Review on Leishmaniasis

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Abstract: Leishmaniasis is a world wide spread parasitic zoonotic diseases caused by protozoans of the genus *Leishmania* and it is transmitted to animals and human being through the bite of *Phlebotamus* female sand flies, not between humans. *Leishmania* are obligatory intracellular protozoan mononuclear phagocytes. Worldwide, there are 2 million new cases each year and 1/10 of the world's population is at risk of infection. This paper reviews leshmaniasis with the objective of highlighting etiology, epidemiology, pathogenesis, clinical sign, diagnosis, treatment and control and prevention of leshmaniasis and also its public health and economic impact. The disease mostly occurs in tropical and sub-tropical areas, mainly in Asia, Europe, Africa, and the Americas. The disease shows different clinical signs. There are several methods of laboratory diagnosis, including parasitological, immunological and molecular. Different forms of treatments are available including oral, parenteral, and topical medications. To date, there are no vaccines against leishmaniasis and control measures rely on chemotherapy to alleviate disease and on vector control to reduce transmission Finally Health education via the public media and training should be implemented by international organizations and governmental agencies in collaboration with research institutions. Fully protection during transmission season, using bed nets and insecticides and reservoirs' control is recommended for personal protection.
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1. Introduction

Leishmaniasis is an important contagious parasitic zoonotic disease whose agent is transmitted by insects called *Phlebotamus* found in wild and urban environments. It affects domestic and wild animals. The parasite has great medical and veterinary public health significance. It infects numerous mammal species, including humans. Leishmaniasis has been known many hundreds of years, with one of the first clinical descriptions made in 1756 by Alexander Russell, and called Aleppo boil. Many names correspond to this group of diseases such as Kala–azar, Dum-dum fever, white leprosy, espundia and so on (Hide *et al.,* 2007). *Leishmania* is, a spectrum of diseases caused by *Leishmania* species, affects ~12 million people around the world, mostly in developing countries. It is transmitted by sand flies (*Phlebotamus* species) as extracellular flagellated promastigotes and replicate as intracellular, flagellated amastigotes in mononuclear phagocytes in mammalian host (Desjeux, 1996).

There are three forms of leishmaniasis, visceral (VL), cutaneous (CL), and mucocutaneous (MCL). Of the three forms VL is the most prevalent in eastern Africa, followed by CL and MCL (Desjesus, 2004). The primary reservoir hosts of *Leishmania* species are sylvatic mammals, such as forest rodents, hyraxes, wild candies. Among domestic animals, dogs are the most important species in the epidemiology of the disease. In addition to becoming ill, dogs are reservoir hosts for *Leshmania. Infantum (L.infantum*), one of the two most important organisms in human visceral leishmaniasis (Pal, 2005).

The increase in *Leishmania* in worldwide incidence is mainly attributed to the increase of several risk factors that are clearly man made and includes massive migration, deforestation, urbanization, immune suppression, malnutrition and treatment failure (Desjeux, 2001). Therefore man made changes to the environment, as well as the population movement may lead to alteration in the range and density of the vectors and reservoirs and consequently may increase human exposure to infected sand flies (Zavitsanou *et al.,*2008). Leishmaniasis is endemic in large areas of the tropics, subtropics, and the mediterranean basin, including more than 98 countries, where there are a total of 350 million people at risk and 12 million cases of infection. Canine leishmaniasis is a serious problem, and it is estimated that 2.5 million dogs are infected in the mediterranean basin only (Moreno, 2002).

Depending on the species, the disease symptoms may range from self-healing skin lesions to the fatal visceral form known as kala-azar or visceral leishmaniasis (Kala-azar) is the most severe form of the leishmaniasis and accounts for 200–400 thousands

new cases and over 50,000 deaths annually (WHO, 2011). Anthroponotic transmission of VL is caused by *Leishmania donovani* and prevails in Indian subcontinent and East Africa; while zoonotic transmission of VL is caused by *L. infantum* in the mediterranean region, South America, and Southwest and Central Asia. The majority of all cases (90%) are found in India, Nepal, Bangladesh, Brazil, South Sudan, and Ethiopia (Alvar *et al.,* 2012).

In Ethiopia, the disease affects people living in a significant portion of the country. Recurrent epidemics of visceral leishmaniasis have occurred in Metema and Humera. Following agricultural development in the region, a large number of labor migrants from the highlands were moved to the endemic areas in the late 1970 for crop harvesting. This led to out breaks of VL, which resulted in high morbidity and mortality (Desta *et al.,* 2005). Recent study investigating risk factors associated with the outbreak in libo Kemkem (Addis zemen), identified dog ownership and habitual outdoor-sleeping to be risk factors for infection (Bashaye *et al.*, 2009).

Therefore the objectives of this seminar paper are:-

- To review the epidemiology of the disease and its prevalence.
- To emphasize public health and economic importance of Leishmaniasis.
- To assess the control and prevention of the diseases in animals and human.

2. Literature Review

The term leishmaniasis refers to the infection of vertebrate hosts by protozoan of the genus *Leishmani*a, Similar to other trypanosomes; they typically present extra nuclear DNA in their cytoplasm within a mitochondrial organelle called the Kinetoplastida (Desjesus, 1992).

2.1. Taxonomic Classification

Leishmania is an intracellular protozoan parasite, belonging to the family Trypanosomatidae (order Kinetoplastida) (Bari, *2008*). These organisms fall within two main groups, the old world species occurring in Europe, Africa and Asia, and the new world species occurring in America (CFSPH, 2009).

Table 1: Taxonomic classification of Leishmaniasis

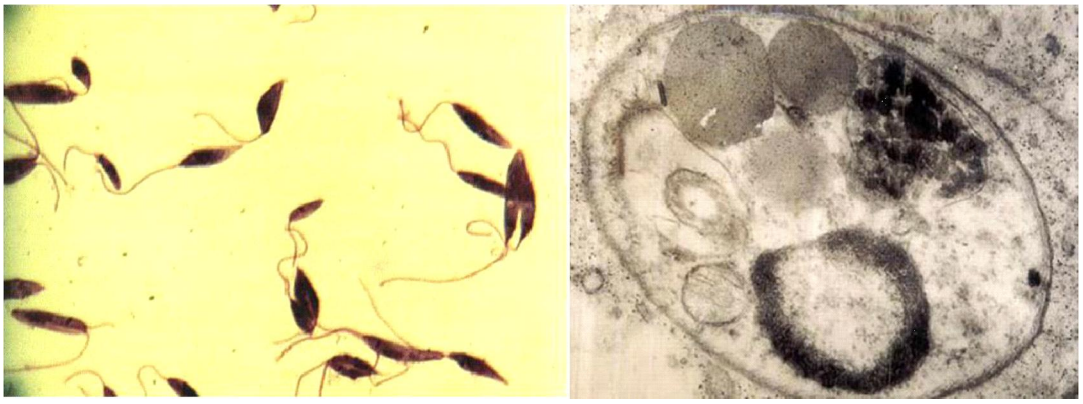
Kingdom	Protista
Subkingdom	Protozoa
Phylum	Sarcomastigophora
Subphylum	Mastigophora
Class	Zoomastigophora
Order	Kinetoplastida
Family	Trypanosomatidae
Section	Salivaria
Genus	*Leishmania*
Species	donovani, tropica, braziliensis infantum

Source: Bari, 2008.

2.2. Etiology

It is caused by the protozoan parasite of the genus *Leishmania.* These agents (causes) are grouped in to two. Those are: old world *Leishman*ia and new world *Leishmania.* In the old world *L.infantum* is the agent of human and canine viscera leishmaniasis, *L.tropica*is the agent of human and canine cutaneous leishmaniasis. In the new world, *L.chagasi* is the agent of human and canine visceral leishmaniasis, *L.mexicana* is the agent of human and canine cutaneous leishmaniasis, and *L.braziliensis* is the agent of human and canine mucocutaneous leishmaniasis (Rose, 2003).

2.4. Morphology of *Leishmania* parasite



B **A**

Figures 1: Stages of *Leishmania.* (A) promastigotes and (B) amastigotes.
Source: Morsy, 1996.

The promastigotes forms are seen in the gut of the sand fly, that the parasite reaches the buccal cavity, which becomes the insect vector of the parasite. They are motile, slender organism's measuring10-15µm in length, with a single anterior flagellum and it runs like a spiral course from the region of the flagella base towards the posterior apical end. One of the membranes is lost when it transform in to amastigotes form. However the fibrils are retained (Hide *et al*., 2007). The amastigotes are small, round to oval bodies, which measure about 3-5µm, and found only in the macrophages of infected vertebrate hosts. They are colorless, have a homogenous cytoplasm, and are surrounded by a pellicle and have a double membrane supported by layer of sub pellicular fibrils (Singh, 2006).

2.5. Epidemiology

2.5.1. Diseases occurrence

Human and animal leishmaniasis shows a wider geographic distribution than previously known. So leishmaniasis is widely distributed around the world. They range over inter tropical zones of America, Africa and extend in temperate region of South America, southern Europe and Asia. Their extension limits are altitude 45 degree north and 32 degree south. The burden of VL remains unknown since several cases are not diagnosed (Kolaczinski *et al.,* 2008). The disease caused byinfection with *Leishmania* continues to have a major impact on much of the world's population. By now estimates have indicates that the annual incidence of visceral leishmaniasis is as high as 500,000 and that of cutaneous leishmaniasis 1-1.5 million that brings the global annual incidence of leishmaniasis to an estimate of 1.5 -2 million cases. Leishmaniasis is the third most important vector born disease (after malaria and sleeping sickness) and accounts for 1.98 million disabilities and 57,000 deaths (WHO, 2001).

Diseases status in Ethiopia: Both CL and VL are growing health problems in Ethiopia, with endemic areas that are continually spreading. The first case of VL in Ethiopia was documented in 1942 in the southern parts of the country. Now, there are an estimated 2,000 to 4,500 cases yearly, with endemic areas in the lowlands of the North West, central, south and south western parts of the country. In the north, the vector is associated with Red Acacia and Balanites trees, in the south with termite hills. Visceral leishmaniasis affects mainly children and young adults. Cutaneous leishmaniasis has been well known since 1913 and is endemic in most regions (Ashford *et al.,* 1973).

There are three clinical forms of cutaneous leishmaniasis in Ethiopia: localized CL, mucosal leishmaniasis and diffuse cutaneous leishmaniasis (DCL); all mainly caused by *L. aethiopica*. The first case of DCL was reported in 1960; currently the incidence of this form is high in the highlands of Ethiopia (Bryceson, 1970). CL is most common in children, with the highest prevalence occurring between 10 and 15 years of age. The visceral leishmaniasis is distributed throughout the low lands while cutaneous leishmaniasis distributed in high lands of Ethiopia, with varying degree of endemicity. Several out breaks occurred in Ethiopia in the last 5 years. Between 2005 and 2008, an outbreak of VL occurred in Amhara Region (Libo Kemkem), where VL had not been reported before, with 2,500 cases and initially a very high mortality (Herrero *et al.,* 2009). The disease was probably imported from the endemic areas in Humera and Metema, wolkaite tsegedi, Segen and Woito valleys in Gemu Gofa. An outbreak of 300 CL cases took place in highlands of Ethiopia and the main areas of transmission includes the Ochollo focus in the Rift Valley escarpment above Lake Abaya, the Kutaber area in the eastern Ethiopian plateau near Dessie, the Aleku area of Wollega zone, the southwest highlands of Bale and Sidamo, Sebeta area near Addis Ababa (Negera et al., 2008) and Silti district between 2003 and 2005. In 2010, 30 cases of VL formed the beginning of an outbreak in a formerly non-endemic area in Tigray (Shiraro district), and 40 VL cases more, mainly children, were diagnosed in East Imey, a district in Somali region, previously non endemic (Bashaye *et al.,* 2009).

2.5.2. The vector

Sand flies do not live on or near the sand, as their name would imply. Their primary habitat is in forests, the cracks of stone or mud walls, or animal burrows. Approximately, 600 species of Phlebotominae are known, most of which belong to the genera *Phlebotamus* in the Old World and *Lutzomyia* in the New World. Adult sand flies are small and one fourth of mosquitoes in size and may reach up to 4 mm in body length. They are covered with dense hairs, black eyes, and long stilt –like legs and hold their wings in a characteristic 'V' shape over hairs and their backs when at rest. They range in color from white to black. The legs are very long and delicate. Both males and females feed on sugary secretions from plants or from honeydew produced by homopterous aphids. But only female sand flies feed blood and transmit the disease (Molyneux and Ashford, 1983).

The flight speed of phlebotomies is considerably slowerthan that of mosquitoes and is <1 m/s and theseasonal activity of adult sand flies is affected by temperature and rainfalls. Adults are active in the evening, at night and in the early morning, although they can bite during the day if disturbed (Kellick *et al*., 1986). The phlebotomies species that are known to transmit the different form of leishmaniasis in Ethiopia includes *p.martinis, P.orientali, P.pedifer P.longipus*

and *P.duboscqi*.other potential vector species like *P.alexandri* and *p.saevus* are known to exist in the endemic areas have been found infected naturally with un identified *Leishmania* species (Asrate *et al*.,2006).

Table (2). *Leishmani*a species, host range and main vector pathogenic to man and animals.

Species	Host range	Main vector
L.donovani	Dogs,savannahrodents , humans	*P.argentpes, L.longipalpis*
L.majoa	Desert and savannah rodents, Rhombomys, Arvicanthis	*P.papatasi*
L.tropia	Humans	*P.sergenti*
L.aethiopica	Rock hyrax	*P.longipes*
L.braziliensis	Sloth, dog	*L. umbratilis* and many others
L.mexicana	Forest rodent	*L.flaviscutellata,L.omecta*

Source: Kerya and Damel, 2004.

2.5.4. Life cycle

The life-cycle starts when a parasitized female sand fly takes a blood meal from a human. These parasites have two basic life cycle stages: one extracellular stage with in the invertebrate host (phlebotomies sand fly), and one intracellular stage within a vertebrate host. The parasites exist in two main morphological forms: the amastigotes and promastigotes, which are found in vertebrate and invertebrate hosts, respectively (Koutis, 2007). The promastigotes are then phagocytosed by the host's macrophages, and consequently, the parasite evolve into amastigotes forms spherical, intracellular forms without flagellum, which they reproduce by binary fission. The multiplication of the parasites occurs inside the macrophages, which are their main targets. The macrophage lyses and the cycle continue when other hosts' phagocytes are being infected (Bañuls and Prugnolle, 2007).

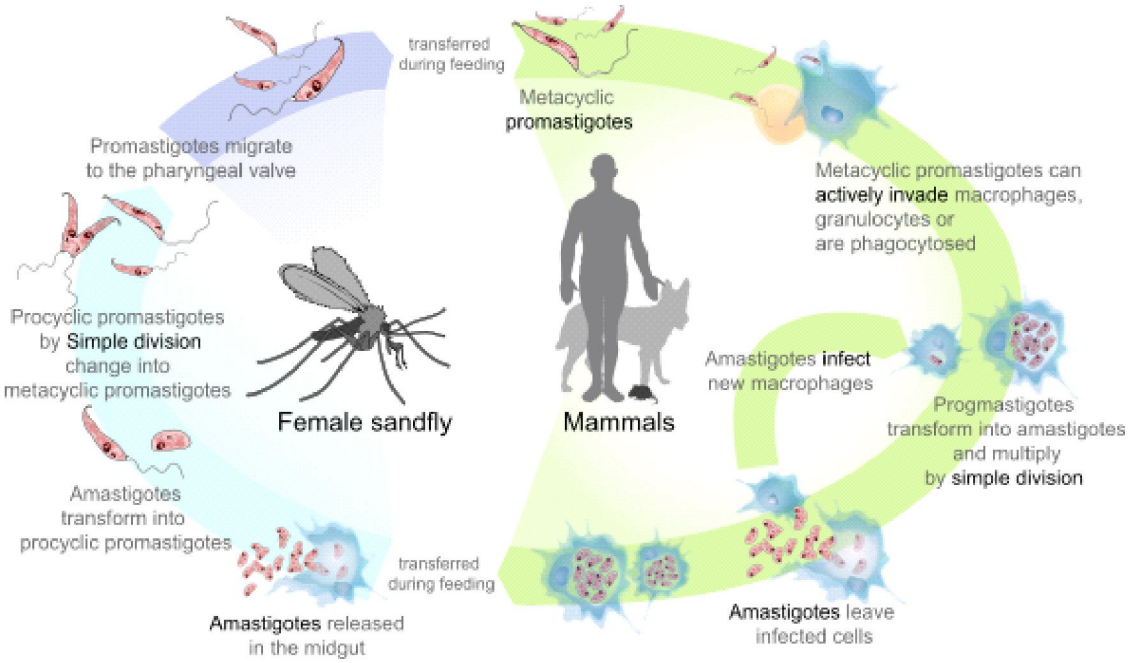


Figure 2: The life cycle of *Leishmania* parasites
Source: (Jump up ^. Tharakaram, 2014).

2.5.5. Transmission

The disease is transmitted to vertebrate host by the bite of female infected sand fly. Then sand fly inject the infective stage, promastigotes during blood meals and the promastigotes that reach wound are phagotized by macrophages and the promastigotes transform in to amastigotes. Then amastigotes multiply in the infected cells and affects different tissues (Sanjay, 2014). In a rare cases horizontal transmission have been reported between dogs in the same household or kennel. Canine leishmaniasis caused by *L. infantum*, the parasites can sometimes be found in saliva, urine, semen and conjunctival secretions, as well as in blood. So these parasites can also be transmitted via blood transfusions in people and dogs and by trans-placental transmission in dogs, mice and humans. Venereal transmission has been proven to occur in dogs, and other routes of spread might be possible (Desta *et al.,* 2005).

2.5.6. Risk factors

Socio-economic factors: Leishmaniasis, especially the visceral form, tends to affect the poorest people and marginalized societies particularly those people that are close to water resources, live in humid houses, and are in vicinity of accumulated rubbish, sewerage and farms of livestock may increase sand fly breeding and resting sites, as well as their access to humans. Lack of access to healthcare causes delays in appropriate diagnosis and treatment and increases leishmaniasis morbidity and mortality (Hasker *et al*., 2012)

Malnutrition: Diets lacking protein-energy, vitamins and minerals increase the risk that an infection will progress to clinically manifest visceral leishmaniasis and also reduces the immune system of the body defense mechanisms. In these case children are at greater risk than adults in endemic areas and also AIDS patients have a greater risk of developing visceral leishmaniasis in certain areas. Recent experiments in nutrients indicates that deficiency of these nutrient can leads to effect of functional failure of the lymph node barrier and increased early visceralization of the parasite (Malaria Consortium,2010).

Population mobility: Leishmaniasis is increasingly reported among travelers returning from tropical and subtropical regions and behavior, such as sleeping outside under acacia trees and living in houses constructed of grassy material, appears to increase risk for the disease (WHO, 2010). This is often associated with migration and the introduction of non-immune people into areas with existing endemic or enzootic transmission cycles and limited data exists on the incidence of leishmaniasis in the travelers in most developed countries, because the number of exposed travelers is often unknown. This often leads to wrong initial diagnosis. So Prediction of such outbreaks depends on the availability of ecological information and on evaluation of development areas (Desta *et a*l., 2005).

Environmental changes: The prevalence and development of leishmaniasis are largely dependent on environmental factors and natural conditions. In addition to the economic, social and cultural conditions, prevalence of leishmaniasis is influenced by ecological factors too. Vegetation area and climatic factors have important roles in proliferation and growth process of sand flies and subsequent outbreak of leishmaniasis. Global warming and land degradation together are expected to affect the epidemiology of leishmaniasis through different mechanism (Yazdanpanah and Rostamianpur, 2013).

2.6. Pathogenesis

When sand flies take blood meals from an infected host, they take up macrophages infected with amastigotes. The amastigotes transforms into promastigotes in the mid gut of the vector fly. They multiply and finally migrate to the fly's pharynx. The feeding sand fly then clears out its pharynx by expelling promastigotes into the skin of the host, from where they pass into the blood and tissues of the human host (Rogers *et al.,* 2004).

Promastigotes are phagocytosed into macrophages of the human's reticuloendothelial system, where they shed their flagella and become amastigotes again. Amastigotes multiply by binary fission. The infected cells then rupture, causing the infection to spread to other macrophages, and are then carried throughout the body (Killick-Kendrick, 1990). These cells process and present parasitic antigens on their surface and are able to primenaive T helper (Th) cells and direct their response to the infection (Fondevila, 1997). The clinical expression of leishmaniasis depends not only on tropism of the parasite but also on immune status of the patient. Species responsible for localized cutaneous leishmaniasis can cause visceral or diffuse cutaneous leishmaniasis in immune compromised patients (Abyot *et al*., 2005).

2.7. Clinical Sign of Leishmaniasis

In animals: The clinical symptoms and time of appearance of the disease vary extensively, from a total absence of symptoms to a severe clinical syndrome suggested that the period of incubation varies between 2 and 8 months (Gaeta *et al*., 1994). The primary lesion of canine leishmaniasis consists of granulomatous inflammatory reaction with parasitized and non-parasitized macrophages, lymphocyte and plasma cells. Inflamatory reactions may be present in any part of the body including joints and central nervous system. Deposition of immune complex may occurs resulting in, uveitis and glomerulonephritis (Rose, 2003). Lymphadenopathy, skin lesions and weakness are the most usual manifestation of the disease in the dog. Skin lesions include alopecia, scaling ulceration (ear and limbs) and nodules. In most sever forms renal failures and hemorrhages (mainly epitaxis) occurred (Aiello and Mays, 1998).

In human being: cutaneous leishmaniasis often involves only the skin, and may be characterized by one to dozens of lesions. Depending on the species of *Leishmania*, ulcers, smooth nodules, flat plaques or hyperkeratosis wart-like lesions may be seen and the initial lesions occur on skin which is exposed to sand flies, are usually papules (Couppie *et al*., 2004). The first sign of an infection is a small erythema. The erythema develops into a papule, then into a nodule, and the nodule ulcerates over a period of two weeks to six months, to become a lesion that is characteristic of the cutaneous leishmaniasis (Dedet, 2003).

Visceral Leishmaniasis: VL is a life threatening tropical infectious disease which mainly affects the

poorest of the poor and usually an insidious, chronic disease among the inhabitants of endemic areas. The most common symptoms of visceral leishmaniasis are a prolonged undulant fever, weight loss, decreased appetite, signs of anemia, and abdominal distension with splenomegaly and hepatomegaly. Thrombocytopenia may cause bleeding tendencies, including petechiae or hemorrhages on the mucous membranes, and leucopenia can result in increased susceptibility to other infections (Kolaczinski *et al.,* 2008**)**. Other symptoms may include coughing, chronic diarrhea, darkening of the skin, lymphadenopathy, and in many cases, signs of chronic kidney disease. Mild cases with only a few symptoms may resolve spontaneously (CFSPH, 2009).

Mucocutaneous leishmaniasis (MCL): It is usually occurs in Latin America, where it is caused by *L.braziliensis* and less often, by *L.panamensis/L.guyanensis* (Arfan *et al.,* 2006). It tends to occur1 to 5 years after cutaneous leishmaniasis. The initial signs are erythema and ulcerations at the nares, followed by destructive inflammation that can spread to involve the nasal septum, and in some cases, the pharynx or larynx. Frequent nosebleeds can be an early sign the inflammation may perforate the nasal septum, cause severe disfigurement of the face, or block the pharynx or larynx. In some cases, the genitalia may also be involved (Gupte, 2002).

2.8. Diagnosis of Leishmaniasis

Diagnosis of cutaneous and mucocutaneous leishmaniasi*s*: In the laboratory, diagnosis is made microscopically by direct identification of amastigotes in Giemsa-stained lesion smears of biopsies, scrapings or impression smears. Amastigotes are observed around or oval bodies, 2–4μm in diameter, with characteristic nuclei and kineto plasts. The material from the ulcer base usually has the highest yield; however, other authors have not found significant differences in the diagnostic outcomes when smears or culture samples are taken from the center or the border of the ulcer or from an incision made tangential from the ulcer. A combination of microscopy and culture increases diagnostic sensitivity to more than 85 % (Weina *et al.,* 2004).

Anti leishmanial antibodies can be detected by serological tests; however, these are not the usual methods, because antibodies tend to be undetectable or present in low titers due to poor hum oral response. Culture and DNA detection by PCR are sensitive but are not currently practical in developing countries (Romero *et al*., 2005). Diagnosis of visceral leishmaniasis: Laboratory diagnosis of VL includes microscopic observation and culture from adequate samples, antigen detection, serological tests and detection of parasite DNA (Santarem and Cordeiro da Silva, 2007).

2.8.1. Differential diagnosis

The differential diagnosis of visceral leishmaniasis includes other tropical and infectious diseases that cause fever or organomegaly (e.g. typhoid fever, brucellosis, histoplasmosis, malaria, tropical splenomegaly syndrome and schistosomiasis), as well as diseases such as leukemia and lymphoma. Post-kala-azar dermal leishmaniasis should be differentiated from syphilis and leprosy (WHO, 2010).

Cutaneous leishmaniasis is frequently confused with tropical, traumatic and venous stasis, ulcers, foreign body reactions, super infected insect bites, myiasis, impetigo, fungal infections (Herwaldt, 2005).

2.9. Treatment

In human: Patients should be referred to a specialist tropical disease unit for diagnosis and treatment of all forms of leishmaniasis, depending upon the form of the disease. There are several drug treatments available including oral, parenteral, and topical medications. Pentavalent antimonials such as sodium stibogluconate and meglumine antimonite, liposomal and amphotericin B (Herwaldt, 2005).

In animals, Treatment can produce clinical improvement, although it may not eliminate the parasite. Pentavalent antimonials drugs are used; such as allpurinol, amphotericin B, or second line drugs may also be employed, either alone or in combination. Allpurinol has been used as a maintenance drug to prevent relapses (CFSPH, 2009).

2.10. Control strategies and Prevention measures

Prevention thus remains the only proven method for controlling leishmaniasis. The preventive measures include self-prevention, vector control and medical intervention. Self-measures include wearing long clothing to cover the body and using insecticide-impregnated bed nets. Vector control includes reducing sand fly breeding sites, controlling animal reservoirs, and using insecticides. Medical intervention includes early detection and treatment, education on the disease and preventive measures, and clinical research and study for vaccinations (WHO, 2008).

Control of reservoir hosts: New tools have been developed for the surveillance and control of zoonotic VL, based on the control of the canine domestic reservoir. Culling of infected dogs is not considered an acceptable measure, both for ethical reasons and the low impact of measure in situations of permanent transmission (Assimina *et al*., 2008). But the elimination of stray and feral dogs is justified for many reasons connected with health, the environment and conservation. Before control activities begin, the distribution and frequency of the infection in dogs should be determined. Mass screening of domestic

dogs is usually done by serological examination (ELISA, IFAT). All symptomatic or seropositive dogs should be eliminated and also active case detection, surveillance and effective treatment, accompanied by measures for preventing re-infection, depending on the coverage achieved, should reduce or eliminate the parasite load and reduce transmission. The use of insecticide-treated bed nets and other materials by patients with kala-azar and chronic *L. tropical* skin lesions may also decrease the likelihood of that sand flies will feed on infected individuals (WHO, 2010). Control of hyraxes around villages may reduce the transmission of East African cutaneous leishmaniasis caused *L. aethiopica*. So elimination of hyraxes within 1 km of settlements is thought to be effective in reducing transmission (Getachew *et al.,* 2006).

Vector control: The primary purpose of a vector control program is to reduce or interrupt transmission of disease. An effective strategy for reducing human leishmaniasis is to control sand fly vectors, especially in domestic and per domestic transmission habitats. A number of control methods are available, including chemicals, environmental management and personal protection. Health education is a core element in implementation of any disease prevention and control programme. Multidisciplinary working groups should be established (WHO, 2010). Repellent tools of topical insecticides treatment of dogs exposed to sand fly bites in order to control the canine reservoir of *L. infantum*. It is now widely accepted that the prevention of sandfly bites on dogs is efficient in reducing not only the incidence of Canine leishmaniasis but also the risk of human infections (Maroli *et al.,* 2010).

There are three different types of topical preventive tools, namely, collars, spot-on and spray formulations, all based on synthetic pyrethroids at various concentrations: permethrin 50%-imidacloprid 10% (spot-on), permethrin 65% (spot-on), permethrin 1.9%-pyriproxyfen 0.02% (spray), and deltamethrin 4% (collar) (Mencke *et al*., 2003). The use of an anti-Leishmania dog vaccine could be the most practical and efficient tool for the control and, possibly, the eradication of the disease in endemic areas but it is not well developed and no effective vaccine until now produced and treatment of dogs with the use of pentavalent antimonial compounds (Gradoni, 2001).

It is mandatory to use fine-mesh screens on dog houses in residences and mainly in pet shops, veterinary clinics, animal shelters, and public veterinary hospitals, in order to prevent the access of phlebotomines and consequently reduce their contact with dogs. A number of works have demonstrated that, in experimental conditions, 4% Deltamethrin-impregnated dog collars were effective in protecting dogs against phlebotomine bites, with reduction of canine transmission in epidemic regions (Brasil,2005). The Brazilian Ministry of Agriculture authorized in 2003 the use of a canine vaccine indicated for visceral leishmniasis, named Leishmune® and produced by Fort Dodge Saúde Animal Ltda. Experimental studies indicated it showed 76.0% efficacy against moderate and severe clinical signs of the disease in dogs.

3. Public Health Significance Of Leishmaniasis

People can carry some species of *Leishmania* asymptomatically for long periods, without becoming ill. In humans, the reported incubation period for cutaneous leishmaniasis can be as short as 1-2 weeks or as long as several months when it is caused by New World species, and up to three years when Old World species are involved. The incubation period for visceral leishmaniasis is 10 days to several years; most cases seem to become apparent in two to six months (Saint, 1997). All types of leishmaniasis are growing health problems in the world, with endemic areas that are continually spreading. The form of the diseases and the usual clinical signs vary with the species of *Leishmania*. Some infections remain asymptomatic (Ferrer *et al.*, 1991).

The primary zoonotic for canine leishmaniasis is from dogs acting as reservoir host for the origanism. Direct contact with amastigotes in draining lesion is unlikely to result in human infection (Nelson and Guilermo, 2003). infected symptomatic dogs are consider to be the main reservoir of zoonotic visceral leishmaniasis. Currently entomological data reporting the presence of *Lutzomyia longipus* together with *L.infantum* infection in urban dogs indicated that the transmission of zoonotic visceral leishmaniasis could be established and that further cases of human visceral leishmaniasis are likely to appear. Ithas been shown in Brazil that human epidemic of VL usually preceded or concomitant to infection rates in canine population (Cruz et al., 2010).

People in endemic regions share the same habitat and frequently in close physical contact with infected dogs several studies indicated that the association between canine and human leishmaniasis in the region and examined to what degree of infection in dogs poses risk for human disease. These studies reported that: - increased prevalence in canine population is associated with increased incidence of human leishmaniasis and poorsocioeconomical conditions (Solano-Gallego, and Baneth,2008). In HIV infected person with or without AIDS, visceral leishmaniasis can be an opportunistic infection. This patient may show a short duration of symptoms, no fever or splenomegaly but a poor response to treatment (Tierney and Mephee, 1998).

4. Economic Impact Of Leishmaniasis

In addition to public health significance, Leishmaniasis imposes a negative impact on the economy of the people in particular and the country in general. These economic impacts are due to high cost of treatment, and time lost during hospitalization. The disease affects mainly the rural poor society and usually outbreak is during harvesting seasons (Bashaye *et al*., 2009). Higher rates of morbidity and mortality, especially related to infectious diseases, are well-recognized concomitants of poverty. Leishmaniasis has strong links with poverty and is generally ranked as one of the 'most neglected' diseases. The concept of neglected diseases originally developed to urge investment in development of new drugs to combat infectious diseases such as leishmaniasis. Leishmaniasis diagnosis and treatment are expensive and families must sell assets and take loans to pay for care, leading to further impoverishment and reinforcement of the vicious cycle of disease and poverty (Yamey and Torreele, 2002).

5. Conclusion And Recommendations

Leishmaniasis is a zoonotic disease caused by a protozoan parasite and it is transmitted from one host to another through the bite of female sand fly. The parasites have two basic life cycle stages. The primary reservoir hosts of *Leishmani*a are sylvatic mammals, and wild candies, and among domesticated animals, dogs are the most important species in the epidemiology of this disease. Currently, leishmaniasis has a wider geographical distribution pattern than before, and it is considered to be a growing public health concern for several countries, including Ethiopia. Risk factors such as environmental, demographic and human behavior contribute to the changing landscape of Leishmaniasis and the disease shows different clinical signs in animals and human beings. So taking this consideration, it is possible treat and prevents the disease through different methods such as, vector control, reservoir host control and creation of awareness about leishmaniasis for the people. Since the methods used until the present moment have been partially effective in preventing and controlling the disease, new control strategies should be developed to produce effective Immunogens to control canine and human leishmaniasis.

Therefore, based on the above review and conclusions the following recommendations are forwarded:

- Priority should be given to the establishment of control programs and governments should take the lion share to empower and support concerned institutions to address control programs.
- Studies should be conducted on the epidemiology of canine Leishmaniasi*s* and other possible reservoir hosts that are found in Ethiopia.
- Campaigns to control canine Leishmaniasi*s* should always be considered to reduce the risk of infection to human beings.
- Extensive research in epidemiology of Leishmaniasis should also be conducted in non-endemic areas too.
- Should be focused on prevention and control of visceral Leishmaniasis, which results highest fatality rate.
- The cost of treatment should be not expensive to treat leishmaniasis effectively.

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