

## Visceral and Cutaneous Leishmaniasis in a City in Syria and the Effects of the Syrian Conflict

Alexey Youssef,<sup>1</sup> Rim Harfouch,<sup>2†</sup> Said El Zein,<sup>3†</sup> Zuheir Alshehabi,<sup>4</sup> Rafea Shaaban,<sup>5</sup> and Souha S. Kanj<sup>3\*</sup>

<sup>1</sup>Faculty of Medicine, Tishreen University, Latakia, Syria; <sup>2</sup>Microbiology and Biochemistry Department, Faculty of Pharmacy, Al Andalus University, Tartous, Syria; <sup>3</sup>Infectious Diseases Division, Department of Internal Medicine, American University of Beirut Medical Center, Beirut, Lebanon; <sup>4</sup>Pathology Department, Faculty of Medicine, Tishreen University, Latakia, Syria; <sup>5</sup>Biostatistics Department, Faculty of Medicine, Tishreen University, Latakia, Syria

**Abstract.** War provides ideal grounds for the outbreak of infectious diseases, and the Syrian war is not an exception to this rule. Following the civil crisis, Syria and refugee camps of neighboring countries witnessed an outbreak of leishmaniasis. We accessed the database of the central leishmaniasis registry in Latakia city and obtained the leishmaniasis data of the period 2008–2016. Our data showed that the years 2013 and 2014 recorded a surge in the number of both cutaneous leishmaniasis (CL) and visceral leishmaniasis (VL) cases. This surge coincided with the massive internal displacement waves that struck Latakia governorate during that time. Subsequently, after 2015, the number of recorded CL and VL cases gradually decreased. This drop coincided with a reduced influx of internally displaced persons into Latakia governorate. Our report depicts the effects of the Syrian crisis on the epidemiology of leishmaniasis by outlining the experience of Latakia governorate. Similar results may have occurred in other refugee-hosting Syrian governorates.

Leishmaniasis is a major public health concern, especially in areas of internal displacement and refugee camps.<sup>1</sup> It has been given less attention than other infectious diseases such as malaria and AIDS. Leishmaniasis can manifest in different forms: cutaneous leishmaniasis (CL), mucocutaneous leishmaniasis (ML), or visceral leishmaniasis (VL).<sup>2</sup>

Inflicting a major burden on the social, economic, and psychological welfare of the patients, along with enforcing the loop between poverty and disease, leishmaniasis has been classified by the WHO as a neglected tropical disease (NTD).<sup>3</sup> Although endemic in 98 countries, almost two-thirds of CL cases are reported from Afghanistan, Algeria, Brazil, Colombia, Iran, and the Syrian Arab Republic. Approximately 0.7 to 1.2 million CL cases and 0.2 to 0.4 million VL cases occur each year. These account for 20,000 to 40,000 annual deaths.<sup>2,4</sup>

Cutaneous leishmaniasis has been endemic in Aleppo since hundreds of years<sup>5</sup>; however, based on epidemiological data dating back to the 1950s, its incidence in Aleppo was low. This was likely due to the antimalarial spraying programs that decreased the density of the sand fly vector.<sup>6</sup> However, CL incidence in Aleppo witnessed a significant rise since the late 1980s despite the vector control programs implemented in 1991.<sup>2,3,6,7</sup> *Leishmania* is transmitted by the bite of a female phlebotomine sand fly.<sup>8</sup> Eight species of the sand fly vector were identified in Syria, with *Phlebotomus sergenti* and *Phlebotomus papatasi* being the most predominant.<sup>2,9</sup> Cutaneous leishmaniasis is caused by *Leishmania tropica* in northern Syria and urban areas such as Aleppo, Idlib, Latakia, Hama, and Damascus,<sup>6,10</sup> whereas *Leishmania major* on the other hand accounts for 10% of the CL cases in Syria and is prevalent in rural areas close to Damascus, Deir al-Zour, and Al-Hasakah.<sup>11</sup> *Leishmania infantum* is the causative agent of most VL cases.<sup>2</sup> In this study, we aim to evaluate the epidemiology of CL and VL in the Latakia governorate by comparing the available pre- and post-conflict *Leishmania* epidemiological data. To our knowledge, this is the first study to assess

leishmaniasis and its epidemiological characteristics in this part of Syria at this specific time.

This study was reviewed and approved by the Institutional Review Board at Tishreen University under a waiver of informed consent. We collected our data from the database of the central leishmaniasis registry in Latakia city. The data represent the years 2008–2016 and include diagnosis data and a number of epidemiological parameters: gender, age, year of diagnosis, city of origin, season of diagnosis, and location of lesions. This database is representative of Latakia; it includes the leishmaniasis cases diagnosed in all local leishmaniasis and external health-care centers in the Latakia governorate. Diagnosis was made by histopathologic demonstration of the parasite on Giemsa and hematoxylin and eosin stains. All analyses were completed using the Statistical Package for the Social Sciences (SPSS) version 18 (SPSS Inc., Chicago, IL). Descriptive statistics using frequencies (%) for categorical data were calculated.

The number of CL patients reached 8,168 between the years 2008 and 2016, and the majority were males (57%). Around 60% of the patients were younger than 30 years. Sixty-five percent of the lesions affected exposed areas of the body such as the hands and head. Thirty percent of the cases were diagnosed in 2013 alone, in which only 17.5% of the patients were original residents of the Latakia governorate, whereas the majority were displaced from the Aleppo governorate (Figures 1 and 2A, Table 1). Overall, more than half of the total patients were from Latakia, whereas approximately 40% were from Aleppo. Our data showed a progressive decrease in the number of CL cases in the long-term residents of Latakia city, especially after 2014 (Figure 2).

The number of VL patients reached 107. The number of cases increased after 2010. Most patients were long-term residents of Latakia Province (62 cases), whereas 29 cases came from Idlib Province Table 1. The lowest number of CL and VL cases was diagnosed in autumn. The seasonal prevalence varies among different geographies; vector population dynamics should be studied to explain this phenomenon.

Similar to CL, VL cases in patients from Aleppo, Idlib, and Hama peaked in 2013–2014 (Figure 2B). However, the number of VL cases in long-term residents of Latakia city did not follow a specific pattern like that of CL.

\* Address correspondence to Souha S. Kanj, Infectious Diseases Division, Department of Internal Medicine, American University of Beirut Medical Center, P.O. Box 11-0236, Riad El Solh, Beirut 1107 2020, Lebanon. E-mail: sk11@aub.edu.lb

† These authors contributed equally to this work.

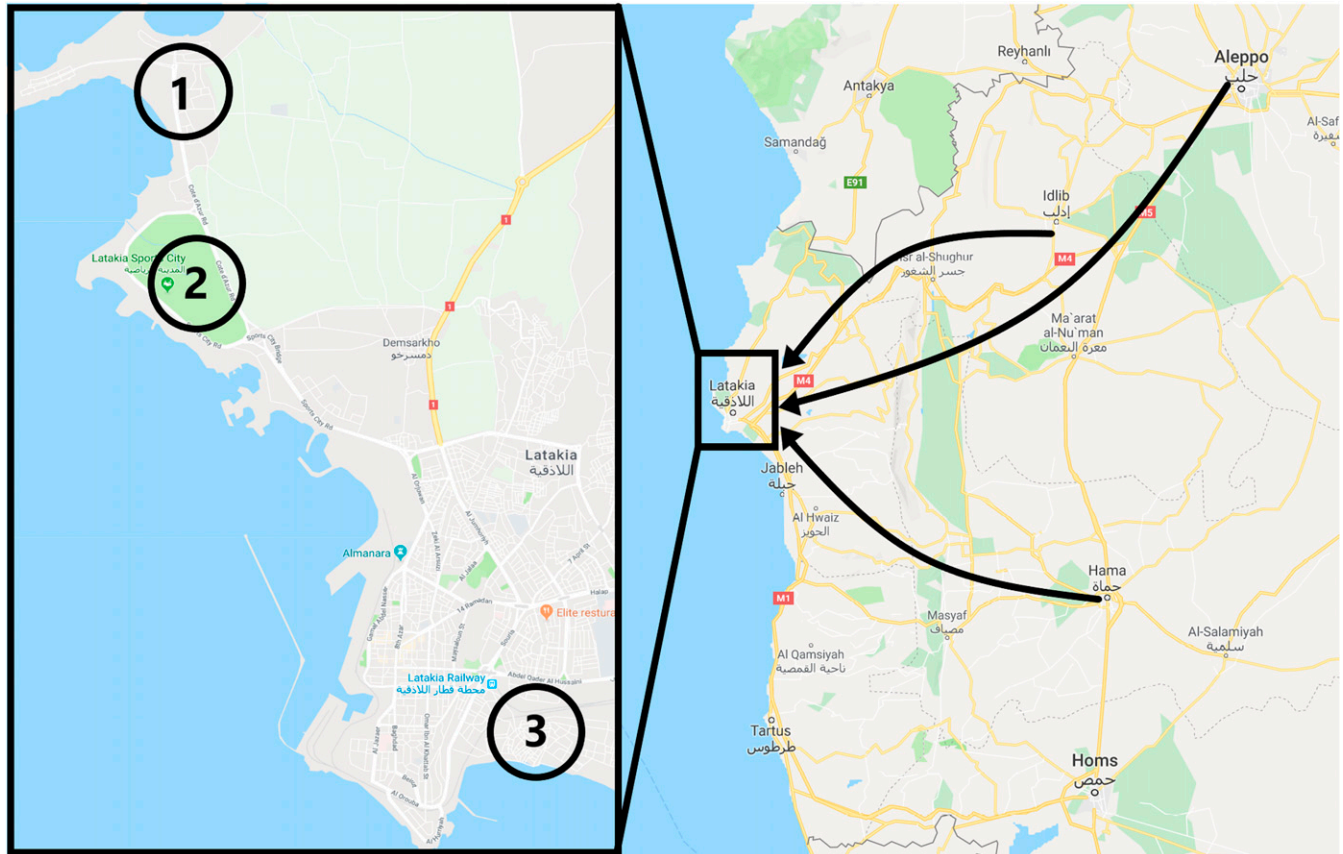


FIGURE 1. Map of Syria highlighting the influx (black arrows) of internally displaced persons (IDPs) from Aleppo, Idlib, and Hama to Latakia. The map also shows a number of IDP-dense neighborhoods in Latakia city (1: Al-Shatee Al-Azraq, 2: Al-Madina Al-Riadia, and 3: Al-Ramel Al-Filastini). This figure appears in color at [www.ajtmh.org](http://www.ajtmh.org).

In this study, CL affected males (57%) more frequently than females (43%). These results were consistent with findings from other studies,<sup>12–14</sup> which were explained by the fact that males engage in more outdoor activities compared to females. Also, we hypothesize that during the Syrian war, males were recruited to the army and therefore were more likely to be exposed to the sand fly bites during that period of time.

Cutaneous leishmaniasis affected individuals of all ages; however, the highest frequency of infection was observed in patients younger than 30 years, with almost equal distribution among the different age groups. Elderly individuals develop a lifelong immunity against the disease by being exposed to the parasite at a younger age, which might explain the lower number of affected individuals older than 50 years.<sup>13</sup> Moreover, people older than 30 years were less likely to be recruited into the army and therefore are less likely to be exposed to the sand fly vector. Children are most likely infected indoors or in areas around their dwellings, which are the most common breeding sites for the vectors.<sup>15</sup> The high percentage of infection seen in children might be due to the lack of immunity against the parasite and to the immature immune system, especially in children aged 0–4 years,<sup>15</sup> which might also hold true for VL infections as 87% of the individuals with VL were younger than 10 years and the majority (52%) were younger than 2 years.

Cutaneous leishmaniasis lesions commonly affected exposed areas of the body such as the hands and face (65%) followed by the feet (8.8%), which might be due to garments

worn during peak exposure times to the sand fly vector, leaving the hands and face exposed.

Our data depicted a surge in the number of CL and VL cases, coinciding with a wave of internal displacement from different regions in Syria into the Latakia governorate (Figures 1 and 2A and B). The number of CL cases in internally displaced persons (IDPs) from Aleppo and Idlib surged starting from the year 2013, whereas the number of CL cases in Hama's patients surged starting from the year 2011. This difference can be explained by the fact that the internal displacement waves from the Hama governorate started earlier than that of the other two governorates Table 1. It is difficult to discern whether reported individuals from Hama, Aleppo, Idlib, and other Syrian governorates were infected in their original residence and diagnosed in Latakia or infected and diagnosed in Latakia.

Similarly, CL cases peaked in nearby countries that received an influx of Syrian refugees. Outbreaks have been reported in the neighboring non-endemic countries such as Lebanon and Turkey.<sup>1,3,16</sup> However, VL cases do not follow a similar pattern possibly because of the lower numbers and different epidemiology. No surge in CL cases was seen in the original residents of Latakia. This can be attributed to the fact that the IDPs may have been infected in their original residence areas and diagnosed later in Latakia. Another explanation could be that a substantial proportion of these patients had been staying in camps or refugee-dense neighborhoods isolated from the rest of the city (Figure 1). However, this does not apply to all IDPs as

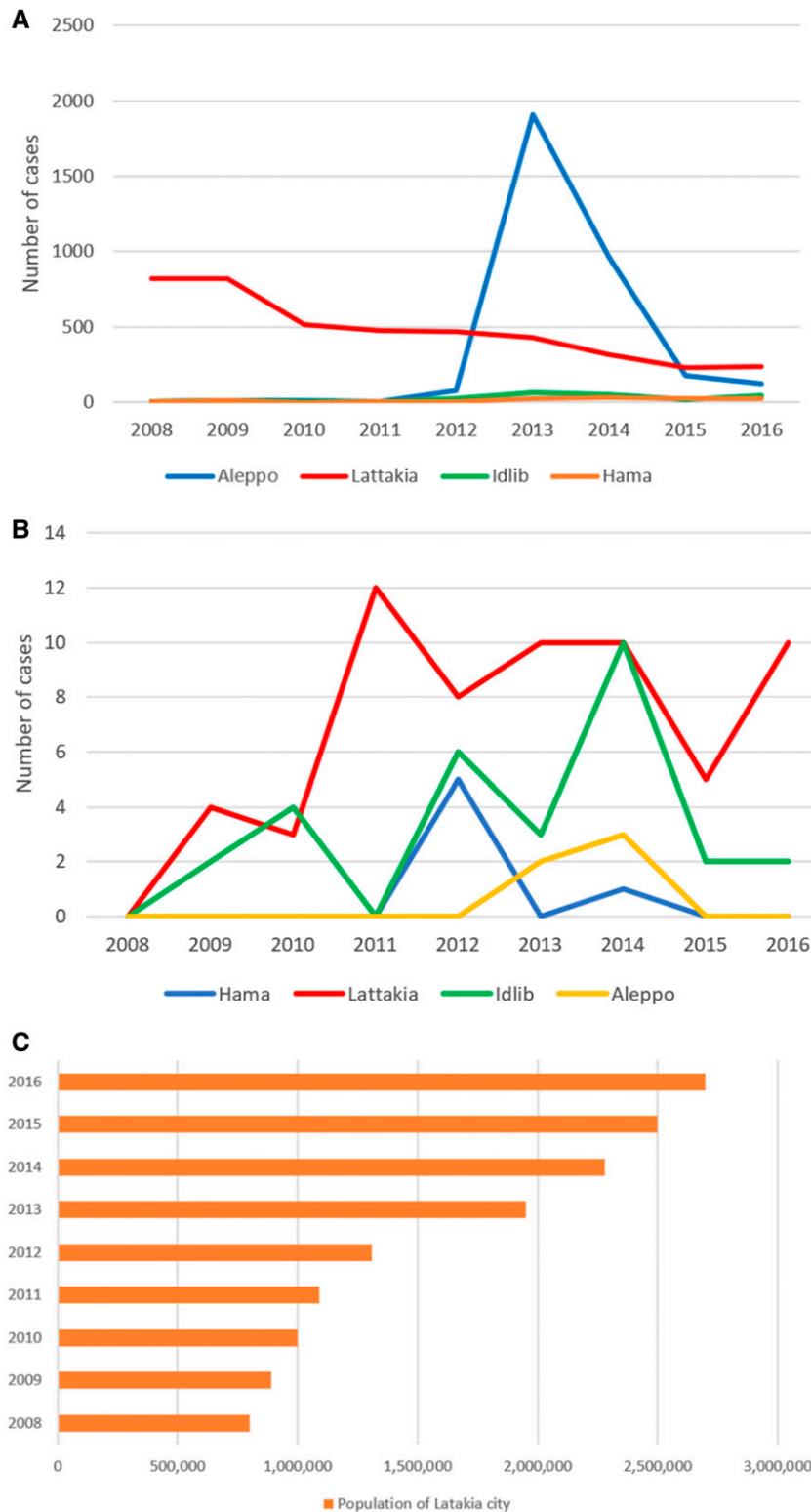


FIGURE 2. (A) Number of cutaneous leishmaniasis cases diagnosed in Lattakia, including the cities of residence of internally displaced persons (IDPs) between the years 2008 and 2016. (B) Number of visceral leishmaniasis cases diagnosed in Lattakia, including the cities of residence of IDPs between the years 2008 and 2016. (C) Bar graph showing the total population of the Lattakia governate between the years 2008 and 2016. This figure appears in color at [www.ajtmh.org](http://www.ajtmh.org).

many were living in regular residential neighborhoods. Visceral leishmaniasis cases in Lattakia remain significantly lower than that of CL, with only 46 cases reported during the same time period. Interestingly, most IDPs diagnosed with CL were from

Aleppo, whereas the majority diagnosed with VL were from Idlib Table 1. This may reflect the fact that VL is most endemic in Idlib, where there is more exposure to vectors carrying *L. infantum*, whereas CL is most endemic in Aleppo. Our

TABLE 1  
Characteristics of patients with cutaneous and VL registered in the central Latakia governorate database between 2008 and 2016

Cutaneous leishmaniasis			VL		
	Number	Percentage		Number	Percentage
Gender			Gender		
F	3,511	42.99	F	57	53.27
Age (years)			Age (years)		
(0–10)	1,975	24.18	(0–10)	93	86.92
(10–20)	1,899	23.25	(10–20)	3	2.8
(20–30)	1,752	21.45	(20–30)	6	5.61
(30–40)	964	11.8	≥ 30	5	4.67
(40–50)	730	8.94			
(50–60)	432	5.29			
(60–70)	257	3.15			
(70–80)	118	1.44			
(80–)	40	0.49			
City of origin			City of origin		
Latakia	4,321	52.91	Latakia	62	57.94
Aleppo	3,289	40.27	Aleppo	5	4.67
Idlib	230	2.82	Idlib	29	27.10
Hama	127	1.56	Hama	6	5.61
Other*	200	3.5	Other*	5	4.66
Season of diagnosis			Season of diagnosis		
Winter	2,154	26.37	Winter	15	14.02
Spring	2,717	33.27	Spring	36	33.64
Summer	1,996	24.44	Summer	37	34.58
Autumn	1,300	15.92	Autumn	19	17.76
Location of lesions					
Hand	2,681	32.83			
Foot	719	8.8			
Head	2,655	32.51			
Other locations	2,213	27.1			

VL = visceral leishmaniasis.

\*Other: Al-Hasaka, Homs, Damascus, Deir Al-Zur, Tartous, Al-Raqqa, Al-Sweida, Al-Quneitira, and Daraa.

findings are supported by reports in the literature that associate civil unrest, displacement, and refugee waves, with both VL and CL endemics and outbreaks.<sup>17,18</sup> Dogs play a role in the transmission of zoonotic leishmaniasis. According to personal communication with public health officers in Latakia, there was an issue of stray dogs in one of the IDP-dense neighborhoods (Al-Ramel Al-Filastini). In addition, malnutrition is a risk factor for VL. Accurate data on malnutrition in Latakia and Syria are scarce. However, because of growing concerns of malnutrition in the conflict setting, the WHO implemented a large-scale malnutrition field response program in many governorates, including Latakia.<sup>19,20</sup>

There has always existed an association between war and infectious diseases.<sup>1</sup> Beginning in 2011, the Syrian turmoil has displaced more than 6.5 million people, causing a crisis comparable to the World War II refugee crisis.<sup>21</sup> It has also devastated the Syrian health-care infrastructures, severely damaging 60% of the Syrian hospitals, and greatly reducing the pharmaceutical production capacity of the country.<sup>1</sup> The destruction of the health-care infrastructure, the crowding of what was considered “safer Syrian cities” and their remaining health-care facilities, and the displacement of a large population from leishmaniasis-endemic areas constituted the right setup for a potential *Leishmania* outbreak. During the crisis, Latakia governorate was considered a safer haven for millions of IDPs from all over Syria, especially from leishmaniasis-endemic areas such as Aleppo, Idlib, and Hama. According to the central statistical office of Latakia governorate, Latakia’s population was 800,000 in 2009. According to the same source, its population almost reached 2.5 million by 2015 (Figure 2C), mainly because of the internal

displacement. Based on the Latakia governorate refugee office data, the years 2013–2014 have witnessed the largest displacement waves over the course of the conflict. This resulted in a surge in the number of leishmaniasis cases diagnosed in the governorate, which, in turn, led the local health-care authorities to implement a control program aiming to counter this outbreak.

Control programs are the cornerstone of limiting leishmaniasis. The Lebanese Ministry of Public Health initiated a control campaign following the 2013 outbreak in the Lebanese refugee camps. It included vector control, early detection, and free treatment of leishmaniasis cases and has proven to be effective.<sup>22</sup> According to the central leishmaniasis registry of Latakia, a similar campaign was implemented in the Latakia governorate to counter the leishmaniasis outbreak after 2013. This campaign consisted of vector control mainly indoor residual spraying, early detection and treatment, and public education.

This study was limited by the lack of data on the medical history of the patients, their comorbidities, treatment regimens, and treatment outcomes. Also, because of the ongoing war in Syria and lack of access to health-care services, we expect an underestimation of the true number of reported cases. Leishmaniasis is an NTD, with a high global burden of disease accounting yearly for thousands of deaths from VL and millions of disfiguring lesions from CL and ML. Improving the living circumstances in sites with high population densities, enforcing better health-care services, and activating surveillance, early diagnosis, vector control, and public education should constitute an integral part of any plan to successfully control and eliminate leishmaniasis.

Received September 24, 2018. Accepted for publication May 6, 2019.

Published online June 3, 2019.

Acknowledgment: The American Society of Tropical Medicine and Hygiene (ASTMH) assisted with publication expenses.

Authors' addresses: Alexey Youssef, Faculty of Medicine, Tishreen University, Latakia, Syria, E-mail: alexeyyousef1994@gmail.com. Rim Harfouch, Microbiology and biochemistry Department, Faculty of Pharmacy, Al Andalus University, Tartous, Syria, E-mail: rimharf@yahoo.com. Said El Zein and Souha S. Kanj, Infectious Diseases Division, Department of Internal Medicine, American University of Beirut Medical Center, Beirut, Lebanon, E-mails: selzein20@gmail.com and sk11@aub.edu.lb. Zuheir Alshehbi, Pathology Department, Faculty of Medicine, Tishreen University, Latakia, Syria, E-mail: alshehabizuheir08@gmail.com. Rafea Shaaban, Biostatistics Department, Faculty of Medicine, Tishreen University, Latakia, Syria, E-mail: shaabanrafea@yahoo.fr.

## REFERENCES

- Sharara SL, Kanj SS, 2014. War and infectious diseases: challenges of the Syrian civil war. *PLoS Pathog* 10: e1004438.
- Salam N, Al-Shaqha WM, Azzi A, 2014. Leishmaniasis in the middle east: incidence and epidemiology. *PLoS Negl Trop Dis* 8: e3208.
- Du R, Hotez PJ, Al-Salem WS, Acosta-Serrano A, 2016. Old world cutaneous leishmaniasis and refugee crises in the middle east and north Africa. *PLoS Negl Trop Dis* 10: e0004545.
- Alvar J, Velez ID, Bern C, Herrero M, Desjeux P, Cano J, Jannin J, den Boer M, 2012. Leishmaniasis worldwide and global estimates of its incidence. *PLoS One* 7: e35671.
- Russel A, 1756. *The Natural History of Aleppo and Parts Adjacent*. London, United Kingdom: A. Millar.
- Tayeh A, Jalouk L, Cairncross S, 1997. Twenty years of cutaneous leishmaniasis in Aleppo, Syria. *Trans R Soc Trop Med Hyg* 91: 657–659.
- Abazid N, Jones C, Davies CR, 2012. Knowledge, attitudes and practices about leishmaniasis among cutaneous leishmaniasis patients in Aleppo, Syrian Arab Republic. *East Mediterr Health J* 18: 7–14.
- Gossage SM, Rogers ME, Bates PA, 2003. Two separate growth phases during the development of *Leishmania* in sand flies: implications for understanding the life cycle. *Int J Parasitol* 33: 1027–1034.
- Haddad N, Saliba H, Altawil A, Villinsky J, Al-Nahhas S, 2015. Cutaneous leishmaniasis in the central provinces of Hama and Edlib in Syria: vector identification and parasite typing. *Parasit Vectors* 8: 524.
- Rehman K, Walochnik J, Mischlinger J, Alassil B, Allan R, Ramharter M, 2018. Leishmaniasis in northern Syria during civil war. *Emerg Infect Dis* 24: 1973–1981.
- Rioux JA, Dereure J, Khiami A, Pralong F, Sirdar K, Lambert M, 1990. [Ecoepidemiology of leishmaniasis in Syria. 1. *Leishmania* major Yakimoff and Schokhor (Kinetoplastida-Trypanosomatidae) infestation of *Psammomys obesus* cretzenschmar (Rodentia-Gerbillidae)]. *Ann Parasitol Hum Comp* 65: 203–207.
- Abdellatif MZM, El-Mabrouk K, Ewis AA, 2013. An epidemiological study of cutaneous leishmaniasis in Al-jabal Al-gharbi, Libya. *Korean J Parasitol* 51: 75–84.
- Feiz-Haddad M-H, Kassiri H, Kasiri N, Panahandeh A, Lotfi M, 2015. Prevalence and epidemiologic profile of acute cutaneous leishmaniasis in an endemic focus, Southwestern Iran. *J Acute Dis* 4: 292–297.
- Siriwardena HV, Udagedara CU, Karunaweera ND, 2003. Clinical features, risk factors and efficacy of cryotherapy in cutaneous leishmaniasis in Sri Lanka. *Ceylon Med J* 48: 10–12.
- Agrawal S, Khandelwal K, Bumb RA, Oghumu S, Salotra P, Satoskar AR, 2014. Pediatric cutaneous leishmaniasis in an endemic region in India. *Am J Trop Med Hyg* 91: 901–904.
- Saroufim M, Charafeddine K, Issa G, Khalifeh H, Habib RH, Berry A, Ghosn N, Rady A, Khalifeh I, 2014. Ongoing epidemic of cutaneous leishmaniasis among Syrian refugees, Lebanon. *Emerg Infect Dis* 20: 1712–1715.
- Al-Salem W, Herricks JR, Hotez PJ, 2016. A review of visceral leishmaniasis during the conflict in South Sudan and the consequences for East African countries. *Parasit Vectors* 9: 460.
- Hussain M, Munir S, Jamal MA, Ayaz S, Akhouni M, Mohamed K, 2017. Epidemic outbreak of anthroponotic cutaneous leishmaniasis in Kohat District, Khyber Pakhtunkhwa, Pakistan. *Acta Trop* 172: 147–155.
- Khudari H, Bozo M, Hoff E, 2015. *WHO Response to Malnutrition in Syria: A Focus on Surveillance, Case Detection and Clinical Management*. Available at: <https://www.ennonline.net/fex/48/whosyria>. Accessed February 24, 2019.
- Miró G, Müller A, Montoya A, Checa R, Marino V, Marino E, Fuster F, Escacena C, Descalzo MA, Gálvez R, 2017. Epidemiological role of dogs since the human leishmaniasis outbreak in Madrid. *Parasit Vectors* 10: 209.
- Al-Salem WS, Pigott DM, Subramaniam K, Haines LR, Kelly-Hope L, Molyneux DH, Hay SI, Acosta-Serrano A, 2016. Cutaneous leishmaniasis and conflict in Syria. *Emerg Infect Dis* 22: 931–933.
- Alawieh A, Musharrafieh U, Jaber A, Berry A, Ghosn N, Bizri AR, 2014. Revisiting leishmaniasis in the time of war: the Syrian conflict and the Lebanese outbreak. *Int J Infect Dis* 29: 115–119.