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Review about Prevalence of *Leishmania SSP* in Humans and Dogs

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A B S T R A C T

Leishmaniasis is a protozoan parasitic disease caused by various strains of *Leishmania* spp. Leishmaniasis is one of the most common zoonotic infectious diseases worldwide. It is considered one of a major public health problem, with three diseases forms, cutaneous, mucocutaneous and visceral. It is known by various names but in Iraq cutaneous form is known as Baghdad boil. This paper includes the review of prevalence of *Leishmania* species in humans and dogs throughout Iraqi governorates and this dependes on Iraqi researches that have been published in different International and local journals .This study reportes wide variation in the infection rate of parasite due to many reasons such as Propaganda of public health, spread of insects, uncontrolled roaming of stray dogs and the different methods of diagnosis of parasite that lead to variation of prevalence rate in Iraq .

1. INTRODUCTION

Leishmaniasis is a serious infection that occurs by intracellular protozoan parasites, returns to the genus *Leishmania*, order Kinetoplastida, family *Trypanosomatidae*, sand flies, female *Phlebotominae* of the genus *Lutzomyia* in America (New World) on the other hand in the *Phlebotomus* in the Asia, Africa and Europe (Old World) that are transmitted the infection of leishmaniasis [1]. The bite of an infected *Phlebotomine* sandfly can spread the protozoan parasites of the genus *Leishmania*, which cause a series of disorders known as leishmaniasis [2]. Depending on the parasite type and the host immune response, the illness can present as cutaneous (CL), visceral (VL), mucocutaneous (MCL), or postkala-azar dermal leishmaniasis (PKDL). In many parts of Sudan, leishmaniasis is endemic. The most prevalent kind is CL, whereas VL is mostly found in the country's eastern, western, and southern regions. [3].

A tropical illness of significant public health concern is cutaneous leishmaniasis [4]. The cycle of transmission infection for this categories is too complex because the various *Leishmania* species, present in various kinds of mammals by the bite of *Phlebotomies*, human infected due to bitten by the insect female sandflies as vector in seeking for blood meal [5]. Perhaps, as a result of risk factors such urbanization, anthropogenic environmental changes, human behavior, medication resistance, population expansion and relocation, and new agricultural methods, the prevalence of CL has grown and the illness has spread to new foci. [6]. As more people travel to endemic regions worldwide, imported cutaneous leishmaniasis (CL) has become a bigger issue. Because doctors in non-endemic areas are not aware of the disease, returned travelers with CL are susceptible to incorrect diagnoses and treatment, which might have negative consequences [7]. Cutaneous form is the more prevalence type of disease caused by *Leishmania* species. Cutaneous leishmaniasis has been diagnosed in more than 98 countries [8]. Cutaneous form in Iraq is considered one of the endemic disease [9].

2. HISTORICAL BACKGROUND

In the Mesozoic era, leishmaniasis illness was a member of the genus *Leishmania* and later expanded geographically the first evidence of the illness early times, initial accounts of the disease in the middle times, investigation *Leishmaina* parasite as etiologic factor leishmaniasis in new age [10]. The prevalence of

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leishmaniasis in ancient human history is only briefly described. Tablets in the library of the Assyrian King Ashurbanipal from the 7th century BCE describe lesions that resemble Oriental sores; it is even believed that these were taken from earlier texts that date back to 1500–2500 BCE [11]. In 42 Egyptian mummies of middle tomb in West Thebes (2050–1650 BCE) that have been studied by paleoparasitological that indicate presence of the mitochondria DNA of *Leishmania* parasite in four samples [12]. The amplified DNA fragment for sequencing indicated that *Leishmania donovani* in the four mummies samples and this revealed that the ancient Egyptian were infected by visceral leishmaniasis. The Ebers Papyrus, a compilation of medical records from ancient Egypt that date back to 1500 BCE, also makes reference to leishmaniasis [13]. The visceral leishmaniasis pathogen, which was initially identified by the doctors *Leishman* and Donovan in 1903, was discovered in stained smears from the spleen of infected patients who displayed symptoms resembling those of malaria. They subsequently named it *Leishmania donovani* [14]. Only a small percentage of the 0.9 to 1.7 million newly infected individuals per year are expected to acquire the disease, and 20,000 to 30,000 of them will ultimately pass away [15].

3. MORPHOLOGY

3.1. Amastigote

In the amastigote form, the parasite resides in the cells of reticulo-endothelial system of vertebrates such as spleen, liver, bone marrow and lymph nodes. Its shape is oval, non-flattened and non-motile, measuring 1-3 μm in width and 3-8 μm in length. The flagellum is being devoid and ineffective. The short flagellum does not project out and it is embedded at the anterior end. The cytoplasm contains mitochondria, vacuoles and volutin granules. The kinetoplast consists of para basal body and blepharoplasty, which are connected by one or more fibrils [16-17].

3.2. The Promastigote

It is located inside the gastrointestinal tract of the insect sand fly and in the culture media. Promastigotes is an extracellular and motile form. Considerably, thin elongate cells fusiform or lance-like in shape and ranging from 1.5-3.5 μm in width and 5-20 μm in length containing a lengthy flagellum that protruded from the front end. The kinetoplast and the basal body are in front of the nucleus, which is at the center [16-17].

4. VECTOR of LEISHMANIA SPP.

Beginning in the early 1900s, sand flies were identified as the vectors of leishmaniasis transmission.They found new species of sand flies and Leishmania far into the twenty-first century [10]. Leishmania parasites, of which there are 98 species, can be transmitted by the bite of an infected *phlebotomine* sand fly. *Lutzomyia* and *Phlebotomus* have been identified as proven or suspected vectors of human leishmaniasis [18]. Only female sand flies bite animals to collect blood meals needed to complete egg development.Sand flies have a wide range of hosts, including canids, rodents, marsupials, and hyraxes, whereas others mainly feed on humans. Consequently, the transmission patterns of human leishmaniasis can be either anthroponotic or zoonotic [10]. The parasite spread to *Phlebotomus* in the Old World (Asia, Africa, and Europe) via female Phlebotominae sand flies of the genus *Lutzomyia* in the New World (America)[1].

5. LIFE CYCLE

When a female sandfly becomes infected while feeding on blood from an amastigote, whether it be an animal or human host, the life cycle of *Leishmania* begins. The amastigote develops in the vector's midgut before changing into a promastigote stage, when it multiplies via binary fission in the midgut and migrates in the direction of the moth parts. Promastigotes will bite the host while feeding on the blood since the infection will go away a few days after ingestion. [19].
When sand fly containing Promastigote feeding on the blood, is injected into an uninfected host, the organisms lose the flagella.Amastigotes are formed and continued multiplying until the cells of infected host get filled with the organisms then rupture releasing free amastigotes which invade new cells [20].

6. CLINICAL SYMPTOMS IN HUMAN

Although there are many distinct clinical presentations of leishmaniasis, Visceral, mucosal, and cutaneous are the three main types of the disease. Lesions at the site of the sand fly bite often manifest as a single, non-suppurative papule. However, many lesions may appear [21]. Over the course of weeks to months, the papules develop into painless ulcers with piled-up borders. Over the course of months to years, these ulcers may cure themselves., or they may leave scars and deformities behind [22]. Outside the plaque or ulcer, there may be nodular, sporotrichoid, disseminated, psoriasiform, verrucous, zosteriform, eczematous, erysipeloid, and small satellite lesions (nodular lymphangitis), are among the many unusual cutaneous symptoms [23]. Dermal signs may co-occur with mucosal lesions, and the most deformative kind of the illness, ML (also called espundia in Latin America), creates deformities on the face, generally years after the first cutaneous signs have gone away, Patients often describe chronic nasal symptoms, including pain, secretions, and epistaxis. Physical tests often show

mucosal involvement of the mouth and nose, followed by involvement of the oropharynx and larynx, ulceration, bleeding, and inflammation. Unlike cutaneous disease, nasal septal perforation is possible, and the cartilaginous septum inside the anterior nares is often impacted [22]. Visceral leishmaniasis, the most deadly kind of leishmaniasis, can result in systemic infections that impact the hematogenous, lymphatic, liver, and spleen, severe illness symptoms, such as fever, pancytopenia, hepatosplenomegaly, cachexia, and hypergammaglobulinemia. Patients with visceral leishmaniasis frequently report subjective symptoms such as exhaustion, stomach discomfort, and weight loss [24].

7. CLINICAL SIGNS in DOGS

Most symptomatology is caused by granulomatous inflammatory responses caused by macrophages infected with *L. infantum*, which are present in parasitized tissues. The majority of dogs exhibit cachexia, or poor bodily condition; they are often underweight and prone to anorexia. Exfoliative dermatitis, cutaneous lesions (nodular, ulcerative, and pustular), and skin peeling are the main symptoms of skin disease. Erythematous responses, pale mucosa, and alopecia are also frequent. In the absence of parasites, onychogryphosis, or nail overgrowth, is quite prevalent and linked to lichenoid and interface mononuclear dermatitis [25]. Because blepharitis, uveitis, and conjunctivitis are so prevalent, ocular injury can also be discovered. Dogs that exhibit symptoms frequently have adenopathy, which is characterized by enlarged lymph nodes as a result of nodal structural hypertrophy [26].

Because amastigotes cause macrophage infiltration and alter the spleen's microstructure, they can cause spleen enlargement or splenomegaly. Along with the skin and bone marrow, the spleen is one of the organs most frequently impacted by infection. The liver exhibits a similar pattern, and in certain cases, the condition develops into hepatitis. Due to its high parasite burden, the spleen exhibits notable morphological alterations, such as red pulp enlargement and hyperplasia as well as mononuclear and plasma cell infiltration. Because of the spleen's enlargement and hyperplasia, the white pulp exhibits lymphocyte replacement of macrophages [27-28]. In the majority of infected dogs, renal involvement manifests as glomerulonephritis, which is linked to immune complex deposition and can lead to kidney failure. Proteinuria and elevated blood creatinine levels are only signs of kidney damage in its latter stages, albeit can occur at the onset of the illness [29].

8. PREVALENCE in HUMAN IRAQ

Depended on database collect from many reports, Iraq is endemic by Cutaneous leishmaniasis and visceral leishmaniasis in human and dogs[30-31] . The first occurrence of leishmaniasis in Iraq was reported in Baghdad and Mosul cities [32]. The disease's popular name, "Baghdad boil," indicates that it has a lengthy history in the area [33]. In human the prevalence of disease varies through Iraqi provenances; the state represented 53% and 62% of the total cases in Baghdad reported respectively [34-35]. Another study in Baghdad indicated that the prevalence rate in male was 55.6 [36]. The study about Visceral Leishmaniasis in Baghdad was reported rate of infection 26.78% [37]. Al-Akash et al have confirmed in their study that the 49 patients (29 male and 20 female) in 5 refugee's camps show cutaneous lesions (CL) in Mosul city in Iraq [38]. Rashid etal., recorded 451 case among total of 2749 person from Ninewa governorate [39]. In Hawija area the rate of infection was 58% [40]. The prevalence rate in Erbil provenance was 66% [41]. Human Cutaneous Leishmaniasis has been identified in Diyala and the infection rate was 51.2% [42]. In Al-Ramadi the prevalence of infection rate was 59/100,000 [43]. The occurrence of humans cutaneous leishmaniasis in Iraq, middle Euphrates was 35% has been reported by (9) [44]. In Karbala city, one hundred patients cases of the cutaneous leishmaniasis are detected (92). Another study about visceral leishmaniasis was conducted in Karbala Governorate with a percentage of 8.24% [45]. The spread of cutaneous form of Leishmaniasis in Najaf governorate was detected 40% [46]. In Babil provenance the cutaneous leishmaniasis were diagnosed in males and the rate was (73.5%)while in female the rate was (26.4%) [47]. A further study was conducted in Babil governorate that found that the variation in infection rate between male and female were 57.89% , 42.11% respectively [48]. In Thi-Qar Province, South of Iraq, the prevalence of infection was 81.25% [49]. L. infantum that caused visceral leishmaniasis In central and south Iraq, the epidemiology of visceral leishmaniasis in Thi-Qar province was (55.35%) in males and (44.64%) in females [50]. In Wasit provenance the infection rate was 76.1% by cultivation on RPMI 1640 medium [51]. A study involved visceral leishmaniasis in Al-Kut Citywhere the infection rate was prevaled 8.25% [31]. The infection rate in Misan city was high in Al-Amarah district 93.807% patients were diagnosed [52]. According to the prevalence study in Al-Muthanna governorate, the highest infection rate of cutaneous leishmaniasis was recorded in 2016 (33.4%) [53]. The prevalence of cutaneous leishmaniasis in Basrah province south Iraq are regarded (34.28%) in females wheal (65.71%) in males [54]. The high level of infection with visceral leishmaniasis reported in Basrah, Southern Iraq was (84.9%) recorded by [55]. The low level of disease incidence recoded in Kirkuk governorate 15

cases/10000 [56]. Iraq is considered endemic by Visceral Leishmaniasis and the infection rate was 81% [57]. Finally, the infections rate of leishmaniasis that were reported in all Iraqi governorates during the period from2011–2013, was a 44.6% [58].

9. PREVALENCE in HUMA and DOGS IRAQ.

The primary host of *Leishmania* species, a parasite that causes canine leishmaniasis, an incurable disease, is dogs. In subtropical and tropical regions, the parasite is spread by sand fly bites, but there is also direct transmission among dogs and between dogs who are pregnant and they are offspring [59]. In the Middle Euphrates, dogs in Iraq are identified as the primary source of zoonotic parasites that cause leishmaniasis in humans [9]. In Spite of well care, German shepherd police dog was reported with cutaneous leishmaniasis in Diyala governorate [60]. The prevalence of Leishmaniasis in dogs in Misan governorate were (63.295%) males and (36.704%) females [52]. Middle Euphrates, Iraq: an investigation of the prevalence of cutaneous leishmaniasis in dogs recorded 88.33% [9]. The higher occurrence of leishmaniasis in dogs were observed in l-Qadisiyah and they were 90% [61]. Other research was conducted in Al -Qadisiyah, (Diwaniya city)and it was reported (46.8%) [62]. In Nineveh province the results showed that the total infection rate Leishmaniasis in dogs was 55%, [63]. Also another study was conducted in Nineveh governorate (Mosul city) found that infection rate was (23.9%) [64]. The lack to control the movement of stray dogs and Leishmaniasis's global escalation and geographic expansion are still associated with the vector population's spread (9).

10. CONCLUSION

In conclusion, this study investigates that Leishmaniasis is endemic in Iraq for many reasons such as the close relationship between Leishmaniasis in humans and dogs, whether dogs are domestic or stray. This paper detects that dogs play a substantial role in the zoonotic transfer of infections to humans and are key parasite reservoirs.. The high infection rate in the middle and south of Iraq belongs to presence worm wither, humidity and marshes. All these factors lead to improve the environment for increasing the population of intermediate host, sand fly.

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Arabic Abstract

داء الليشمانيات هو مرض طفيلي تسببه انواع مختلفة من طفيلي الليشمانيا. يعد داء الليشمانيات أحد أكثر الأمراض المعدية الانتقالية شيوعًا في جميع أنحاء العالم. وتعتبر من اكبر المشاكل الصحية. و المرض له ثلاث اشكال، الجلدية والمخاطية الجلدية والحشوية. وله أسماء مختلفة ولكن في العراق شكله جلدي يعرف حبة بغداد. يتضمن هذا البحث مراجعة لانتشار أنواع الليشمانيا في الإنسان والكلاب في جميع المحافظات العراقية وهذا يعتمد على الأبحاث العراقية التي تم نشرها في مجلات عالمية ومحلية مختلفة، وقد أفادت هذه الدراسة بتباين واسع في معدل الإصابة بالطفيلي لأسباب عديدة مثل التوعية الصحية، انتشار الحشرات، التجوال غير المسيطر علية للكلاب السائبة واختلاف طرق تشخيص الطفيلي جميع هذه العوال ادت إلى اختلاف معدل الانتشار في العراق.