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Update on the Seroepidemiology of Human Cystic Echinococcosis and Associated Risk Factors in Iran: A Systematic Review and Meta-Analysis

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ABSTRACT

Background and Aims: Cystic echinococcosis (CE) poses a significant public health challenge in developing countries, including Iran. This systematic review and meta-analysis aim to enhance our understanding of CE prevalence by providing an updated assessment of the general prevalence of human CE in Iran through a comprehensive review of the literature.

Methods: PubMed, Scopus, Web of Science, Google Scholar, Magiran, and Scientific Information Database (SID) databases were searched for relevant literature published between January 1990 and December 2023. All peer-reviewed original papers evaluating the seroprevalence of human CE were included. Meta-analysis was performed using a random-effects model with 95% confidence intervals (CIs). Heterogeneity among the included studies was assessed using Cochran's Q and I^2 tests. The funnel plot and Egger's test were used to evaluate potential publication bias.

Results: Sixty-eight studies met the inclusion criteria. The overall seroprevalence of human CE in Iran's general population was 4% (95% CI 3%−6%). Significant differences in seropositivity to human CE were observed among age groups, urban versus rural residence, diagnostic methods, and in relation to the presence of dogs at home or on farm. Substantial heterogeneity was observed across the included studies ($I^2 = 99.47\%$; $p < 0.001$). The funnel plot and Egger's test revealed considerable publication bias (Egger's test; $p < 0.001$).

Conclusion: Our findings demonstrate that CE remains prevalent in Iran, necessitating intensified health interventions and the development of targeted strategies for prevention and control. Recommendations include deworming dogs with praziquantel and vaccination of sheep with recombinant EG95 protein, removing raw offal or carcasses from the diet of dogs, hand washing, fencing of slaughterhouses with offal disposal systems, community participation for the control program and screening strategies for the diagnosis of asymptomatic cases and their timely treatment.

Summary

- The overall prevalence of human cystic echinococcosis (CE) in the general population of Iran is 4%.
- The seroprevalence of human CE is significantly associated with age, residence, diagnostic methods and the presence of dogs at home or on farms.
- The seroepidemiology of human CE in Iran has not decreased over time.
- Findings emphasize the need for increased awareness and effective control strategies to combat human CE.

1 | Introduction

Cystic echinococcosis (CE) is a neglected chronic parasitic zoonotic disease caused by the larval stage of the tapeworm *Echinococcus granulosus* (*E. granulosus*), belonging to the family Taeniidae. The life cycle of *E. granulosus* involves domestic and wild canids as definitive hosts (harboring the adult form) and various ungulates such as sheep, cattle, pigs, and goats as intermediate hosts that harbor the larval form or hydatid cysts [1]. Humans become infected through accidental ingestion of *E. granulosus* eggs shed in the feces of infected canids, resulting in CE [1]. The incubation period of CE is prolonged with many infected individuals remaining asymptomatic for years or exhibiting nonspecific symptoms, leading to incidental diagnosis [2]. Consequently, the World Health Organization (WHO) classifies CE as a "Neglected Tropical Disease" due to its significant underestimation [3]. CE is endemic in regions where cattle and sheep are raised [1]. The global annual human incidence of CE is approximately 50 cases per 10,000 population. According to the WHO Foodborne Disease estimates, echinococcosis results in 19,300 deaths and 871,000 disability-adjusted life years (DALYs) annually [4].

Iran is a major hotspot for CE due to favorable climatic conditions and reliance on agriculture and animal husbandry. Infection rates among definitive hosts (dogs, foxes, jackals, wolves) and intermediate hosts (slaughtered livestock) have been reported as 23.6% and 13.9%, respectively [5, 6]. About 1% of hospital surgeries in Iran involve CE [5].

Diagnosis relies on clinical findings supported by serological testing and imaging techniques. Considering the health and economic significance of human CE in Iran, various methods have been employed to estimate the prevalence of human CE in different provinces, including ultrasonography, serological and surgery methods, as well as reporting surgical cases of CE. While imaging methods offer higher diagnostic sensitivity, serological approaches remain the preferred tool for large-scale population screening due to their cost-effectiveness [7, 8].

Since the last meta-analysis in 2019 (including studies published from 1990 to 2017) on the prevalence of human CE in Iran [9], numerous studies have focused on CE in different provinces, which have been incorporated into this updated meta-analysis. The accumulation of more recent evidence not only necessitates an updated meta-analysis but also enhances the generalizability of the results at the community level. On the other hand, the prevalence of CE in different regions depends on various biotic and abiotic factors. To the best of the authors' knowledge, there is not yet a comprehensive study that pools all evidence to provide estimates of risk. To address the gap in knowledge, we conducted a systematic review and meta-analysis to estimate the seroprevalence and associated risk factors of human CE in the general population of Iran. The information presented in our systematic review is the critical first step for healthcare professionals to develop health programs and formulating appropriate strategies for human CE prevention and control.

2 | Materials and Methods

2.1 | Study Design

The present systematic review and meta-analysis were performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Table S1) [10].

2.2 | Search Strategy

The literature search focused on the seroepidemiology of CE in the general Iranian population. A comprehensive search to identify all relevant studies was conducted across four English databases (PubMed, Scopus, Web of Science, and Google Scholar) and two Persian databases (Magiran and Scientific Information Database [SID]) between January 1990 and December 2023. This review was conducted using medical subject headings (MeSH) terms in combination or alone: (*E. granulosus* OR echinococcosis OR hydatidosis) AND (prevalence OR epidemiology OR seroepidemiology OR seroprevalence) AND Iran. Furthermore, we manually searched the reference lists of retrieved articles and existing reviews for additional studies.

2.3 | Inclusion and Exclusion Criteria

The inclusion criteria were peer-reviewed original articles and cross-sectional studies that estimated the seroepidemiology of CE in the Persian general population. Studies on patients with suspected CE, retrospective studies based on hospital records, studies reporting the prevalence of *Echinococcus multilocularis*, case reports, reviews, meeting reports, letters to editors, abstracts, case series, congress articles, literature reporting inadequate data, articles in languages other than Persian and English, and those with confusing or unclear analyses were excluded.

2.4 | Study Selection

The articles retrieved from the systematic search were imported into EndNote (version X7) and checked for duplicates. Subsequently, two independent reviewers (A.B. and A.G.) evaluated all publications individually based on their titles and abstracts for study selection. Discrepancies were resolved through discussion and consensus with other investigators.

2.5 | Data Extraction

For each eligible study, the following variables were extracted into a preprepared Microsoft Excel spreadsheet: first author's name, publication year, implementation year, study province, geographical location, patient demographic details (gender, age, educational level, occupation, area of residence), diagnostic methods, sample size, number of positive samples for CE and associated risk factors (such as contact with dogs and soil, and washing methods for vegetables). Two trained members of our research group (A.R.G. and S.A.K.) independently conducted the data extraction, while two others reviewed the data (A.B. and A.D.). Any disagreements were resolved through consensus between the two reviewers or by involving a third researcher.

2.6 | Quality Evaluation

We used the Joanna Briggs Institute (JBI) checklist for prevalence studies to assess the methodological quality of the included studies. This tool comprises nine items (questions) concerning the sampling process, analytical methods for controlling confounding, study population, measurement tools, and response rate. Each item scored 1 for a "Yes" answer, and 0 for other responses, including "No," "Unclear," and "Not applicable." Based on the scores, studies were categorized into high-quality (7−9 points), moderate-quality (4−6 points), and low-quality (0−3 points) groups. Quality assessments were carried out independently by two authors (H.E. and S.A.K.), with a third author (A.B.) involved in resolving any disagreements.

2.7 | Meta-Analysis

The meta-analysis was conducted using STATA version 17 (STATA Corp., College Station, Texas, USA). To estimate the weighted-mean prevalence of human CE across the included studies, we employed a random-effects model with 95% confidence intervals (CIs) for pooling the studies. Heterogeneity among studies was assessed using Cochran's *Q*-test and the inverse variance index (I^2) [11]. Additionally, subgroup analysis was performed to explore sources of heterogeneity. This analysis computed the pooled seroprevalence of CE based on characteristics such as gender, age group, education, residence, vegetable washing methods, and contact with soil or dogs. A chi-square test was utilized to identify differences within subgroups. Furthermore, sensitivity analysis was conducted to evaluate the influence of individual studies on the pooled prevalence estimates. Meta-regression was performed to assess the impact of time (1990−2023) and sample size as factors affecting heterogeneity on prevalence. Publication bias was evaluated using Begg's Funnel plot and Egger's regression test. A significance level of 0.05 was set for all analyses.

3 | Results

3.1 | Study Selection

The systematic search and article selection process for the meta-analysis is illustrated in Figure 1 and Table S2. Initially, a total of 960 studies were identified. After removing 310 duplicate studies and excluding 608 irrelevant studies through a detailed screening of titles and abstracts, 42 studies remained for eligibility screening. Among these, 9 studies were excluded for various reasons, as detailed in Figure 1. In total, 33 studies met our inclusion criteria, in addition to the 35 studies reviewed by [9] and [5], resulting in a comprehensive total of 68 studies in our review.

3.2 | Features of the Selected Studies

Table 1 presents the general characteristics of the studies that were ultimately included in this analysis. The cross-sectional studies were published between September 1990 and February 2023. These studies originated from 25 provinces across the country, with Ardabil contributing the most reports (five reports). Six provinces, namely Bushehr, Hormozgan, Yazd, Gilan, South Khorasan, and Qazvin, did not present any separate reports on the seroepidemiology of human CE. Sample sizes varied significantly, ranging from 91 to 4138 individuals, totaling 65,893 analyzed individuals. The seropositivity rate for CE ranged from less than 1%−32%. The most frequently employed serological test was the enzyme-linked immunosorbent assay (ELISA) (54 studies, 79.4%), followed by the indirect fluorescent antibody (IFA) method (6 studies, 8.9%), counter immunoelectrophoresis (CIEP) (2 studies, 2.9%), and indirect haemagglutination (IHA) method (2 studies, 2.9%). Two studies (2.9%) used both ELISA and IFA, while one study (1.5%) employed ELISA and CIEP methods. Finally, one study (1.5%) employed ELISA, IHA, and western blot analysis.

3.3 | Overall Effects

The overall prevalence rate of CE infection in humans, as determined by the random effects model in the meta-analysis, was 4% (95% CI 3%–6%) (Figure 2). The heterogeneity among studies was substantial ($I^2 = 99.47\%$). Figure 3 displays the seroepidemiology of human CE in the general population of Iran based on the provinces studied. Sensitivity analysis showed that none of the studies substantially affected the pooled seroprevalence of human CE and we can include all studies in the meta-analysis (Figure S1).

3.4 | Quality Assessment

The evaluation of article quality revealed that 38 out of 68 studies scored 4–6, indicating moderate quality, while 30 studies scored 7–9, indicating high quality (see Table 1).

3.5 | Factors Associated With CE Infection in Iran

Ten factors related to CE infection in humans were examined, including gender, age, education level, residence, diagnostic method, geographical zone, occupation, contact with dogs, contact with soil, and the method of washing vegetables.

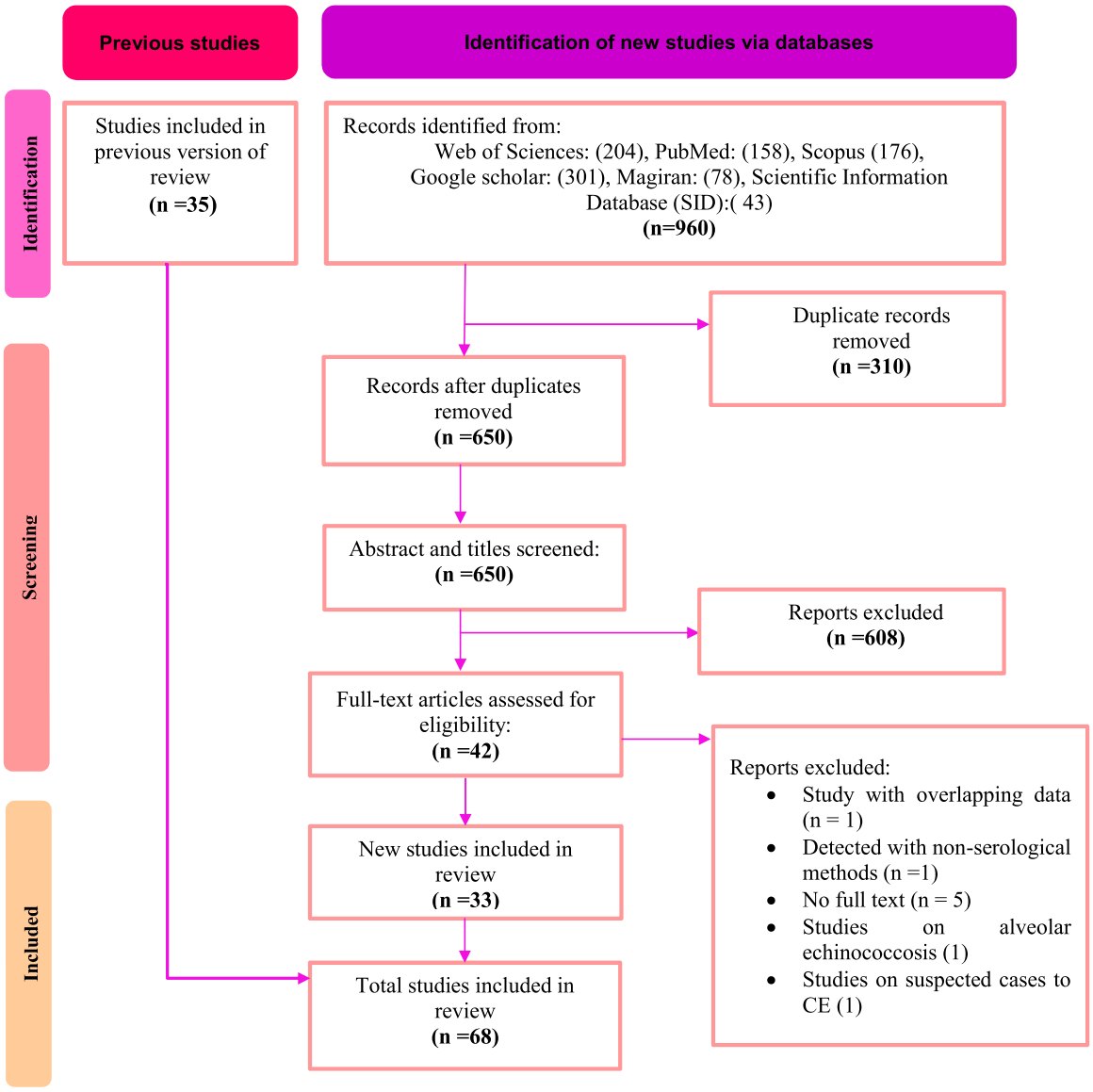

FIGURE 1 | Flowchart of the study design process.

The overall prevalence was 5% (95% CI 3%–6%) in males and 4% (95% CI 3%–5%) in females ($p = 0.51$). Among individuals aged 0−19 years, the prevalence was 2% (95% CI 1%–3%), while it was 4% (95% CI 2%–6%) in individuals aged 20−39, 5% (95% CI 3%–6%) in those aged 40−59, and 4% (95% CI 2%–6%) in individuals aged 60 years and older ($p = 0.04$) (see Table 2).

The estimated prevalence of human CE was 3% (95% CI 2% −5%) in urban settings, while it was 6% (95% CI 3%−10%) in rural areas and 8% (95% CI 4%−12%) among nomadic populations ($p = 0.04$). This meta-analysis showed that having a dog at home/on the farm/at work as a sheep-dog ($p = 0.05$) was significantly associated with the seroprevalence of CE.

Higher prevalence was obtained when using the ELISA test with 5% (95% CI 3%−6%), compared to the CCIEP (4%, 95% CI 1%−8%), IFA (3%, 95% CI 2%−5%), IHA (3%, 95% CI 2%−4%), and WB (1%, 95% CI 0%−1%) ($p < 0.001$). There was no significant difference in the prevalence of human CE based on the method of washing vegetables ($p = 0.82$), and contact with soil ($p = 0.30$) and geographical zone ($p = 0.06$).

3.6 | Meta-Regression

There were no significant associations between the seroprevalence of human CE and publication year (Reg Coef = −0.0002, $p = 0.55$) or sample size (Reg Coef = 4.74, $p = 0.76$), indicating that these quantitative variables may not affect the seroprevalence of CE in the general population of Iran (Figure 4).

3.7 | Publication Bias

The presence of publication bias was evaluated subjectively using funnel plots and objectively using the Egger's test. The systematic review and meta-analysis revealed significant publication bias ($p \leq 0.001$) (Figure 5).

TABLE 1 | Characteristics of studies included in the present review.

No	References	Sampling time	Study site	Population	No tested	No positive	Seroprevalence, % (95% CI)	Laboratory diagnostic method	Quality score
1	[12]	—	Ilam	The community level	1200	27	2 (1–3)	ELISA	Moderate
2	[13]	2020	Sistan and Baluchestan/ Zahedan	Health centers	773	28	4 (2–5)	ELISA	High
3	[14]	—	Ilam	The community level	3000	37	1 (1–2)	ELISA	Moderate
4	[15]	—	Kurdistan/Sanandaj, Divandareh	The community level	1114	81	7 (6–9)	IFA	Moderate
5	[16]	2006	Tehran/Tehran	Blood transfusion center	1100	18	2 (1–2)	ELISA	Moderate
6	[17]	2020	—	Military personnel	205	30	15 (10–19)	ELISA	High
7	[18]	2021	Sistan and Baluchestan/ Zabol, Zahedan, Iranshahr, Saravan, Chabahar	Farmers and Ranchers	500	4	1 (0–2)	CCIEP	High
8	[19]	1991	Hamadan/Hamadan	Health centers	1530	46	3 (2–4)	IFA	Moderate
9	[20]	—	Isfahan/Kashan	The community level	500	12	2 (1–4)	IHA	Moderate
10	[21]	2018	West Azerbaijan/Urmia	Municipal workers (gardeners and sweepers)	220	5	2 (0–4)	ELISA	Moderate
11	[22]	—	Arak/Arak	Medical diagnostic laboratories, health centers	578	20	3 (2–5)	ELISA	Moderate
12	[23]	—	Golestan/Gorgan, Gonbad-e Kavus, Aliabad-e Katul and Kordkuy	Health centers	1024	24	2 (1–3)	ELISA, IFA	Moderate
13	[24]	2017	Hamadan/Hamadan	Health centers	1000	4	0 (0–1)	ELISA	High
14	[25]	2017	Hamadan/Kaboodarahang	The community level	1232	12	2 (0–2)	ELISA	High
15	[26]	2015	Khuzestan	The community level	410	20	5 (3–7)	ELISA	High
16	[27]	2016	Lorestan/Aligudarz and Sepiddasht	The community level	315	18	6 (3–8)	ELISA	Moderate
17	[28]	2011	Alborz/Najmabad, Mahdasht, Taleghan, Sira, Chaharbagh, and Hyve	The community level, Blood transfusion center	680	23	3 (2–5)	ELISA	Moderate
18	[29]	—	Eest Azerbaijan/Sarab	The community level	280	8	3 (1–5)	IFA	Moderate

(Continues)

TABLE 1 | (Continued)

No	References	Sampling time	Study site	Population	No tested	No positive	Seroprevalence, % (95% CI)	Laboratory diagnostic method	Quality score
19	[30]	2022	Arak/Arak	Health centers	456	6	1 (0–2)	ELISA	High
20	[31]	2019	Mazandaran/Qaemshahr	Health centers	403	11	3 (1–4)	ELISA	Moderate
21	[32]	2016	Tehran/Tehran	Medical diagnostic laboratories	909	7	1 (0–1)	ELISA	Moderate
22	[33]	2008	Isfahan/Kashan	Health centers	361	11	3 (1–5)	ELISA, IFA	High
23	[34]	2018	Kermanshah/Sarpol-e Zahab	Health center	736	8	1 (0–2)	ELISA	High
24	[35]	2019	East Azarbaijan/Khoda Afarin	Health center	295	12	4 (2–6)	ELISA	High
25	[36]	2019	Hamadan/Hamadan	Medical diagnostic laboratories	300	16	5 (3–8)	ELISA	High
26	[37]	2015	Lorestan/Doroud	The community level	927	25	3 (2–4)	ELISA	High
27	[38]	—	Tehran/Shemiranat	Health centers	427	1	0 (0–1)	IFA	Moderate
28	[39]	2017	Golestan/Gorgan	Medical diagnostic laboratories	612	16	3 (1–4)	ELISA	High
29	[40]	2009	East-Azarbaijan/Bonab, Sarab, Marand, Azarshahr, Tabriz, Maragheh, Mianeh, Ahar	The community level	1500	19	1 (1–2)	ELISA	Moderate
30	[41]	2006	Kurdistan	The community level	1979	22	1 (1–2)	ELISA	Moderate
31	[42]	2018	Semnan/Semnan, Sorkheh	Health centers	957	48	5 (4–6)	ELISA	High
32	[43]	2002	Zanjan/Zanjan	The community level	2367	71	3 (2–4)	ELISA	Moderate
33	[44]	2008	Kerman/Kerman	The community level	1062	77	7 (6–9)	ELISA	High
34	[45]	2018	Sistan and Baluchestan	Health centers	830	0	0 (0–0)	ELISA	Moderate
35	[46]	2010	Ardabil/Meshkinshahr	Health centers	670	12	2 (1–3)	ELISA	Moderate
36	[47]	2020	Ardabil/Parsa-bad, Nir, Meshkinshahr, Khalkhal	The community level	952	42	4 (3–6)	ELISA	Moderate
37	[48]	—	Isfahan/Isfahan	Health centers	635	7	1 (0–2)	ELISA	Moderate
38	[49]	2016	Khuzestan/Behbahan	The community level	180	5	3 (0–5)	ELISA	Moderate
39	[50]	2020	Sistan and Baluchestan/ Zahedan	Health centers	551	22	4 (2–6)	ELISA	High

(Continues)

TABLE 1 | (Continued)

No	References	Sampling time	Study site	Population	No tested	No positive	Seroprevalence, % (95% CI)	Laboratory diagnostic method	Quality score
40	[51]	—	Ardabil/Moghan plain	The community level	2001	184	9 (8–10)	ELISA	High
41	[52]	—	Ardabil/Moghan plain	The community level	1003	92	9 (7–11)	ELISA	Moderate
42	[53]	—	Ardabil/Moghan plain	The community level	2003	164	8 (7–9)	ELISA	Moderate
43	[54]	2007	Kerman/Shahdad and Chatroud of Kerman	The community level	451	37	8 (6–11)	ELISA	High
44	[55]	2014	Shahrebabk, Kerman	The community level	536	1	0 (0–1)	ELISA	Moderate
45	[56]	2016	Kohgiluyeh and Boyer-Ahmad/Boyer-Ahmad	The community level	1005	81	8 (6–10)	ELISA	High
46	[57]	2019	Kurdistan/Sanandaj	Health centers	500	11	2 (1–3)	ELISA	High
47	[58]	—	Ardabil, West Azerbaijan, Ease Azerbaijan/Sarab, Meshkinshahr, Moghan plain, Urmia	The community level	852	30	4 (2–5)	IFA	Moderate
48	[59]	—	Isfahan/Faridan	The community level	1000	39	4 (3–5)	IHA	Moderate
49	[60]	2016	Khuzestan	The community level	314	3	1 (0–2)	ELISA	Moderate
50	[61]	—	Khuzestan/Izeh, Masjed Soleiman, Behbahan, Shush	The community level	3446	475	14 (13–15)	ELISA	High
51	[62]	2014	Zanjan/Abhar	The community level	810	1	0 (0–0)	ELISA	Moderate
52	[63]	2012	Qom	The community level	1564	25	2 (1–2)	ELISA	High
53	[64]	1995	South of Iran	The community level	1000	137	14 (12–16)	ELISA, CIE	Moderate
54	[65]	—	Fars/Kavar	The community level	1500	131	9 (7–10)	ELISA	High
55	[66]	2018	East Azerbaijan/Jolfa	The community level	1296	11	1 (0–1)	ELISA, IHA, WB	High
56	[67]	2014	Fars/Darab, Firooz Abad, Kazeroon, Jahrom, Noor Abad	Blood transfusion center	1068	60	6 (4–7)	ELISA	Moderate
57	[68]	—	Kohgiluyeh and Boyer-Ahmad/Yasuj	Health centers	500	36	7 (5–9)	ELISA	Moderate
58	[69]	—	Fars/Sar Mashhad, ToleSaman, Hossein Abad of Kazeroon	The community level	578	39	7 (5–9)	ELISA	High
59	[70]	1999	Tehran/Shahriar	The community level	1052	62	2 (1–3)	IFA	Moderate

(Continues)

TABLE 1 | (Continued)

No	References	Sampling time	Study site	Population	No tested	No positive	Seroprevalence, % (95% CI)	Laboratory diagnostic method	Quality score
60	[71]	2018	North Khorasan/Bojnurd, Shirvan, Maneh and Samalqan, Faruj, Raz and Jargaran, Garmeh and Jajarm	Health centers	932	37	4 (3–5)	ELISA	High
61	[72]	2012	Kerman/Rafsanjan	The community level	486	9	2 (1–3)	ELISA	Moderate
62	[73]	2007	Fars/Jahrom	Medical diagnostic laboratories	1096	69	6 (5–8)	ELISA	Moderate
63	[74]	2001	Chaharmahal and Bakhtiari	Blood transfusion center, Medical diagnostic laboratories	2524	120	5 (4–6)	CCIEP	Moderate
64	[75]	2012	Mazandaran and Gilan	Greengroceries	160	4	3 (0–5)	ELISA	High
65	[76]	2016	Central Khorasan/Mashhad	Slaughterhouse workers	91	5	5 (1–10)	ELISA	High
66	[77]	—	Ardabil, East Azabaijan, West Azarbaijan, Kurdistan, Ilam, Hamadan, Lorestan	The community level	4138	230	6 (5–6)	ELISA	Moderate
67	[78]	2014	Mazandaran/Neka, Sari, Ghaemshahr, Babol, Babolsar-Amircola, Polasafid-Zirab, Amol, Tonekabon, Ramsar	Health centers	600	190	32 (28–35)	ELISA	High
68	[79]	2011	Lorestan, Khorram Abad	Health centers	617	95	15 (13–18)	ELISA	High

Abbreviations: CCIEP, counter current immunoelectrophresis test; CIE, counterimmunoelectrophoresis test; ELISA, enzyme-linked immunosorbent assay test; IFA, indirect fluorescent antibody test; IHA, indirect hemagglutination test; WB, western blot test.

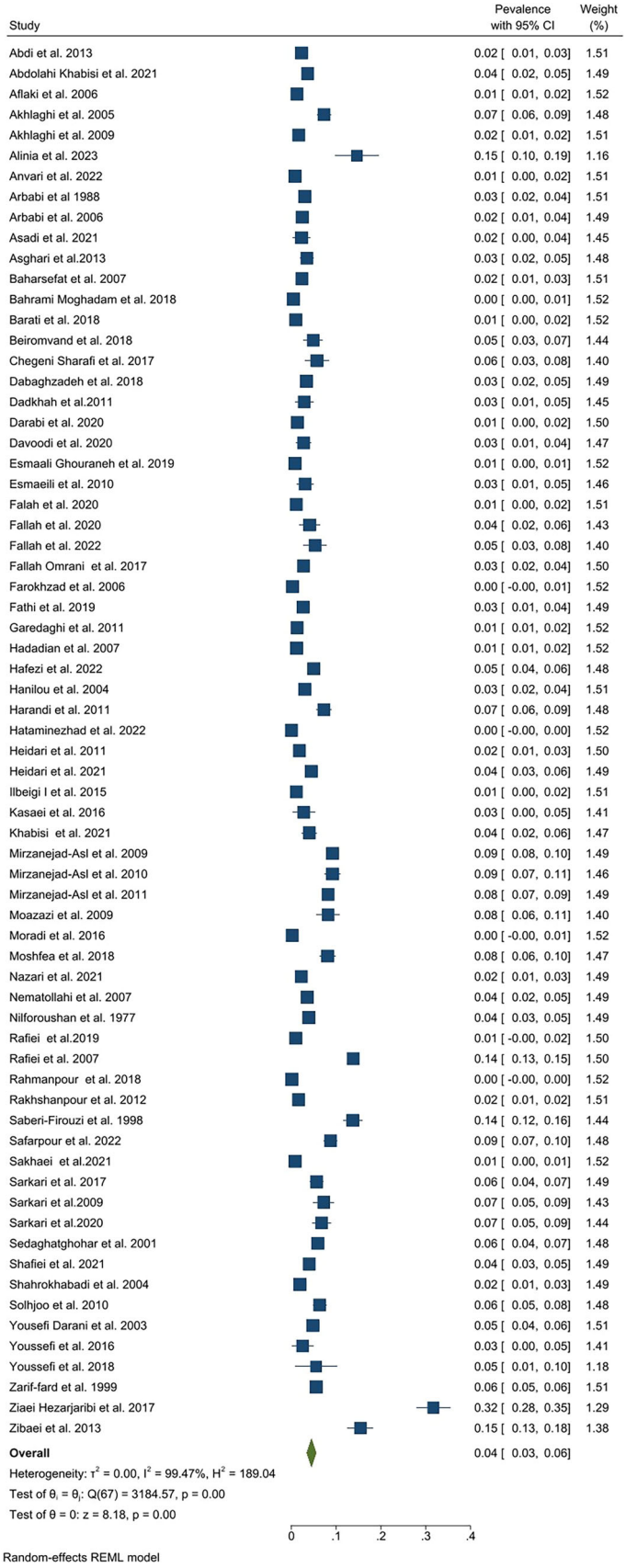

FIGURE 2 | Forest plot of human cystic echinococcosis seroprevalence in the general population of Iran based on articles published between January 1990 and December 2023 (the size of squares represents the relative weight of studies).

FIGURE 3 | Province-based seroprevalence and distribution of articles on human cystic echinococcosis in Iran.

4 | Discussion

The present systematic review and meta-analysis aimed to determine the seroepidemiology of CE, drawing data from 68 eligible prevalence studies including 65,893 participants across 25 provinces in Iran. Several previous systematic reviews and meta-analyses have reported the prevalence of human CE in Iran. The most recent study found a prevalence of 5% within 37 studies conducted from 1990 to 2017 [9]. In contrast, our study revealed a prevalence of 4%, which is lower than the reported range in China (5.66%) [80] and higher than that in Africa (1.7%) [81]. These variations may be attributed to factors such as the number of free-roaming dogs and dog ownership, climatic parameters (temperature, rainfall, and humidity), residents' lifestyles, awareness of echinococcosis prevention, and the effectiveness of local control efforts.

Our investigation found that 85.3% of the included studies employed the ELISA method, while others utilized a broader range of serological techniques. Hydatid fluid, antigen B (AgB), and antigen 5 are the most commonly used sources of antigen for the detection of antibodies in serum. However, the lack of standardization in antigen preparation, varying sensitivities and specificities of the immunodiagnostic tests used, and differences in the strains of the parasite from which antigens have been purified undoubtedly contribute to the variability in estimates of the seroprevalence of CE infection.

Diversity in urban, rural, and nomadic habitats can lead to varying prevalences of parasitic infections. Our study found that nomadism is a risk factor for CE, which is consistent with the findings of a previous meta-analysis conducted in China [80]. An estimated 1.6 million people, or about 2% of Iran's population, are nomadic or semi-nomadic [82, 83]. Many nomads lack

TABLE 2 | Subgroup analyses of the seroprevalence of human CE in general population of Iran among selected studies.

Subgroup	Number of studies	Seroprevalence, % (95% CI)	Heterogeneity[a]			Test for subgroup differences
			Q	I^2	*p* value	
Gender						
Male	54	5 (3–6)	1307.81	99.87	< 0.001	$p = 0.51$
Female	52	4 (3–5)	1459.79	98.37	< 0.001	
Age group						
0–19	19	2 (1–3)	86.15	99.75	< 0.001	$p = 0.04$
20–39	20	4 (2–6)	418.23	99.83	< 0.001	
40–59	20	5 (3–6)	280.19	96.21	< 0.001	
≥ 60	19	4 (2–6)	164.95	99.79	< 0.001	
Educational						
Illiterate	12	4 (3–6)	70.40	70.40	< 0.001	$p = 0.81$
Diploma and less than	13	4 (2–5)	153.71	95.22	< 0.001	
Academic	12	4 (1–7)	65.74	97.63	< 0.001	
Occupation						
Farmer and rancher	18	6 (3–9)	216.65	98.94	< 0.001	$p = 0.41$
Housewife	18	4 (2–5)	208.25	94.99	< 0.001	
Student	13	3 (1–5)	87.08	99.91	< 0.001	
Other	20	4 (2–6)	223.44	97.81	< 0.001	
Residence						
Urban	21	3 (2–5)	320.37	98.61	< 0.001	$p = 0.05$
Rural	27	6 (3–10)	607.13	99.70	< 0.001	
Nomadic/semi-nomadic	7	8 (4–12)	306.79	96.97	< 0.001	
Diagnostic methods						
ELISA	58	5 (3–6)	2988.63	99.82	< 0.001	$p < 0.001$
IFA	8	3 (2–5)	145.05	94.07	< 0.001	
CCIEP	3	4 (1–8)	70.16	97.28	0.02	
IHA	3	3 (2–4)	7.47	72.25	< 0.001	
WB	1	1 (0–1)	—	—	—	
Geographical zones						
North	5	8 (3–20)	229.21	99.61	< 0.001	$p = 0.06$
West and North West	27	4 (3–5)	993.39	99.07	< 0.001	
Center	15	3 (2–4)	233.98	94.81	< 0.001	
South	14	6 (4–9)	853.16	97.64	< 0.001	
East	6	3 (1–4)	98.21	94.70	< 0.001	
Contact with soil						
Yes	4	14 (−6–35)	231.49	99.57	< 0.001	$p = 0.30$
No	4	4 (−2–9)	44.18	98.15	< 0.001	
Method of washing vegetables						
With water	6	7 (3–10)	91.23	92.85	< 0.001	$p = 0.8$

(Continues)

TABLE 2 | (Continued)

Subgroup	Number of studies	Seroprevalence, % (95% CI)	Heterogeneity[a]			Test for subgroup differences
			Q	I^2	*p* value	
With detergent or salt	6	6 (2–11)	146.45	97.25	< 0.001	
Keeping dog						
Yes	23	9 (3–14)	814.67	99.36	< 0.001	$p = 0.05$
No	23	3 (2–5)	440.70	99.98	< 0.001	

[a]Heterogeneity between studies was evaluated using Cochrane's *Q* test and the I^2 statistic.

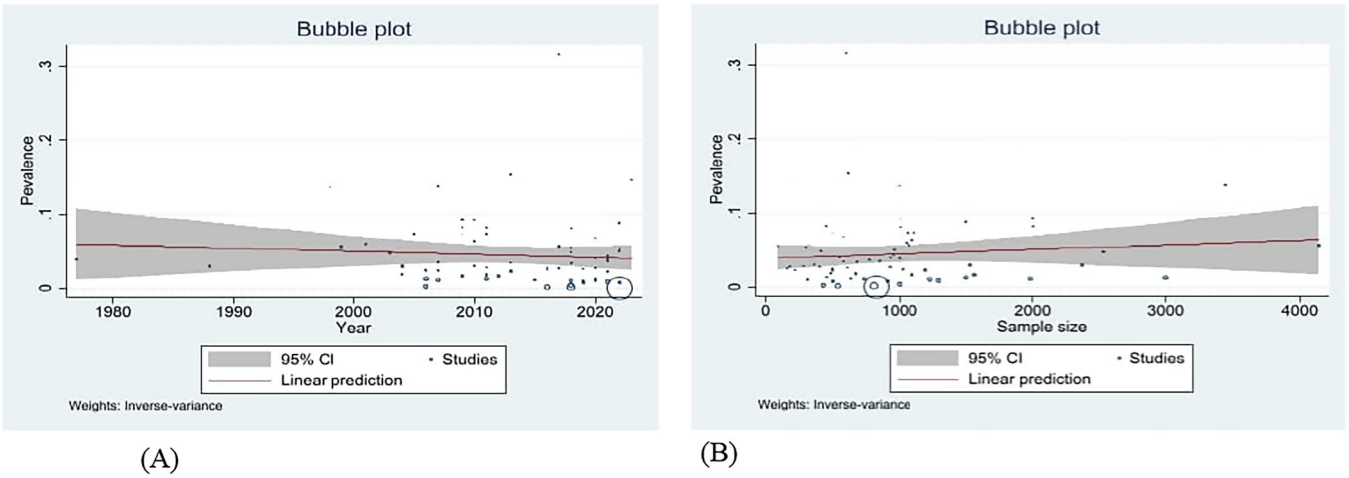

FIGURE 4 | The meta-regression shows an absence of a statistically significant association between human cystic echinococcosis in Iran and quantitative variables such as (A) publication year and (B) sample size in the general population of Iran.

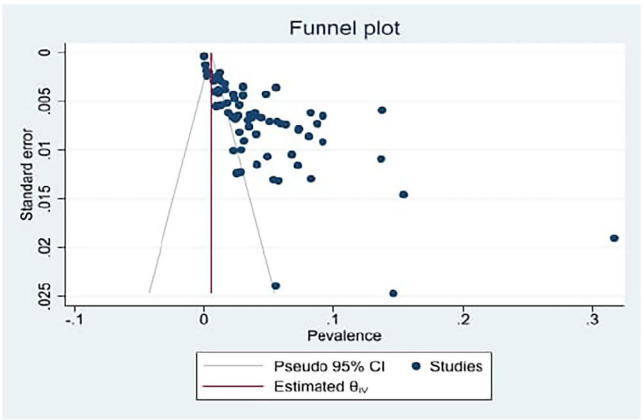

FIGURE 5 | Funnel plot for the determination of publication bias of the seroprevalence estimates of human cystic echinococcosis in Iran.

access to safe drinking water, face inadequate sanitation, and practice poor hygiene. On the other hand, the lower level of formal education among pastoralists compared to other communities living in more developed areas can lead to a decrease in knowledge about CE transmission mechanisms and prevention and control measures. Furthermore, their pastoralist lifestyle involves frequent contact with livestock, as they regularly import and export herds to other regions [84]. These individuals also play a significant role in the production and handling of dairy products. Moreover, herd dogs, guard dogs, and strays are often present in their living environment. As a result, people can easily become infected due to the establishment of the parasite's life cycle and the lack of education, information, and poor health conditions.

We found that the infection rate of human CE in people who kept dogs was significantly higher in individuals who kept dogs compared to those who did not ($p < 0.05$). The primary source of CE in humans is dogs, as definitive hosts. Environmental contamination with *E. granulosus* eggs is known to pose a risk to human health. The frequency of *E. granulosus* eggs in dog feces was reported as 3.47% in the west, 6.8% in the southeastern regions, and 16% in a systematic review in Iran, indicating high environmental contamination with *Echinococcus* eggs [85–87]. Therefore, keeping infected dogs is risky for both the dog owner and the neighboring community due to environmental contamination and the possibility of fecal-oral transmission of infection. In a study in southern Iran, the knowledge, attitude, and practices of 180 hydatid cyst surgically operated patients toward the disease were investigated [88]. The investigators reported that only 11.1% of the participants demonstrated good knowledge, 45.6% demonstrated a positive attitude, and 11.6% of dog owners and 47.5% of participants with no dogs demonstrated suitable practice toward CE, indicating poor knowledge and attitude.

We observed that human CE was positively and significantly correlated with age. This may be attributed to the chronic

nature of the disease, increased exposure to the parasite over time, or a weakened immune system in elderly individuals. Also, more exposure to livestock and agricultural activities can be associated with higher CE seroprevalence in adults. This is consistent with studies conducted in Africa [81], China [89], and Poland [90]. However, the seroepidemiology of CE in children reflects the active transmission of the parasite in endemic areas and can indicate the effectiveness of infection prevention and control programs [91].

In Iran, salt solutions, water and vinegar, dish detergent, and calcium hypochlorite are the most commonly used methods for washing vegetables. Due to the irrigation of some vegetables with animal fertilizers or untreated sewage systems in Iran, it is recommended to use these detergents for deparasitization and disinfection. Evidence indicates a high level of taeniid eggs (5%) recovered from raw vegetables in the country [92], although the eggs of *Echinococcus* and *Taenia* spp. are not morphologically distinguishable. In the present study, contrary to expectations, no significant difference was observed between the method of washing vegetables and seropositivity to human CE. However, only six studies included in the analysis reported seropositivity to human CE based on the method of washing vegetables; therefore, these findings may not fully reflect the true situation, and the results must be interpreted with caution.

Based on the results of the present study, no significant change was observed in the prevalence of human CE over the 33 years of study (1990–2023). A systematic review and meta-analysis that included 31 articles published between 1970 and 2020 showed that the prevalence of CE in livestock in Iran has increased over time [6]. On the other hand, the number of hydatid cyst surgeries has increased in recent years in the country [91], although this increase may be related to improvements in hospital documentation systems and advances in diagnostic techniques.

Despite the climate diversity across different regions of Iran, which affects egg survival rates and the parasite transmission cycle [93], the seroprevalence of CE remains relatively high in most provinces of the country. In developing countries, including Iran, traditional animal husbandry and herding practices have become popular. The close contact among dogs, livestock, and humans creates favorable conditions for CE. Therefore, it is believed that behavioral factors, along with a lack of knowledge, awareness, and poor hygiene practices about CE—especially in rural areas—play a significant role in the transmission of the disease. In general, more attention should be given to the control and prevention of echinococcosis in various hosts in Iran and other countries. This is why the WHO, in collaboration with other members, has included the prevention, control, elimination, and eradication of echinococcosis as part of the roadmap for neglected tropical diseases (NTDs) targets by 2030.

According to the Q test, the results indicated high heterogeneity between the reported prevalence rates ($I^2 = 99\%$, $p < 0.001$). Thus, the random effects model was used for the meta-analysis, and sources of heterogeneity were explored through subgroup analysis. Overall, heterogeneity across all pooled prevalence estimates was high; therefore, the results should be interpreted with caution. The heterogeneity among studies may be attributed to differences in geographic areas, publication years, sample sizes, study methods, gender, age, education, occupation, and other factors. Furthermore, other factors not assessed in this study, such as the type of water used and environmental and climatic conditions may have influenced the results. Additionally, the results of the funnel plot and Egger's tests revealed substantial publication bias (Egger's test; $p < 0.001$). Potential publication bias may have affected our results, as small studies with low or zero prevalence may have been conducted but not published, leading to an overestimation of the findings.

Using a long-term data set with a large sample size, we were able to enhance the accuracy of estimates regarding the prevalence of human CE and related epidemiological variables. However, our study has some limitations. First, in certain provinces of the country, only one report on the prevalence of human CE has been published in the past 33 years. Second, there was a lack of information on some risk factors. Third, substantial heterogeneity was observed among the studies included, as well as in the subgroup analysis. Additionally, some of the overall estimates were affected by significant publication bias, which impacts the interpretation of the results.

5 | Conclusions

According to this review, the pooled prevalence of human CE was found to be 4%. Residence, age, and having a dog at home, on the farm, or as a sheepdog were significantly associated with the prevalence of human CE. No significant change was observed in the prevalence over the 33 years of the study. This study highlights the importance of targeted programs such as deworming dogs with praziquantel and vaccination of sheep with recombinant EG95 protein. Other complementary measures to improve program effectiveness are also recommended, such as hygiene education (e.g., removing raw offal or carcasses from the diet of dogs and hand washing), fenced slaughterhouses with offal disposal systems, community participation and social support for the control program (e.g., by taking dogs to deworming sessions or accepting ultrasound studies in children). In addition, screening strategies for the diagnosis of asymptomatic cases and their timely treatment are recommended. Although this does not play a role in interrupting the cycle of parasite transmission, it has a high health impact by improving the prognosis of cases, limiting costly surgeries and the risk of developing complicated cases, reducing hospital stays, and reducing mortality rate.

Author Contributions

Nashmin Mohemmi: data curation, conceptualization, writing – original draft. **Mohammad Taghi Khodayari:** formal analysis, software. **Seyed Ahmad Karamati:** data curation. **Mohammad Reza Shiee:** data curation. **Hossein Effatpanah:** data curation, writing – review and editing. **Afshin Davari:** data curation. **Ali Reza Ghorbani:** data curation. **Arezoo Bozorgomid:** conceptualization, writing – original draft, writing – review and editing, validation.

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Ethics Statement

The protocol was approved by the Ethics Committee of Kermanshah University of Medical Sciences (IR.KUMS.MED.REC.1402.002).

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The authors have nothing to report.

Transparency Statement

The lead author, Arezoo Bozorgomid, affirms that this manuscript is an honest, accurate, and transparent account of the study being reported, that no important aspects of the study have been omitted, and that any discrepancies from the study as planned (and if relevant, registered) have been explained.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.