Leishmaniasis: A Review on Parasite, Vector and Reservoir Host

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Received date: 02 August 2017; Accepted date: 24 August 2017; Published date: 31 August 2017

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Citation: Alemayehu B, Alemayehu M (2017) Leishmaniasis: A Review on Parasite, Vector and Reservoir Host. Health Sci J. Vol. 11 No. 4: 519.

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, diffuse cutaneous leishmaniasis | Ethiopia, Kenya | Rock hyraxes | *Phlebotomus longipes,* *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; mucocutaneous leishmaniasis | South America, | Forest rodents, | *Psychodopygus* |
| *L. peruviana* | Localised cutaneous leishmaniasis | West Andes of Peru, Argentine highlands | Peridomestic animals | *Lutzomyia spp.* |
| *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. pomciosus,* *P. arias* |
| *L. donovani* | Visceral leishmaniasis | Ethiopia, Sudan, Kenya, India, China, Bangladesh, Burma | Human anthroponosis, Rodents Sudan, Canines | *Phlebotomus argentipes,* *P. ornitalis,* *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].

### 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 |

**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].
mongoose, dogs, cats, foxes, jackals, wolves, bats, primates, and armadillos and other domestic animals are among the multiple 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 anthropocontact 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

| Species                          | Region                          |
|---------------------------------|---------------------------------|
| Phlebotomus argentinipes, 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 trapidii              | 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 moves 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 leishmaniasis, zoonotic leishmaniasises, in which the reservoir hosts are wild animals, commensals or domestic animals, and anthropocontact leishmaniasises, 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 anthropocontact 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, and 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].
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 Guiana, Guadeloupe, Guatemal, 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 |
Acknowledgement

The authors are thankful to Wolaita Sodo University for provision of full internet service, e-books and library to access books and journals for the review.

Conflict of Interests

The authors declare that they have no conflicting interests.

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