



Risk mapping of human HIV-Leishmaniasis co-infection in Morocco

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ABSTRACT

Background: HIV/AIDS is frequently associated with opportunistic diseases such as leishmaniasis. Hence, the co-infection HIV-*Leishmania* spp. is the result of the geographical overlap between leishmaniasis and HIV/AIDS cases. To the best of our knowledge, this is the first report describing the spatial distribution of HIV-Leishmaniasis co-infection in Morocco where both infections are endemic.

Methods: In the current study, we discuss the HIV-*Leishmania* spp. co-infection vulnerability in Morocco by using the cartography tools. Thus, epidemiological data of both infections (Leishmaniasis and HIV/AIDS) in different administrative regions of Morocco were collected and co-registered for Digital maps making.

Results & conclusion: The results showed a high risk of HIV-*Leishmania infantum* co-infection in northern and central regions in Morocco. These results should be taken into account for efficient control strategies and epidemiological surveillance of HIV -*Leishmania* spp. co-infection in Morocco.

1. Introduction

Acquired Immunodeficiency Syndrome (AIDS) and leishmaniasis are among the priority diseases of the World Health Organization (WHO, 2000).

Human Immunodeficiency Virus (HIV) responsible of AIDS, is now attacking the entire world and it is changing the society's future, particularly in developing countries (WHO, 2012). One of the essential characteristics of AIDS is its frequent association with opportunistic diseases, such as leishmaniasis (Lindoso et al., 2016). These opportunistic infections take advantage of a very weak immune system, or immunodeficiency caused by HIV, to occur more frequently and more severe diseases (Mofenson et al., 2009).

Leishmaniasis are a common parasitosis to humans and certain mammals. They are caused by flagellate protozoa of the genus *Leishmania* and transmitted by the bite of an infested sand fly (*Diptera: Psychodidae*) (Torres-Guerrero et al., 2017). Currently, leishmaniasis corresponds to a group of diseases comprising different clinical forms: visceral leishmaniasis, localized or diffuse cutaneous leishmaniasis and cutaneous-mucous

leishmaniasis (Scorza et al., 2017).

In Morocco, both infections exist and constitute a public health concern (Rhajaoui, 2011). The number of Moroccans living with HIV was estimated to be 32 000 in 2014 and the cumulative total number of HIV/AIDS cases reported from 1986 to 2014 was 10 017 (MMH, 2015a).

Regarding leishmaniasis, three *Leishmania* species representing two leishmaniasis forms (cutaneous CL and visceral leishmaniasis VL) co-occur in Morocco: *Leishmania major*, *L. tropica* and *L. infantum*. A total of 27 257 cases of zoonotic cutaneous leishmaniasis (ZCL by *Leishmania major*) was reported during the period of 2000–2013 with an annual incidence of 5000 cases per year (MMH, 2015b); followed by anthroponotic cutaneous leishmaniasis (ACL by *L. tropica*) with 17 882 reported cases during the last 10 years (MMH, 2015b); while, an average of 150 cases of visceral leishmaniasis (VL by *L. infantum*) is annually recorded (Rhajaoui, 2011; MMH, 2015b).

Understanding and predicting patterns of HIV/AIDS-Leishmaniasis co-infection risk is an important component of an effective control

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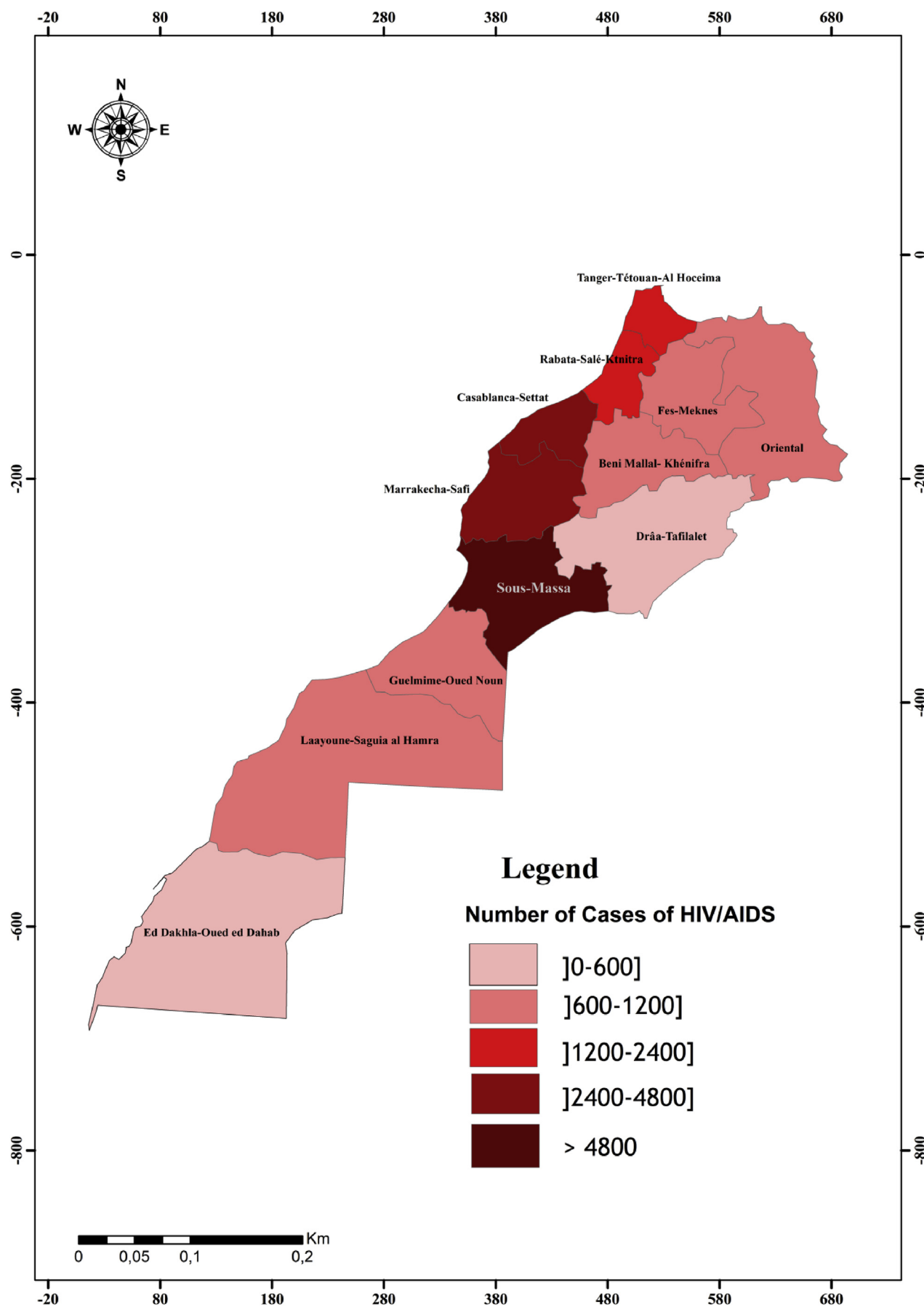


Fig. 1. Geographical distribution of HIV/AIDS cases in Morocco.

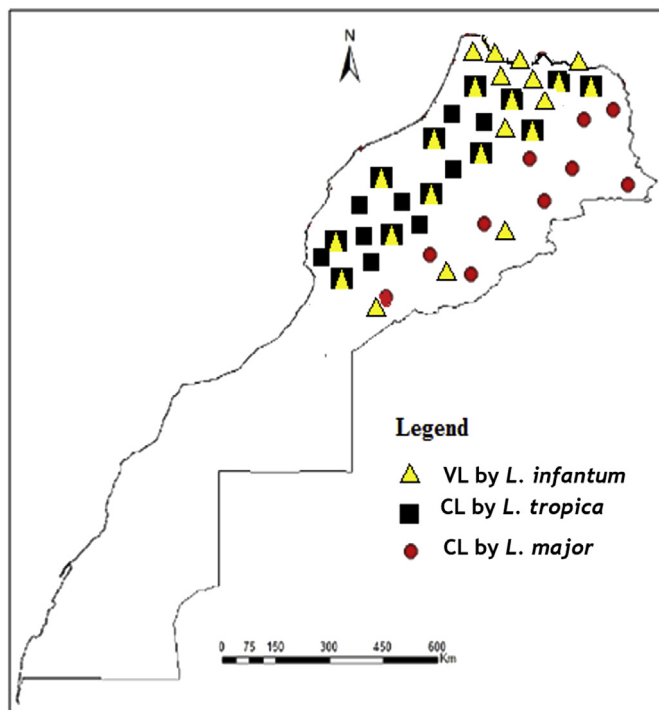


Fig. 2. Geographical distribution of cutaneous (CL) and visceral (VL) leishmaniasis entities in Morocco.

campaign. Knowing that HIV- *Leishmania* spp. co-infection is the result of their geographical overlapping (Alvar et al., 2008), we determine here, the area with a high risk of HIV-*Leishmania* spp. co-infection for the first time in Morocco.

2. Materials and methods

2.1. Study area

Morocco, officially the Kingdom of Morocco, is a country located in North Africa, bordering the North Atlantic Ocean and the Mediterranean Sea. Total population of Morocco is 33 million with a total of area of 710850 km². The mean rate of urbanization recorded in Morocco is 61.9 % with differences according to regions (HCP, 2014).

2.2. Epidemiological data

In this retrospective study, digital maps were produced by matching the number of cases of leishmaniasis and HIV/AIDS. Epidemiological data were collected from the bulletins, registers and annual reports published by the local and national medical services; and completed from the local Ministry of Health offices, after official authorization from the regional delegations of Moroccan Ministry of Health.

2.3. Cartography

Arc Gis® software was used for mapping (Version 10.4), an information system designed to collect, store, process, analyze, manage and present spatial and geographic data.

3. Results & discussion

Cases of HIV-*Leishmania* co-infections have been reported in 33 countries, most of them were in southwestern Europe (France, Italy, Portugal and Spain) (Lindoso et al., 2016). In some parts of East Africa and India, large migration flows (refugees, seasonal workers) and certain at-risk populations (truck drivers, sex workers) are causing a growing overlap between the two diseases. In addition, the incidence of both diseases increased sharply in both regions, increasing the likelihood of co-infections (Desjeux and Alvar, 2003). This worrying situation prompted WHO/UNAIDS (WHO, 1998) to set up a global network for HIV-*Leishmania* co-infection.

In Morocco, despite the high incidence of both leishmaniasis and HIV (Figs. 1 and 2) infections, to date, little is known about the Leishmaniasis – HIV/AIDS co-infection.

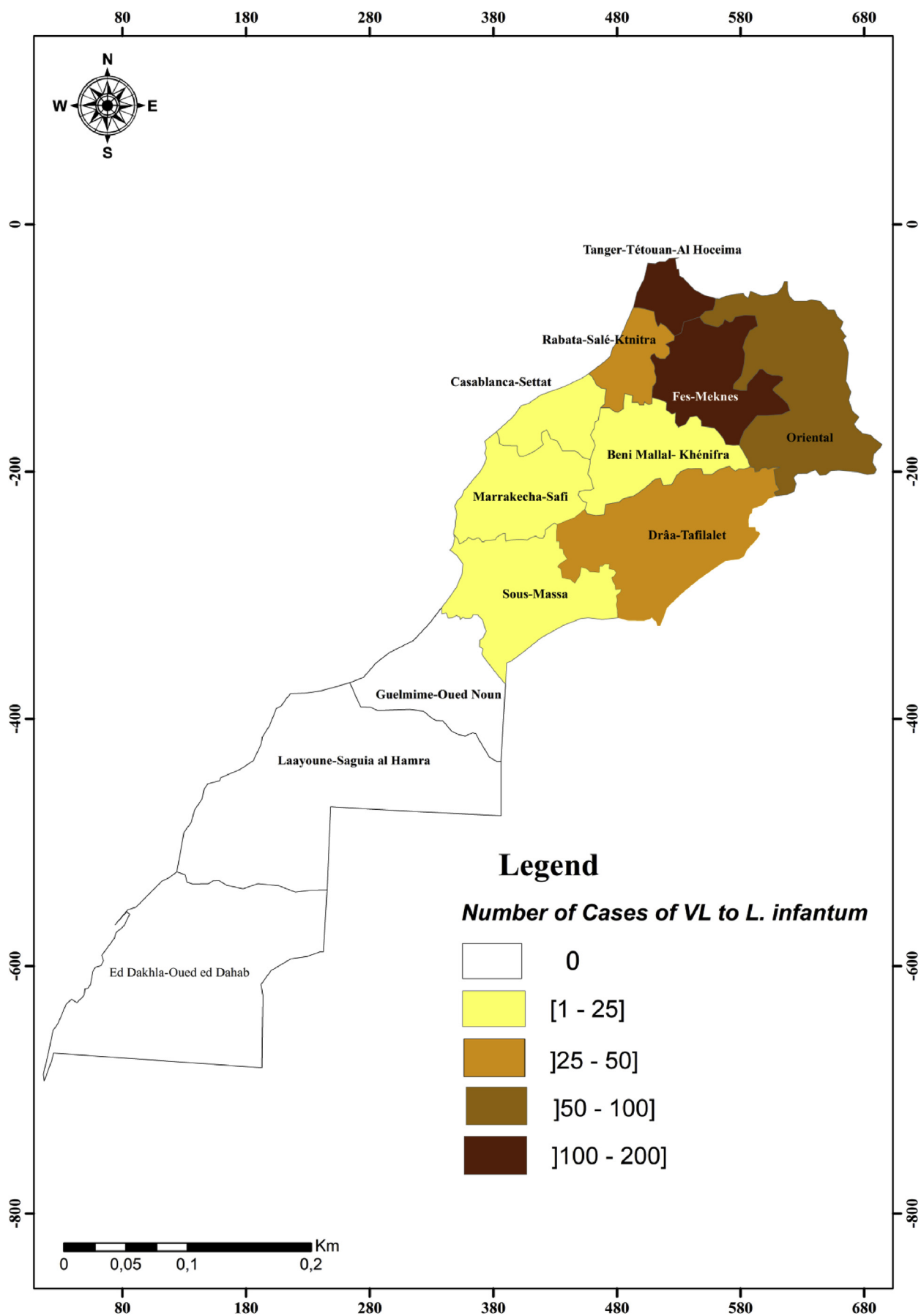
Depending on the origin of the infection, leishmaniasis in Morocco can be grouped into three eco-epidemiological entities. Zoonotic Visceral Leishmaniasis (ZVL) and less frequently Zoonotic Cutaneous Leishmaniasis (ZCL) caused by *L. infantum* which is maintained in long term by dogs and bites of three vector species; *Phlebotomus ariasi*, *P. perniciosus* and *P. longicuspis* (Zarrouk et al., 2015). The Ministry of Health is still considering *L. infantum* as evolving sporadically mainly in northern Morocco (Fig. 2) with some 150 cases per year, while, many authors estimated that the VL incidence may be as high as 600 cases per year (Tachfouti et al., 2016). ZCL caused by *L. major*, where the parasite is maintained among small mammals and human by the bites of *P. papatasi* (Echchakery et al., 2015). ZCL has been known to exist in the vast arid pre-Saharan regions (Fig. 2). ACL caused by *L. tropica* and transmitted by the bites of *P. sergenti*. Human is the main host-reservoir with the possibility of zoonotic cycle (Echchakery et al., 2017). ACL has been known to occur mainly in north and central of Morocco were many foci were reported (Guessous-Idrissi et al., 1997; Ramaoui et al., 2008; Boussaa et al., 2009; Rhajaoui et al., 2012; Ajaoud et al., 2013).

Currently, the change in the epidemiological trends of leishmaniasis was noted in Morocco with the spread of *L. tropica* and *L. infantum* to areas known until then as free and consequently, the overlap of the spatial distribution areas of the three *Leishmania* species (Hakkour et al., 2016; Hmamouch et al., 2017). Geographical distribution of our epidemiological data (Fig. 2) shows the widespread of *L. infantum* and *L. tropica* leishmaniasis in northern and central Morocco and confirms the overlapping of these two species in these areas. According to region, VL due to *L. infantum* is more marked in Fez-Meknes and Tanger-Tetouan-Al Hoceima regions, followed by Oriental, Rabat-Sale-Kenitra and Draa-Tafilelt regions (Fig. 3).

Regarding HIV infection, we noted the presence of the cases through Morocco. Sous-Massa and Marrakech-Safi are the most administrative regions concerned; with respectively, 24% and 18% of people living with HIV in Morocco (Fig. 1). The evolution of HIV/AIDS pandemic in Morocco between 1980 and 2015 shows an exponential increase (Fig. 4). The number of HIV/AIDS reported cases between 2009 and 2014 was 1312768 cases accounted for 51% cases of the total cases (MMH, 2015a).

70 % of the new infections would arise at the people the most exposed at the risk of the infection HIV or among their stable sexual partners. Men are more affected (63%) and the majority (73%) of the contaminated women is expected to be infected with the spouse (Fig. 4). The contamination of the man is in 92 % of the cases linked to the behavior at high risk (specially the multi-sexual partnership).

Among the notified cases, the heterosexual mode is the dominant mode of transmission (85.1 %), while the transfusional way is not clearly incriminated in the transmission of the HIV in Morocco (0.1 %). In contrast, the perinatal mode is responsible of 3.6 % of transmission

Fig. 3. Geographical distribution of cases of VL by *L. infantum* in Morocco.

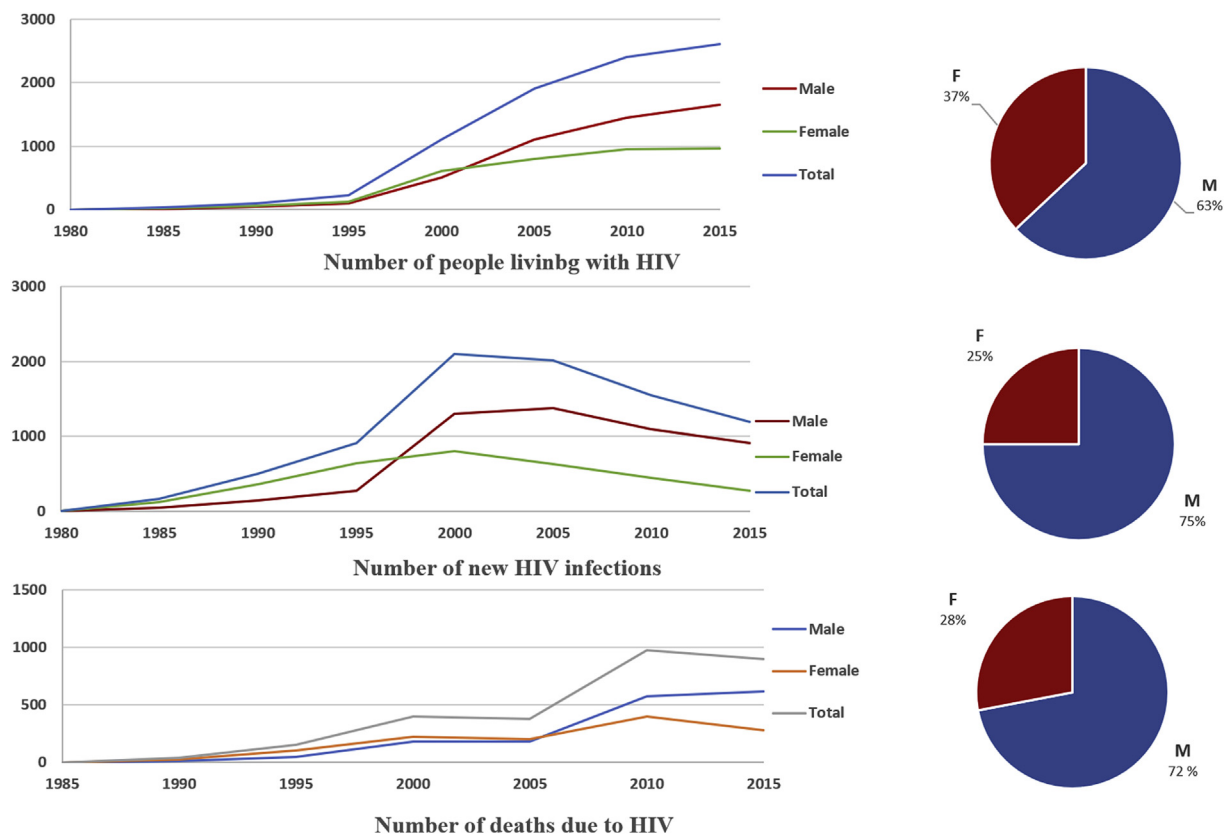


Fig. 4. Evolution of HIV-AIDS prevalence, incidence and lethality in Morocco by gender between 1980 and 2015 (MMH, 2015a).

proportion.

According to Alvar et al. (2008) the HIV-*Leishmania* spp. co-infection is the result of the geographical overlap between Leishmaniasis and AIDS cases. Thus, the cartography technique represents the geographical distribution of these two conditions in the different areas of Morocco. The superposition of the two maps, of leishmaniasis and HIV-AIDS, can identify the area at risk of HIV-*Leishmania* co-infection in Morocco.

Consequently, seven regions out of twelve (Marrakech-Safi, Casablanca-Settat, Rabat-Sale-Kenitra, Fez-Meknes, Tanger-Tetouan-Al Hoceima, Oriental and Sous Massa) are at high risk of HIV-*Leishmania infantum* VL co-infection (Fig. 5). These results are confirmed recently in Marrakech-Safi region where specific anti-*L. infantum* antibodies were detected in 5% of HIV-infected patients (Echchakery et al., 2018). Furthermore, canine *L. infantum* VL might contribute to increase the risk of HIV-VL coinfection. In Morocco, Canine leishmaniasis was reported in northern (Rami et al., 2003) as well as in central Morocco (Boussaa et al., 2014).

Majority of the mortality due to *Leishmania* spp. in the context of HIV co-infection arises from visceral leishmaniasis (Jarvis and Lockwood, 2013). CL-HIV co-infection is much less common than VL-HIV co-infection. In HIV infected patients, CL is characterized by several clinical forms: diffused cutaneous form, ulcerated form and pseudo lepromatous form (Jebbouri, 2013). Also, some atypical cutaneous leishmaniasis and the more severe mucocutaneous variants have been reported in HIV-infected patients (Ngouateu et al., 2012).

In Morocco, considerable clinic variability was noted in many CL foci

in northern and central Morocco (Iguermia et al., 2011; Mouttaki et al., 2014) suggesting possible HIV-CL coinfection. In addition, HIV-CL co-infection case was recorded recently in Sous Massa region (Ouadia et al., 2016).

HIV-*Leishmania* co-infection is seemed to be linked to the urbanization process. According to WHO (2000), HIV-*Leishmania* spp. co-infection is favored by the spread of HIV/AIDS to rural areas and urbanization of leishmaniasis. HIV-AIDS is known as urban disease (Hall et al., 2010). In Morocco, 95% of HIV-AIDS patients reside in urban areas (MMH, 2015a), whereas, the urbanization of leishmaniasis is noted recently in Morocco, specially its anthroponotic cutaneous form (Boussaa et al., 2007) and visceral form (Kahime et al., 2017).

Co-existence of both HIV/AIDS and leishmaniasis in the same region increases the risk of both health problems (Alvar et al., 2008). That is alarming regarding the epidemiological role that can play the HIV-infected individuals as a reservoir host for leishmaniasis and that which *Leishmania*-infected patients can play in the development of HIV infection.

Indeed, the immunosuppressed individuals, including HIV-infected patients, present a higher risk of developing leishmaniasis than immunocompetent individuals (WHO, 2010). In addition, HIV-infected patients are known to be highly infectious to sand fly vectors (Monge-Maillo et al., 2014) because of the abundance of the parasite in their peripheral blood compared to immunocompetent patients (Desjeux et al., 2001). At the same time, leishmaniasis promotes the clinical progression of HIV disease and the development of AIDS-defining conditions (Alvar et al., 2008).

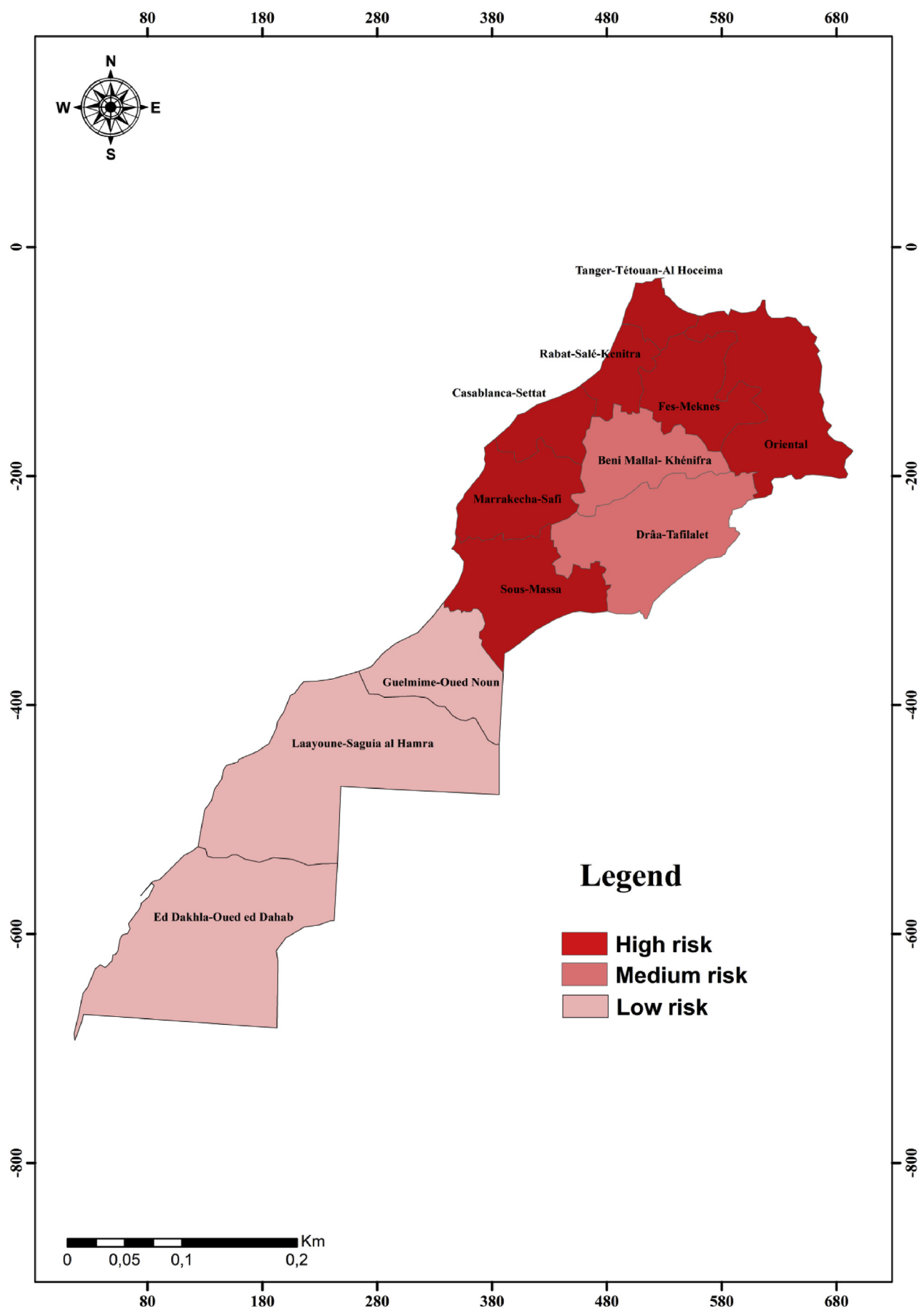


Fig. 5. Map of vulnerability areas for HIV- *Leishmania infantum* co-infection in Morocco.

4. Conclusion

In the sum, northern and central Morocco have a very high risk of HIV-*Leishmania* spp. co-infection. The change in the epidemiological trends of leishmaniasis in Morocco can be explained by the overlap with major areas of HIV transmission; hence, the need to mobilize for the control and epidemiological surveillance of HIV-*Leishmania* co-infection in Morocco. This research provides a general overview of the incidence and risk of HIV-*Leishmania* co-infection in Morocco, the epidemiological significance of these results merits' future investigations.

Declarations

Author contribution statement

Daoudi M: Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Boussaa S: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.

Echchakery M: Performed the experiments; Wrote the paper.

Boumezzough A: Conceived and designed the experiments; Wrote the paper.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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