Leishmaniasis: A Review on Parasite, Vector and Reservoir Host

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Abstract

Leishmaniasis is a vector-borne disease affecting millions of people worldwide. The disease is caused by different species of Leishmania, and it is manifested by three major clinical forms namely cutaneous, muco-cutaneous and visceral leishmaniasis. This review is aimed to address briefly the parasite, the vector and the reservoir aspects in transmission of leishmaniasis in different regions of the world. The complexity of transmission of the disease lays on the complex life cycle of the parasite which involves sand fly vectors and mammalian reservoirs. The transmission can either be zoonotic and/or anthroponotic through the bite of an infected female sand fly. There is uneven global distribution of the disease often because of the various distribution patterns of the parasite, the vector and the reservoir host species. Various sand fly species in the genus Phlebotomus and Lutzomyia are responsible for transmission of leishmaniasis in the old and new worlds. Animal reservoirs are important for maintaining infections in various areas, and hence are important for zoonotic and rural/sylvatic transmission of the disease. A high prevalence of infection has been reported from small to large domestic and wild mammals. Control and elimination of leishmaniasis require detection of human and animal cases, identification of reservoir hosts, and implementation of effective vector control strategies in areas.

Keywords: Leishmaniasis; Leishmania spp; Sand fly; Zoonosis; Anthroponosis; Reservoir host; Vector-borne

Introduction

Leishmaniasis is a vector-borne zoonotic disease caused by obligate intracellular parasitic protozoa of the genus Leishmania. The disease gets into human population when human, flies and the reservoir hosts share the same environment [1-3]. Leishmania infection is transmitted to humans and to other mammals by the bite of an infected sand fly vector [4]. The infection can rarely be transmitted by other means such as blood transfusions [5], needle sharing [6], or from mother to child during pregnancy [7]. The World Health Organization (WHO) has stated that leishmaniasis is one of the most neglected diseases, with 350 million people considered at risk of contracting the disease, a burden of about 12 million people currently infected in 98 countries, and two million new cases estimated to occur annually [8,9]. There are three clinical forms of leishmaniasis in human namely cutaneous, mucocutaneous, and visceral involving the skin, mucous membranes and visceral organs respectively. Cutaneous leishmaniasis is a less severe form of the disease which usually manifests self-healing ulcers. Mucocutaneous leishmaniasis results in disfiguring lesions of the nose, mouth and throat mucous membranes. Visceral leishmaniasis is the most severe form of the disease which can result in 100% mortality of infected patients if not treated.

The present paper reviewed the interplay of the parasite, the vector, and the hosts in the transmission dynamics of leishmaniasis.

The parasite

The genus Leishmania belongs to a family Trypanosomatidae (order Kinetoplastida) [10,11]. The parasite is categorized in two main groups; the old world species occurring in Europe, Africa and Asia, and the new world species occurring in America [11,12]. About 53 species of the parasite have been described from different regions of the world; of these, 31 species are known to be parasites of mammals and 20 species are pathogenic for human beings [9,13]. Many of the leishmania species infecting human are zoonotic, having a complex variation in domestic and wild mammal reservoir hosts; while, other species of the parasite are anthroponotic, having human-to-human transmission in the presence of the vector [9]. *Leishmania donovani* is usually considered to be an anthroponotic parasite though studies reported the presence of parasite or circulating antibodies against the parasite antigens in domestic and wild animals of India and East [8,14]. The global distribution of each of Leishmania species determines the type of disease that occurs in an area. *L. donovani* causes visceral leishmaniasis in South Asia and Africa; while *L. infantum* causes this disease in the

Mediterranean, the Middle East, Latin America and parts of Asia. Leishmania major causes cutaneous leishmaniasis in Africa, the Middle East and parts of Asia; while *L. tropica* causes this disease in the Middle East, the Mediterranean and parts of Asia, and *L. aethiopica* causes cutaneous disease in the horn of Africa. In south America, again several species of Leishmania cause cutaneous form of the disease [11,15] **(Table 1)**.

Table 1 The main species of leishmania that cause human disease [11,15,16].

Leishmania species	Disease form in humans	Geographical distribution	Reservoir hosts	Vectors
Leishmania aethiopica@	Localised cutaneous leishmaniasis,			*Phlebotomus longipes*,
	Diffuse cutaneous leishmaniasis	Ethiopia, Kenya	Rock hyraxes	*P. pedifer*
L. major@	Localised cutaneous leishmaniasis	North Africa, Middle East and Central Asia, Sub- Saharan Africa and Sahel belt, Sudan, North India, Pakistan	Rodents	*P. papatassi*, *P. duboscqi*
*L. mexicana**	Localised cutaneous leishmaniasis	Central America	Forest rodents	*Lutzomyia olmeca*
*L.amazonensis**	Localised cutaneous leishmaniasis	South America, north of the Amazon	Forest rodents	*L. flaviscutellata*
*L.braziliensis**	Localised cutaneous leishmaniasis;	South America,	Forest rodents,	*Psychodopygus*
	Mucocutaneous leishmaniasis	Central America and Mexico	peridomestic animals	*Lutzomyia spp.*
*L. peruviana**	Localised cutaenous leishmaniasis	West Andes of Peru., Argentine highlands	Dog	*L. verrucarurn*, *L. pvmenis*
L. infantum@	Visceral leishmaniasis; Localised cutaneous leishmaniasis	Mediterranean basin; Middle East and Central Asia to Pakistan; China; Central and South America, southern Europe, northwest Africa	Dogs, cats, foxes, jackals	*P. pcrniciosufi*, *P. arias*
L. donovani@	Visceral leishmaniasis	Ethiopia, Sudan, Kenya, India, China, Bangladesh, Burma	Human anthroponosis, Rodents Sudan, Canines	*Phiebotomus argentipes*, *P. orinntalis*, *P. martini*
@Old world species				
*New world species				

Leishmania species have a heteroxenous life cycle. The parasite exhibits two morphological forms in its life cycle; amastigote in macrophages of the mammalian host and promastigote in the gut of the sand fly vectors [11]. Human stage of the life-cycle starts when a parasitized female sand fly injects metacyclic promastigotes into human body. The promastigotes are then phagocytosed by the host's macrophages, and consequently, the parasite transforms into non-flagellated form, amastigote, which reproduce by binary fission. The multiplication of the parasites occurs inside the macrophages. The macrophage lyses and the multiplication cycle continues when other hosts' phagocytes are infected [11,15].

The vector

Leishmaniasis is transmitted by the bite of infected female sand flies. There are over 600 species of sand flies divided into five genera: Phlebotomus and Sergentomyia in the Old World and Lutzomyia, Brumptomyia, and Warileya in the New World [4,16,17]. Although human-biting sandflies occur in various genera, the only proven vectors of human leishmaniasis are species and subspecies of the genus Phlebotomus and Lutzomyia **(Table 2)**. Various species in the genus Phlebotomus are responsible for transmission of leishmaniasis in the Old World and Lutzomyia species in the New World. Each sand fly species typically transmits only one species of parasite and each parasite leads to a particular type of disease [8,18,19].

Table 2 Sand flies transmitting most human leishmaniasis [18].

Sand fly species	Geographical distribution
Phlebotomus papatasi, Phlebotomus dubosqi, Phlebotomus salehi	Central and West Asia, North Africa, Sahel of Africa, Central and West Africa
Phlebotomus sergenti	Central and West Asia, North Africa
Phlebotomus longipes, Phlebotomus pedifer	Ethiopia, Kenya

Phlebotomus argentipes, Phlebotomus orientalis, Phlebotomus martini	Indian subcontinent, East Africa
Phlebotomus ariasi, Phlebotomus perniciosus	Mediterranean basin, Central and West Asia
Lutzomyia longipalpis	Central and South America
Lutzomyia olmeca olmeca	Central America
Lutzomyia flaviscutellata	South America
Lutzomyia wellcomei, Lutzomyia complexus, Lutzomyia carrerai	Central and South America
Lutzomyia peruensis, Lutzomyia verrucarum	Peru
Lutzomyia umbratilis	South America
Lutzomyia trapidoi	Central America

The development of leishmania parasite within the vector sand flies is an inevitable stage for the transmission of leishmaniasis among various hosts. Female sand flies acquire leishmania parasites when they feed on an infected mammalian host in search of a blood-meal. The amastigote forms of the parasites taken up by sand flies are not usually found in the peripheral circulation; rather they are present in the skin itself. Parasites present in organs such as liver and spleen are not accessible to sand flies. Amastigotes are intracellular parasites found in phagolysosomes of macrophages and other phagocytes [20], and their uptake by the blood-feeding sand fly is assisted by the cutting action of the mouthparts. Thus sand flies are pool feeders, meaning they insert their saw-like mouthparts into the skin and agitate them to produce a small wound into which the blood flows from superficial capillaries [21]. It is this tissue damage associated with the creation of the wound that releases skin macrophages and/or freed amastigotes into the pool of blood, and enables their subsequent uptake into the abdomen of the sand fly. Then the parasite multiplies and further differentiates into other stages, metacyclic promastigote being the final mammalian-infective stage which movies to the foregut of the vector sand fly [22]. The metacyclic promastigotes are deposited in the skin of a new mammalian host when the fly takes another blood meal, leading to the transmission of disease.

The reservoir host

Animal reservoirs are important for maintaining the life cycle of many Leishmania species and hence are important for transmission of zoonotic and rural/sylvatic infections. There are two main sources of human leishmaniases, zoonotic leishmaniases, in which the reservoir hosts are wild animals, commensals or domestic animals, and anthroponotic leishmaniases, in which the reservoir host is human. Although each Leishmania species generally falls into one or the other of these categories, there are exceptions where the anthroponotic species cause zoonotic transmissions [8]. Several species of wild, domestic and synanthropic mammals have been recorded as hosts and/or reservoirs of Leishmania spp. in different parts of the world. Rock hyraxes, rodents, mongoose, dogs, cats, foxes, jackals, wolves, bats, primates, armadillos and other domestic animals are among the multi-host reservoirs to maintain transmission of leishmaniasis in different localities [23-25]. However, leishmania reservoirs are so complex that they show regional and temporal variations [26], and only a local studies involving ecological and parasitological analysis can determine whether these animals are playing a role as reservoir in a given environment [24].

The sylvatic transmission of leishmaniasis is effected as a result of established wildlife populations in and around human settlements in the presence of appropriate vector. Dogs and cats may be involved in the transmission cycles of these parasites in urban areas, and the presence and frequency of these animals may have a significant effect on disease pressure to humans. In urban and peri-urban areas, the frequency of contact between wildlife and humans changes from sporadic encounters to permanently sharing the environment, thus greatly increasing the chance of transmission of leishmania parasite to humans [27].

Human beings are directly involved as a principal reservoir host in two forms of the disease: visceral leishmaniasis caused by L. donovani and cutaneous leishmaniasis caused by L. tropica. Although infections due to L. tropica and L. donovani have been assumed to be anthroponotic by most reports [18,28], there is evidence for the possible involvement of zoonotic transmission of these two species with uncertain reservoir hosts in some foci [8,29]. In addition, there are recent reports on zoonotic involvement of L. donovani as natural infections of dogs [30], domestic animals [23] and rodents [31] with L. donovani complex were reported in different regions of both old and new world.

Although dogs are considered the most important domestic reservoirs of L. infantum, the role of other domesticated mammals as reservoirs have also been implied and their synanthropic capability could facilitate the connection between wild and peri-domestic environments [8].

Moreover, many rodent species have been identified as reservoirs of different species of leishmania showing competence to maintain the parasite. Small mammals like rodents are important reservoir hosts to maintain leishmania transmission cycle [1]. Even though few studies done on flying animals to confirm their reservoir host status, leishmania

parasites (*L. infantum*) were isolated from the blood of bats [32-34] **(Table 3)**.

Table 3 Reservoir hosts of human leishmaniasis in some endemic countries [8,24,27,35,36].

Region	Countries	Reservoir hosts
Old world	North Africa, central and west Asia	Dog, human, rodent
	Ethiopia, Kenya	Rodents, dog, domestic animals, bats, human, rock hyrax
	Indian subcontinent, (India, Nepal, Bangladesh) and east Africa	Dog, human, rock hyrax, rodent
	Mediterranean basin, central, west Asia and west Africa	Dog, fox, rodent, human
	Europe	Dog, fox
New world	Argentina, Belize, Bolivia, Brazil, Colombia, Costa Rica, Dominican, Ecuador, El Salvador, French Guyana, Guadeloupe, Guatemala, Guyana, Honduras, Martinique, Mexico, Nicaragua, USA, Venezuela, Paraguay, Peru, Surinam, Panama,	Dog, cats, rodent, marsupials, anteater, fox, monkey, coati, sloth, armadillo, porcupines, kinkajou, raccoon, red squirrel,

The transmissibility competence of the reservoir host species and accessibility of the leishmania parasite to the vector are important factors for maintenance of leishmania transmission in an area [35-37]. A host plays a role as a reservoir host if it can transmit the parasite into the next stage that is into the vector. The infectivity of a reservoir host for the sand fly is therefore an important condition for any mammal to be a leishmania reservoir [24]. The vectoral competency is also a factor which determines the transmission of leishmania parasite among multi-hosts. In leishmaniasis endemic areas, where reservoir hosts could sustain as many bites as possible from the sand fly vectors, the infectivity of the reservoir host to the vector would be high [38]. In a study done in Brazil, even low-level infectivity among reservoir hosts corresponded to a substantial infection of the vector, because of the high prevalence of leishmania reactivity in the endemic area [39].

Human activity and leishmania transmission

The epidemiology of leishmaniasis depends on the co-existence and interaction of the parasite, the vector and the host population. The local ecological characteristics of the transmission sites, the current and past exposure of the human population to the parasite and widely varying human behaviour determine the infection status in human [40,41]. Altering the local ecology by human driven forces such as deforestation for socio-economic reasons increases the inflow of leishmania transmitting vectors and possible reservoir hosts from forest-rural areas into semi-urban and urban human settlements [42-44]. Therefore transmission of leishmaniasis is influenced by human effected environmental changes [41]. The co-existence and interaction of the parasite, the vector and the host are affected by changes in both biotic and abiotic setups [44]. Human population pressure is a main reason to bring changes in these setups [45,46]. This human activity is also reason for change in climate, which in-turn influences the transmission of leishmaniasis in an area. It has been suggested that the distribution and burden of such diseases are affected by climate change [41,47,48].

In many areas the intrusion of humans into sylvatic cycles results in a higher risk for leishmania infection. The human may inter this cycle in search of agricultural land, human settlement, timber production, road construction and other economic benefits in forests and other enzootic areas [49]. With regard to human settlement, the disease transmission tends to be high in agricultural villages where houses are frequently constructed with mud walls and earthen floors, and cattle and other livestock are kept close to human dwellings [50-52]. The human behavior of keeping domestic animals in the house and the surrounding attracts sand flies into human settlement, and therefore favor transmission of the disease to human [51]. In endemic areas, building houses near the natural habitats of the vector and the reservoir hosts would increase human-sand fly contact, and hence increases the risk for human leishmaniasis [49]. Human population movement from endemic rural environments into urban areas is a major reason for the establishment of leishmaniasis in peri-urban and urban settlements [53,54].

Conclusion

Although leishmaniasis remains a series public health problem in several countries, its epidemiological status is unevenly situated in different parts of the world [8]. The observed temporal and spatial difference in the epidemiology of leishmaniasis is mainly due to the differences in the distribution of Leishmania spp. (the parasite), sand fly species (the vector) and host species (reservoir and principal hosts) [26,55]. The leishmania parasite is transmitted by the bite of infected female sand flies: Phlebotomus in the Old World and Lutzomyia in the New World (central and south America) [56]. The complexity of leishmania transmission lays on its involvement of various mammalian hosts, ranging from small rodents to big domestic animals, as reservoir hosts [57]. Human imposed environmental changes result in the modification of the micro-ecology of the parasite, the vector and the reservoir host favoring the higher transmission of leishmaniasis in areas [58]. Human activities such as deforestation, agricultural development and settlements near

forested areas and domestication of animals are reasons for occurrence of both zoonotic and anthroponotic transmissions of leishmaniasis [59]. Hence, control and elimination of leishmaniasis largely depends on the understanding of how leishmaniasis involves various mammalian reservoir hosts, whose epidemiological role is yet to be fully understood [60,61]. Epidemiological investigations should not only target human cases, but also focus on animal reservoir and their transmissibility competences [24,57,62,63].

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Conflict of Interests

The authors declare that they have no conflicting interests.

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