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# Prevalence of cutaneous Leishmaniasis in the Middle East: a systematic review and meta-analysis

Mohsen Karami[a], Tahmineh Gorgani-Firouzjaee[a] and Mohammad Chehrazi[b]

[a]Department of Mycology and Parasitology, School of Medicine, Babol University of Medical Sciences, Babol, Iran; [b]Department of Biostatistics and Epidemiology, School of Health Science, Babol University of Medical Sciences, Babol, Iran

**ABSTRACT**

Cutaneous leishmaniasis (CL), caused by an obligate intracellular protozoan parasite from the genus Leishmania, imposing a significant burden on underdeveloped countries especially those located in the Middle East. Four electronic databases were searched to evaluate the prevalence of CL in the Middle East. The random effects model (95% confidence intervals (CI)) were applied to determine the overall and subgroup pooled prevalence. Heterogeneity was assessed by Cochran's Q test and I2 statistics. Among 2424 peer-reviewed papers, 37 datasets from 34 studies were included in the current meta-analysis. 285560 individuals were assessed across 9 Middle Eastern countries. The pooled prevalence of CL was estimated at 12% (95% CI 9-15 %; 10718/285560). The highest prevalence rate was observed in Syria (39%, 37-42%), and the lowest one was found in Iraq and Lebanon (0%, 0-1%). The prevalence of CL in studies that applied LST assays had the highest rate (48%, 17-80%). The infection rate in males was similar to females (7%, 4-10%). The prevalence of infection in individuals living in urban areas was higher than in rural areas (14%, 10-19%). The prevalence of CL in the age group 0-15 years was higher than in individuals 16-40 and >40 years (9%, 6-13%). Most of the lesions were found on the face, and single lesions were more prevalent than two and three ones. In conclusion, the occurrence of CL was considerable in Middle Eastern countries. Therefore, more efforts should be made to precisely report the CL in this region for developing appropriate preventive and controlling strategies.

**KEYWORDS**
Cutaneous leismaniasis; prevalence; Middle East

## 1. Introduction

Leishmaniasis is one of the neglected tropical diseases, according to the World Health Organization (WHO) report [1]. This disease is caused by an obligate protozoan parasite, which belongs to the genus *Leishmania*. It commonly occurs through the bite of sand flies, which inject metacyclic promastigotes (infective stage of *Leishmania*) into the skin [2]. Almost 90 species of sand flies are known to be vectors of *Leishmania* parasites, with the two mainly implicated vector species being *Phlebotomus* and *Lutzomyia* [2,3].

According to the WHO, almost 102 countries/areas are endemic for *Leishmania* infections [4]. This disease appears in four major clinical forms, including visceral leishmaniasis (VL, kala-azar), cutaneous leishmaniasis (CL), post-kala-azar dermal leishmaniasis (PKDL), and mucocutaneous leishmaniasis [4,5]. Globally, 70 countries are endemic for CL, and nearly 10 countries (Afghanistan, Algeria, Brazil, Colombia, Iran, Iraq, Libya, Pakistan, the Syrian Arab Republic, and Tunisia) have reported about 87% of new CL cases. The annual incidence of CL was estimated at 600,000 to 1,000,000 new cases [4,6]. It is also commonly found in two main forms in the Middle East, namely, zoonotic CL (ZCL) caused by *L. major* and anthroponotic CL (ACL) caused by *L. tropica* [2,7].

Considering the emergence of lesions, ACL is the so-called dry type, which is mainly transmitted among humans in urban areas. On the other hand, in ZCL, as the wet type of lesions, rodents are usually reservoir hosts in rural regions [2,8]. The active phase of CL is characterized by lesions that advance from papules and nodules to plaques and ulcers. Another phase of CL is inactive or scaring lesions which commonly develop following an active phase [9]. These lesions are generally found on the face, hands, legs, and to a lesser extent, in other parts of the body. According to epidemiological studies, approximately 50% of lesions occur on the face [9]. Since facial scars can persist for a long time, they are considered social stigmas with psychological consequences, including depression, seclusion, and decrease of quality of life (QOL) [10,11].

The facial scars due to CL can lead to the loss of job opportunities and also a decrease in self-confidence to participate in social activities, especially in women and children [12]. In recent years, several factors, including environmental conditions, climate changes, lack of urbanization management, war and migration, use of

**CONTACT** Tahmineh Gorgani-Firouzjaee t.gorgani@gmail.com Department of Mycology and Parasitology, School of Medicine, Babol University of Medical Sciences, Ganj-Afroz Ave.Babol, Babol, I.R Iran
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agricultural lands for residential purposes, and changes in vector populations, are associated with a considerable increase in leishmaniasis [13]. In recent years, some countries in the Middle East, such as Syria and Lebanon, have faced a war crisis, which caused an influx of refugees to the border areas of neighboring countries. With the migration of people from endemic areas to non-endemic areas and vice versa, the prevalence of CL increased significantly. To implement control programs and increase the level of public health, knowledge of the latest occurrence rate of this disease can be helpful in the region. Therefore, a systematic review and meta-analysis study of existing data on the prevalence of cutaneous leishmaniasis in the Middle East was performed.

## 2. Material and methods

### 2.1. Search scheme and selection criteria eligibility

We conducted a systematic review and meta-analysis study according to instructions from the Predefined Protocol Items for Systematic Reviews and Meta-Analyses (PRISMA) statements [14].

A comprehensive literature search was conducted from English language databases (PubMed, Web of Science, Scopus, and Google Scholar) up to the 1st June 2021. An additional literature search was performed through the references of key studies. The main search terms were applied alone or in combination, as follows: "Cutaneous Leishmaniases", "old world Leishmaniasis", "*Leishmania* infection", "diffuse cutaneous leishmaniasis", "prevalence", "epidemiology, "incidence", "Frequency" and each country which located in the Middle East region (Bahrain, Cyprus, Egypt, Iran, Iraq, Jordan, Kuwait, Lebanon, Oman, Palestine, Qatar, Saudi Arabia, Syria, Turkey, United Arab Emirates, and Yemen) was also included.

In the next step, duplicate publications were removed, and the initial title and abstract were screened by two independent researchers according to inclusion and exclusion criteria (T.G.F. and M.K.). Only studies conducted on human subjects without time limitations, all population-based, cross-sectional, and cohort peer-reviewed original observational studies reporting the prevalence of cutaneous leishmaniasis in the Middle East, studies that applied different diagnostic methods such as skin examination, serological and molecular techniques for evaluation of the prevalence of CL were considered for inclusion. Studies which assessed the frequency of cutaneous leishmaniasis on suspected individuals/patients were not eligible for inclusion. In addition, studies that were carried out on non-human subjects, duplicate articles, non-English language papers, experimental research, conference papers, reviews, case reports, case series, and letters or correspondences were excluded from the current work.

### 2.2. Data extraction and study quality assessment

The full-text of all selected papers was reviewed for inclusion by two independent authors. Then, data was extracted from selected studies and included in an Excel sheet. After that, variables were taken out from eligible studies that included the followings: the first author's last name, publication year, operation year, implementation country, mean age or age range of the studied population, gender, diagnostic methods, location (urban/rural), total sample size and number of infected subjects. Any dissimilarity in data extraction was resolved with the contribution of the third author. The quality assessment (risk of bias) was evaluated using the Joanna Briggs Institute Critical Appraisal Tool (JBI) for prevalence studies. According to the JBI protocol, nine questions were answered for each study, and they were categorized based on the total score to show poor quality (high risk of bias), 0–3 points; moderate quality (moderate risk of bias), 4–6 points; and high quality (low risk of bias), 7–9 points [15].

### 2.3. Data synthesis and statistical analysis

All statistical analysis was performed by Stata version 15 (College Station, Texas 77,845 USA), and the significance level was considered as *P*- value <0.05.

In the current meta-analysis, for evaluation of the pooled (weighted) proportion of cutaneous leishmaniasis, a random-effects model was used, and the $I^2$ statistic was considered to measure the discrepancy in the prevalence estimates across the studies. Subgroup analyses were applied to find the sources of heterogeneity. Subgroup analysis was performed based on several variables, including each Middle Eastern country, study period, type of diagnostic methods, sample size, gender, age, location (urban/rural), *Leishmania* identified species.

## 3. Results

### 3.1. Main characteristics of the studies

The study selection process according to the PRISMA statements is shown in Figure 1. The preliminary search resulted in 2424 studies. Subsequently, duplicate papers and unrelated studies were removed according to the title and abstract. Finally, 212 full texts of eligible articles were assessed, from which 37 datasets were included in the quantitative analysis based on the inclusion and exclusion criteria. Also, 6 articles were found through searching the references

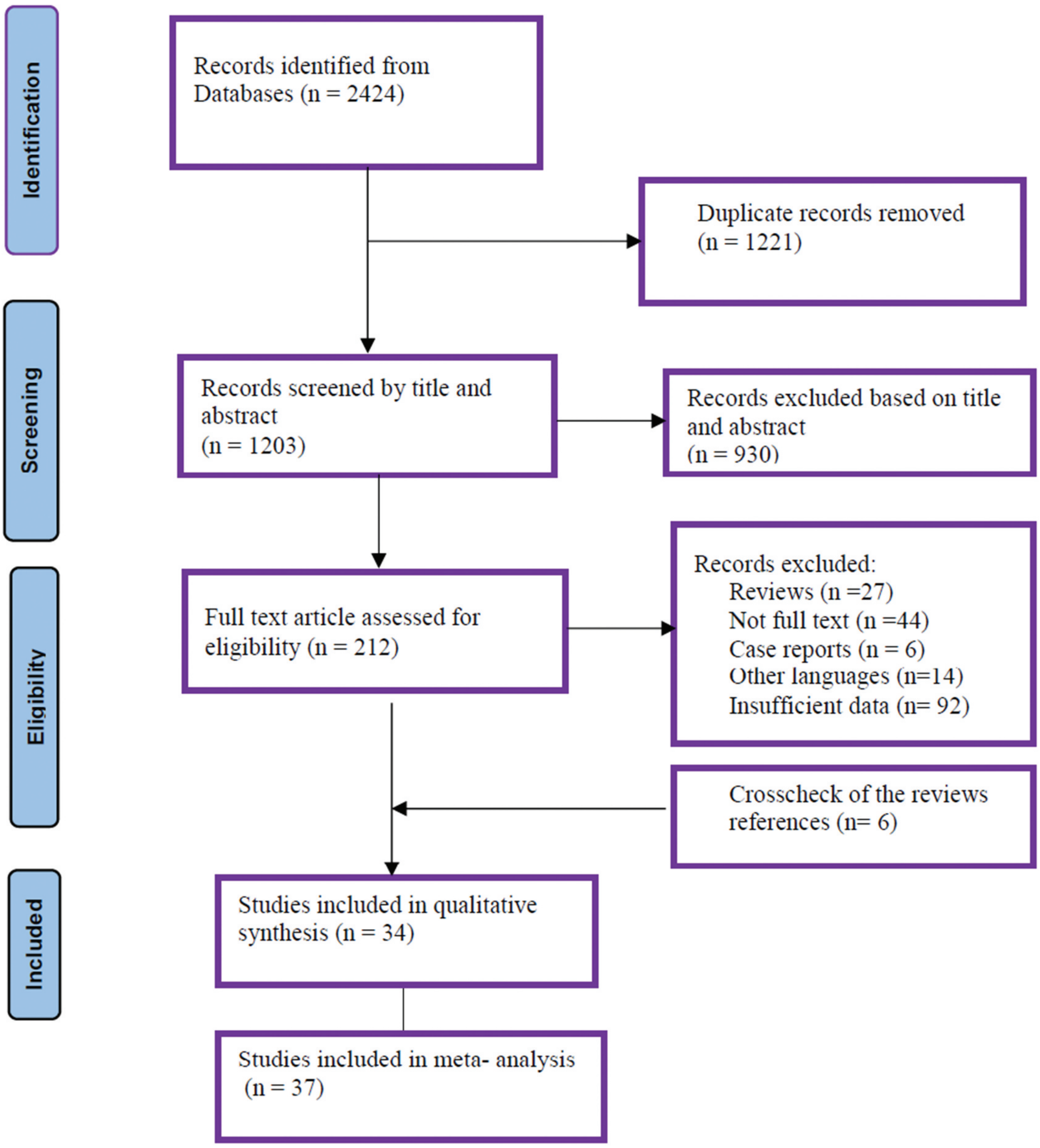


Figure 1. PRISMA flow chart of study identification and selection.

of relevant studies included in the quantitative analysis (Figure 1).

Out of 37 articles, 31, 4, and 2 studies evaluated CL infection by microscopy examination, leishmanin skin test (LST), and serological methods, respectively. Two studies used microscopy and LST methods [16,17]. Two other studies reported the CL prevalence based on the LST technique (Table 1) [23,34]. Totally, 37 datasets from 34 studies were included in the current meta-analysis. These studies illustrated data on 285,560 individuals from the 37 datasets across 9 countries of Middle Eastern regions as follow: 22 datasets for Iran (164595 individuals), 2 for Saudi Arabia (9253 individuals), 3 for Yemen (2855 individuals), 3 for Jordan (1897 individuals), 2 for Syria (1106 individuals), 1 for Lebanon (81486 individuals), 1 for Iraq (23778 individuals), 1 for Egypt (141 individuals), and 1 for Palestine (190 individuals) (Table 1).

### *3.2. Overall prevalence of cutaneous leishmaniasis in the Middle East*

The random effects pooled prevalence of CL in the Middle East was 12% (95% CI 9–15 %; 10718/285560) with a very high heterogeneity ($Q = 25403.63$, $df = 35$, $I^2 = 99.86\%$, $P < 0.001$). According to Middle Eastern regions, Syria (39%, 37–42%) has the highest prevalence of CL, and the lowest prevalence rate was found in Iraq and Lebanon (0%, 0–0%). The Pooled prevalence in other Middle Eastern countries was as follows: Jordan (34%,0–86%), Palestine (26%, 21–33%), Yemen (19%,19–20%), Saudi Arabia (16%15–16%), Iran (7%, 4–10%), and Egypt (4%, 2–9%) (Table 2) (Figure 2). Figure 3 shows a Geographic Information System (GIS) map summarizing the prevalence of cutaneous leishmaniasis in individual countries in Middle Eastern region.

Table 1. Main characteristics of included studies reporting prevalence of cutaneous leishmaniasis in the Middle East.

| First author/year/Reference | Study period | Country | specimen | Location | Gender | Age | Methods | Sample Size | Case | Active lesion | Scar lesion | PCR+ | Species |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Aflatoonian et al 2013 [18] | 2010 | Iran | Skin scrap | rural | both | 1–96 | Microscopy/PCR | 5544 | 67 | NA | NA | 15 | *L. tropica* |
| Akhavan et al 2007a [19] | 2003 | Iran | Skin scrap | rural | both | 1>->25 | microscopy | 2441 | 280 | 27 | 253 | NA | *L. major* |
| Akhavan et al 2007b [19] | 2003 | Iran | Skin scrap | rural | both | 6-12 | microscopy | 1662 | 263 | 19 | 244 | NA | *L. major* |
| Al-Jawabreh et al 2003 [20] | 1994–99 | Palestine | Serum | rural | NA | NA | Serology | 190 | 50 | NA | NA | NA | *NA* |
| Alkulaibi et al 2019a [16] | 2015 | Yemen | Skin scrap | rural | both | 16->45 | microscopy | 1165 | 215 | 189 | 26 | NA | *NA* |
| Alkulaibi et al 2019b [16] | 2015 | Yemen | NA | rural | both | 16->45 | LST | 1165 | 215 | NA | NA | NA | *NA* |
| AlSamarai et al 2009 [21] | 2004-05 | Iraq | Skin scrap | urban | both | 1-60 | microscopy | 23778 | 107 | NA | NA | NA | *NA* |
| Amin et al 2012 [22] | 2009 | Saudi Arabia | Skin scrap | both | both | 15- ≥50 | microscopy | 1824 | 1313 | NA | NA | NA | *NA* |
| Arbaji et al 1993 [23] | 1991 | Jordan | NA | rural | NA | 3->9 | LST | 399 | 350 | NA | NA | NA | *NA* |
| Asgari Nezhad et al 2012 [24] | 2009 | Iran | Skin scrap | urban | both | 5-19 | Microscopy/PCR | 7555 | 767 | 32 | 735 | NA | *L. major* |
| Ashford et al 1993a [17] | 1990-91 | Syria | NA | rural | NA | <5-10 | LST | 259 | 160 | NA | NA | NA | *NA* |
| Ashford et al 1993a [17] | 1990-91 | Syria | NA | rural | NA | <5-10 | Microscopy | 847 | 278 | NA | NA | NA | *NA* |
| Askari et al 2018 [25] | 2015-16 | Iran | Skin scrap | both | both | 1-83 | Microscopy/PCR | 46799 | 160 | 160 | 0 | 160 | *L. major* |
| Asmaa et al 2017 [26] | 2012-13 | Yemen | Skin scrap | Rural | both | 1-60 | Microscopy | 525 | 99 | NA | NA | NA | *NA* |
| Dye et al 1989 [27] | 1982-83 | Saudi Arabia | NA | Rural | NA | 0-60 | Microscopy | 7411 | 474 | 202 | 272 | NA | *NA* |
| Emami et al 2009 [28] | 2000-02 | Iran | Skin scrap | Rural | both | 0-≥25 | Microscopy/PCR | 3277 | 144 | 57 | 87 | 28 | *L. major* |
| Faris et al 1988 [29] | 1967-73 | Egypt | Skin scrap | Rural | both | <10- >21 | Microscopy | 141 | 6 | NA | NA | NA | *NA* |
| Fazaeli et al 2009 [30] | 2005–2006 | Iran | Skin scrap | urban | both | <10- >40 | Microscopy | 762 | 102 | NA | NA | NA | *L. Major* |
| Hamzavi rt al 2018 [31] | 2104-15 | Iran | Skin scrap | urban | both | 0- >80 | Microscopy | 5277 | 254 | 60 | 194 | NA | *NA* |
| Hanafi Majd et al 2006 [32] | 2005 | Iran | Skin scrap | Rural | both | NA | Microscopy/PCR | 1392 | 129 | 14 | 115 | 129 | *L. major* |
| Jafari et al 2020 [33] | 2015-16 | Iran | Skin scrap | Rural | both | 0-≥25 | Microscopy/PCR | 914 | 15 | 1 | 14 | 5 | *L. major* |
| Kamhawi et al 1995 [34] | 1994 | Jordan | NA | Rural | both | 5>->40 | LST | 626 | 146 | NA | 56 | NA | *NA* |
| Khosravi et al 2013 [35] | 2011-12 | Iran | Skin scrap | Rural | both | ≤10- >50 | Microscopy/PCR | 18308 | 869 | 30 | 839 | 29 | *L. tropica/major* |
| Kolivand et al 2015 [36] | 2013-14 | Iran | Skin scrap | both | both | 7-12 | Microscopy/PCR | 4800 | 31 | 15 | 16 | 15 | *L. major* |
| Mirzaei et al 2012 [37] | 2008 | Iran | Skin scrap | both | both | 10-40 | Microscopy/PCR | 3516 | 188 | 26 | 162 | | *L. tropica* |
| Nuwayri-Salti et al 2000 [38] | 1993-97 | Lebanon | Skin scrap | both | both | <20- >50 | Microscopy | 81486 | 224 | 124 | 100 | NA | *NA* |
| Obaidat and Roess, 2019 [39] | 2015–2016 | Jordan | Serum | both | both | <30->50 | Serology | 872 | 22 | NA | NA | NA | *NA* |
| Razavinasab et al 2019 [40] | 2015-16 | Iran | Skin scrap | Rural | both | <6- >40 | Microscopy/PCR | 11021 | 58 | NA | NA | 50 | *L. tropica* |
| Razmjou et al 2009 [41] | 2004-05 | Iran | Skin scrap | Rural | both | <10- ≥10 | Microscopy/PCR | 1000 | 232 | 70 | 162 | 27 | *L. major* |
| Sharifi et al 2010 [42] | 1994–06 | Iran | Skin scrap | urban | both | 6-18 | Microscopy/PCR | 22 838 | 523 | 523 | 0 | 9 | *L. tropica* |
| Sharifi et al 2011 [43] | NA | Iran | Skin scrap | urban | both | ≤10- >40 | Microscopy | 3884 | 204 | 69 | 135 | 26 | *L. tropica* |
| Talari et al 2006 [44] | 2001-03 | Iran | Skin scrap | urban | both | 6-15 | Microscopy | 1625 | 117 | 49 | 68 | NA | *L. major* |
| Yaghoobi-Ershadi et al 2001 [45] | 1997-98 | Iran | Skin scrap | both | both | 7-15 | Microscopy | 1960 | 48 | 18 | 30 | NA | *L. major* |
| Yaghoobi-Ershadi et al 2003 [46] | 2001–2002 | Iran | Skin scrap | Rural | both | 0-≥25 | Microscopy | 807 | 108 | 24 | 84 | NA | *L. major* |
| Yaghoobi-Ershadi et al 2004 [47] | 2001–2002 | Iran | Skin scrap | Rural | NA | 0->25 | Microscopy | 3024 | 1663 | 743 | 919 | NA | *NA* |
| Zahraei-Ramazani et al 2007 [48] | NA | Iran | Skin scrap | Rural | NA | 6- >11 | Microscopy/PCR | 16380 | 734 | 685 | 49 | NA | *NA* |

Table 2. Sub-group analysis of potential factors influencing the prevalence of Cutaneous Leishmaniasis in Middle Eastern region.

| Potential factors | Number of datasets | Prevalence (CI 95%) | $X^2$ | $I^2$ |
|---|---|---|---|---|
| **Middle East countries** | | | | |
| Egypt | 1 | 4(2–9) | NA | NA |
| Iran | 24 | 7(4–10) | 15123.01 | 99.85 |
| Iraq | 1 | 0(0–1) | NA | NA |
| Jordon | 3 | 34(0–86) | NA | NA |
| Lebanon | 1 | 0(0–0) | NA | NA |
| Palestine | 1 | 26(21–33) | NA | NA |
| Saudi Arabia | 2 | 16(15–16) | NA | NA |
| Syria | 2 | 39(37–42) | NA | NA |
| Yemen | 3 | 19(17–20) | NA | NA |
| **Location** | | | | |
| Urban | 7 | 10(5–11) | NA | NA |
| Rural | 20 | 14(10–19) | 5037.79 | 99.62 |
| **Gender** | | | | |
| Female | 18 | 7(4–10) | 6024.63 | 99.70 |
| Male | 18 | 7(4–10) | 5811.95 | 99.69 |
| **Age** | | | | |
| 0-15 | 20 | 9(6–13) | 3224.71 | 99.38 |
| 16-40 | 16 | 6(4–9) | 1930.03 | 99.17 |
| >40 | 9 | 4(3–5) | 965.58 | 99.07 |
| **Type of lesion** | | | | |
| Active | 24 | 48(28–69) | 8166.88 | 99.74 |
| Scar | 22 | 62(42–81) | 6534.16 | 99.71 |
| **No. Lesion** | | | | |
| Single | 12 | 57(49–66) | 360.61 | 96.7 |
| Two | 12 | 15(6–26) | 1034.39 | 98.84 |
| Three/more | 12 | 23(13–34) | 808.86 | 98.52 |
| **Site of lesion** | | | | |
| Face | 18 | 39(19–50) | 1143.51 | 98.43 |
| Hand | 18 | 30(23–40) | 910.85 | 98.13 |
| Leg | 18 | 13(10–17) | 281.50 | 93.61 |
| Other parts | 14 | 12(6–21) | 903.72 | 98.45 |
| **Sample size** | | | | |
| ≤200 | 5 | 9(4–17) | 75.44 | 94.70 |
| 201-1500 | 13 | 20(16–40) | 6628.59 | 99.79 |
| >1501 | 20 | 7(4–11) | 21516.44 | 99.92 |
| **Study period** | | | | |
| < 2009 | 22 | 4(1–30) | 3324.01 | 99.09 |
| 2010–2015 | 12 | 6(2–8) | NA | NA |
| ≥2016 | 3 | 0(0–1) | NA | NA |
| **Methods** | | | | |
| Microscopy | 32 | 12(8–16) | 31217.69 | 99.9 |
| serology | 3 | 8(7–9) | NA | NA |
| LST | 4 | 48(17–80) | 1391.64 | 99.63 |
| ***Leishmania* species** | | | | |
| *L.tropica* | 6 | 3(1–7) | 2188.13 | 99.82 |
| *L. major* | 12 | 7(3–12) | 4247.43 | 99.74 |
| *L. tropica/major* | 4 | 10(2–12) | 2364.27 | 99.87 |
| **Quality assessment** | | | | |
| Low | 5 | 16(10–29) | 4296.62 | 99.88 |
| Moderate | 32 | 15(10–20) | 27300.18 | 99.89 |
| High | 1 | 1(0–1) | NA | NA |

### 3.3. Prevalence of CL infection according to study characteristics

In subgroup analysis, we observed high heterogeneity in the prevalence rate among study characteristics. According to the diagnostic methods, the prevalence of CL in studies that applied LST assay had the highest rate (35, 10–68%). Regarding gender, the prevalence of infection in males was similar to that in females (7%, 4–10%). The pooled prevalence of infection in individuals living in rural areas was higher than in urban areas with no significant variations (14%, 10–19%) ($P > 0.05$). The prevalence of CL in the age group 0–15 years was higher than (9%, 6–13%) in individuals 16–40 and >40 years. The number of scar lesions was higher than active lesions (62%, 42–81%) with significant differences ($P < 0.05$). Most of the lesions were observed on the face, with a prevalence rate of 39% (19–50%). Single lesions were more prevalent than two or three lesions (57%, 49–66%). The details of pooled prevalence of CL infection obtained from subgroups analysis are shown in Table 2.

### 3.4. Sensitivity analysis

A sensitivity analysis was performed, in which a particular study was removed from the meta-analysis at each time

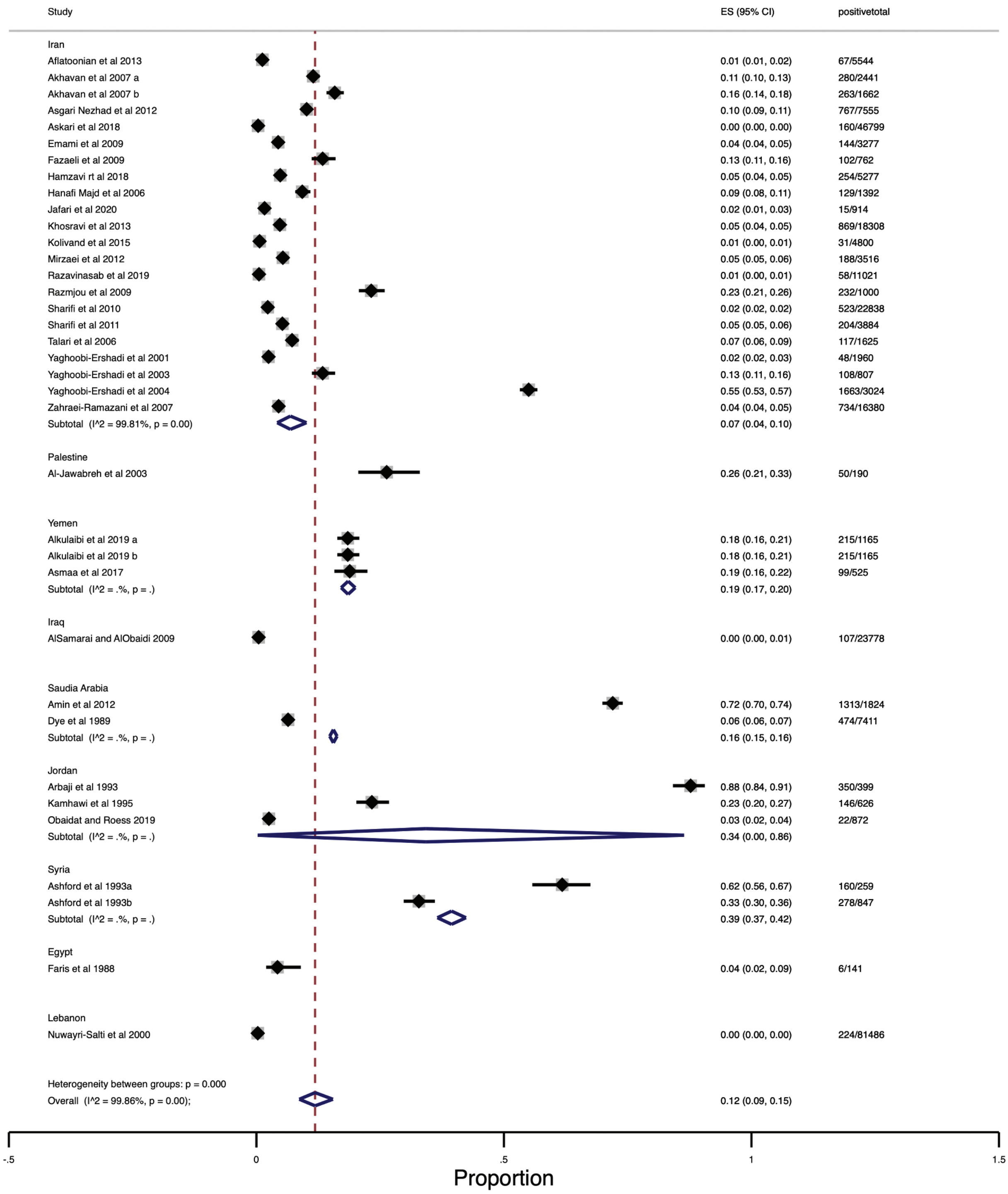


Figure 2. Forest Plot of the prevalence of cutaneous leishmaniasis in the Middle East.

to calculate the stability of the results. The obtained results did not show any considerable changes in the heterogeneity of the studies ($P < 0.0001$) (Figure S1).

### 3.5. Quality assessment

Quality assessment of the included studies for the prevalence of CL was estimated and summarized in Supplementary Table S1. Analysis of the risk of bias showed that the prevalence rates of CL in studies with low (16%, 10–29%) and moderate (15%,10–20%) risks of bias were considerable (Table 2).

## 4. Discussion

The results of this systematic review and meta-analysis indicated that the occurrence of CL was considerable in the Middle East at 12% (95% CI, 9–15 %). These studies illustrated data on 285,560 individuals across 9 Middle Eastern countries. Based on the findings, this prevalence rate may be underestimated due to misdiagnosis and insufficient reporting strategies in more than half of the endemic countries. It should be noted that some Middle Eastern countries, such as Syria, have faced war crisis in recent years. These war-torn

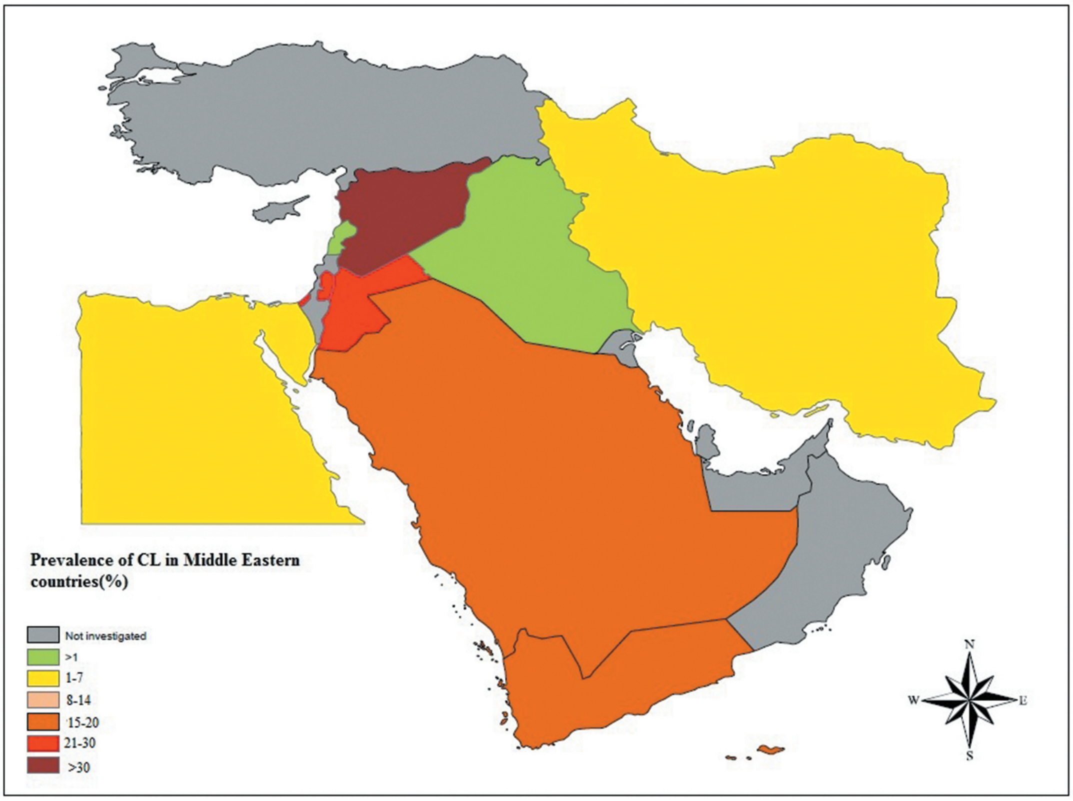


Figure 3. Prevalence of cutaneous leishmaniasis in Middle Eastern countries using geographic information system (GIS).

countries face problems, such as migration and the influx of refugees to the borders of other countries. Turkey and Jordan were the most affected countries in this region [49].

According to the results of the current study, the pooled estimates for the prevalence of CL were (39%, 37–42 %), (34%, 0–86%) and (26%, 21–33%) in Syria, Jordan, and Palestine, respectively. In a study by Al-Salem et al. in 2016, it was found that only two regions of Aleppo and Damascus in Syria were endemic for CL until 1960, while with the outbreak of a war, a significant increase was reported in the number of CL cases [50]. As mentioned above, Turkey is one of the countries affected by the crisis of the Syrian war. Currently, 4.4 % of Turkey's population is allocated to Syrian refugees. Some provinces bordering Syria, such as Sanlurfa and Gaziantep, have reported CL more often since 2011 [51]. The study, which was performed in Gaziantep in southeast Turkey revealed that 81.1% (900/1110) of suspected individuals were positive for CL, of which 93.8% (845/900) were Syrian refugees, and 6.2% (55/900) were Turkish citizens [52]. Besides, in a study conducted between 2009 and 2015 in the border towns of Turkey, the frequency of CL among suspected patients was estimated 46.4%; in this study and 66% of the patients were Syrian refugees [53]. Moreover, an investigation performed in Lebanon confirmed that all CL patients were Syrian refugees [49]. All studies in Turkey were accomplished on suspected CL individuals, and the target population did not precisely represent the general population since they were not eligible for analysis in the present study.

The results of the current study revealed that the prevalence rate of CL increased by the year 2015 (Table 2). As mentioned above, a possible explanation for this finding is inefficient surveillance and control programs in some countries due to instabilities in the Middle East. The prevalence of CL was higher in the age group of 0–15 years compared to the age group of >15- >40 years. The higher infection rate in younger people may be associated with a weak immune system for protecting against sand-fly bites. The higher infection rate in younger people may be due to the immune system's inefficiency in inhibiting the parasite's propagation [26,53,54].

Based on the findings, the prevalence rate of scar lesions was higher than active lesions (62%, 42–81%). The number of active and scar lesions in urban areas was more than in rural areas. Regarding the number of lesions, single lesions were more prevalent than two or three concurrent lesions in this study. The possible reason may be related to the variations in the nutritional behaviors of sand flies and blood feeding from multiple hosts [26,55]. Concerning the lesion site, the face was the most common site of involvement (39%, 19–50%), followed by the hands and legs. It is well documented that CL lesions usually develop on uncovered body parts and are more exposed to sand-fly bites. The present results were in agreement with some previous studies [8,53,55]. One of the consequences of facial lesions is the permanent scar with lifelong stigma for individuals [8,56]. In a recent investigation by Bennis et al. in 2018, CL lesions were a source of psychological problems, stigmatization, and decreased QOL in patients, especially women and young girls [56]. Several studies evaluating QOL in patients with CL scars concluded that CL had considerable effects on QOL and different aspects of life, such as social activities, education, and job opportunities [57,58]. The pooled prevalence of *L. major* and mixed infection with *L. tropica/major* were high in the Middle East, which is in agreement with a previous study [59].

### 4.1. Limitations

There are some limitations to the present study. First, the epidemiological data were not available for several Middle Eastern countries. Second, the full-text of some potentially eligible papers was not available in this systematic review. Third, some potentially relevant studies were not in English, and consequently, they were excluded from the analysis. Fourth, many studies had only assessed the frequency of CL in suspected patients and were not eligible for inclusion. Therefore, selection bias can occur due to the exclusion of some relevant data.

## 5. Conclusion

According to this systematic review, the pooled prevalence of CL is considerable in the Middle East. Since different factors, including environmental and weather changes, war and migration, and changes in vector populations, influence the burden of CL in this region, awareness of the disease prevalence can help us implement more appropriate control and preventive programs.

## Disclosure statement

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## ORCID

Tahmineh Gorgani-Firouzjaee http://orcid.org/0000-0001-6017-836X

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