking untreated water is associated with a higher risk of *Fasciola* spp. infection.[2,3]

Fascioliasis significantly impacts the livestock industry, with wild ruminant reservoirs as a source of disease introduction. Between 10% and 80% of cattle are infected globally.[2] Livestock production losses and increased associated treatment costs contribute to lowered meat, milk, and wool production and a predisposition for peracute mortality caused by *Clostridium noyvi*. Worldwide studies have reported losses of up to millions of US dollars annually.[4,5] These losses perpetuate poverty and deny smallholder farmers much-needed income and subsistence.[6]

Human fascioliasis has been a public health concern for the last three decades, prompting the World Health Organization's (WHO) declaration as a neglected tropical disease.[7,8] Fascioliasis is asymptomatic in most patients, but right upper quadrant discomfort and anorexia can occur. It is associated with anemia and weight loss in children, who are especially vulnerable to devastating long-term complications, such as delayed growth and poor neurocognitive development.[2,9] In addition, the disease is estimated to incur 90,000 disability-adjusted life years (DALYs) due to associated abdominal symptoms such as nausea, vomiting, diarrhea, and pain.[10] Infestation has also been associated with liver fibrosis in humans and animals.[11,12] The complications following *Fasciola* infections may include acute cholecystitis, biliary obstruction, and liver abscesses, often requiring abdominal surgeries.[13]

The number of humans infected by *Fasciola* spp. in 1998 increased in 51 countries on 5 continents, with 7071 reported human cases.[14] In 2012, the estimated number was 2.6 million cases reported in 81 countries worldwide. The prevalence varies by continent, but the highest has been reported in the Andes region of Latin America.[9]

Human fascioliasis may be emerging due to more favorable wet weather for fluke egg survival due to climate change. There is a gap in knowledge about the global status of this neglected parasitic disease. Current studies are mainly limited to the regional level, but cost-effective serological tests are lacking in the most affected areas.[15–17] There is an urgent need for assessments of disease burden to monitor the prevalence dynamics of human fascioliasis to promote stakeholders' engagement in implementing effective public health programs aimed at disease prevention. Given changes in climate and food habits that could increase the presence of intermediate hosts and suitable conditions for their growth, it is essential to assess changes to fascioliasis human cases worldwide. This study aims to perform a systematic review and meta-analysis to estimate the global prevalence of human fascioliasis and examine prevalence variation by demographic and clinical characteristics.

Methods

Search strategy

The Joanna Briggs Institute (JBI) methodology for systematic reviews and meta-analysis with a three-phase search strategy was utilized.[18] Initial keywords were identified, database-specific search filters were constructed, and the included studies' reference list was searched. We considered articles published in English, Portuguese, or Spanish from December 1985 to October 2022. Results of a web of science core collection search of the topic field "Fascioliasis" listed by language revealed that 95% of entries were in English, Portuguese, or Spanish (supplementary material). An initial comprehensive literature search was conducted in May 2022 by a Medical Librarian, with an update on October 2022. The following databases were searched: MEDLINE, Web of Science Core, Scopus, Cochrane Library, SciELO, Crossref, LILACS, and Google Scholar. Relevant publications were identified by a search strategy using a combination of keywords related to fascioliasis in humans were used, such as "Fascioliasis,", "*F. hepatica*,", "*F. gigantica*," "helminthiasis,", "liver fluke," "Fasciola," "prevalence,", "seroprevalence." See detailed

MEDLINE search strategy (supplementary material). Search terms included Fasciola AND Prevalence, excluding animal studies. This review considered longitudinal studies, prospective and retrospective cohorts, case series, and randomized clinical trials (RCTs). Filters were used to limit results to human studies. A search for additional research and the manual addition of other significant papers in the field was done on the reference list of every study chosen.

Study selection

After the systematic search, all registered articles were uploaded to "ProQuest RefWorks" (Ann Arbor, Michigan, USA), where duplicate reports were removed. Then, a screening of the title and abstract was carried out, which were reviewed by two authors, while a third one resolved the differences. Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia) was used for screening and full-text review. Through Covidence, a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram was generated with the number of results found, the number excluded during title/abstract screening, and the number excluded during full-text assessments and methodological appraisals, along with reasons for exclusion. We reported the estimates according to the GATHER statement.[19]

Eligibility criteria

We included studies with evidence of endemicity data for *F. hepatica* or *F. gigantica* reported worldwide in the general population (Table 1). We assessed each study for an adequate estimated population size,[20] appropriate serological and coprological diagnostic methodology, and availability of prevalence data. We excluded studies of participants with comorbidities or significant risk factors that may alter the course of the disease, such as relatives diagnosed with the disease, significant eosinophilia, occupational exposure, or who have been previously diagnosed with fascioliasis, and also those that did not provide enough pertinent outcome data or were determined not to have an acceptable quality methodologic assessment. We also excluded any gray literature or expert opinion data due to the absence of a peer-reviewed quality evaluation.

Table 1. Eligibility criteria per the POS criterion.

Criterion	Definition
Population	We included studies with evidence of endemicity data for *F. hepatica* or *F. gigantica* reported worldwide in the general population.
Outcome	Prevalence, number of positive samples divided by the total number of patients assessed on each study expressed as a percentage
Study	Full text primary studies published in English, Spanish or Portuguese in eligible Databases from December 1985 to October 2022

Data analysis

Study data were collected and managed using Microsoft Excel 2020 electronic data capture tools. We performed data visualization and quality control in GraphPad (version 9.4.1 for Windows, GraphPad Software, San Diego, California, USA). Extracted data included the year of the study, type of study, country/continent of origin, duration of the study, number of infected patients, number of participants, length of follow-up, population demographics, diagnostic technique (Fas2-enzyme-linked immunosorbent assay [ELISA], microscopy on stool samples and antibody ELISA test), type of infection (symptomatic, asymptomatic or both), and kind of endemicity of the area studied. Endemicity was defined by the percentage of the arithmetic mean intensity of eggs per gram of feces (EPG). Hypoendemic if the prevalence is less than 1%, mesoendemic region if the prevalence is between 1% and 10% (50–300 EPG), and hyperendemic area if prevalence >10% (>300 EPG).[21] If a study reported stool microscopy and serology, we extracted numbers for serology only, the most sensitive methodology. The primary outcome was the prevalence.

Quality assessment

Two reviewers independently reviewed the selected studies for methodological quality, performing quality critical standard measures from the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI; Joanna Briggs Institute, Adelaide, Australia). A third independent reviewer resolved assessment differences between the two reviewers.

Critical appraisals were performed utilizing the JBI Reviewer's Manual checklists for longitudinal studies. All studies with greater than 60% of "yes" answers to the essential appraisal questions were subject to data extraction and synthesis per JBI guidelines. The risk of bias was assessed using the QUIPS tool.[22]

Statistical analysis

The prevalence proportion was calculated by dividing the cases of Fasciola in each study by the total number of participants. We computed each study's Freeman–Tukey double-arcsine-transformed proportion to obtain the effect sizes using the meta-analysis of prevalence package.[23,24] Confidence intervals for individual studies were calculated with the exact or the score (Wilson) method. A random-effects model was performed in the meta-analysis as prevalence and estimated effect sizes are expected to change between different studied populations.

To calculate the heterogeneity and variability of the meta-analysis, we estimated the I^2 statistic and the τ^2 coefficient. We established a heterogeneity of $\geqslant$75% as considerable heterogeneity based on the Cochrane Handbook for Systematic Reviews of Interventions. The studies were analyzed by subgroups: type of study, age group, symptomatology, the decade in which the study was carried out, country, continent, female percentage, study population size, diagnostic method, endemicity, and study duration. The pooled effect was recalculated after excluding one study from the analysis and repeating this single-study exclusion for each study.

The variables associated with the pooled prevalence ($p < 0.05$) and continuous explanatory variables (study population size, study year, and percentage of women) were included in a random-effects multi meta-regression analysis. In addition, Egger's regression test and a Galbraith plot were performed to generate a funnel plot that assesses publication bias and the existence of minor study effects. A p-value < 0.05 for the Egger test was considered significant for possible publication bias. Statistical analysis was performed using the STATA software program, version 18.0 (StataCorp, College Station, Texas, USA).

Results

Study population and characteristics

We initially identified 5617 studies. After deduplication, 740 studies were screened for eligibility based on titles and abstracts. Of these, 171 full-text articles were assessed, of which four were excluded due to lack of accessibility to the full text. The remaining 167 studies were thoroughly evaluated, considering the inclusion and exclusion criteria. They were also subjected to quality assessment using the JBI Critical Appraisal tool. We manually included 5 studies and excluded 117 for different reasons (Figure 1). A total of 55 articles were eligible. Among them, 52 cross-sectional studies, 2 retrospectives, and 1 clinical trial, composed of 154,697 patients and 3987 cases of fascioliasis, were utilized for the meta-analysis (Figure 1).

Of the 55 studies, most were cross-sectional seroprevalence from South America and Asia and enrolled patients between 1990 and 2019. Studies sample sizes varied from 42 to 69,633 patients, with a mean of 2,812 participants per study. Fascioliasis cases per study ranged from 1 to 932, with a mean of 73 cases per study. Gender distribution had a slight female predominance at 57.7% (44 studies). Twenty-six (47%) studies included information from patients between 0 and 17 years old. The prevalence of human fascioliasis ranged from 0.03% to 32.5% (Table 2). A few studies had missing data for demographic data. The mean follow-up study duration was 1.8 years, ranging from 1 to 11 years.

We found a pooled estimated prevalence of 4.5% [95% confidence interval (CI): 3.1–6.1; $I^2 = 99.4\%$; $T^2 = 0.07$] (Figure 2). The I^2 variable suggested significant heterogeneity among these studies, as well as the τ^2, which represents the variability of the prevalence of each study.

The final dataset included data from 16 countries, with generally only a few studies from each represented country (Figure 3). More studies were included from Peru (12) and Iran (13) than other countries. The prevalence in South America, Africa, and Asia was 9.0%, 4.7%, and 2.0%, respectively. (Table 3, Supplementary material Figures 1 S and 2 S). The highest prevalence was

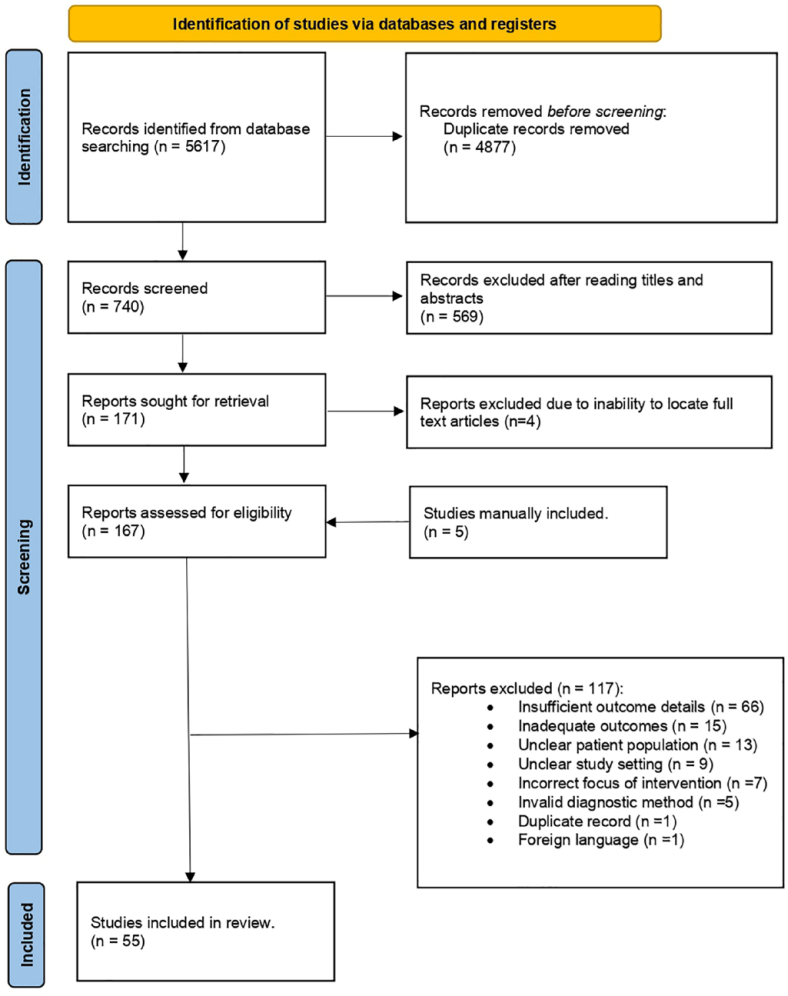


Figure 1. PRISMA flow diagram.

found in Bolivia (21%), Peru (11%), and Egypt (6%) (Figure 3, Heat map).

Subgroup analysis

We performed a subgroup analysis to explore the high heterogeneity. The subgroup was separated by decades from 1985 to 1994, 1995 to 2004, 2005 to 2014, and 2015 to 2021. Older decades had higher prevalences but were not statistically significant (Table 3, Figure 3 S). Across age groups, the prevalence was higher and statistically different in patients younger than 18 years compared with those 18 years or older and of mixed ages (Table 3, Figure 4 S). Prevalence was also higher when Fas2-ELISA was used as a diagnostic tool compared with microscopy stool study or antibody ELISA test (Table 3, Figure 5 S). When comparing the results by endemicity of the place where the study was conducted, a significantly higher prevalence was found in hyperendemic areas compared to hypoendemic and mesoendemic (Table 3, Figure 6 S). We did not find differences in prevalence when comparing according to the type of study, symptomatic status, or study duration (Supplemental Figures 7S–9S). A larger study sample size ($p = 0.027$) and an increase in female percentage ($p = 0.043$) correlated with a decrease in prevalence.

Multiple meta-regression

Prevalence was higher for hyperendemic than hypoendemic ($p = 0.002$) or mesoendemic ($p = 0.013$). Estimated differences on the scale of the Freeman-Tukey double arcsin transform were

Table 2. Studies characteristics and *Fasciola* prevalence.

Study	Study type	Study size (*n*)	Cases (*n*)	Study duration (years)	Prevalence %, (CI 95%)	Age	Symptoms	Diagnostic method	Country
Abdi *et al.*[25]	Cross-sectional	600	4	1	0.7 (0.3–1.7)	18–60 years old	Asymptomatic	ELISA	Iran
Abo-Madyan *et al.*[26]	Clinical trial	1019	17	2	1.7 (1–2.7)	Mixed ages	Mixed	Stool microscopy	Egypt
Afshan *et al.*[27]	Cross-sectional	546	130	1	23.8 (20.4–27.6)	Mixed ages	Mixed	ELISA	Pakistan
Aguiar *et al.*[28]	Cross-sectional	558	11	1	2 (1.1–3.5)	0–17 years old	Mixed	Stool microscopy	Brazil
Apt *et al.*[29]	Cross-sectional	5861	41	4	0.7 (0.5–0.9)	Mixed ages	Asymptomatic	ELISA	Chile
Asadian *et al.*[30]	Cross-sectional	458	9	1	2 (1–3.7)	Mixed ages	Mixed	ELISA	Iran
Ashrafi *et al.*[31]	Cross-sectional	1984	30	3	1.5 (1.1–2.2)	Mixed ages	Mixed	ELISA	Iran
Bahram *et al.*[32]	Cross-sectional	612	11	1	1.8 (1–3.2)	Mixed ages	—	ELISA	Iran
Bekana *et al.*[33]	Cross-sectional	798	44	1	5.5 (4.1–7.3)	0–17 years old	Mixed	Stool microscopy	Ethiopia
Beyhan *et al.*[34]	Cross-sectional	817	45	8	5.5 (4.1–7.3)	Mixed ages	Mixed	ELISA	Turkey
Bless *et al.*[35]	Cross-sectional	221	1	1	0.5 (0.1–2.5)	0–17 years old	Symptomatic	ELISA	Cambodia
Bozorgomid *et al.*[36]	Cross-sectional	975	5	3	0.5 (0.2–1.2)	18–60 years old	Mixed	ELISA	Iran
Cabada *et al.*[37]	Cross-sectional	2515	253	5	10.1 (8.9–11.3)	0–17 years old	Mixed	Fas2-ELISAlisa	Peru
Cabada *et al.*[38]	Cross-sectional	227	22	1	9.7 (6.5–14.2)	0–17 years old	Mixed	Stool microscopy	Peru
Carnevale *et al.*[39]	Cross-sectional	42	5	1	11.9 (5.2–25)	18–60 years old	Symptomatic	ELISA	Argentina
Cengiz *et al.*[40]	Cross-sectional	1600	89	2	5.6 (4.5–6.8)	Mixed ages	Mixed	ELISA	Turkey
Curtale *et al.*[41]	Cross-sectional	1783	54	1	3 (2.3–3.9)	0–17 years old	Mixed	Stool microscopy	Egypt
Curtale *et al.*[42]	Cross-sectional	21,477	932	4	4.3 (4.1–4.6)	0–17 years old	Mixed	Stool microscopy	Egypt
Curtale *et al.*[43]	Cross-sectional	1331	72	1	5.4 (4.3–6.8)	Mixed ages	Asymptomatic	Stool microscopy	Egypt
Davoodi *et al.*[44]	Cross-sectional	2418	60	2	2.5 (1.9–3.2)	Mixed ages	Mixed	ELISA	Iran
Eshrati *et al.*[45]	Cross-sectional	1053	28	1	2.7 (1.8–3.8)	Mixed ages	Mixed	ELISA	Iran
Esteban *et al.*[21]	Cross-sectional	2723	419	6	15.4 (14.1–16.8)	0–17 years old	Mixed	Stool microscopy	Bolivia
Esteban *et al.*[46]	Cross-sectional	558	154	1	27.6 (24.1–31.5)	0–17 years old	Symptomatic	Stool microscopy	Bolivia
Esteban *et al.*[47]	Cross-sectional	338	82	1	24.3 (20–29.1)	0–17 years old	Mixed	Stool microscopy	Peru
Esteban *et al.*[48]	Cross-sectional	678	87	1	12.8 (10.5–15.6)	Mixed ages	Mixed	Stool microscopy	Egypt
Fentie *et al.*[49]	Cross-sectional	520	17	1	3.3 (2.1–5.2)	0–17 years old	Mixed	Stool microscopy	Ethiopia
Gonzalez *et al.*[50]	Cross-sectional	476	116	1	24.4 (20.7–28.4)	0–17 years old	Mixed	Stool microscopy	Peru
Hassan *et al.*[51]	Cross-sectional	1350	147	1	10.9 (9.3–12.7)	0–17 years old	Mixed	ELISA	Egypt

(Continued)

Table 2. (Continued)

Study	Study type	Study size (*n*)	Cases (*n*)	Study duration (years)	Prevalence %, (CI 95%)	Age	Symptoms	Diagnostic method	Country
Heydarian *et al.*[52]	Cross-sectional	1256	16	1	1.3 (0.8–2.1)	Mixed ages	–	ELISA	Iran
Hosseini *et al.*[53]	Cross-sectional	1025	2	1	0.2 (0.1–0.7)	Mixed ages	Symptomatic	ELISA	Iran
Kaya *et al.*[54]	Cross-sectional	586	26	1	4.4 (3–6.4)	18–60 years old	Mixed	ELISA	Turkey
Kheirandish *et al.*[55]	Cross-sectional	801	6	1	0.7 (0.3–1.6)	Mixed ages	Asymptomatic	ELISA	Iran
Lopez *et al.*[56]	Cross-sectional	223	23	1	10.3 (7–15)	0–17 years old	Asymptomatic	Stool microscopy	Peru
Maciel *et al.*[57]	Cross-sectional	434	36	1	8.3 (6.1–11.3)	Mixed ages	Mixed	ELISA	Brazil
Manouchehri *et al.*[58]	Cross-sectional	1475	2	3	0.1 (0–0.5)	>60 years old	Mixed	ELISA	Iran
Manrique *et al.*[59]	Cross-sectional	507	2	1	0.4 (0.1–1.4)	0–17 years old	Mixed	Stool microscopy	Colombia
Mantari *et al.*[60]	Cross-sectional	312	16	1	5.1 (3.2–8.2)	0–17 years old	Mixed	Stool microscopy	Peru
Marcos *et al.*[61]	Cross-sectional	157	51	1	32.5 (25.7–40.2)	0–17 years old	Mixed	Fas2-ELISAlisa	Peru
Marcos *et al.*[62]	Cross-sectional	291	25	1	8.6 (5.9–12.4)	0–17 years old	Mixed	Stool microscopy	Peru
Natividad *et al.*[63]	Cross-sectional	132	4	1	3 (1.2–7.5)	Mixed ages	Mixed	Stool microscopy	Peru
Nguyen *et al.*[64]	Retrospective	10,084	590	1	5.9 (5.4–6.3)	Mixed ages	Mixed	ELISA	Vietnam
Nxsana *et al.*[65]	Cross-sectional	162	1	1	0.6 (0.1–3.4)	0–17 years old	Asymptomatic	Stool microscopy	South Africa
Özturhan *et al.*[66]	Cross-sectional	884	7	1	0.8 (0.4–1.6)	Mixed ages	Mixed	ELISA	Turkey
Qureshi *et al.*[67]	Cross-sectional	540	4	1	0.7 (0.3–1.9)	0–17 years old	Mixed	Stool microscopy	Pakistan
Qureshi *et al.*[68]	Cross-sectional	7200	85	2	1.2 (1–1.5)	Mixed ages	Asymptomatic	Stool microscopy	Pakistan
Rodríguez *et al.*[69]	Cross-sectional	253	13	1	5.1 (3–8.6)	0–17 years old	Mixed	Stool microscopy	Peru
Rodríguez *et al.*[70]	Cross-sectional	270	17	1	6.3 (4–9.9)	0–17 years old	Mixed	Stool microscopy	Peru
Saberinasab *et al.*[71]	Cross-sectional	471	8	1	1.7 (0.9–3.3)	Mixed ages	Mixed	ELISA	Iran
Steinmann *et al.*[72]	Cross-sectional	1262	24	1	1.9 (1.3–2.8)	0–17 years old	Mixed	Stool microscopy	Kyrgyzstan
Taş Cengiz *et al.*[73]	Retrospective	69,633	25	11	0 (0–0.1)	Mixed ages	Mixed	ELISA	Turkey
Valencia *et al.*[74]	Cross-sectional	842	33	1	3.9 (2.8–5.5)	0–17 years old	Mixed	Fas2-ELISAlisa	Peru
Wilches *et al.*[75]	Cross-sectional	61	3	1	4.9 (1.7–13.5)	Mixed ages	Mixed	ELISA	Colombia
Yilmaz and Godekmerdan[76]	Cross-sectional	500	9	1	1.8 (0.9–3.4)	0–17 years old	Asymptomatic	ELISA	Turkey
Zoghi *et al.*[77]	Cross-sectional	933	24	1	2.6 (1.7–3.8)	Mixed ages	Mixed	ELISA	Iran
Zumaquero *et al.*[78]	Cross-sectional	865	50	1	5.8 (4.4–7.5)	0–17 years old	Symptomatic	ELISA	Mexico

CI, confidence interval; ELISA, enzyme-linked immunosorbent assay.

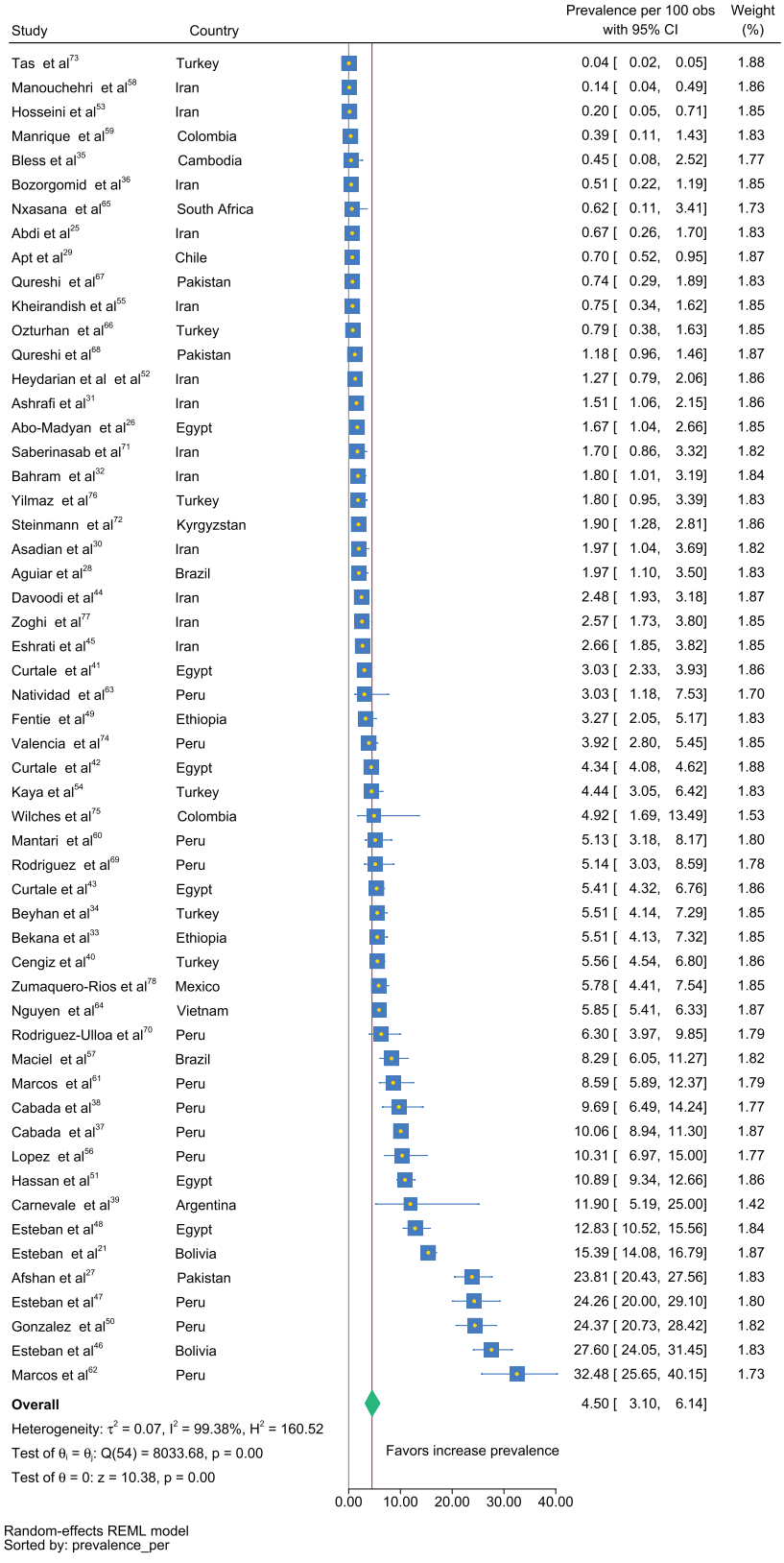


Figure 2. Forest plot of global estimated prevalence of fascioliasis by study.

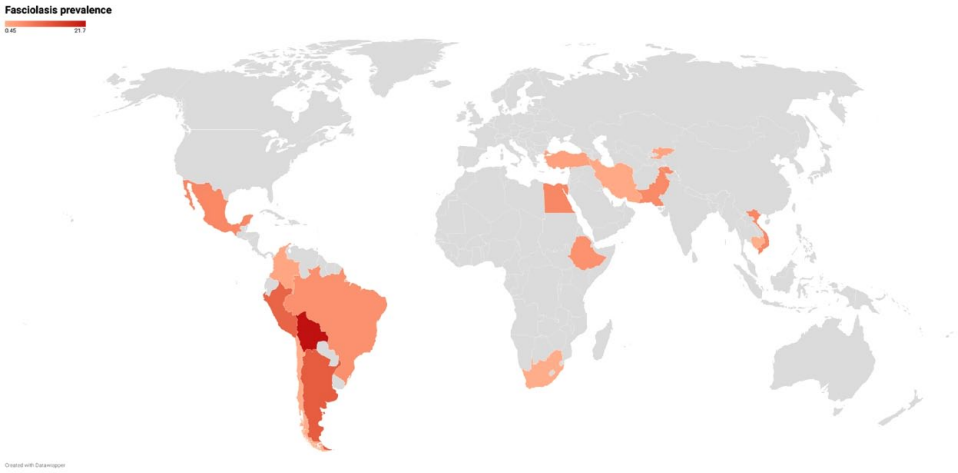


Figure 3. Heat map of unique datasets from each country depicting the prevalence of fascioliasis.

0.536 (95% CI: 0.208, 0.865) and 0.344 (0.077, 0.610), respectively.

Sensitivity analysis

Sensitivity analysis of the 55 studies (after excluding each study) did not significantly change the overall prevalence. There was also no significant change in heterogeneity. Furthermore, prevalence effect sizes did not vary after decreasing the variance to 0.25. The rates declined to 2.5%, assuming an I^2 of 10%. The Egger test showed a *p*-value of 0.03. A funnel plot for publication bias indicated asymmetry on the right side of the graph, and more studies are found in the upper part, suggesting possible publication bias (Figure 10 S). Galbraith plot showed a cluster of studies close to the Y axis, suggesting low precision for them (supplementary material Figure 11 S). Our assessment of the certainty of the estimated prevalence is low, based on the limited geographic studies included, the potential publication bias, and the high heterogeneity. The actual effect may be substantially different from the estimated effect.

Discussion

Our systematic review found a prevalence of global fascioliasis of 4.5%. However, most studies came from Iran and Peru; ELISA testing could have detected prior resolved infections, and included studies could have sampled populations already at risk. The variable most strongly associated with increased prevalence was a known area of hyperendemicity, suggesting some studies targeted at-risk populations. The current burden estimate of infected patients is unclear, but nearly 50 million people represent 4.5% of the population of countries reporting prevalence for this study.[79]

Human fascioliasis is an emerging zoonosis due to the increased reported cases in non-endemic countries. The global prevalence of this disease was unknown.[1,80] Global estimates performed in 2012 found a much higher estimated prevalence of fascioliasis of 14%, mainly using expert opinion studies.[81] In the early 1990s, 2594 cases were reported in approximately 42 countries—the WHO estimated about 2.4 million infected people worldwide after surveying experts. Currently, about 2.6 to 17 million people with fascioliasis are estimated worldwide. However, these estimates used outdated reports.[9,80,82] Conversely, some experts argued that an increase in diagnosis artificially drives the emergence observed.

We found a decreasing trend in the fascioliasis prevalence from 1985 to 1994 through 2015 to 2021. In 2006, a plan for epidemiological surveillance, control, and treatment was launched by the WHO.[83] The WHO promoted a mass drug administration of triclabendazole to decrease the human prevalence of fascioliasis in high-burden countries such as Bolivia, Egypt, Peru, and Vietnam. In two districts of Bolivia, a significant reduction in prevalence was observed, being 26.9% and 12.6% in 1999 to only 0.7% and 1% in 2017, respectively.[84] Also, in Egypt, a decrease

Table 3. Subgroup analysis of Fasciola prevalence.

Characteristic	Studies (n)	Prevalence (%)	95% CI	I^2	*p*-value
Type of study				99.4%	0.431
Retrospective	2	1.7	0.0–0.12		
Cross-sectional	52	4.7	3.2–6.4		
Age groups				99.4%	0.049
0–17 years old	26	6.8	4.2–10.0		
18–60 years old	4	2.6	0.0–7.8		
Mixed ages	24	3.0	1.7–4.7		
Symptoms				99.4%	0.058
Symptomatic	5	6.2	0.2–18.1		
Asymptomatic	8	2.0	0.6–4.1		
Mixed	40	5.1	3.4–7.2		
Decade				99.4%	0.148
1985–1994	2	9.8	0.0–49.3		
1995–2004	12	8.3	4.2–13.5		
2005–2014	28	3.2	1.9–4.9		
2015–2021	13	3.7	1.6–6.8		
Country[a]				99.4%	<0.0001
Bolivia	2	21.1	10.5–34.2		
Peru	12	10.7	6.3–15.9		
Egypt	6	5.7	2.8–9.6		
Pakistan	3	5.4	0.0–23.3		
Brazil	2	4.6	0.4–12.7		
Ethiopia	2	4.4	2.5–6.8		
Turkey	6	2.4	0.6–5.1		
Colombia	2	1.6	0.0–8.9		
Iran	13	1.2	0.8–1.8		
Continent				99.4%	<0.0001
South America	20	9.0	5.5–13.2		
Asia	25	2.0	1.1–3.2		
Africa	9	4.7	2.6–7.5		

(Continued)

Table 3. (Continued)

Characteristic	Studies (n)	Prevalence (%)	95% CI	I^2	*p*-value
Diagnostic method				99.4%	0.022
ELISA	28	2.7	1.5–4.2		
Fas2-ELISA	3	13.3	1.8–32.6		
Stool Microscopy	24	6.1	3.7–9.0		
Endemicity				99.4%	0.0002
Hypoendemic	6	1.0	0.4–1.8		
Mesoendemic	37	3.6	2.4–5.0		
Hyperendemic	11	12.0	6.3–19.2		
Study duration				99.4%	0.524
⩽1 year	42	4.8	3.2–6.7		
>1 year	13	3.7	1.3–7.3		

CI, confidence interval; ELISA, enzyme-linked immunosorbent assay.
[a]Including countries with at least 2 studies.

in prevalence was observed from 1998 to 2002, from 5.6% to 1.2%, respectively.[85] A recent systematic review from Pakistan, including two studies, found a prevalence of 0.3% among humans.[86] The availability of livestock and human antiparasitic treatment can potentially affect or decrease the disease prevalence. However, a surge of new cases is expected since the intermediate host (*Lymmnae* spp.) and untreated animals, particularly wildlife species, continue to contaminate the environment with fluke eggs and cercariae, not to mention the emergent problem of triclabendazole-resistant fascioliasis in both humans and animals (the only drug effective against Fasciola).[12]

Our results suggest the prevalence of fascioliasis is high. However, the number of infected people could still be higher since only a few prevalence studies are available, especially in the most affected areas.[87] Furthermore, the population studied in hyperendemic regions is relatively small and commonly has school-age population groups. Since fascioliasis is not a notifiable disease, its prevalence in many countries is unavailable. Also, the prevalence in endemic areas is heterogeneous, with local prevalence as high as 62%. In contrast, close-proximity regions may have a prevalence as low as 0%.[21] Therefore, further well-powered epidemiological surveillance studies are needed to estimate the number of infected individuals per region and globally.[80]

In all, 81 countries have reported the presence of fascioliasis. The most affected regions are South America and Africa; however, no country is free of *Fasciola* spp. infection.[88] In our analysis, the prevalence of only 16 nations was available, far lower than the actual number of affected countries, reflecting the pronounced lack of epidemiological and clinical data. We found a high prevalence in Bolivia (21%), Peru (10.7%), and Egypt (5.7%). In South America, a global prevalence reached 15.4% in 24 communities. Peru, one of the countries with the highest prevalence, reported numbers up to 24.3% in 3 communities, classified as hyperendemic areas.[89,90]

We found the highest prevalence in South America and Africa. These results are within the range reported by other systematic reviews, such as in Africa, with prevalence studies ranging from 0.29% to 19.3%. In South America, previous reports indicated a high prevalence ranging from

15% to 66% annually.[91,92] Fascioliasis predominantly affects impoverished human populations lacking essential resources and infrastructure, such as deficient health systems.[93]

We found a higher prevalence when using the Fas2 ELISA than ELISA and coprological methods. Coprological methods (microscopic visualization of eggs in the stool) are the most commonly used techniques for diagnosing fascioliasis since they are more accessible in hyperendemic areas with lower technological input required. Among these methods, the WHO recommends using the Kato-Katz technique in regions of high prevalence; however, the Lumbreras rapid sedimentation test has a higher sensitivity than other methods.[83] Nonetheless, these techniques are limited by the stage of the disease, being more sensitive during chronic infection, given a long pre-patent period of many months before egg production in feces. Coprological studies are often misused during the early stages of disease—often asymptomatic and with very low to no egg production. As a result, coprological tests have lower sensitivity during this stage, raising concerns about an increase in false negative rates in asymptomatic patients.[94] Due to its higher positive predictive value, the Fas2 ELISA could be considered the method of choice for large-scale prevalence screening tests.[2,16] However, the MM3 coproantigen and serological CL-1 ELISA test are commercially available with an increased performance.[95,96]

We found an increased prevalence of fascioliasis with a decreased percentage of women. A study from Egypt observed a higher prevalence in women than men, with 5.1% and 3.6%, respectively, while a study in Peru found no gender differences.[42,50]

In most prevalence studies, children are the most predominant group infected, which peaks between 9 and 11 years.[1] Similarly, we found that children aged 0 and 17 years had a higher prevalence compared to the groups of 18 and 60 years. The higher prevalence of fascioliasis in children could be due to their habit of placing aquatic plants in their mouths, lack of hygiene, and proximity to rivers and drains.[93,97] Although not statistically significant, we also found a higher prevalence among symptomatic subjects, who may not seek medical attention until biliary complications occur.

Finally, our systematic review suggests more people have been infected by fascioliasis than previously reported. These results concern public health since fascioliasis is not considered a fatal disease but rather a disabling one, like most neglected tropical diseases. WHO calculated 90,041 DALYs and a global loss of 3.2 billion dollars annually in animal production.[98,99] We expect an increase in global disease burden given associations with climate change, ecotourism, exports, agriculture, sociocultural factors, and eating habits. Additional funding and epidemiological studies are needed to specify regional disease burden for implementing surveillance, health promotion, disease control, and adequate treatment programs according to each country's health policies.

Limitations

The potential limitations of this study may be attributed to the low number of published studies included, which could have introduced selection bias. If studies were biased toward at-risk populations, that could overestimate the overall prevalence, which can explain the large estimated number of people with a history of infection worldwide. These studies varied in sample size, study design, epidemiologic settings, population characteristics, disease stages, and follow-up durations, translating to high heterogeneity. Many studies were performed in South America and Asia, where there is a systemic lack of diagnostic tests for fascioliasis, which may have been selected for populations with greater access to diagnostics. Also, we only included reports published in English, Portuguese, or Spanish, limiting the inclusion of additional regional studies as revealed in the funnel plot; however, we covered >95% of the published literature. Finally, the obtained global estimates are intended to inform a projected global disease burden and by no means a particular local geographic zone. It is well known that the prevalence of fascioliasis is patchy and can even vary drastically from adjacent areas.

Conclusion

The estimated global prevalence of human fascioliasis was 4.5% in the included studies, translating into a high disease burden. Based on our findings, fascioliasis continues to expand as a globally neglected tropical disease. A clear data

gap persists for human fascioliasis prevalence worldwide. High-quality studies in those settings are crucial to improving the burden of disease estimates. As this neglected tropical disease affects the most underprivileged populations, strengthening epidemiological surveillance, and implementing measures to control and treat fascioliasis is imperative in the most affected areas to prevent long-term complications.

Declarations

Ethics approval and consent to participate

As the research project is a systematic review, it does not involve participation or action on humans or animals. The Institutional Ethics Committee exonerated the project, so it only required the approval of the University Directorate of Research, Science, and Technology (DUICT) of the Universidad Peruana Cayetano Heredia, Lima, Peru.

Consent for publication

Not applicable.

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Acknowledgements

None.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study was supported by grant UL1 RR025780 from the National Institutes of Health/National Center for Research Resources, Colorado Clinical Translational Science Institute.

Competing interests

The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: We declare no competing interests related to this work. Dr. Sillau reported receiving grants from the Alzheimer's Association, the Benign Essential Blepharospasm Research Foundation, the Colorado Department of Public Health, the Davis Phinney Foundation, the Hewitt Family Foundation, the Michael J. Fox Foundation, the National Institutes of Health, the National Institute of Nursing Research, the Patient-Centered Outcomes Research Institute, and the Rocky Mountain Alzheimer's Disease Center outside the submitted work. Dr. Henao-Martínez reported being the recipient of a K12-clinical trial award as a co-principal investigator for the

Expanded Access IND Program (EAP) to provide the Yellow Fever vaccine (Stamaril) to Persons in the United States outside the submitted work. The Editor in Chief and Associate Editor of Therapeutic Advances in Infectious Disease are authors of this paper. Therefore, the peer review process was managed by alternative members of the Editorial Board and the submitting Editors had no involvement in the decision-making process. No other disclosures were reported.

Availability of data and materials

The corresponding author had full access to data in the study and had final responsibility for the decision to submit the manuscript for publication. The datasets generated and analyzed in the current study are available from the corresponding author at reasonable request. The protocol was sought to be registered in PROSPERO. However, it was declined to give COVID-19-related research priority

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Supplemental material

Supplemental material for this article is available online.

References

1. Mas-Coma S, Valero MA and Bargues MD. Fascioliasis. *Adv Exp Med Biol* 2019; 1154: 71–103.
2. Caravedo MA and Cabada MM. Human Fascioliasis: current epidemiological status and strategies for diagnosis, treatment, and control. *Res Rep Trop Med* 2020; 11: 149–158.
3. Marcos L, Maco V, Terashima A, *et al.* Fascioliasis in relatives of patients with Fasciola hepatica infection in Peru. *Rev Inst Med Trop Sao Paulo* 2005; 47: 219–222.
4. Charlier J, Rinaldi L, Musella V, *et al.* Initial assessment of the economic burden of major parasitic helminth infections to the ruminant livestock industry in Europe. *Prev Vet Med* 2020; 182: 105103.
5. Arias-Pacheco C, Lucas JR, Rodriguez A, *et al.* Economic impact of the liver condemnation of cattle infected with Fasciola hepatica in the Peruvian Andes. *Trop Anim Health Prod* 2020; 52: 1927–1932.
6. Terashima A, Canales M, Maco V, *et al.* Observational study on the effectiveness and safety of multiple regimens of triclabendazole in human fascioliasis after failure to standard-of-care regimens. *J Glob Antimicrob Resist* 2021; 25: 264–267.
7. World Health Organization. *Research priorities for zoonoses and marginalized infections: WHO TRS N°971*. Geneva: World Health Organization, 2012.
8. Mas-Coma S, Funatsu IR, Angles R, *et al.* Domestic pig prioritized in one health action against fascioliasis in human endemic areas: experimental assessment of transmission capacity and epidemiological evaluation of reservoir role. *One Health* 2021; 13: 100249.
9. Webb CM and Cabada MM. Recent developments in the epidemiology, diagnosis, and treatment of Fasciola infection. *Curr Opin Infect Dis* 2018; 31: 409–414.
10. Havelaar AH, Kirk MD, Torgerson PR, *et al.* World Health Organization Global estimates and regional comparisons of the burden of foodborne disease in 2010. *PLoS Med* 2015; 12: e1001923.
11. Machicado C, Machicado JD, Maco V, *et al.* Association of Fasciola hepatica infection with liver fibrosis, cirrhosis, and cancer: a systematic review. *PLoS Negl Trop Dis* 2016; 10: e0004962.
12. Marcos LA, Terashima A, Yi P, *et al.* Mechanisms of liver fibrosis associated with experimental Fasciola hepatica infection: roles of Fas2 proteinase and hepatic stellate cell activation. *J Parasitol* 2011; 97: 82–87.
13. Chang Wong MR, Pinto Elera JO, Guzman Rojas P, *et al.* Demographic and clinical aspects of hepatic fascioliasis between 2013–2010 in National Hospital Cayetano Heredia, Lima, Peru. *Rev Gastroenterol Peru* 2016; 36: 23–28.
14. Mas-Coma S. Epidemiology of fascioliasis in human endemic areas. *J Helminthol* 2005; 79: 207–216.
15. Marcos L, Maco V and Terashima A. Triclabendazole for the treatment of human

fascioliasis and the threat of treatment failures. *Expert Rev Anti Infect Ther* 2021; 19: 817–823.

16. Flores VM, Raymundo LM, Iwashita AT, *et al.* Fas2-ELISA y la técnica de sedimentación rápida modificada por lumbreras en el diagnóstico de la infección por Fasciola hepática. *Rev Med Hered* 2002; 13: 49–57.
17. Terashima A and Marcos LA. Fracaso de dosis única de triclabendazole para el tratamiento de fasciolosis humana. *Acta Médica Peruana* 2016; 33: 228–231.
18. Aromataris EMZ. Joanna Briggs institute reviewer's manual, 2017, https://jbi.global/sites/default/files/2020-08/Checklist_for_Prevalence_Studies.pdf
19. Stevens GA, Alkema L, Black RE, *et al.* Guidelines for accurate and transparent health estimates reporting: the GATHER statement. *Lancet* 2016; 388: e19–e23.
20. Pourhoseingholi MA, Vahedi M and Rahimzadeh M. Sample size calculation in medical studies. *Gastroenterol Hepatol Bed Bench* 2013; 6: 14–17.
21. Esteban JG, Flores A, Angles R, *et al.* High endemicity of human fascioliasis between Lake Titicaca and La Paz valley, Bolivia. *Trans R Soc Trop Med Hyg* 1999; 93: 151–156.
22. Hayden JA, Van der Windt DA, Cartwright JL, *et al.* Assessing bias in studies of prognostic factors. *Ann Intern Med* 2013; 158: 280–286.
23. Nyaga VN, Arbyn M and Aerts M. Metaprop: a Stata command to perform meta-analysis of binomial data. *Arch Public Health* 2014; 72: 39.
24. Barendregt JJ, Doi SA, Lee YY, *et al.* Meta-analysis of prevalence. *J Epidemiol Community Health* 2013; 67: 974–978.
25. Abdi J, Naserifar R, Rostami Nejad M, *et al.* New features of fascioliasis in human and animal infections in Ilam Province, Western Iran. *Gastroenterol Hepatol Bed Bench* 2013; 6: 152–155.
26. Abo-Madyan A, Morsy TA, Motawea SM, *et al.* Clinical trial of Mirazid in treatment of human fascioliasis, Ezbet El-Bakly (Tamyia Center) Al-Fayoum Governorate. *J Egypt Soc Parasitol* 2004; 34: 807–818.
27. Afshan K, Kabeer S, Firasat S, *et al.* Seroepidemiology of human fascioliasis and its relationship with anti-Fasciola IgG and liver enzymes as biomarkers of pathogenicity. *Afr Health Sci* 2020; 20: 208–218.
28. Aguiar Oliveira A, Da SilvaNascimento A, Dos Santos TAM, *et al.* Estudo de prevalência e fatores associados à fasciolose no Município de Canutama, Estado do Amazonas, Brasil. *Epidemiolservsaúde* 2007; 16: 251–259.
29. Apt W, Aguilera X, Vega F, *et al.* Prevalence of fascioliasis in humans, horses, pigs, and wild rabbits in 3 Chilean provinces. *Bol Oficina Sanit Panam* 1993; 115: 405–414.
30. Asadian S, Mohebali M, Moudi M, *et al.* Seroprevalence of human fascioliasis in Meshkin-Shahr district, Ardabil province, northwestern Iran in 2012. *Iran J Parasitol* 2013; 8: 516–521.
31. Ashrafi K, Saadat F, O'Neill S, *et al.* The endemicity of human fascioliasis in Guilan Province, Northern Iran: the baseline for implementation of control strategies. *Iran J Public Health* 2015; 44: 501–511.
32. Bahram N, Sharbatkhori M, Tohidi F, *et al.* Serological study of Fascioliasis using indirect ELISA in Gorgan City, Golestan Province, Northern Iran. *Iran J Parasitol* 2020; 15: 418–424.
33. Bekana T, Berhe N, Eguale T, *et al.* Prevalence and factors associated with intestinal schistosomiasis and human fascioliasis among school children in Amhara Regional State, Ethiopia. *Trop Med Health* 2021; 49: 35.
34. Beyhan YE and Yilmaz H. Seroprevalence of fascioliasis in the eastern region of Turkey: an eight-year investigation. *Turk J Gastroenterol* 2020; 31: 746–751.
35. Bless PJ, Schar F, Khieu V, *et al.* High prevalence of large trematode eggs in schoolchildren in Cambodia. *Acta Trop* 2015; 141: 295–302.
36. Bozorgomid A, Nazari N, Kia EB, *et al.* Epidemiology of fascioliasis in Kermanshah Province, Western Iran. *Iran J Public Health* 2018; 47: 967–972.
37. Cabada MM, Morales ML, Webb CM, *et al.* Socioeconomic factors associated with fasciola hepatica infection among children from 26 communities of the Cusco Region of Peru. *Am J Trop Med Hyg* 2018; 99: 1180–1185.
38. Cabada MM, Goodrich MR, Graham B, *et al.* Fascioliasis and eosinophilia in the highlands of Cuzco, Peru and their association with water and socioeconomic factors. *Am J Trop Med Hyg* 2014; 91: 989–993.
39. Carnevale S, Cabrera MG, Cucher MA, *et al.* Direct, immunological and molecular techniques for a fasciolosis survey in a rural area of San Luis, Argentina. *J Parasit Dis* 2013; 37: 251–259.

40. Cengiz ZT, Yilmaz H, Dulger AC, *et al.* Seroprevalence of human fascioliasis in Van Province, Turkey. *Turk J Gastroenterol* 2015; 26: 259–262.

41. Curtale F, Nabil M, El Wakeel A, *et al.* Anaemia and intestinal parasitic infections among school age children in Behera Governorate, Egypt. Behera survey team. *J Trop Pediatr* 1998; 44: 323–328.

42. Curtale F, Hassanein YA, Barduagni P, *et al.* Human fascioliasis infection: gender differences within school-age children from endemic areas of the Nile Delta, Egypt. *Trans R Soc Trop Med Hyg* 2007; 101: 155–160.

43. Curtale F, Abd El-Wahab Hassanein Y, El Wakeel A, *et al.* Distribution of human fascioliasis by age and gender among rural population in the Nile Delta, Egypt. *J Trop Pediatr* 2003; 49: 264–268.

44. Davoodi L, Mizani A, Najafi-Vosough R, *et al.* A descriptive study of human fascioliasis in Qaemshahr, Mazandaran Province, Iran: its prevalence and risk factors. *Arch Clin Infect Dis* 2022; 17: e123682.

45. Eshrati B, Mokhayeri H, Rokni MB, *et al.* Seroepidemiology of human fascioliasis in rural and nomad areas of Lorestan province, western Iran, in 2016 and 2017. *J Parasit Dis* 2020; 44: 806–812.

46. Esteban JG, Flores A, Aguirre C, *et al.* Presence of very high prevalence and intensity of infection with Fasciola hepatica among Aymara children from the Northern Bolivian Altiplano. *Acta Trop* 1997; 66: 1–14.

47. Esteban JG, Gonzalez C, Bargues MD, *et al.* High fascioliasis infection in children linked to a man-made irrigation zone in Peru. *Trop Med Int Health* 2002; 7: 339–348.

48. Esteban JG, Gonzalez C, Curtale F, *et al.* Hyperendemic fascioliasis associated with schistosomiasis in villages in the Nile Delta of Egypt. *Am J Trop Med Hyg* 2003; 69: 429–437.

49. Fentie T, Erqou S, Gedefaw M, *et al.* Epidemiology of human fascioliasis and intestinal parasitosis among schoolchildren in Lake Tana Basin, northwest Ethiopia. *Trans R Soc Trop Med Hyg* 2013; 107: 480–486.

50. Gonzalez LC, Esteban JG, Bargues MD, *et al.* Hyperendemic human fascioliasis in Andean valleys: an altitudinal transect analysis in children of Cajamarca Province, Peru. *Acta Trop* 2011; 120: 119–129.

51. Hassan MM, Moustafa NE, Mahmoud LA, *et al.* Prevalence of fasciola infection among school children in Sharkia Governorate, Egypt. *J Egypt Soc Parasitol* 1995; 25: 543–549.

52. Heydarian P, Ashrafi K, Mohebali M, *et al.* Seroprevalence of human fasciolosis in Lorestan Province, Western Iran, in 2015–16. *Iran J Parasitol* 2017; 12: 389–397.

53. Hosseini G, Sarkari B, Moshfe A, *et al.* Epidemiology of human fascioliasis and intestinal helminthes in rural areas of Boyer-Ahmad Township, Southwest Iran; a population based study. *Iran J Public Health* 2015; 44: 1520–1525.

54. Kaya S, Demirci M, Demirel R, *et al.* Seroprevalence of fasciolosis and the difference of fasciolosis between rural area and city center in Isparta, Turkey. *Saudi Med J* 2006; 27: 1152–1156.

55. Kheirandish F, Kayedi MH, Ezatpour B, *et al.* Seroprevalence of human fasciolosis in Pirabad, Lorestan Province, Western Iran. *Iran J Parasitol* 2016; 11: 24–29.

56. Lopez M, White AC Jr and Cabada MM. Burden of fasciola hepatica infection among children from Paucartambo in Cusco, Peru. *Am J Trop Med Hyg* 2012; 86: 481–485.

57. Maciel MG, Lima WDS, De Almeida FLM, *et al.* Cross-sectional serological survey of human fascioliasis in Canutama municipality in Western Amazon, Brazil. *J Parasitol Res* 2018; 2018: 6823638.

58. Naeini KM, Nasiri FM, Rokni MB, *et al.* Seroprevalence of human fascioliasis in Chaharmahal and Bakhtiyari Province, Southwestern Iran. *Iran J Public Health* 2016; 45: 774–780.

59. Manrique-Abril F and Suescun-Carrero S. Prevalencia de parasitismo intestinal y situacion nutricional en escolares y adolescentes de Tunja. (Perspectiva general de la enfermedad/trastorno). *Cesmedicina* 2011; 25: 20–30.

60. Mantari TC, Chávez V A, Suárez A F, *et al.* Fasciolasis en ninos de tres distritos del departamento de Junin, Peru. *Rev Investig Vet Perú* 2012; 23: 454–461.

61. Marcos Raymundo LA, Flores VM, Terashima A, *et al.* Hyperendemicity of human fasciolosis in the Mantaro Valley, Peru: factors for infection with Fasciole hepatica. *Rev Gastroenterol Peru* 2004; 24: 158–164.

62. Marcos L, Romani L, Florencio L, *et al.* Hyperendemic and mesoendemic zones of Fasciola

infection surrounding urban Lima: an emerging disease?. *Rev Gastroenterol Peru* 2007; 27: 31–36.

63. Natividad Carpio I and Terashima Iwashita A. Prevalencia de infección humana por Fasciola hepática en pobladores del distrito de Caujul provincia de Oyon, region de Lima, Perú. *Acta Méd Peru* 2008; 25: 77–80.
64. Nguyen T, Cheong FW, Liew JW, *et al*. Seroprevalence of fascioliasis, toxocariasis, strongyloidiasis and cysticercosis in blood samples diagnosed in Medic Medical Center Laboratory, Ho Chi Minh City, Vietnam in 2012. *Parasit Vectors* 2016; 9: 486.
65. Nxasana N, Baba K, Bhat V, *et al*. Prevalence of intestinal parasites in primary school children of Mthatha, eastern Cape Province, South Africa. *Ann Med Health Sci Res* 2013; 3: 511–516.
66. Ozturhan H, Emekdas G, Sezgin O, *et al*. Seroepidemiology of Fasciola Hepatica in Mersin province and surrounding towns and the role of family history of the Fascioliasis in the transmission of the parasite. *Turk J Gastroenterol* 2009; 20: 198–203.
67. Qureshi AW, Zeb A, Mansoor A, *et al*. Fasciola hepatica infection in children actively detected in a survey in rural areas of Mardan district, Khyber Pakhtunkhawa province, northern Pakistan. *Parasitol Int* 2019; 69: 39–46.
68. Qureshi AW, Tanveer A and Mas-Coma S. Epidemiological analysis of human fascioliasis in northeastern Punjab, Pakistan. *Acta Trop* 2016; 156: 157–164.
69. Rodríguez-Ulloa C, Rivera-Jacinto M, Chilón YS, *et al*. Infección por Fasciola hepatica en escolares del distrito de Condebamba, Cajamarca. *Rev Invest Vet Perú* 2018; 29: 1411–1420.
70. Rodríguez-Ulloa C, Rivera-Jacinto M, Del Valle-Mendoza J, *et al*. Risk factors for human fascioliasis in schoolchildren in Banos del Inca, Cajamarca, Peru. *Trans R Soc Trop Med Hyg* 2018; 112: 216–222.
71. Saberinasab M, Mohebali M, Molawi G, *et al*. Seroprevalence of human fascioliasis using indirect ELISA in isfahan district, central iran in 2013. *Iran J Parasitol* 2014; 9: 461–465.
72. Steinmann P, Usubalieva J, Imanalieva C, *et al*. Rapid appraisal of human intestinal helminth infections among schoolchildren in Osh oblast, Kyrgyzstan. *Acta Trop* 2010; 116: 178–184.
73. Taş Cengiz Z, Yilmaz H, Beyhan YE, *et al*. A Comprehensive retrospective study: intestinal parasites in human in Van Province. *Turkiye Parazitol Derg* 2019; 43: 70–73.
74. Valencia M Nicasio, Pariona D Andrea, Huaman A Margarita, *et al*. Seroprevalencia de fasciolosis en escolares y en ganado vacuno en la provincia de Huancavelica, Perú. *Rev Peru Med Exp Salud Públ* 2005; 22: 96–102.
75. Wilches C, Jaramillo JG, Muñoz DL, *et al*. Presencia de infestación por Fasciola hepatica en habitantes del valle de San Nicolás, oriente antioqueño. *Infectio* 2009; 13: 92–99.
76. Yilmaz H and Godekmerdan A. Human fasciolosis in Van Province, Turkey. *Acta Trop* 2004; 92: 161–162.
77. Zoghi S, Emami M, Shahriarirad S, *et al*. Human fascioliasis in nomads: a population-based serosurvey in southwest Iran. *Infez Med* 2019; 27: 68–72.
78. Zumaquero-Rios JL, Sarracent-Perez J, Rojas-Garcia R, *et al*. Fascioliasis and intestinal parasitoses affecting schoolchildren in Atlixco, Puebla State, Mexico: epidemiology and treatment with nitazoxanide. *PLoS Negl Trop Dis* 2013; 7: e2553.
79. Worldometer. Population by country, 2022, https://www.worldometers.info/
80. Alba A, Vazquez AA and Hurtrez-Bousses S. Towards the comprehension of fasciolosis (re-) emergence: an integrative overview. *Parasitology* 2021; 148: 385–407.
81. Furst T, Keiser J and Utzinger J. Global burden of human food-borne trematodiasis: a systematic review and meta-analysis. *Lancet Infect Dis* 2012; 12: 210–221.
82. Nyindo M and Lukambagire AH. Fascioliasis: an ongoing zoonotic trematode infection. *Biomed Res Int* 2015; 2015: 786195.
83. World Health Organization. Report of the WHO informal meeting on use of triclabendazole in fascioliasis control, WHO headquarters, Geneva, Switzerland, 17–18 October 2006, 2007, https://www.who.int/publications/i/item/WHO-CDS-NTD-PCT-2007.1
84. Mollinedo S, Gutierrez P, Azurduy R, *et al*. Mass drug administration of triclabendazole for Fasciola Hepatica in Bolivia. *Am J Trop Med Hyg* 2019; 100: 1494–1497.
85. Curtale F, Hassanein YA and Savioli L. Control of human fascioliasis by selective chemotherapy: design, cost and effect of the first public health, school-based intervention implemented in endemic areas of the Nile delta, Egypt. *Trans R Soc Trop Med Hyg* 2005; 99: 599–609.

86. Rizwan M, Khan MR, Afzal MS, *et al*. Prevalence of fascioliasis in livestock and humans in Pakistan: a systematic review and meta-analysis. *Trop Med Infect Dis* 2022; 7: 126.

87. Zhou XN. Prioritizing research for 'one health—one world'. *Infect Dis Pover* 2012; 1: 1.

88. Savioli L DD and Crompton DWT. *Sustaining the drive to overcome the global impact of neglected tropical diseases. Second WHO report on neglected tropical diseases*. Geneva: World Health Organization, 2013.

89. Parkinson M, O'Neill SM and Dalton JP. Endemic human fasciolosis in the Bolivian Altiplano. *Epidemiol Infect* 2007; 135: 669–674.

90. Marcos L, Romani L, Florencio L, *et al*. Zonas hiperendémicas y mesoendémicas de la infección por fasciola hepática aledañas a la ciudad de lima: una enfermedad emergente. *Rev de Gastroenterol del Perú* 2007; 27: 31–36.

91. Carmona C and Tort JF. Fasciolosis in South America: epidemiology and control challenges. *J Helminthol* 2017; 91: 99–109.

92. Dermauw V, Muchai J, Al Kappany Y, *et al*. Human fascioliasis in Africa: a systematic review. *PLoS ONE* 2021; 16: e0261166.

93. Sabourin E, Alda P, Vazquez A, *et al*. Impact of human activities on fasciolosis transmission. *Trends Parasitol* 2018; 34: 891–903.

94. Mas-Coma S, Bargues MD and Valero MA. Diagnosis of human fascioliasis by stool and blood techniques: update for the present global scenario. *Parasitology* 2014; 141: 1918–1946.

95. Martinez-Sernandez V, Orbegozo-Medina RA, Gonzalez-Warleta M, *et al*. Rapid Enhanced MM3-COPRO ELISA for detection of fasciola coproantigens. *PLoS Negl Trop Dis* 2016; 10: e0004872.

96. Munita MP, Rea R, Martinez-Ibeas AM, *et al*. Comparison of four commercially available ELISA kits for diagnosis of Fasciola hepatica in Irish cattle. *BMC Vet Res* 2019; 15: 414.

97. Marcos L, Terashima A, Leguia G, *et al*. La infección por Fasciola Hepática en el Perú: una enfermedad emergente. *Rev Gastroenterol Perú* 2007; 27: 389–396.

98. Torgerson PR, Devleesschauwer B, Praet N, *et al*. World Health Organization estimates of the global and regional disease burden of 11 foodborne parasitic diseases, 2010: a data synthesis. *PLoS Med* 2015; 12: e1001920.

99. Mehmood K, Zhang H, Sabir AJ, *et al*. A review on epidemiology, global prevalence and economical losses of fasciolosis in ruminants. *Microb Pathog* 2017; 109: 253–262.

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