



# Canine visceral leishmaniasis in Iran: A systematic review and meta-analysis



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## ABSTRACT

Visceral leishmaniasis is considered an endemic zoonosis in some parts of Iran and dogs are main reservoirs, which play role in the transmission cycle of human leishmaniasis. This systematic review and meta-analysis was performed to determine the prevalence of canine visceral leishmaniasis (CVL) in Iran. Data were systematically collected from 1982 to 2015 in Iran on the following electronic databases: PubMed, Google Scholar, Science Direct, Scopus, Web of Science, Magiran, Irandoc, Iran medex and Scientific Information Database (SID). A total of 39 articles concerning dogs, 6 articles on jackals, 4 articles on wolves and 4 articles on foxes, reporting the prevalence of CVL from different regions of Iran fulfilled our eligibility criteria. Totally, 19903 dogs, 151 jackals, 42 wolves and 44 foxes were examined and the overall prevalence rate of CVL in Iran was estimated to be as following: in dogs 16% (95% CI: 13–19%), in jackals 10% (95% CI: 5–15%), in wolves 10% (95% CI: 5–15%) and in foxes 10% (95% CI: 1k19%), respectively. There was a significant difference in infection rate between male and female dogs, the infection in males 9% (95% CI: 8.8–10.5%) was more than females 7% (95% CI: 5.5–7.5%) ( $p=0.024$ ). Also, the rate of infection was significantly higher in older dogs than younger ones ( $p<0.047$ ) while in dogs younger than 1 year was 12% (95% CI: 6–18%), in 1–2 years 10% (95% CI: 6–14%), in 3–5 years 16% (95% CI: 9–22%) and in those which were over 7 years 31% (95% CI: 19–44%), respectively. Our meta-regression analysis revealed the significant correlation between stray and owned dogs: the infection rate in stray 10% (95% CI: 5–4%) was higher than those owned 6% (95% CI: 3–8%) ( $p=0.037$ ). Also, the prevalence of infection in rural dogs 36% (95% CI: -1–72%) is significantly higher than urban dogs, 19% (95% CI: -1–40%) ( $p=0.013$ ). Although most (81%) of infected dogs had no clinical signs (asymptomatic), meta-regression analysis showed that the infection rate in asymptomatic dogs was 14% (95% CI: 11–18%) and in those with clinical signs 3% (95% CI: 2–4%), and the correlation is statistically significant ( $p=0.001$ ). The present systematic review and meta-analysis indicates that CVL is common at least in some districts of more than half of provinces of Iran. Further investigation and monitoring will be required to improve the surveillance and control strategies to reduce the incidence of CVL in Iran.

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## 1. Introduction

Visceral leishmaniasis (VL) or kala-azar is a parasitic disease caused by protozoa of the *Leishmania donovani* complex (order Kinetoplastida). In this order, two parasites including *L. donovani*

and *L. infantum* are known as causative agents of VL in the Old World and *L. chagasi* in the New World (Palatnik-De-Sousa et al., 2001).

The disease affects approximately 500,000 cases annually worldwide and is fatal if left untreated (Mohebali et al., 2005; Alvar et al., 2012). However, the annual incidence of human visceral leishmaniasis in Iran is about 100–300 cases (Mohebali, 2013). The parasite is transmitted by phlebotomus sand fly. In Iran, South and Northwest regions are known as old endemic foci for VL and most of these cases (90%) have reported from the Fars and Bushehr provinces, particularly among communities of nomadic tribes (Asgari et al., 2006; Hajjarian et al., 2013). *L. infantum* is the main causative agent of the infection in human, dogs and

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wild canids in the country. In general, domestic dogs (*Canis familiaris*) are main reservoir hosts for VL in endemic regions of Iran, and most of them are asymptomatic (Fakhar et al., 2012). Clinical signs in infected dogs including cachexia, hair loss, dermal wounds, weight loss, lymphadenopathy and lethargy. Secondary infections such as pneumonia, hematological changes and hemorrhagic rhinitis are not observed in all infected animals (Baneth et al., 2008). Detection of *Leishmania* parasite in asymptomatic dogs and wild canids is difficult. Antibody detection by direct agglutination test (DAT), indirect immunofluorescent assay (IFA) and enzyme-linked immunosorbent assay (ELISA) is valid and has been used for many years in human as well as dogs; hence polymerase chain reaction (PCR) can reveal the load and also the type of parasite (Mohebbali, 2013; Fakhar et al., 2011). It is important to know the exact prevalence of visceral leishmaniasis among dogs in Iran to manage controlling programs. For this purpose, this is the first systematic review about the prevalence of canine visceral leishmaniasis (CVL) in Iran; so, the present study aimed to determine CVL in different regions of the country.

## 2. Methods

### 2.1. Bibliographic search

The search was carried out in databases including: Pub Med, Google Scholar, Science Direct, Scopus, Web of Science, Magiran, Iran doc, Iran medex and Scientific Information Database (SID) from 1982 to 2015. Duplicates, human based studies and studies out of Iran were excluded. All original descriptive studies (designated as cross-sectional) in dogs visceral leishmaniasis were concerned. The process is shown in Fig. 1.

### 2.2. Search strategy

The search was performed using such terms as follows “dog,” “leishmaniasis,” “leishmaniosis,” “Iran,” “canine,” “wild canids,”

“canine leishmaniasis,” “dog visceral leishmaniasis,” “*Leishmania infantum*,” “anti-Leishmania antibody,” “epidemiology,” and “prevalence” alone or in combination, both in Persian and English languages.

### 2.3. Data collection

A diverse search conducted in all databases following which the collected papers screened carefully to eliminate duplicates, studies out of Iran and human based studies. Finally, papers with epidemiological parameters of interest were selected and 39 articles fulfilled the inclusion criteria. Those that reported visceral leishmaniasis in dogs and wild canids were included in the study (Table 1). Data were extracted from articles including: author(s), year of study, publication year, demographic information such as age, sex, breed and also geographical region of study, number of examined dogs, number of seropositive, prevalence rate, laboratory method used for study, sensitivity and specificity of diagnostic methods, clinical signs and molecular tests for parasite detecting. Data recorded in selection sheet (see appendix).

### 2.4. Statistical analysis

The quality of meta-analysis was evaluated with STROBE checklist. A checklist including 22 items was considered for well reporting of observational studies. These items related to the article’s title, abstract, introduction, methods, results, and discussion sections. The score under 7.75 considered poor quality, between 7.76–15.5 low, between 15.6–23.5 moderate and more than 23.6 high quality (Von Elm et al., 2007). Mean score of STROBE checklist for 39 analyzed articles was obtained 18.03, which considered moderate quality. Point estimates and their 95% confidence intervals of prevalence of all included studies were calculated. The prevalence (P) and standard error (Se) of each study estimated with respect of binomial distribution and studies combined according to sample size and variance. An overall prevalence and group-specific

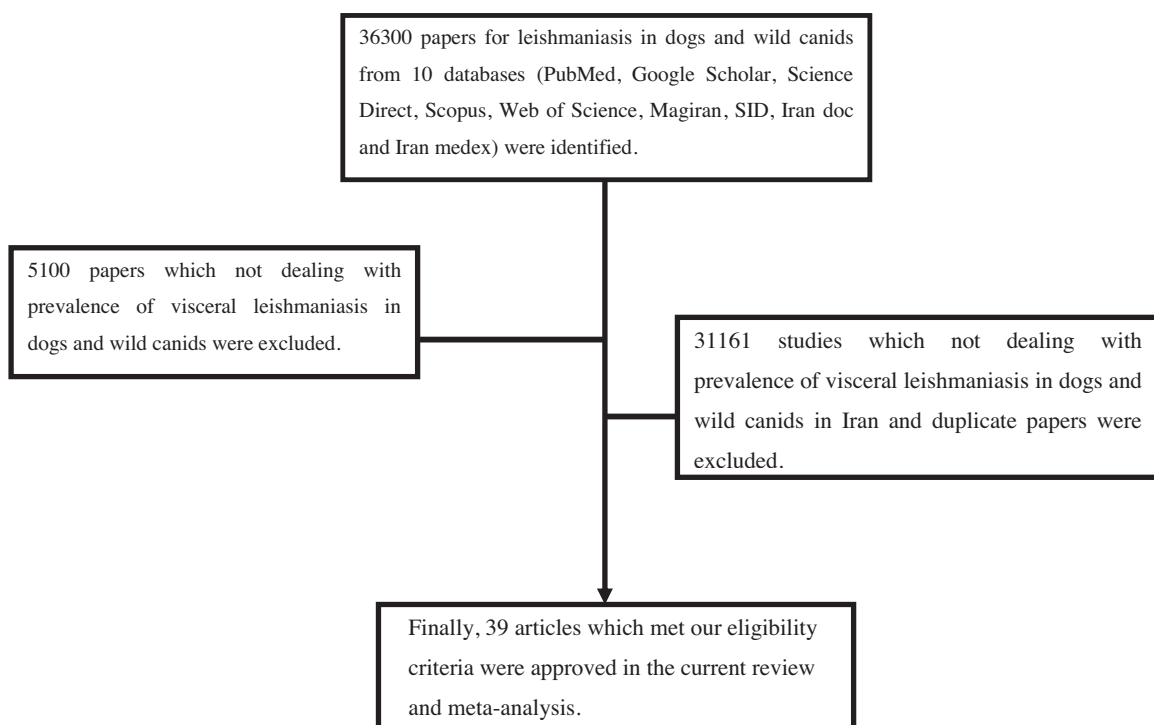


Fig. 1. Flow diagram describing the study design process for canine visceral leishmaniasis in Iran.

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