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Chapter

Epidemiology and Ecology of Leishmaniasis

Tonay Inceboz

Abstract

Leishmaniasis is the third most important vector-borne disease after malaria and lymphatic filariasis. It is common disease in all over the world. The vector for leishmaniasis is *Phlebotomus* and there have found around 20 different types of this vector. There are different clinical forms under the name of leishmaniasis such as kala-azar, dum-dum fever, white leprosy, espundia, pian bois, chicleros ulcer, uta. Environmental factors leading to climate changes and global warming are major risk factors for the spreading of the disease. *Leishmania* spp. to prevent the spread of the definitive host and intermediate hosts is difficult compared to *Plasmodium* spp. Therefore; leishmaniasis disease will retain its importance for many years.

**Keywords:** leishmaniasis, neglected tropical diseases, vector-borne disease, epidemiology, ecology

1. Introduction

This fact is mainly due to the presence of many different species of *leishmania*, its vectors and hosts in different parts of the world. More than 20 pathologic species of *leishmania* and over 30 species of *Phlebotomus*—the vector—are known worldwide (Figure 1, Table 1).

On the other hand, deterioration of the eco-systems by human beings also contribute to the spread of the disease in the world.

Leishmaniasis has four clinical forms. These are cutaneous leishmaniasis (CL, local—LCL or diffuse—DCL), mucocutaneous leishmaniasis (MCL), visceral leishmaniasis (VL), post-kala-azar dermal leishmaniasis (PKDL), (Table 1).

![Figure 1. Taxonomy of leishmania family [1].](image)
In this section we aimed to reveal the epidemiologic analysis of different types of leishmaniasis in all over the world in every aspect.

2. Geographic distribution and incidence

Leishmaniasis, as being one of the world’s most neglected diseases, affects mainly the poor, developing countries; 350 million people are thought to be at risk of contracting leishmaniasis. It is estimated that approximately 12 million men are ill and 2 million new cases occur annually [1, 2].

With new epidemics occurring in endemic areas and the spread of leishmaniasis to previously free areas because of migration, tourism, and military activities. Leishmaniasis is a disease of the poor, occurring mostly in remote rural villages with poor housing and little or no access to modern health-care facilities. In endemic areas, diagnosis of any form of leishmaniasis puts a huge financial strain on an already meagre financial resource at both the individual and community levels [3].

Visceral leishmaniasis: approximately 90% of new cases occur in the world’s cases of India, Bangladesh, Nepal, Ethiopia, Sudan and Brazil are seen. The annual number of cases worldwide has been estimated to be visceral leishmaniasis, between 200,000 and 400,000. The two important causative agents of visceral leishmaniasis (VL), namely Leishmania (L) donovani and L. infantum, cause significant health problems [1, 4].

Visceral leishmaniasis (VL), also known as “kala azar,” is caused by parasites of the L. donovani complex in some parts of the world. The L. donovani complex can be found throughout Asia, North Africa, Latin America and Southern Europe, affecting mostly vulnerable and uncared populations. As being the most severe form, VL is almost always fatal if left untreated. It is characterized by undulating fever, loss
of weight, splenomegaly, hepatomegaly and/or lymphadenopathies and anemia
L. infantum, the other causative agent of VL, is found in Southern Europe, North
Africa and West and Central Asia [1, 5].

Post-kala-azar dermal leishmaniasis (PKDL) is another clinical composition of
kala azar and it is seen in all areas endemic for L. donovani. It especially comments
in East Africa and on the Indian subcontinent with a prevalence of 50 and 10%,
respectively [1, 6].

Cutaneous leishmaniasis: approximately 90% of the world’s cases of
Afghanistan, Pakistan, Sudan, Syria, Saudi Arabia, Algeria, Iran, Iraq, is seen in
Brazil and Peru. The annual number of cases worldwide has been estimated to be
visceral leishmaniasis, cutaneous leishmaniasis: between 700,000 and 1.2 million
[1]. Old World species: L. major, L. infantum, and L. tropica, New World species,
such as, L. amazonensis, L. chagasi, L. mexicana, L. viannia (V) naiffi, L. (V)
brasiliensis, and L. (V) guyanensis [6, 7]. Antroponotic cutaneous leishmaniasis
(ACL) is caused by most Leishmania species, occur in most subtropical and tropical
regions (for example, L. major from Africa and Asia, and L. mexicana from Central
and South America), and by many species in the subgenus Viannia, which are
limited to Latin America (for example, L. (V) brasiliensis) [6].

Old World cutaneous leishmaniasis caused by L. tropica (seen particularly in the
Mediterranean Basin, the Middle East, Pakistan and India) and L. infantum,
(found sporadically in the Middle East, South Russia, and rural regions of Africa).
New World cutaneous leishmaniasis, caused by L. braziliensis and L. mexicana is
seen in Mexico and South America. Leishmaniasis exists on every continent except
Australia, the Pacific Islands and Antarctica. The parasites that cause leishmaniasis
are found in 98 countries around the world [7].

L. tropica, L. major, L. aethiopica and L. infantum causes Old World cutaneous leish-
maniasis. Leishmania tropica is mainly seen in urban areas and causes ACL. Related
vectors are Phlebotomus sergenti and Phlebotomus papatasi. Lesions are generally dry
and remain without ulceration. During the course lesions change to papules [1, 8].

L. tropica is found in urban areas. It causes ACL via the vectors Phlebotomus
sergenti and Phlebotomus papatasi. The lesions are dry and stay for a long period of
time without ulceration. Thereafter, painless lesions as papules, tubercles or nodules
subside without scarring in 9–12 months [8].

L. major infections generally cause wet lesions in habitants of rural areas.
Incubation period is less than 4 months. Lesions are usually seen on the legs. They
start as acute papillary infection in the bite area and advances into pustular ulcers
in 1–3 weeks. The infection is categorized as “zoonotic cutaneous leishmaniasis
(ZCL)” due to the transmission to rodents, dogs via Phlebotomus papatasi [9].

L. infantum often causes small (0.5–1 cm), solitary ulcers on the face [10].

L. aetropica lesions are seen in the mouth and nose with local or wide spread
dermal involvement. Lesions rarely become ulcerated. Healing may take 1–3 years
or more [11].

L. braziliensis, L. mexicana, L. amazonensis, L. guyanensis, L. panamensis and L.
peruviana cause New World cutaneous leishmaniasis [8, 12].

The disease caused by L. braziliensis is named “espundia.” The infection leads
to metastatic lesions, damages and deformation of the cartilage and soft tissues by
affecting buccal and nasal mucosa [13].

L. mexicana causes usually solitary, painless lesions in the pinna. It leads to
chronic lesions in the pinna called “chiclero’s ulcer” [14].

L. guyanensis infection is consisted of flat ulcerative plaques with leakage in
whole body. The lesion is called “pianbois” in Uruguay and Venezuela [15].

L. amazonensis causes solitary or multiple lesions with rarely spontaneous remis-
ion. It is rare in humans [8].
*L. peruviana* infection causes solitary or multiple painless dermal lesions they usually subsided spontaneously in 4–5 months. This infection is called uta [16]. Lesions of *L. panamensis* are ulcers without spontaneous improvement the reservoirs are dogs and monkeys [12].

*L. venezuelensis* generally causes solitary painless nodular lesion. [12, 17].

*L. garnhami* usually causes solitary or multiple lesions and may spontaneously be healed in 6 months [12].

The Eastern Hemisphere (Old World): leishmaniasis is found in some parts of Asia, the Middle East, Africa (especially in the tropical region and North Africa), and Southern Europe.

The Western Hemisphere (New World), leishmaniasis is found in some parts of Mexico, Central America, and South America. It is not found in Chile or Uruguay. Leishmaniasis is seen in most tropical and subtropical regions with climate, mainly in South and Central America, Africa, Asia, and Southern Europe. The leishmaniasis is considered as one of the neglected tropical diseases (NTD) (Figures 2 and 3) [18].
3. Epidemiology of leishmaniasis according to vector


b. *Lutzomyia* spp. (New World).

Humidity and moisture, whether from rainfall or in the soil, have often been identified as important for the sandfly, with humidity influencing breeding and resting [6].

Sandflies belonging to either *Phlebotomus* spp. (Old World) or *Lutzomyia* spp. (New World) are the primary vectors; domestic dogs, rodents, sloths, and opossums are amongst a long list of mammals that are either incriminated or suspected reservoir hosts [1, 21, 22]. Most of its foci in the Old World have a Mediterranean climate and sand fly vectors, usually *Phlebotomus* (Larroussius) species, *Phlebotomus* species (*P. papatasi*, *P. sergenti*, *Phlebotomus alexandri*, *P. tobbi*, *Phlebotomus syriacus*, *Phlebotomus neglectus*, *Phlebotomus perfiliewi*, *Phlebotomus galilaeus*, *Phlebotomus transcaucasicus*, and *Phlebotomus halepensis*) two *Sergentomyia* species (*Sergentomyia theodori* and *Sergentomyia dentata*), (*Phlebotomus ariasi* and *Phlebotomus perniciosus*, *Phlebotomus longicuspis*) can diapauses for human visceral leishmaniasis [21–24]. In contrast to malaria, there is little evidence for the effect of vector control in leishmaniasis because terrestrial habitat of *Phlebotomus* is mostly unknown.

4. Host

4.1 Human

*Leishmania* species are transmitted to human via vectors, blood transfusion, organ transplantation or vertically via transplacental route. Other factors that cause the transmission of the disease are contact with contaminated materials or needle stick injuries in the labs [25–27].

*Leishmania*-infected humans especially in poor socioeconomic conditions play a pivotal role as a reservoir in transmission of the agent to vectors or to other hosts. In another words, one can say that human beings contribute the disease transmission by themselves [26, 27]. Poor living conditions in adobe, wooden houses, barns create a tendency towards an increase of vectors [27–29].

In all three clinical types of *Leishmania* spp., antimonials (sodium stibogluconate [SSG]), miltefosin (MIL), amfoterisin B (AmB) veparomomisin (PMM)) are being used [30]. Children and people with immune suppression, HIV infection or malignant diseases cause rapid spread of leishmaniasis. Apart from these, undiagnosed or untreated infected people create an important risk factor. Especially drug resistance and high expense of the medication cause insufficient treatment [27–29]. The first drug resistance was reported in VL treatment against SSG and against MIL, in India and Nepal, respectively [31–33]. Later, resistance against MIL was also reported in one patient with HIV and another two patients with Indian origin [34, 35]. Verma et al. showed that the effectiveness of PMM was decreased by 6 times for the promastigote forms of *L. donovani* [36]. Invasion of macrophages by PMM-R parasites led to increased nitric oxide (NO), whereas the levels of reactive oxygen species (ROS) remained unchanged. This finding shows resistance of *Leishmania* spp. against PMM [36]. Similarly, Deep et al., reported high recurrence rates in patients with VL and PKDL when treated with MIL [37].

In conclusion, due to immune problems of the patient, co-existence of other diseases, inappropriate use of the drugs during the medical treatment of leishmaniasis, “drug resistance” may occur via gene over-expression, deletion, single nucleotide
<table>
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<td><em>L. donovani</em></td>
<td>AVL, DCL, CL</td>
<td>Northeast India, Nepal, Bangladesh, (Bhutan), Sri Lanka, Republic of China, Sudan, Ethiopia, (Chad), (Yemen), Kenya</td>
<td>Rural, peri-domestic</td>
<td>Human anthroponosis</td>
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<tr>
<td><em>L. donovani</em></td>
<td>AVL</td>
<td>People's Republic of China</td>
<td>Rural, peri-domestic</td>
<td>Unknown</td>
<td><em>P. (Du.) alexandri, P. (Ad.) species</em></td>
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<td><em>L. donovani</em> (L. archibaldi)</td>
<td>AVL, ZVL, ML</td>
<td>Sudan, Ethiopia, (Chad), (Yemen)</td>
<td>Rural, <em>Acacia</em>—<em>Balanites</em> forest</td>
<td>Human anthroponosis</td>
<td><em>P. (Larroussius) orientalis</em></td>
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<td>AVL, DCL</td>
<td>Sudan, Ethiopia, Kenya, (Uganda)</td>
<td>Rural, savannatermite mounds</td>
<td>Human anthroponosis</td>
<td><em>P. (Sy.) martini</em></td>
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<td><em>L. infantum</em></td>
<td>ZVL, ZCL</td>
<td>Med Europe, North Africa, Southwest Asia, People's Republic of China</td>
<td>Rural, peri-domestic</td>
<td>Domestic dog, wild canids, domestic cat</td>
<td><em>P. (La.) ariasi, perniciosus</em></td>
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<td><em>L. infantum</em> (L. chagasi)</td>
<td>VL, CL</td>
<td>Latin America: not Peru or Guianas</td>
<td>Rural, peri-domestic</td>
<td>Domestic dog, wild canids</td>
<td><em>L. (L.) longipalpis</em></td>
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<tr>
<td><em>L. major</em></td>
<td>ZCL</td>
<td>North Africa, Ethiopia, Kenya, Sudan, Middle Asia India</td>
<td>Peri-domestic</td>
<td>Human anthroponosis</td>
<td><em>P. papatasi, P. duboscqi</em></td>
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<td><em>Le. (Le.) tropica</em></td>
<td>ACL</td>
<td>North Africa, Middle East, Iran, Afghanistan</td>
<td>Urban</td>
<td>Peridomestic, including suburbs; human</td>
<td><em>P. (Paraphlebotomus) sergenti</em></td>
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<td><em>Le. (Le.) tropicae</em> (Le. (Le.) killicki)</td>
<td>ZCL</td>
<td>North Africa, Middle East, Sub-Saharan Africa</td>
<td>Rural</td>
<td>Rocky arid; hyraxes, Rodents</td>
<td><em>P. (Adlerius) arabicus P. (La.) guggisbergi</em></td>
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<td><em>Le. (Le.) aethiopica</em>;</td>
<td>ZCL, DCL, ML</td>
<td>Ethiopia, Kenya</td>
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<td><strong>New World</strong></td>
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<td><em>Leishmania</em> (Leishmania) infantum</td>
<td>ZVL, ZCL</td>
<td>Latin America: not Peru, Guianas</td>
<td>Peridomestic, including suburbs</td>
<td>Domestic dog</td>
<td><em>Lutzomyia (Lutzomyia) longipalpis s.l.</em></td>
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<tr>
<td><em>Leishmania</em> (Viannia) braziliensis</td>
<td>ZCL, ML</td>
<td>East of Andes: not Guyana, Suriname</td>
<td>Peridomestic, silvatic</td>
<td>Rodents, marsupials, dog</td>
<td><em>L. (Psychodopygus) wellcomei L. (Nyssomyia) neivai L. (Ny.) whitmani</em></td>
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<td>Leishmaniaspecies</td>
<td>Disease</td>
<td>Countries (suspected)</td>
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<td><em>Le. (V.) braziliensis</em></td>
<td>ZCL, ML</td>
<td>West of Andes, northern Venezuela: not El Salvador</td>
<td>Peridomestic, silvatic</td>
<td>Rodents, marsupials, dog</td>
<td><em>L. (Pifanomyia) ovallesi</em></td>
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<td><em>Le. (V.) peruviana</em></td>
<td>ZCL, ML</td>
<td>Peru</td>
<td>Peridomestic, silvatic</td>
<td>Rodents, marsupials, dog</td>
<td><em>L. (He.) peruanus</em> L. (Pf.)</td>
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<td><em>Le. (V.) guyanensis</em></td>
<td>ZCL, ML</td>
<td>East of Andes: not Paraguay</td>
<td>Silvatic</td>
<td>Arboreal edentates, Others</td>
<td><em>L. (Ny.) umbratilis</em></td>
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<tr>
<td><em>Le. (V.) panamensis</em></td>
<td>ZCL, ML</td>
<td>West of Andes, northern Venezuela: not Mexico, Belize, El Salvador</td>
<td>Silvatic</td>
<td>Arboreal edentates, Others</td>
<td><em>L. (Ny.) triapodi</em> L. (Ny.)</td>
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<td><em>L. (Ny.) edentula</em> L. (Tricholateralis)</td>
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<td>gomezi</td>
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<td><em>Le. (V.) shawi</em></td>
<td>ZCL</td>
<td>Brazil</td>
<td>Silvatic</td>
<td>Arboreal</td>
<td><em>L. (Trichophoromyia) ubiquitalis</em> L. (Pf.) nuneztovari</td>
</tr>
<tr>
<td><em>Le. (V.) lainsoni</em></td>
<td>ZCL</td>
<td>Bolivia, Peru, Brazil, French Guiana, Suriname</td>
<td>Silvatic</td>
<td>Rodent <em>Agouti paca</em></td>
<td><em>L. (Trichophoromyia) ubiquitalis</em> L. (Pf.) nuneztovari</td>
</tr>
<tr>
<td><em>Le. (V.) colombiensis</em></td>
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<td>Panama, Colombia, Venezuela</td>
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<td>Choloepushoffmani</td>
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<td><em>Le. (V.) naifi</em></td>
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<td>Brazil, French Guiana, Panama</td>
<td>Silvatic</td>
<td>Dasypunonemecinctus</td>
<td><em>L. (Pr.) ayozae and other species</em> L. (Ny.) trupidicic</td>
</tr>
<tr>
<td><em>Le. (L.) amazonensis</em></td>
<td>ZCL, DCL</td>
<td>East of Andes: not Guyana, Paraguay</td>
<td>Silvatic, non-climax forest</td>
<td>Terrestrial Rodents, Marsupials</td>
<td><em>L. (Ny.) flaviscutellata</em></td>
</tr>
<tr>
<td><em>Le. (L.) mexicana</em></td>
<td>ZCL, DCL, ML</td>
<td>West of Andes, southern United States: not Peri</td>
<td>Silvatic, non-climax forest</td>
<td>Terrestrial Rodents, Marsupials</td>
<td><em>L. (Ny.) olmecabmeca</em></td>
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<tr>
<td><em>Le. (L.) venezuelensis</em></td>
<td>ZCL, DCL</td>
<td>Northern Venezuela</td>
<td>Silvatic</td>
<td>Unknown</td>
<td><em>L. (Ny.) olmecacicolor</em></td>
</tr>
</tbody>
</table>

Abbreviations: TC, transmission cycle; A, anthroponotic; Z, zoonotic; V, visceral; C, cutaneous; M, mucosal; D, diffuse; L, leishmaniasis. P., Phlebotomus; Pa., Paraphlebotomus; Pf., Pifanomyia; Sy., Synphlebotomus La., Larroussius; Lu., Lutzomyia.

Table 2. Disease types and transmission cycles of leishmaniasis worldwide [6, 20, 21].
polymorphisms generating stop codons or amplification of sets of genes [38–40]. This very important for epidemiological standpoint and thus proper use of drugs when needed should be stressed, and also new drug formulations and/or vaccine should be investigated.

Technological advances let the people travel all over the world. This may cause vectored spread or spread directly by infected people [41].

4.2 Dogs

Dogs are very important in terms of the epidemiology of leishmaniasis. All forms of leishmaniasis namely cutaneous, mucocutaneous and visceral types may be found in dogs. Since the infected dogs are important reservoir of the disease, their controls and treatments are mandatory for the disease control. Dogs as pets are being controlled by vets however stray or wild dogs, fox species like Lycalopex vetulus [42], Cercocyon thous [43] may cause outbreaks. Dogs are natural hosts for L. infantum, L. chagasi, L. tropica and L. peruviana as well as being infected by them. Especially they are endemic in dogs in Mediterranean region, Asia and Latin America. Leishmania infantum is the causative agent of visceral leishmaniasis and it is prevalent especially in Mediterranean region. Vectors for this type are Phlebotomus ariasi, P. major, P. perniciosus, P. longicuspis, P. chienisa, P. mongolensis, P. papatasi [44, 45]. In the same region, the causative agent of zoonotic cutaneous leishmaniasis is L. tropica and the vectors are P. perfilievi, P. papatasi and P. sergenti [1, 46]. In South America, the causative agent of canine cutaneous leishmaniasis is L. chagasi and the vectors are Lu. longipalpalis, Lu. evansi, Lu. gomezi [1].

4.3 Rodents

Comparing to dogs, eradication of the infectious agent of leishmaniasis from the rodents is more difficult and even sometimes impossible.

Different rodents such as Didelphis albiventris (opossum), Mus musculus (domestic mouse), Microtus socialis, Rattus rattus (black rat), Cercomys cunicularius (wild rat), Mesocricetus auratus (Syrian hamsters) in America, Africa and Asia lead to spread of leishmaniasis [47–51].

Phlebotomus papatasi, vector of L. tropica, transmitted cutaneous leishmaniasis to small rodents such as Psammomys obesus (Israel), Meriones crassus (Israel), Meriones libycus (Iran), Rhombomys opimus (Iran), Rhombomys opimus (Iran), Meriones sacramenti (Egypt) [9].

Rattus rattus and Rattus norvegicus have been found naturally infected with L. infantum in the Mediterranean and in Next Orient endemic areas (Table 2) [49, 52, 53].

5. Transmission cycle

There are two different types of transmission;

1. In many geographic areas, infected people are not needed to sustain the transmission cycle of the parasite in nature; transmission cycle continue via the infected animals (rodents or dogs, felines). Leishmania infection in reservoir animals are specifically named; if it is in dogs, it is named as canine leishmaniasis whereas in cats, it is called feline leishmaniasis dogs species of Leishmania species in the reservoir in animals, canine leishmaniasis, which is in feline called leishmaniasis. L. infantum is the most common and important cause of canine leishmaniasis worldwide. The zoonotic transmission of L.
infantum, from canine to humans, is not only in the Mediterranean region where it may have originated, but also it may be found in many of the drier regions of Latin America. *Leishmania* species reported from dogs include *L. mexicana*, *L. donovani*, and *L. braziliensis*. These *Leishmania* species are occasionally reported from the cats. Cats are at risk of infection especially in areas where these parasites are endemic [6, 54, 55].

2. In some parts of the world, infected people are needed to sustain the cycle; this kind of transmission (human—*Phlebotomus*—human) is called anthroponotic transmission.

Full knowledge on these two transmission cycles is very important in effective prevention of leishmaniasis [54, 55].

6. Effect of deteriorated eco-system on spread of leishmaniasis

Unlike other parasites, it is extremely difficult to eradicate whole kinds of species of *Leishmania* in nature. This is contrary to some other parasites. As example *Plasmodium vivax* is specific to human, thus it can be eradicated by vector control. However, this is not the case for *Leishmania* spp. [54, 55].

There are many check points to establish the control of the disease. Firstly, all patients with leishmaniasis should be properly treated. *Leishmania* transmission is dependent on the togetherness of contaminated sandflies with the reservoir hosts, and humans. Additionally, climatic and environment factors are important, too.

As the development of chemical insecticides use such as dichlorodiphenyltrichloroethane (DDT) against mosquito was a key component of the eradication, similarly they were proposed to have an effect on the sandflies, vectors of visceral leishmaniasis [56–58]. Since DDT use is found to be harmful to the environment and people, its use is prohibited by the World Health Organization [59]. At the moment there isn’t any strategy to control *Phlebotomine* by using insecticides by governments [60, 61]. Preliminary experiments for developing a vaccine against *Leishmania* spp. was reported [62]. However, the vaccine did not appear to protect against visceral leishmaniasis [63]. fucose-mannose ligand from an extract of *L. donovani* has been used in conjunction with a saponin adjuvant in attempts to vaccine [64]. Further studies are needed to develop an effective vaccine against leishmaniasis.

7. Summary

Leishmaniasis is still an important parasite disease in all over the world. The reasons are presence of many different species of *Leishmania*, and their ability to survive in many different organisms, such as vectors, dogs, rodents, humans. *Leishmania* spp. may cause different clinical scenarios by affecting different tissues and organs. As eukaryotic cells, *Leishmania* spp. can survive in the immune system of the most advanced organism, human. Presence of amastigote forms even in the hosts’ defensive cells shows the strength of the parasite.

Leishmaniasis is an important public health problem. Thus, relevant public health policies such as education of the people especially in endemic areas, multi-disciplinary approach, diagnosis, treatment will be helpful in the elimination of the disease. Additionally, further epidemiological studies as well as vaccination studies will continue to strive for eradication.
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