



## Revisiting leishmaniasis in the time of war: the Syrian conflict and the Lebanese outbreak



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### SUMMARY

**Background:** Leishmaniasis is a neglected tropical disease, endemic in many worldwide foci including the Middle East. Several outbreaks have occurred in the Middle East over the past decades, mostly related to war-associated population migration. With the start of the Syrian war, the frequency and magnitude of these outbreaks increased alarmingly. We describe the epidemiology of Leishmania infection in Lebanon and the most recent outbreak relevant to the Syrian war.

**Methods:** We reviewed all leishmaniasis cases reported to the Epidemiological Surveillance Department at the Lebanese Ministry of Public Health between 2001 and the first quarter of 2014. The demographics and distribution of Syrian refugees in Lebanon were linked to reports of new Leishmania cases.

**Results:** In total, 1033 new cases of leishmaniasis were reported in 2013 compared to a previous annual number in the range of 0–6 cases. The majority of cases reported in 2013 involved Syrian refugees and their relevant areas of concentration.

**Conclusions:** This new outbreak of leishmaniasis in Lebanon is the first of its kind for more than a decade. The sudden increase in Leishmania cases in Lebanon in 2013 is attributed to the increasing numbers and wide distribution of Syrian refugees in Lebanon. This serves as an example of the risks associated with military conflicts and the ability of communicable diseases to cross borders.

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### 1. Introduction

Leishmaniasis is caused by the obligate intracellular parasites of *Leishmania* species and is transmitted by the female phlebotomine sandfly. Classified as a neglected tropical disease, leishmaniasis has focal areas of prevalence in tropical and subtropical regions and the Mediterranean Basin.<sup>1</sup> Depending on the endemic species of *Leishmania*, human and/or animal reservoirs maintain the propagation of the parasite. Some species like *Leishmania tropica* are anthroponotic, having solely human hosts. Other species like *Leishmania major* are zoonotic, exhibiting animal reservoirs.<sup>2</sup>

The clinical manifestations of leishmaniasis tend to occur months after exposure and can be one of three presentations

depending on host and parasite characteristics.<sup>1</sup> Cutaneous leishmaniasis (CL) is characterized merely by skin manifestations including papules and nodules that may ulcerate. Although these skin lesions tend to heal spontaneously, they may result in disfiguring and stigmatizing scars with a considerable impact on quality of life. Mucocutaneous leishmaniasis (ML) is a consequence of an untreated cutaneous infection that spreads into adjacent mucosal surfaces, and these tend not to heal spontaneously. The most severe and potentially fatal form is visceral leishmaniasis (VL), which affects internal organs including the bone marrow, liver, and spleen, and may exhibit a latent form reviving during states of immunodeficiency.<sup>1,3,4</sup>

No vaccine is available for *Leishmania* and the only preventative method is to limit exposure to the vector through vector control, insect repellents, insecticide-impregnated bed nets, and other modalities. The traditional approach to the treatment of leishmaniasis includes amphotericin B or its lipid formulations for visceral

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forms, and sodium stibogluconate for cutaneous forms; however, several other treatment modalities have been proposed.<sup>4,5</sup>

According to the World Health Organization (WHO), around two million cases of Leishmania are reported annually from 88 countries.<sup>6</sup> This figure is believed to be an underestimate of the true numbers by five to eight times, since reporting of the disease is obligatory in only 32 of the 88 endemic countries.<sup>6,7</sup> Over the past decade, the global burden of Leishmania has nearly reduced by half,<sup>8</sup> but its incidence is still on the rise in several regions, mainly the Middle East and South America.<sup>9</sup>

Leishmania is the most important protozoan infection in the Middle East and North Africa (MENA) region,<sup>10,11</sup> where several risk factors contribute to an increased frequency of infection. The most significant are those associated with wars and population clustering and relocation, resulting in the exposure of unimmunized individuals to the parasite.<sup>6</sup> Among the different countries of the MENA region, Syria is known to have the highest prevalence of CL,<sup>10</sup> which is often referred to in the area as 'Aleppo boil' after Aleppo, the Syrian city. Recently, owing to different war-related factors, new outbreaks have been reported by the mass media from different areas bordering Syria, including Turkey and Iraq.<sup>11,12</sup> Leishmaniasis is a mandatory reportable disease in Lebanon, and the Lebanese Ministry of Public Health (LMOPH) has implemented active surveillance for leishmaniasis since the beginning of the Syrian conflict.<sup>13</sup>

In this study, we evaluated the current leishmaniasis situation in Lebanon in light of the increasing numbers of Syrian refugees in the country, the fact that Lebanon has adopted an open border policy with Syria allowing the free flow of refugees, and the decrease in United Nations (UN) allocated resources coupled with the limited assets available to the Lebanese government to control the situation.<sup>14</sup> We also revisited the association between war and Leishmania, and the main challenges faced in the control of this infection in Lebanon are discussed herein.

## 2. Methods

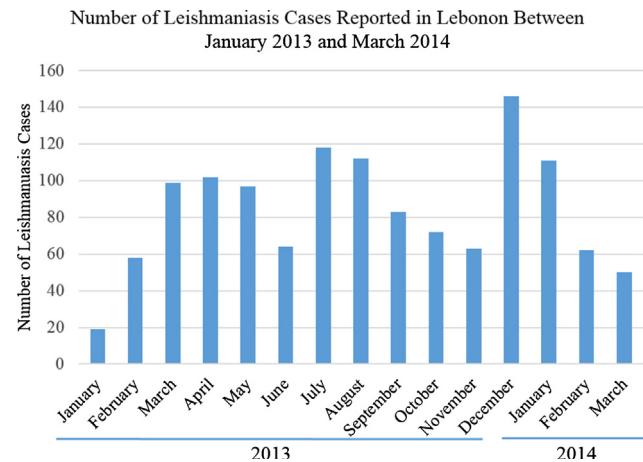
Records from the Epidemiological Surveillance Department, Lebanese Ministry of Public Health (ESDMOH) were reviewed for cases of leishmaniasis in Lebanon reported between January 2001 and March 2014. All cases reported were reviewed in terms of area of residence, age and gender, clinical presentation, treatment, and outcome. As per the LMOPH recommendations, all cases were diagnosed by the traditional diagnostic techniques of smear, parasite culture, and histological analysis of skin biopsies obtained by qualified physicians assigned to various districts. A case is classified as 'probable' if the person is showing only clinical signs without parasitological confirmation, or as 'confirmed' after punch biopsy and parasitological confirmation by a positive smear or culture.<sup>15</sup>

Cases affecting Lebanese nationals were also distinguished from those of Syrian refugees, and the locations of Syrian refugee tented settlements were reviewed in terms of their distribution across various Lebanese districts. The number of Syrian refugees and their distribution all over Lebanon was obtained from the United Nations Refugee Agency (UNHCR).<sup>16</sup>

Cases obtained from ESDMOH records were used to draw an epidemiological map eliciting the distribution of new leishmaniasis cases across various Lebanese districts, along with the locations of concentrations of Syrian refugees.

## 3. Results

Over the 12 years of 2000–2012, an annual number ranging between 0 and 6 cases of Leishmania infection were reported to the ESDMOH. In 2013, 1033 cases of Leishmania were reported; 998 cases



**Figure 1.** Reported cases of Leishmania in Lebanon per month from January 2013 through March 2014. The graph shows that cases have continued to occur in 2014 at a high rate relative to the previous years (2001–2012); however, the number of cases has started to decrease since a peak in December 2013.

(96.6%) were identified among Syrian refugees and the remaining cases (3.4%) involved both Lebanese nationals and Palestinian refugees. An additional 217 cases were reported this year (January through March 2014), of which 208 involved Syrian refugees. As illustrated in Figure 1, the distribution of leishmaniasis cases per month showed a peak number in December 2013 (146 cases), with numbers appearing to decrease thereafter (January through March 2014). Only two nonfatal cases of VL were reported and the remaining cases were of the cutaneous form. All cases reported to the ESDMOH were confirmed by biopsy and parasitological examination (smear and/or culture). The two VL cases were treated successfully with liposomal amphotericin B, while cases of CL were treated with intralesional or systemic meglumine antimonate (Glucantime), both provided free of charge by the LMOPH.

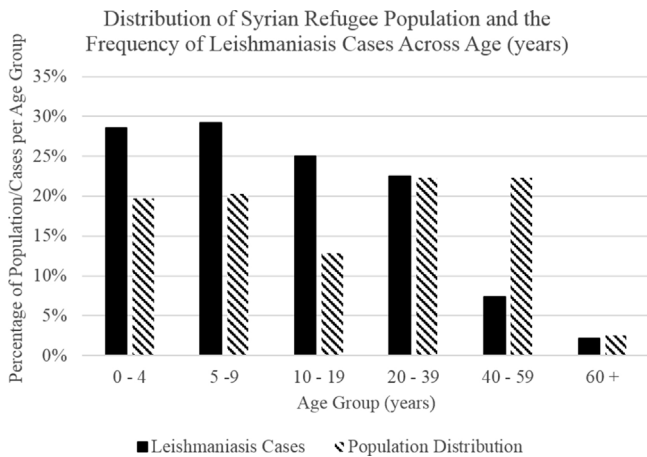
Children and adolescents (less than 20 years of age) were the most affected age group. Table 1 shows the age distribution of leishmaniasis cases reported. Less than 10% of cases occurred in people over 40 years of age. Of note, the distribution of the Syrian refugee population across the different age groups was not skewed towards the younger age groups (Figure 2).

The cases were reported from several Lebanese districts, but Bekaa district had the highest percentage of cases (726 cases, 70.3%), as well as highest incidence among Syrian refugees (38 cases/100 000). Figure 3 shows two epidemiological maps representing the distribution of Leishmania infection among the

**Table 1**

Distribution of Leishmania cases reported to the Lebanese Ministry of Public Health, by age group and gender (modified from <http://www.moph.gov.lb>).

	Number of cases	Percentage
Age group, years		
0–4	239	24%
5–9	245	25%
10–19	210	21%
20–39	189	19%
40–59	62	6%
60+	18	2%
Unknown	34	3%
Gender		
Male	505	48.9%
Female	527	51%
Unknown	1	0.1%
Nationality		
Syrian	998	96.6%
Others	35	3.4%
Total	1033	100%



**Figure 2.** Distribution of the Syrian refugee population and cases of leishmaniasis among the different age groups. The graph shows that although a higher frequency of cases occurred in the younger age groups (<10 years old), these age groups do not account for the majority of the population. Data on the Syrian refugee population were obtained from UNHCR.<sup>16</sup>

Lebanese districts and the incidence of leishmaniasis among the concentrations of Syrian refugees.

In Lebanon, around 985 346 Syrian refugees are registered at the United Nations Refugee Agency (UNHCR), the majority being in the Bekaa and North provinces (62%) (Figure 3). They are distributed all over Lebanon, in more than 540 locations, and are not restricted to special camps or tented settlements. However, the Lebanese government has reported that the true number of Syrian refugees in the country has exceeded one million.<sup>16,17</sup>

**4. Discussion**

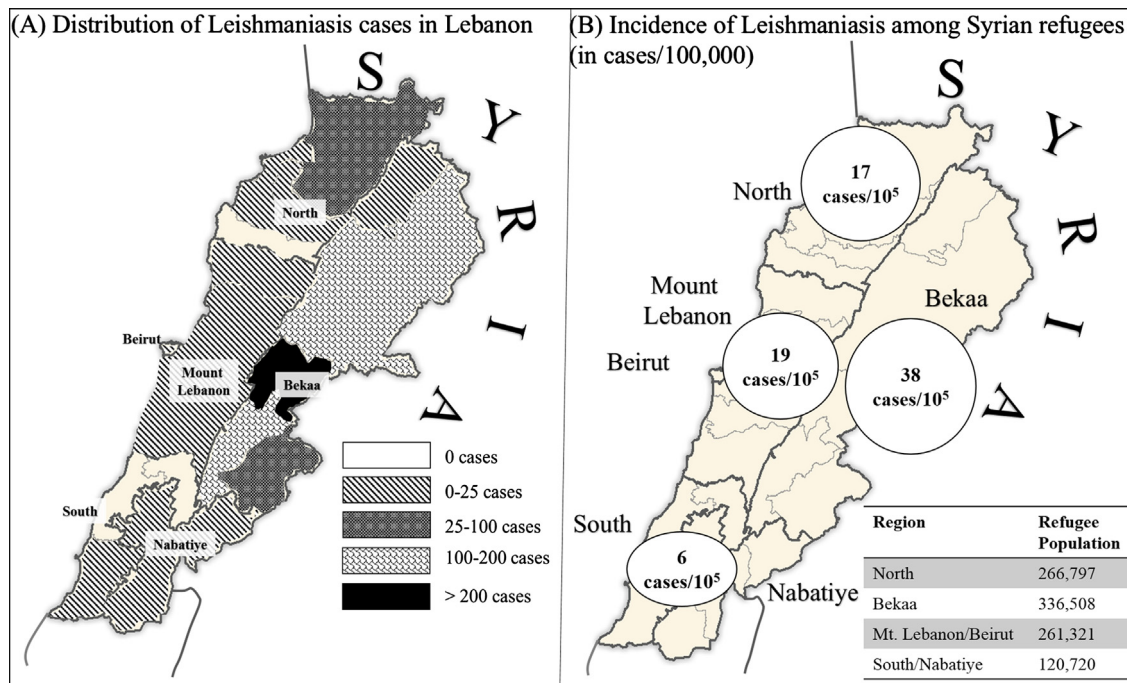
According to McDowell et al. in 2011, the MENA region reported 0.04 million cases of CL caused by *L. tropica*, with Syria being the

country with the highest prevalence, and 0.03 million cases of CL caused by *L. major*, with Iran being the country with the highest prevalence.<sup>10</sup> Both species, *L. major* and *L. tropica*, have been reported previously to be the major causative agents of Leishmania in Lebanon and Syria, compared to *Leishmania arabica* in Saudi Arabia.<sup>18</sup> However, data from the MENA region as well as other regions of endemic leishmaniasis are an underestimate, especially given that some countries do not report the various pathological forms of Leishmania and others do not report at all. For VL, records of its occurrence are more obscure; the WHO has reported an estimated number of 875 cases per year from the entire Mediterranean Area.<sup>19</sup>

Although leishmaniasis is endemic in Lebanon and has been reported mainly from the North district, the drastic increase in number of cases seen during the 2013–2014 period is a call for concern and a warning for the potential of a future major outbreak.<sup>20,21</sup> Before 2013, the highest number of cases reported per year was six cases in 2010; hence the Lebanese health care professionals, facilities, and authorities are unprepared to handle an outbreak of the disease, especially if it occurs in rural areas where health care assets are minimal.

The current outbreak in 2013–2014 correlates with the massive increase in arrival of Syrian refugees.<sup>16</sup> Although this outbreak has predominantly involved the Syrian refugees, cases among Lebanese citizens and residents have also been reported. Despite this strong correlation with the influx of Syrian refugees, and given the fact that Leishmania is known to occur in some Lebanese regions, Lebanon may be witnessing a pseudo-outbreak owing to the increase in surveillance and reporting measures instigated by the LMOPH with the escalation in the Syrian crisis. Although this hypothesis is possible, the majority of cases having involved Syrian refugees and the cases being clustered in their areas of concentration are strongly against this argument.

The fear of a spread of the infection outside the Syrian refugee community has driven the LMOPH as well as other relevant governmental departments to initiate a coordinated campaign to



**Figure 3.** (A) Map showing the distribution of Leishmania cases among the different districts of Lebanon: areas along the Syrian–Lebanese border had the highest number of Leishmania cases reported in 2013. (B) Map showing the incidence of leishmaniasis among Syrian refugees in different regions of Lebanon: Bekaa area had the highest incidence (38 cases/100 000) compared to South area (6 cases/100 000) due to the concentration and high density of Syrian refugees in the Bekaa area compared to southern Lebanon.

contain the spread of infection. This includes spraying pesticides to kill the vector, providing free treatment and diagnosis for emerging cases, distributing medications free of charge to the different primary care centers, and vigilant monitoring of disease activity.<sup>13</sup> Measures taken by the LMOPH have also involved promoting surveillance measures to ensure disease detection and adequate treatment of all cases. These measures include training physicians and health care workers on disease symptoms, raising their index of suspicion, as well as educating the Lebanese public and Syrian refugees about the disease symptoms and how to seek medical advice and treatment. In addition, the ministry has also assigned new centers for Leishmania detection and treatment in all Lebanese hospitals, including those in rural areas and near refugee camps.<sup>13</sup> These measures may explain the decrease in disease occurrence since December 2013, even though the rate of refugee influx into Lebanon has remained the same.

This new outbreak has raised concerns that the parasite may be able to form new circles of disease propagation in different foci in Lebanon, where the vector may find a favorable habitat and where appropriate zoonotic reservoirs are present. One main region of particular risk is Bekaa district (Figure 3) located on the northeastern border with Syria, which has had the highest share of leishmaniasis cases (70.3%) as well as the highest density of Syrian refugees. Reasons contributing to the higher burden in this area include the presence of high numbers of Syrian refugees in dense concentrates, which facilitates the spread of infection. In addition, this area has environmental conditions similar to those of many Syrian districts and is also rural and less developed, with limited health care assets.

The age distribution of those infected with Leishmania has been skewed towards the younger age groups despite the fact that the reported demographics of the Syrian refugees do not show a higher population of young vs. older age groups (Figure 2). The increased frequency of leishmaniasis among the younger Syrian population cannot simply be explained by higher numbers, but rather by the fact that older Syrian refugees are more likely to have been exposed to the disease previously. Such a finding is very common in areas of high prevalence where new cases are more predominant among the youth.<sup>22</sup>

Several factors contribute to the complexity of the situation in Lebanon, magnifying the consequences of the outbreak at the national level. They include: (1) an influx of refugees at a rapid rate, not allowing the government to cope with their needs; (2) the infiltration of refugees into different regions of Lebanon without restriction to designated camps; (3) a lack of familiarity of Lebanese physicians with the manifestations of the disease, leading to a delay in diagnosis; (4) the absence of well-trained laboratory personnel required to detect the parasite; and (5) the limited access to treatment, which is only available at a few designated locations.

The Syrian war-associated outbreaks are not one of a kind in the Middle East. In Iraq, war and instability between the years 2002 and 2004 were believed to be responsible for the high occurrence of the disease, ranging between 3000 and 4000 cases a year.<sup>23</sup> A large epidemic occurred during the civil war in Sudan between 1984 and 1994 in which VL was estimated to have caused around 100 000 deaths.<sup>24</sup> War-associated leishmaniasis outbreaks in the Middle East have also been reported historically among foreign troops serving in the area.<sup>25–27</sup>

Leishmaniasis continues to be endemic in the Middle East owing to several obstacles preventing proper control. According to the WHO initiative, the Leishmania control plan consists of (1) early diagnosis and prompt treatment; (2) vector and reservoir control, especially for zoonotic forms; (3) population health education; (4) monitoring of epidemics and early containment; and (5) management of Leishmania–HIV co-infection.<sup>6</sup> Several challenges have impeded the success of this program in many endemic areas; the main obstacle is under-reporting and poor

monitoring of the disease. CL is among the most under-reported diseases. The fact that the disease occurs in poor rural areas is a major reason for under-reporting. Limited access to medical care and the stigmatizing morbidity associated with CL, make families tend to hide rather than report the disease.<sup>9</sup> The lack of efficient governmental efforts and poor surveillance contribute to the spread of infection especially in times of war and political instability. The media has an important role in reporting war-associated diseases like Leishmania, as is the case for Syria.<sup>28</sup>

The absence of an effective vaccine or any preventative drug for Leishmania adds to the challenge of control and restricts containment efforts to limiting human exposure to the potential vectors and vector and reservoir eradication.<sup>3,4</sup> In addition, treatment alternatives for resistant Leishmania strains are still limited, as most trials have been poorly designed and reported, resulting in a lack of evidence for potentially beneficial treatment outcomes.<sup>29</sup>

The potential global impact of leishmaniasis was emphasized in 2009 during a Leishmania research and policy conference held in Tunisia to enhance collaborative efforts between the USA and countries of the Old World with endemic leishmaniasis.<sup>10</sup> The interest of the USA and other developed countries in Leishmania in the Middle East arises from the possibility of the disease being imported through immigrants, travelers, troops, reporters, non-governmental organization (NGO) workers, and even tourists, contributing to the globalization of this disease. Today, this threat is now more concerning given the recent outbreaks and status of instability in the regions endemic for leishmaniasis.

In conclusion, Lebanon is experiencing an outbreak of leishmaniasis possibly as a result of the Syrian crisis and the influx of refugees. This should be a solid aide memoire to remind us of the ability of wars and military conflicts to cause and spread disease and infection. The measures taken by the LMOPH are key and central to any response, but require the cooperation of other concerned parties to ensure success. The importance of coordinating efforts among various governmental departments, international agencies, local authorities, medical associations, and NGOs is crucial for containing this or similar outbreaks in Lebanon, or any other country in the region. With no near end in sight for the Syrian conflict, it is of the utmost importance to emphasize the need for characterizing the different *Leishmania* species involved in this outbreak, as well as the need to conduct risk assessments on the probability of the further spread of Leishmania to other areas in the immediate future. Of note, the Syrian conflict has also resulted in other major challenges to the Lebanese and regional health care systems, with concerns about the spread of other serious infectious diseases. These include poliomyelitis, which has recently re-emerged in Syria, and other vaccine-preventable diseases in Syria.<sup>30</sup>

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