



Coexistence of Cutaneous and Visceral Leishmaniasis in the Province of Moulay Yaâcoub, North-Central Morocco

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ABSTRACT

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Leishmaniasis is an infectious disease transmitted to humans by the bite of a female sandfly. In Morocco, leishmaniasis is considered a real health concern. The aims of this study were to analyze the epidemiological situation and identify localities at risk of transmission of leishmaniasis in the province of Moulay Yaâcoub. The study was a retrospective analysis of leishmaniasis cases reported over a period of 11 years from 2005 to 2015 in Moulay Yaâcoub Province. The data were collected from the registries of the Prefectural Cell of the Moulay Yaâcoub Province Medical Delegation, Regional Directorate of Health, Fez-Meknes, and analyzed statistically. The results showed that leishmaniasis was present, with an annual average of 18.63 cases. A total of 205 cases of leishmaniasis were recorded, with 53% cutaneous leishmaniasis and 47% visceral leishmaniasis. Females were the most affected, at 53.7%, mainly by cutaneous leishmaniasis, although the difference was not statistically significant ($\chi^2 = 0.7$, p-value = 0.79). Cutaneous leishmaniasis affected all age groups, whereas visceral leishmaniasis affected only young people under 30. The communes most affected were Ain Chkef and Ain Kansara, and the difference between the proportions of cases detected in the different sites was statistically significant ($\chi^2 = 96.03$, p-value < 0.05). To the best of our knowledge, this is the first time such a study has been conducted in Moulay Yaâcoub Province.

Keywords: Central Morocco, Cutaneous leishmaniasis, Epidemiological study, Moulay Yaâcoub Province, Visceral leishmaniasis

Introduction

Leishmaniasis is a vector-borne parasitic disease that poses a public health concern. According to the World Health Organization (WHO) reports, leishmaniasis affects 2 million people each year and 350 million people are at risk of being affected by leishmaniasis.^{1,2} In 2013, a total of 72,026 cases of leishmaniasis were reported worldwide.³ In Morocco, due to climatic and geographic diversity, leishmaniasis presents a considerable nosological diversity.⁴ According to Laamrani-Idrissi,⁵ leishmaniasis can be illustrated in three epidemiological entities: visceral leishmaniasis (VL) caused by *Leishmania infantum* (L.), zoonotic cutaneous leishmaniasis (ZCL) brought about by *L. major*, and anthroponotic cutaneous leishmaniasis (ACL) caused by *L. tropica*. *Leishmania infantum* MON1 is the species responsible for the VL for which three vector species are responsible, namely, *Phlebotomus ariasi*, *P. perniciosus*, and *P. (Larroussius) longicuspis* Nitzulescu (1930).^{6,7} Meanwhile, CL is

caused by three parasites: *L. tropica* MON102, whose vector species is *P. (Paraphlebotomus) sergenti* Parrot,^{8,9}

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L. major, which is transmitted by touching *P. papatasi* Scopoli (1786),^{10,11} and sometimes by *L. infantum* MON24 in a sporadic form. Since 1995, leishmaniasis in Morocco has been a reportable disease (Ministerial Order No. 683-95 of March 31, 1995).

Among 23 species of sandflies described in Morocco, only five were vectors of leishmaniasis.¹² *Phlebotomus sergentis*, the only vector of the *L. tropica* species in Morocco and the main vector in the countries of the Mediterranean.¹² This sandfly is widespread throughout Morocco, and it is considered one of the most frequent species, especially in semi-arid regions.¹³ *Phlebotomus papatasi* is proven as a vector of *L. major*.¹⁴ The subgenus *Larrousius* represents a very particular group of species characterized by their typical morphology on the one hand, and their epidemiological role in the transmission of *L. infantum*, the causative agent of visceral leishmaniasis in humans and dogs on the other hand.¹⁵ *Phlebotomus longicuspis* is suspected as a vector of *L. infantum* in Mediterranean countries.¹⁶ *Phlebotomus perniciosus* is the proven vector of canine and human visceral leishmaniasis in the Mediterranean region.¹⁷ In the subgenus *Larrousius*, *P. ariasi* and the proven role of *P. perniciosus* and *P. longicuspis* in *L. infantum*.¹⁸ As part of the fight against leishmaniasis in Morocco, several initiatives have been taken by the Ministry of Health. These initiatives have targeted the three main actors of leishmaniasis, which are the vector, the reservoir, and the parasite.¹⁹ Among the actions on the parasite are the screening, oversight, and treatment of cases of leishmaniasis. The region of Zouagha Moulay Yaâcoub, a region which was part of Moulay Yaâcoub Province (former administrative division) has been identified as a CL hotspot.²⁰

The present study was, therefore, conducted to analyze the epidemiological situation of leishmaniasis and identify the localities at risk of transmission of the disease in Moulay Yaâcoub Province in central Morocco.

Materials and Methods

Study area

Moulay Yaâcoub Province is an area located in central Morocco (Figure 1). It is subdivided into eleven municipalities. Sebti Loudaya, Sidi Daoud, Ouled Mimoun, Louadan, and Ain Kansara communes in the south. The communes of Mikkes and Sbaâ Rouadi in the west, Ain Chkef in the south, and Laâjajra, Ain Bouali, and Moulay Yaâcoub in the east.

Type and duration of the study

This is a retrospective study of all cases of CL and VL, recorded over a period of 11 years from 2005 to 2015. The recorded data were in the registers of the Prefectural Cell of the Medical Delegation of Moulay Yaâcoub Province, Regional Directorate of Health, Fez-Meknes.

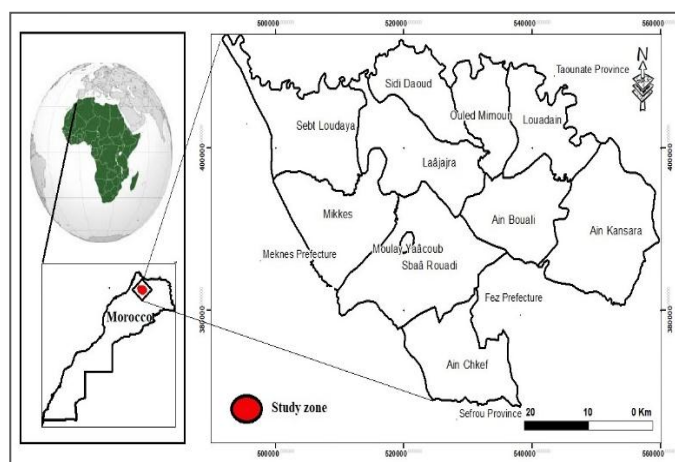


Figure 1: Map of the Province of Moulay Yaâcoub and the studied communes.

Data analysis

The descriptive analysis included age, gender, and a description of how cases evolved across time and space. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS; version 20). The χ^2 test was used to compare the categorical variables. For all the analyses, the significant level was $p < 0.05$. The distribution of CL and VL cases was evaluated using the Qgis 2.18 software by integrating data on leishmaniasis in the geographic information system.

Results and Discussion

The results of this study revealed for the first that Moulay Yaâcoub Province is a mixed epicentre where the two forms of CL and VL coexist. Between 2005 and 2015, the total number of leishmaniasis cases reported in the Moulay Yaâcoub Province was 205 cases. Among them, 109 cases (53%) were in the form of CL and 96 cases (47%) were in the VL form (Figure 2). This coexistence is not marked by a dominance of one species to another since the difference between the proportions of the cases detected in the different sites was significant. The province of Moulay Yaâcoub is a hotspot of submerged leishmaniasis occurring from March to April at the level of the Zouagha Discreet Dispensary, according to a prospective study conducted in 2002, which was reported by Rhajaoui *et al.*²¹ Another prospective study, which was carried out from March to May in the same year observed that 135 cases of CL in humans and no case of the form of VL was reported. The enzymatic typology of the species in question has been shown to belong to *L. tropica* MON102.²¹ According to the declaration of the Ministry of Health in 2010, the visceral form in Morocco resembles the visceral form found in the Mediterranean region,²² with the species *L. infantum* acting as the pathogenic agent.²³ In Morocco, this infestation developed in a hypo-endemic form throughout the rif and pre-rif regions, with Al Hoceima, Tétouan, Chefchaouen, Taza, sidiKacem, Fès, Meknès, and Nador being the most impacted.^{4,24}

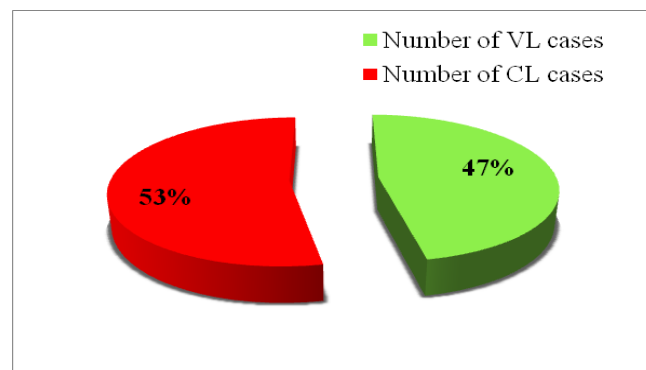


Figure 2: Distribution of the form of cases of leishmaniasis recorded in the Moulay Yaâcoub Province from 2005 to 2015.

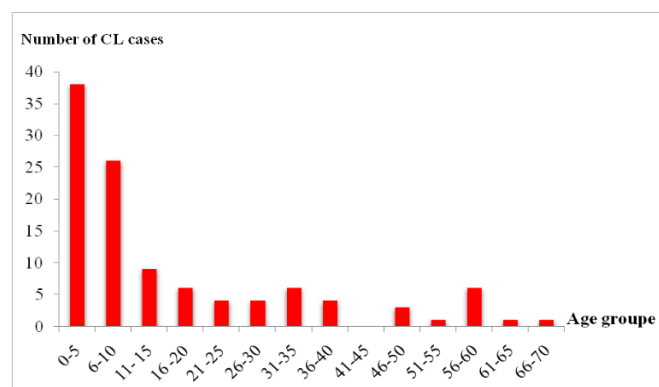


Figure 3: Distribution of cutaneous leishmaniasis cases according to age groups at Moulay Yaâcoub Province from 2005 to 2015.

The presence of VL in the Province of Moulay Yaâcoub is not surprising given that the province is bordered to the south by the Province of Taounate, as demonstrated by Guessous-Idrissi *et al.*²⁵ The pathogen was *L. infantum* MON1, and *P. ariasi* has been found naturally infested by *L. infantum*, indicating that this species is at least one of the vectors of the parasite. Therefore, with the use of a molecular PCR-RLFP analysis, *L. infantum* MON1 was found in dogs from southern regions, including Taounate, which suggests that the dog is the reservoir of this parasite. At the locality of ZMY, 13.2% were found to be seropositive.²⁶ The evolution of the number of cases from 2005 to 2015 generally follows the evolution of leishmaniasis at the national level. The results of the present study corroborate with those of the Ministry of Health, which declared an increase in cases of leishmaniasis at the national level from 2005 to 2010, with an increase from 3,153 to 8,846 cases in the same period.¹⁹ Meanwhile, the number of cases has decreased from 8,846 recorded in 2010 to 2,641 in 2014.²⁷ In the same region of Fez Meknes, this temporal evolution was noticed in Sefrou Province.²⁸ Cutaneous leishmaniasis was recorded during the study period, with a very remarkable drop in 2011. This is consistent with the findings of Kahim *et al.*,²⁹ on cases of CL in Morocco, which showed that the highest number of CL cases was observed between 2008 and 2011 for the ZCL and between 2010 and 2013 for the ACL. The overall case limit for both forms was reported in 2010. However, the number of cases of VL were decreased during this study period. The highest number was recorded in 2006. This result is in agreement with the situation of VL in the country, which experienced a decrease in cases in 2006 (170 cases), the number decreased to 86 cases in 2014.²⁷

Of the 205 cases of leishmaniasis recorded, 109 cases (53.17%) were recorded in females compared to only 96 cases (46.92%) that were recorded in males as presented in Table 1. The sex ratio was around 0.88, indicating that human leishmaniasis affects both males and females equally; the two genders were almost equally affected. The difference between the proportions of detected cases was not significant. Taking each form into account, the VL distribution according to human gender has a sex ratio of 1.08 in favour of males. The latter were affected at 52.08% (50 cases) against 47.92% (46 cases) for females (Table 1). For the visceral form, the distribution of cases by human gender was marked by a sex ratio of 0.73 in favour of females. These were affected at 57.8% (63 cases) against 42.2% (46 cases) for males (Table 1).

It was observed by the Chi-square percentage comparison test that there was no statistically significant ($\chi^2 = 1.25$, p-value = 0.26) relationship between the form of leishmaniasis and the sex of people with the disease. This result is in agreement with those reported in other Moroccan foci, notably in Sefrou Province.²⁸ The hypothesis of human dependence on leishmaniasis is refuted. Leishmaniasis, whether visceral or cutaneous, affects both men and women without preference towards one sex or another. The CL was in favour of women (sex ratio = 0.73), while the VL was in favour of men (sex ratio = 1.08). This result is in agreement with that obtained in Sefrou Province,²⁸ and El Hajeb City where the predominance was marked among females at adult age.³⁰ In several epidemiological studies, the distribution of leishmaniasis according to the human gender was demonstrated by focusing on the calculation of the sex ratio. Thus, for CL, Chiheb *et al.* found a sex ratio of 0.67.³¹ At the level of ZMY, they also obtained a sex ratio in favour of women.³² At the Chichaoua level, they calculated a sex ratio of 0.8.³³ Moreover, in Algiers, Algeria, a sex ratio of around 0.95 was observed, while in Tunisia, a sex ratio of 1.02 was recorded.³⁴ The sex ratio of the VL was found in several studies in favour of men in Rabat where they calculated a sex ratio of 1.82.³⁵ Zait *et al.*,³⁶ found a sex ratio of 1.53 in Algiers, Algeria. Furthermore, in Tunisia, Aoun *et al.*,³⁷ reported a sex ratio of 1.03.

Cutaneous leishmaniasis instances were recorded for all age groups ranging from 0 to 70 years. However, children from 0 to 10 years old were the most affected, which represents 31.21% of the infested population (Figure 3). For VL, only children under the age of 5 (adolescents) and young people under the age of 30 were affected. As presented in Figure 4, there was no case of VL was recorded in the other age groups (31-70). The distribution across these six impacted

age groups is inconsistent, with data available for all age groups from 0 to 70 years. The VL has been recorded in children less than five years of age. This latter bracket alone accounts for 77.08% of all cases, followed by the age group (6-10) accounting for 16.66%. A few cases not exceeding 6% of the total cases have been recorded in other age groups ranging from [11- 30].

Table 1: The distribution of leishmaniasis according to sex in Moulay Yaâcoub Province from 2005 to 2015

Type of leishmaniasis		Sex		Total
		Male	Female	
Visceral leishmaniasis (VL)	Effective	50.00	46.00	96
	Percentage of VL (%)	52.08	47.92	100
Cutaneous leishmaniasis (CL)	Effective	46.00	63.00	109
	Percentage of CL (%)	42.20	57.80	100
Total	Effectif	96.00	109.00	205
	%	46.83	53.17	100

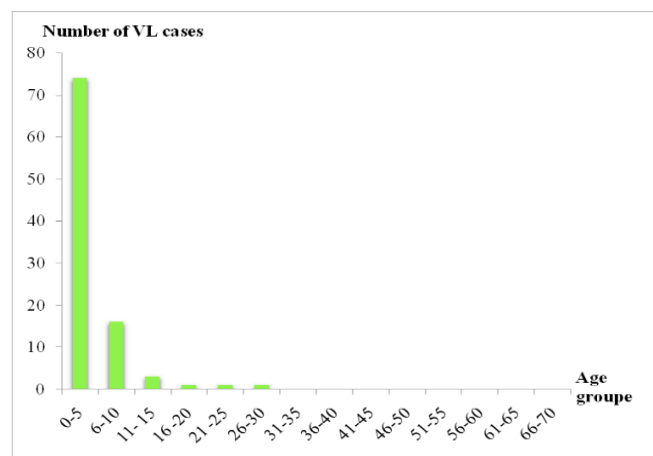


Figure 4: Distribution of the number of visceral leishmaniasis cases according to age groups in the Moulay Yaâcoub Province from 2005 to 2015.

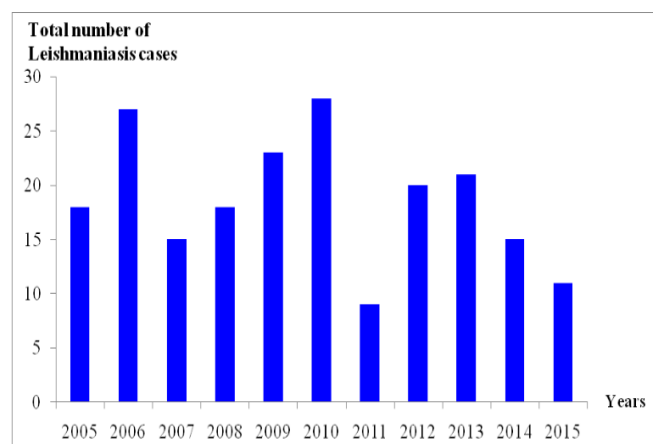


Figure 5: Temporal evolution of cases of leishmaniasis recorded in the Moulay Yaâcoub Province from 2005 to 2015.

The results obtained by the age distribution study showed that CL affects all age groups, children and adolescents were the most affected, which corroborates with several studies.^{22,33,32,38,39} These results indicate that CL affects all ages with predominance among children under 10 years of age. Visceral leishmaniasis was only detected in children under the age of 5 among adolescents and young people under the age of 30. The results of this study highlight the juvenile origin of VL and support the findings of Zait *et al.*,³⁶ where it was observed that 88.7% of the study population was made up of children, with 56.3% being between the ages of 1 and 2. A similar report was made by Zougaghi *et al.*³⁵

From 2005 to 2015, leishmaniasis was present in the province with an annual average of 18.63 cases. The total number of cases increased significantly between 2005 and 2010. Two peaks were observed, the first was recorded in 2006 and the second one was marked in 2010 with, respectively, 26 and 28 cases per year. With 9 occurrences of leishmaniasis, 2011 was the year with the lowest number of cases (Figure 5). The cases of CL occurred with an annual average of 9.9 cases as illustrated in Figure 6. The progression of CL followed the same curve as the total number of cases, as demonstrated in Figure 6. The highest number was recorded in 2010 and the lowest in 2005. The visceral form was recorded with an annual average of 8.72 during the period from 2005 to 2015. A peak was observed in 2006 with 22 cases. Since then, a decrease in the number of cases has been observed. The lowest number was recorded in 2015 with 3 cases (Figure 7).

The distribution of the cases does not occur in a homogeneous way in all the communes. Thus, the municipalities of Ain Chkef and Ain Kansara represent the largest share of the total number of cases (Figure 8). The spatial distribution of leishmaniasis cases according to the localities shows that the commune of Ain Chkef contained the majority of the cases recorded on the territory of the province, with 40% of the total cases, followed by the commune of Ain Kansara with 17%, the commune of Ain Bouali with 10%, the communes of Sbaâ Rouadi and Laâjajra with 7% each, then the communes of Sebt Loudaya, Louadain and Ouled Mimoun with 5%, and the commune of Sidi Daoud with 3% of the total. Only 2% of cases have been recorded in the commune of Moulay Yaâcoub, the province's only urban commune. During the research period, however, no cases were reported in the commune of Mikkes (Figure 8).

The spatial distribution of CL and VL cases shows a dominance of CL in only two communes, which are Ain Chkef and Ain Kansara among the eleven communes of Moulay Yaâcoub Province. According to the χ^2 test, the difference between the proportions of cases detected in the sampling sites is statistically significant ($\chi^2 = 96.03$, p-value < 0.001), so there is a relationship between the municipality and the number of cases of leishmaniasis. On the other hand, the VL form applies to all municipalities except Mikkes, where no cases were recorded during the study period (Figure 9). As shown in Figure 8, the commune of Ain Chkef had the largest number of CL cases with 71 cases (39.51%), followed by the commune of Ain Kansara with 25 cases (17.07%). The commune of Ain Bouali was the most affected by the visceral form (15 cases; 10%), followed by the commune of Sbaâ Rouadi and Laâjajra (14 cases; 7%). Furthermore, these two municipalities are almost the only ones affected by the CL. They accounted for 84.95% of all instances, whereas the total number of cases in the remaining municipalities did not surpass 15.05%. According to the Chi-square test, there is a statistically significant ($\chi^2 = 67.5$, p-value < 0.001) relationship between the sampling sites and the types of leishmaniasis detected. The dependency hypothesis, which suggests that the percentages of CL and VL forms are statistically different from one site to another., should be retained.

The results of the present study demonstrated that the epidemiological situation of the two localities, Ain Chkef and Ain Kansara was different from the other municipalities. The greatest number of cases of leishmaniasis was recorded in these two communes. Among the 11 communes of the Moulay Yaâcoub Province, 9 communes were found with VL. This observation suggests that the Moulay Yaâcoub Province is a home for the CL and VL. The high number of cases of leishmaniasis in the two communes of Ain Chkef and Ain Kansara could be explained by the diversification of risk factors, favourable

ecological and weather conditions, the proliferation of the sandfly vector, the presence of the parasite, as well as the existence of the reservoir. The emergence or re-emergence of leishmaniasis is directly linked to the increase in risk factors which are essentially anthropogenic in nature.⁴⁰ Climate change is also a major contributor to the increase and spread of vector-borne diseases, including leishmaniasis.^{41,42}

Studies and research on factors affecting the distribution of CL and VL, as the impact of urbanization and socio-economic factors should be conducted in this province. The findings of these studies will help to understand the pathology in this province, as well as to control its distribution compared to the other provinces of the region.^{43,28,44}

In 2016, it was discovered that the Moulay Yacoub Province has a diverse phlebotomy fauna, which differs from one site to the next, with some localities having more species than others.⁴⁵ The diversity of species, abundance of sandflies, climatic factors, urbanization, and socio-economic situation could make this province more vulnerable to the leishmaniasis risk.

Conclusion

The findings of the present study have established for the first time the coexistence of CL and VL in the Moulay Yaâcoub Province. The retrospective study of the province of Moulay Yaâcoub has shown the existence of cases of leishmaniasis in both forms.

Therefore, efforts to combat this disease remain critical, and there is a significant need to raise awareness and information campaigns among populations at risk, as well as to implement a strategy to combat this disease.

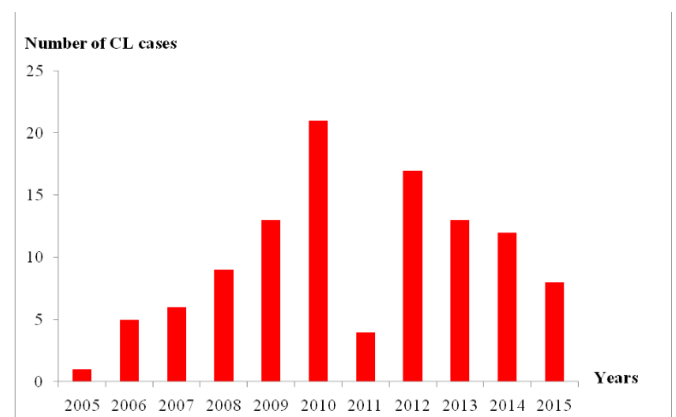


Figure 6: Temporal evolution of cutaneous leishmaniasis cases in Moulay Yaâcoub Province from 2005 to 2015.

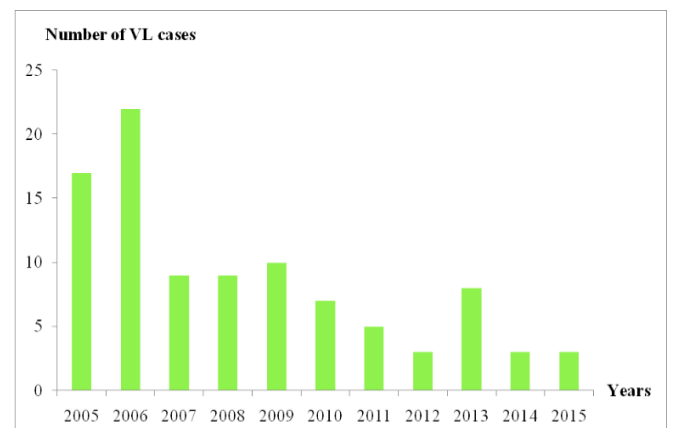


Figure 7: Temporal evolution of cases of visceral leishmaniasis in the Moulay Yaâcoub Province from 2005 to 2015.

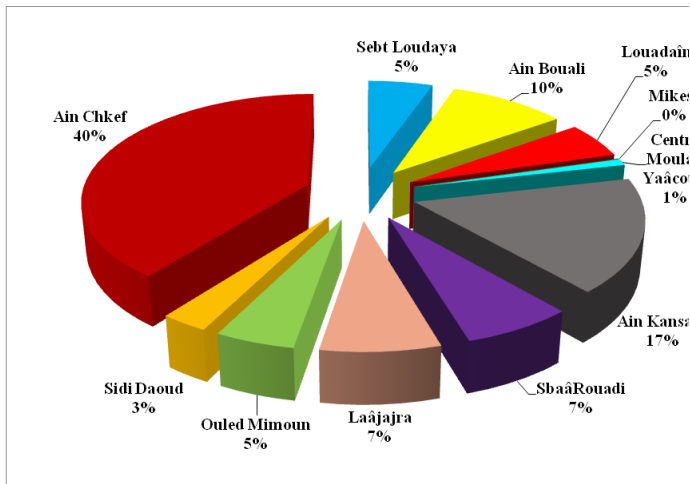


Figure 8: Spatial distribution of leishmaniasis cases in Moulay Yaâcoub Province from 2005 to 2015.

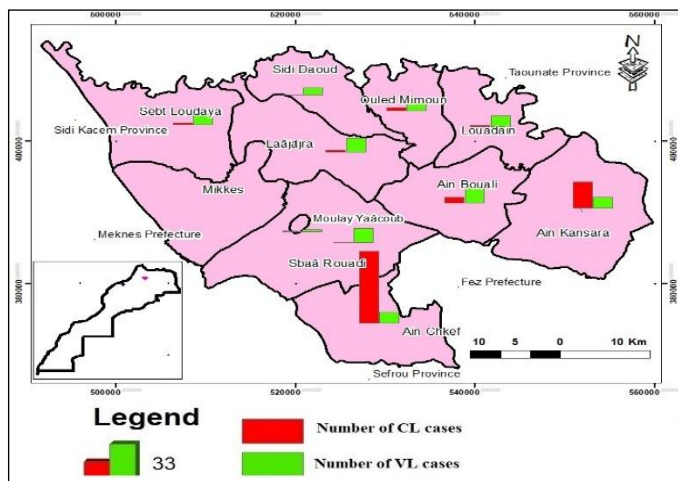


Figure 9: Spatial distribution of the number of cutaneous and visceral leishmaniasis cases recorded in Moulay Yaâcoub Province from 2005 to 2015.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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