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Epidemiological study on acute cutaneous leishmaniasis in Morocco

Kholoud Kahime[1*], Samia Boussaa[1,2], Abderrahmane Laamrani-El Idrissi[3], Haddou Nhammi[3], Ali Boumezzough[1*]

[1]*Laboratory of Ecology & Environment, (URAC 32, CNRST; ERACNERS 06), Faculty of Sciences Semlalia, Cadi Ayyad University, Marrakesh, Morocco*

[2]*ISPITS-Institut Supérieur des Professions Infirmières et des Techniques de Santé, Marrakesh, Morocco*

[3]*Directorate of Epidemiology and Disease Control, Ministry of Health, Rabat, Morocco*

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ABSTRACT

Objective: To describe and compare the epidemiological features of anthroponotic cutaneous leishmaniasis (ACL) caused by *Leishmania tropica*, and zoonotic cutaneous leishmaniasis (ZCL) due to *Leishmania major* in Morocco.
Methods: We performed a retrospective study of ZCL and ACL cases reported during the last ten years in Morocco (2004–2013). Epidemiological data were analyzed by using Pearson's correlation method as well as Tukey test and digital maps were produced for incidence repartition calculated by using ArcMap GIS version 10.
Results: A total of 41 656 cases of cutaneous leishmaniasis were notified between 2004 and 2013 in Morocco. The mean incidence was 139 cases/100 000 population/10 years and it was significantly higher in 2010. In the spatial context, ACL form was the most common in Morocco, while ZCL was the most important in terms of the number of reported cases. For both forms, the highest incidence occurred in females and children (0–14 years). When analyzed according to the number of cases in each province, Errachidia (8 728 cases) and Azilal (3 523 cases) were the most affected by ZCL and ACL, respectively, while the highest incidence was noted in Zagora (231 cases/100 000 population/10 years) and in Chichaoua (97 cases/100 000 population/10 years), for ZCL and ACL, respectively. Maps of incidence repartition were performed to identify the risk area of ZCL and ACL.
Conclusions: ZCL and ACL are still major health problems in Morocco. We highlight the spatiotemporal change of cutaneous leishmaniasis incidence through the country during the last ten years and we underline the correlation between ZCL incidence and the percentage of rural population in Morocco.

1. Introduction

Leishmaniases are parasitic diseases with a wide range of clinical symptoms. In the skin, they range from localized cutaneous and mucocutaneous leishmaniasis to diffuse cutaneous leishmaniasis (CL), whereas in the viscera they range from subclinical to potentially fatal disease[1,2]. These parasitic protozoans are usually transmitted to a human host via a bite by an infected female phlebotomine sandfly (Diptera: Psychodidae) on exposed parts of the human body. Leishmaniasis currently threaten 350 million persons in 88 countries[2].

Caused by three *Leishmania* species [*Leishmania major* (*L. major*), *Leishmania tropica* (*L. tropica*) and *Leishmania infantum* (*L. infantum*)], CLs are endemic, widespread and represent a public health problem in most countries in the Mediterranean basin[3].

In Morocco, CL is widely distributed as three nosogeographic entities. *L. major* is transmitted by *Phlebotomus papatasi* and is associated with zoonotic cutaneous leishmaniasis (ZCL) in the arid regions along the northern edge of the Sahara desert[4–6]. *L. infantum* is transmitted by *Phlebotomus ariasi* and causes zoonotic cutaneous disease (and mainly zoonotic visceral form) in the north and centre-south regions of the country[5–7]. Lastly, *L. tropica*, causative agent of anthroponotic cutaneous leishmaniasis (ACL), is widespread in the semi-arid regions of

*Corresponding authors: Kholoud Kahime, Laboratory of Ecology & Environment, (URAC 32, CNRST; ERACNERS 06), Faculty of Sciences Semlalia, Cadi Ayyad University, Marrakesh, Morocco.
E-mail: kahimkholoud@gmail.com
Ali Boumezzough, Laboratory of Ecology & Environment, (URAC 32, CNRST; ERACNERS 06), Faculty of Sciences Semlalia, Cadi Ayyad University, Marrakesh, Morocco.
E-mail: aboumezzough@gmail.com
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Central and South-western Morocco, and transmitted by *Phlebotomus sergenti* (*P. sergenti*)[5,6,8]. The main reservoirs for ZCL by *L. infantum* and *L. major*, respectively, are dogs and rodents[9,10], with humans fulfilling this function for ACL by *L. tropica*[11].

Over the past decade, the epidemiological situation of CL has changed significantly. It is acquiring an increasingly epidemic status with geographic expansion to previously free areas and the emergence of new foci in several provinces of Morocco. A total of 24 804 cases of *L. major* CL and 16 852 cases of *L. tropica* CL were recorded between 2004 and 2013 in Morocco. *L. infantum* CL meanwhile is a rare condition with a few sporadic cases in the north of the country (especially in Sidi Kacem Province) and few epidemiological data are available[5,12]. This study was designed to describe and compare the epidemiological features of *L. major* and *L. tropica* CL cases during a ten year period (2004–2013) in Morocco.

2. Materials and methods

2.1. Study area and population

Located between the Atlantic and the Mediterranean between latitudes 21N–36N and longitudes 1W–17W, Morocco was placed in the extreme northwest of the African continent. It had the most important permanent rivers in the Maghreb but suffers in semi-arid to arid areas from a lack of water during all seasons[13]. Morocco's climate was Mediterranean and mainly characterized by hot and dry summer where rainfall was almost completely absent except in mountain areas (which have significant thunderstorm activity) and particularly high evaporation. It was characterized also by a temperate to mild winter in the coastal strip, cool to cold in the country's interior, on the chains of the Atlas, in the Rif and the highlands of the eastern[14].

Morocco had a surface area of 710 850 km^2 and a population of 29 891 708 with 13 428 074 inhabitants in rural areas[15].

2.2. Epidemiological data

The present study was a retrospective analysis of the CL in Morocco. Epidemiological data were obtained from the bulletins, registers and reports published by the local and national medical services. These epidemiological data were recorded after active or passive screening (leishmaniasis is a certifiable disease in Morocco). We used clinical and epidemiological data provided by the Moroccan Directorate of Epidemiology and Fight Against Diseases, during 2004–2013[16].

2.3. GIS data base and statistic analysis

Digital maps were produced for incidence repartition calculated for the studied area by using ArcMap GIS version 10. The output was two maps each depicting the incidence of ZCL and ACL.

All data were analyzed by using SPSS software and Pearson's correlation method. Results were considered significant when the *P*-value was less than 0.05 by using a Tukey test.

3. Results

Table 1 shows the general characteristics of all provinces ($n = 52$) affected by CL (ZCL and ACL) and the incidence (cases/100 000 inhabitants/10 years) of CL in Morocco. For ZCL, the

Table 1

Geographic, demographic and epidemiologic characteristics of each province affected by CL in Morocco.

CL form	Provinces	Latitude	Longitude	Rural population (%)	Incidence (cases/100 000 inhabitants/ 10 years)
ZCL	Boulemane*	33.363	−4.730	70.93	35.01
	Errachidia*	31.934	−4.423	64.89	156.81
	Figuig	32.213	−1.368	51.20	179.32
	Jrada	34.312	−2.164	38.77	99.58
	Midelt	32.684	−4.735	100.00	39.75
	Ouarzazate*	30.907	−6.908	70.29	87.60
	Taourirte	34.416	−2.900	42.29	0.10
	Tata	29.746	−7.970	67.88	15.29
	Tinghir	31.522	5.518	78.27	15.18
	Zagora	30.332	−5.837	661.06	231.08
ACL	Agadir I Outanane	30.412	−9.604	21.10	0.23
	Al haouz	31.307	−7.858	89.22	14.64
	Al Hoceima	35.249	−3.938	70.06	2.65
	Azilal	31.967	−6.569	83.81	69.83
	Ben Slimane	33.616	−7.131	63.18	0.05
	Béni Mellal	32.339	−6.355	52.71	5.99
	Berkane	34.924	−2.320	42.24	0.22
	Boulemane*	33.363	−4.730	70.93	11.61
	Chefchaouen	35.171	−5.272	89.56	2.02
	Chichaoua	31.545	−8.765	87.09	96.96
	Chtouka Ait Baha	30.071	−9.162	86.65	0.44
	Driouach	34.982	−3.383	70.64	5.02
	El jadida	33.241	−8.505	72.92	0.01
	El kelaa Sraghna	32.050	−7.409	75.95	1.07
	Errachidia*	31.934	−4.423	64.89	0.45
	Essaouira	31.514	−9.770	421.73	66.55
	El Hajeb	33.693	−5.372	57.32	0.46
	Fahs Anjra	35.766	−5.667	100.00	1.13
	Fès	34.035	−5.000	2.33	0.84
	Fkih Ben salah	32.508	−6.694	100.00	6.31
	Guelmim	34.234	−3.351	31.18	4.50
	Guercif	34.233	−3.351	100.00	6.11
	Inezgane A Melloul	30.356	−9.550	8.10	0.17
	Kenitra	34.263	−6.581	50.94	0.05
	Khemisset	33.821	−6.069	58.03	0.19
	Khenifra	32.939	−5.668	47.23	0.31
	Larache	35.184	−6.151	53.52	1.40
	Marrakech	31.637	−7.997	21.22	0.33
	Meknes	33.893	−5.556	19.99	0.91
	Mdiq Fnideq	35.684	−5.330	6.40	0.58
	Moulay Yacoub	34.088	−5.181	97.90	5.32
	Nador	35.168	−2.939	49.34	2.55
	Ouazzane	34.800	−5.583	18.88	8.56
	Ouarzazate*	30.907	−6.908	70.29	15.64
	Sale	34.038	−6.803	6.56	1.03
	Safi	32.321	−9.219	52.86	0.05
	Sefrou	33.831	−4.840	53.18	32.94
	Settat	33.002	−7.621	66.16	6.11
	Sidi Kacem	34.236	−5.713	69.91	17.88
	Sidi Slimane	34.261	−5.923	100.00	37.66
	Tanger Assilah	35.777	−5.839	7.73	0.17
	Taounate	35.249	−3.940	89.83	15.31
	Taroudannte	30.468	−8.869	76.11	5.67
	Taza	34.228	−4.021	66.33	12.96
	Tetouan	35.577	−5.368	24.37	4.19
	Tiznit	29.708	−9.730	75.97	0.26

*:Provinces with both ZCL and ACL forms.

highest incidence was observed in Zagora (231.08 cases/100 000 inhabitants/study decade) and Figuig (179.32 cases/100 000 inhabitants/study decade), followed by Errachidia (156.81 cases/100 000 inhabitants/study decade). This high incidence could be linked to the elevated percentage of rural populations in these areas. The lowest incidence was determined in Taourirte (0.10 cases/100 000 inhabitants/study decade) (Table 1).

Figure 1 presents the temporal evolution of CL (ZCL and ACL) cases in Morocco between 2004 and 2013. The highest CL cases were noted between 2008 and 2011 for ZCL and between 2010 and 2013 for ACL. The overall maximum of cases, for both forms, was reported in 2010.

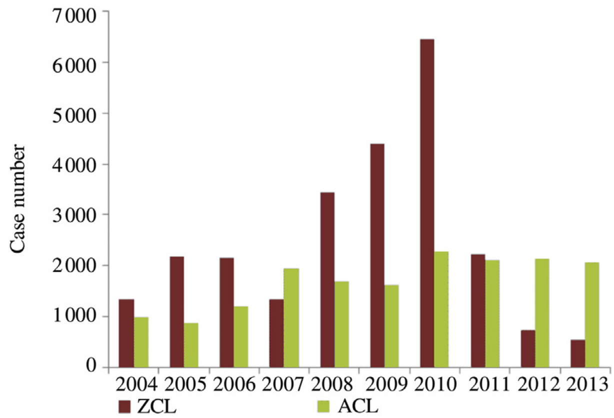

Figure 1. Temporal evolution of CL (ZCL and ACL) cases in Morocco, 2004–2013.

Spatiotemporal analysis of ZCL (from 2004 to 2013) showed a northward migration of the disease to Jrada and Taourirt (Figure 2).

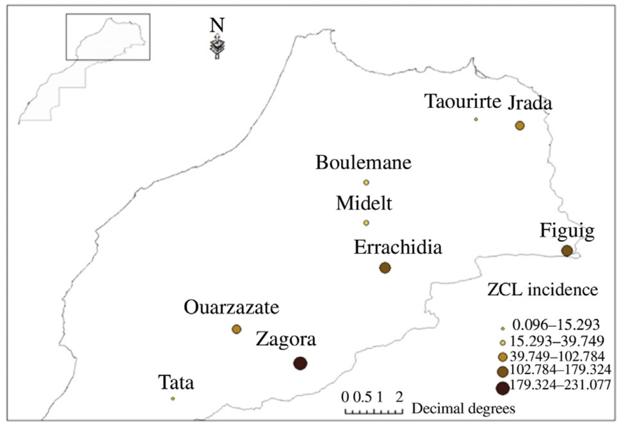

Figure 2. Map showing geographical distribution of ZCL incidence (cases due to *L. major*/100 000 population/(2003–2014 period) in Morocco provinces. Ouarzazate: Ouarzazat + Thinghir.

Concerning ACL, the highest incidence was observed in Chichaoua (96.96 cases/100 000 inhabitants/study decade) followed by Azilal (69.83 cases/100 000 inhabitants/study decade), whereas the lowest incidence occurred in Kenitra, Ben Slimane, Safi, El Jadida with incidence between 0.05 and 0.01 cases/100 000 inhabitants/study decade (Table 1, Figure 3).

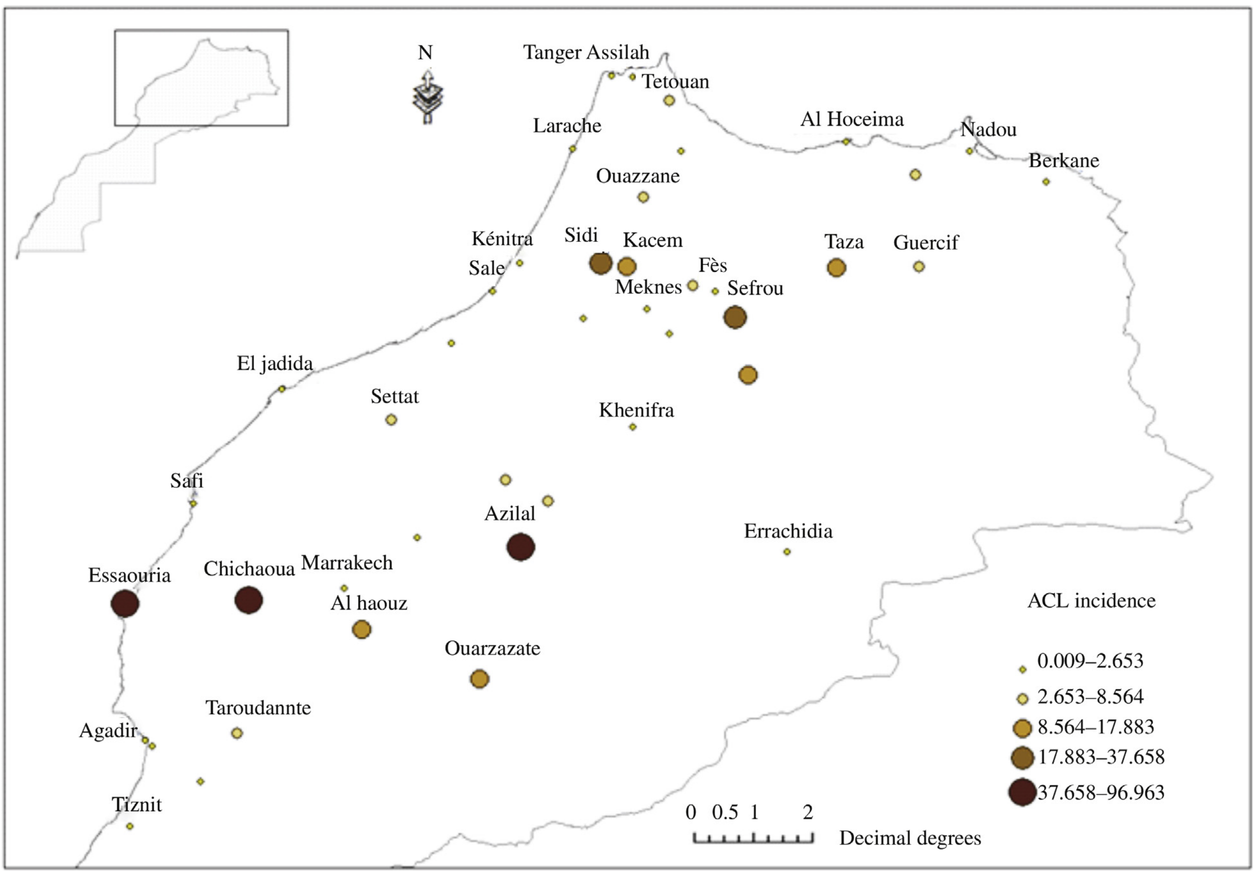

Figure 3. Map showing geographical distribution of ACL incidence (cases due to *L. tropica*/100 000 population/10 years) in Morocco (cases recorded between 2003 and 2014).

Epidemiological analysis of CL distribution according to age and gender showed that all ages and both genders were affected by the different forms of disease (Table 2). The analysis with respect to age groups showed that children (less than 14 years) were significantly ($P < 0.05$) affected (62%; 67%) compared to adults (38%; 33%) for ZCL and ACL, respectively (Table 2).

Table 2
Epidemiological characteristics of CL in Morocco (2004–2013).

CL form	Parameters		Year										Total	*P*
			2004	2005	2006	2007	2008	2009	2010	2011	2012	2013		
ZCL	Gender	Male	619	998	971	598	1 458	1 897	2 757	995	351	243	10 887	N.S
		Female	722	1 176	1 193	754	1 973	2 505	3 687	1 224	389	294	13 917	
		Total	1 341	2 174	2 164	1 352	3 431	4 402	6 444	2 219	740	537	24 804	
	Age group	< 5 years	202	273	334	210	523	816	1 038	414	214	188	4 212	$P < 0.05$
		5–14 years	536	828	875	479	1 392	1 933	3 408	1 156	322	134	11 063	
		15 years and above	603	1 073	955	663	1 516	1 653	1 998	649	204	215	9 529	
		Total	1 341	2 174	2 164	1 352	3431	4 402	6 444	2 219	740	537	24 804	
ACL	Gender	Male	406	381	506	816	729	699	1 037	970	1 009	929	7 482	N.S
		Female	585	483	691	1 122	968	912	1 226	1 130	1 127	1 126	9 370	
		Total	991	864	1 197	1 938	1 697	1 611	2 263	2 100	2 136	2 055	16 852	
	Age group	< 5 years	232	214	359	470	610	584	896	858	864	926	6 013	$P < 0.05$
		5–14 years	364	304	380	644	560	533	690	694	688	513	5 370	
		15 years and above	395	346	458	824	527	494	677	548	584	616	5 469	
		Total	991	864	1 197	1 938	1 697	1 611	2 263	2 100	2 136	2 055	16 852	

N.S: Not significant.

4. Discussion

Human CL is widely distributed in Morocco. Compared with visceral leishmaniasis (3.17%), CL accounted for 96.83% of leishmaniasis cases between 2004 and 2013. Within this CL form, ZCL presented 57.63% (about 24 804 cases), while ACL recorded 39.20% (16 852 cases) of CL cases reported in the same period.

ZCL is the oldest leishmaniasis form in Morocco. In the pre-Saharan area, it has been identified since 1914[17], in the palm grove of Oued Tata, where a subsequent and major CL epidemic was manifested during the late 1970s. After Tata, two new epidemics were identified: one located along the Draa, in the depression of Ouarzazate and the other on the high plateau, south of Oujda[4,18]. Now identified as rampant in the country, the disease has spread endemically both in the per-arid Moroccan palm grove zone (the Tata-Akka-Foum Z'Guid triangle in Ouarzazate Province and in the Northern Oriental Highlands in the arid Ain-Beni Mathar strip[4,19]. Actually, ZCL in Morocco is caused by *L. major* zymodeme MON-25 and transmitted by *P. papatasi*, with *Meriones shawi grandis* as the main reservoir host[6].

About 73 years after ZCL's Moroccan identification, the ACL form was identified in 1987. Since 1997, it has been considered as a major threat to public health[5]. It was widespread in semi-arid regions, provinces in central and western slopes of the Atlas Mountains, from Azilal in the centre up to Essaouira in the west and Agadir-Guelmim in the south[8]. Currently, ACL is transmitted by the sandfly *P. sergenti*, with human as the only reservoir and caused by *L. tropica* with many zymodemes (MON-102, MON-107, MON-109, MON-112, MON-113, MON-122 and MON-123)[6].

Leishmaniasis affects both genders with an equal distribution of cases between genders (56% female and 44% male for both infections of ZCL and ACL). This may be related to the fact that women sufferers seek medical advice more often than male counterparts because of the unsightly lesions and the socio-economic consequences for women of a perception of ‘unmarriageability’ due to unpleasing appearance[20].

All ages are affected by the different forms of disease, with a high incidence for young children who are at most risk. The same result was recorded for *L. tropica* and *L. major* foci in Morocco[21–23]. This marked correlation may be explained by the inability of children's immune systems to fight CL infection, as well as the comparative resistance of older people to sandfly bites[24]. The large numbers of women and children infected also indicate that leishmania transmission may have occurred in the peridomiciliary habitat[6].

According to urbanization, ACL (also known as the dry or urban) is characterized by its strong rural and urban population, in contrast to the high positive correlation between the ZCL (also recognized as the wet or rural) incidence and percentage of rural population ($R^2 > 0.49$).

Moreover, over the past two decades, the epidemiological situation of CL has changed significantly. It acquired an increasingly epidemic status with geographic expansion into previously free areas in several provinces of South-east Morocco[23]. According to Bounoua *et al.*[25], changes in climate may have resulted in an increase in ZCL incidence in Errachidia. In addition to noted global change, socio-economic factors such as poverty, lack of infrastructure, lifestyle and factors influencing the environment, appear to be among the major underlying determinants of leishmaniasis in the region, a result in agreement with previous studies[23,25,26].

Concerning ACL, the highest incidence was observed in Chichaoua (96.96 cases/100 000 inhabitants/study decade) and Azilal (69.83 cases/100 000 inhabitants/study decade). This propagation may be related to the vector distribution. *P. sergenti* had an extensive geographical distribution and it was also reported in all bioclimatic rural as well as urban population habitats[6]. Furthermore, since humans constitute the only reservoir host for ACL, the movement of populations (travel, migration, *etc.*) may present a source of risk for the spread of the disease. These hypotheses may explain the increase of the incidence of ACL and its extension to new non-endemic areas in all directions.

This study reveals that ZCL and ACL pose a continuous and important health problem in Morocco. In the light of our findings, the change of spatiotemporal CL incidence was identified.

Epidemiological data clearly demonstrate the correlation between incidence of ZCL and the percentage of rural population in different provinces. The cosmopolitan character of species vector of ACL, and population movement may form a source of risk for the spread of ACL disease. Additionally, theses diseases may be linked to vector preferences, socio-economic conditions, climate and environmental factors. Finally, the use of spatial analyses is a highly useful tool in determining high incidence risk zones.

Conflict of interest statement

The authors report no conflict of interest.

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