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Overview of Leishmaniasis

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Abstract: Leishmaniasis is a disease through a parasitic organism that invades and thrives within human cells when a sand fly takes a blood meal from the infected person. This specie is commonly found in Asia, Africa, the Americas, and the Mediterranean region. Annually, there are 1. 50 to 200 new cases of Leishmaniasis every year with about three hundred and fifty million people at risk of getting the disease. In addition, Leishmaniasis is a major killer which claims 70, 000 lives every year. The clinical manifestations depend on the apropos Leishmania species and its host's immunological responses. These manifestations can occur restricted to the skin or may involve internal organs and, in some cases, may be fatal. It has diverse medications employed in its therapy, yet the single effective cure is realized through the existing antimonies in today's dispensary.

Introduction

Leishmaniasis is a protozoal infection that is transmitted through the bite of an infected female sandfly and involves the Leishmania organism. This disease impacts greatly on the health of the human. Leishmania is a flagellated protozoan parasite that evolves in the intestines of the infected animal and belongs to the order Kinetoplastida and the Trypanosomatidae family (Thomas et al. , 2017; Shu-ichi Tao and Ling Jia, 2024). Leishmania spp. The infection has prevalence at nearly 12 million people worldwide, while others estimate 350 million people are prone to infection (Lockard et al. , 2019). Leishmaniasis thusmainly impacts people in poor, less-developed countries that have paid scarce attention to the control programmes, received negligible funding from the pharmaceutical industry, and poor healthcare systems (Choi et al. , 2021; Oliìas-Molero et al. , 2021; Scarpini et al. , 2022). There are some of the factors that may affect the transmission and dissemination of Leishmaniasis. This sickness is commonly reported in Asia, the Middle East, North of Africa, East Africa, Mediterranean countries, as well as South and Central America (Tabbabi, 2019 as cited in El Idrissi et al. , 2022). Leishmaniasis is an infection that occurs from one of the approximately 20 reported standard types of Leishmania parasites that are transmitted to humans through several generic categories of sand fly called phlebotomine. The transmission of the Leishmania parasites may differ as to its process, specifically with regards to the extent to how efficient the interaction between the parasites, sand flies, and the disease is. Restrictive vectors are conveyed by a precise connection between the sphingolipid base and a species of Leishmania species, Phlebotomus papatasi and Phlebotomus sergenti. Permissive mosquito vectors activate development of multiple Leishmania species, including Phlebotomus arabicus and Lutzomyia longipalpis within the midgut of sandflies. Cecílio et al. (2022) reveal that this development has a negative impact on immunological signal pathways.

Life cycle

There is largely a nocturnal female phlebotomine sand fly involved in the transmission of Leishmania parasite to man or other anthropoid hosts. Leishmania sp. is protozoan parasites which in transmission, life cycle and pathology involves a complex interaction between the host and parasite. consists of two different stages: The infectious form is the extracellular promastigote and the intracellular amastigote (Who 2020b; Chávez-Ruvalcaba et al. , 2021). The promastigote form is also capable of mobility, as it is equipped with flagella; this form of the parasite travels through the

digestive tract of the sand fly (WHO, 2020b). During the blood meal the mouth parts of the sand fly penetrates the skin and injects promastigote form. To enter the mammalian host, the promastigote form of the parasite becomes engulfed by mononuclear cells and then transforms into the amastigote form, referred to as a Leishman-Donovan body. In the host's RES, amastigotes multiply and transform through schizogony, becoming a symptomatic or latent form depending on numerous factors tied to the host and parasite (Cecílio et al. , 2022). It has been revealed that amastigotes are not limited to the bloodstream and have the potential to move through the lymphatic fluid, and as a result, mucosal and visceral diseases arise (Chávez-Ruvalcaba et al. , 2021; Ness et al. , 2022). The transmission of Leishmania sp. mostly occurs through symptomatic infection and post-kala-azaria cutaneous Leishmaniasis (PKDL), while sandflies are not infected by asymptomatic cases (Burza et al., 2022). Certain areas need individuals to adhere to the specific life cycle (anthroponotic spread) associated with L. tropical (causing CL in the New World) and L. donovoni (causing VL in India) (Davidson and Croft, 1992; Burza et al., 2022). Nevertheless, animals can sustain their life cycle and exhibit indications or manifestations of the illness, but not always. The susceptible hosts encompass canines, rodents, marsupials, primates, and simians.

Dogs are very crucial animals for L. infantum, as stated by Faye et al. (2010). Leishmaniasis can be spread by less frequent means such as organ transplantation, blood transfusion, intravenous drug usage, or congenital transmission.

Types of Leishmaniasis

Leishmaniasis presents itself in several clinical forms, including cutaneous (CL), mucocutaneous (ML), and visceral (VL) manifestations. Among these, cutaneous Leishmaniasis is the most often described kind, characterised by the presence of inflammatory skin lesions. The life-cycle of L. major is controlled by P. Papatasi is the vector for L. major and is acquired from Psammomys obesus, Meriones libycus, Nesokia indica and Rhombomys opimus which serve as the reservoir host for the disease (Rafati and Modabber, 2014; De Vries and Schallig, 2022). Pulmonary leishmaniasis or kala-azar is the most serious form of the disease and is defined by the extension of the disease to the different internal organs, including the liver, spleen or bone marrow. The source of the infection is L. infantum, which affects numerous plant species such as P. galilaeus, P. syriacus, P. tobbi, and P. halepensis among others. Furthermore, dog species of Canis familiaris also act as vectors to the infection in other animals. Anthroponotal CL is a disease that is caused by L. tropica and the transmission channel is through the P. Sergenti. It is only observed in humans Notably, the disorder is symptomatic of general health deterioration among patients. Furthermore, Anthroponotic Visceral Leishmaniasis (AVL) is the causative agent of L. donovani and is transmitted by the P. alexandri vector (Ready, 2013; WHO 2020b).

Leishmaniasis in Iraq

Leishmania daisies is endemic in Iraq, with the first cases recorded in the cities of Mosul and Baghdad (Latif et al., 1974). Regarding (Sukker, 1986), he mentioned that the central part of Iraq is infected by kala-azar, 12038 cases were recorded between 1971 and 1984 and most of them were children, especially in rural areas. Although (Bray and Rahim, 1969; El-Yazachi, 1975) found that northern Iraq is one of the endemic areas of cutaneous Leishmaniasis, especially in Mosul.

In 2001, the World Health Organisation conducted a study which found that there were 10.9 cases of visceral Leishmaniasis per 100,000 individuals in the governorates of Baghdad, Dhiqar, Muthanna, Maysan, and Basra (WHO, 2004). In their work, Al-Hussaini et al. (2017) shown that in 2002, health facilities in Baghdad identified 14,502 cases of Kala-azar infection throughout sixteen regions in Iraq using the use of the indirect fluorescent antibody test (IFAT). The provinces exhibiting the greatest incidence of infections were Diala, Babylon, and Baghdad. In addition, a research carried out by Peter et al. in 2004 recorded a total of 310 cases of both cutaneous and visceral Leishmaniasis among American troops who had returned from the Iraq war. The overall data of Basra governorate health department states that 608 of cases of Leishmaniasis with 210 of those particularly reported in Korna. (Jafer, 2005). Yusuf (2006) elaborated while Jassim et al. (2006) confirmed it by on the account of some cities of Dhiqar county: 877 cases of visceral

infection in 2003 as opposed to 573 seen in the period of 1999 to 2002. Visceral Leishmaniasis in Iraq has annual reporting of far over 1000 casesreported. Registrar General, Department of Endemic Diseases, stated that within 1971–1984 the overall number of cases was 12 038 and 88% of them identified in the Baghdad and Central Governorates. In the current years, Hashim et al. (2007) have identified that there are the increased numbers of counties in the southern region. He explained that the national average incidence of this disease is approximately 1,711 cases per annum while according to the World Health Organisation, the current figure of the infection stands between 3,400 and 6,800 between 2004 and 2008 (WHO, 2018). Rabeea also conducted a research in Wasit city in 2008 aimed at determining the rate of Leishmania among the population. In the study , 178 patients were diagnosed with infection in total. Interestingly, another research also by Al-Samarai and Al-Obaidi identified that there were 107 cases of cutaneous Leishmaniasis in Hawija city in the Kirkuk governorate for the period October 2004 to April 2005. In a research carried out by Al-Ani et al. , (2012), it was estimated that there were about 32 visceral infections cases among the patients in Ramadi hospital situated in the Anbar Governorate. In addition, it was ascertained that 75 percent of such cases were in children, and most of them were less than two years old.

Conducted by Qader et al in 2009, it was found that 103 new CL cases were confirmed in Al-Qadessia province from 2005- 2007. The visceral Leishmaniasis was reported at a rate of approximately 1049 in the year 2008, and it estimated by scholars that nine out of every ten minor were infected. According to Majeed et al. (2013), the majority of the cases were reported in the eastern provinces such as Diyala, Wasit, Misan, and Basrah. Another comparative cross-sectional study conducted by Al-Warid et al in 2017 showed that, from the year 2011 to 2013, Iraq experienced an approximate 7,112 cumulative confirmed Cutaneous Leishmaniasis cases. More particularly the IAC reported 2,978 cases in the year 2011, 2,486 cases in the year 2012 and 1,648 cases in the year 2013. The World Health Organisation (WHO) stated in 2015 that Iraq falls in to the category of high endemic countries and according to the figures, it estimated that approximately 1000 – 4999 cases were reported in the year 2013. A cross-sectional descriptive study conducted by Al-Samarai et al. , found that out of 120 patients who presented in three health centers in Kirkuk, Iraq, with cutaneous symptoms, 571 patients were confirmed to have cutaneous Leishmaniasis between April 2015 and April 2016. Consequently, Hassan (2018) established that out of the 100 patients who were admitted, 58 of them contracted the skin disease. out of 58 people affected by leishmaniasis, 35 were men and 23 were women, aged between 4 and 56 years, who developed lesion in the face, arms and leg in samples collected from Rizgary & Komary hospitals in Erbil. Additionally, (Abdulla *et al.,* 2018) showed that data from the Kurdistan Regional Health Agency showed that no cases of cutaneous Leishmaniasis were recorded before 2010. In 2008, the incidence of infection was zero. In 2010, approximately 15 cases were reported. 34 in 2011 and then 88 in 2014, while in 2015 the number of cases was around 228. In addition to the 259 cases reported in 2017, more (41%) cases were from the Maxima region, while 8%. were refugees and (21%) internally displaced persons. On the other hand (Ali *et al.,* 2018) they show that visceral and cutaneous Leishmaniasis are endemic in different parts of Iraq, 1,800 cases of diseases of internal organs are registered every year, in recent years it is estimated that there are almost 4,000-5,000 cases. Previous reports indicated that the skin infection was indeed endemic in northern parts of Iraq such as Kirkuk, Salah-Eldin, Diyala, Missan and Wasit. Thousands of skin diseases have also been recorded by American soldiers in Iraq since the war. In addition, approximately 700 cases of cutaneous Leishmaniasis are collected from eight Iraqi provinces as follows: Salah-Edin 76, Diyala 78, Baghdad 80, Basrah 82, Thiqar 91, Najaf 94, Wasit 99 and Diwaniyah 100. See, (Al-Khayat *et al.,* 2018) shows that from January 2015 to January 2017, 1,264 cases of cutaneous Leishmaniasis were diagnosed in the city of Makhmur, 67 kilometers southwest of Erbil. In addition, (Hussein *et al*., 2019) reported that 1482 cases of cutaneous Leishmaniasis were recorded in the Rabeea area of Mosul city during a 12-month period from September 2016 to November 2017. This number may be due to the significant reduction in health services after the war, as well as poor sanitation in the city, which may cause an increase in vector populations. In addition, the number of cases may have been increased by the internal movement of people from endemic areas. . Other researchers confirmed that 60 cutaneous Leishmaniasis patients aged 3-71 years were collected from Al-

Diwaniyah Teaching Hospital and the study showed that 35% of them had single lesions and 65% had multiple lesions. According to the location of the lesion, 50% of patients had facial lesions, 30% upper limbs, and 20% lower limbs (Abdul-Reda, 2019). Researchers (Al-Waaly and Shubber, 2020) show that among 4,276 samples taken from people admitted to Al-Diwaniyah Teaching Hospital, 1,489 cases of cutaneous Leishmaniasis were confirmed in 2018 after external diagnosis by a specialist. It was also explained that there were 800 cases of injuries in men and 689 cases in women. In the study of the city of AlKut (Alhachami *et al.,* 2024), which showed the prevalence of infections in this governorate by collecting 230 samples from Al Karama Teaching Hospital and Al Zahra Teaching Hospital the results were 6.95% and the prevalence of infections in 15-40 year olds was 10.07%, in men 7.87%. and female 5.82%. In addition, infection rates increased in January and February (16.37% and 13.79%) during the rest of the months defined in the study. The infection rate of rural and semi-rural population increased (8.38%) compared to urban or civilized population (3.17%).

Diagnostic Method of Leishmaniasis

Several methods have been used to identify Leishmania parasites in skin lesions of human patients, including histological examinations, rectal smears, cultures, and serological tests (Al-Bajalan et al., 2018, 2021). However, only a few studies have used PCR to examine and identify the specific Leishmania strains seen in human skin lesions. A phylogenetic study was conducted at a United States military base in southern Iraq to investigate the occurrence of several Leishmania species in sandflies. The investigation was conducted using molecular and phylogenetic methods (Al-Bajalan et al., 2018, 2021). Several studies conducted all over Iraq for the period 2011, 2012 and 2013 established that men were most vulnerable to the occurrence of CL compared to women. From the findings, the highest number of cases was reported among those in the age bracket of five to fourteen and fifteen to forty-five. Moreover, more than fifty percent of cases were reported from regions with ground elevation below 2,000 meters having moderate annual precipitation, and a large rural population (Al-Warid et al. , 2017). Justification for this research was done between the years 2014 and 2017 with several researches being conducted to assess the risk of occurrence of Cutaneous Leishmaniasis (CL) in Iraq. These research used study of the cytochrome b gene sequence and specifically the investigation of the epidemiological, molecular and phylogenetic aspects of the species. In the study findings it was noted that the CL cases in the border of northern and central Iraq were mainly as a result of L. major parasite. These outcomes established the genetic association between the L. major strain found in Iraq and the L. major MRHO/IR/75/ER strain reported in Iran. A research reveals Diyala province bears the highest incidence rates for visceral and cutaneous Leishmaniasis from years 2014 till 2017 with 21. 91% and 13. 85% respectively for prevalence rates. This happened in the backdrop of the warfare that resulted in the displacement of a significant percentage of the population in Diyala (Lehlewa et al. , 2021). 51% with the most common age group being 1-4 years representing 62% of the patients. 04%. By comparing the ages of patients with cutaneous leishmaniasis found in this study with those of other studies, it can be observed that the age range most significantly affected was between 5-14 years, with a proportion of 37%. 81%. The study done by Ali et al (2018) was helpful in triangling data on the parasitic diseases which enabled the authors to offer important information for methodological approaches aimed at tackling the scourge in Iraq. In a cross-sectional study, Modey et al. focused on US troops in Iraq diagnosed with VL between 2015 and 2017. They used enzyme-linked immunosorbent assay (ELISA), rk39 test strip, quantitative polymerase chain reactant (PCR) and interferon-gamma release assay (IGRA) in their study. The prevalence of VL was 19 confirmed via microscopy and/or culture in the splenic aspirate. 5% of the soldiers who took part in the OIF during a visit to a country in northern Iraq, which has been established to have a link with infection (Mody et al. , 2019; Ibiapina et al. , 2022). Some recent investigations carried out by Iraqi researchers discussed the present epidemiological and clinicopathological study in order to enhance characterisation of Leishmania species associated with CL diseases in patients of Iraq. This was done using sequencing analysis of the Internal Transcribed Spacer 1 (ITS1) in the Waist province. The results revealed a high proportion of cutaneous Leishmaniasis of 83. 3% with gender as a significant parameter the

results obtained were significant at 0. 001**level of significance. Similarly, males were more probable to have CL as 56. 4% while females as 43. The authors suppositions were that the conflict witnessed the popularization and increased expression of CL and its prevalence areas with little health care facilities (Ali et al. , 2018). The Iraqi study identified that the principal species of Leishmania that leads to Leishmaniasis in Iraq is Leishmania major. Immunocompromised individuals have spontaneous healing of lesions, which results in the formation of depressed scars.

Treatment and prevention

Taken together, the results provided point towards the risks of Leishciania parasites and the vectors in the free zones and other neighboring countries inclusive of Saudi Arabia, Turkey, Jordan, and Iran. Sodium stibogluconate which has pentavalent antimony is the only licensed drug for CL in Iraq as recommended by the ministry of health (Lehlewa et al. , 2021). Therefore, further and long-term studies are required to determine value of the long proposed treatment algorithms for visceral and cutaneous Leishmaniasis and to improve the quality and standardization of treatment of these neglected diseases.

Prevention and Control

Preventing and managing diseases To prevent the transmission of leishmaniasis, many intervention measures are necessary. as it manifests inside an intricate biological system including of a human or animal host, parasites, and a vector, in the following manner: 1. Prompt identification and swift intervention of infection can significantly decrease the occurrence of illness and avert harm or fatality. Presently, there exist efficacious and secure medications that can function as Leishmania therapeutics, particularly in cases of visceral Leishmaniasis, but their administration can be challenging. Vector control is an effective method for mitigating the spread of infectious illnesses by decreasing the number of sand flies. Control strategies encompass pesticide spraying indoors or at the site, use of insecticide-treated bed nets, environmental management, and personal protection. 3. Timely and precise monitoring of the disease can facilitate the implementation of effective healthcare and behavioural interventions during epidemics, as well as the treatment of cases with high fatality rates. 4. Implementing reservoir host control can be highly successful, particularly in cases of zoonotic transmission.

Conclusions

Leishmaniasis is a complex clinical syndrome that is difficult to diagnose and treat. Advances in vaccine development, diagnosis, reporting and treatment can prevent significant morbidity and mortality from this disease.

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