Review Article

Cutaneous Leishmaniasis Based on Climate Regions in Iran (1998-2021): A Systematic Review and Meta-Analysis

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Abstract

Background: Climate change can facilitate the expansion of leishmaniasis and create the suitable habitat for vector and reservoir species. The objective of this study was to estimate the prevalence of cutaneous leishmaniasis (CL) at the climatic regions of Iran.

Materials and Methods: The literature search was conducted to identify all published studies reporting the prevalence or incidence of CL in humans in Iran. A total of 350 articles that reported leishmaniasis in Iran were retrieved, due to eligibility criteria, only 42 studies were selected to the final systematic review and meta-analysis procedure. Random effects meta-analysis was done with the estimate of heterogeneity being taken from an inverse-variance model. Subgroup analysis was conducted and it stratified the studies according to climatic regions. Between-study heterogeneity was assessed by using I^2 and Cochran's Q method I^2 value of heterogeneity. Meta regression was used to investigate factors potentially contributed the between-study heterogeneity.

Results: Individual studies showed that prevalence per 100,000 population estimated the range from 1.5 to 318.7 with the overall random pooled prevalence of 83.3 (95% confidence interval 74.5–92.1). Subgroup analysis by climatic regions showed that many studies were conducted in the desert areas and also, it has more prevalent than the other climatic regions.

Conclusions: Leishmaniasis was more prevalent in regions with dry and desert climates than the other climatic regions. One of the advantages of this work is that the majority of selected studies have been conducted on population-base. However, some of the studies have been designed poorly or have had a lack of internal validity.

Keywords: Cutaneous leishmaniasis, human reservoirs, Iran, prevalence

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Introduction

Leishmaniasis is one of the most important vector-borne diseases transmitted to humans and other animals through the bite of infected sandflies.[1,2] It is also the third-most important vector-borne parasitic disease after malaria and lymphatic filariasis.[2,3] In general, over 350 million persons are at risk globally[4,5] and 0.7–1.3 million new cases occur annually.[6,7] According to the World Health Organization, 2 million new cases are infected with leishmaniasis annually, including 1.5 million of cutaneous leishmaniasis (CL), and 20,000–40,000 die each year.[6,8] CL which represents a significant public health problem over a wide geographical area,[9,10] is an endemic parasitic disease in 98 countries of the world.[11] Most

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cases of CL occur in Afghanistan, Algeria, Brazil, Colombia, Iran, Pakistan, Peru, Saudi Arabia, and Syria.[12] However, the disease remains a public health problem worldwide.[13] The estimated world prevalence of all forms of the disease is 12 million annually.[14-17]

The cutaneous and visceral forms of CL have been mainly reported in 14 countries in the Eastern Mediterranean Region including Iran.[18] CL is endemic in 17 out of 31 provinces of Iran.[2,5,12,18] The disease is prevalent in southern Khorasan, Fars, Isfahan, Khuzestan, Kerman, Ilam, and Bushehr provinces. The Western and northwest provinces of Iran have the lowest incidence of CL.[19] About 20000 cases of CL are reported in many parts of Iran annually.[20] Isfahan has recorded the highest prevalence of the disease with many endemic foci.[20] Among the main ecological factors, the average temperature and type of soil can determine the sandflies activities and ultimately the outbreak of CL.[21] Climate change can facilitate the expansion of leishmaniasis and create the suitable habitat for vector and reservoir species.[22] Phlebotomine sandflies are assumed to be specific to areas with warmer climatic conditions (mainly to the tropics and subtropics) and so they are generally characterized as thermophilic species.[23]

Although there has been an increase in the number of studies on CL prevalence across Iran, based on our knowledge, the country does not have an overall estimation of the prevalence of CL at the Iranian's climatic regions. In the present systematic review and meta-analysis, we reviewed and retrieved publications relating to leishmaniasis in Iran based on six climatic regions that classified according to Thermal, humidity and cloudiness, precipitation, wind and dust, and Thunder factors and also the atmosphere pressure.

The objective of this study was to estimate the prevalence of CL in the climatic regions of Iran. This study may help policymakers to develop better control and prevention programs.

Materials and Methods

Literature search strategy

The literature search was conducted by three reviewers independently to identify all published studies reporting the prevalence or incidence of CL in Iranian people. The search was conducted in electronic databases of ISI web of sciences, PubMed, Google Scholar, Magiran, Irandoc, IranMedex, Sciencedirect, Scientific Information Database, and Scopus with no time limitation. The search was performed using such terms as follows: "Leishmania*," "cutaneous Leishmania*," "cutaneous Leishmaniasis and Iran," "Leishmaniasis prevalence and Iran," "Leishmaniasis incidence and Iran" both in Persian and English languages. For instance, the term strategy in ISI is as follows: TS= (Prevalence or incidence) AND TS= (leishmania* OR cutaneous) AND TS= (Iran(. The process of search is shown in Figure 1.

Eligibility criteria and data extraction procedure

All articles on CL in Iran were downloaded and added to the Endnote reference manager. Duplicates were rigorously checked and removed. Studies that were conducted out of Iran and also the animal-based studies were removed. The inclusion criteria include on observational studies that report the prevalence or incidence of the disease in Iran. In addition, one of the employed diagnostic approaches such as microscopic, serological, molecular, and culture methods were checked.

Data which were extracted from articles including Author(s) name, years of the study, year of the published paper, sample size, number of positive cases, prevalence, diagnosis method used, type of CL studied, demographic information such as age, sex ratio, and climatic regions. The Iran climatic regions included coastal areas of the Caspian Sea West-East parts, coastal areas of the Persian Gulf and Oman sea west part, coastal areas of the Persian Gulf and Oman sea east part, mountainous and high areas of the central plateau, foothills of the central plateau, and desert areas. Geographical regions of the study also were noted. The above data were recorded and extracted to the preprepared data extraction excel sheets. Based on the intensive literature search, a total of 350 studies that report on CL in Iran were retrieved. Due to eligibility criteria, only 42 studies were selected to the final systematic review and meta-analysis procedure. All of the studies were on human reservoirs. It should be noted that the results of some selected studies have been done in more than 1 year or in more than one province and the results were presented for either separate years or provinces. As a result, the mentioned studies collapsed to the number of reported either year or province results. The summation of them transferred from 42 to 150 included studies for the meta-analysis.

Quality assessment and publication bias

In this study, the Joanna Briggs Institute critical appraisal was used to evaluate the quality of articles that reported prevalence data (last amended in 2017). This checklist consists of 9 different questions that the minimum and maximum scores for each study varied between 0 and 9. More information is shown in Table 1.

Besides, the quality assessment or publication bias was assessed using the Begg and Eggers test, as well as visual inspection of the funnel plot.

Statistical analyses

Statistical analyses were performed using STATA 14 software (StataCorp LLC; College Station, Texas, USA). Descriptive statistics of data were analyzed to estimate the pooled prevalence and its 95% confidence intervals (CIs). Because substantial heterogeneity was expected, random-effects meta-analysis was performed with the estimate of heterogeneity being taken from an inverse-variance model. Subgroup analysis was conducted and it stratified the studies according to climatic regions affected human hosts.

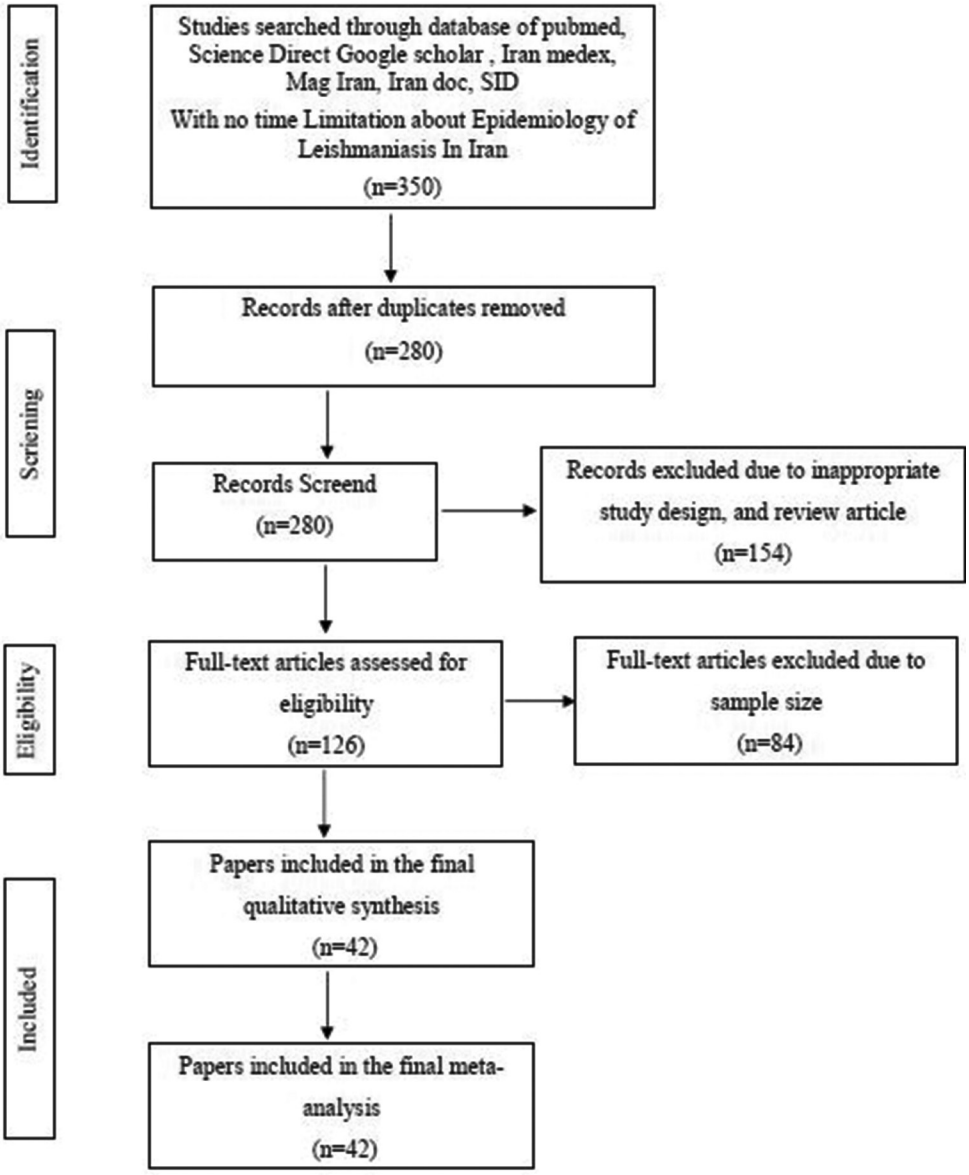

Figure 1: Flowchart of literature search and inclusion/exclusion process

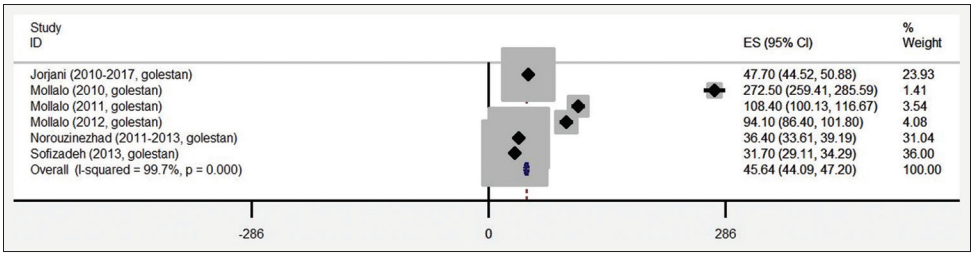

Figure 2: Forest plot of leishmaniasis prevalence per 100,000 population in coastal areas of the Caspian Sea east and west (climatic region 1) part of Iran

Between-studies heterogeneity was assessed using I^2 and Cochran's Q method and I^2 values of 25%, 50%, and 75% that were considered low, moderate, and high heterogeneity respectively. Meta-regression was used to investigate factors potentially contributing to the between-study heterogeneity.

Results

Descriptive results of eligible studies

Descriptive summary statistics were calculated to determine the total number of the population samples and the range of

Table 1: The Joanna Briggs Institute critical appraisal checklist for studies reporting prevalence data

Selected studies	1	2	3	4	5	6	7	8	9	Total score (%)
Jorjani (2019)	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Unclear	6 (67)
Mollalo (2015)	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Unclear	6 (67)
Sofizadeh (2016)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Fekri (2018)	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Unclear	6 (67)
Zare (2001)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Dehghani (2019)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Kassiri (2018)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Kassiri (2018)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Kassiri (2018)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	7 (78)
Azimi (2017)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Akhlagh (2019)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Zohirnia (2009)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Hamzavi (2015)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Ahmadi (2013)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Roghani (2013)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	6 (67)
Nikouee (2017)	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Unclear	6 (67)
Nazari (2016)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Ahmadi (2013)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Saghafipour (2012)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Hashemi (2011)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Khajedaluee (2014)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Nilforoushzadeh (2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	8 (89)
Abdollahzadeh (2018)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Doroodgar (2018)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	8 (89)
Doroodgar (2019)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Shiravand (2018)	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Unclear	6 (67)
Abedi-Astaneh (2016)	Yes	yes	yes	yes	yes	yes	Yes	Yes	Unclear	8 (89)
Nateghi Rostami (2013)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Sharifi (2011)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Razavinasab (2019)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Elyasi (2017)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Shirzadi (2020)	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Unclear	6 (67)
Shirzadi (2019)	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Unclear	6 (67)
Ramezankhani (2018)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Shirzadi (2015)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Athari (2006)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Heydarpour (2016)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Holakouie Naieni (2017)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Khazaei (2015)	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	6 (76)
Piroozi (2019)	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Unclear	6 (67)
Ayubi (2018)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)
Norouzinezhad (2016)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear	7 (78)

1 - Was the sample frame appropriate to address the target population?. 2 - Were study participants sampled in an appropriate way?. 3 - Was the sample size adequate?. 4 - Were the study subjects and the setting described in detail?. 5 - Was the data analysis conducted with sufficient coverage of the identified sample?. 6 - Were valid methods used for the identification of the condition?. 7 - Was the condition measured in a standard, reliable way for all participants?. 8 - Was there appropriate statistical analysis?. 9 - Was the response rate adequate, and if not, was the low response rate managed appropriately?

prevalence estimates [Table 2]. The flowchart of literature search is shown in Figure 1.

Meta-analysis

Random-effects meta-analysis was carried out using the total sample size and number of positive cases. Effect size (standard error [SE]) was used to estimate the prevalence of CL at the climatic regions. Variation in SE attributed to heterogeneity ($\pi^2 = 3e^{+3}$; heterogeneity $I = 100\%$ with heterogeneity Chi-square $= 2.3e^{+4}$ a degree of freedom = 150 and $P < 0.001$). Individual studies showed that prevalence per 100,000 population estimates ranged from 1.5 to 318.7 with the overall random pooled prevalence of 83.3 (95% CI: 74.5–92.1). Studies weighted on individual studies varied from 0.26% to 0.67%. The forest plot aren't shown here.

Subgroup meta-analysis

Subgroup analysis was done for 6 climatic regions. Furthermore, meta-regression analysis was done for selected

variable groups such as sex ratio, age, and the year of study. Subgroup analysis by climatic regions showed that many studies were conducted in the desert areas and also, it has more prevalent than the other climatic regions. More results are shown in Figures 2-7. Based on the selected eligible studies, CL was reported in 6 climatic regions of Iran as (1) Coastal areas of Caspian sea west, east and central part including 6 study reports, (2) Coastal areas of Persian Gulf and Oman sea east part including 3 study reports, (3) Coastal areas of Persian Gulf and Oman sea west part including 7 study reports, (4) Mountains and high areas of central plateau part including 18 study reports, (5) Foothills of the central plateau

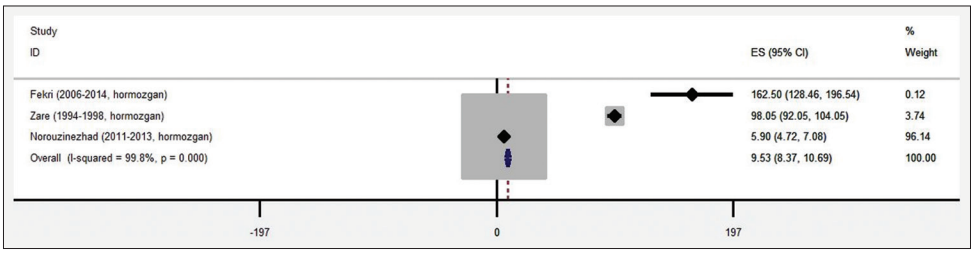

Figure 3: Forest plat sf leishmaniasis prevalence per 100,000 population in Persian Gulf and Oman Sea east (climatic region 2) part of Iran

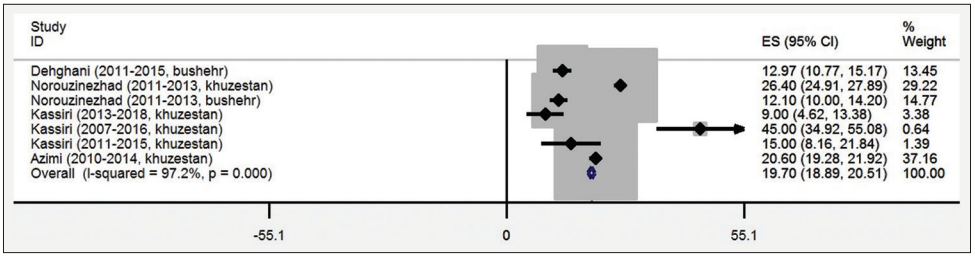

Figure 4: Forest plot of leishmaniasis prevalence per 100,000 population in Persian Gulf and Oman sea West (climatic region 3) part of Iran

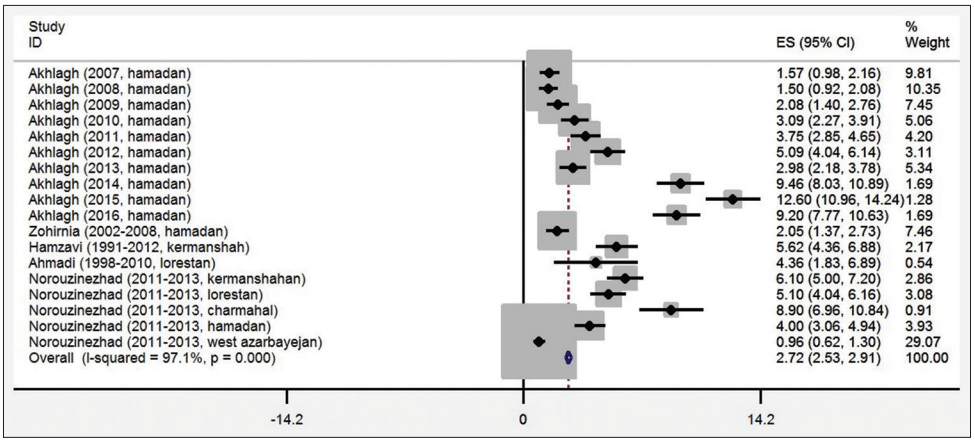

Figure 5: Forest plot of leishmaniasis prevalence Per 100,000 population in mountains and high areas of central plateau (climatic region 4) of Iran

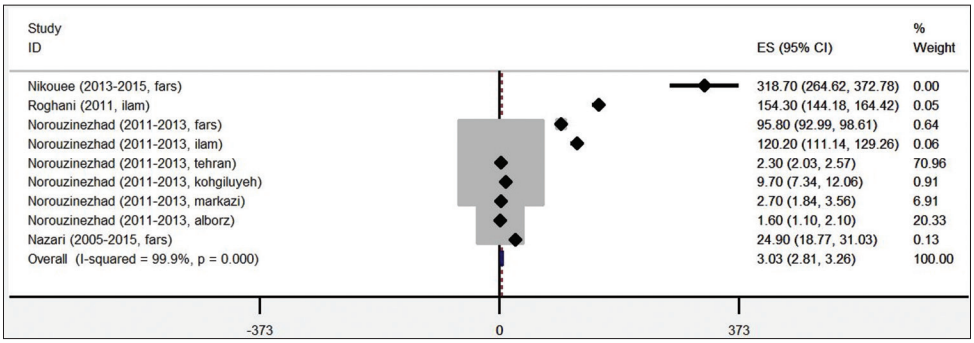

Figure 6: Forest plot of leishmaniasis prevalence per 100,000 population in Foothills of the Central plateau (climatic region 5) of Iran

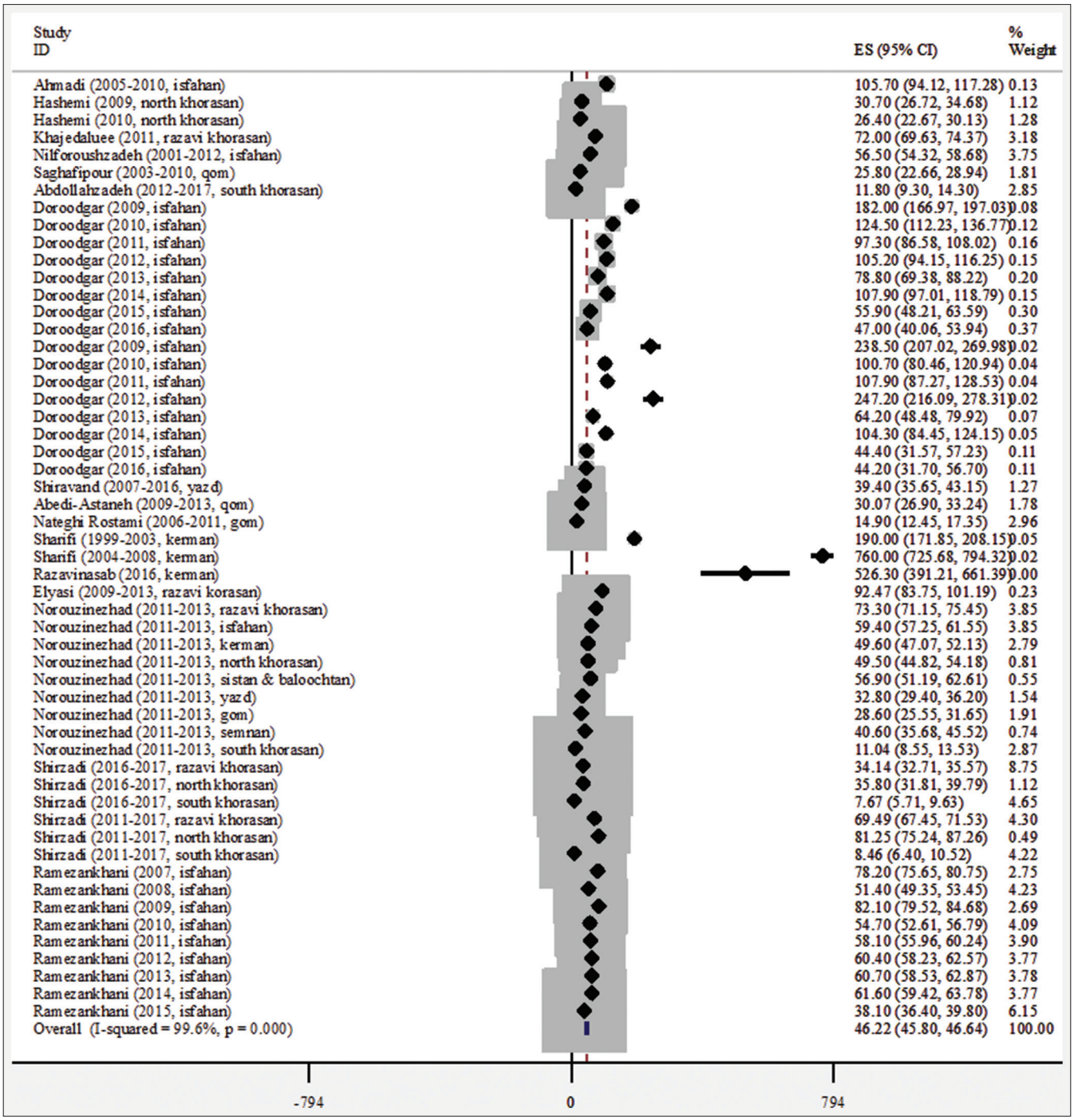

Figure 7: Forest plot of leishmaniasis prevalence per 100,000 population in desert areas (climatic region 6) of Iran

part including 9 study reports, and (6) Desert areas including 54 study reports. Forest plots of CL prevalence (95% CI) per 100,000 population were 45.6 (44.1–47.2), 9.5 (8.4–10.7), 19.7 (18.9–20.5), 2.7 (2.5–2.9), 3.1 (2.8–3.3), and 46.2 (45.8–46.6), respectively, in climatic regions 1–6 [Figures 2-8].

There were 53 reports from the total regions of Iran. The forest plot showed that the prevalence of CL per 100,000 population was 57.5 (57.4–57.6) [Figure 9].

Meta-regression

Meta-regression was done for age means, sex ratio (female/male), and the study year. The study year was not significantly associated with the prevalence of CL in the final multiple meta-regression ($P = 0.762$). The results showed that the sex ratio had a positive correlation with the prevalence of CL ($P = 0.039$). Furthermore, the higher mean age significantly had less CL prevalence ($P = 0.033$).

Biases in the review

We found no specific bias in this review process.

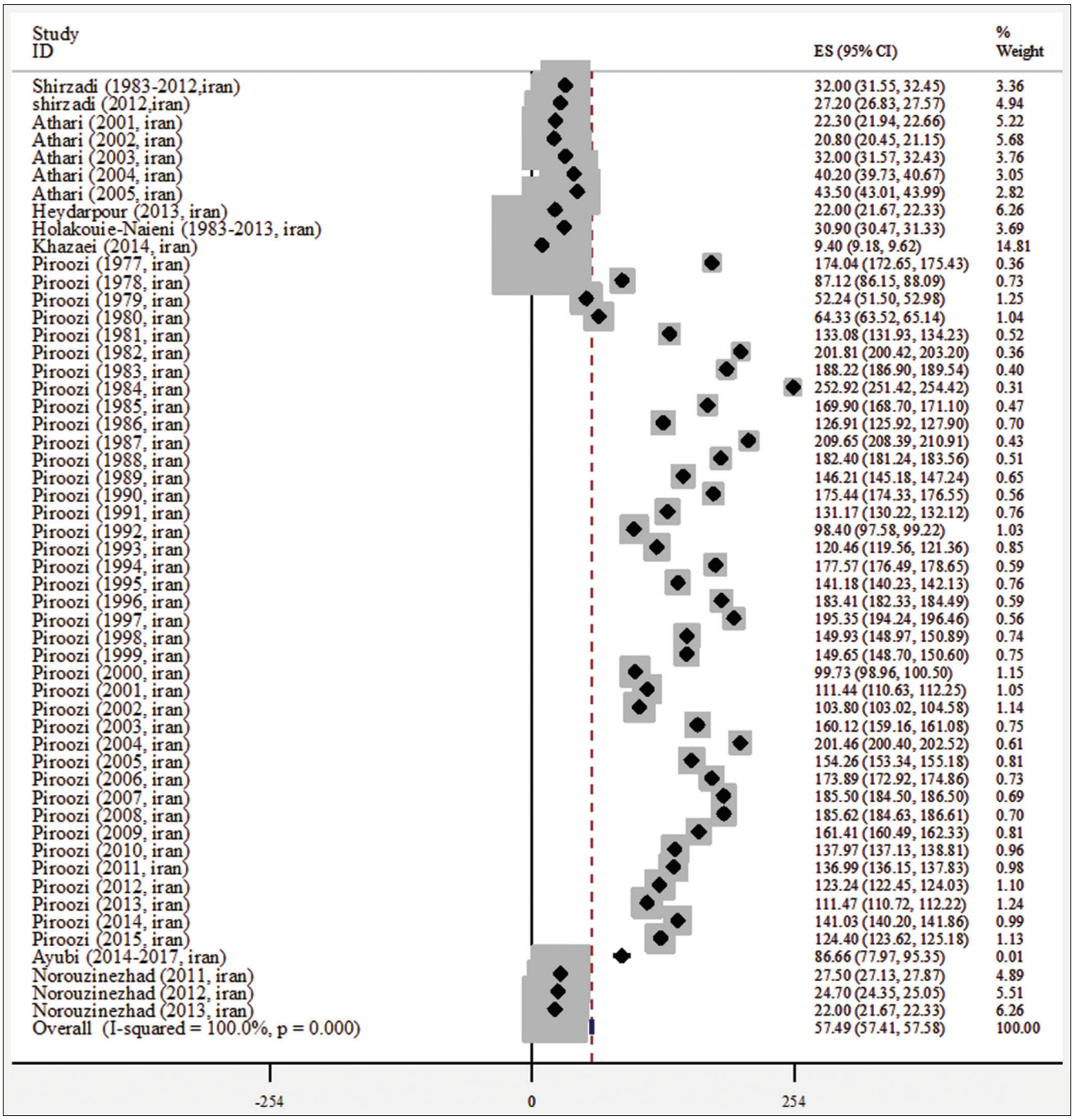

Figure 8: Spatial geographic distribution of climatic regions of Iran

Discussion

According to our knowledge, this is the first systematic review and meta-analysis on the prevalence of CL based on climatic regions of Iran. The final descriptive results and meta-analysis of the prevalence were done on 42 selected articles in humans. The results of the meta-analysis showed high variability between studies using Higgin's I^2. Because of the considerable variability between studies, the random-effects meta-analysis was used. It was demonstrated that pooled prevalence of CL was 85/100,000 in Iran which it was most prominently occurred in regions with dry and desert climates. Leishmaniasis was more prevalent (46.2/00,000) in these regions than in the other climatic regions. Most cases in these regions were observed in the provinces of southern Khorasan, Khorasan-e-Razavi, northern Khorasan, Sistan and Baluchestan, Semnan, Isfahan, Qom, and Yazd.[24-29] According to the current study, it was highly prevalent in the desert area, coastal areas of Caspian sea east, Persian Gulf and Oman sea west, and Persian Gulf and Oman sea east, respectively.

Table 2: Descriptive statistics of included in the final systematic review and meta-analysis

References	Author (publication time)	Date of study	Age, mean±SD	Gender proportion (female/male)	Study location	Climatic regions	Diagnosis method	Annual average prevalence (per 100,000)	Number of positive	Sample size	Quality assessment score (%)
[5]	Jorjani *et al.*(2019)	2010-2017	20.7±16.9	0.76	Golestan	1	Unclear	47.7	6873	1,813,091	67
[34]	Mollalo *et al.*(2015)	2010-2012	19.3±14.4	0.69	Golestan	1	Laboratory	158.3	2893	609,053	67
[35]	Sofizadeh *et al.*(2016)	2013	18.8±25.3	0.66	Golestan	1	Unclear	31.7	573	1,813,091	78
[20]	Fekri *et al.*(2018)	2006-2014	18.6±17.1	0.82	Hormozgan (Jask)	2	Unclear	162.5	874	53,770	67
[36]	Zare S and Baghestani (2001)	1994-1998	14.5±14.7	0.74	Hormozgan	2	Clinical laboratory	98.05	4094	1,043,855	78
[21]	Dehghani *et al.*(2019)	2011-2015	21.9±17	0.68	Bushehr	3	Unclear	12.97	663	1,032,949	78
[37]	Kassiri and Mehr-Aghaei (2018)	2013-2018	24.9±16.3	0.72	Khuzestan (karun)	3	Laboratory	9	81	180,000	78
[38]	Kassiri *et al.*(2018)	2007-2016	14.1±22.4	0.93	Khuzestan (Khorramshahr)	3	Laboratory	45	745	170,000	78
[39]	Kassiri *et al.*(2018)	2011-2015	25.6±17.6	0.83	Khuzestan (Abadan)	3	Laboratory	15	179	123,000	78
[40]	Azimi *et al.*(2017)	2010-2014	-	-	Khuzestan	3	Unclear	20.6	4672	4,531,720	78
[18]	Akhlagh *et al.*(2019)	2007-2016	34.4±13.2	0.06	Hamedan	4	Laboratory	5.1	908	1,764,087	78
[41]	Zohirnia *et al.*(2009)	2002-2008	28.7±11.7	0.07	Hamedan	4	Clinical laboratory	2.05	210	1,707,317	78
[42]	Hamzavi and Khademi (2015)	1990-2012	37.3±19.3	0.75	Kermanshah	4	Laboratory	5.62	1684	1,362,018	67
[43]	Ahmadi *et al.*(2013)	1998-2010	18.8±10.2	0.09	Lorestan (Borujerd)	4	Laboratory	4.36	137	261,850	78
[7]	Roghani *et al.*(2013)	2011	-	0.56	Ilam	5	Unclear	154.3	891	577,599	67
[6]	Nikouee *et al.*(2017)	2013-2015	11.3±17.2	1.37	Fars (Zarindasht)	5	Unclear	318.7	266	41,729	67
[44]	Nazari *et al.*(2017	2005-2015	15.7±24.1	0.78	Fars	5	Unclear	24.9	700	254,704	78
[45]	Ahmadi *et al.*(2013)	2005-2010	24.8±18.1	0.82	Kashan	6	Clinical laboratory	105.7	1599	302,637	78
[26]	Saghafipour *et al.*(2012)	2003-2009	-	0.73	Qom	6	Clinical laboratory	25.8	1812	1,003,322	78
[24]	Hashemi *et al.*(2011)	2009-2010	-	0.66	North Khorasan	6	Clinical laboratory	28.3	485	855,957	78
[25]	Khajehdalavi *et al.*(2014)	2011	25.3±17.8	0.92	Razavi Khorasan	6	Laboratory	72	3558	4,929,471	78
[46]	Nilforoushzadeh *et al.*(2015)	2001-2012	21.9±0.94	1.62	Isfahan	6	Laboratory	56.5	28,315	4,559,256	89
[47]	Abdollahzadeh *et al.*(2018)	2012-2017	26.9±17.7	0.61	South Khorasan	6	Clinical laboratory	11.8	426	724,391	78
[12]	Doroodgar (2018)	2009-2016	32.9±20.3	0.72	Kashan	6	Laboratory	100.9	2676	331,352	89
[48]	Doroodgar (2019)	2009-2016	27.9±20.7	0.71	Aran va Bidgol	6	Laboratory	118.9	926	97,330	78
[49]	Shiravand *et al.*(2018)	2007-2016	31.2±19.3	-	Yazd	6	Unclear	39.4	4229	1,074,428	67
[50]	Abedi-Astaneh *et al.*(2016)	2009-2013	-	054	Qom	6	Laboratory	30.07	1767	1,151,672	89
[29]	Nateghi Rostami *et al.*(2013)	2006-2011	28.7±18.3	0.69	Qom	6	Laboratory	14.9	849	949,664	78
[51]	Sharifi *et al.*(2011)	1999-2008	15.5±16.7	0.96	Kerman (Bam)	6	Laboratory	475	11,448	241,011	78
[52]	Razavinasab (2019)	2016	-	1.52	Kerman	6	Laboratory	526.3	58	11,021	78
[53]	Elyasi (2017)	2009-2013	31.1±20.5	0.76	Razavi Khorasan	6	Clinical laboratory	92.47	2158	466,740	78
[54]	Shirzadi *et al.*(2020)	2016-2017	-	-	Khorasan	6	Unclear	25.66	2565	8,066,491	67
[55]	Shirzadi *et al.*(2019)	2011-2017	-	-	Khorasan	6	Clinical laboratory	53.07	31,036	8,066,491	67
[56]	Ramezankhani *et al.*(2018)	2007-2015	-	-	Isfahan	6	Clinical laboratory	60.4	26,347	48,632,767	78
[57]	Shirzadi *et al.*(2015)	1983-2012	-	-	Iran	7	Laboratory	32	566,532	60,055,488	78
[58]	Athari and Jalal Lu (2006)	2001-2005	-	0.72	Iran	7	Laboratory	31.8	107,097	67,256,250	78
[59]	Heydarpour *et al.*(2016)	2013	-	0.78	Iran	7	Unclear	22	16,980	76,945,000	78

Contd...

Table 2: Contd...

References	Author (publication time)	Date of study	Age, mean±SD	Gender proportion (female/male)	Study location	Climatic regions	Diagnosis method	Annual average prevalence (per 100,000)	Number of positive	Sample size	Quality assessment score (%)
[27]	Holakouie Naieni *et al*.(2017)	1983-2013	-	-	Iran	7	Clinical laboratory	30.9	589,913	63,636,785	78
[28]	Khazaei *et al*.(2015)	2014	31.4±22.1	0.81	Iran	7	clinical laboratory	9.4	3684	77,800,000	67
[60]	Piroozi *et al*.(2019)	1977-2015	-	-	Iran	7	Unclear	149.3	3,427,583	58,855,560	67
[61]	Ayubi *et al*.(2018)	2014-2017	-	-	Iranian army units	7	Unclear	86.66	1144	440,000	78
[62]	Norouzinezhad *et al*.(2016)	2011-2013	28.1±17.4	0.77	Iran	7	Laboratory	24.7	56,546	76,072,338	78

Climatic regions: 1. Coastal areas of Caspian Sea, East, and West part, 2. Coastal areas of the Persian Gulf and Oman Sea, East part, 3. Coastal areas of the Persian Gulf and Oman Sea, West part, 4. Mountains and high areas of central plateau part, 5. Foothills of the central plateau part, 6. Desert areas part, 7. All climates. SD: Standard deviation

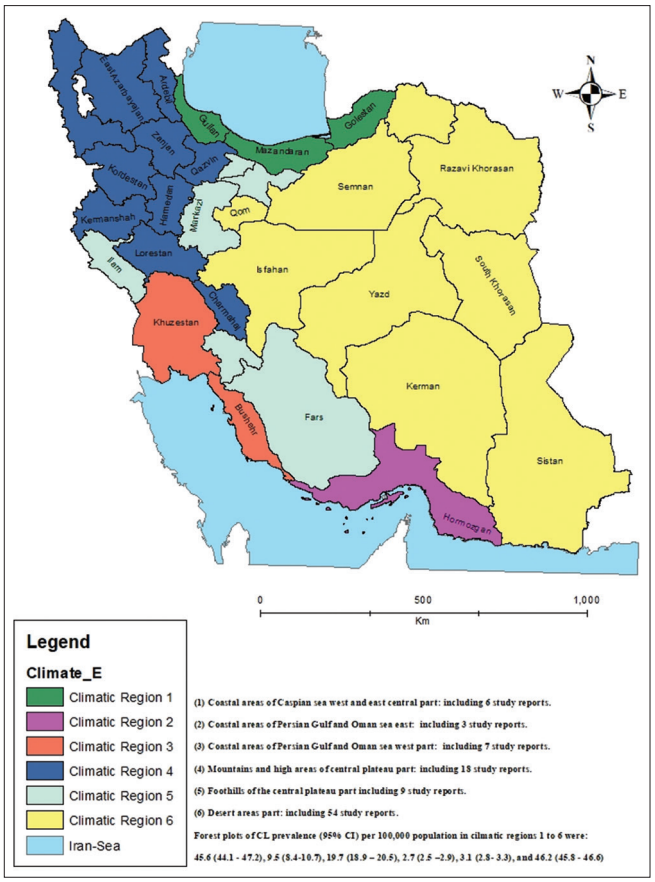

Figure 9: Forest plot of leishmaniasis prevalence per 100,000 population in Iran

A systematic review and meta-analysis was done by Sabzevari *et al*. on CL in Iran from 2000 to 2019 in which 84 studies were selected. Using random-effect model, the pooled prevalence was estimated about 45/100,000 population. The prevalence was calculated based on both *Leishmania tropica* and *Leishmania major* spices were caused by anthroponotic CL and zoonotic CL (ZCL), respectively.[30] In another systematic review and meta-analysis of CL which was conducted by Panahi *et al*. in Iran from 2000 to 2016 including 44 selected studies, the pooled prevalence was 77 per 100,000 population based on both *L. tropica* and *L. major* spices.[31] In contrast, the current study prevalence is calculated based on only ZCL. However, the effects of climatic factors on the occurrence of ZCL were similar to CL incidence in previous studies. Therefore, depending on the various Leishmania species, the variability of the climate factors may have different impacts on the occurrence of CL.[32] In a systematic review and meta-analysis of leishmaniasis that was performed in Ethiopia, the overall estimated prevalence was 19.1% in both humans and animals. It was highly prevalent in the northern and southern parts of the country.[33] Mohammadbeigi *et al*. in their systematic review study concluded that leishmaniasis is a climate-sensitive disease, and changes in environmental factors such as temperature, rainfall, and humidity can impact the epidemiology of the

disease with the changes they make on population size, distribution, and the survival of sandflies.[32]

The current study revealed a higher prevalence of CL in females than males. These results were inconsistent with those which were reported by Sabzevari *et al*.[30] This study demonstrated that there has been an increase in the number and also the quality of works in recent years.

Conclusion

The prevalence of CL in this study that was estimated based on climatic regions showed that it was highly prevalent in Iran. One of the advantages of this work is that majority of selected studies have been conducted on population base. However, disadvantages might be because of poor design of some studies or the lack of interval validity [Table 1]. Moreover, one of the major limitations in this study is that some of the study locations were nested in more than one climate condition. As a result, we considered a dominant climate condition for every province of Iran and then we assigned every climatic region for each province. Finally, we concluded that climatic factors impact on CL incidence and our results revealed that leishmaniasis was more prevalent in dry and arid regions. Therefore, it should be noted that a unified strategy cannot be applied to the whole country, and control programs should be used according to climate change in each region.

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Conflicts of interest

There are no conflicts of interest.

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