A meta-analysis of *Entamoeba histolytica/dispar* in Iraq

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Abstract

Background

Amebiasis is a major health problem caused by the protozoan parasite *Entamoeba histolytica* with a worldwide distribution, especially in developing countries. The aim of this systematic review and meta-analysis was to estimate the proportion prevalence of *E. histolytica/dispar* in human in Iraq.

Methodology/Principal Findings

Published studies on human infection with *E. histolytica/dispar* in Iraq were searched in electronic databases using Google scholar, Iraqi Academic Scientific Journals (IASJ), PubMed, ScienceDirect and WHO Global Health Library (GHL). Eligible studies were cross-sectional and used fecal and/or serological methods to diagnose *E. histolytica/dispar* infection in human in Iraq, and published between 1970 and July 2017. The pooled prevalence was calculated using random effect model meta-analyses with 95% confidence interval (CI). Ninety nine studies were eligible for the meta-analysis that included 117694 individuals. The pooled proportion for *E. histolytica/dispar* infection in Iraq was estimated at 20.61% with a 95% confidence interval (CI) of 17.83, 23.53. A high level of heterogeneity was found among the studies. The prevalence among Iraqi population ranged between 1.66 and 90.5% per study (mean: 22.36%). The pooled prevalence of infection was 58.43% (95% CI: 54.71%–62.1%) and 43.10% (95% CI: 39.66%–46.6%) for males and females respectively. Parasite screening using microscopy did not differentiate between the pathogenic and nonpathogenic species of *Entamoeba* resulted in higher proportion prevalence than PCR proportion prevalence, (20.32%, 95% CI: 17.80%–22.96%) (17.57%, 95% CI: 8.07%–29.75%) respectively. Hospital based studies recorded the highest prevalence of *E. histolytica/dispar* infection at 22.69% (95% CI: 19.55%–25.99%). The prevalence decreased into 18.46 (95% CI: 14.28%–23.04%) between 2010 and 2017.

Conclusions/Significance

Although there was a reduction in prevalence of amebiasis since 2010, the prevalence of amebiasis is still considerable in population of Iraq. Therefore, prevention strategies of fecal contamination are required to reduce the infection.

Author summary

Amebiasis is the infection with *Entamoeba histolytica* an invasive parasite dwelling the intestine or other organs such as liver, lungs, or skin of human. Infection with this parasite could be acquired by consumption of contaminated water, vegetables, and fruits with feces of infected human. The infection may be asymptomatic or symptomatic causing dysentery. We performed this meta-analysis to estimate the prevalence of amebiasis in the population of Iraq between 1970 and 2017. Ninety nine published studies were identified and the data were extracted from them to use in our meta-analysis and the total included individuals were 117694. The prevalence of population infection in Iraq was evaluated at 20.61%. The infection prevalence was higher in males than in females. The infection prevalence decreased during the period 2010 to 2017 in Iraqi population. This level of infection needs further efforts to eradicate amebiasis, these efforts begin with the prevention of the disease transmission through water and food and treatment of infected people. So awareness of simple hygienic principles can control the disease by boiling water and washing vegetables and fruits thoroughly.

Introduction

Amebiasis is a human infection caused by the intestinal protozoan parasite *Entamoeba histolytica*, with a cosmopolitan distribution. It is considered as third parasitic cause of human mortality after malaria and schistosomiasis, especially in developing countries with poor sanitations. The infection with amebiasis is estimated to be more than 50 million cases throughout the world and 40,000–110,000 deaths annually [1,2]. *E. histolytica* is endemic in most tropical and subtropical countries [3]. Infection with amebiasis can be intestinal and extraintestinal especially in liver; intestinal amebiasis varies widely from asymptomatic infection to dysentery [4]. The common route for infection of the host with amebiasis is by the ingestion of *E. histolytica* cysts in water or food, which are contaminated with feces [5]. *E. histolytica* has been reclassified into *Entamoeba* complex that include pathogenic *E. histolytica* and two nonpathogenic species (*E. dispar* and *E. moshkovskii*), the three species are morphologically indistinguishable [6].

To our knowledge, there is no study which has determined the overall prevalence of *E. histolytica* infection of human in Iraq. Therefore, the objectives of this study were to determine the prevalence of *E. histolytica* infection and related data (age, sex and study setting) of humans in Iraq, by using meta-analytical methods. The data of the current study can be used to eliminate or reduce the human infection with amebiasis in Iraq through providing more targeted programs for prevention and control.

Methods

The study was conducted based on the PRISMA guideline (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [7]. The PRISMA checklist was used to ensure inclusion of relevant information in the analysis (S1 Checklist).

Search strategy

The literature search was conducted in the following electronic databases: Google scholar, Iraqi Academic Scientific Journals (IASJ), PubMed, ScienceDirect and WHO Global Health Library (GHL). The electronic search was limited to studies published in English or Arabic between 1970 and July 2017.

For searching, Boolean operators OR and/or AND were used for combination of terms. The following terms were used in the electronic database search: “amebiasis”, “amoebiasis”, “Entamoeba histolytica”, “Entamoeba dispar”, “Iraq”, “human”, “prevalence” and “Infection”.

Study selection

The process of study selection was performed by identifying relevant publications about human amebiasis in Iraq. The selection of articles was based on their titles and then their abstracts, which were relevant to the outcomes of interest. The search results were imported into Mendeley, for management of articles, to exclude duplicate publications. Then articles were screened, they were excluded if did not meet the eligibility criteria. A study was eligible if it fulfilled the following eligibility criteria: (i) full text and published in English or Arabic; (ii) cross-sectional; (iii) carried out on humans; (iv) conducted in Iraq; (v) used coprological and/or serological methods for diagnosis; (vi) sample size > 35; (vii) clarity of results. If more than one study presented the same data, the study with data that are more complete were included.

Data extraction

From each study included, the following data were extracted: the first author, year of publication, year of study, province, method of detection, sample size, positive samples, prevalence, sex, age group and study setting.

If the data values were not clearly mentioned in the text, the information was extracted from available data tables.

Data analysis

Proportion meta-analyses had been conducted for data analysis. For each study, the proportions of the prevalence of amebiasis were calculated, and then the pooled proportions were derived with 95% confidence intervals (CIs). Freeman-Tukey transformation (arcsine square root transformation) was used for calculation of the weighted summary proportion for the random effects model (DerSimonian and Laird).

If a study did not record the year of data collection, the year of publication was used as the year of data collection. If detailed data were available, we stratified the prevalence of amebiasis by sex (male and female), by method of detection (Microscopy and PCR), by setting (hospital, hospital/primary schools pupils, primary school pupils, foodhandlers, village and nursery schools/children from some houses), by Year of study (less than 1990, 1990-1999, 2000-2009 and 2010-2018) and by province (Al-Anbar, Al-Najaf, Babylon, Baghdad, Basrah, Diwaniya, Diyala, Duhok, Erbil, Karbala, Kirkuk, Ninevah, Saladin, Sulaimani, Thi-Qar and Wasit).

Data analysis was performed using MedCalc Statistical Software (version 17.9.2) (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2017) and Microsoft Office Excel 2013.

Forest plot was generated to display the results of each study and the heterogeneity among studies. Heterogeneity between studies was assessed by the Cochran's Q test and inverse variance index (I^2). The I^2 index indicates that the variation between studies that is due to heterogeneity rather than chance. I^2 values greater than 75% were considered as high heterogeneity [8]. A funnel plot was used to visually investigate the across study bias.

Results

Study selection

A total of 164 studies were found of which 16 were duplicates and were excluded, resulting in 148 records (Fig 1). After screening the title and abstract of 148 records, 17 records were excluded because the abstracts and the full-texts of eight and nine studies were not accessible, respectively. Out of 131 full-text reports were assessed for eligibility, 32 were excluded because: 2 studies did not use coprological and/or serological methods for diagnosis of amebiasis; 2 studies had the same data by the same author; 4 studies were not epidemiological; 2 studies presented the data of infection with amebiasis as a combined infection with other parasite; 19 studies did not provide data of prevalence; 2 studies were conducted on the samples of fingernails; 1 study was carried out on infectious agents in stool samples of children with nosocomial diarrhea. Finally, 99 entries were included in the meta-analysis [9-107].

Fig 1. Flow diagram of study selection process for meta-analysis.

Study characteristics

Table 1 shows the characteristics of the studies included in the meta-analysis, which covered 16 provinces in Iraq. The studies included 24383 positive cases out of 117694 individuals. Most of the studies used microscopy method (95 studies) followed by PCR method (3 studies) for detection of *E. histolytica/dispar* in stool, one study did not mention the method. There was no study used serological methods for detection of *E. histolytica/dispar*. The studies have been carried out from 1988 to 2016 and published between 1999 and 2017. The studies included in the meta-analyses were undertaken in subjects of all ages, ranging from less than 1 year to 90 years, 47 studies included only children and 45 studies included both children and adults, seven studies did not specify the age groups. The sample sizes of the eligible studies ranged from 70 to 18450. The prevalence of infection with *E. histolytica/dispar* ranged from 1.66 to 90.5%

(mean: 22.36%). In the selected articles, 84 studies were hospital based, 3 studies were conducted in individuals from hospitals / primary schools, 3 studies in pupils of primary schools, 3 studies in foodhandlers, 2 studies in individuals from villages, 1 study in children from nursery schools / some houses, 3 studies did not specify the sources of stool samples.

Table 1. Characteristics of studies included in the meta-analysis.

First author	Year of publication	Year of study	Province	Detection method in stool	Sample size	Positive cases	Prevalence %	Male No (%)	Female No (%)	Age in years	Study setting
Al-Mosawi	2016	2015	Thi-Qar	Microscopy	200	35	17.5				hospital
Al-Sorchee	2013	2007	Erbil	Microscopy	500	175	35			1-10	hospital
Rabatti	2008	2002	Erbil	Microscopy	116	70	60.34			0-12	hospital
Khudair	2011	2008 - 2009	Diyala	Microscopy	975	93	9.54			0-10	hospital
Nasser	2014	2013 - 2014	Wasit	Microscopy	596	100	16.78			<5->46	hospital
Ali	2015	2013 - 2014	Babylon	Microscopy	492	115	23.37			0 -<30	hospital
Al-Ammash	2015	2014 - 2015	Saladin	Microscopy	304	55	18.09	35 (63.64)	20 (36.36)	0-50	hospital
Muhsin	2016	2012	Karbala	Microscopy	5670	332	5.86	193 (58.13)	139 (41.87)	<12	hospital
Mahfoth	2010	2007 - 2008	Ninevah	Microscopy	1220	347	28.44			<5	nursery schools / children

											from some houses
Hussein	2011	2009	Baghdad	Microscopy	730	103	14.11	40 (38.83)	63 (61.17)	0-18	hospital
Al-Fahdawi	2007	2004 - 2005	Al-Anbar	Microscopy	896	237	26.45	120 (50.63)	117 (49.37)	1-71	hospital
Jamil	2008	2006	Diyala	Microscopy	220	155	70.45			<1->41	hospital
Al-Zigibi (a)	2011	2009 - 2010	Karbala	Microscopy	776	61	7.86	29 (47.54)	32 (52.46)	0-70	hospital
Al-Jeburi	2010	2007 - 2008	Diyala	Microscopy	161	43	26.71	23 (53.49)	20 (46.51)	<1-70	hospital
Al-Zigibi (b)	2011		Babylon	Microscopy	250	34	13.6	19 (55.88)	15 (44.12)		primary school pupils
AL-Aboody	2010	2009	Thi-Qar	Microscopy	1000	249	24.9			1->16	hospital
Mohammed	2010	2008	Thi-Qar	Microscopy	960	392	40.83	210 (53.57)	182 (46.43)	<10-> 51	hospital
Al-Tae	2008	2000 - 2001	Baghdad	Microscopy	354	103	29.10			1->70	hospital
Al-Azzawi	2010	2009	Diyala	Microscopy	18450	2640	14.31	1490 (56.44)	1150 (43.56)	0-15	hospital
Jasim	2009	2001	Saladin	Microscopy	133	57	42.86			0-5	hospital
Al-Kaisi	2007	2002	Saladin	Microscopy	1050	140	13.33	82 (58.57)	58 (41.43)	0-81	hospital
Saael	2009	2005	Baghdad	Microscopy	1268	394	31.07	204 (51.78)	190 (48.22)	1-12	hospital
Al-Warid	2012	2009 - 2010	Baghdad	Microscopy	737	27	3.66			various ages	hospital

Al-Tikrity	2009	2006 - 2007	Saladin	Microscopy	218	154	70.64	78 (50.65)	76 (49.35)	1->25	hospital
Al-Marzoqi	2008	2008	Babylon	Microscopy	173	40	23.12			<1	hospital
Al-Mosa	2007	2004 - 2005	Babylon	Microscopy	540	91	16.85			various ages	hospital
Ftohe	2008	2005 - 2006	Ninevah	Microscopy	600	139	23.17	82 (58.99)	57 (41.01)	<6	hospital
Nayyef	2011	2008	Baghdad	Microscopy	800	317	39.63	163 (51.42)	154 (48.58)	0-90	hospital
Al-Taie	2006	2003 - 2004	Babylon	Microscopy	865	146	16.88			1->50	hospital
Abdullah (a)	2005	1998 - 1999	Kirkuk	Microscopy	806	75	9.31			6-13	primary school pupils
Abdullah (b)	2005	1998 - 1999	Kirkuk	Microscopy	325	12	3.69	325		9-79	foodhandlers
Saeed	2005		Ninevah	Microscopy	754	67	8.89			1-69	hospital
Jaeffer	2011	2009 - 2010	Baghdad	Microscopy	513	15	2.92	7 (46.67)	8 (53.33)	0-12	hospital
Thhaib	2008	2005 - 2006	Diwaniya	Microscopy	75	8	10.67			0-2	hospital
Al-Yasari	2009	2008	Babylon	Microscopy	115	6	5.22			5-50	hospital
Al-Morshidy	2007	2003 - 2004	Babylon	Microscopy	243	68	27.98				hospital
Yousif	2011		Baghdad	Microscopy	722	12	1.66			1->18	

Ibraheem	2010	2007 - 2008	Baghdad	Microscopy	316	64	20.25			0-10	hospital
Al-Reikaby	2010	2007	Thi-Qar		4006	2470	61.66			<1->45	hospital
Al-Kubaisy	2008	2006 - 2007	Babylon	Microscopy	1224	222	18.14	135 (60.81)	87 (39.19)	<1->45	hospital
Kadhum	2011	2009 - 2010	Al-Najaf	Microscopy	70	3	4.29			<1	hospital
Al-Najar	2006	2001	Baghdad	Microscopy	125	51	40.8			0-12	hospital
Ali	2010	2009 - 2010	Wasit	Microscopy	600	60	10	34 (56.67)	26 (43.33)	0-50	hospital
Ibrahim (a)	2012	2010	Baghdad	Microscopy	1520	149	9.80	91 (61.07)	58 (38.93)	0-12	hospital
Rahi (a)	2011	2009 - 2010	Wasit	Microscopy	424	68	16.04	38 (55.88)	30 (44.12)	0-50	hospital
Rahi (b)	2011		Wasit	Microscopy	78	13	16.67	10 (76.92)	3 (23.08)	0-60	hospital
Raddam	2008	2006	Thi-Qar	Microscopy	3600	1400	38.89	725 (51.79)	675 (48.21)	0-12	hospital
Kadum	2007	2005 - 2006	Babylon	Microscopy	1312	228	17.38			1->50	hospital / primary schools pupils
Al-Kubaisy	2007	2005 - 2006	Karbala	Microscopy	2052	554	27	359 (64.80)	195 (35.20)	various ages	hospital
Al-Jabouri	2007	2006 - 2007	Karbala	Microscopy	557	286	51.35	157 (54.90)	129 (45.10)	<1-70	hospital

Al-Dulaimi	2007	2005	Babylon	Microscopy	515	48	9.32			1->30	hospital
AL-Shaheen	2007	2005	Basrah	Microscopy	7537	2203	29.23	1374 (62.37)	829 (37.63)	1->45	hospital
Hamad	2011	1998 - 2004	Erbil	Microscopy	5768	711	12.33	430 (60.48)	281 (39.52)		hospital
Jasim	2011	2009	Baghdad	Microscopy	2177	377	17.32	206 (54.64)	171 (45.36)	Children	hospital
Ibrahim (b)	2012	2010	Baghdad	Microscopy	223	43	19.28			0-5	hospital
Guirges	2006		Baghdad	Microscopy	3564	938	26.32			0-70	hospital
Al-Jebory	2012	2010 - 2011	Saladin	Microscopy	1500	188	12.53	119 (63.30)	69 (36.70)	0-70	hospital
Hussan	2012		Baghdad	Microscopy	250	22	8.8			<5	hospital
Raof	2012	2009 - 2010	Baghdad	Microscopy	300	67	22.33	41 (61.19)	26 (38.81)	>1-<19	hospital
Hussein	2013	2012 - 2013	Al-Najaf	Microscopy	678	162	23.89			1-70	hospital
Kadir	2013	2008 - 2009	Kirkuk	Microscopy	600	154	25.67			<1-60	hospital
Zaidan	2013	2005	Baghdad	Microscopy	400	362	90.5	211 (58.29)	151 (41.71)	<5	hospital
Al-Hameedawi	2014	2013	Al-Najaf	PCR	104	25	24.04			1-58	hospital
Aljanabi	2014	2011 - 2012	Baghdad	Microscopy	1712	270	15.77	169 (62.59)	101 (37.41)	0-15	hospital
Alshawi	2013	2010	Baghdad	Microscopy	1356	331	24.41	186 (56.19)	145 (43.81)	1->50	hospital

Al-Bayati	2014	2011 - 2012	Diwaniya	Microscopy	1057	149	14.1			0-12	hospital
Racine	2014		Diwaniya	Microscopy	220	13	5.91			15-45	foodhandlers
Hussein	2014	2011 - 2012	Baghdad	Microscopy	2449	453	18.5				hospital
Abed	2015	2007	Baghdad	Microscopy	200	55	27.5			0-10	hospital
Al-Garawi	2015	2013	Karbala	Microscopy	2036	410	20.14	253 (61.71)	157 (38.29)	<1-12	hospital
Obaid	2015		Kirkuk	Microscopy	430	123	28.6			<1-12	hospital
Shaker	2016	2014	Baghdad	Microscopy	320	60	18.75			1-50	hospital
Shlash	2016	2015 - 2016	Al-Najaf	Microscopy	120	90	75	32 (35.56)	58 (64.44)	<6-14	hospital
Ali	2017	2013 - 2014	Karbala, Babylon & Al-Najaf	Microscopy	1350	203	15.04			1->60	hospital
Al-Khalidi	2016	2014	Diwaniya	PCR	170	39	22.94			0-2	hospital
Atiyah	2016	2015	Wasit	Microscopy	3550	1780	50.14	1447 (81.29)	333 (18.71)	0-45	hospital
Hussein	2016	2008	Thi-Qar	Microscopy	780	49	6.28			0-6	hospital
Al-Moussawi	2005	2002 - 2003	Babylon	Microscopy	681	69	10.13			1->30	village
Kadir	1999	1988 - 1989	Kirkuk	Microscopy	1681	130	7.73			6-12	primary school pupils
Al-Joudi	2005	1992 - 1997	Al-Anbar	Microscopy	6330	509	8.04			1-67	hospital
Ali	2016	2014	Sulaimani	Microscopy	300	31	10.33			0-14	hospital

Abid	2012	2009 - 2010	Saladin	Microscopy	317	54	17.03				hospital
Badry	2014	2012 - 2013	Duhok	Microscopy	522	134	25.67			0-14	hospital
Mero	2013	2008 - 2009	Duhok	Microscopy	1132	121	10.69			0-13	hospital / primary schools pupils
Al-Kubaisy	2015		Baghdad	Microscopy	1500	351	23.4			<10	hospital
Mahdi	2002	1997 - 1998	Basrah	Microscopy	215	5	2.33	2 (40)	3 (60)	<6-65	
Shebib	2003	1999 - 2000	Baghdad	Microscopy	200	50	25				hospital
Salman	2013	2010	Kirkuk	Microscopy	221	44	19.91			<2	hospital
Al-Kaissi	2006		Baghdad	Microscopy	200	4	2			0-2	hospital
Amin	2015	2014	Sulaimani	Microscopy	300	110	36.67			1-50	hospital
Obaid	2014	2013 - 2014	Kirkuk	Microscopy	207	84	40.58	46 (54.76)	38 (45.24)	<1-50	hospital
Mero	2015	2013 - 2014	Duhok	Microscopy	600	158	26.33			<2-12	hospital / primary schools pupils
Al-Azawi	2009	2006 - 2007	Baghdad	Microscopy	600	195	32.5			2-11	hospital

Al-Kubaisy	2014	2003 - 2004	Baghdad	Microscopy	2033	105	5.16			≤15	hospital
Jarallah	2012	2011	Basrah	Microscopy	294	80	27.21	47 (58.75)	33 (41.25)	<1-14	village
Hussein	2015	2014 - 2015	Baghdad	PCR	100	7	7			0-18	hospital
Hamad	2012	2010 - 2011	Erbil	Microscopy	200	60	30	32 (53.33)	28 (46.67)	<1-12	hospital
Faraj	2012	2005 - 2006	Erbil	Microscopy	587	75	12.78	75 (100)		≥10->50	foodhandlers
Salman	2016	2014 - 2015	Kirkuk	Microscopy	417	7	1.68			<1-60	

Prevalence and heterogeneity

The random effect pooled prevalence of *E. histolytica/dispar* infection was 20.61% (95% CI: 17.83%–23.53%) in Iraq. The prevalence estimates of *E. histolytica/dispar* are shown in a forest plot (Fig 2). The results of Cochran's Q test and inverse variance index (I^2) among studies included in the meta-analysis were 14169.34 and 99.31%, respectively.

Fig 2. Forest plot of the proportion prevalence of *E. histolytica/dispar* in Iraq.

The pooled estimates by subgroup are summarised in Table 2. Of the 99 studies, 39 provided information on the gender of individuals investigated (38 studies presented data from both males and females, 1 study presented data from just males). The pooled prevalence of *E. histolytica/dispar* in males (58.43%, 95% CI: 54.71%–62.1%) was higher than in females (43.10%, 95% CI: 39.66%–46.6%).

Table 2. Pooled prevalence of *E. histolytica/dispar* in Iraq stratified by subgroups

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Characteristics		Number of studies	Proportion %	95% CI	heterogeneity			
					Q	P-value	I^2 %	95% CI for I^2
Overall		99	20.61	17.83–23.53	14169.34	P < 0.0001	99.31	99.26 – 99.35
Sex	**Male**	39	58.43	54.71–62.1	686.28	P < 0.0001	94.46	93.24 – 95.47
	Female	38	43.10	39.66–46.6	568.85	P < 0.0001	93.50	91.95 – 94.74
Detection method in stool	**Microscopy**	95	20.32	17.80–22.96	10813.55	P < 0.0001	99.13	99.07 – 99.19
	PCR	3	17.57	8.07–29.75	15.81	P = 0.0004	87.35	64.15 – 95.53
Study setting	**hospitals**	84	22.69	19.55–25.99	12965.76	P < 0.0001	99.36	99.32 – 99.40
	hospitals / primary schools pupils	3	17.66	10.34–26.43	68.38	P < 0.0001	97.08	94.14 – 98.54

	primary school pupils	3	9.68	7.17–12.52	8.89	P = 0.0118	77.49	26.97 – 93.06
	foodhandlers	3	7.79	1.36–18.83	24.08	P < 0.0001	95.85	88.14 – 98.55
	villages	2	17.85	4.59–37.25	41.60	P < 0.0001	97.60	94.09 – 99.02
	nursery schools / children from some houses	1						
Year of study	**<1990**	1						
	>=1990–<=1999	4	5.98	3.72–8.73	25.73	P < 0.0001	88.34	72.63 – 95.03
	>=2000–<=2009	46	26.68	22.12–31.51	8143.53	P < 0.0001	99.45	99.40 – 99.49
	>=2010–<=2017	38	18.46	14.28–23.04	3758.65	P < 0.0001	99.02	98.89 – 99.12
Province	**Al-Anbar**	2	16.15	2.72–37.73	200.94	P < 0.0001	99.50	99.14 – 99.71

	Al-Najaf	5	26.80	11.96–44.98	175.82	P < 0.0001	97.73	96.39 – 98.56
	Babylon	12	15.98	13.24–18.93	109.12	P < 0.0001	89.92	84.33 – 93.52
	Baghdad	27	19.51	14.49–25.07	2867.75	P < 0.0001	99.09	98.96 – 99.21
	Basrah	3	17.29	4.43–36.19	142.09	P < 0.0001	98.59	97.55 – 99.19
	Diwaniya	4	13.08	7.46–19.97	25.59	P < 0.0001	88.28	72.46 – 95.01
	Diyala	4	28.02	13.28–45.72	361.20	P < 0.0001	99.17	98.78 – 99.43
	Duhok	3	20.32	10.05–33.07	92.35	P < 0.0001	97.83	95.92 – 98.85
	Erbil	5	28.34	15.89–42.76	287.69	P < 0.0001	98.61	97.94 – 99.06

	Karbala	6	19.43	9.07–32.54	1121.22	P < 0.0001	99.55	99.43 – 99.65
	Kirkuk	8	14.88	7.69–23.92	411.34	P < 0.0001	98.30	97.66 – 98.76
	Ninevah	3	19.43	8.63–33.27	128.04	P < 0.0001	98.44	97.23 – 99.12
	Saladin	6	27.33	14.91–41.87	365.82	P < 0.0001	98.63	98.06 – 99.04
	Sulaimani	2	22.16	3.04–51.980	62.21	P < 0.0001	98.39	96.43 – 99.28
	Thi-Qar	6	30.12	15.47–47.22	1467.28	P < 0.0001	99.66	99.58 – 99.73
	Wasit	5	20.92	5.71–42.370	756.71	P < 0.0001	99.47	99.30 – 99.60

The proportion of *E. histolytica/dispar* infection was higher in studies used microscopic detection method (20.32%, 95% CI: 17.80%–22.96%) compared to studies used PCR method (17.57%, 95% CI: 8.07%–29.75%).

Most of the studies were hospital based studies reported a prevalence of *E. histolytica/dispar* of 22.69% (95% CI: 19.55%–25.99%). The estimated prevalence across the hospitals / primary schools pupils-based studies was 17.66% (95% CI: 10.34%–26.43%). The pooled prevalence in primary school pupils and residents of villages was 9.68% (95% CI: 7.17%–12.52%) and 17.85% (95% CI: 4.59%–37.25%), respectively. Foodhandlers showed the lowest proportion of infection (7.79%, 95% CI: 1.36%–18.83%). There was one nursery schools / children from some houses-based study.

According to the subgroup of study year, there was one study conducted before 1990, the pooled prevalence was 5.98% (95% CI: 3.72%–8.73%) between 1990 and 1999, then increased into 26.68% (95% CI: 22.12%–31.51%) between 2000 and 2009, lastly, decreased into 18.46 (95% CI: 14.28%–23.04%) between 2010 and 2017.

On the basis of provinces, the highest pooled prevalence was observed in the province of Thi-Qar (30.12%, 95% CI: 15.47%–47.22%), while the lowest pooled prevalence was in the province of Diwaniya (13.08%, 95% CI: 7.46%–19.97%).

Fig 3. Funnel plots of the proportion prevalence of *E. histolytica/dispar* in Iraq.

Discussion

This the first systematic review and meta-analysis to estimate the nationwide prevalence of *E. histolytica/dispar* in Iraq. The findings of this study could have important implications to develop prevention and control strategies for amebiasis.

This study showed that the overall prevalence of *E. histolytica/dispar* in Iraq was 20.61%. The *E. histolytica/dispar* prevalence in Iraq is higher than that reported in the United States and Australia which were 7% and 2.9% respectively [108,109]. The prevalence of *E. histolytica/dispar* in Iraq is closer to the prevalence of 23.1% in Pakistan [110] and 19.2% in United Arab Emirates [111], but lower than the estimated prevalence in two neighboring countries, Turkey and Iran which were 1.5% and 1.0% respectively [112,113].

The infection with *E. histolytica* is acquired through the ingestion of cysts from fecally contaminated food or water. Therefore in developing countries, *E. histolytica* is a waterborne and foodborne parasitic protozoa. In Iraq, the most probable sources of *E. histolytica* infection may be due to the contamination of different sources of drinking water with human sewages, as a result of direct dumping of untreated sewage into rivers or leaking sewage pipes or septic tanks resulting in contaminated drinking water network and ground water. In Baghdad city, the capital of Iraq, the contamination proportion of tap water and sewage with *E. histolytica* were 10% and 30% respectively [114].

This meta-analysis showed that the infection rate was higher in males than females in Iraq. This finding is consistent with a previous study of gender distribution in which the reports of invasive amebiasis and population-based studies demonstrated a higher proportion of men than women, whereas asymptomatic infection with *E. histolytica* is equally distributed between males and females [115]. Another study indicated that serum from women had a higher ability to kill *E. histolytica* trophozoites than serum from men and this killing took place via complement [116].

In terms of detection method in stool, the pooled prevalence of microscopy was higher than that of PCR, because microscopic examination of stools does not distinguish *E. dispar* from *E. histolytica*. PCR methods are used to differentiate *E. histolytica* from *E. dispar*. Hence, PCR methods have led to more reliable results compared to microscopy.

In the present study, the maximum prevalence rate of 22.69% occurred in hospital based studies. The hospital setting cases may have intestinal symptoms and require clinical examination in the clinic or hospital to diagnose the causes of these symptoms, and they were routinely to be tested for intestinal parasites compared with cases from the community setting.

Residents of villages presented high prevalence of *E. histolytica* (17.85%). This may reflect the shortages of purified water supplies and compromised sanitation in the villages of Babylon and Basrah provinces where the samples of stools were taken and examined. The contamination of drinking water with *E. histolytica* was reported to be 8% in Basrah marshes villages, south of Iraq [117].

The prevalence of *E. histolytica* in primary school pupils was 9.68% and this is due to the lack of purified water supplies and poor hygiene in both schools and pupils. This can be explained by the fact that out of the three studies conducted only on primary schoolchildren, two studies were carried out among schoolchildren in rural areas [20,87] and one study with samples from rural and low socioeconomic urban areas [64].

Relatively the lowest prevalence (7.79%) has been observed among foodhandlers, this can be attributed to the routine mandatory screening and treatment of registered foodhandlers by the ministry of health. However, the prevalence of *E. histolytica* infection was much higher than in the neighboring countries Jordan and Turkey (0.11% and 0.3% respectively) [118,119].

The majority of included studies were published online after 2003 since there was no internet access before that in Iraq. The prevalence of *E. histolytica* increased from 5.98% in 1990–1999 to 26.68% in 2000–2009. The small number of published researches in 1990–1999 could be the reason for the lower prevalence. The highest prevalence of *E. histolytica* was related to the years 2000–2009, this can be due to the sectarian violence during 2006-2008 in Iraq that led to the emigration and internal displacement of millions and this was associated with poor sanitation and limited access to health services. The overall prevalence *E. histolytica* in Iraq has reported a decrease (18.46%) in 2010–2017 compared to 26.68% in 2000–2009. This relative decrease could be an indicator of improvement in the sanitation and water supplies quality. In spite of that, this may suggest that *E. histolytica* is still considered as a health issue in Iraq.

The prevalence of *E. histolytica* varied among the provinces. The highest prevalence was observed in Thi-Qar province (30.12%). This may be because only individuals from hospitals were analyzed and this increased the rate of prevalence. The largest fraction of identified studies (27 of the 99 included studies) were carried out in Baghdad, the province with the highest density of population in Iraq and a population of more than 7 million, the estimated pooled prevalence of *E. histolytica* was 19.51%, this represents a challenge for health workers. The lowest pooled prevalence (13.08%) of *E. histolytica* in the country was reported from Diwaniya province. This may be because of the low number of studies from this province and the studies were conducted in individuals from hospitals (one of them used PCR for detection of *E. histolytica*) and foodhandlers, the group with the lowest rate of infection. Even if the disease is known to be prevalent to Iraq, no study was reported from provinces of Maysan and Muthanna in the south of Iraq.

There was high heterogeneity in prevalence infection with *E. histolytica* in Iraq among the included studies. This is revealing the variations that could have been due to population of the study, detection method, province and year of study.

Limitations

The study has some limitations. Most of the studies did not report the gender of the persons infected with *E. histolytica/dispar*, thus making it difficult to evaluate the effect of this important factor on the prevalence of infection with *E. histolytica/dispar* in Iraq. In addition, most surveys used microscopic diagnosis, which could not differentiate the pathogenic *E. histolytica* from the nonpathogenic *E. dispar* and these studies may have overestimated the rates of the prevalence. In this meta-analysis, there were few studies that assessed the prevalence of *E. histolytica/dispar* in community populations, most of the studies were hospital based which increased the risk of bias. Another limitation of this study is that all provinces of the country have not been covered in the eligible studies, therefore the pooled prevalence of two provinces have not been estimated and this could affect the overall pooled prevalence of infection with *E. histolytica/dispar* in Iraq.

In conclusion, the overall prevalence of infection with *E. histolytica/dispar* was 20.61% in the population of Iraq and the prevalence of the disease has dropped since 2010. Therefore, in order to reduce the infections of amebiasis in humans, preventive measures including educational programs, proper sanitation, monitoring of foodhandlers and preventing fecal contamination of water, vegetable and fruits should be recommended. Further studies are needed for the molecular diagnosis of intestinal *E. histolytica* to differentiate the pathogenic from nonpathogenic *Entamoeba* species. Also diagnosis of extraintestinal amebiasis in patients is required to estimate the epidemiology of the disease at a national level.

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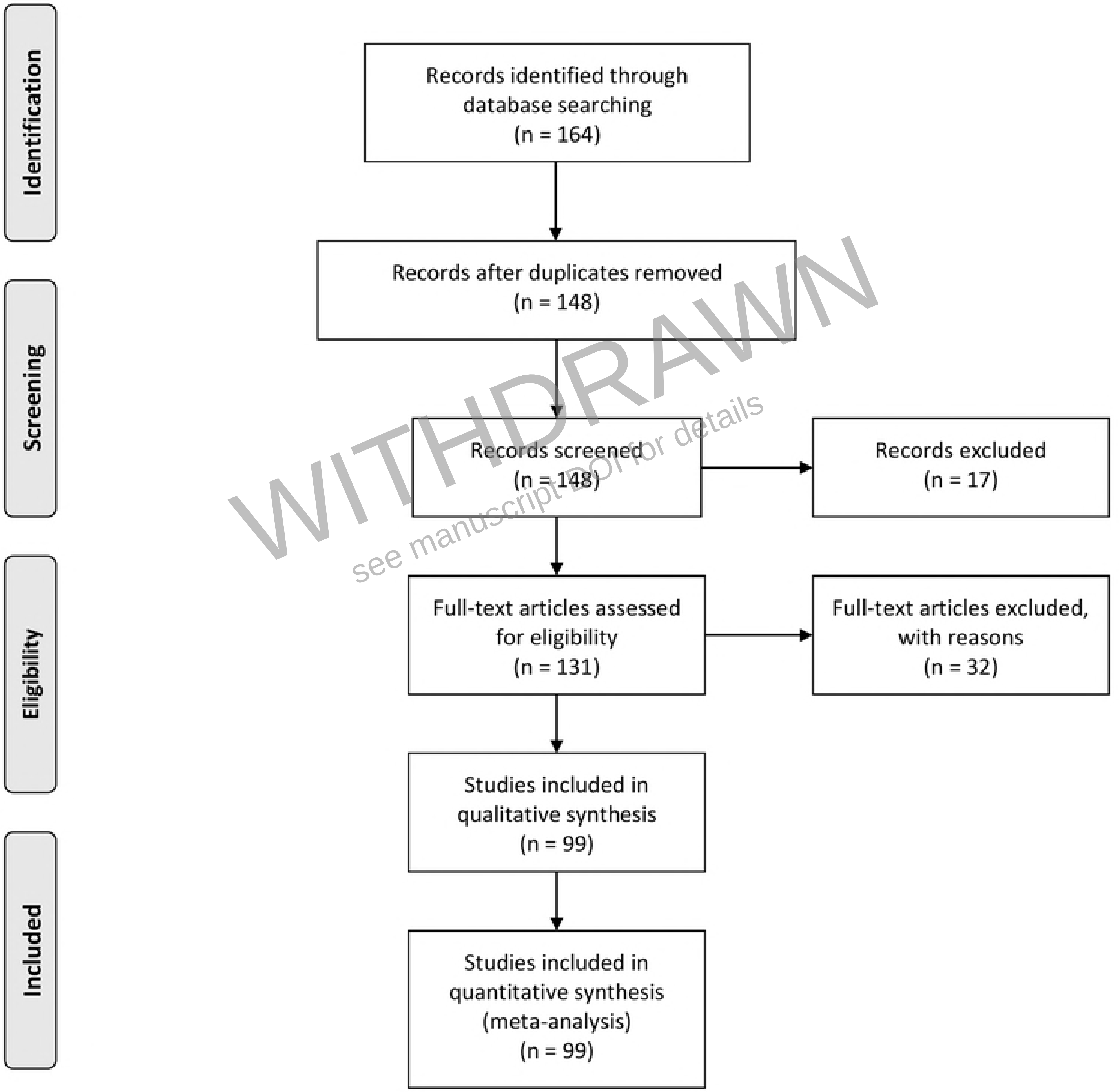
Supporting information

S1 Checklist. PRISMA checklist. PRISMA guideline (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).

S1 Diagram. PRISMA flow diagram. Flow diagram of study selection process for systematic review and meta-analysis.


Identification
Screening
Eligibility
Included
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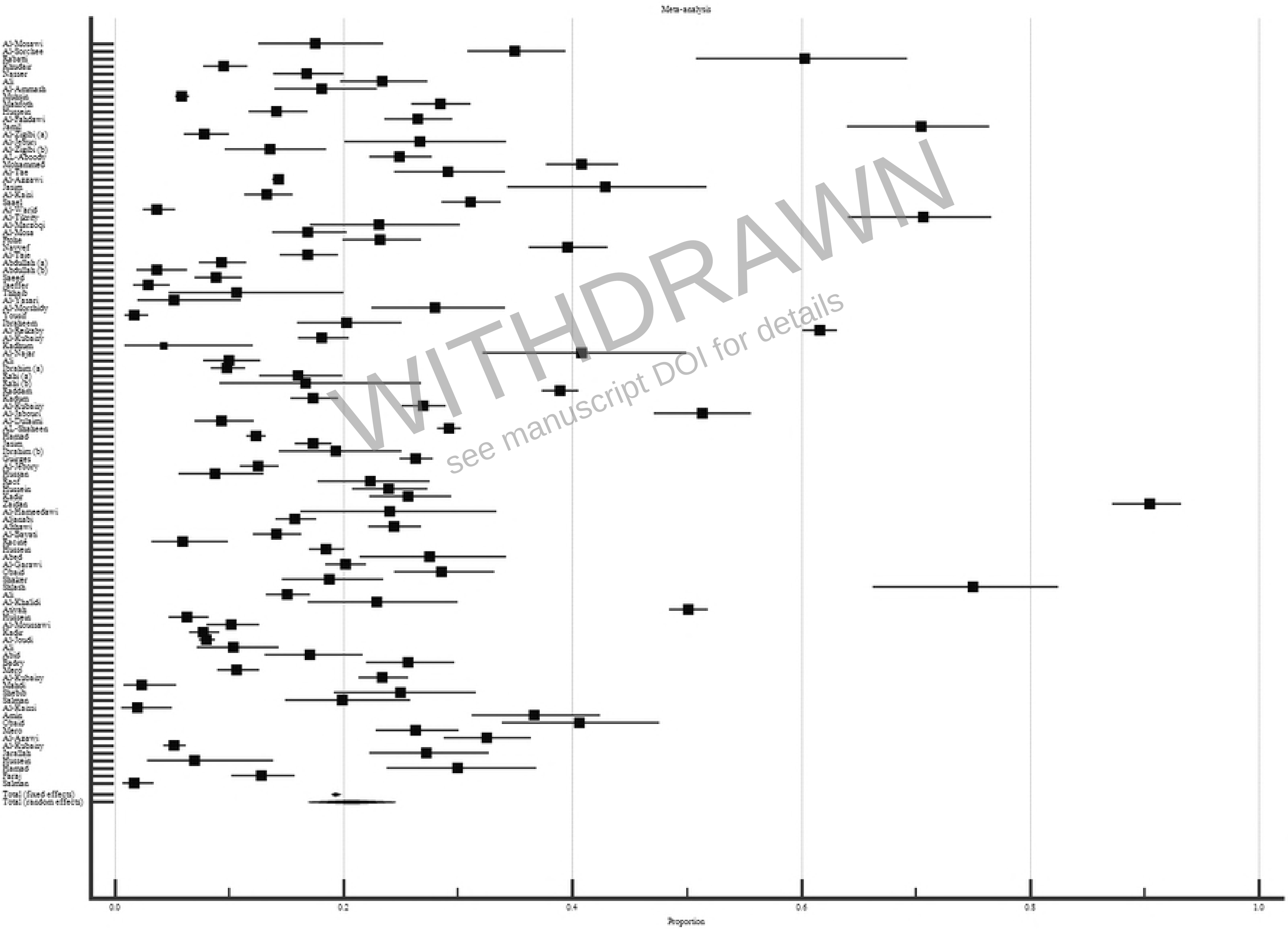
Records after duplicates removed (n = 148)
Records screened (n = 148)
Records excluded (n = 17)
Full-text articles assessed for eligibility (n = 131)
Full-text articles excluded, with reasons (n = 32)
Studies included in qualitative synthesis (n = 99)
Studies included in quantitative synthesis (meta-analysis) (n = 99)


Meta-analysis
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Total (random effects)
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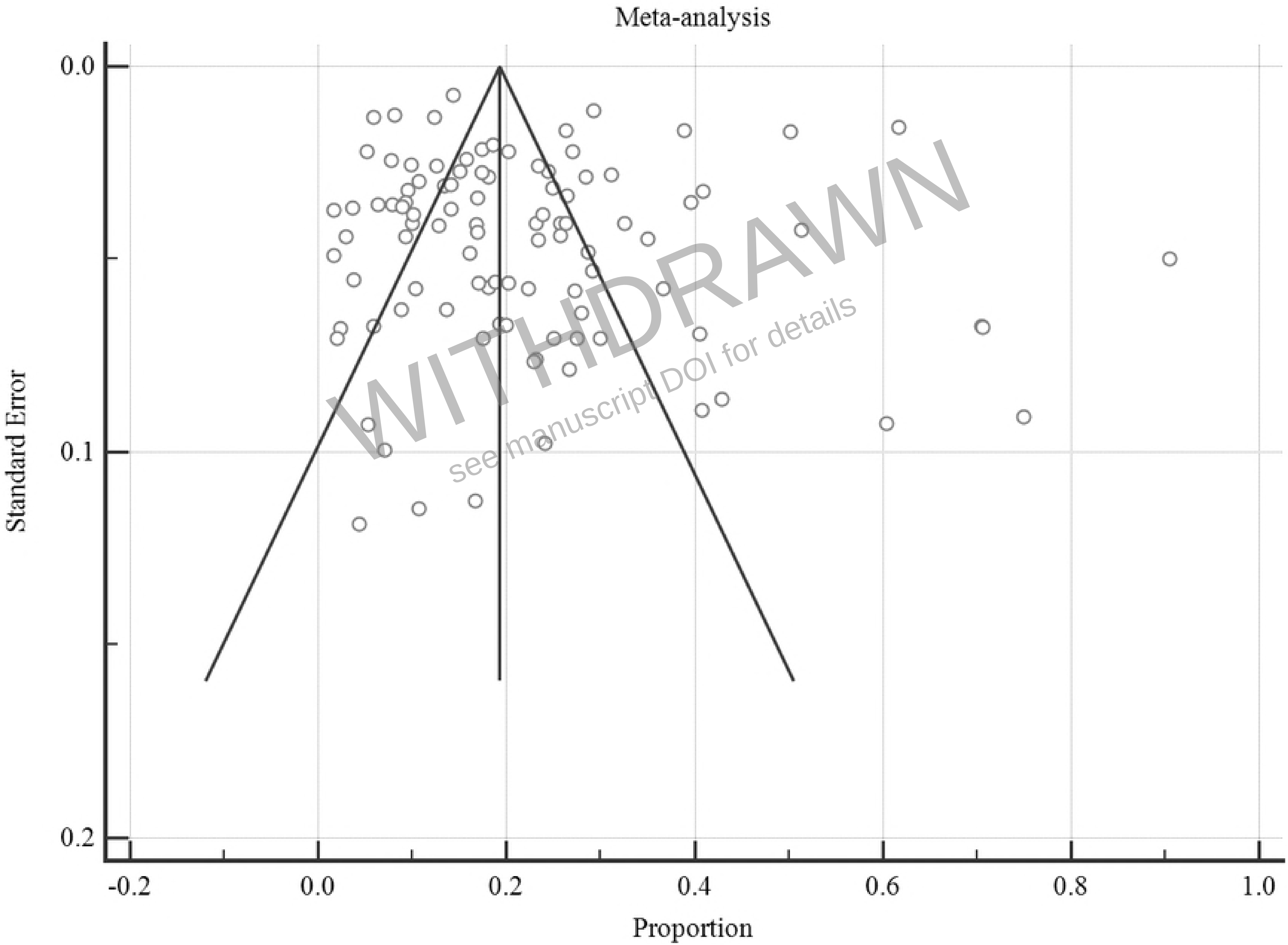
0.2
0.4
0.6
0.8
1.0
Proportion


Meta-analysis
Standard Error
0.0
0.1
0.2
-0.2
0.0
0.2
0.4
0.6
0.8
1.0
Proportion