Distribution of *Leishmania* Infection in Humans, Animal Reservoir Hosts and Sandflies in Golestan Province, Northeastern Iran: A Systematic Review and Meta-Analysis

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**Abstract**

**Background:** Leishmaniasis is one of the most important parasitic diseases in the Golestan Province, northeastern Iran. In this study, we summarize the results of studies on the disease and its causative agent *Leishmania* in humans, vectors and reservoirs in the Golestan Province, Iran.

**Methods:** We retrieved all articles related to leishmaniasis in the Golestan Province, northern Iran from 1994 to 2018 in various databases including PubMed, Scopus and Web of Science. Articles in Persian were retrieved from the IranMedex, SID and Magiran. Reference lists of relevant articles were also hand-searched. Local active researchers in the field of leishmaniasis were contacted to avoid missing any relevant articles. Overall, 54 papers were extracted, later evaluated by two research team members based on inclusion criteria. All analyses were performed using the Stata 14 software. Pooled prevalence was calculated using the metaprop command and a random-effect model. The I² statistic was used for measuring heterogeneity of studies.

**Results:** Ten articles in the province were related to detection of *Leishmania* species in patients with suspected cutaneous or visceral leishmaniasis. Fifteen articles were dedicated to identification of *Leishmania* species in disease reservoirs and five articles were about detection of the parasite in sand flies. The pooled prevalence of *L. major* in patients with acute ulcer, wild rodents and sandflies was 83%, 29% and 11%, respectively.

**Conclusion:** Our findings highlight the need for implementation of control measures among the reservoirs of both cutaneous and visceral leishmaniasis in the Golestan Province, Iran.

**Keywords:** *Leishmania*, Reservoir host; Sand fly; Systematic review; Iran

**Introduction**

Leishmaniasis is one of the most important vector-borne diseases transmitted to humans and other animals through bite of infected sandflies (1). It is also the third most important vector-borne parasitic disease after malaria and lymphatic filariasis (2). There are three main forms of leishmaniasis – visceral (also known as kala-azar and the most serious form of the disease), cutaneous (the most common), and mucocutaneous, it is estimated that 700000 to one million new cases of leishmaniasis and some 26000 to 65000 deaths occur annually. Moreover, about 600000 to one million people become infected with cutaneous leishmaniasis and 50000 to 90000 with visceral leishmaniasis (3).
Iran is facing both form of leishmaniasis: cutaneous and visceral and cutaneous leishmaniasis is reported in two forms: zoonotic cutaneous leishmaniasis (ZCL), anthroponotic cutaneous leishmaniasis (ACL) and visceral leishmaniasis in zoonotic visceral leishmaniasis (ZVL) form. Iran is amongst the six countries where 95% of global cases of cutaneous leishmaniasis occur (3), and each year, more than 22,000 new cases of cutaneous leishmaniasis are reported in Iran, 80% of which are ZCL (4). However, the actual new cases is estimated to be 4-5 fold higher than these reports (5). Golestan Province is amongst the 17 provinces of Iran that are endemic for ZCL (5). In these areas, Leishmania major is the causative agent, while Phlebotomus papatasi and wild rodents (Rhombomys opimus and Meriones libycus) are known as the vectors and reservoir hosts, respectively (5).

In ACL foci, L. tropica is the agent, while Ph. sergenti and dogs and humans are known as the vector and reservoir hosts, respectively (5). Every year, 100–300 new cases of ZVL are reported in Iran. The disease is sporadic in most parts of the country but has become endemic in the northwestern and southern areas. In these areas, L. infantum is the agent, domestic dogs are known as the main and potential reservoir hosts and wild canines (jackal, fox and wolf) have potential role in sylvatic transmission cycle of ZVL (6–8). Ph. neglectus, Ph. kandelakii, Ph. ke Kishtian, Ph. perfiliewi transcaucasicus and Ph. alexandri are considered as probable vectors for ZVL (9–13).

Currently, the health system of Iran’s approach to cope with leishmaniasis has been mainly established on timely recording and reporting of cases, education, providing free rapid diagnosis and treatment of patients as well as implementation of rodents- and sandflies-targeted control measures. The Golestan Province is known as the most important foci of leishmaniasis in Iran. ZCL is endemic and visceral leishmaniasis is sporadic in this province, particularly in its northeastern areas. Given the importance of leishmaniasis in this province, numerous studies have been conducted in this area on features of this disease. Therefore, we aimed to summarize results of these studies to contribute to decision-making for prevention, diagnosis, control and treatment of this disease in this area.

**Methods**

**Study area**

The Golestan Province (53°57′- 56°23′ E, 36°30′- 38°08′ N) is located northeast of Iran, bordering the Caspian Sea and Turkmenistan. The province has a dry and semi-arid climate in the north and northeastern parts, a temperate climate in the central parts and a mountainous and cold climate in the southern parts. It comprises 14 counties and has an area of 20437.74 km² (Fig. 1).
This study has been designed and performed according to the MOOSE guidelines for meta-analyses and systematic reviews of observational studies.

**Search strategy**
First, the following search terms were determined for finding articles related to leishmaniasis in the Golestan Province from 1994 to 2018: Golestan, Gonbad-e Kavus, Maraveh Tappeh, Turkmen Sahra, Leishmaniasis, Leishmania, Kala-azar and sandfly. Since some of the words may have different spelling, the following search syntax was used: (Leishmanian* OR Kala*azar OR Sand*fl*) AND (Golestan OR Turkemen* OR Gonbad* or Maraveh*).

The search was performed using the following databases: Medline, PubMed, Scopus and Web of Science. Related articles in Persian were retrieved from the SID, Magiran and IranMedex. In addition, the "Iranian Journal of Arthropod-Borne Disease" and the "Iranian Journal of Parasitology" were investigated as key journals. Reference lists of relevant articles were also hand-searched. Finally, we contacted local active researchers in the field of leishmaniasis to avoid missing any articles on leishmaniasis in the Golestan Province.

**Selection of articles**
The following inclusion criteria were considered for the entry of articles to the study:

1. Articles on Leishmania and its prevalence in humans, vectors and reservoirs.
2. Articles that solely report the results of research conducted in the Golestan Province.

Articles of studies conducted in other parts of Iran or several provinces were entered in the study only if they had reported data related to the Golestan Province separately and clearly. Subsequently, two research team members evaluated the selected articles independently by reading titles, abstracts, and if necessary full texts. Articles that did not meet the inclusion criteria were excluded from the analysis. Articles repeated in two or more databases were excluded. There was a disagreement regarding inclusion/exclusion of an article, but a consensus was reached after holding a group discussion.

**Data extraction**
Data were extracted from the selected articles using a data extraction form. Quality of the studies was evaluated and scored on a scale of 0 to 10 using the Joanna Briggs Institute's critical evaluation checklist for studies reporting prevalence data. Studies with a quality score of ≥6 were included in the meta-analysis. A table was also designed to present the type, location, date, results and quality of each study.

**Subgroup combination**
The data were classified into subgroups of prevalence, type of parasite in human, reservoirs and vectors.

**Data analysis**
Meta-analysis was performed with the Stata software (ver. 14). Pooled prevalence was calculated using the metaprop command and a random-effect model. Moreover, the I² statistic was used to measure heterogeneity of studies. If heterogeneity (I² ≥ 50%) was noted among studies, sensitivity analysis was carried out by removing studies. We calculated the pooled prevalence of *L. major* in humans, reservoirs (rodents) and sandflies using forest plot (at 95% confidence interval).

**Results**
After searching keywords in Persian and English databases, 235 papers were found in English and 198 in Persian. Overall, 390 papers remain for reviewing their titles and abstracts after reviewing and removing duplicates; and 324 records excluded after title and abstract screening by inclusion criteria, described in methods. The text of 66 papers was carefully investigated and their data entered into the data extraction form. Finally, 34 studies included in qualitative and quantitative study (Fig. 2).
Twelve articles investigated detection of different species of Leishmania in suspected cases of cutaneous or visceral leishmaniasis in the Golestan Province (Table 1) (14-25). In these studies, 2167 patients with acute ulcer and suspected cutaneous leishmaniasis were examined by preparing direct smears from the ulcers, microscopic examination and polymerase chain reaction (PCR) method. In these studies, \textit{L. major}, \textit{L. tropica} and \textit{L. turanica} were isolated from 1561 (72%), 8 (0.7%) and 2 (0.13%) patients, respectively. In Maraveh Tappeh County, 1.3% of the tested humans were positive for \textit{L. infantum} in the serological tests and 2.8% were positive in the PCR method (24). In addition, eight children under five years of age had clinical symptoms and were positive for \textit{L. infantum} (25, 26). We found sixteen articles that investigated reservoirs of Leishmania in the Golestan Province (Table 2). In these studies, \textit{L. major} was detected in \textit{Rh. opimus}, \textit{M. libycus}, \textit{M. persicus}, and \textit{Hemiechinus auritus} (22, 27-34), while \textit{L. infantum} was found in dogs, jackals and \textit{Rh. opimus}. Antibodies against \textit{L. infantum} were also detected in \textit{Mus musculus} (24, 35-39), and \textit{L. (Saurolejshmaini) gymnodactyli} was found in lizard (40).
Table 1: Conducted studies in Golestan Province to investigate human infection to leishmania parasites

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Region</th>
<th>Method</th>
<th>Num.</th>
<th>Num. Positive</th>
<th>Percentage</th>
<th>Parasite</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesgarian Et al.</td>
<td>2010</td>
<td>Gonbad-e Kavus</td>
<td>Smear and PCR</td>
<td>35</td>
<td>35</td>
<td>100</td>
<td>L. major</td>
</tr>
<tr>
<td>Tohidi Et al.</td>
<td>2011a</td>
<td>Golestan</td>
<td>Smear and PCR</td>
<td>63</td>
<td>56</td>
<td>93.6</td>
<td>L. major</td>
</tr>
<tr>
<td>Tohidi Tohidi Et al.</td>
<td>2011b</td>
<td>Golestan</td>
<td>Smear and PCR</td>
<td>63</td>
<td>56</td>
<td>100</td>
<td>L. major</td>
</tr>
<tr>
<td>Pagheh Tohidi Et al.</td>
<td>2012</td>
<td>Gonbad-e Kavus</td>
<td>Smear and PCR</td>
<td>303</td>
<td>238</td>
<td>78.5</td>
<td>L. major</td>
</tr>
<tr>
<td>Mahmoudzadeh-Niknam Tohidi Et al.</td>
<td>2012</td>
<td>Gonbad-e Kavus</td>
<td>Smear and PCR</td>
<td>13</td>
<td>12</td>
<td>92.3</td>
<td>L. major</td>
</tr>
<tr>
<td>Baghchi Tohidi Et al.</td>
<td>2012</td>
<td>East of Golestan</td>
<td>Smear and PCR</td>
<td>121</td>
<td>113</td>
<td>93.4</td>
<td>L. major</td>
</tr>
<tr>
<td>Pagheh Tohidi Et al.</td>
<td>2013</td>
<td>Gonbad-e Kavus</td>
<td>Smear and PCR</td>
<td>1398</td>
<td>946</td>
<td>67.6</td>
<td>L. major</td>
</tr>
<tr>
<td>Bordbar Et al.</td>
<td>2014a</td>
<td>Turkmen Sahra</td>
<td>PCR</td>
<td>164</td>
<td>123</td>
<td>75</td>
<td>L. major</td>
</tr>
<tr>
<td>Bordbar Et al.</td>
<td>2014b</td>
<td>Turkmen Sahra</td>
<td>PCR</td>
<td>164</td>
<td>123</td>
<td>75</td>
<td>L. major</td>
</tr>
<tr>
<td>Hezari Et al.</td>
<td>2016</td>
<td>Kalaleh</td>
<td>Smear and PCR</td>
<td>70</td>
<td>38</td>
<td>54.3</td>
<td>L. major</td>
</tr>
<tr>
<td>Fakhari Et al.</td>
<td>2014</td>
<td>Maraveh Tapeh</td>
<td>DAT and PCR</td>
<td>450</td>
<td>13</td>
<td>2.8</td>
<td>L. infantum</td>
</tr>
<tr>
<td>Asfaram Et al.</td>
<td>2017</td>
<td>Golestan</td>
<td>Rk39, DAT and PCR</td>
<td>6</td>
<td>6</td>
<td>100</td>
<td>L. infantum</td>
</tr>
</tbody>
</table>

L. major: Leishmania major; L. tropica: Leishmania tropica; L. turanica: Leishmania turanica; L. infantum: Leishmania infantum

Table 2: Conducted studies in Golestan Province to investigate reservoir host infection to Leishmania parasites

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Region</th>
<th>Method</th>
<th>Species</th>
<th>Num. Of investigated sample</th>
<th>Num. Positive</th>
<th>Percentage</th>
<th>Isolated parasite</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parvizi Et al.</td>
<td>1999</td>
<td>Gonbad-e Kavus</td>
<td>Smear and Injection to Balb/c mouse</td>
<td>Rb. opimus</td>
<td>94</td>
<td>35</td>
<td>36.8</td>
<td>L. major</td>
</tr>
<tr>
<td>Mohabadi Et al.</td>
<td>2004</td>
<td>Minoo Dasht</td>
<td>PCR</td>
<td>Rb. opimus</td>
<td>27</td>
<td>23</td>
<td>85.5</td>
<td>L. major</td>
</tr>
<tr>
<td>Russo Et al.</td>
<td>2008</td>
<td>Maraveh Tapeh</td>
<td>PCR</td>
<td>M. libycus</td>
<td>16</td>
<td>6</td>
<td>37.5</td>
<td>L. major</td>
</tr>
<tr>
<td>Parvizi Et al.</td>
<td>2010</td>
<td>Gonbad-e Kavus</td>
<td>Smear and Injection to Balb/c mouse</td>
<td>Rb. opimus</td>
<td>27</td>
<td>23</td>
<td>85.5</td>
<td>L. major</td>
</tr>
<tr>
<td>Mirzaei Et al.</td>
<td>2011</td>
<td>Gonbad-e Kavus and Maraveh Tapeh</td>
<td>PCR</td>
<td>Rb. opimus</td>
<td>227</td>
<td>59</td>
<td>26</td>
<td>L. major</td>
</tr>
<tr>
<td>Akhoundi Et al.</td>
<td>2013</td>
<td>Gonbad-e Kavus and Maraveh Tapeh</td>
<td>PCR</td>
<td>Rb. opimus</td>
<td>227</td>
<td>59</td>
<td>36.8</td>
<td>L. major</td>
</tr>
<tr>
<td>Hajiaran Et al.</td>
<td>2013</td>
<td>Gonbad-e Kavus and Maraveh Tapeh</td>
<td>PCR</td>
<td>M. libycus</td>
<td>19</td>
<td>14</td>
<td>6.2</td>
<td>L. major</td>
</tr>
<tr>
<td>Mirzaei Et al.</td>
<td>2014</td>
<td>Turkmen Sahra</td>
<td>PCR</td>
<td>Rb. opimus</td>
<td>227</td>
<td>59</td>
<td>26</td>
<td>L. major</td>
</tr>
</tbody>
</table>

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There were six studies on vectors of the disease in the Golestan Province (Table 3). These studies reported *Ph. papatasi* as the main vector for cutaneous leishmaniasis and *L. major*. Moreover, infection of *Ph. papatasi* with *L. turanica* and *L. closed to gerbil* were observed. The three aforementioned parasites were also isolated from *Ph. caucasicus* group (22, 29, 41-43), and *L. (Saurolejshmaini) gymnodactyli* was found in *S. sintoni* (40).

According to our meta-analysis, the pooled prevalence of *L. major* was 83%, 32.62% and 11% in patients with acute ulcer, rodents and sandflies (Table 4).

**Table 3:** Conducted studies in Golestan Province to investigate sand fly infection to Leishmania parasites

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Region</th>
<th>Method</th>
<th>Species</th>
<th>Num. Of investigated sample</th>
<th>Num. Positive</th>
<th>Percentage</th>
<th>Isolated parasite</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rassi Et al.</td>
<td>2008</td>
<td>Maraveh Tapeh</td>
<td>PCR</td>
<td><em>Ph. papatasi</em></td>
<td>372</td>
<td>1</td>
<td>0.5</td>
<td><em>L. major</em></td>
</tr>
<tr>
<td>Parvizi &amp; Ready</td>
<td>2008</td>
<td>Gonbad-e Ka-</td>
<td>PCR</td>
<td><em>Ph. papatasi</em></td>
<td>52</td>
<td>7</td>
<td>13.5</td>
<td><em>L. major</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td>versus and Maraveh Tapeh</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><em>L. turanica</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td><em>Ph. caucasicus</em></td>
<td>20</td>
<td>1</td>
<td>5</td>
<td><em>L. closed to gerbil</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>20</td>
<td>1</td>
<td>5</td>
<td><em>L. major</em></td>
</tr>
<tr>
<td>Roshanghahb Et al.</td>
<td>2011</td>
<td>Gonbad-e Ka-</td>
<td>PCR</td>
<td><em>Ph. papatasi</em></td>
<td>168</td>
<td>18</td>
<td>10.7</td>
<td><em>L. major</em> &amp; <em>L. turanica</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td>versus and Maraveh Tapeh</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><em>L. turanica</em></td>
</tr>
<tr>
<td>Bordbar Et al.</td>
<td>2014</td>
<td>Gonbad-e Ka-</td>
<td>PCR</td>
<td><em>Ph. papatasi</em></td>
<td>220</td>
<td>25</td>
<td>11.4</td>
<td><em>L. major</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td>versus and Maraveh Tapeh</td>
<td></td>
<td></td>
<td></td>
<td>2</td>
<td>0.9</td>
<td><em>L. turanica</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td><em>Ph. caucasicus</em></td>
<td>98</td>
<td>10</td>
<td>10.2</td>
<td><em>L. major</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4</td>
<td>1</td>
<td>1</td>
<td><em>L. turanica</em></td>
</tr>
<tr>
<td>Sharbhakhtori Et al.</td>
<td>2014</td>
<td>Gonbad-e Ka-</td>
<td>PCR</td>
<td><em>Ph. papatasi</em></td>
<td>168</td>
<td>17</td>
<td>10.1</td>
<td><em>L. major</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td>versus and Maraveh Tapeh</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>0.6</td>
<td><em>L. turanica</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td><em>Ph. caucasicus</em></td>
<td>38</td>
<td>7</td>
<td>18.4</td>
<td><em>L. major</em></td>
</tr>
<tr>
<td>Seyed Rashti Et al.</td>
<td>1994</td>
<td>Turkmen Sahra</td>
<td>Isoenzyme</td>
<td><em>S. sintoni</em></td>
<td>403</td>
<td>60</td>
<td>14.9</td>
<td><em>L. (Saurolejshmaini) gymnodactyli</em></td>
</tr>
</tbody>
</table>

*L. major*: Leishmania major; *L. tropical*: Leishmania tropica; *L. turanica*: Leishmania turanica; *L. infantum*: Leishmania infantum; *L. (Saurolejshmaini) gymnodactyli*: Leishmania (Saurolejshmaini) gymnodactyli; *Ph. papatasi*: Phlebotomus papatasi; *Ph. caucasicus* group: Phlebotomus caucasicus group; *S. sintoni*: Sergentomyia sintoni

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Table 4: Meta-analysis results of Prevalence of *L. major* in humans, wild rodents and sandflies in Golestan Province

<table>
<thead>
<tr>
<th>Examined animal</th>
<th>P value</th>
<th>$I^2$</th>
<th>Prevalence Min</th>
<th>Prevalence Max</th>
<th>Pooled prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>humans</td>
<td>&lt;0.0001</td>
<td>100</td>
<td>0.54</td>
<td>100</td>
<td>0.81</td>
</tr>
<tr>
<td>Wild rodents</td>
<td>&lt;0.0001</td>
<td>89.2</td>
<td>0.27</td>
<td>0.85</td>
<td>0.32</td>
</tr>
<tr>
<td>Sand flies</td>
<td>&lt;0.0001</td>
<td>99.5</td>
<td>0.11</td>
<td>0.13</td>
<td>0.11</td>
</tr>
</tbody>
</table>

Studies on the incidence of *L. major* in humans had high heterogeneity ($I^2=93.29$), which could be due to the difference in the diagnostic methods as well as geographic diversity. For instance, some studies evaluated the incidence rate in a county, while others studied the entire or part of the province (Fig. 3).

A high degree of heterogeneity ($I^2=0.89$) was seen among studies on the pooled prevalence of *L. major* in rodents, which was decreased ($I^2=0.21$) after removing two studies (30, 39), the pooled prevalence of rodents contaminated with the parasite was 32.62% in the Golestan Province (Fig. 4).

**Fig. 3:** Meta-analysis of human infection to *L. major*

**Fig. 4:** Meta-analysis of wild rodent’s infection to *L. major*
Given the diversity of reservoirs of *L. infantum*, it was not possible to report the pooled prevalence or conduct meta-analysis. Moreover, the I² index (92.52) indicated high heterogeneity among these studies.

Of six studies that investigated infection of sand-flies with *L. major*, five studies were jointly carried out in the Gonbad-e-Kavus and Maraveh Tappeh Counties and one study was performed in the Maraveh Tappeh County alone. The heterogeneity was high among these studies (I²=97.07). However, after removing the single study on the Maraveh Tappeh County (29), heterogeneity decreased and the pooled prevalence of *L. major* in sandflies was determined as 11% (Fig. 5).

![Fig. 5: Meta-analysis of Sand flies infection to *L. major*](image)

**Discussion**

Overall, 83% of patients with acute ulcer and suspected cutaneous leishmaniasis were infected with *L. major*. This parasite is dominant in this region and endemic in this province. *L. tropica* was found in a small number of patients, particularly in those with a history of traveling to endemic areas of ACL.

In a previous study in this province, *L. turanica* was isolated from patients (21). *L. turanica* as well as *L. gerbilli* and *L. closeni* to *gerbelli* can infect rodents but not humans. Nevertheless, they can increase stability and persistence of Leishmania in the region (4, 5, 44).

Most cases have been reported from Gonbad-e-Kavus and Maraveh Tappeh Counties, known endemic areas of leishmaniasis (14-19, 21, 23, 45, 46). Human infection with *L. infantum* in the Golesthan Province has been reported in two studies (24, 25).

Of 450 individuals examined in the Maraveh Tappeh County, 1.3% was seropositive and 2.8% were PCR positive. Given the limited number of studies in this area, we were unable to determine the pooled prevalence in the province. In Iran, 4% and 8.7% of blood donors were positive for *L. infantum* using serological and molecular methods, respectively (47) and in Ethiopia, the pooled prevalence of leishmaniasis was 19% (48).

In studies in the Golesthan Province, *L. major* was isolated from *Rb. opimus*, *M. libycus*, *M. persicus* and *Hemiechinus auritus*. Among 1196 *Rb. opimus* tested in this province, 316 (26.4%) were positive for *L. major* and 28 (2.3%) were positive for *L. turanica*. Moreover, *L. major* was detected in 31.8% of *M. libycus* and in a few number of *M. persicus* and *H. auritus* (22, 27-31, 33-34).

In our meta-analysis, the rate of *L. major* infection in rodents was 32.62%. Similarly, in another meta-
analysis in Iran, the weighted prevalence of Leishmania species in rodents was 23\% (95\% CI=18\%-28\%) (49).

Six studies investigated reservoirs of \textit{L. infantum} and detected this parasite in dogs (19\%), jackals (8.7\%) and \textit{Rh. opimus}. In addition, antibodies against \textit{L. infantum} were identified in \textit{Mus musculus} (24, 35-39). The highest rate of \textit{L. infantum} infection was reported from the Maraveh Tappeh County, in a way that 40\% of jackals and 30\% of domestic dogs were infected with this parasite (24, 37). The Maraveh Tappeh County is bordered by the North Khorasan Province, a well-known endemic area for visceral leishmaniasis in Iran (50).

In a systematic review and meta-analysis study in Iran, the rate of \textit{L. infantum} infection in dogs, jackals and wolves was 16\%, 10\% and 10\% respectively (51), which are lower than the rates observed in our study.

Various studies in the Golestan Province have reported \textit{Ph. papatasi} as a main vector of cutaneous leishmaniasis. The rate of \textit{L. major} infection in this species was 11\% in our meta-analysis and ranging between 0.3 and 13.5\% in other studies in the province (22, 29, 41-43). The rates reported for \textit{L. major} infection in other areas of Iran were similar or lower than the rates observed in our study (52-55).

In addition to \textit{L. major}, \textit{L. turanica} and \textit{L. close to gerbilli} have been also detected in \textit{Ph. papatasi} (22, 29, 41-43). These three parasites have been also isolated from \textit{Ph. caniculus} and \textit{Ph. mongolensis}, with the highest prevalence observed in the east and northeast of the Golestan Province (46). The rate of infection with \textit{L. major} and \textit{L. close to gerbil} in the \textit{Ph. caniculus} was 18.4\% and 25\%, respectively (22, 42-43). However, the rate of \textit{L. major} infection in these species in other areas of Iran is lower than the rates observed in our study (54-55). These findings highlight the irrefutable role of these species as vectors of zoonotic cycle of \textit{L. major} between rodents and secondary vector of this species to humans and stability of these parasites in the country (4-5, 44).

Our findings highlight the need for implementation of control measures among the reservoirs of both cutaneous and visceral leishmaniasis in this area.

Conclusion

Given the high rates of \textit{L. major} infection in rodents and abundance of \textit{Ph. papatasi}, the Golestan Province can be considered an endemic area for cutaneous leishmaniasis. Sporadic visceral leishmaniasis may be present in all counties of the province, particularly in the foothill areas and the Maraveh Tappeh County.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interests.

References

2. Inceboz T (2019). Epidemiology and Ecology of Leishmaniasis. DOI: http://dx.doi.org/10.5772/intechopen.86359

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