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(REVIEW ARTICLE)

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Review of epidemiological *Leishmania Ron. Ross*, 1903 in Iraq

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Abstract

Leishmania species are intracellular protozoan parasites that spend a portion of their life cycle in the midgut of sand flies and the remainder in the tissues of mammals. These parasites, which cause a class of human disorders known as leishmaniasis, live mostly in macrophages, where they multiply and survive by employing a variety of defense mechanisms against the oxidative stress and acidity generated by these immune cells. To help control their reaction to heat stress, they also produce heat shock proteins. Furthermore, the promastigote form has a glycocalyx that is necessary for colonizing the gut wall of the sand fly and completing its life cycle. Consequently, a variety of virulence factors contribute to the parasite's pathogenicity. Clinical signs and symptoms vary depending on the species of *Leishmania* and the host's immune system. In cases of cutaneous leishmaniasis, the symptoms may be limited to the skin, but if left untreated, they may spread to internal organs and be lethal.

Keywords: Cutaneous Leishmaniasis; *Leishmania*; Life Cycle; Protozoan

1. Introduction

Leishmania is a mandatory intracellular protozoan parasite that is transmitted by vectors and belongs to the *Trypanosomatidae* family. It causes disorders of the skin, mucosa, and viscera in both the Old and New Worlds. Since leishmaniasis is a complex disease that affects numerous subspecies, each of which has a wide range of clinical signs, even experts can become perplexed by it. This review attempts to compile the current understanding of leishmaniasis, a serious zoonotic and vector-borne disease, and offer recommendations for future research directions in the field. The primary vertebrate hosts of *Leishmania* species are humans, canines, and several rodent species. The collective term for a collection of human illnesses linked to the parasite is leishmaniasis. The world's human-infecting organisms can be found in Africa, Asia, Europe, the Americas, and the Mediterranean. According to studies, there are 70,000 annual deaths, 350 million people believed to be at risk of infection, and 1.5 to 2 million new cases. The symptoms of various *Leishmania* species vary; some may resolve on their own, but others, like visceral leishmaniasis, can be lethal if treatment is not received. [1].

Leishmaniasis is a widespread disease in tropical and subtropical climates caused by an internal parasite carried by sand flies, primarily from the genera *Phlebotomus* and *Lutzomyia*, which are present in Europe, Northern Africa, the Middle East, Asia, and parts of South America. It was surprising to learn that isolated transmission cases resulting from laboratory accidents have been reported [2]. Leishmaniasis is listed by the World Health Organization (WHO) as one of the seven most dangerous tropical diseases. It poses a major threat to world health due to its wide range of clinical manifestations some of which are lethal [3, 4]. This disease affects every continent except Oceania and is endemic in some areas such as Central and South America the Middle East Southeastern Mexico Northeastern Africa and Southern Europe [5]. [4] contend that. The clinical severity of leishmaniasis is largely determined by the hosts immune response and the particular *Leishmania* species involved. The cutaneous-chondral form of the illness also known as chicleros ulcer has been the most prevalent in Mexico [2, 5].

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1.1. Morphology and Life Cycle

Sand flies belonging to the genus Phlebotomus act as both the vector and the intermediate host during their life cycle. The primary disease-carrying sand fly is the female. Blood from an infected person contains an amastigote that changes into a promastigote multiplies in the midgut and then moves to the pharynx to prepare for transmission to another host when the blood is consumed. According to [6] sand flies have a life cycle of about ten days. While feeding the sand fly injects an uninfected host with the infectious stage Promastigote.

The macrophage cells engulf the promastigote, subsequently transforming it into an amastigote that proliferates within the macrophages, leading to their rupture and the release of stages that can infect additional cells. As a result, when another sand fly feeds on the infected individual, the parasite's life cycle in the human host persists [7]. Amastigotes found in mammalian tissues commonly share a spheroid shape and typically range in size from 2.5µm to 5.0µm. PCR has been utilized to amplify kinetoplast DNA from samples to tackle the issue of the uniformity of amastigotes across various tissues and the challenges of distinguishing between different species. [8]. (Figure 1).

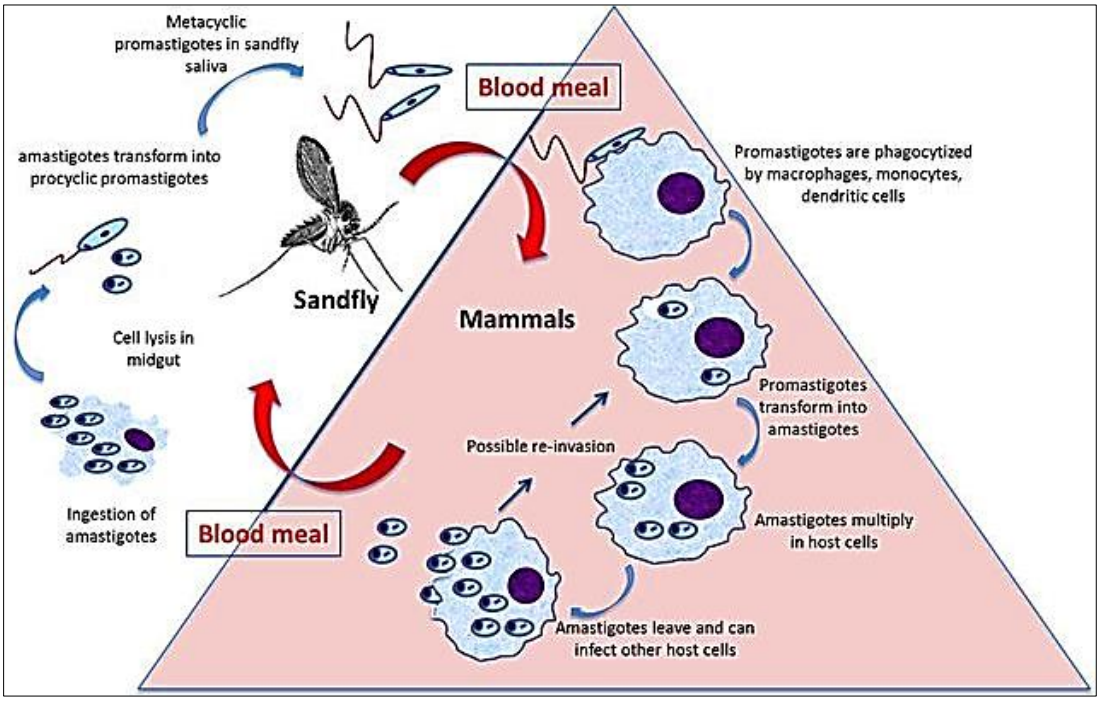

Figure 1 Life Cycle of *Leishmania* species [9]

1.2. Pathogenesis

After being bitten by some sand fly symptoms of cutaneous leishmaniasis may not show up for a few days to months. This condition primarily affects the skin and begins with red lesions that may develop into crusts and underlying ulcers. [3] claim that. These lesions may eventually merge to create larger more uncomfortable areas that are more susceptible to secondary bacterial infections. Mucocutaneous leishmaniasis is caused by the parasite damaging the surrounding cartilage and tissue as it travels from the bite site to the mucous membranes of the mouth nasal passages and ears. This form is commonly linked to secondary bacterial infections necrosis and severe deformities. Additionally, the parasite may affect the larynx and trachea which could result in voice loss. [5]. The parasite responsible for visceral leishmaniasis targets the internal organs of the reticuloendothelial system. Even though there are no outward symptoms the infection can often get worse and eventually cause Kala-azar a dangerous disease. Common symptoms that frequently show up two to four months after a sand fly bite include anemia enlarged liver and spleen and decreased bone marrow function though they can also show up ten days to a year later. Considering [10], this disorder is often associated with bleeding from mucous membranes due to low platelet counts which can have detrimental effects and increased susceptibility to secondary bacterial infections due to compromised immune responses and reduced white blood cell production.

1.3. Epidemiology

There have been reports of both cutaneous and visceral forms of leishmaniasis in Iraq making it a serious health concern. infestations of Leishmania species. are found in greater numbers in the northern and central regions especially

in the hot and dry border region. Commonly known as Oriental sore or Baghdad boil cutaneous leishmaniasis presents locally as a slowly spreading inflammatory skin sore. Via a range of techniques including direct smears cultures histological analyses and serological testing leishmania parasites have been found in human skin lesions. Nevertheless, few studies use PCR techniques to detect Leishmania strains in these skin lesions. Notably a U. S. phylogenetic study. S. A military installation in southern Iraq used phylogenetic and molecular methods to investigate the presence of various Leishmania species in sandflies. A more comprehensive study conducted in all Iraqi provinces between 2011 and 2013 found that men are more likely than women to contract cutaneous leishmaniasis with the majority of cases occurring in the 5–14 and 15–45 age groups. Lowland regions with modest annual rainfall and substantial rural populations have the highest incidence [11]. L was found to be the causative agent of cutaneous leishmaniasis (CL) in the area bordering northern and central Iraq. major based on epidemiological and phylogenetic molecular research conducted between 2014 and 2017. By employing cytochrome b gene sequence analysis these studies assessed the probability of a CL outbreak in Iraq. The findings indicated that the strains of L. had an important connection. There are notable MRHO/IR/75/ER in Iran and Iraq [12,13] . It is noteworthy that during this time the province of Diyala had the highest rates of cutaneous and visceral leishmaniasis infections at 21 and 91 percent respectively. Due to the circumstances of the conflict many locals had to relocate [14].

Children ages 1–4 had the highest percentage of visceral leishmaniasis (VL) infection at 62–0. 04%. On the other hand, the highest prevalence of cutaneous leishmaniasis infections (37–81 percent) was found in those between the ages of 5 and 14. Important data for developing successful strategies for managing parasitic diseases in Iraq were obtained from this epidemiological study [15]. Interferon gamma release assays (IGRA) rk39 test strips quantitative polymerase chain reaction (PCR) and enzyme-linked immunosorbent assay (ELISA) were among the many diagnostic techniques that supported these results. In 2019 a study was carried out on VL among US soldiers who served in Iraq from 2015 to 2017 [16, 17].

Wasit Provinces Internal Transcribed Spacer1 (ITS1) sequence analysis has been used in recent Iraqi studies to determine which Leishmania species cause CL in Iraqi patients. There was a statistically significant correlation between sex and the exceptionally high frequency of CL (83. 3 %) and the results showed that men were more prone to CL (56. 4 %) than women (43. 6 %). The authors claim that wartime operations increased the incidence rate and made it easier for CL to spread especially in areas with limited access to healthcare [15]. In Iraq leishmaniasis cases were found to be primarily caused by Leishmania major. Lesions usually heal on their own in immunocompromised people leaving behind indented scars. All things considered the data shows how dangerous Leishmania parasites and the insects that spread them can be in free zones and nearby nations like Saudi Arabia Turkey Jordan and Iran. According to [14], the only drug authorized by the Iraqi Ministry of Health to treat CL is sodium (Na) stibogluconate a pentavalent antimony compound. Treatment approaches for VL and CL need to be evaluated through long-term comprehensive research in order to improve the standard and caliber of care for these neglected illnesses.

1.4. Diagnosis

The pertinent clinical and epidemiological context is used to establish the diagnosis. Laboratory confirmation and Leishmania species identification are essential. Scraping cutaneous or mucosal ulcerations especially at their margins can reveal the protozoan which may be present in non-ulcerated lesions. Performing a biopsy from the lesions active edge is an additional diagnostic technique. The parasites are visible either in their free form or as a smear inside macrophages. With numbers varying from two to twenty in a single cell polymorphonuclear leukocytes are less common. With a rounded or oval nucleus and an oval or piriform shape this parasite is 2 to 5 μm long and 1 to 2 μm wide. Rarely have flagellated forms been observed. Moreover, vaccination is used for cultural reasons [2, 18]. Treatment

The host, the species involved, and the clinical presentation all affect how cutaneous leishmaniasis is treated. People who have a healthy immune system and no symptoms of mucosal disease usually don't need treatment for cutaneous leishmaniasis caused by L. mexicana and L. major because it usually goes away on its own [19]. On the other hand, small lesions that do not go away on their own should be treated locally, while complicated cutaneous leishmaniasis should be treated systemically. More than five lesions, lesions larger than 5 cm, lesions on the face, fingers, toes, or genital area, regional lymphadenopathy, symptoms lasting longer than six months, diffuse cutaneous leishmaniasis, or the presence of an immunocompromised host are all signs of complex cutaneous leishmaniasis. Pentavalent antimonials are considered the gold standard for systemic therapy of cutaneous leishmaniasis in Latin America, according to [20]. Experts support individualized therapy that takes into account the patient's immune health, any co-existing medical illnesses, plans for pregnancy, the size and location of lesions, and possible drug side effects, even if there is no one-size-fits-all treatment strategy. Unlike cutaneous leishmaniasis, mucosal leishmaniasis does not go away on its own and can cause deformity, gradual tissue damage, and even death (from complications such aspiration pneumonia or respiratory obstruction). Consequently, a thorough evaluation of the naso-oropharyngeal region must be followed by immediate

systemic treatment. For patients at risk for respiratory obstruction which anti-leishmaniasis treatment may worsen the Infectious Diseases Society of America (IDSA) advises both prophylactic steroid medication and inpatient surveillance. Similar to people with complex cutaneous leishmaniasis those with mucosal leishmaniasis should also receive specialized systemic treatment [21].

Since systemic treatment is the most severe form of visceral leishmaniasis (VL) anyone with symptoms and a confirmed diagnosis of the disease should begin it right away. Current concerns center on the possibility of resistance developing to pentavalent antimonials which were once thought to be the most effective treatment for Leishmania species. For those who are not pregnant or nursing miltefosine should be considered however the IDSA recommends liposomal amphotericin B for the treatment of VL in immunocompetent patients. Pentavalent antimonials may be a suitable option for leishmaniasis patients who are unable to take liposomal amphotericin B or miltefosine in areas where there is little indication of treatment resistance. Although miltefosine combination therapy may also be used liposomal amphotericin B is the recommended treatment for immunocompromised individuals such as those with HIV or transplant recipients. HIV patients are advised to take antiretroviral therapy (ART) and secondary prophylaxis that targets the particular parasite but transplant recipients are not [21].

2. Conclusion

Leishmaniasis, a multifaceted clinical syndrome, poses challenges in both diagnosis and treatment. It is conceivable that progress in vaccine development, diagnostic methods, reporting protocols, and treatment strategies will significantly reduce the morbidity and mortality rates associated with this disease.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict-of-interest to be disclosed.

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