Epidemiological trends of Cutaneous Leishmaniasis in Biskra district, Algeria

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ABSTRACT:
Cutaneous leishmaniasis (CL); caused by protozoa of the Leishmania genus, presents a public health concern in Algeria. This study aims to uncover the epidemiological patterns of CL in Biskra Province, Algeria, during the period of 2005 to 2020. The diagnosed patients with CL are registered at the health centers with some information's including sex, age, address. During the survey 43895 CL patients were recorded and the incidence of CL was declining at a stable rate, especially during the last 5 years. The registered cases of CL were distributed through all Biskra district and the most affected areas were Biskra town with 30.1%, followed by Sidi Okba with 10.33% and Zeribet El Oued with 7.33%. Furthermore, 43.3% of the patients were female and 56.7% were male. The highest incidence was found among patients in two age groups, ranging from 0–14 and 20–44 years old, with an incidence of 46.8% and 17.3% respectively. The analysis revealed that the highest frequencies of CL occurred in autumn and the lowest one in the summer period. A definite declining trend in the incidence of CL was noted and this imposes special public health measures in order to control the epidemiological disease in Algeria.
Keywords: cutaneous leishmaniasis, epidemiology, incidence, Biskra district.

INTRODUCTION

Leishmaniasis is a parasitic disease, caused by protozoa of the *Leishmania* genus. The disease comes in several forms, including Cutaneous Leishmaniasis (CL), which this common type results in skin sores and ulcers. Other form, Visceral Leishmaniasis (VL)) or Kala-azar is the most severe type, is affecting internal organs like the spleen, liver and bone marrow. The mucocutaneous leishmaniasis (MCL), this variant targets the mucous membranes of the nose, mouth and throat, causing destructive lesions and disfigurement (Mokni, 2019).Zoonotic Cutaneous Leishmaniasis (ZCL) is a form of cutaneous leishmaniasis, transmitted between animals (usually rodents) and humans through the bite of infected sandflies. With animals serving as reservoir hosts for the parasite; hence, ZCL stands as a significant public health concern, affecting millions of individuals in endemic regions worldwide (Bounoua et al., 2013). The global yearly occurrence of cutaneous leishmaniasis (CL) was predicted to vary between 0.7 and 1.2 million new clinical cases (Zeroual et al., 2019). The prevalence of CL is notably concentrated in specific geographical regions, with South America, particularly countries such as Brazil, Peru, Colombia, and Costa Rica, exhibiting a significant burden. In addition, North Africa and the Middle East, encompassing nations like North Sudan, Algeria, Syria, Iran, Iraq, Saudi Arabia and South Asia, with Afghanistan as a prominent focal point, experience a heightened occurrence of this disease (Firouraghi et al., 2023). A pentavalent antimonial molecule like Glucantime is the most commonly prescribed drug for the disease because of its efficacy, free availability and absence of severe side effects, in the absence of an effective and efficient vaccine against leishmaniasis (Sadeghian & Nilforoushzadeh, 2006). Algeria has been recognized as an endemic region for cutaneous leishmaniasis (CL), with various Leishmania species implicated in human infections (Alcover et al., 2023). Particularly in southeast regions, such as Biskra province, CL occurs in the form of ZCL (Zoonotic cutaneous leishmaniasis) and its etiological agent is
Leishmania major with the proven sandfly vector, *Phlebotomus Papatasi* (Zeroual et al., 2017; Benikhlef et al.,

2021). Biskra province is the gateway of the Sahara and is known as the main focus of the ZCL (Zeroual et al., 2016). It's an arid area. It has dry and hot climates. Often have sparse vegetation, which can lead to an increase in breeding sites for sandflies. They are commonly found in rural and peri-urban areas where there is a close association between humans, reservoir hosts (such as rodents or canines) and sandfly vectors (Aoun & Bouratbine, 2014). Despite extensive efforts to control the disease, along with government initiatives and collaborative research, the disease continues to persist in numerous provinces and new areas, with endemic cases continue to emerge and are regularly reported. Several variables that contribute to the development and occurrence of CL are including a unique set of environmental conditions, such as a warm and dry climate, abundant vegetation, diverse geography and rich biodiversity and these factors provide an ideal habitat for the sandflies, which are the primary vectors of the disease. Additionally, human activities such as deforestation, urbanization and migration contribute to the expansion and spread of the disease. However, challenges such as limited resources, inadequate surveillance systems and the

emergence of drug-resistant parasites continue to hamper effective control and elimination of the disease (Gaouaoui et al., 2017 & Khademvatan et al., 2017).

This study aimed to update and analyze the epidemiological features with descriptive data on the current situation of the CL in Biskra province, southeast of Algeria for 16 consecutive years (2005–2020).

MATERIALS AND METHODS

Study area:

The epidemiological study was conducted in the Biskra province in eastern part of Algeria. It is located in the Saharan Atlas region at the gates of the Sahara (4°15 'and 6°45', 35°15 'and 33°30' N) (Figure 1). The height above sea level ranging between 29 m to 1600 m, which makes it one of the lowest cities. The province covers an area of 20986 km2 and is made up of 33 administrative districts. Biskra Province is renowned for its arid terrains and settlements with oases. The province has hot and dry weather conditions. The city of Biskra is famous for its palm groves and is often referred to as the "City of the Palms." Is recognized as a significant endemic area for cutaneous leishmaniasis in Algeria.

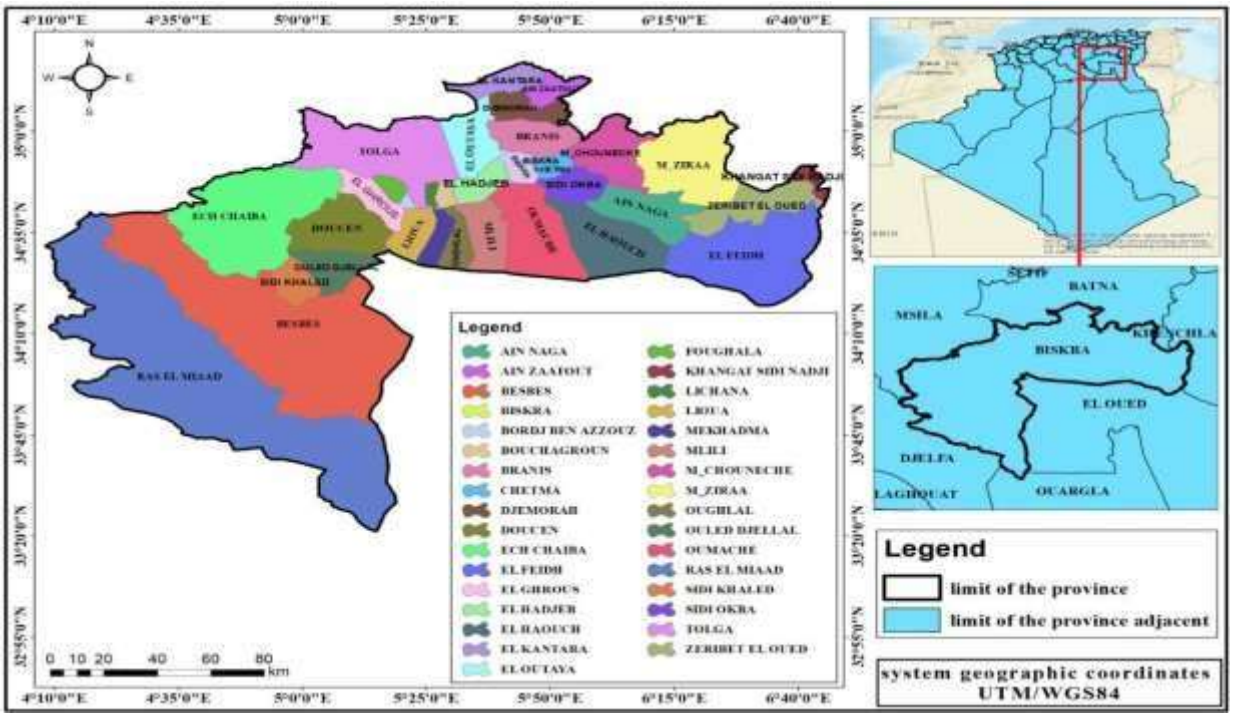

Figure 1. Geographical location of Biskra province and administrative districts.

Data collection and analysis:

The clinical-epidemiological data of microscopically confirmed CL patients were obtained from the health services of Biskra Province from 2005 to 2020. The survey data were obtained on a monthly and yearly basis. Extensive data on each case of CL, including sex, age, and area, was documented according to their availability. The data obtained were analyzed by Excel 2019. Also, in order to determine the spatial distribution of infections in the region between 2005-2020, ArcGIS software by Esri was employed. The district coordinates were acquired from Google Earth Pro (version 7.3), and the average number of CL instances in each district was matched accordingly.

RESULTS 3.1 Number and incidence rate of CL cases

According to Figure 2, There were 43895 cases of cutaneous leishmaniasis (CL) reported between 2005 and 2020. Leishmaniasis in this area showed a fluctuating pattern over the years. The lowest incidence of CL was in 2007 with 1107 cases and an incidence rate of 142.3 per 100,000 population. The greatest incidence was in 2005 with 8375 cases and an incidence rate of 1138.02 per 100,000 population. The number of cases declined by 64.7% in 2006 and by a further 37.5% in 2007. In 2010, there was an 81.54% growth, followed by an 81.6% decline in 2015. The incidence rate has remained consistent at around 180.3 to 200.1 per 100,000 since 2014 (Figure 2).

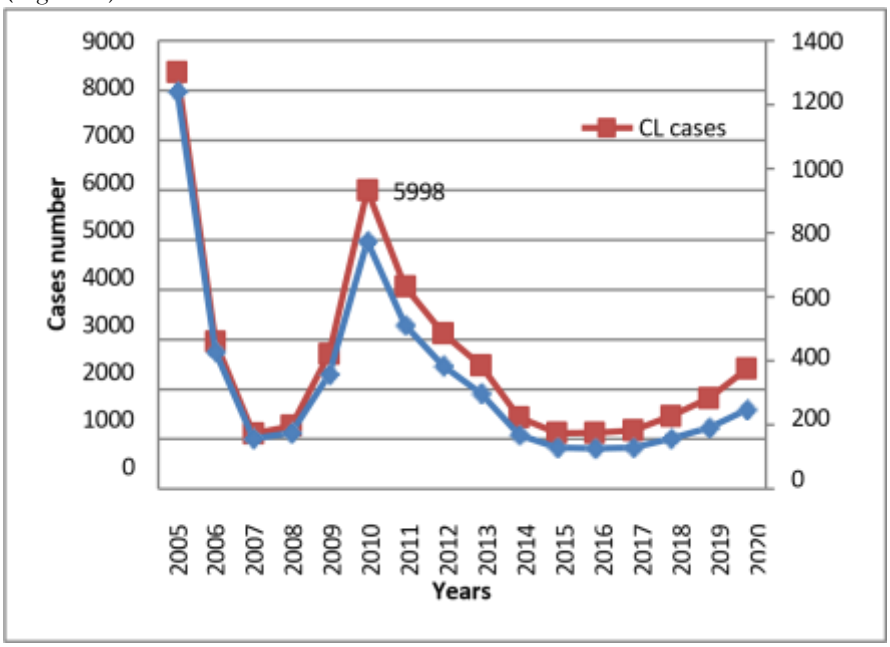

Figure 2. Total number of cases and incidence rate of cutaneous leishmaniasis in Biskra province between 2005 and 2020.

DISTRIBUTION BY DISTRICTS:

The geographical distribution of CL was generally higher in the centre and eastern districts compared to other areas. (Figure3). So Biskra Province could be divided into three regions, including high (10.14%–31.9%), intermediate (2.85–13.3%), and low-level endemic or non-endemic areas (0.27%–2.84%) . Most of the cases originated from three districts located in the center-east of the province, with moderate altitude ranges in the center and east lowlands (1–150 m), namely Biskra as the capital of the province, Sidi Okba, and Ze. El Oued City. The percentage of cases from previous districts were 30.1%, 10.33%, and 7.33%, respectively. Few cases were recorded from 12 districts (ranging from 0.2% to 1%) located in the West Highland (450–657m). While sporadic events (ranging from 1.26.2% to 4.9%) were observed in 16 districts in the West Highland (450– 657m) and the Interior Highland (151–449m).

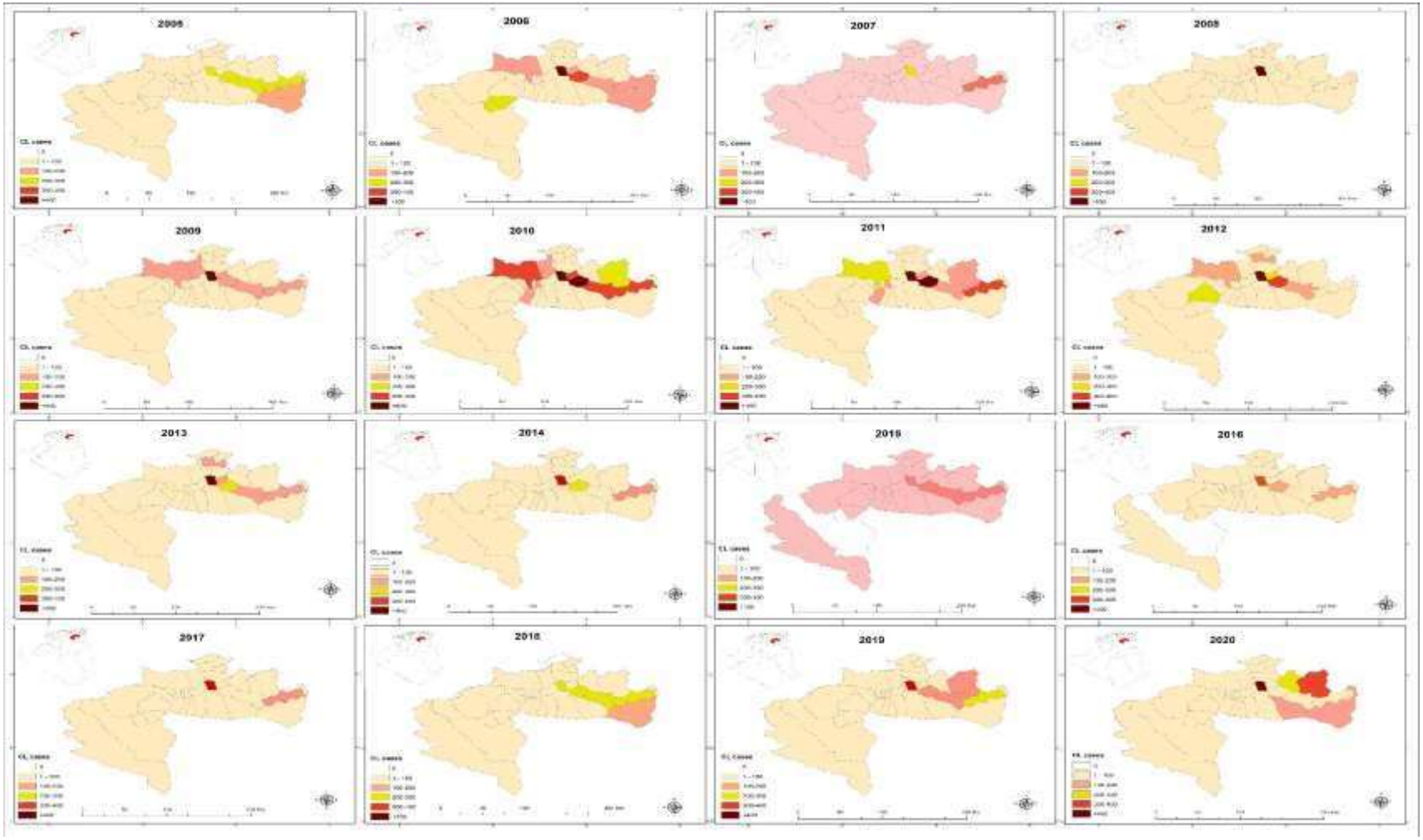
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Figure 3.
Geographical distribution of Cutaneous Leishmaniasis cases in Biskra province at the district level. For each academic year from 2005 to 2020. Low and high endemic areas are depicted using varying gradient colours; light brown signifies the least afflicted regions while dark brown denotes the most impacted regions.

3.3. Monthly distribution:

Furthermore, Figure 4 displays the monthly distribution of incidents from 2005 to 2020.Cases were reported in all months of the year with a heterogenic distribution, whereby the highest frequency of cases was consistently observed in one of the four months: October, November, December, or January, while the lowest numbers were consistently seen throughout the summer season. Generally, we found that the sickness achieves its peak in December (8106 cases) and January (7848 cases) months and continues thereafter to diminish progressively to reach its lowest value in July (447 cases) of the total cases during 16 years. However, there was a persistent occurrence of numerous cases during the summer months.

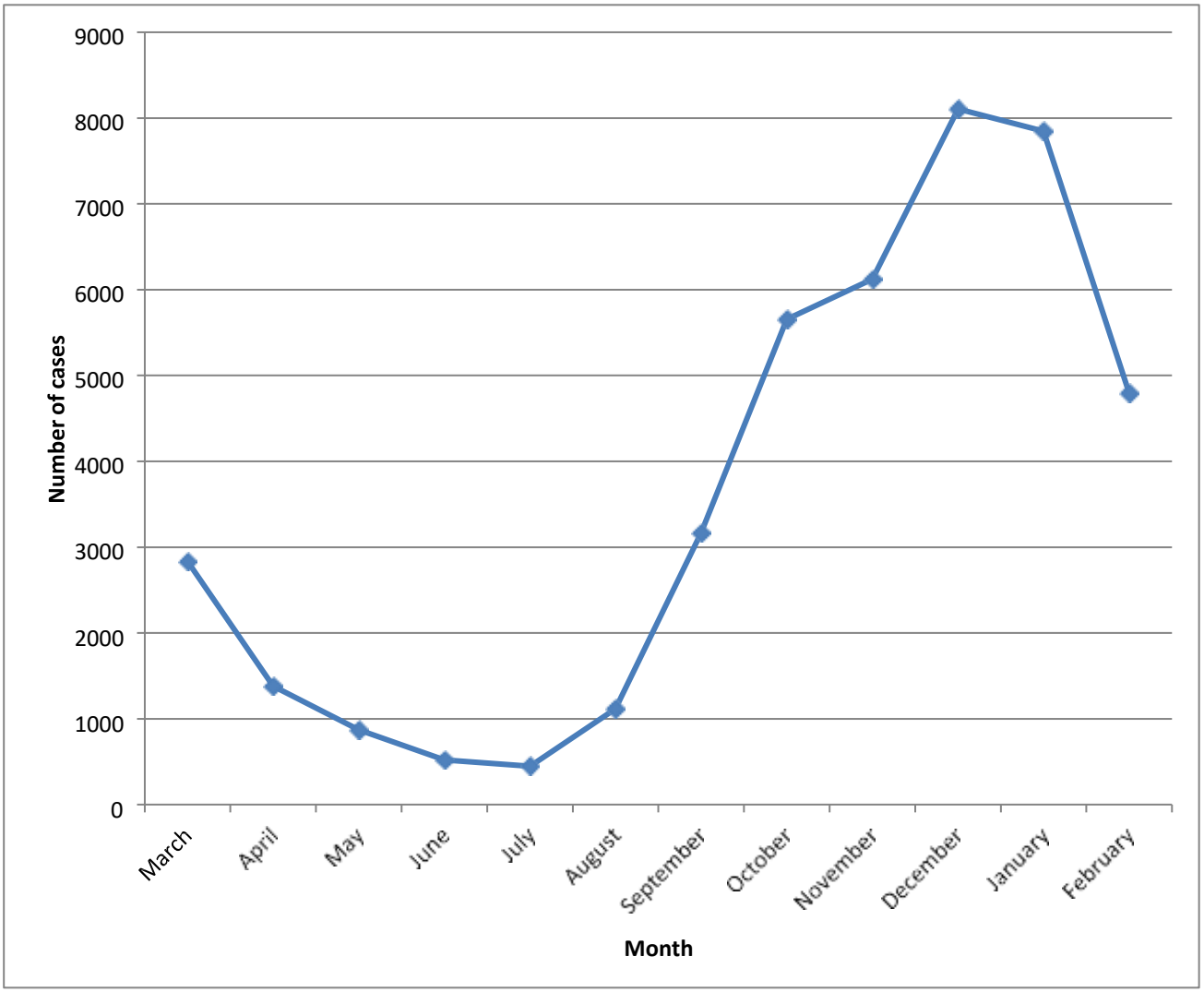

Figure 4. Temporal distribution of reported cutaneous leishmaniasis (CL) cases in Biskra province from 2005 to 2020.

3.4. Gender and age distribution:

The disease is almost evenly distributed among genders in all years of the study period with a total of 24022 cases, (56.71%) being males against 18333 cases (43.28%) for females.

There was no statistically significant change in the gender distribution of patients across various years ($P > 0.05$).The patients' ages varied from under five years to over 65 years with unequal distribution. Upon analyzing our data, we noted that. Children aged 0-14 were the most afflicted group throughout the research period,

whereas individuals aged 45-65 and above were the least affected. The Chi-square test findings indicated a statistically significant difference between infection cases and age categories ($p<0.05$). (Table 1)

Table 1: Distribution of cases of CL by gender and age group, in Biskra province during years of 2005-2020.

Years																		
		2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	**Total**	**P value**
Gender	**Male**	4459	1630	675	705	1478	3341	2332	1674	1386	678	739	699	560	905	1208	1553	24022	NS
	Female	3916	1328	327	554	1239	2657	1729	1344	982	455	485	462	467	663	745	980	18333	
Age Groupe	**≤ 5**	2937	1028	374	533	1039	2302	1457	1026	893	488	423	429	393	545	578	763	15208	p<0.05a
	5-14	1028	936	229	301	761	1600	1048	907	644	315	298	336	379	459	585	952	12410	
	15- 19	715	213	75	83	256	458	297	198	154	66	83	54	36	118	148	119	3073	
	20- 44	1646	626	253	259	514	1275	946	706	555	204	351	283	168	319	504	537	9146	
	45-65	307	103	59	67	107	279	221	139	94	50	51	41	39	103	119	132	1911	
	≥65	110	52	12	16	40	84	92	42	28	10	18	18	12	24	19	30	607	

N.S: *Not significant.*

DISCUSSION

Epidemiological inquiry, disease trend monitoring, and ecological studies are crucial priorities for assessing risk factors and preventative approaches in controlling leishmaniasis. Our work was based on the extensive retrospective investigation on CL done by Zeroual and Benikhlef in the same region. They demonstrated that CL had a very high occurrence, almost reaching epidemic levels in 1987, and then gradually decreased to a stable level by the mid-2001 (Aoun & Bouratbine, 2014; Khademvatanet al., 2017). To effectively manage illnesses carried by insects, it is essential to gather comprehensive epidemiological data including geographical distribution, seasonal patterns, and their correlation with factors including age, gender, employment, and location of infection.This study aimed to analyse the epidemiological pattern of Cutaneous Leishmaniasis (CL) in the Biskra province, Algeria, from 2005 to 2020. There has been an increasing tendency in the occurrence of cutaneous leishmaniasis in Algeria, with numerous new areas of the illness being discovered in the nation in recent years. The study maintained a consistent yearly record of cutaneous leishmaniasis patients over a 16-year period, demonstrating the disease's endemic nature in the Biskra region (Khademvatanet al., 2017). Figure 2 displayed two significant peaks. In 2005, there was a high in CL cases with a total of 8364 cases, representing a rate of 1138.02 per 100,000 people. A prior research in this region determined that L. major is the causal species, *Phlebotomus Papatasi* is the primary vector, *Meriones shawi* as the main reservoir (Harrat et al., 1996 ; Del Giudice et al., 1998) . Continued efforts to eradicate CL from the province have contributed significantly to the decline in the number of cases, declining to 389.9 per 100,000 by 2006 and 2007, possibly modulated by more efficient spraying against sandflies after a year of more cases (Benikhlef et al., 2021). The second high occurred in 2010 and was followed by a slow decline, as shown in Figure 2. However, a sharp rise in disease occurrence in 2010 may be attributed to higher rainfall, failure in disease reservoir control, heightened urbanisation, agricultural practices, and unregulated development of disease reservoirs (Aoun & Bouratbine, 2014; Haddad et al., 2016; Amro et al., 2022)In contrast, such a lowering trend from 2010 to 2020 justified as preventive units had a solid performance in the field of modern ways of prevention via the removal of stray rodents throughout the city. Furthermore, providing training to health professionals and utilising experienced staff are crucial aspects in decreasing the condition (Haddad et al., 2016; Zeroual et al., 2022). The study revealed that the urban area of Biskra had the greatest infection rate, followed by the peri-urban districts of Sidi Okba and Zeribet El-Oued. The high prevalence in these places is attributed to the suitable habitat and breeding conditions for the disease reservoir and sandfly populations, which are greatly influenced by climatic and environmental variables as well as high population density (Benikhlef et al., 2021; Aoun & Bouratbine, 2014; Amro et al., 2022).Residents of these areas normally engage in agricultural activities and are readily exposed to the bite of infected sand flies, which are mainly resident and reproducing within gerbil burrows, and the consequent leishmaniasis infection (Amro et al., 2022; Azmi et al., 2012). In this study, a focal point for the disease was found in the central and eastern parts of the study area. With a unique topography and an average altitude above sea level of less than 70m, there is an inverse relationship between the altitude above sea level and the case number. The disease's transmission is linked to environmental factors like warm temperatures, high humidity, and suitable sand fly vectors. Lower-elevation areas often have these conditions, creating an ideal sand fly habitat and increasing disease transmission. Higher population densities in these areas further raise the risk of exposure and transmission (Gutierrez et al., 2017).The study found that cutaneous leishmaniasis had the highest occurrence during the winter months, particularly in December and January, with a lower prevalence recorded in the summer. In dry and semi-arid environments, the seasonal occurrence of CL infection in humans is closely linked to the seasonal growth of adult sandflies and the extended incubation time of Leishmania infection (Azmi et al., 2012; Aghdaei et al., 2023). During late summer and autumn, sand fly populations peak, leading to the initiation of most human cases during this period (Haddad et al., 2016; Nazari et al., 2017). This correlates with other illness hotspots in Algeria, Banta (Messahel et al., 2021) and M'sila (Khademvatan et al., 2017). Various research from different areas worldwide showed consistent findings that the highest number of cases occurred in November or between November and February, such as those from Palestine (Azmi et al., 2012), Iran (Azimi et al., 2017) and Tunisia (Chraiet- Rezgani et al., 2016). According to physician working in health centers across several districts in Biskra province most patients visited clinics from October to January (Gaouaoui et al., 2022). This pattern followed a silent incubation period of the disease, as which ranged from a few weeks to several months, explaining the

significant emergence of lesions in autumn and winter (Chraiet-Rezgani et al., 2016), which confirm the present finding.In terms of gender CL can affect both men and women (Gaouaoui et al., 2022). Leishmaniasis affects both genders with an equal distribution of cases between genders (56.71% male) and (43.28% female). This suggests that both genders are equally exposed to sandfly bites. Some investigations from other parts of the country such as (Setif, Djelfa, and Souf Ouasis) has shown that CL is affecting males more likely than females (Khezzani & Bouchemal, 2017; Benikhlef et al., 2021; Messahel et al., 2021; Fellahi et al., 2021) . However, Most

studies show that cutaneous leishmaniasis is more common in males due to several factors, such as environmental conditions, socioeconomic status, and human behaviors, household design, and construction material (Gaouaoui et al., 2017). All age groups were affected, but most commonly affected in this study was 0–14 years while groups above 44 years old showed the lowest rate of infection. This strong link may be explained by the lack of immunity in children due to their lack of previous exposure to the parasite. The distribution of cutaneous leishmaniasis findings aligns with the results of previous studies carried out in known ZCL endemic regions of Algeria including Batna[(Messahel et al., 2021), Souf oasis (Hamiroune et al., 2019). Similarly, in studies conducted in, Pakistan (Zeb et al., 2021), Yemen and Afghanistan the CL was more prevalent in young age groups. Although our results is quite different from the results of the study conducted in Iran (Kassiri et al., 2012; Debash et al., 2022) , Saudi Arabia (Hassanein et al., 2023) that have shown most highly infected age group with CL is person of more than 20 years .Generally, the prevalence of CL leishmaniasis in the established endemic areas decreases in those older than 15 years old, probably as a result of the progressive buildup of acquired immunity (Aghdaei et al., 2023).This study reveals that ZCL a continuous and important health problem in the area. Many patients affected by CL, are likely to take treatment from private sector hospitals or outside the province, hence their number might be under reported (Haddad et al., 2016). Nevertheless, it would have been preferable if additional factors were available in the records of these CL patients and are included here; such as variables related to their general clinical data, anatomical distribution and morphological typing (popular, nodular, or ulcerative) of the detected CL species identification and biopsy findings and type and outcome of the applied treatment.

CONCLUSION

According to the present survey, cutaneous leishmaniasis is still considered an endemic disease in the southeast of Algeria, even though its incidence is declining. The data of the present study were drawn from the registers of patients with CL during the period of 2005 to 2020 in the Biskra region and revealed the endemicity of this protozoan parasitic disease in this region. Further screening and monitoring with multidisciplinary approaches are warranted to assess the entire epidemiological profile of CL disease and identify emerging hotspots. This can help identify new risk factors and improve the ability of public health authorities to allocate resources and implement timely interventions.

Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors

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Conflict of interest statement We declare that we have no conflict of interest.

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