

## **Biological Study for Leishmaniasis Cutaneous In Thi-Qar Governorate**

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**Abstract.** General Background: Cutaneous leishmaniasis (CL), a parasitic disease transmitted by sandflies, remains a pressing public health issue in endemic regions. Specific Background: In Iraq, particularly within Dhi-Qar Governorate, CL has shown persistent prevalence, yet comprehensive long-term surveillance is limited. Knowledge Gap: Despite various clinical and diagnostic advancements, there is a lack of regional data analyzing demographic, geographic, and seasonal trends in CL incidence over an extended period. Aims: This study aims to monitor and evaluate the epidemiological patterns of CL in Dhi-Qar from 2020 to 2024 using hospital surveillance data. Results: A total of 3,882 cases were recorded, with a higher prevalence among males (53.16%) and rural residents (52.53%). Children aged 5–15 were the most affected group (41.6%). Infections peaked during winter (40.7%) and were most frequent on lower limbs (43.35%). Novelty: This research represents one of the few longitudinal studies in Iraq detailing the spatial, temporal, and anatomical distribution of CL at the governorate level. Implications: The findings provide critical insights for targeted public health interventions and underscore the need for improved awareness, especially in rural areas, to control disease spread and reduce long-term health impacts.

### **Highlights:**

1. Infection rates were higher among males (53.16%) and in rural areas (52.53%).
2. Children aged 5–15 years had the highest infection rate (41.6%) over the 4-year period.
3. Winter season showed the highest number of cases (40.7%), indicating a seasonal pattern of transmission.

**Keywords:** Cutaneous Leishmaniasis, Dhi-Qar Governorate, Epidemiology, Seasonal Variation, Public Health

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## Introduction

In 190 developing countries, Leishmaniasis, an infectious disease caused by the Protozoa of Genus *Leishmania*, is a significant public health concern. Depending on the specific species causing the infection, *Leishmania* can manifest in one of three main clinical forms. Through genotyping, it has been determined that *Leishmania Infantum* and *L. Chagasi* are essentially the same, originating from imported European strains. Therefore, they should be considered synonymous and addressed in both old world (OW) and new world (NW) regions.

The first clinical form of Leishmaniasis is localized dermal leishmaniasis (CL), which may result in satellite lesions or nodular lymphangitis, leading to one or multiple skin ulcers. The second form is visceral leishmaniasis (VL), a systemic intestinal infection that affects organs like the liver, spleen, and bone marrow, often proving fatal if left untreated. The third type, cutaneous leishmaniasis (CL), does not involve the mucosal areas (Rakhshani, et al., 2017).

A 53-year-old woman, diagnosed with seropositive rheumatoid arthritis in 2000, was initially treated with methotrexate. Due to poor progress, in 2013, she was switched to Adalimumab (an injection every 15 days) in addition to methotrexate (10mg per week). Since then, she has not needed steroids and has responded well to this treatment plan. Recently, she developed mucous, erythematous, and ulcerative lesions in her nasal vestibules and upper lips, causing distortion of her nose. She was referred to the ENT department, where a biopsy revealed a diagnosis of leishmaniasis, confirmed through both Giemsa technology and nested polymerase chain reaction. Despite not traveling to regions where the disease is common, having contact with animals, or a history of insect bites, her Adalimumab treatment was stopped. She was then treated in the infectious disease department with liposomal amphotericin B, which successfully resolved the issue (Khan, et al., 2017).

Leishmaniasis is a disease that is transmitted by sandflies belonging to the genera *Phlebotus* in the ancient world and *Lutzomyia* in the modern world. These flies are part of the Diptera order, Pest class, and Psychodidae family. Sandflies are small insects, around 3mm in length, known for their hopping flight. They have delicate bodies, long legs, dagger-shaped mouthparts, large dark eyes, long antennae, and mouthparts located on the bottom (Hejazi, et al., 2013).

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When bitten by female sandflies, humans can contract one of 20 different species of Leishmania, with the disease being spread by 30 species of sandflies. Humans, as well as domestic animals and wildlife, can act as reservoir hosts for the parasite. Transmission can also occur through the sharing of contaminated needles among infected individuals. Common species of Leishmania include *L. Chagasi*, *L. Infantum*, and *L. Donovan*i. There has been a potential rise in Leishmaniasis cases in urban areas due to the migration of people from unstable regions in the last two decades. Visiting individuals in these regions can also lead to the spread of Leishmaniasis (Anbareen, et al., 2014).

Leishmaniasis, a common clinical type of disease caused by Leishmania parasites, is most prevalent in seven nations: Algeria, Afghanistan, Brazil, Iran, Peru, Syria, and Saudi Arabia, which account for 90% of all cases worldwide. The species of Leishmania vary between the old world (*L. Infantum*, *L. Tropica*, *L. Major*) and the new world (*L. Chagasi*), with different regions affected by different species (Abazid, et al., 2012, Zanetti, et al., 2019).

The disease is zoonotic, primarily found in Spain, India, Bangladesh, Sudan, and Brazil, and is transmitted through the bite of infected sandflies. Symptoms range from self-limiting ulcers to more severe forms like mucocutaneous involvement and a systemic illness known as visceral leishmaniasis. Diagnosis methods include culture, direct visualization, and polymerase chain reaction testing. Treatment typically involves medications like amphotericin B (Akram, et al., 2015, Freire, et al., 2021).

Initially developed for the treatment of rheumatoid arthritis, Biological DMARDs have found utility in addressing a range of autoimmune conditions such as spondyloarthropathies, juvenile idiopathic arthritis, skin psoriasis, Crohn's disease, ulcerative colitis, uveitis, and suppurative hidradenitis (specifically with adalimumab). A notable downside to these medications is their immunosuppressive nature, which heightens susceptibility to opportunistic infections, particularly those caused by mycobacteria. While occurrences of infections from other agents are less frequent, they have been documented in some instances. It is important to recognize that such infections are not isolated to Biological DMARDs; for example, leishmaniasis has been observed in patients treated with traditional steroids and DMARDs. The quandary arises when contemplating reintroducing an immunosuppressant during a rheumatic flare-up, as relapses of leishmaniasis have been noted. Under such circumstances, certain experts advocate for etanercept as the preferred treatment. Furthermore, it may prove beneficial to consider therapeutic alternatives beyond anti-TNF therapies. In any case, it is crucial

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to maintain vigilant monitoring for any signs of leishmaniasis reactivation (Sunyoto, et al., 2015, Carvalho, et al., 2017).

As a result, it is crucial for healthcare providers to promptly evaluate any patient showing skin lesions described in the text and taking immunosuppressant drugs, especially anti-TNF- $\alpha$  for autoimmune rheumatic conditions, for possible leishmaniasis. Additionally, individuals on these medications who travel to areas where the disease is common must be closely monitored for any signs of infection (Martins, et al., 2014, Vink, et al., 2018).

Patients diagnosed with cutaneous leishmaniasis may be treated with an intralesional injection of sodium stibogluconate (SSG) at a concentration of 100 mg/ml, with a volume ranging from 1 to 5 ml every other day for three days per month. Typically, this regimen results in complete healing within two months. However, for larger or multiple lesions, a higher dose and more treatment cycles may be required. In some cases, intramuscular SSG at a daily dose of 800 mg was utilized by Henten et al. 2022 along with intralesional SSG for multiple lesions. Meglumine antimoniate is an alternative medication option and is the preferred treatment in Ecuador. Meanwhile, in Nepal, sodium antimony gluconate is administered intramuscularly at a dosage of 20 mg/kg per day for a period lasting 30 to 72 days for patients with post-kala-azar dermal leishmaniasis (PKDL) (Sunyoto, et al., 2018, van Henten, et al., 2022).

Drug resistance is a significant challenge in the treatment of leishmaniasis, with reports of resistance to sodium stibogluconate (SSG) in cases of visceral leishmaniasis in Nepal. Fortunately, resistance to SSG has not been noted in cases of cutaneous leishmaniasis in the country. The most effective treatment for American cutaneous and mucocutaneous leishmaniasis (ACML) remains uncertain. Since the 1940s, pentavalent antimonial drugs like SSG and meglumine antimonate (Glucantime, MA) have been used, but they are costly, toxic, and uncomfortable for patients. Unfortunately, leishmaniasis tends to be overlooked in wealthier countries, and the available treatments are often toxic and come with severe side effects (Moreira, et al., 2018, Ergönül, et al., 2020).

When compared to parenteral therapy, this method results in higher concentrations at the affected area and fewer side effects throughout the body. Thirty-three cases of cutaneous leishmaniasis were treated with intralesional SSG during the study period. The patients consist of 26 males and 7 females and there were a total of 93 lesions. Within 3 months from treatment onset, 91% (30/33) had completed healing of the cutaneous lesions after an average of 3 treatments (range 1-6). Side-effects were

mild and were mostly pain during injection, with two patients developing mild local site reaction after the injection (Solomon, et al., 2009).

The study aims to monitor cases of cutaneous leishmaniasis in Dhi-Qar Governorate over a period of 4 years and to assess the general situation of the disease spread.

## Method

### A. Sampling and Data Collection

The current research analyzed reported cases of Cutaneous Leishmaniasis using data from the surveillance database of governmental hospitals in Dhi-Qar, Iraq from January 2020 to December 2024.

Data on diseases were collected from primary health centers and hospitals throughout Dhi-Qar province. Physicians in these health facilities conducted the diagnoses. Their diagnostic method involved taking skin lesion smears, air-drying them, fixing with methanol, and staining with Giemsa stain before culturing in NNN media. The collected data were organized into age groups as follows: A (under 1 year), B (1-5 years), C (over 5-15 years), D (over 15-40 years), and E (over 40 years).

### B. Statistical Analysis

In the current study, SPSS (Version 19) was utilized for conducting descriptive statistics, calculating percentages, performing ANOVA, t-tests, Pearson Chi-Square analysis, and identifying results as statistically significant at a significance level of  $P < 0.05$ .

## Results and Discussion

The study aims to monitor cases of cutaneous leishmaniasis in Dhi-Qar Governorate over a period of 4 years and to assess the general situation of the disease spread.

The results of the study during the period from January 2020 to December 2024 showed that the percentage of males is greater than the percentage of females. The percentage of males to the total number of cases infected with Cutaneous Leishmaniasis during the study period (four years) reached 53.16% and the percentage of females reached 46.84%, as shown in Table 1 and Figure 1.

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Patients infected with leishmaniasis display a variety of immune responses. Some show a robust T cell response, characterized by delayed-type hypersensitivity (DTH) and increased levels of interferon  $\gamma$  (IFN $\gamma$ ). On the other hand, some patients may have high levels of antibodies but lack a DTH response. Those with a strong DTH response typically have low levels of parasites in their lesions, as the *Leishmania* species are eradicated by macrophages activated by IFN $\gamma$ , rather than being countered by antibodies. Conversely, individuals who mainly rely on a humoral response struggle to manage the parasite burden (Heras-Mosteiro, et al., 2017).

**Table 1.** Cutaneous Leishmaniasis Recorded Cases in Dhi-Qar Governorate in the period of 2020 to 2024.

No.	Region	Years	Male	Female	Total
1	Dhi-Qar city	2020	351	293	644
2	West of the Dhi-Qar	2021	390	324	714
3	East of the Dhi-Qar	2022	409	334	743
4	North of the Dhi-Qar	2023	446	416	862
5	South of the Dhi-Qar	2024	468	451	919
6	<b>Total Cases</b>		2064	1818	3882

According to Table 2 and Figure 2, the age groups most impacted by cutaneous leishmaniasis are individuals aged 5-15 years, with a total infection rate of 41.6% during the study period. This is followed by the age group over 40 years, with a rate of 26.42%, then the age group from 15 to 40 years, with an infection rate of 18.08%. The least affected group was those aged 1-5 years, with an infection rate of 13.88%.

Samples from skin scrapes, often collected from lesions, are typically looked at under a microscope to help with diagnosis. This approach is fast and affordable, but it doesn't work well for long-lasting lesions. Plus, cultures of these lesions can be contaminated by bacteria and fungi present in biopsy samples. Different species also have varying needs for growth. While isoenzyme electrophoresis can pinpoint certain *Leishmania* species, it takes a lot of time and money, and requires a lot of effort to grow the parasites (Savioli, et al., 2014).

PCR is often the go-to technique for examining clinical samples directly, but monoclonal antibodies can help identify species in cultured strains, too. This method stands out because it's fast and can accurately identify and characterize *Leishmania*'s genetics at the same time. In a study focused on American cutaneous leishmaniasis, PCR showed a remarkable sensitivity of 100%. On the other hand, detecting antibodies might not work as well in cutaneous leishmaniasis cases since there's not much antibody production happening (De Brito RCF, et al., 2020).

**Table 2.** Cutaneous Leishmaniasis Recorded Cases in Dhi-Qar Governorate in the period of 2020 to 2024 (Distributed Based on the Age).

No.	Region	Years	Age (1-5)	Age (5-15)	Age (15-40)	Age (over 40)
1	Dhi-Qar city	2020	78	274	118	174
2	West of the Dhi-Qar	2021	102	303	124	185
3	East of the Dhi-Qar	2022	99	304	134	206
4	North of the Dhi-Qar	2023	122	356	158	226
5	South of the Dhi-Qar	2024	138	378	168	235
6	<b>Total Cases</b>		539	1615	702	1026

Table 3 and Figure 3 show the percentages and numbers of cases of cutaneous leishmaniasis during seasonal changes (seasons of the year). The highest percentages were during the winter season, at 40.7%, followed by the percentages of infection during the spring season, at 23.54%. Then the percentages of infection during the fall and summer seasons, respectively, were 20.09% and 15.66%.

Not all species of *Leishmania* respond to the current treatment options available. As a result, identifying the specific species is crucial for the clinical outcomes of patients with cutaneous leishmaniasis (CL) or mucocutaneous leishmaniasis (MCL) caused by unidentified species. This situation frequently arises in ill travelers, such as backpackers, who have visited multiple regions where leishmaniasis is endemic and where various species with different susceptibility patterns exist. Advances in molecular techniques for identifying *Leishmania* species have revealed new disease manifestations linked to specific parasite species in different parts of the world. For instance, the *L. donovani* complex, typically associated with visceral leishmaniasis (VL), has also been found to cause CL. Additionally, earlier reports have noted the overlap between the clinical presentations of VL and CL in cases of *L. infantum* (Sousa, et al., 2014).

**Table 3.** Cutaneous Leishmaniasis Recorded Cases in Dhi-Qar Governorate in the period of 2020 to 2024 (Seasonal variation).

No.	Region	Years	Summer	Autumn	Winter	Spring
1	Dhi-Qar city	2020	115	141	274	114
2	West of the Dhi-Qar	2021	116	146	286	166
3	East of the Dhi-Qar	2022	117	148	303	175
4	North of the Dhi-Qar	2023	127	167	342	226
5	South of the Dhi-Qar	2024	133	178	375	233
6	<b>Total Cases</b>		608	780	1580	914

The results monitored in Table 4 and Figure 4 showed that the infection rates in rural areas were higher than in urban areas during the study period, reaching 52.53% in rural areas, while the infection rates in urban areas were 43.47%.

The awareness regarding breeding sites for sandflies reveals a concerning



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tendency among surveyed populations, with slightly more than one-third of respondents recognizing unclean environments as potential habitats for this vector. However, the capacity to articulate specific characteristics of these sites appears insufficient among both urban and rural demographics, as they predominantly referenced general moist habitats and freshwater without elaboration. Moreover, the investigation conducted by Akram et al. (2015) corroborates this lack of comprehensive knowledge, with findings indicating that the majority of participants were inadequately informed about the typical breeding environments. Their responses frequently identified unhygienic surroundings, moist areas, freshwater sources, and the disposal of medical waste in hospitals as key locations conducive to breeding.

The research conducted in Shiraz, Iran (Aronson et al., 2017) revealed that the participants' knowledge was below the average level. Approximately half of those surveyed identified sandflies as the disease vector in Afghanistan (Bracamonte et al., 2020), which is attributed to the disease being endemic in the region. Conversely, a significant lack of knowledge was particularly evident in Isfahan concerning the identification and behavior of sandflies, methods of vector control, and the application of control strategies such as insecticides and repellent-treated bed nets (Zanetti et al., 2019).

**Table 4.** Cutaneous Leishmaniasis Recorded Cases in Dhi-Qar Governorate in the period of 2020 to 2024 (Urban and Rural).

No.	Region	Years	Urban Area	Rural Area
1	Dhi-Qar city	2020	312	332
2	West of the Dhi-Qar	2021	339	375
3	East of the Dhi-Qar	2022	342	401
4	North of the Dhi-Qar	2023	402	460
5	South of the Dhi-Qar	2024	448	471
6	<b>Total Cases</b>		1843	2039

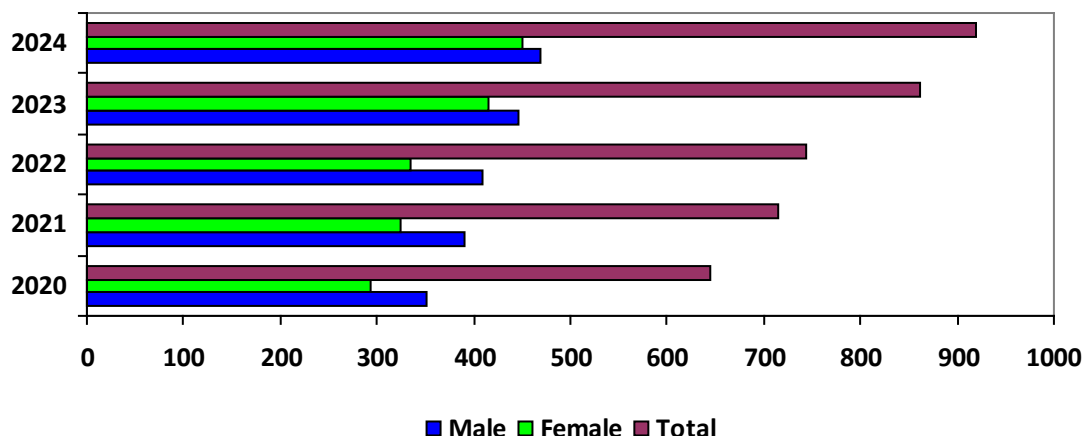
The results monitored in Table 5 and Figure 5 showed that the rates of infection in the human body regions, where infection in the lower limbs was the highest at 43.35%, followed by the upper limbs at 26.86%, then the face at 17.56% and the head at 12.21%.

**Table 5.** Cutaneous Leishmaniasis Recorded Cases in Dhi-Qar Governorate in the period of 2020 to 2024 (Body location).

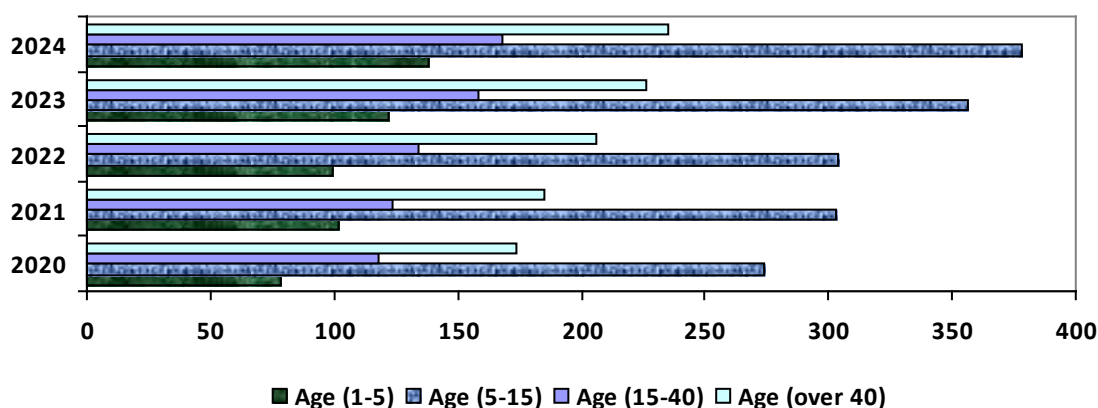
No.	Region	Years	Head	Face	Upper limbs	Lower limbs
1	Dhi-Qar city	2020	84	92	178	290
2	West of the Dhi-Qar	2021	88	96	206	324
3	East of the Dhi-Qar	2022	94	115	202	332
4	North of the Dhi-Qar	2023	93	185	226	358



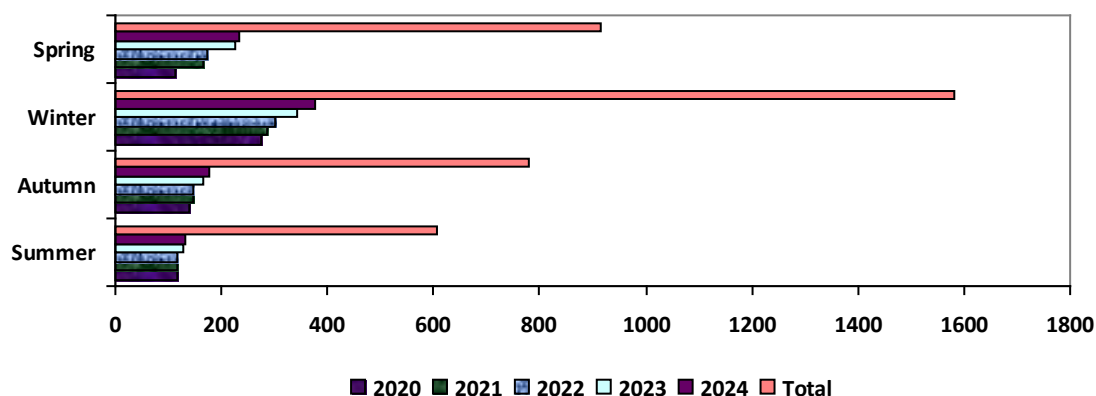
5	South of the Dhi-Qar	2024	115	194	231	379
6	<b>Total Cases</b>		474	682	1043	1683



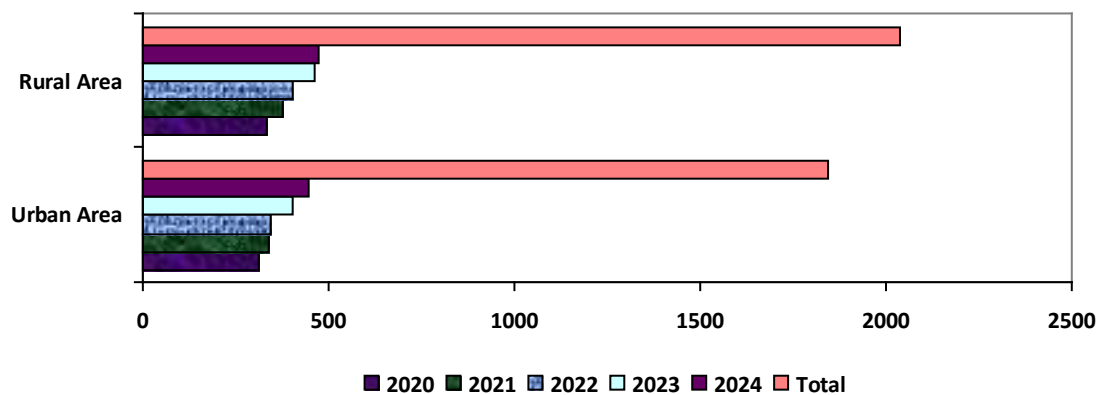
**Figure 1.** Cutaneous Leishmaniasis Recorded Cases in Dhi-Qar Governorate in the period of 2020 to 2024.



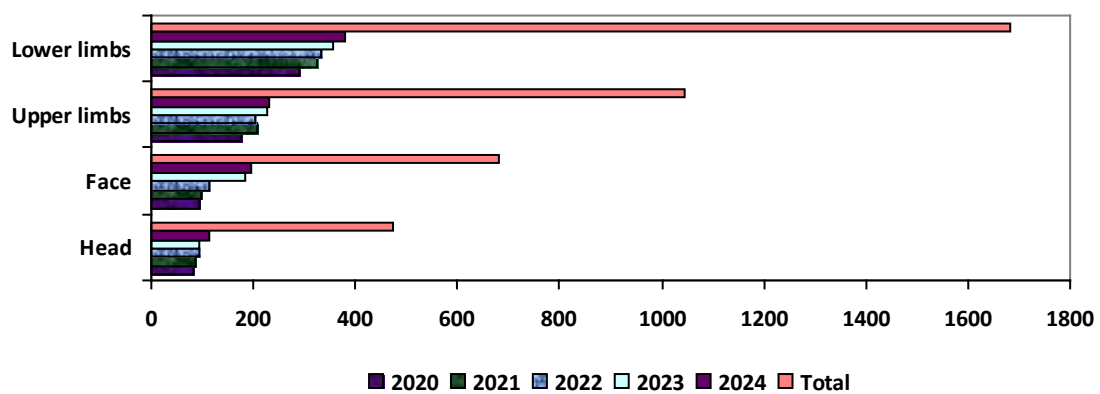
**Figure 2.** Cutaneous Leishmaniasis Recorded Cases in Dhi-Qar Governorate in the period of 2020 to 2024 (Distributed Based on the Age).



**Figure 3.** Cutaneous Leishmaniasis Recorded Cases in Dhi-Qar Governorate in the period of 2020 to 2024 (Seasonal variation).



**Figure 4.** Cutaneous Leishmaniasis Recorded Cases in Dhi-Qar Governorate in the period of 2020 to 2024 (Urban and Rural).



**Figure 5.** Cutaneous Leishmaniasis Recorded Cases in Dhi-Qar Governorate in the period of 2020 to 2024 (Urban and Rural)

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**Table 6.** Statistical analysis of Cutaneous Leishmaniasis Recorded Cases in Dhi-Qar Governorate in the period of 2020 to 2024.

<i>Age (1-5)</i>		<i>Age (5-15)</i>		<i>Age (15-40)</i>		<i>Age (over 40)</i>	
Mean	179.6667	Mean	538.3333	Mean	234	Mean	342
Standard Error	72.35499	Standard Error	215.8958	Standard Error	93.93473	Standard Error	137.1289
Median	112	Median	330	Median	146	Median	216
Mode	#N/A	Mode	#N/A	Mode	#N/A	Mode	#N/A
Standard Deviation	177.2328	Standard Deviation	528.8344	Standard Deviation	230.0922	Standard Deviation	335.8958
Sample Variance	31411.47	Sample Variance	279665.9	Sample Variance	52942.4	Sample Variance	112826
Kurtosis	5.719641	Kurtosis	5.890575	Kurtosis	5.850308	Kurtosis	5.899798
Skewness	2.375847	Skewness	2.421004	Skewness	2.410634	Skewness	2.423102
Range	461	Range	1341	Range	584	Range	852
Minimum	78	Minimum	274	Minimum	118	Minimum	174
Maximum	539	Maximum	1615	Maximum	702	Maximum	1026
Sum	1078	Sum	3230	Sum	1404	Sum	2052
Count	6	Count	6	Count	6	Count	6
Largest(1)	539	Largest(1)	1615	Largest(1)	702	Largest(1)	1026
Smallest(1)	78	Smallest(1)	274	Smallest(1)	118	Smallest(1)	174
Confidence Level(95.0%)	185.9944	Confidence Level(95.0%)	554.9777	Confidence Level(95.0%)	241.4669	Confidence Level(95.0%)	352.501

## Conclusions

The percentage of males to the total number of cases infected with Cutaneous Leishmaniasis during the study period (four years) reached 53.16% and the percentage of females reached 46.84%.

The results showed also the infection rates in rural areas were higher than in urban areas during the study period, reaching 52.53% in rural areas, while the infection rates in urban areas were 43.47%.

The percentages and numbers of cases of cutaneous leishmaniasis during seasonal changes (seasons of the year). The highest percentages were during the winter season, at 40.7%, followed by the percentages of infection during the spring season, at 23.54%. Then the percentages of infection during the fall and summer seasons, respectively, were 20.09% and 15.66%.

The findings indicated that the infection rates in various regions of the human body were highest in the lower limbs at 43.35%, followed by the upper limbs at 26.86%,

the face at 17.56%, and the head at 12.21%. Additionally, infections in the lower limbs are linked to a reduced quality of life when compared to those affecting the head/face and upper limbs.

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