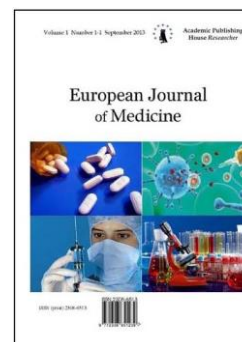


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Articles

Study of Leishmaniasis Disease: A Systematic Review

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Abstract

Sand flies are characterized by their inability to fly continuously and spread over a wide range, as they rarely spread more than one kilometer away from their breeding areas. It was found that wind does not affect the intensity of its spread, but on the contrary, these insects are ineffective when the wind speed is more than one kilometer per second and resort to their homes when the wind blows.

Leishmaniasis has been known for a long time and is still one of the ten most important infectious diseases in the world, in addition to being a public health problem in many countries of Africa, South America, Central and South West Asia and Indian subcontinent. It is also one of diseases endemic in Iraq and parasite has caused a healthy problem to be underestimated in Southern Iraq, especially in Dhi Qar Governorate.

Leishmaniasis is a main careless tropical disease related with high attribution of disability and death. This illness is linked with destitution, which can be reflected in housing housing quality, especially in rural territory. This sickness is transported amidst mammalian hosts through bites of blood sucking vector sand fly. So, Lack of realization among local societies also decrease the efficiency of reservoir host and vector control schemes. Until now parasites transition to mammalian host has never been immediately determined, so this disease has a great impact to public good health of Individuals. The form of protozoan parasite is closely related to pathogenicity. Therefore, many instant actions must done in order to excess scientific information on this disease and higher achievement, of the patients and observation programmers need be carried out by raise realization around the sickness between common public and stringent sharing of local society in surveillance and safeguard actions.

Keywords: *Leishmania*, Epidemiology, diseases, review.

1. Introduction

Leishmaniasis is occasion by a protozoa parasite (that is transmitted by the bite of infected female sand flies) of more than 20 species, the number of sand flies known to transmit *Leishmania* parasites exceeds 90 (Giraud et al., 2019). The disease effects on the poorest people in the world, and is linked to malnutrition, population displacement, poor housing, a weak immune system, and a lack of financial resources (Kimblin et al., 2008). Leishmaniasis is associated with environmental changes such as dams building, deforestation, establishing irrigation systems and urbanization (Kholoud et al., 2018). The number of cases of this disease is estimated between 700,000 and one

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million annually, the disease appears only in a small percentage of infected with parasite will ultimately develop Leishmaniasis (Abdullah et al., 2017). *Leishmania* disease is classified as a parasitic disease of animal origin, man is infected by bite of a female type of mosquito called sand bug, this small-sized insect is silent when flying and lives in the hot humid climate and its activity increases in the summer and feeds on human or animal blood and absorbs this Blood from an infected person or animals (such as dogs and foxes, where these animals are a reservoir for the disease parasite) and this blood is loaded with the disease parasite that multiplies in the stomach of the insect and then reaches its saliva and when it bites a healthy person or animal, it injects these parasites into his body, causing him disease (Giraud et al., 2019). There are three main forms of disease include visceral leishmaniasis (also known as kalaazar, the most serious form of the disease), cutaneous (most common) and mucocutaneous disease (Hendrickx et al., 2020).

2. Results and discussion

Fundamental species of leishmania

It appears in three forms: eastern sorts, diffuse cutaneous and mucocutaneous form. The lesions may take from 2-5 years to heal.

1) Visceral leishmaniasis, also known as kala azar, is fatal in 95 % of cases if left untreated, it is characterized by irregular bouts of fever, weight loss, an enlarged spleen and liver and anemia. This type is often found in people with double infection between leishmaniasis vascular and AIDS .Most of its cases are concentrated in Brazil, East Africa and India. Number of new cases around the world is estimated at between 50,000 and 90,000 annually, of which only 25-45 percent are reported to the World Health Organization. In 2018, more than 95 % of the new cases were concentrated in 10 countries: Brazil, China, Ethiopia, India, Iraq, Kenya, Nepal, Somalia, South Sudan and Sudan (Kholoud et al., 2018).

2) Cutaneous leishmaniasis, which is the most widespread form of leishmaniasis, causes skin lesions, actually ulcers on visible parts of the body, leaving permanent scars, serious disability or eschar. About 95 % of cutaneous leishmaniasis cases occur in the Americas, Middle East and Central Asia. In 2018, more than 85 percent of new cases were concentrated in 10 countries: Afghanistan, Algeria, Bolivia, Brazil, Colombia, Islamic Republic of Iran, Iraq, Pakistan, Syrian Arab Republic and Tunisia. The number of new cases per year is estimated at between 600,000 to one million globally (Hendrickx et al., 2020).

3) Mucocutaneous leishmaniasis, which causes partial or complete damage to mucous membranes of nose, mouth and throat. More than 90 % of mucocutaneous leishmaniasis cases are concentrated in the Plurinational State of Bolivia, Brazil and Ethiopia (Kholoud et al., 2018).

Major risk factors

1) Socio-economic conditions

Poverty increases the risk of leishmaniasis, it may worsen housing conditions and health conditions in homes (such as insufficient waste management or open sanitation) from sand fly breeding and resting sites, as well as the possibility of reaching people. Sand flies are attracted to overcrowded dwellings because they provide a good source of blood that they feed on. Also, human behavior, such as sleeping outside or on the ground, may increase the odds of developing this disease (Okwor, Uzoona, 2016).

2) Malnutrition

Diets that lack protein, energy, iron, vitamin A and zinc increase risk of infection developing into advanced disease (Wijerathna et al., 2017).

3) Population mobility

Epidemics of cutaneous leishmaniasis and epidemics of visceral leishmaniasis are often associated with migration and the movement of unimmunized people to areas with disease transmission cycles. Occupational exposure as well as large-scale deforestation remain important factors (Calderon et al., 2018).

4) Environmental changes

Incidence of leishmaniasis may be affected by changes in civilization and human live into forested areas (Wijerathna et al., 2017).

5) Climate change

Leishmaniasis is a climate-sensitive disease that affects its epidemiological characteristics in many ways, including the following (Ghazanfar, Malik, 2016):

- * Changes in temperature, rainfall and humidity may severely affect the host vectors and reservoirs by changing their distribution and affecting their survival and numbers.

- * Simple fluctuations in temperature may significantly influence the development cycle of the leishmaniasis in sand flies, allowing the parasites to move to areas that were not endemic to the disease.

- * Droughts, famines and floods may lead to mass displacement and migration of people to areas where leishmaniasis is transmitted, and malnutrition may Weaken their immunity.

Shape and life cycle

There are two phases of the parasite, 1)(Amastigote) which is oval in shape and its diameter is (3-5) micrometers and contains one nucleus and has a kinetic structure (Kinzooplast) (Sunter, Gull, 2017). As well as the presence of flagella that is present in macrophages and cells of the internal retinal system, which includes liver, spleen and lymph nodes, which enriched the bones 2)(Promastigote), second form, this species is found in the vector insect and is fusiform-shaped and has a length of about (20-30) μm , it has one flagellum at the front of the body, during its life the parasite needs two hosts, one of which is vertebrate and the other is invertebrate (sand fly) and the parasite transforms in the insect's intestine from (Amastigote) to (Promastigote). In fact, it multiplies by longitudinal fission and then migrates after several days (Sunter, Gull, 2017).

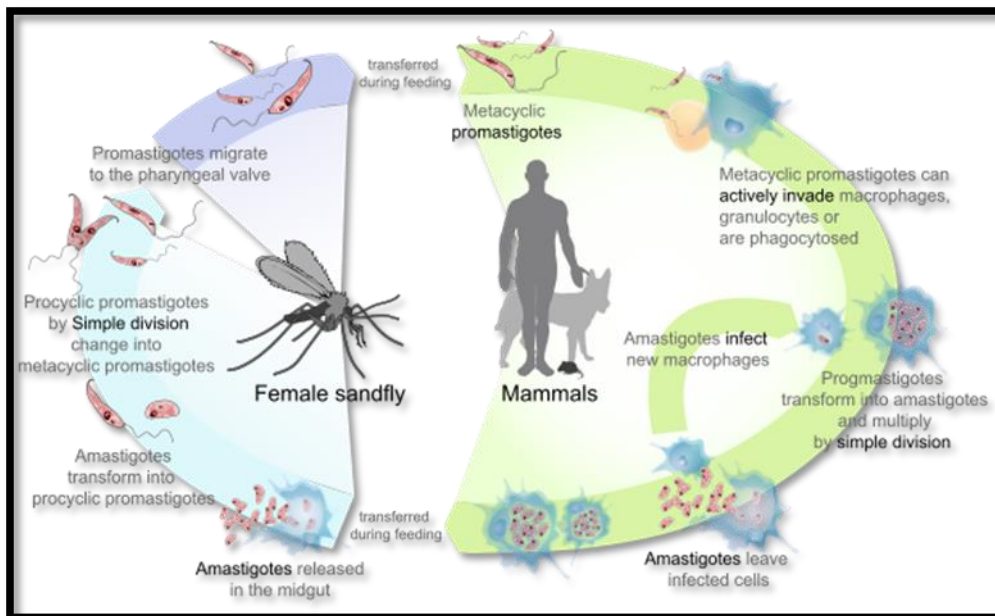


Fig. 1. Life cycle of *leishmania* (Harkins et al., 2016)

Host carrier (Sand fly)

Sand fly is considered the host for the leishmaniasis parasite and this insect is seasonal in its appearance in temperate regions of the world, adults appear only in the summer, that is, the breeding season is confined to the summer season in the tropics, and some species seem almost constant throughout the year, but in other species there may be significant changes to an extent that is considered for the group of adults, especially in the dry and wet climates (Harkins et al., 2016).

In fact, there is no evidence of eggs hatching in nature, and from some studies the eggs hatch within 3-4 days of laying in the summer and the period may increase to (7) days in the winter season so that they lay the female is from (30-40) eggs throughout her life, and the larva is found in the same places where the eggs were laid, and it feeds on the same materials. The duration of the larva is two weeks in the summer, and the period may increase or decrease in the winter season,

in this time, the larva goes through three alienations and has four stages, the number of insects in Iraq increases in two seasons (Blume, Eloi, 2019).

Spring season, the numbers start to increase from the end of the month of March and increase more in the month of April and May, as well as in the first half of June, then their number begins to decrease, and their quantities remain low in the rest of June, July and the first half of the month of August, and then the number begins to increase, reaching a large extent and very high in late September and early October, subsequently the number begins to decrease until the insects fertilize or multiply in late November and for a period of months: December, January and February, and do not start in public places, homes and cities during the winter, and this is not a strange thing (Casanova et al., 2019). Rather, they come to houses to provide warm conditions. Females leave the residence before sunset and then return and enter them at about eleven o'clock in the evening (Kumar et al., 2015). Sand insect is spread in tropical regions, but it does not exist in submerged and cold areas, and its presence is limited between 4 degrees south and 40 degrees north, and in America, Europe and parts of Asia its presence reaches 95 degrees north, and the southern presence is unknown. As for Iraq, it is present in all governorates, but it is few in Basra, which indicates that soil moisture affected its reproduction and there are (16) species of insect, although recent studies have revealed many types of them (Mauldin, Peters, 2016).

The insect's saliva is mixed inside the vertebral host while feeding on it, where it is consumed by the macrophage cells and transformed inside them into (amastigote) , it begins to proliferate within macrophages, after which these cells divide and the parasites are released to be consumed by other phagocytes, thus, reproduction continues when the large macrophage cells split into the body of the vertebral host, and numbers of parasites move through the lymph nodes and body fluids to the internal viscera, such as, liver, spleen and lymph nodes, which subsequently cause these organs to enlarge (Menezes, Madeira, 2016).

Clinical Symptoms of leishmaniasis

Symptoms of cutaneous leishmaniasis have skin ulcers that appear at the site of the bite, usually in the exposed areas of the body include limbs and face, period of parasite harbor lasts from two months to several months, however hosting duration depends on parasite genus and immune response of the infected person , yet, lesions, which are small at first, grow into sores that usually heal themselves after sundry months (up to 24 months), while about skin harm often disappear without any medication, most of the suffering caused by *Leishmania* major recover within 6-12 months. In most cases, symptoms caused by *Lishmania* Tropica will recover within 24 months. But in visceral *leishmania* include regular signs such as fever, depression, weight loss, anemia, enlarged spleen, liver and lymph nodes, these symptoms occur as a result of a weakened immune system of infected person. It also causes leukopenia and thrombocytopenia and shows secondary infection and bleeding tendency (Terio et al., 2018).

Diagnosis and Treatment

Method of diagnosis depends on infection type. In cutaneous leishmaniasis, clinical symptoms are clear, the examiner is isolating parasite from damage skin of known laboratory methods according to the fluids around the skin and cultivated it in the medium, then checked the parasite in a Promastigote stage. while other methods, especially in cases of visceral leishmaniasis, depend on several procedure, inclusive (Kimblin et al., 2008).

1) Laboratory methods that have isolation and diagnosis of parasite when a part of the live tissue (biopsy) is not taken from the iliac bone, thereafter sample is implanted in the culture medium as resemble a cross, and observed parasite in (promstigote phase) after staining the sample directly with Leishmania stain , and in this time can viewing parasite in an amasigote phase inside the cells (Abdullah et al., 2017).

2) Serological examinations which comprise (fat, Elisa) and others. These tests depend on specific antibodies presence to leishmaniasis parasite in the serum of patient or suspected person (Obaid, 2018).

3) Possible to use other methods in state of disease progression, such as using X-rays or sonar (ultrasound) to detect cases of enlarged liver and spleen in advanced stages of the illness (Kholoud et al., 2018).

Often cutaneous leishmaniasis infection cures automatically without any treatment, and healing of these ulcers takes a period from one to two years, sometimes it may extend to more than this time (Calderon-Anyosa et al., 2018).

As for the infection with visceral leishmaniasis, it leads to death of patients if it is left untreated, death cause is often an accidental harm with another disease and sometimes injury returns again after complete recovery, these relapses occur even after years of treatment period, but, most cases of visceral leishmaniasis respond well to treatment. There are now several treatments available to cure visceral leishmaniasis disease, but some studies confirmed that the disease is difficult to treat, therefore used antimonial in symptoms appear, but it is not known whether this chemical element directly effect on parasite activity in (Amastigot) stage inside cells, or indirectly, by accelerate macrophages and other elements of the immune system. A recent study about visceral leishmaniasis suggests that work should be done by reducing current levels of cytokines (Giraud et al., 2019).

For treatment of chronic leishmaniasis, use Pentostam, which is sodium stibo glnconate for a period of (6) days. aside from rest, protein and vitamins intake and good care, there are many remediation, such as (Choline to Promastigot), which is new class of inhibitors, whose may be used to treat leishmaniasis and this it completely effective and gives a cure rate of 97 % for 28 days (100 mg/l a day) (Abudallah et al., 2017).

Review in the previous studies carried out of Leishmaniasis

Due to medical prominence of Leishmaniasis, it is a main assembly health issue that can cause dangerous human diseases, as well as, economical damage to the person, family and society, there have been numerous studies on leshmaniasis illness and transact with many portion, subsequent section of these studies:

Kimblin et al. (2008) study on quantification of number Leishmania for main parasites injected inside the ears of living mice within nutrition during persons infected flies. Al-Samarai (2009) study to locate the rang of cutaneous leishmaniasis (C L) in Alhaweja zone and to enquire the subaltern bacterial contamination in C L. Another study which also included ecological agents related with apportionment of visceral leishmania disease (kala-azar) in chronic regions of Bangladesh and which increased morbidity and mortality rates in these areas: design of environmental variables (Abdullah et al., 2017). While other study of Obaid (2018) involved clinical study on Leishmania kinds and distribution areas in Kirkuk city, Iraq, for one year from 2014 to April 2015, conducted on inside and outside patients of Pediatric, Kirkuk General and Azadi Teaching hospitals. As for the study of Kholoud et al. (2018) on epidemiology consequences of leishmaniasis to distinguish advice and define topic recommendations to fight this illness by study climate variation influence on spread and distribution of this disease in Morocco. Other study Calderon-Anyosa et al. (2018) about housing features and Leishmaniasis, these study revealed found that clay walls with puncture and cracks, moist, and dusky houses it hazard agents for leishmaniasis transmission because these factors make suitable places for sand flies nurture and resting as sand fly choose warmth, wet and preservation from sunlight through midday. Finally, (Giraud et al., 2019) conducted on survey of comprehension of transportation strategy by using Real-Time Quantitative (PCR) to quantify contagious Non-metacyclic and metacyclic kinds in mouse lacing from singular sand fly biting to reveals role and prevalence of heterogeneity dose of sand flies.

3. Conclusion

1. Leishmaniasis is a parasitic illness transmitted by the female sand fly G: phleptomas.
2. There are three major kinds of this disease, visceral, cutaneous and Mucocutaneous leishmaniasis.
3. This parasite has two main phases in its life cycle: Amastigote and Promastigote.
4. Leishmaniasis is one of the most widespread diseases in the world, especially in Iraq, for both visceral and cutaneous types.

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