مجلة الدراسات التربوية والعلمية - كلية التربية - الجامعة العراقية
العدد الخامس والعشرون - المجلد الثاني عشر - علوم الحياة - آب 2025 م
doi.org/10.52866/esj.2023.12.25.12

Epidemiological Study of Cutaneous Leishmaniasis in Iraq between 2015 to 2020

Maha Mustafa Assem[1], Ghuffran Muhammed Hassan[2], Dalya Falih Ahmed[3], Ihab Raqeeb Aakef[4]
Ibn Sina University of Medical and Pharmaceutical Sciences, Baghdad, Iraq[1]
Department of Biology, College of Science, University of Baghdad[2]
Department of Biotechnology, College of Applied Science, AL-Fallujah University [3]
Communicable Diseases Control Center/ MoH/ Baghdad/ Iraq4
***Corresponding author** ghufran.muhammed@sc.uobaghdad.edu.iq

Abstract :

Objective: Cutaneous leishmaniasis (CL) caused by infection with a parasitic protozoan called Leishmania. Incidence of the disease ranging from painless single sore to severe chronic lesions, using classical drugs may demonstrate resistance or not to the treatment. Coordination between parasitic species, early immune responses and environmental parameters, play pivotal role in the development of lesions. Iraq is one of the six most endemic countries in the world. Because of the medical importance of the parasite, this study elucidates the valiance of CL in Iraq within a time frame spanning from 2015 to 2020.

Materials and Methods: The Communicable Diseases Control Center (CDC), under the Ministry of Health, in Baghdad, Iraq, compiled data from all 18 province hospitals on patients admitted to Iraqi hospitals between 2015 and 2020. The clinical record was captured like gender, and age, as well as their annual and month-by-month recorded patterns.

Results: A total of 81099 CL patients were reported during the said period. They were included (44544 male and 36555 female). Additionally, in 2017 the majority (7207) of these CL patients were in the age group of 15– 45 years ($p < 0.5$), and the lowest number was reported in 2019 in the age group of less than one year. Significantly, a consistent and comprehensive record of these patients was maintained on an annual and monthly basis, providing valuable insights on the prevalence of CL in Iraq.

Conclusions: The current findings suggest that CL is widespread in Iraq. Given the recent surge in human immigration, it is imperative to establish effective and sustainable monitoring systems for communicable diseases (CDs) and improve control methods accordingly.

Recommendations: Eradication of sand flies annually in September and October to minimize the number of infections, as well as getting rid of stray dogs (must be), Eradication of wild rodents in farms is not only a problem for cutaneous leishmaniasis, but these animals are big problems for poultry farms and agriculture farms. Educational and media programs about how to protect people from this disease and avoid infection and utilize immunological and molecular techniques to diagnose and differentiate between parasite species and to help identify appropriate treatments.

Keywords: Cutaneous leishmaniasis, demographic, *Leishmania major, Leishmania tropica*, prevalence.

دراسة وبائية لداء الليشمانيات الجلدي في العراق بين الاعوام 2015 و2020

مها مصطفى عاصم[1] ، غفران محمد حسان[2] ، داليا فالح أحمد[3] ، إيهاب رقيب عاكف[4]
[1] جامعة ابن سينا للعلوم الطبية والصيدلانية، بغداد، العراق
[2] جامعة بغداد، كلية العلوم، قسم علوم الحياة، بغداد، العراق
[3] جامعة الفلوجة، كلية العلوم التطبيقية، قسم التقنيات الاحيائية، الانبار، العراق
[4] وزارة الصحة، دائرة الصحة العامة، مركز السيطرة على الامراض الانتقالية/ بغداد/ العراق.

مستخلص:

خلفية البحث: داء الليشمانيات الجلدي (CL) ناتج عن عدوى بطفيلي أولي يُسمى الليشمانيا. يتراوح معدل الإصابة بالمرض بين قرحة واحدة غير مؤلمة الى آفات مزمنة شديدة، وقد يُظهر استخدام الأدوية التقليدية مقاومة للعلاج من عدمه. تلعب العلاقة ما بين الأنواع الطفيلية، والاستجابات المناعية المبكرة، والمعايير البيئية دورًا محوريًا في تطور الآفات. يُعد العراق من أكثر الدول الست توطنًا بهذا المرض في العالم. ونظرًا للأهمية الطبية لهذا الطفيلي، تُلقي هذه الدراسة الضوء على ثبات معدل الإصابة بداء الليشمانيات الجلدي (CL) في العراق خلال الفترة الزمنية الممتدة من عام 2015 إلى عام 2020.

المواد وطريقة العمل: تم الحصول على البيانات الإحصائية من مركز السيطرة على الأمراض الانتقالية (CDC)، التابع لوزارة الصحة العراقية في بغداد والتي تم جمعها من جميع مستشفيات المحافظات الثمانية عشر بين عامي 2015 و2020.

النتائج: تشمل هذه البيانات: الجنس والعمر، والحالات المسجلة سنويًا وشهريًا. حيث شملت نتائج الدراسة الحالية 81099 مريضاً بداء الليشمانيات الجلدي (CL) بين الأعوام من 2015 و2020 من بينهم 44544) ذكر و36555 انثى). بالإضافة إلى ذلك، في 2017 تم تسجيل غالبية حالات الإصابة داء الليشمانيات الجلدي (CL)(7207) في الفئة العمرية 45–15 سنة ($P < 0.5$)، في حين تم تسجيل في 2019 أقل عدد في الفئة العمرية أقل من سنة واحدة. ومن الجدير بالذكر أنه تم الحفاظ على سجل ثابت وشامل لهؤلاء المرضى على أساس سنوي وشهري، مما يوفر رؤى قيمة حول مدى انتشار داء الليشمانيات الجلدي (CL) في العراق.

الاستنتاج: تشير النتائج الحالية إلى أن داء الليشمانيات الجلدي (CL) منتشر على نطاق واسع في العراق ونظرا للزيادة الأخيرة في الهجرة البشرية، من الضروري إنشاء أنظمة رصد فعالة ومستدامة للأمراض المعدية وتحسين أساليب مكافحتها وفقاً لذلك.

التوصيات: القضاء على ذبابة الرمل سنويًا في شهري سبتمبر وأكتوبر لتقليل عدد الإصابات، والتخلص من الكلاب الضالة (أمرٌ لا مفر منه). لا يقتصر القضاء على القوارض البرية في المزارع على مشكلة داء الليشمانيات الجلدي فحسب، بل تُشكل هذه الحيوانات أيضًا مشكلة كبيرة لمزارع الدواجن والمزارع الزراعية. يجب وضع برامج تثقيفية وإعلامية حول كيفية حماية الناس من هذا المرض وتجنب العدوى، واستخدام التقنيات المناعية والجزيئية لتشخيص أنواع الطفيليات والتمييز بينها، والمساعدة في تحديد العلاجات المناسبة.

الكلمات المفتاحية: داء الليشمانيات الجلدي، التوزيع الديموغرافي، *Leishmania major, Leishmania tropica* ، نسبة الانتشار.

1. Introduction

Leishmania are protozoan parasites that, in nature, are transmitted by the bites of sandflies. In the tropical and semi-tropical areas of the world, leishmaniasis described as a health problem, because it was reported 350 million cases annually [1, 2] . Leishmaniasis can manifest in one of three forms: Cutaneous Leishmaniasis (CL), Mucocutaneous Leishmaniasis (MCL), or Visceral leishmaniasis (VL) depending on the infecting species involved and the host's immune response [3]. The presently available treatment choices are associated with several restrictions, including side effects, cost, poor efficacy, and the need for multiple injections. The main medical therapies for leishmaniasis are the use of sodium stibogluconate, a drug containing antimony, and amphotericin B, a prescription with antifungal properties [4, 5]. Despite the potential for underreporting, the current estimates for the prevalence of cutaneous leishmaniasis (CL) can be reached to 1.2 million cases annually. Approximately 96% of these instances are concentrated in the Americas, the Mediterranean basin, the Middle East, and Central Asia. The current yearly estimates for visceral leishmaniasis (VL) are around 100,000, a substantial reduction from previous predictions of 400,000. Over 95% of reported cases are from Brazil, Ethiopia, China, India, Kenya, Somalia, Nepal, and Sudan, according to the World Health Organization (WHO) [6, 7]. More than 20 species of the *Leishmania* parasite have been identified. These parasites are spread by over seventy different varieties of phlebotomine sand- flies. These sandflies belong to the Diptera family of Psychodidae, which is further classified into *Phlebotomus* in the old world and *Lutzomyia* in the new world [5, 8]. During their life cycle, the female phlebotomine sand fly, primarily active during nocturnal periods, transmits the leishmaniasis parasite to humans or other animal reservoirs. When a blood meal is taken from an infected person, the blood contains an amastigote phase that turns into a promastigote phase. The promastigote form possesses a flagellum, which enables it to move into the intestines of the sand fly (Fig. 1) [9,10, 11]. Leishmaniasis is traditionally

understood as a disruption in the equilibrium between T helper 1 (Th1) and T helper 2 (Th2) (12). People with a primary Th1 response are very good at getting rid of parasites and have low levels of parasitemia. However, they are more likely to get mucocutaneous disease because their immune systems are overactive and cells are being destroyed[13, 14]. But those with a Th2 response have an increased parasite load as antibody neutralization is incapable against the intracellular parasite[12, 15].

Leishmania tropica, Leishmania major, and *Leishmania aethiopica* species are the causes of it. Rural areas suffer more CL than urban ones do. The incubation period is 2-8 weeks. Symptoms of CL vary depending on parasite species and the patient's immune system. Cutaneous leishmaniasis begins as an erythematous papule that develops into a nodule, then ulcerates and crusts over the boundary [16, 17]. Cutaneous leishmaniasis, is common across Iraq, except for the three governorates in the northeast, bordering Turkey and Iran, where cases are rare. While Iran and Syria reported a higher incidence of more than 5000 new cases, Iraq is in the high endemic area, with a range of 1000-4999 new cases recorded in 2013, along with Turkey, Saudi Arabia, and Kuwait [18, 19]. The major method of diagnosing CL in an endemic area is clinical appearance, which is consider clouded in non-endemic areas (20). Additionally, a secondary infection or improper care might change the clinical picture of CL, making a diagnosis challenging and prolonging treatment. When this occurs, the diagnosis should be verified using histological analysis, culture, and inspection of smears from the lesion [21]. Laboratory equipment such as ELISA test kits and PCR technique, are limited in developing countries such as Iraq. As a result, dermatologists must mostly depend on the clinical characteristics of the lesion. A quick way to diagnose is with Giemsa- or Leishman-stained smears taken from the lesions [21]. Consequently, the World Health Organization (WHO) focused on research projects which deals with the control of CL in endemic countries [22]. Both CL and VL are present in Iraq. Following the Second Gulf War in 1992, the number of CL cases reported reached its highest level, reaching 45.5

cases per 100,000 persons [23]. When Islamic state of Iraq and Syria (ISIS) captured large portions of Iraq in 2014, the health system collapsed, and infection statistics resumed their downward trajectory. Furthermore, with the internal displacement of people, infectious diseases had a fair opportunity of spreading to other places [24]. There has been an increase in the occurrence of leishmaniasis in recent years. The numbers are expected to continue increasing as a result of heightened human mobility, which includes travel and involuntary migration. This is further compounded by the growth of reservoir host populations, as well as the expansion and spread of vector species due to climate and habitat changes, urbanization, and globalization [25, 26]. The study's objectives are to identify the prevalence and epidemiology of CT in all of Iraq's governorates.

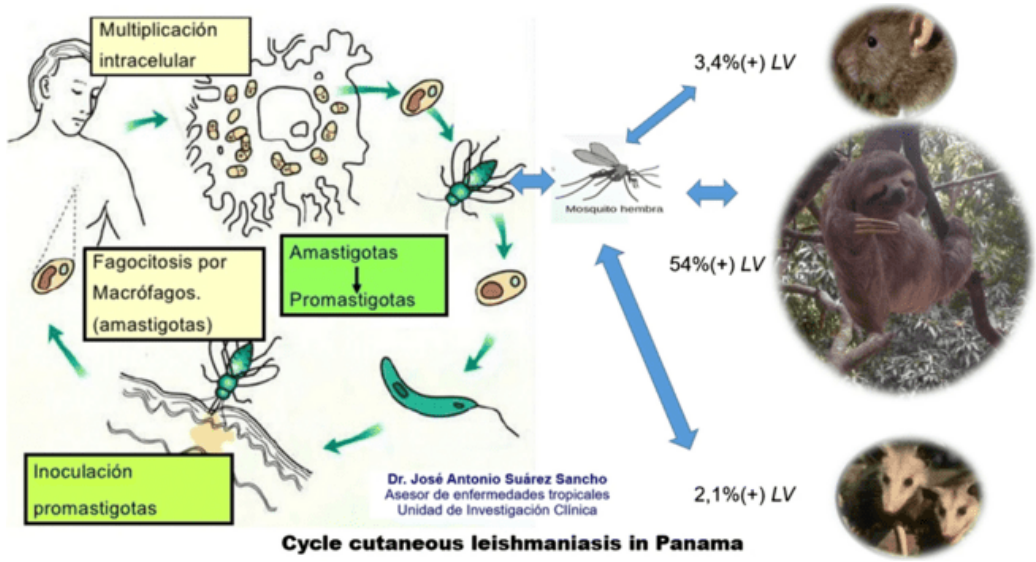

Figure (1): Leishmaniasis life cycle [27].

2. Materials and Methods

2.1. Study description

The retrospective study has included the analysis of the reported cases of cutaneous leishmaniosis. The study used the available surveillance database for the disease from the Center for Disease Control and Prevention (CDC) in Iraq, under the Ministry of Health, in Baghdad, Iraq, and compiled the data

from all of the 18 provinces hospitals on patients admitted to Iraqi hospitals between 2015 to 2020.

2.2. Diagnosis of Cutaneous Leishmaniasis

Parasitological techniques are widely used for diagnosing leishmaniasis by visually detecting the presence of *Leishmania* amastigote forms in affected tissues [28]. Although these approaches are extremely specific for detecting leishmaniasis, they lack sufficient sensitivity [29]. Furthermore, these approaches lack the ability to differentiate between several *Leishmania* species. In clinical practice, the sample is obtained via biopsy, punch, or scrape from mucosal or cutaneous lesions. For skin ulcers , it is advisable to employ scrapings and cytology brushes as an alternative to the more intrusive biopsy procedure [30, 31]. Furthermore, the most sensitive, quick, cheap method is press-imprint-smear method. The smears undergoes to air dried, fixed in methanol, stained with Giemsa, and examined microscopically using oil immersion lens [32, 33]. In this study, the sample sent for a microscopic examination where amastigotes were found.

2.3. Statistical Analysis:

ArcGIS version 10.4 was used to map geospatial and related demographic information. The Statistical Analysis System (SAS 2018) program was used to detect the effect of different factors on study parameters. A chi-square test was used to significantly compare between percentages (0.05 and 0.01 probability) in this study [34].

3. Results and Discussion

3.1. Relationship between gender and the infection with cutaneous leishmaniasis

In this study, from 2015 to 2020 it was shown that there was a higher incidence of infection in males (44544) than in females (36555), and there were highly significant differences (0.0001**) as shown in table (1) and figure (2).

Table 1: Relationship between gender and the infection with cutaneous leishmaniasis, (refers to statistical difference where p-value ≤ 0.0001)**

Year	Males with CL	Females with CL	P-value
2015	9025	8500	** 0.0001
2016	9859	7707	** 0.0001
2017	10604	8250	** 0.0001
2018	6353	5073	** 0.0001
2019	3905	3151	** 0.0001
2020	4798	3874	** 0.0001
Total	44544	36555	** 0.0001
P-value	** 0.0001	** 0.0001	---
.(P≤0.01) **			

3.2. Cutaneous leishmaniasis distributed according to the age groups.

Regarding the age groups, the present study indicated that the infection rate of cutaneous leishmaniasis (2015) was highest in the age group (5–14), while in 2016–2017-2018–2019–2020, the infection rate was highest in the age group (15–45), with highly significant differences (P≤0.01) as shown in table (2).

Table 2: Cutaneous leishmaniasis distributed according to the age groups, (refers to statistical difference where p-value ≤ 0.0001)**

Year	Less than one year	year (1-4)	(5-14) year	(15-45) year	more than 45 years	P-value
2015	659	SD 3810±	6924	5231	901	** 0.0001
2016	584	3403	6174	6382	1039	** 0.0001
2017	761	3671	5655	7207	1560	** 0.0001
2018	485	2192	3785	4197	767	** 0.0001
2019	371	1480	2166	2399	550	** 0.0001
2020	508	1947	2607	2924	610	** 0.0001
P-value	** 0.0001	** 0.0001	** 0.0001	** 0.0001	** 0.0001	---

3.3. Relationship between province and year with cutaneous leishmaniasis

According to this study, the rate of CL infection in 18 Iraqi provinces from 2015 to 2020 was as follows: in 2015, 2016, 2017, 2018, 2019, and 2020, the rate of infection was higher in Diyala (4460, 2621, 4250, 3372, 2386, and 3798), with very big differences between years; in 2016, the rate of infection was highest in Thi-Qar (2828). All previous cases were tested using Giemsa-smeared with two types of lesions: wet and dry.

Table 3: Relationship between province and year with cutaneous leishmaniasis, (refers to statistical difference where p-value ≤ 0.0001)**

Governorate	2015	2016	2017	2018	2019	2020	P-value
Baghdad/Al-karkh	232	334	220	132	90	146	** 0.0002
Baghdad/Al-Rusafa	473	277	219	106	74	202	** 0.0001
Al-Basra	139	142	82	108	38	27	** 0.0001
Ninewa	105	1578	3365	1225	852	710	** 0.0001
Maysan	1982	653	392	286	433	263	** 0.0001
Al-Qadissiya	1362	2266	859	447	162	184	** 0.0001
Diyala	4460	2621	4250	3372	2386	3798	** 0.0001
Al-Anbar	62	285	2891	1675	344	415	** 0.0001
Babylon	323	660	536	216	165	488	** 0.0001
Kerbela	439	1065	992	444	171	138	** 0.0001
Kirkuk	337	960	1095	494	419	462	** 0.0001
Wassit	1120	277	329	378	169	449	** 0.0001
Thi-Qar	3927	2828	693	411	178	71	** 0.0001
Al-Muthanna	687	776	217	312	528	149	** 0.0001
Salah Al –Din	370	1125	1194	867	576	1030	** 0.0001
Al-Najaf	699	1123	637	197	316	129	** 0.0001
Erbil	31	385	151	95	12	4	** 0.0001
Duhouk	10	13	3	13	29	6	* 0.049
Al-Sulaimaniya	767	198	729	648	114	1	** 0.0001
P-value	0.0001 **	0.0001 **	0.0001 **	0.0001 **	0.0001 **	0.0001 **	---
.(P≤0.05), ** (P≤0.01) *							

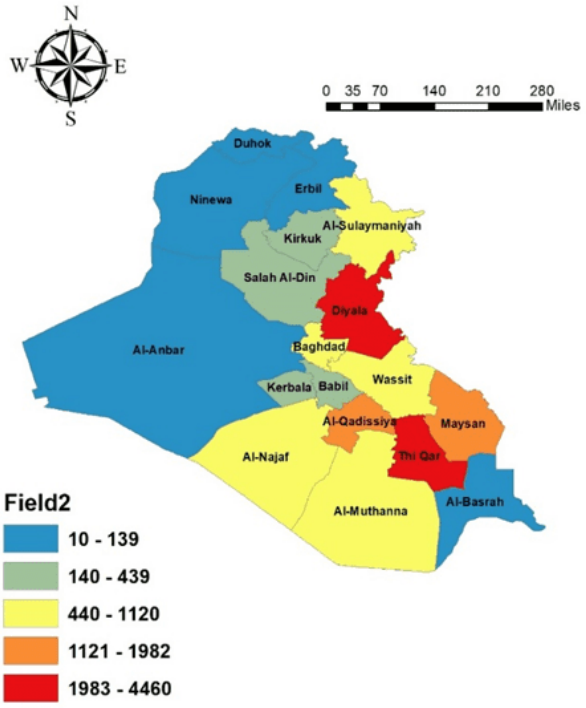

Figure 2: Distribution of Cutaneous Leishmaniasis (CL) in Iraqi governors in 2015 (CDC) in Iraq.

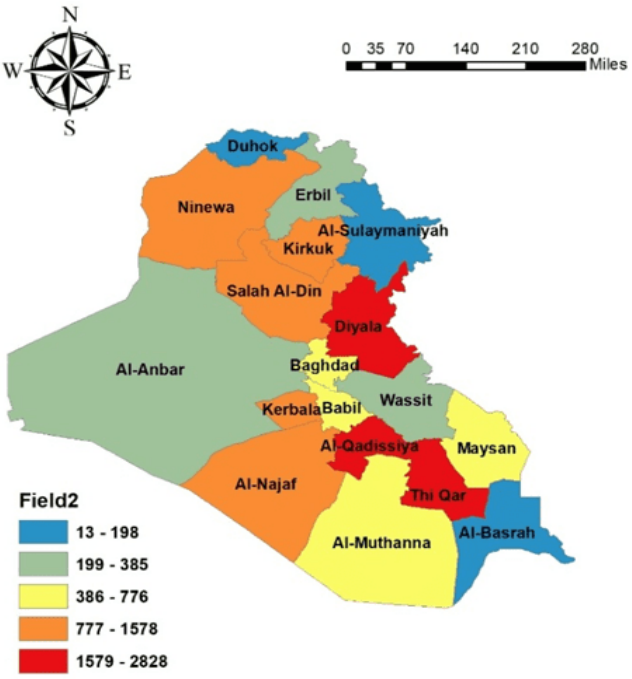

Figure 3: Distribution of Cutaneous Leishmaniasis (CL) in Iraqi governors in 2016 (CDC) in Iraq.

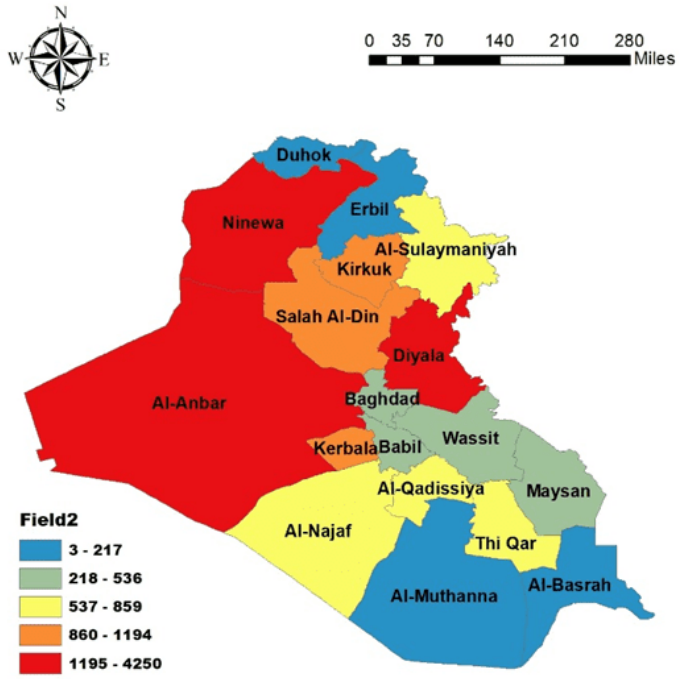

Figure 4: Distribution of Cutaneous Leishmaniasis (CL) in Iraqi governors in 2017 (CDC) in Iraq.

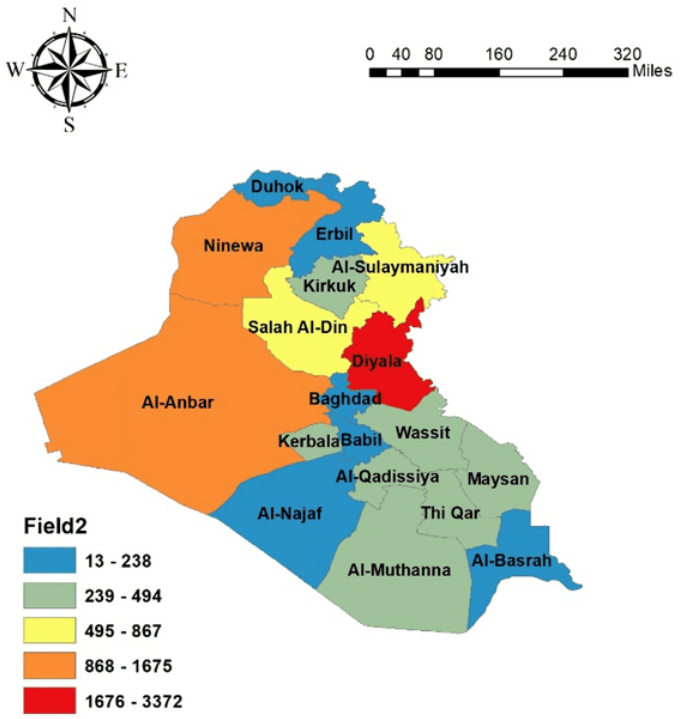

Figure 5: Distribution of Cutaneous Leishmaniasis (CL) in Iraqi governors in 2018 (CDC) in Iraq.

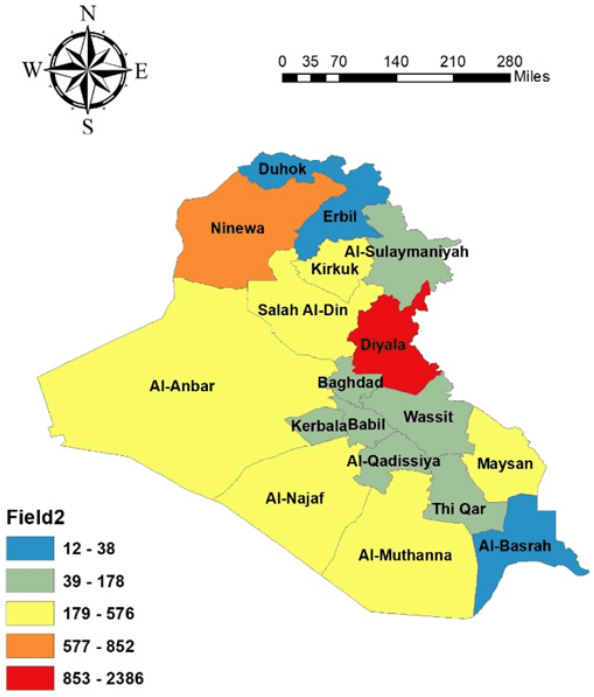

Figure 6: Distribution of Cutaneous Leishmaniasis (CL) in Iraqi governors in 2019 (CDC) in Iraq.

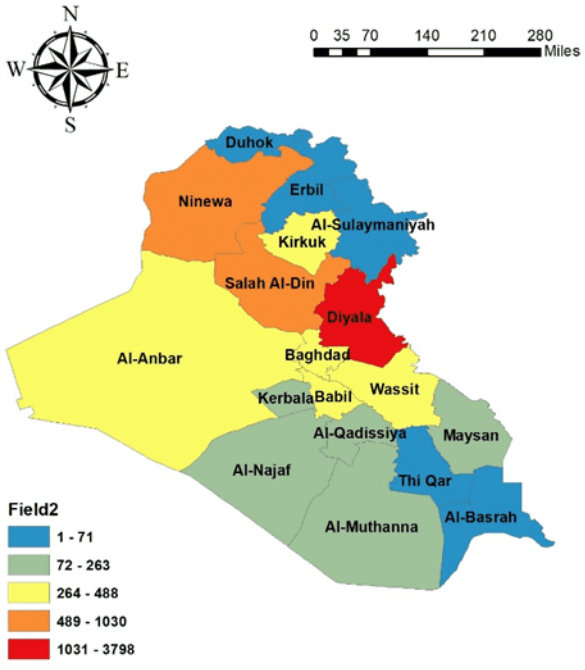

Figure 7: Distribution of Cutaneous Leishmaniasis (CL) in Iraqi governors in 2020 (CDC) in Iraq.

Cutaneous leishmaniasis is prevalent in Iraq, with cases of cutaneous forms of the illness being documented for all Iraqi governors, as shown in figure maps (Figures 2 to 7). In the five years from 2015 to 2020, several techniques and instruments have been created to detect, measure, and classify the parasite belonging to the genus *Leishmania*. Despite the progress made in these techniques, the accuracy and precision of leishmaniasis diagnosis have been enhanced. However, there are certain obstacles that need to be addressed [35, 36]. Because of the environment in Iraq, both *Leishmania major* and *Leishmania tropica* are the main causes of CL. Annual outbreaks of leishmaniasis are a common illness in Iraq [23]. The term "Baghdad boil or Oriental sore" is commonly used to refer to this particular medical problem, indicating its extensive historical presence within the region of Iraq [37]. Consequently, a significant number of substantial cases have been documented. As a result of the collaborative efforts between the WHO and the Iraqi Ministry of Health, there has been a notable decline in the incidence of CL in Iraq. Furthermore, disease control protocols need to be established [38]. The outcome of *Leishmania* infection depends on the delicate balance of pro- and anti-inflammatory immune responses produced by the host. The innate and adaptive immune systems are closely interconnected, as the cytokines generated by innate immune cells play a crucial role in determining the extent and result of the adaptive immune response [14, 39].

The number of officially reported cases decreased from 2978 in 2011 to 1648 in 2013 [40]. The current study's findings corroborate prior research indicating a higher prevalence of infection among males compared to females [41,42,43]. This aligns with another study that revealed that men are more exposed to infection compared to women because men cover their bodies less than women, in addition to seasonal migration for factory or farm work, which explains increasing contact with sandflies [44]. Previous studies conducted in Turkey and Iraq/Baghdad have indicated a higher proportion of females, with percentages of 53.84% and 56%, respectively [45, 46].

The observed variations can be described as disparities in the study's methodology, the magnitude of the sample, the specific demographic under investigation, and prevailing meteorological circumstances. Moreover, within our societal context, the limited engagement in outdoor activities and the adoption of more modest dress choices among females are influential factors that contribute to the comparatively lower incidence rates observed within this demographic. Consequently, it is more probable for males to come into occupational contact with sand fly vectors in outdoor environments [16, 40, 45, 46].The potential association between gender and parasite infection remains uncertain, as it is unclear whether other hormonal or physiological factors contribute to the observed disparity. Furthermore, the current study findings indicate a higher prevalence of leishmaniasis infection among individuals classified as employees compared to those who are not employed. This observation might be attributed to an elevated susceptibility to vector insect exposure when individuals are engaged in outdoor activities [47,48].

The present study revealed a higher prevalence of instances in individuals aged more than 14 years (Table 2). Results of this study came in agreement with previous studies done in Iran (31.6% in the age group less than 10 years) [49]. In similar vein, a study conducted in Baghdad, Iraq, revealed that the age groups of 5–14 and 15–45 years exhibited a higher susceptibility to cutaneous leishmaniasis (CL). The observed variations in these studies could potentially be associated with the specific school and occupational age groups of males and females in Iraq. It is reasonable that individuals within these age groups, regardless of gender, are more inclined to engage in outdoor activities and consequently encounter environmental conditions conducive to sandfly exposure, as compared to individuals from different age groups [50]. The results of the current study came in disagreement with a previous study done by (Norouzinezhad *et al.,* 2016), which found that the highest occurrence of CL occurred in the age groups less than 9 years old. (Norouzinezhad *et al.,* 2016), conclude this may be because children of this

age play outdoors; that's why they increase their chance of infection [22]. The southern and eastern regions of Iraq exhibited the highest incidence of CL infections throughout the period spanning from (2015 to 2020). Diyala and Salahuddin recorded the highest incidence of insect bites, which then developed into CL. That's because of the distribution of houses, which are made of clay (Table 3). Clay maintains a sufficient level of moisture in the sandfly larval habitat, so these houses facilitate sandfly breeding [51]. An engaged and vigilant global community has the potential to reverse the adverse effects on human health caused by political instability, violence, and conflicts. The collaboration between governments and non-governmental organizations in the past has successfully eliminated life-threatening and incapacitating diseases such as smallpox and polio. Control and elimination of leishmaniasis necessitate comparable measures [23, 52].

4. Conclusions

This study reveals a higher proportion of CL in rural regions, among pediatric populations, and among individuals of male sex. This condition primarily impacts the facial region. Despite a decrease in the prevalence of the disease, cutaneous leishmaniasis (CL) continues to be a significant public health concern, necessitating the implementation of disease control measures.

References

1. Hepburn NC. Cutaneous leishmaniasis: an overview. Journal of postgraduate medicine. 2003;49(1):50.

Ismail HH, Hasoon SA, Saheb .2
EJ. The anti-Leishmaniasis activity of green synthesis silver oxide nanoparticles. Annals of Tropical Medicine and .Health. 2019;22:28-38

3. Torres-Guerrero E, Quintanilla-Cedillo MR, Ruiz-Esmenjaud J, Arenas R. Leishmaniasis: a review. F1000Research. 2017;6.

4. Neamah SD, Ali HZ, Al-Halbosiy MM. Artemisinin Efficacy on iNOS Production in U937 Cell-line Infected with Leishmania donovani. Iraqi Journal of Science. 2023:525-35.

5. Abdullah MS, Alqaisi AQI. Evaluating the in vitro anti-Leishmanial activity of essential oil extracted from

Cymbopogon Citratus against Leishmania Donovani. Iraqi Journal of Science. 2022:1453-63.

6. Ikedionwu CA, Dongarwar D, Williams C, Odeh E, Peh MPN, Hooker H, et al. Trends and risk factors for leishmaniasis among reproductive aged women in the United States. International Journal of Maternal and Child Health and AIDS. 2021;10(2):166.

7. Ruiz-Postigo JA, Jain S, Mikhailov A, Maia-Elkhoury AN, Valadas S, Warusavithana S, et al. Global leishmaniasis surveillance: 2019-2020, a baseline for the 2030 roadmap/Surveillance mondiale de la leishmaniose: 2019-2020, une periode de reference pour la feuille de route a l'horizon 2030. Weekly epidemiological record. 2021;96(35):401-20.

8. Farrar J, Hotez PJ, Junghanss T, Kang G, Lalloo D, White NJ, et al. Manson's Tropical Diseases E-Book: Elsevier health sciences; 2023.

9. Hussein, A.M. and Ali, H.Z., 2022. Detection of TNF Alpha level as biomarker in different stages of cutaneous leishmaniasis infection. *Iraqi Journal of Science*, pp.3313-3321.

10. Organization WH. Manual of procedures for leishmaniases surveillance and control in the Americas. Pan American Health Organization. 2019.

11. González C, Wang O, Strutz SE, González-Salazar C, Sánchez-Cordero V, Sarkar S. Climate change and riskof leishmaniasis in North America: predictions from ecological niche models of vector and reservoir species. PLoS neglected tropical diseases. 2010;4(1):e585.

12. Scott P, Novais FO. Cutaneous leishmaniasis: immune responses in protection and pathogenesis. Nature Reviews Immunology. 2016;16(9):581-92.

13. Mandell G. Mandell, Douglas and Bennett's Principles and Practice of Infectious Diseases. 2000.

14. Mahamdallie SS, Ready PD. No recent adaptive selection on the apyrase of Mediterranean Phlebotomus: implications for using salivary peptides to vaccinate against canine leishmaniasis. Evolutionary Applications. 2012;5(3):293-305.

15. Hassan GM, Ali HZ, Hussein WM. Evaluation of IL-8, nitric oxide and macrophage inhibitory factor as clinical circulatory markers in patients

with cutaneous leishmaniasis, before and during sodium stibogluconate treatment. Cytokine. 2024;173:156450.

16. Al-Obaidi MJ, Abd Al-Hussein MY, Al-Saqur IM. Survey study on the prevalence of cutaneous leishmaniasis in Iraq. Iraqi Journal of Science. 2016:2181-7.

17. Ahmed ME, Mousa IS, Al-Halbosiy MM, Jabar E. The anti-Leishmaniasis activity of Purified Bacteriocin Staphylococcin and Pyocin Isolated from Staphylococcus aureus and Pseudomonas aeruginosa. Iraqi Journal of Science. 2018:645-53.

18. Organization WH. Investing to overcome the global impact of neglected tropical diseases: third WHO report on neglected tropical diseases 2015: World Health Organization; 2015.

19. Hassan GM, Ali HZ. Ex vivo study of Anti-leishmanial activity of Artemisinin against Leishmania tropica amastigote. Research Journal of Pharmacy and Technology. 2020;13(8):3787-91.

20. Bari A, Rahman S. Correlation of clinical, histopathological, and microbiological findings in 60 cases of cutaneous leishmaniasis. Indian Journal of Dermatology Venereology and Leprology. 2006;72(1):28.

21. Singh S, Sivakumar R. Recent advances in the diagnosis of leishmaniasis. Journal of postgraduate medicine. 2003;49(1):55.

22. Norouzinezhad F, Ghaffari F, Norouzinejad A, Kaveh F, Gouya MM. Cutaneous leishmaniasis in Iran: results from an epidemiological study in urban and rural provinces. Asian Pacific journal of tropical biomedicine. 2016;6(7):614-9.

23. Salam N, Al-Shaqha WM, Azzi A. Leishmaniasis in the Middle East: incidence and epidemiology. PLoS neglected tropical diseases. 2014;8(10):e3208.

24. Hussein NR, Balatay AA, Saleem ZS, Hassan SM, Assafi MS, Sheikhan RS, et al. A clinical study of cutaneous leishmaniasis in a new focus in the Kurdistan region, Iraq. PloS one. 2019;14(5):e0217683.

25. Riebenbauer K, Czerny S, Egg M, Urban N, Kinaciyan T, Hampel A, et al. The changing epidemiology of human leishmaniasis in the non-endemic country of Austria between 2000 to 2021, including a congenital case.

PLOS Neglected Tropical Diseases. 2024;18(1):e0011875.

26. Ghasemloo H, Rasti S, Delavari M, Doroodgar A. Molecular diagnosis of clinical isolates of cutaneous leishmaniasis using ITS1 and KDNA genes and genetic polymorphism of leishmania in Kashan, Iran. Pakistan Journal of Biological Sciences. 2016;19(3):136.

27. Mann S, Frasca K, Scherrer S, Henao-Martínez AF, Newman S, Ramanan P, et al. A review of leishmaniasis: current knowledge and future directions. Current tropical medicine reports. 2021;8:121-32.

28. Srivastava P, Dayama A, Mehrotra S, Sundar S. Diagnosis of visceral leishmaniasis. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2011;105(1):1-6.

29. Suárez M, Valencia BM, Jara M, Alba M, Boggild AK, Dujardin J-C, et al. Quantification of Leishmania (Viannia) kinetoplast DNA in ulcers of cutaneous leishmaniasis reveals inter-site and inter-sampling variability in parasite load. PLoS neglected tropical diseases. 2015;9(7):e0003936.

30. Reimão JQ, Coser EM, Lee MR, Coelho AC. Laboratory diagnosis of cutaneous and visceral leishmaniasis: current and future methods. Microorganisms. 2020;8(11):1632.

31. Akhlagh A, Salehzadeh A, Zahirnia AH, Davari B. 10-year trends in epidemiology, diagnosis, and treatment of cutaneous leishmaniasis in Hamadan Province, West of Iran (2007–2016). Frontiers in public health. 2019;7:27.

32. Sousa AQ, Pompeu MM, Frutuoso MS, Lima JW, Tinel JM, Pearson RD. Press imprint smear: a rapid, simple, and cheap method for the diagnosis of cutaneous leishmaniasis caused by Leishmania (Viannia) braziliensis. The American journal of tropical medicine and hygiene. 2014;91(5):905.

33. Bayram DM, Ali HZ. Molecular Detection of Suspected Leishmania Isolates Using Polymerase Chain Reaction. Iraqi Journal of Science. 2017:2076-82.

34. Cary N. Statistical analysis system, User's guide. Statistical. Version 9. SAS Inst Inc USA. 2012.

35. Akhoundi M, Kuhls K, Cannet A, Votýpka J, Marty P, Delaunay P, et al. A historical overview of the classification, evolution, and dispersion of Leishmania parasites and sandflies.

PLoS neglected tropical diseases. 2016;10(3):e0004349.

36. Chappuis F, Sundar S, Hailu A, Ghalib H, Rijal S, Peeling RW, et al. Visceral leishmaniasis: what are the needs for diagnosis, treatment and control? Nature reviews microbiology. 2007;5(11):873-82.

37. Nazzaro G, Rovaris M, Veraldi S. Leishmaniasis: a disease with many names. JAMA dermatology. 2014;150(11):1204-.

38. Bayram DM, Hassan GM, Ali HZ. Detection of some CC Chemokine Ligands in Patients with Cutaneous Leishmaniasis. Iraqi Journal of Science. 2022:1431-7.

39. Saidi N, Blaizot R, Prévot G, Aoun K, Demar M, Cazenave PA, et al. Clinical and immunological spectra of human cutaneous leishmaniasis in North Africa and French Guiana. Frontiers in Immunology. 2023;14:1134020.

40. Kumar R, Bumb RA, Ansari NA, Mehta RD, Salotra P. Cutaneous leishmaniasis caused by Leishmania tropica in Bikaner, India: parasite identification and characterization using molecular and immunologic tools. The American journal of tropical medicine and hygiene. 2007;76(5):896-901.

41. Abdul-Hussein A, Yousif AA, Abed OT, Jabbar AA. Cutaneous Leishmaniasis: A clinicoepidemiological Study in Al Muthanna Governorate/Iraq. Al-Anbar Medical Journal. 2023;19(1):30-5.

42. Khamaes ES, Al-Bayati NY, Abbas AH. A Demographic and Epidemiological Investigation of Patients Afflicted with Cutaneous Leishmaniasis in The Diyala Government Region of Iraq. Basrah Journal of Sciences. 2023;41(2):324-36.

43. Cloots K, Burza S, Malaviya P, Hasker E, Kansal S, Mollett G, et al. Male predominance in reported Visceral Leishmaniasis cases: Nature or nurture? A comparison of population-based with health facility-reported data. PLoS neglected tropical diseases. 2020;14(1):e0007995.

44. Zahirnia A, Moradi A, Norozi NA, Bathaii SJN, Erfani H, Moradi A. Epidemiological survey of cutaneous Leishmaniasis in Hamadan province (2002-2007). Avicenna Journal of Clinical Medicine. 2009;16(1):43-7.

45. Akçalı C, Çulha G, İnalöz HS, Savaş N, Önlen Y, Savaş L, et al. Cuta-

neous leishmaniasis in Hatay. Journal of The Turkish Academy of Dermatology. 2007;1(1).

46. Al-Mafraji KH, Al-Rubaey MG, Alkaisy KK. Clinco-Epidemiological Study of Cutaneous Leishmaniasis in Al-Yarmouk Teaching Hospital. IRAQI JOURNAL OF COMMUNITY MEDICINE. 2008;21(3).

47. Salimi M, Shakiba E, Moradi-Asl E, Abbasi-Ghahramanloo A, Khassi K. Classification of cutaneous leishmaniasis patients based on its risk factors using latent class analysis. Tropical Doctor. 2021;51(1):91-5.

48. Al-Bajalan, M.M., Al-Jaf, S.M., Niranji, S.S., Abdulkareem, D.R., Al-Kayali, K.K. and Kato, H., 2018. An outbreak of Leishmania major from an endemic to a non-endemic region posed a public health threat in Iraq from 2014-2017: Epidemiological, molecular and phylogenetic studies. *PLoS neglected tropical diseases*, *12*(3), p.e0006255.

49. Mahnaz T, Katrin K, Amer A-J, Isabel M, Gabriele S, Safar F, et al. Leishmania major: genetic heterogeneity of Iranian isolates by single-strand conformation polymorphism and sequence analysis of ribosomal DNA internal transcribed spacer. Acta tropica. 2006;98(1):52-8.

50. Mendonça SC. Differences in immune responses against Leishmania induced by infection and by immunization with killed parasite antigen: implications for vaccine discovery. Parasites & vectors. 2016;9(1):1-9.

51. Al-Warid HS, Al-Saqur IM, Al-Tuwaijari SB, Zadawi KAA. The distribution of cutaneous leishmaniasis in Iraq: demographic and climate aspects. Asian Biomedicine. 2017;11(3):255-60.

52. Al Hilfi TK, Lafta R, Burnham G. Health services in Iraq. The Lancet. 2013;381(9870):939-48.