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Review

Prevalence of human visceral leishmaniasis in Iran: A systematic review and meta-analysis

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ABSTRACT

Leishmania infantum is the main cause of human visceral leishmaniasis (HVL; also known as kala-azar) in the Middle East and may be fatal if left untreated. This disease was first reported in 1949 in Iran. Despite marked improvements in hygiene and sanitation conditions, the disease is still endemic in some parts of Iran. It is difficult to determine the current prevalence of HVL in Iran due to the scarcity of comprehensive studies in this regard. In response to this gap, a systematic review and meta-analysis was conducted to gain better understanding of HVL epidemiology in the general population of Iran. English and Persian databases were searched for studies reporting the prevalence and risk factors associated with HVL in the Iranian people from January 1995 to December 2019. The reported data were selected according to inclusion and exclusion criteria. The pooled prevalence of HVL infection and its 95 % confidence intervals were calculated. Quality assessment, heterogeneity testing and publication bias assessment were also done. Literature search revealed 3634 studies, of which 35 studies met our eligibility criteria, with a total of 50,716 individuals. The meta-analysis was performed on 31 out of 35 included studies. The estimated pooled prevalence of HVL infection according to seropositivity was 2% (95 % CI: 1–2%) in the general population of Iran in which western and northern provinces had the lowest and the highest prevalence, 0.5 % (95 %CI, 0.2−0.7%) and 3% (95 %CI, 1–5 %), respectively. The seroprevalence of HVL among females (2%; 95 %CI, 1–2 %) was more than males (1%; 95 %CI, 1–2 %). The ≤10 and >10 years age groups had similar seroprevalence rates (1%, 95 %CI, 1–2 % versus 1%, 95 %CI, 0–1 %, respectively). There was no significant difference in terms of geographic area, age and sex. Of 31 studies included in the meta-analysis, the most common diagnostic test was the direct agglutination test (96.77 %). To the best of our knowledge, this is the first systematic review of the prevalence of HVL in Iran. The results showed a low seroprevalence of HVL infection. However, the lack of published reports of HVL in an area does not exclusively mean the absence of the disease or carrier. We therefore recommend further studies in this regard.

1. Introduction

Visceral leishmaniasis (VL), also known as kala- azar, is a protozoan neglected disease. It is the most severe form of leishmaniasis and may be fatal if left untreated. Common clinical symptoms of human visceral leishmaniasis (HVL) infection include fever, weight loss, hepatomegaly, splenomegaly, anemia, and lymphadenopathy [1,2]. More than 94 % of global HVL cases occur in South Asia, South and Central Americans. The

Abbreviations: L. infantum, *Leishmania infantum*; ELISA, Enzyme-linked immunosorbent assay; DAT, Direct agglutination test; MAT, Modified agglutination test; PCR, Polymerase chain reaction; JBI, Joanna Briggs Institute; LAT, Latex agglutination test; IFA, Indirect Immunofluorescence Assay; SID, Scientific information database; STATA, Statistics and data; HVL, Human visceral leishmaniasis; VL, Visceral leishmaniasis.

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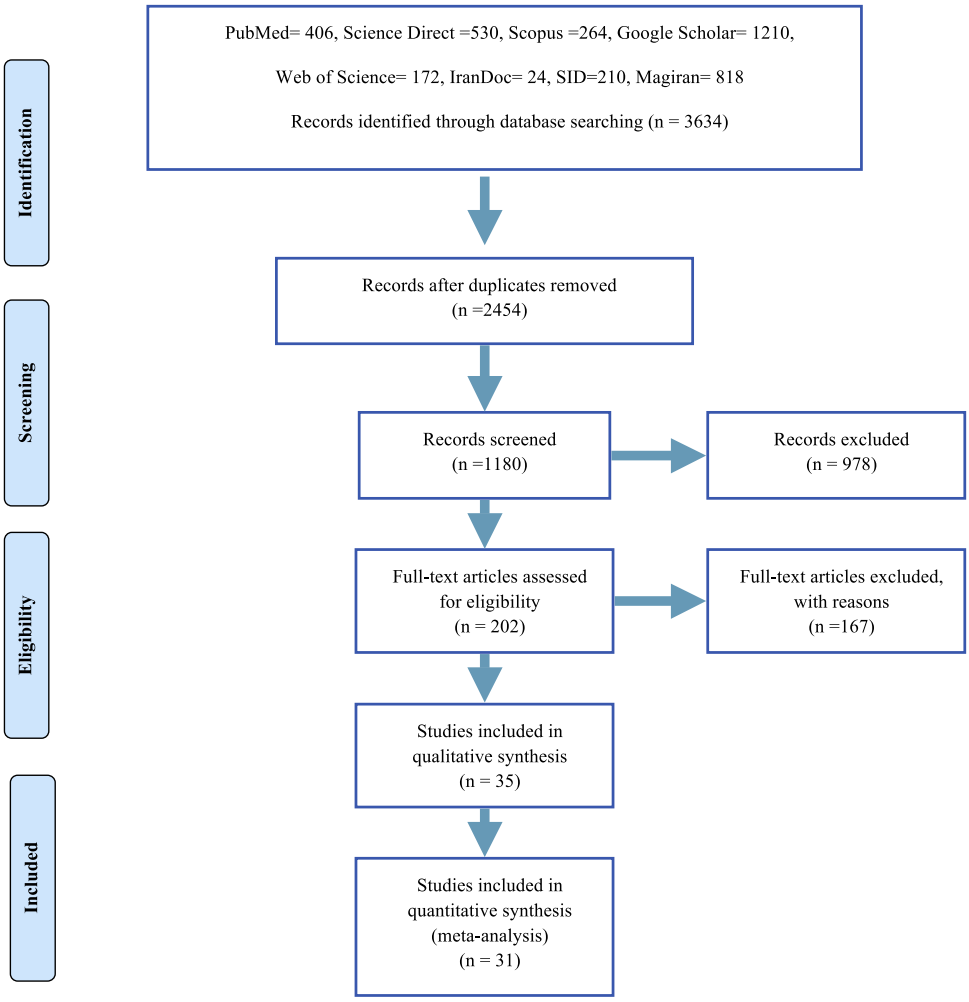

Fig. 1. Flowchart of study selection.

estimated world prevalence of VL is 500 000 cases and about 50 000 deaths from the disease each year [3]. VL is transmitted by the bite of infected female sand flies (Diptera: Psychodidae) of the genus *Phlebotomus* in the Old World and *Lutzomyia* in the New World. The primary etiologic agents for VL are *Leishmania(L.) donovani* and *L. infantum/chagasi* complex parasites, however, it has been reported that VL may be rarely caused by *L.tropica, L. amazonensis* and *L.major* [1].

Iran has a subtropical climate providing optimal conditions for the survival and breeding of sand flies and many other vector arthropods. Three forms of leishmaniasis have been identified in Iran: VL, cutaneous leishmaniasis and mucocutaneous leishmaniasis [4,5].The first documented case of HVL in Iran was reported from Mazandaran Province in 1949 followed by other geographical areas based on microscopic or molecular confirmation [5,6]. In Iran and throughout the Middle East, *L. infantum* is the main causative agent of HVL and usually affects children in endemic regions where dogs (Canis familiaris) are regarded as the primary reservoir of the disease [7]. Nevertheless, *L. tropica* and *L. major* associated VL cases have been also reported from southern Iran [8,9]. In addition, sand flies from genus *Phlebotomus* including *Ph. kandelakii*, *Ph. neglectus*, *Ph. keshishiani*, *Ph. perfiliewi transcaucasicus*, *Ph. alexandri* and *Ph. tobbi* are distributed in country, increasing the chance for parasite transmission [10].

During the last decades, several researchers have worked on HVL prevalence in Iran. Sarkari et al., found 380 hospitalized cases of VL during 1999–2014 in Fars Province, southwestern Iran and reported that 91.5 % of HVL cases were 5 years old [11]. In another study in 2011, the investigators reported that anti-*Leishmania* antibodies with titers 1:3200 found from 4.3 % human serum samples collected from 4 distinct geographical locations of the country by DAT method [12]. Furthermore, according to data extracted from the national leishmaniasis surveillance system from 1983 to 2012, the average annual incidence of HVL was 0.18 per 100 000 in Iran [5]. Although there is a substantial decline in the global incidence of VL mainly due to improved hygienic conditions as a result of better living conditions [5,13], given the increasing number of immunocompromised cases such as those with HIV, cancer, and organ transplant recipients, VL as an opportunistic infection may threaten the lives of these patients [14,15].

The exact measurement of disease prevalence is of vital importance for policy makers, health care providers, and the general population. Policy makers often encounter incompatible reports of disease prevalence in the literature. Systematic reviews are now well accepted as an ideal method to summarize these incompatible reports. Many studies have evaluated the prevalence of VL in Iran [16,17] but there is no comprehensive review of the HVL prevalence in the Iranian population. Hence, the present study was conducted to understand the prevalence of HVL in the general population of Iran to determine the various risk factors associated with this infection.

2. Material and methods

The objective of this study was to determine the prevalence of HVL in different provinces of Iran. This study was performed based on PRISMA guideline (preferred reporting items for systematic reviews and meta-

Table 1
Baseline characteristics of included studies for human visceral leishmaniasis in Iran.

No.	Province	Year	Sample size (n)	Prevalence n (%)	Method	Cut off value	References
North							
1	Ardabil	ND	730	57 (7.8)	DAT	≥1. 3200	Arshi et al. 2002 [19]
			723	103 (14.2)	MST		
2	East Azerbaijan	2000–2001	1252	24 (1.91)	DAT/	≥1. 3200/	Mirsamadi et al. 2003 [20]
				30 (2.39)	IFAT	≥1. 60	
3	Ardabil	2004	1155	7 (0.60)	DAT/IFAT/ ELISA	≥1. 3200	Mahami et al. 2006 [21], Mahami et al. 2009 [22]
4	Mazandaran	2009–2010	402	0	DAT/ PCR	≥1. 3200	Fakhar et al.2011 [23]
5	Northwest of Iran	2006	1584	106 (6.69)	DAT	≥1. 3200	Mazloumi Gavgani et al. 2011 [24]
			1566	246 (15.7)	MST		
6	Golestan	2011–2012	450	6 (1.33)	DAT/ PCR	≥1. 3200	Fakhar et al.2014 [25]
7	Ardabil	2015	180	0	DAT	≥1. 3200	Shirmohammad et al. 2016 [26]
8	Ardabil	2016	600	8 (1.33)	DAT/PCR	≥1. 3200	Asfaram et al. 2017 [27]
9	Ardabil	2014–2015	776	1 (0.1)	DAT	≥1. 3200	Ebrahimzade-Parikhani et al. 2017 [28]
10	East Azerbaijan	2017	1420	13 (0.63)	DAT	≥1. 3200	Behniafar et al. 2019 [29]
West							
11	Lorestan	2004 – 2005	530	6 (1.13)	DAT/PCR	≥1. 3200	Chegeni et al. 2005 [30]
12	Kermanshah	2011–2012	1800	6 (0.33)	DAT	≥1. 3200	Hamzavi et. 2012 ([4]
13	Ilam	2013	456	2 (0.43)	DAT	≥1. 3200	Abdi et al. 2015 [31]
14	Ilam	2014–2015	872	0	DAT	≥1. 3200	Khazaei et al. 2017 [32]
15	Lorestan	2012	800	5 (0.62)	DAT	≥1. 3200	Masoori et al. 2018 [33,34]
Center							
16	Tehran	1995	925	1 (0.1)	DAT	≥1. 3200	Faghihi et al. 2002 [35]
				0	LAT		
17	Qom	2001	416	7 (1.68)	DAT	≥1. 3200	Fakhar et al. 2004 [36]
18	Qom	2011–2012	1564	1 (0.06)	DAT	≥1. 3200	Rakhshanpour et al. 2014 [37]
19	Alborz	2013–2014	1007	37 (3.67)	DAT	≥1:800	Heidari et al. 2015 [38]
20	Qom	2017	960	2 (0.2)	DAT	≥1:800	Zanjirani Farahani et al. 2019 [39]
East							
21	North Khorasan	2007–2008	1608	9 (0.55)	DAT	≥1. 3200	Torabi et al. 2009 [40]
22	North and Razavi Khorasan	2016	442	22 (5.21)	DAT	≥1. 3200	Ashkanifar et al. 2016 [41]
				0	rK39		
South							
23	Bushehr	1998–1999	1496	51 (3.4)	DAT	≥1. 3200	Mohebali et al. 2001 [42]
24	Fars	NR	321	6 (1.86)	DAT	≥1. 3200	Asgari et. 2006 [43]
25	Fars	2005	321	6 (1.86)	DAT	≥1. 3200	Fakhar et al. 2006 [44]
26	Fars	2004–2006	802	13 (1.6)	DAT	≥1. 3200	Fakhar et al. 2008 [45]
				100 (12.5)	PCR		
27	Fars	2010	376	5 (1.33)	DAT/ PCR	≥1. 3200	Fakhar et al. 2010 [46]
28	Kohgiluyeh and Boyer-Ahmad	2005–2006	1628	50 (3.07)	DAT	≥1. 3200	Sarkari et al. 2010 [47]
29	Kerman	2009–2010	1476	14 (0.94)	DAT	≥1. 3200	Mahmoudvand et al.2011 [48]
30	Kerman	2014–2015	862	6 (0.69)	DAT	≥1. 3200	Abbaszadeh-Afshar et al. 2015 [49]
31	Fars	NR	2003	28 (1.39)	DAT/PCR	≥1:800	Sarkari et al. 2015 [50]
32	Bushehr	2014–2015	1221	0	DAT	≥1. 3200	Gorgipour et al. 2017 [51]
33	Fars	2017	617	17 (2.8)	ELISA	*	Layegh Gigloo et al. 2018 [52]
				8 (1.29)	PCR		
34	East-Azerbaijan, Bushehr, Ardabil	1996	19,693	1274(6.47)	DAT	≥1. 3200	Edrissian et al. 2002 [53]
35	Northwest& east, Central, South and Southeast regions	2007–2009	5206	68 (1.30)	DAT	≥1. 3200	Mohebali et al. 2011 [12]

* The cutoff point was calculated at 2SD above the mean of control samples.

analysis) (Additional file 1: Table S1) [18].

2.1. Search strategy

Systematic search was performed on the literature about prevalence of HVL in Iran. Electronic database including PubMed, Science Direct, Scopus, Google Scholar, Web of Science, the Iranian Research Institute for Information Science and Technology (IranDoc), the Scientific Information Database (SID), and Magiran were comprehensively searched for published articles on HVL prevalence in Iran from January 1995 until December 2019. Search was carried out using following keywords and terms: "*Leishmania* spp.", "*Leishmania infantum*", "visceral leishmaniasis", "leishmaniasis", "Kalaazar'', "human leishmaniosis", "prevalence'', "epidemiology'' and "Iran'', alone or in combination with "OR'' and/or "AND'' operators. Finally, the studies were recorded in EndNote X7.1 software (Thomson Reuters).

2.2. Inclusion and exclusion criteria

Inclusion criteria

i Studies conducted on human subjects in Iran
ii Studies reporting the prevalence of VL infection and positive samples in the groups
iii Observational studies, including case-control and cross-sectional studies based on serological and molecular tests
iv Studies published between 1995–2019

Exclusion criteria

i Studies such as review articles, experimental, case reports, case series, non-human studies, hospital-based retrospective studies, duplicate publications, and conference papers were excluded from the study

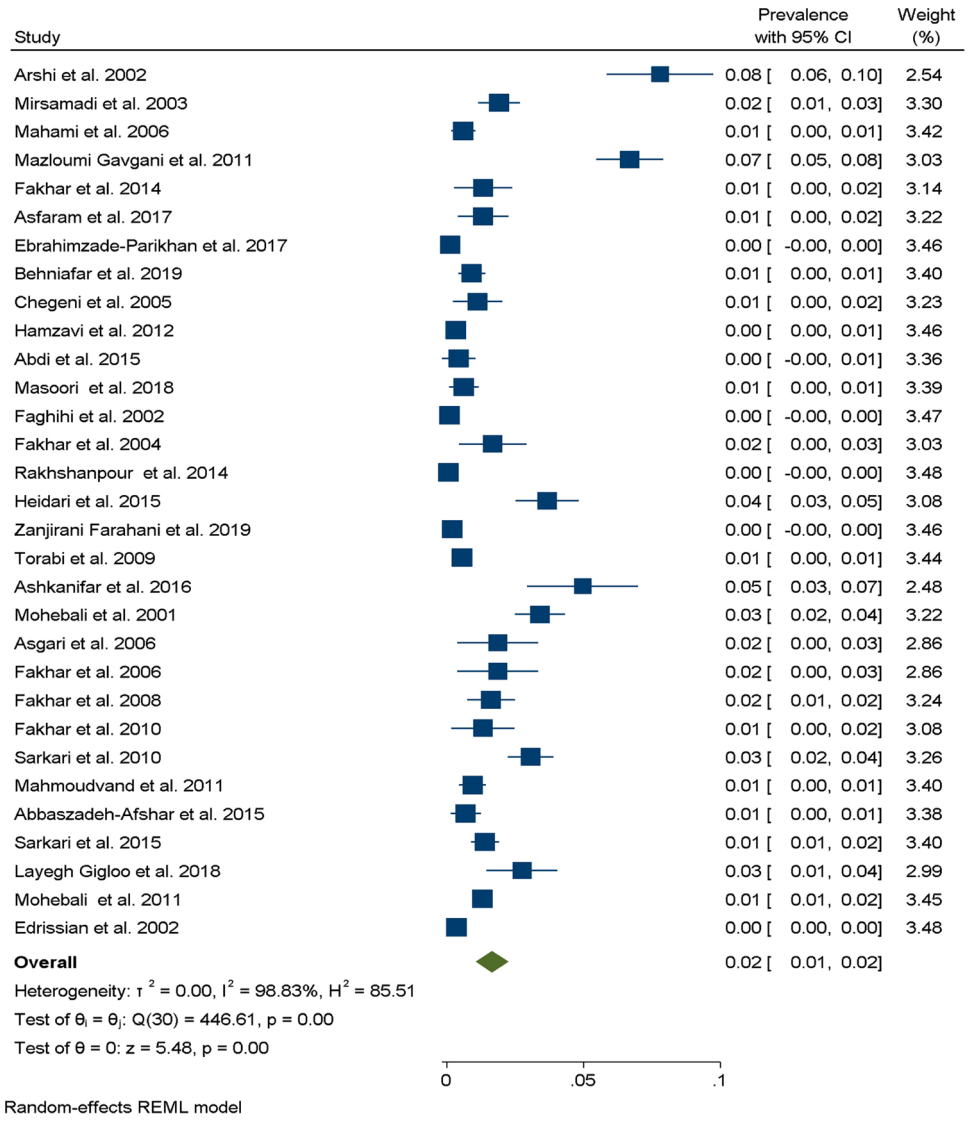

Fig. 2. Forest plot showing the pooled prevalence of HVL infection among the Iranian population, 1995 to 2019.

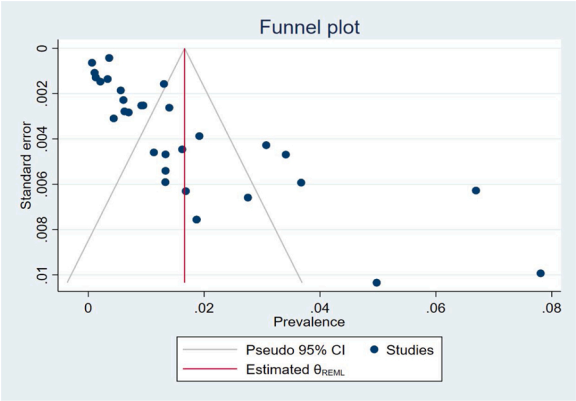

Fig. 3. Egger test for publication bias of HVL infection in the general population in Iran.

ii Studies published outside the determined period of this systematic review
iii Studies with unclear diagnostic methods and cut-offs

2.3. Data extraction

After the primary screening based on inclusion and exclusion criteria, the titles and abstracts of the articles were screened by two independent investigators to eliminate studies that were unrelated to the a priori defined research questions. Any disagreement was resolved by discussion. If still no agreement was achieved, the decision was made by a third reviewer. Furthermore, the reference lists of eligible studies also were checked manually and appropriate articles were included. Afterwards, the following items was extracted by an author and was checked by another one: the first author's name, year of publication, type of study, age category, province, geographical region (north, east, west, south, and center), gender, place of residence (urban, rural and nomadic), sample size, diagnostic method, cut off value or antibody titer for serological testes, number of positive samples, prevalence (%).

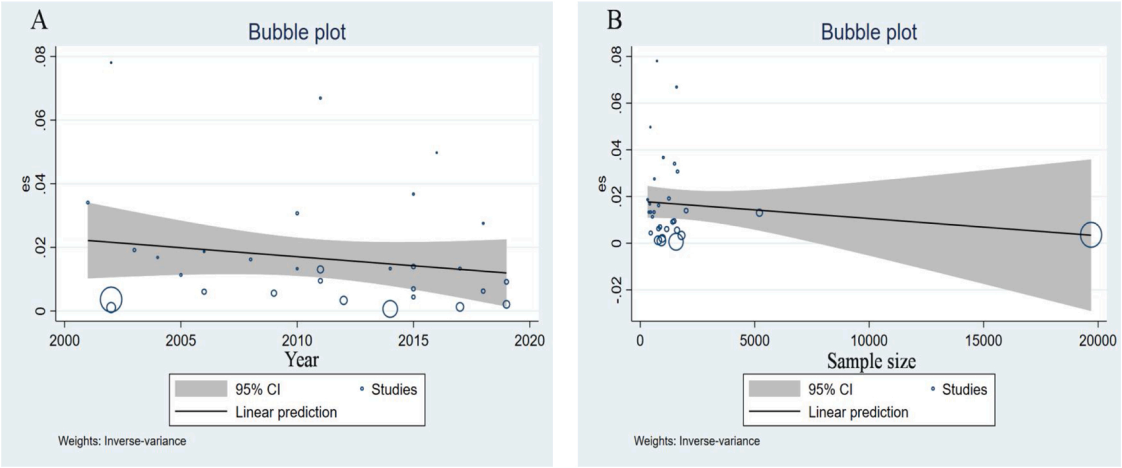

Fig. 4. Meta-regression plot of seroprevalence of HIV in Iran according to sample size (A) and year of publication (B), 1995 to 2019.

2.4. Quality assessment

The quality of the selected studies was evaluated using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist which contains nine items for quality assessment of cross-sectional/prevalence studies. These items are related to the study groups, sample size, study setting, and statistical analysis. Each question is assigned one score. Finally, the quality of each article was scored accordingly from 0 to 9. The studies achieved that scored six or higher were considered eligible for meta-analysis. Quality assessment was independently done by two reviewers (K. Ghadiri, S. Raeghi). Any disagreement was resolved by consulting A. Bozorgomid and M. Rostamian.

2.5. Statistical analysis

The meta-analysis was performed using Stata software, version 14 (StataCorp, College Station, 144 TX, USA) and P values < 0.05 were considered significant. We estimated the pooled prevalence of HVL in Iran with its 95 % confidence interval (CI) using a random-effects model assuming that the true effect size varies between studies. Forest plots were used to visualize the heterogeneity among studies. The results of each study and the pooled outcome are presented as forest plots (reported as effect size with a 95 % CI). Heterogeneity testing was performed using the degree of inconsistency (I^2) with a range from 0 to 100% and values of 25 %, 50 %, and 75 % were considered as low, medium, and high heterogeneity, respectively. Subgroup analysis was used to compare the prevalence of visceral leishmaniasis among age groups, gender, different regions, and urban or rural areas. Meta-regression analysis was used to investigate the relationship between the prevalence of HVL, year of publication, and sample size. Publication bias was assessed graphically using a funnel plot and formally using the Egger's test (significance at $P < 0.05$).

3. Result

3.1. Study characteristics

Following a systematic search of the mentioned electronic databases and using the reference lists of the articles, 35 human studies investigating visceral leishmaniasis were found to be eligible (Fig. 1). The characteristics of the 35 studies with 50,716 subjects included in this review are summarized in Table 1. The studies covered sixteen provinces in Iran, which includes Kermanshah, Golestan, Mazandran, Ardabil, Kerman, Ilam, Fars, Lorestan, Qom, North Khorasan, Razavi Khorasan, Alborz, Bushehr, Kohgiluyeh & Boyer-ahmad, Tehran and East Azerbaijan. The diagnostic methods used included the direct agglutination test (DAT, 34 studies), enzyme-linked immunosorbent assay (ELISA, 2 studies), the modified agglutination test (MAT, 2 studies), polymerase chain reaction (PCR, 8 studies), the latex agglutination test (LAT, 1 studies), indirect Immunofluorescence assay (IFA,2 studies) and rK39 dipstick test (1 study) (Table S2). Thirty-four studies were cross-sectional and one was a case control study. Because of inadequate information with different diagnostic methods, only seroprevalence studies of HVL were analyzed. Moreover, it has been shown that four studies with zero prevalence (0%) had the high effect on pooled effect size; thus, we excluded it from the meta-analysis.

The quality of the studies included in this review was generally acceptable with 31 high-quality studies. Therefore, all studies were considered eligible for final meta-analysis. Details of the scoring system are demonstrated in Additional file 1: Table S3.

3.1.1. Prevalence of HVL infection in the general population

The pooled prevalence of HVL according to seropositivity was 2% (95 % CI: 1–2%) from 1995 to 2019 (Fig. 2). The results of funnel plots and Egger's test showed the absence of publication bias in the studies included for the prevalence of HVL infection ($P > 0.05$; Fig. 3).

As shown in Fig. 4, meta-regression analysis of the publication year showed a statistically insignificant declining trend of HVL infection in the Iranian population from 1995 to 2019 ($B = -1.05$, $P = 0.293$). Similarly, there was no statistically significant correlation between the seroprevalence of HVL infection and sample size ($B = -0.85$, $P = 0.403$).

3.2. Subgroup analysis of HVL infection according to regions, age groups, gender, and urban or rural areas

As for different geographical zones of Iran, northern provinces had the highest seroprevalence of HVL, 3% (95 % CI: 1–5 %) followed by southern 2.1% (95 % CI: 1.4–2.8 %), eastern 0.7% (95 % CI: 0–1 %) and western 0.5% (95 % CI: 0–1 %). With respect to gender, the seroprevalence of HVL among females was more (2%; 95 %CI, 1–2 %) than males (1%; 95 %CI, 1–2 %) (Fig. 5). Of 31 studies included in this meta-analysis, only one study had reported the seroprevalence rate of *Leishmania* infection in urban residents, fourteen studies in rural residents and five studies in nomads. The pooled seroprevalence of HVL was in 4% (95 % CI: 3–5 %) urban residents, 2% (95 % CI: 1–4 %) in rural residents, and 3% (95 % CI: 0–7 %) in nomads (Fig. 6). Furthermore, the $\leq$10 and >10 years age groups had similar seroprevalence rates (1%, 95 %CI, 1–2 % versus 1%, 95 %CI, 0–1 %, respectively). More details are shown in the Fig. 7.

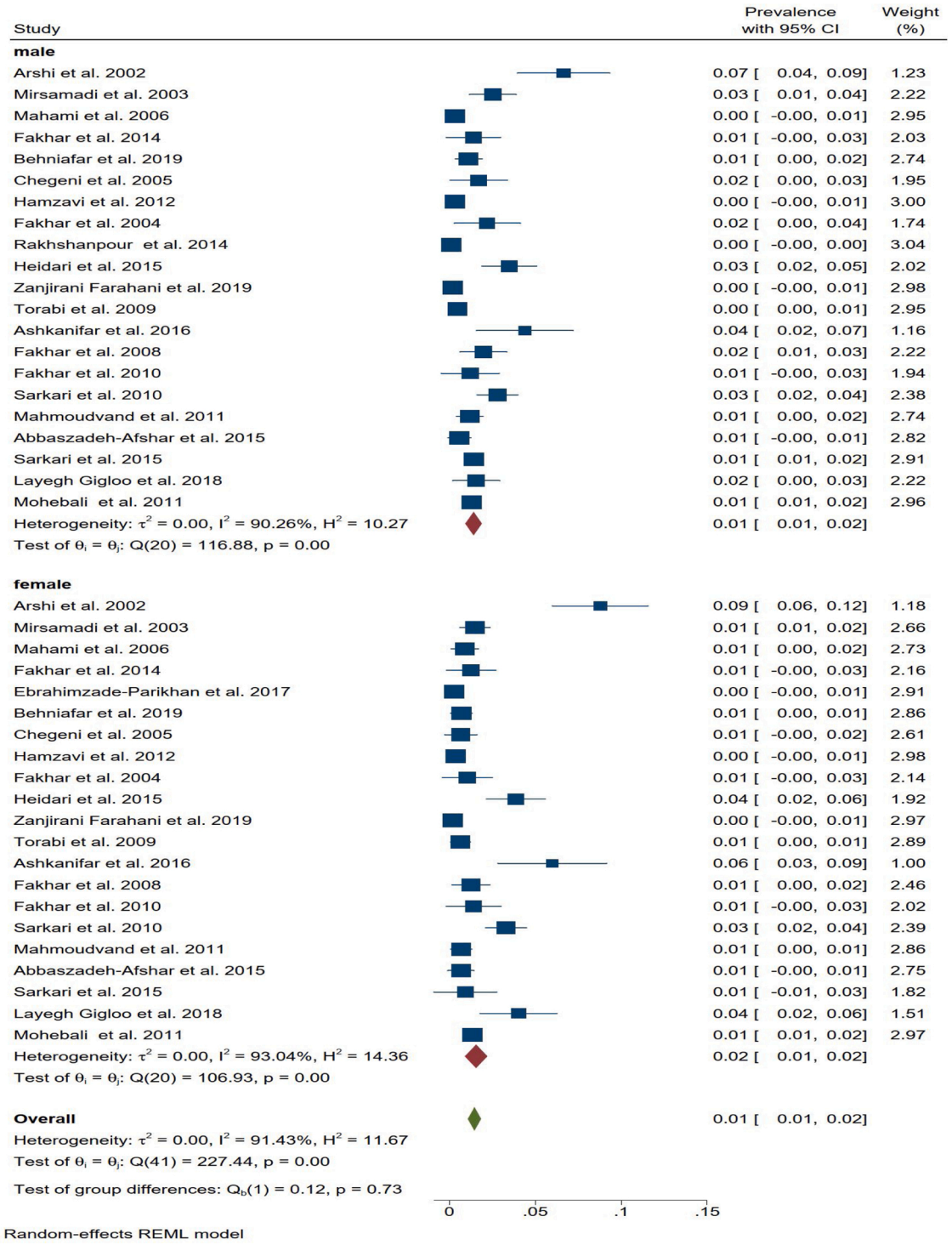

Fig. 5. The prevalence of HVL by gender in Iran.

4. Discussion

To the best of our knowledge, this is the first systematic review and meta-analyses of the prevalence of human VL in Iran. In this study, thirty-five publications were collected investigating 50,716 individuals of whom 1796 were VL positive from 1995 to 2019. The results showed an overall pooled prevalence of 2% (95 % CI: 1–2%) for HVL according to seropositivity in Iran, but it showed variations in diff ;erent regions with no statistical significance. This was lower than the rate reported from Brazil (46.2 %) and Drama in the north of Greece (6.9 %) [54,55]. However, the finding of this systematic review and meta-analysis is higher than that of Iran (1%), Ethiopia 0.87 % and Cyprus (Turkey) (1.2 %) [7,56,57]. Differences in the prevalence of HVL in various studies can be due to the different way of living the communities, climatic conditions, socio-economic factors, vector factors, diagnostic method, and sampling method [58]. For example, a study in Iran showed that HVL was more common in individuals living in riversides and nomadic villages lacking health-centers [59].

In this study, the highest prevalence of HVL was found in the northern (3%, 95 % CI: 1–5%) and southern (2.1 %, 95 % CI: 1.4–2.8 %)

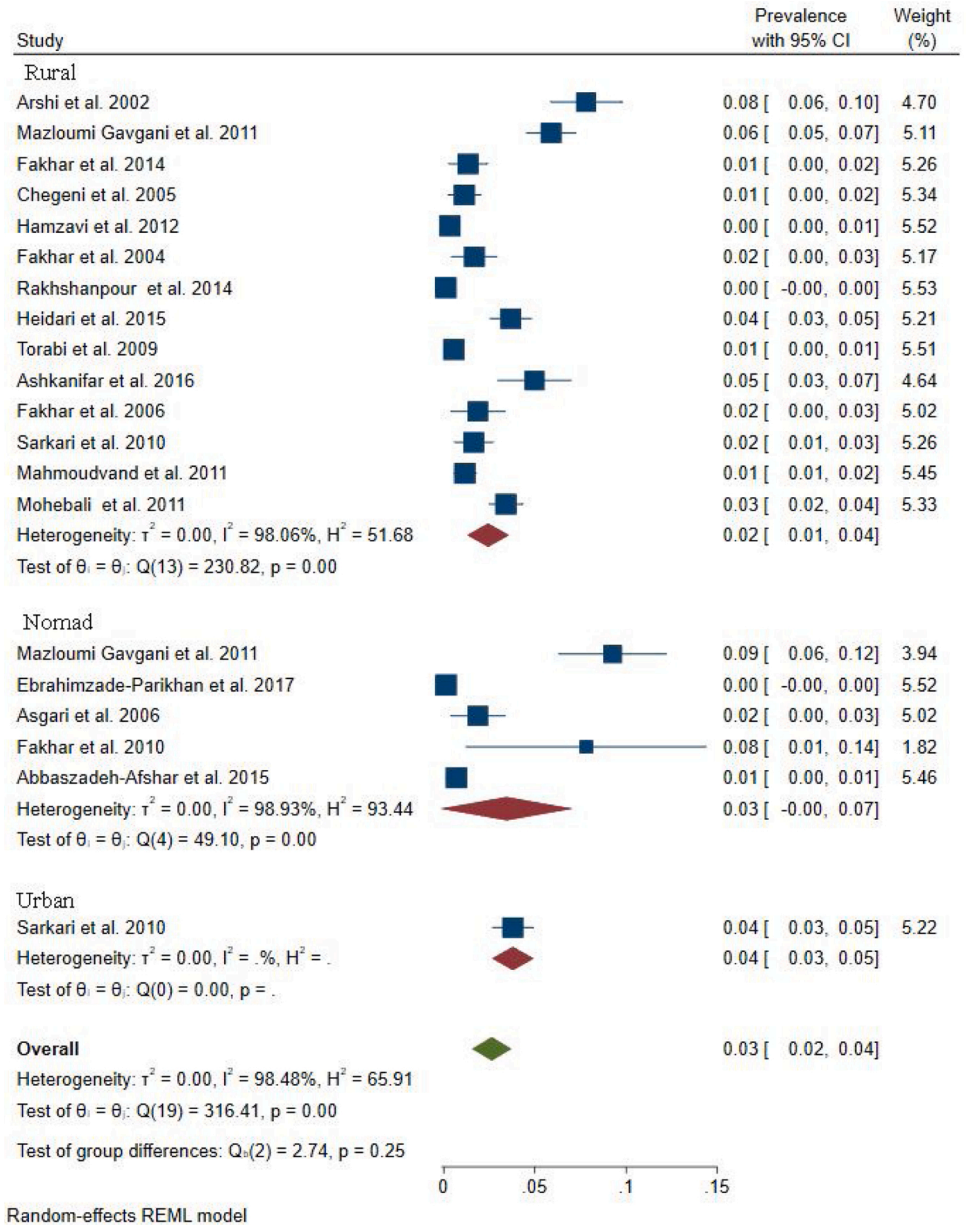

Fig. 6. The prevalence of HVL by sex in Iran.

areas of Iran. This was consistent with the results of Shirzadi et al., [5] and Yaghoobi-Ershadi et al. [60], that the highest rates were related to the north and south of Iran. The northwest of Iran is generally cold with an average daily temperature of below 0 °C in at least one-third of the year. In rural areas, dry cattle feces are traditionally used for heating the rooms in the winter. For this purpose, the cattle feces are handled in blocks and kept in large conical structures called "Galakhs" in the local language in the summer. These structures provide a good niche for vectors of *Leishmania* parasite. The Galakhs structures are also usually used as dog shelters in the winter and summer. It could be concluded that Galakhs structures have crucial roles in high prevalence of HVL in these areas [61]. Furthermore, *Phlebotomine* sand flies including *Ph. kandelakii*, *Ph. perfiliewi*, *Ph.* tobbi, *Ph.* Major, *Ph. keshishiani* and *Ph. alexandri* as potential vectors for the transmission of HVL are frequently found in the northwest and southwest of Iran [7,62].

In Iran, HVL is mainly found in the northwestern (Ardabil and East Azerbaijan) and southern areas (Fars and Bushehr) of the country [7]. In the current study, the highest prevalence of HVL was observed in Ardabil [5.51 %] and East-Azerbaijan (5.55 %) Provinces (Table 1). A meta-analysis study found a median positivity of 10.2–23.3 % for *L. infantum* in dogs in the two mentioned regions [63]. Domestic dogs and wild canines are considered as the main reservoirs of *L. infantum* parasites in Iran and the presence of these animals in endemic areas suggests the potential transmission of the disease to humans due to the role of these animals in spreading infection in phlebotomine sand flies [64]. Likewise, there were other regions with high prevalence rates such as Razavi Khorasan with 6.6 %, Alborz with 3.67 % and Kohgiluyeh and Boyer-Ahmad with 3.07 % [38,41,47]. The high prevalence of HVL in these regions may be due to the small sample size or the emergence of endemic foci in the country.

In this systematic review and meta-analysis, data on HVL in urban setting are very limited. Therefore, the results should be interpreted with caution and indicating more work to be done in the future to resolve this issue. However, the prevalence of HVL was higher in nomads compared to the rural average during the study years. The results of studies conducted in Iran confirmed the role of travel and nomadic lifestyle on the incidence of visceral leishmaniasis [59]. The nomads lifestyle is defined as commuting from one place to another as a way of

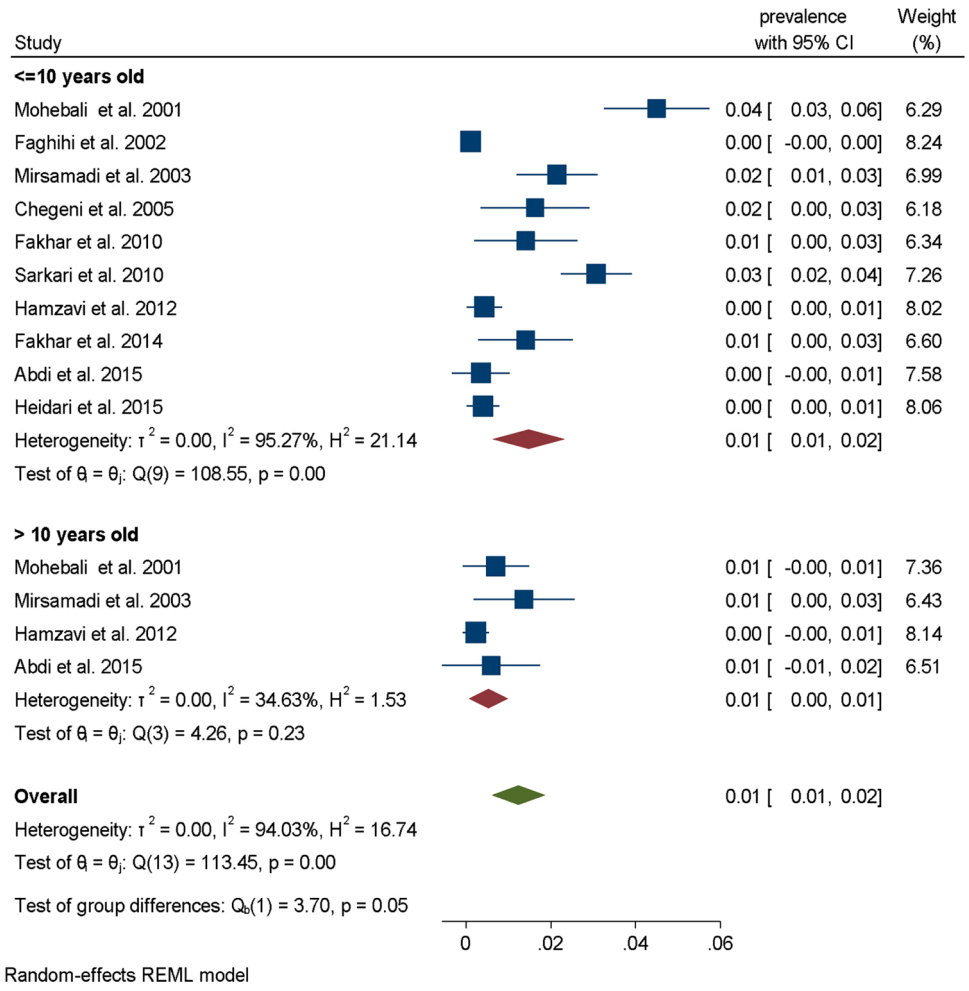

Fig. 7. Forest plot showing the seroprevalence of HVL by age in Iran.

finding food, water, and place for livestock. They therefore have a higher risk of exposure to sand fly bites due to living outdoors during VL transmission seasons. This is also a major risk factor for the distribution of the disease, especially in new areas where VL is not previously reported.

Mediterranean visceral leishmaniasis is a pediatric disease though the children under 10 years old are the main victims of the infection in Iran [11]. While many investigations reported that the age group of ≤10 years are affected more than the age group of >10 years by HVL [7,65], contrary to expectations in our study, the ≤10 and >10 years age groups had similar seroprevalence rates (1%, 95 %CI, 1–2 % versus 1%, 95 %CI, 0–1 %), respectively. This finding is due to doing fewer studies concerned with detecting HVL in the age group of >10 years in Iran. Nevertheless, HVL is not assumed as a serious infection in older people. However, the growth of the elderly population accelerates may make HVL as a great challenge to public health [66].

Accurate diagnosis of VL is important since clinical features of VL mimic some other common diseases. Invasive diagnostic methods for observing the parasite in tissue smears taken from bone marrow and splenic aspirate are the first-line approach in VL diagnosis [67]. Seven different diagnostic tests used to detect HVL infection in Iran include: DAT, ELISA, IFAT, PCR, MST, LAT, and rK39 dipstick. The present meta-analysis showed that the most common examinations were DAT and molecular methods. However, there are questions about the diagnostic accuracy of PCR for detecting VL when the parasite burden is low and in endemic areas. In addition, it is time consuming and expensive for routine use in health monitoring programmes [68]. DAT is a semi qualitative test, cost-effective and field applicable method that has been used for the diagnosis of VL and has been widely validated in several countries including Iran, India, Nepal, Bangladesh, Sudan, Ethiopia, Kenya, and Brazil [69,70].

This study had some limitations, for example, some of the related risk factors such as the socioeconomic status and the presence of dogs in or around the house were not investigated due to the lack of relevant information in most of the studies. Different diagnostic tests with different sensitivity and specificity values were used for the detection of HVL infection. Despite numerous studies investigating the HVL prevalence in Iran, particularly in endemic areas, there are still research gaps and many areas of the country have not been evaluated. These limitations may have influenced the pooled prevalence estimate; therefore, the results should be interpreted with caution.

5. Conclusions

This study found that the pooled prevalence of HVL infection was low in Iran. According to the results, the prevalence of HVL infection has decreased in Iran over the last two decades (24 years). However, despite the efforts made by Iranian public health authorities for controlling and preventing HVL, not only new human cases of VL continue to occur in old endemic foci, but also the disease has been reported in new areas where it was non-endemic previously. In this regard, appropriate measures should be taken to control VL and prevent its spread to other areas.

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Ethics approval and consent to participate

The protocol was approved by the Kurdistan University of Medical Sciences Ethics Committee [IR.MUK.REC.1398.204].

Declaration of Competing Interest

The authors report no declarations of interest.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.cimid.2020.101604.

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