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A Review on Canine Leishmaniasis; Etiology, Clinical Sign, Pathogenesis, Treatment and Control Methods

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Abstract: Canine Leishmaniasis is a vector borne zoonotic disease caused by protozoan parasite belonging to the genus Leishmania. It is basically a disease of animals that gets in to the human population when man, flies and the animal reservoirs coexist in the same environment. The disease is transmitted to human and animals by blood sucking sand fly of the genus Lutzomyia in the new world and Phlebotomus in the old world. The primary reservoir hosts of *Leishmania* species are sylvatic mammals such as forest rodents, hyraxes and wild canides. From domestic animals, dogs play an important role in the epidemiology of this disease. Leishmania species are flagellated and have two basic life cycle stages: the extracellular stage within the invertebrate host and the intracellular stage within vertebrate host. Clinically, imported dogs from endemic areas may develop the disease months or years later. The disease is endemic in parts of Africa, India, Middle East, Southern Europe and central and South America. Leishmaniasis can be diagnosed using various methods, such as: parasitological, immunological and molecular techniques. Different forms of treatments are available including oral parentral and topical medications such as pentavalent antimonials, liposomal amphoteracin B, miltefosine and paromomycin. However, control methods are largely limited to: destruction of animal reservoirs, treatment of infected human and animals and management of sand fly populations. Development of an effective vaccine against leishmaniasis has been largely unsuccessful and hinders its prevention.

Key words: Canine Leishmaniasis · Control · Diagnosis · Epidemiology · Sand Fly · Treatmen

INTRODUCTION

Leishmaniasis is a vector-borne zoonotic disease caused by obligate intra-macrophage protozoan parasite of the genus Leishmania. Kala-azar, dum-dum fever white leprosy and espundia are names corresponding to Leishmaniasis. It is transmitted by the bite of phleboptomine female sand flies of the genera *Phlebotomus* and *Lutzomyia*, in the old and new world, respectively [1]. The causative agent has great medical and veterinary public health significance. It infects numerous mammals including humans. *Leishmania* species are primarily parasites of animals and secondary to man. They infect lizard, carnivores, insectivores and man. The primary reservoir hosts of leishmaniasis are sylvatic mammals, such as forest rodents, hyraxes and wild canides. Among domesticated animals, dogs are the most important reservoir host and play a key role in the epidemiology of this disease [2].

Vectors that transmit leishmaniasis are widely distributed in many countries. About 350 million people are considered at risk of leishmaniasis and some 2 million new cases occur yearly in 88 countries [3]. Canine leishmaniasis exists in about 50 countries among the 88 world countries where human leishmaniasis is present, mainly affecting three major foci: china, the Mediterranean basin and Brazil [4]. The geographical distribution of leishmaniasis is dependent on its vectors. Currently, leishmaniasis has a wider geographical distribution than before due to the climate change which favors the breeding and survival of its vector sand fly. Further, several risk factors including massive migration, deforestation, urbanization, immune suppression and malnutrition and treatment failure attribute the incidence of leishmaniasis to increase worldwide [5].

Depending on the species *Leishmania* involved, the host's immunity and clinical manifestations, there are three major forms: cutaneous leishmaniasis,

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mucocutaneous leishmaniasis and visceral leishmaniasis. Visceral leishmaniasis is the most important and severe form of leishmaniasis and it is a frequent cause of clinical illness in dog. Dog is considered the most reservoir animal of it [6].

The common clinical signs of canine leishmaniasis are: skin lesion, weight loss, anorexia, lymphadenopathy, ocular lesions, nasal bleeding, locomotary problem and muscular athrophy. Chronic enteritis and renal failure are the most cause of death [7].

Diagnoses of canine leishmaniasis are difficult because the disease have variable clinical outcomes. However, the definitive diagnosis is obtained by direct observation of the parasite or using serological tests [6]. No drug has yet been developed that safely and quickly eliminate the disease. But various treatment options are available in different countries. Pentavalent antimonial agents with alloprunole are the best available therapy today [7]. Use of repellants, early detection and treatment of infected dogs are strategies for the prevention and control of canine leishmaniasis [8].

Discussion and creating awareness about canine leishmaniasis in Ethiopia is very important since the disease is endemic in some parts of the country especially in low lands of Northwest areas bordering eastern Sudan (Metema and Humera) and areas around Abay and Omo river [9]. It is also important to prevent importation of dogs from countries where the disease is endemic. Therefore, the objectives of this seminar paper are:-

- To review the epidemiology, public health significance and diagnostic methods of canine leishmaniasis
- To highlight the control and prevention strategies of the disease

Canine Leishmaniasis: Canine leishmaniasis is an important vector borne parasitic disease occurring in all continents, except Oceania [10]. In dogs, the infection may be asymptomatic or may evolve to life-threatening overt disease, with the wide range of clinical signs. Clinically, the signs of canine leishmaniasis range from localized skin alterations to severe loss of weight and generalized lymphadenomegaly. In this regard the prevention of canine leishmaniasis should include measures targeting animals (At individual and population) and the environment. However, the adoption and transportation of dogs from areas of canine leishmaniasis endemicity has resulted in the introduction and spread of disease to regions where infections were not previously found [12].

Table 1: Taxonomy of the Genus *Leishmania*

Kingdom	Protozoa
Phylum	Sarcomastigophora
Class	Zoomastigophora
Order	Kinetoplasitida
Family	Trypanosomatidae
Genus	Leishmania

Source: Robert [14]

The causative agent, *Leishmania* species, requires two different hosts; a vertebrate and an insect to complete its life cycle [13]. There is no age, breed or sex predilections difference for the occurrence of infection. In endemic areas, the disease is rarely seen in very young and very old dogs because of long incubation period and very low cure rate [7]. The protozoa multiply within the macrophages continuously until the macrophages are filled up and burst and then the librated parasite infects other macrophages. This disease is a chronic and slowly progressive in some naturally infected dogs [13].

Etiology: Leishmaniasis is caused by numerous protozoan parasites, belonging to the family Trypanosomatidae, genus Leishmania [13]. The parasite is flagellated and intracellular. Morphological, immunological, biological, geographical, clinical and behavioral characteristics are ranges of criteria used to separate Leishmania species. The following table below shows the modern classification of *Leishmania* parasite.

Approximately, 30 species of leishmania have been described and 20 of them are pathogenic for mammals [15]. 18 of the pathogenic leishmania do have zoonotic nature [8].

Morphology: The parasite exists in to two forms, the amastigote and the promastigotes. The amastigote are small, round to oval bodies which measures about 3-5 µm, in length, no flagella and found inside monocytes, leucocytes/macrophages and endothelial cells of infected vertebrate hosts [16]. They are colour less, have a homogenous cytoplasm and are surrounded by a pellicle. They have large nucleus and small kinetoplast as shown in Figure 1 below.

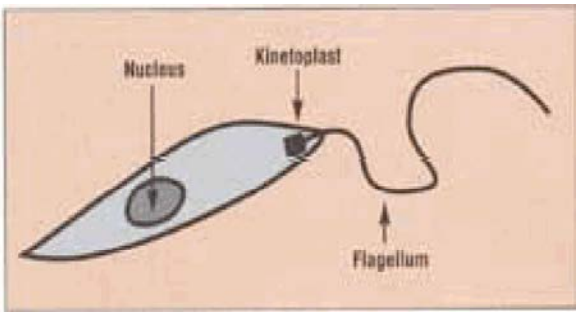

Fig. 1: Morphological description of the promastigotes of *Leishmania* species

The promastigotes are found in digestive system of sand flies. They are 2.5 µm in length and 1.5-3.5 µm in width [17].

Life Cycle: *Leishmania* species have two basic life cycle stages. These are the extracellular stage with in the invertebrate host and then intracellular stage with in vertebrate host. The parasite exists in to two main morphological forms, the amastigote and the promastigotes, which are found in vertebrate and invertebrate hosts, respectively [18]. The life cycle starts when a female sand fly takes a blood meal from vertebrate host and injects the promastigotes in to the host circulation. After inoculation into vertebrate host, the promastigotes are phagocytosed by the host's macrophages. Then the parasite evolves into amastigote form which they reproduce by binary fission continuously with in macrophages [10]. As many as so to 200 amastigote may be present in the cytoplasm of enlarged cell, so that the macrophage ruptured and releases a large number of amastigotes into the circulation. Then they invade monocytes and macrophages of spleen, liver, bone marrow, lymph node and other tissue of reticulo-endothelial cells [19]. Free amastigotes in the blood as well as intracellular amastigotes in the monocyte are ingested by female sand flies. After a period of 6 to 9 days, the promastigotes migrate from the midgut to the pharynx and bucal cavity of sand fly. Consequently, it can be transmitted to other new host where these fly feed on blood meal [17].

Host: *Leishmania* species infect man, lizard, rodents and carnivores. In some endemic areas of the Mediterranean the incidence of seropositive is about 5-15% of the canine population and from these; 20-40 % of seropositive population is asymptomatic carriers. This makes the disease to be unrecognized of the infection for other dogs and human beings. The disease primarily affects dogs and rural animals especially who spend the night outdoors [20].

Vectors: Leishmaniasis is a vector born disease. These vectors are different species of sand files grouped under the genus *Phlebotomus* and *Lutzomyia* in the Psychodidae family. Sand fly species under the genus *Phlebotomus* are a vector of leishmaniasis in old word whereas those under *Lutzomyia* are in the new world. Psychodidae are small, nematoceran flies with long antenna, pendulous pulps, hairy bodies and wings. Brownish, long legged narrow, lancets. Their wings are less than 3mm long and erect above their body [21]. Phlebotomine mostly found in rural areas between 100 and 800m above sea level and spend their life in limited areas not exceeded 1.5 km around their birth place [22]. The activities of sand fly vary seasonally, their number is increased during rainy season [23] and fly transmits the disease during feeding on the definitive host [24].

Epidemiology: Human and animal leishmaniases show a wider geographical distribution than previously known. Canine leishmaniasis is widely distributed around the world: it is found in five continents. The disease is endemic in the tropical and subtropical regions of 50 countries among the 88 world countries where human leishmaniasis is present [25]. The existence of canine leishmaniasis is determined by a number of epidemiological facts that allow very intimate contact between the infected sand flies and the vertebrate host, allowing the biological cycle of leishmaniasis to develop. Geographical distribution of the disease depends on sand fly species acting as vectors, their ecology and the conditions of internal development of the parasite [5]. It seems that its distribution is limited to the areas of natural distribution of sand flies, which are a small (2-3 mm), silent, nocturnal, blood-sucking insect belonging to the family Psychodidae [7]. *Phlebotomus* species are mostly found in rural areas between 100 and 800meter above sea level and spent their life in a limited areas not exceeding 1.5 km around their birth place. However, economic developments including wide spread urbanization, deforestation and development of new settlements are responsible for the spreading of sand flies as well as the reservoir system of leishmania [24].

The endemic areas and the total number of affected animals have been increasing in recent years [22]. This could reflect greater mobility of dog owners with their pets and/or a change in the climatic conditions that favor the sand flies survival in new areas [2]. The following table below shows the reservoir host, geographical distribution and the disease that occur in dog and human.

There is no age, breed or sex predilection for the infection although it is thought that toy breeds are less affected, as they often have an indoor lifestyle. Further, in the endemic areas, the disease is rarely seen in very young and very old dogs because of the long incubation period (Usually more than four months) and the very low cure rate respectively [7].

Status of Leishmaniasis in Ethiopia: Visceral leishmaniasis has been known to exist in Northwestern Ethiopia (Humera-Metema lowlands) since the early 1970s associated with large scale agricultural development activities after resulting in outbreak [26]. The latest outbreak of the disease that has started around 1995 in both regions has led to the present primary entomological surveys held from 1996-2005. Today Ethiopian low lands (Less than 1500 meter above sea level) including Abay and Omo river basins are endemic to the parasite infestation [9]. At least 19 species of genus *Phlebotomus* exists in Ethiopia. However, the main vectors of VL in Ethiopia are *P. martini* and *P. colida* in south and *P. orientalis* in south west part of Ethiopia [27].

Generally leishmaniasis is an important public health concern in Ethiopia. Its outbreak usually occurs during harvesting season mainly in rural poor community [28]. Having this challenge in the country from veterinary aspect, there has not been any report about canine leishmaniasis in Ethiopia except 1970th report [26]

Pathogenesis: The insect vector sucks blood from an infected vertebrate and ingests the amastigotes. The amastigotes multiply in the infested tissues and transform in to promastigotes. The flagellum enables them to migrate in to the insects sucking apparatus, with each blood meal parasites are deposited in to the skin of the new host. The parasites are internalizing by macrophages and other dendrite cells in the dermis and transform into amastigotes by losing their flagella. They multiply and survive in phagolysosomes through a complex parasite-host interaction [29]. The parasites disseminate through the lymphatic and vascular systems and infect other monocytes and macrophages in the reticulo-endothelial system, resulting in infiltration of the bone marrow, hepatosplenomegaly and sometimes enlarged lymph nodes (Lymphadenopathy). Ability of leishmania organisms to live in the endothelial reticulum of host cells is that they can neutralize the host cells PH and detoxify oxygen metabolites. In macrophages the parasites are multiplied by binary fusion continuously until they rupture the cell and spread to other macrophages. The cell mediated immune system of susceptible dogs is impaired and the lymphocytes proliferative capacity is decreased when stimulated with leishmania agents [7].

The basic lesion is foci of activated proliferating macrophages infected with leishmania organisms. In some cases they are ultimately surrounded by plasma cells and lymphocytes [20]. Reticulo-endothelial cells are increased in number and invade by parasites. The liver is enlarged with fatty infiltration of kuppfer cells. Macrophages monotypes and neutrophils of bone marrow are filled with the parasite. Lymph nodes are usually enlarged and interstitial mucosa is infiltrated with macrophages containing the parasite [19].

In dog, *Leishmania Donovan* may cause either visceral or cutaneous lesions. It may take many months or even years to develop clinical sign in dog, so that the disease may only become apparent long after dog have left endemic areas. The disease is usually chronic with low mortality although it can manifest as an acute rapidly fatal form. Recovery depends on the proper expression of cell mediated immunity. If these does not occur, the active lesion persists and leading to chronic enlargement of spleen, liver, lymph node and cutaneous lesions [19].

Clinical Sign: Several organs may be affected, as parasites have been found in every part of the body, except probably, the central nervous system. With this reason leishmaniasis may have several variable clinical features. The main presenting signs are weakness, decreased physical activity, skin disease and weight loss [7]. The dogs usually appear much older than they are because of the prominent muscular atrophy, particularly on the head. Anorexia, if present, is probably related to renal failure. Weakness and decreased activity may be the consequences of anemia, muscle atrophy, polyarthropathy, or chronic renal failure. Locomotary problems are not very frequent and include shifting leg lameness, due to immune-mediated polyarthritis, polymiositis and bone lesions, in which parasites are found in granulomatous inflammatory groups [24].

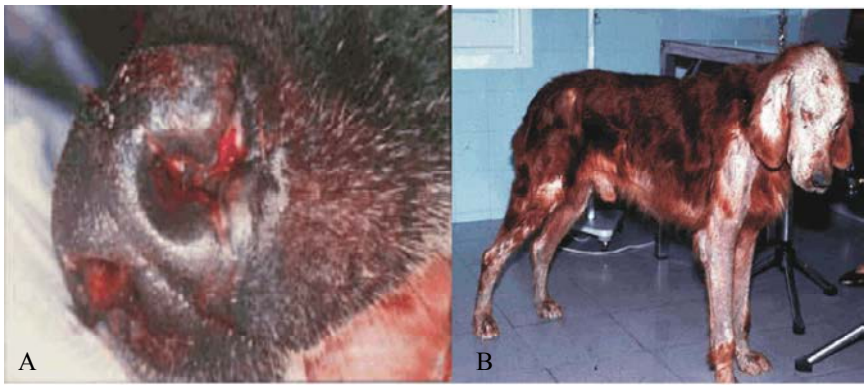

Fig. 2: Different clinical features of *Leishmania* infection in dogs Fig A. severs lesions on muzzle, Fig B. alopecia around different body parts.

On physical examination, pyrexia, weight loss, geneneralized lymphadenomegaly, pale mucosa membrane, alopecia, exudative dermatitis, hyperkeratosis of foot pad,excessive growth of claws and nodular dermatitis due to vasculitis and granulomatous inflammation and shifting lameness are common [30]. Visceral leishmaniasis starts as a cutaneous lesion and the infection spreads systematically. The disease mainly infects spleen, liver and bone marrow. The main dermatologic sign of visceral leishmaniasis consists of emaciation, keratitis, scaling of skin seborrhea and alopecia, which is often systematical in distribution. Dogs usually appear much older than they are because of the prominent muscular atrophy, particularly on the head [7].

Public Health Significance of Leishmaniasis: Infected dogs are considered to be the main reservoir of zoonotic visceral leishmaniasis (ZVL). Current entomological data reporting the presence of *Lutzomyia longspurs* together with *Leishmania infantum* infection in urban dogs indicates that the transmission cycle of zoonotic visceral leishmaniasis could be established and that further cases of human visceral leishmaniasis are likely to be appeared. People in the endemic region those share the same habitat and are frequently in close physical contact with infected dogs have high probability of exposing to leishmaniasis. Several studies have investigated the association between canine and human leishmaniasis in the same region and examined to what degree infection in dog poses a risk for human disease. These studies report that:- Increasing of the prevalence of leishmaniasis in canine population is associated with increasing of the incidence of human leishmaniasis; Poor soscio-economical conditions are risk factors for the association between canine and human infection and Dog density and infected dog ownership are factors for leishmaniasis to occur [32].

DIAGNOSIS: The diagnosis of leishmaniasis is difficult for three main reasons [7, 33]. The clinical sign are very variable and may look similar to other diseases; The histopathological appearance is extremely nonspecific and the microscopic lesions are also observed in other immune-mediated disease and infections; and no available diagnostic test can offer a specificity and a sensitivity of 100%.The clinical appearance of the affected dog may suggest the diagnosis but confirmation of the diagnosis is necessary. To confirm whether there is leishmania infection or not, currently there are three main diagnostic techniques:

- Parasitological techniques, whose aim is to visualize the microorganisms
- Serologic or immunological tests, which identify circulating anti-leishmanial antibodies.
- Molecular methods (Polymerase chain reaction), where parasite DNA is amplified and detected in host tissues.

Parasitological Diagnosis*:* The detection by optical microscopy of the parasite using cytological or histopathological observations of amastigotes in Giemsa stained smears from spleen aspirate, lymph node and bone marrow tissues has high specificity, allowing confirmation of CL diagnosis. This is the simplest and most commonly performed procedure [34]. However, the sensitivity of this method is less than 30%, since the direct parasite identification may be limited, especially in mildly and asymptomatic dogs that have low parasitic

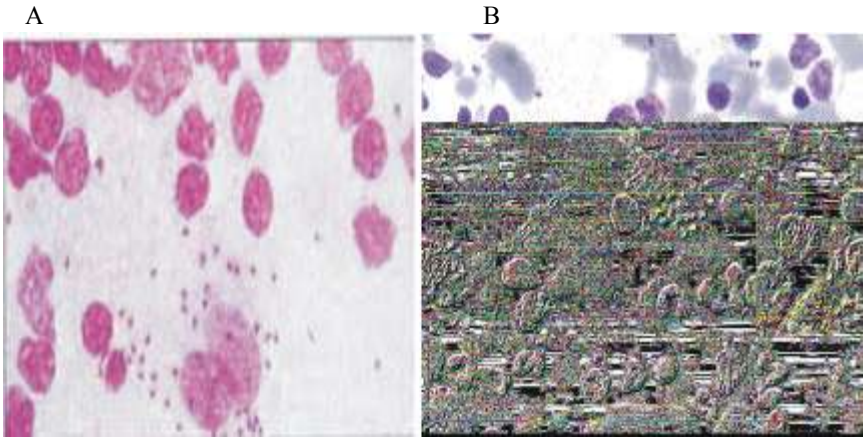

Fig. 3: Giemsa stained amastigotes from bone marrow aspirates (FIG A) and lymph node aspirates (FIG B) (Source: 7)

load, producing false negative results Immuno-peroxidase staining improves the detection of amastigotes in the infected tissue. This method is highly specific and cheap but it has a low sensitivity [35].

Another method that can identify the parasite in tissues is the culturing of tissue fragments or aspirates, preferably in a biphasic medium [34] composed by Novy-MacNeal-Nicolle (NNN).

This parasitological diagnostic method offers high specificity allowing isolation and characterization of parasites, as well as determination of which species and/or variants are circulating in endemic areas [36]. However, the culturing consists of an indirect test, because when the parasites are isolated from various tissues, they are present in amastigote form and during cultivation they transform into the promastigote form. This process may be impaired as a result of parasite death due to a failure of temperature-control during transport of the tissue sample, or contamination during collection or cultivation [4].

Immunologic Diagnostic Methods: They are based on the presence of specific humoral immune response against the pathogen or purified fraction or recombinant proteins of the pathogen. These techniques allow the detection of antibodies (Mainly immunoglobulin G/IgG/ and especially IgG1) levels against the pathogen or specific cell mediated response. Thus tests becoming an essential tool for the diagnosis of canine visceral leishmaniasis. These tests are simple to carryout and therefore they are frequently used to determine the prevalence of leishmaniasis in epidemiological status [34]. To detect immunological responses, there are four main serological techniques such as: IFAt, ELISA, DAT, rK39 rapid diagnostic test and western bloat.

Despite the practicality and simplicity of serological tests, they do not have 100% sensitivity because some dogs, especially those that are resistant or in the early stages of the disease, have negative results. Thus, the results of such tests should be evaluated carefully, always associating test results with epidemiological history, clinical state of the animal and the result of a more specific diagnostic test [37]. In addition, since titers of anti-Leishmania antibodies remain detectable for long periods, serological tests are not a good alternative for assessing healing or monitoring dogs after treatment [38].

From immunological tests, IFAt is considered as the gold standard test because it has a high specificity and sensitivity. However, it is laborious technique that presents difficulties for both standardization and interpretation of the results. ELISA is useful for laboratory analysis or field applications and to screen a large number of samples at a rapid pace. However, it is less precise than IFAt and cross react with *Trypanosome cruzi* and Babesia species [34].

***Molecular* Methods (Amplification and Detection of Leishmania DNA):** This method of diagnoses relies on polymerase chain reaction (PCR). PCR technique has been developed recently and is a highly sensitive and specific, diagnostic test for leishmaniasis [7]. Parasitic kinetoplast DNA in liver, spleen, skin, lymph node and bone marrow biopsies or heparinized whole blood is selectively identified and amplified [34] and both fresh and formalin-fixed paraffin embedded tissue can be used for this technique. This test can identify the presence of parasites, even in animals which have been clinically cured for years [20]. Unfortunately, PCR for *Leishmania* spp. is currently only available in specialized laboratories.

Table 2: Drugs used for treating canine leishmaniasis

1	Meglumine antimonite	Pentavalent antimonial	50mg/kg	SC	3-4 week
2	Allopurinol	Primedine derivative	10-30 mg /kg	oral	9-12 month
3	Amphoteracin B	Polyene macrolide	0.5-0.8mg/kg	IV/SC	2-3 weeks
4	Sodium stibogluconate	Pentavalent antimonial	5-10 mg/kg	SC	10-30 days
5	Aminosidine	Polyene macrolide	5-10mg/kg		2-3 weeks

Source: Noli [7]

Differential Diagnosis: The differential diagnosis of leishmaniasis is legion, since its clinical appearance is extremely variable [7]. In endemic areas canine leishmaniasis can be confused with many other diseases and the differential diagnosis is complicated with high rate of concomitant infection such as demodicosis, dermatophylosis, keratinization disorders, sebaceous adenitis, pyoderma, sarcoptic mange, filariasis, lupus erythematosus, haemparasitosis like ehrilichiosis, deep mycoses, cutaneous neoplasia, skin tumors and polyarthritis [39].

Treatment: Although treatment of canine leishmaniasis achieves clinical cure, it rarely results in complete elimination of the parasites and recurrences are frequent. No drug has yet been developed that safely and quickly eliminates the infection [8]. Current research aims at new therapeutic protocols with drugs already in use and the development of new drugs. Current treatment protocols are summarized in the table 2.

Before starting treatment, a complete blood count, biochemical profile and urine analysis should be performed in order to assess the renal and hepatic status. Several drugs are used for treating canine leishmaniasis. These include pentavalent antimonials of which meglumine antimonate is the main drug used either alone or in combination with other drugs. Amphoteracin B, pentamidine, aminoside and ketoconazole are other alternative drugs [19]. One study showed that the combination of antimony and allopurinol was superior to treatment with either drugs alone [40].

Controle and Prevention: Canine leishmaniasis is among the most neglected vector-borne parasitic diseases of dogs, occurring on all continents, except Oceania [12]. the infection may be asymptomatic (Over 80% of cases in some areas) or may evolve to life-threatening overt disease, with a wide range of clinical signs (From localized skin alterations to severe loss of weight and generalized lymphadenomegaly). For its potential severity in dogs and its zoonotic nature, the prevention of this infection is not only desirable but also a must for both dog and human health (Figure 1). Because the infection to a receptive host occurs through the bite of sand flies of the genus *Phlebotomus* (In the Old World) and genus *Lutzomyia* (In the Americas) [11] the management of this disease is extremely complex [10].

In this regard, the prevention of CanL should include measures targeting animals (At individual and population level) and the environment. However, the adoption and transportation of dogs from areas of CanL endemicity has resulted in the introduction and spread of disease to regions where infections were not previously found [11] which may create new epidemiological scenarios, further complicating the zoonotic potential. This often occurs in combination with emerging immunosuppressive conditions in humans (e.g., HIV/AIDS) that may increase the risk of zoonotic diseases such as visceral leishmaniasis (VL) [38]. Although the risk of canine leishmaniasis (CanL) transmission is reputed to be low in the absence of sand flies, other ways of transmission, such as venereal and transplacental transmission, should be seriously considered [7].

The control of CanL is a difficult task because of the complex transmission cycle of Leishmania species. A proper assessment of the infection status of dogs is fundamental for a better determination of actions to be taken, to start the treatment in the initial stages of the disease and to monitor the effectiveness of control measures. Based on current knowledge and considering the tools available, the current control and prevention strategies for canine leishmaniasis rely on reservoir and vector control, the use of insecticide-impregnated materials and active case detection and treatment [40] anti-leishmanial vaccines are still being developed. In endemic areas dogs should not spend the night outdoors and fine mesh nets should be applied to the windows. Recent studies demonstrated that the application of a repellant deltamethrin collar to dog can protect them from sand flies' bites and prevent *Leishmania* infection [7].

The environmental control of immature sand flies is unfeasible because the microhabitats of larvae and pupae are extremely variable, including, for example, tree roots, animal burrows, decaying foliage and tree holes [11]. Similarly, evidence indicates that spatial fogging for adults and fly control is useless and that the residual effect of house wall spraying is very short making the residual spraying of houses impractical and ineffective, particularly in rural areas [11].

The elimination of all clinically affected dogs has not improved the human infection rate where it has been imposed [4]. However, treatment of all seropositive (Symptomatic and asymptomatic dogs) has significantly decreased the prevalence of new infection cases in endemic areas [18].

CONCULUSION

Canine leishmaniasis is caused by a protozoan parasite. The parasites are transmitted from one host to another through the bite of female sand fly during blood meal time. The primary reservoir hosts of leishmania are sylvatic mammals such as forest rodents, hyraxes and wild canides. Among domesticated animals, dogs are the most important reservoir host. Currently, leishmaniasis has a wide geographic distribution pattern than before and it is considered to be a growing public health concern for several countries including Ethiopia. Both visceral and cutaneous leishmaniasis are endemic in Ethiopia. Based on the above conclusion the following recommendations are forwarded.

- Since sand flies play pan important role in transmission of leishmaniasis in dogs and humans, destroying of the breeding and resting sites of the vector is very important.
- Applying of insecticides to pre-domestic animals and improved construction of house which is not suitable for breeding and entrance of sand flies are good for fly controlling.
- It is important to educate the public and settlement to avoid them around the forest area.
- Suitable, cost effective and simple control strategies of reservoir hosts should be designed and implemented.
- Avoid importation of infected dogs from endemic areas.
- Keeping dogs indoor in the evening and applying of deltamethrin impregnated collar on all dogs is also essential to reduce the prevalence of infection.

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REFERENCES

1. Assimina, Z., K. Charilaos and B. Fotoula, 2008. Leishmaniasis: an overlooked public health concern, Health science journal, 1: 196-205.
2. Hide, M., B. Bruceton, S. Kamhawi, R. Brass-Goncalves and S. Sunadr, 2007. Understanding Human Leishmaniasis: The need for an integrated approach in encyclopedia of infectious disease book of microbiology. John Wiley and Sons Inc, pp: 87-107.
3. WHO, 2010. control of the leishaniases. Report of a meeting of the WHO committee on the control of leishmaniases, 22-26 March 2010, Geneva pp: 5-88.
4. Alvar, J., C. Canavate, R. Molina, J. Moreno and J. Nieto, 2004. Canine leishmaniasis. Adv. Parasitol., 57: 1-88.
5. Desjeux, P., 2001. the increase in risk factors for leishmaniasis worldwide: Trans R Soc Trop Med Hyg, 95: 239-243.
6. Rose, K., J. Curtis, T. Baldwin, A. Mathis, B. Kumar, A. Sakthianandeswaren, T. Spurck, J. Low Choy and E. Handman., 2004. Cutaneous leishmaniasis in red Kangaroos: isolation and characterization of the causative organisms. Int J. parasitol, 34: 655-664.
7. Noli, C., 1999. canine Leishmaniais walth foucs, 9/2/ 16-24.
8. Otranto, D., F. Paradies, R.F. Lia, M.S. Latrofa, G. Testini, C. Cantacessi, N. Menchke, G. Galli, G. Cappeli and D. Stanneck,, 2007. Efficacy of a combination of 10% imidachlorid and 50% permethrin for the prevention of leishmaniasis in kenneled dogs in an endemic area. Vet. Parasitol, 144: 270-278.

9. Fuller, G.K., A. Lemma, T. Haile and Gemdan, 1979. Kala azar in Ethiopia,survey of south west Ethiopia, the lesishamnd in the skin test and epidemiological studies Analsis of Tropical Medicine and parasitology, 70: 417- 431.
10. Dantas- Torres, F., L. Salano-Gallego, G. Baneth, V.M. Ribeiro, M. de Paiva-Cavalcanti and D. Otranto, 2012. Canine leishmaniasis in the old and new world: Unveiled similarities and differences. Trends. Parasitol, 28: 531-538.
11. Maroli, M., M.D. Felicianqeli, L. Bichaud, R.N. Charrel and L. Gradoni, 2013. phlebotomies sand flies: and the spreading of leishmaniases and other diseases of public health concern. Med. Vet. Entomol, 27: 123-147.
12. Otranto, D., P. Paradies, D. de Caprariis, D. Stanneck, G. Testinni, F. Grimm, P. Deplazes and G. Capelli, 2009. Toward diagnosing Leishmania infantum infection in asymptomatic dogs in an area where leishmaniasis is endemic. Clin. Vaccine Immunol, 16: 337-343.
13. Mullen and L. Durden, 2002. Madical & vet Entomology Elsesevier Inc.China, pp: 158-160.
14. Robert, M.T., 2006. Current understandings on the immunology leishmaniasis and recent developments in prevention and treatment. Br Med Bull, 75: 115-130.
15. Gramiccia, M. and L. Gradoni, 2005. the current status of zoonetic leishmaniasis and approaches to disease control. Innt J. parasitol, 35: 1169-1180.
16. Pal, M., 2005. Importance of zoonoses in public heath, J Ani Sci, 75: 586-591.
17. Parija, S., 2004. Textbook of Medicinal parasitology ended Indica PN 94-100.
18. Koutis, C.H., 2007. Special Epidemiology.Editions, technological Educational Institute of Athens: Athens, Greece.
19. Taylor, M.A., R.L. Coop and R.L. Wall, 2007. veterinary parasitology 3rd edd. Oxford Black well publishing, pp: 407- 408.
20. Urquhart, G.M., J. Armour, J.L. Duncan, A.M. Dunn and F. Jennings, 1996. veterinary pakasizology, 2nd ed. London: black well, pp: 218-219.
21. Kettle, D.S., 1995. Medical and veterinary Entomology Cambridge, University press, Uk, pp: 177-188.
22. Maroli, M., V. Mizzon, C. Siraqusa, A. D'Oorazi and L. Gradoni, 2001. Evidence for an impact on the incidence of canine leishmaniasis by the use of deltamethrin- impregnated dog collars in southern Itlay.Med.Vet. Entomol, 15: 358-363.
23. Soulsby, E.J., 1974. parasitic Zoonoses, finical& experimental studies subsidiary of Horcourt brdce, New York: Jovanovich publishers, pp: 65-70.
24. Stephen, B., 2006. Sounders of small animals practice application and language, USA, oo 228-229.
25. Da Silva, E.S., W.F. Vander Meide, G.J. Schoone, C.M. Gontijo, H.D. Schallig and R.P. Brazil, 2006. Diagnosis of canine leishmaniasis in the endemic area of Belo Horizonte, Minas Gerais, Brazil by parasite, antibody and DNA detection assays. Vet. Res. Commun., 30(6): 637-43.
26. Elsevier, B. and M. Abuhay, 1978. Kala-azar among labors migrant Tropical and Geographic Medicine, 1: 199-206.
27. WHO., 1991. Report information on the epidemiology of leishmaniasis by country or territory Geneva, world heath org. Wlto /Leosj/ 91-30.
28. Bashaye, S., N. Nombela, A. Kassa, D. Argaw, A. Mulugeta, M. Herrero, *et al*., 2009. Risk factors for visceral leishmaniasis in new epidemic site in Amhara region, Ethiopia, Am J Trop Med Hyg, 81: 34-39.
29. Rittia, M.G. and C. Bogdan, 2000. Leishmania–host-cell interaction: complexities and alternative views. Parasitol. Today, 16: 292-297.
30. Ramsey, K. and B. Tennany, 2001. Mannval of canine and feilen infections Dx. UK., pp: 85-88.
31. Cruz, I., J. Nieto, C. Canavate, P. Desjeux and J. Alvar, 2006. Leishmania-HIV co- infections in the second decade. India J Med Res, 123: 357-388.
32. Solano-Gallego, L. and G. Baneth, 2008. canine leishmaniasis a challenging zoonesis, the Europian journal of companion animal practice/EJCAP/, 18/13/ 231-241.
33. Tierney, M.L. and J.P. Mephee, 1998. Current medical diagnoses and treatment of leishmaniasis, 37th ed. Appleton and language, USA., pp: 1339-1345.
34. Veras, T., D.B.M. Fraga, M.S. Solcá and C.E.S. Guedes, 2014. new advances in the diagnosis of canine visceral leishmaniasis. March, 11: 2014.
35. Gomes, Y.M., C. Paiva, M. Avalcanti, R.A. Lira, F.G. Abath and L.C. Alves, 2008. Diagnosis of canine visceral leishmaniasis: biotechnological advances. Vet. J., 175(1): 45-52.
36. De Almeida, M.E., F.J. Steurer, O. Koru, B.L. Herwaldt, N.J. Pieniazek and A.J. Da Silva, 2011. Identification of Leishmania spp. by molecular amplification and DNA sequencing analysis of a fragment of rRNA internal transcribed spacer 2. J. Clin. Microbiol., 49(9): 3143-9.

37. Ferret, L., M.J. Aisa, X. Roura and M. Portus, 1995. Serological diagnosis and treatment of canine leishmaniasis. Vet. Rec., 136(20): 514-6.
38. Rose, M., 2003. Canine leishmaniasis an update in dx & Rx. In 28th world congress of small animal association, USA, pp: 65-70.
39. Nelson, W. and C. Guilermo, 2003. small animal Internal Medicine 3rd china, pp: 1303.
40. Chappuis, F., S. Sundar, A. Hailu, H. Ghalib, S. Rijal, R. Peeling, J. Alvar and M. Boelaert, 2007. Visceral leishmaniasis: what are the needs for diagnosis, treatment and control? Nature Rev. Microbiol, 5: 873-882.