Asian Journal of Medicine and Health

19(7): 8-20, 2021; Article no.AJMAH.69965
ISSN: 2456-8414

Systematic Review of Visceral Leishmaniasis in Central Africa

Demba Kodindo Israël[1], Cheick Amadou Coulibaly[2], John C. Beier[3], Gunter C. Muller[4] and Seydou Doumbia[2*]

[1]Ministry of Public Health N'Djaména, Chad.
[2]Leishmaniasis Unit, International Center for Excellence in Research (ICER-Mali), Faculty of Medicine and Odonto-stomatology, University of Science, Techniques and Technologies of Bamako (USTTB), BP 1805, Mali.
[3]Department of Public Health Sciences, University of Miami Miller School of Medicine Miami, Florida 33136 USA.
[4]Department of Parasitology, Kuvin Centre for the Study of Infectious and Tropical Diseases. The Hebrew University - Hadassah-Medical School Jerusalem, Israel.

Authors' contributions

This work was carried out in collaboration among all authors. Author DKI did the concept of this study and drafting. The article was critically reviewed by authors CAC, JCB, GCM, SD and finally approved by author SD. All authors read and approved the final manuscript. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/AJMAH/2021/v19i730341
Editor(s):
(1) Dr. Ashish Anand, G. V. Montgomery Veteran Affairs Medical Center, USA.
Reviewers:
(1) Levi Eduardo Soares Reis, Brazil.
(2) Andrea Cristina Alpoim Botelho, University of São Paulo, Brazil.
Complete Peer review History: http://www.sdiarticle4.com/review-history/69965

Review Article

Received 20 April 2021
Accepted 24 June 2021
Published 30 June 2021

ABSTRACT

In underdeveloped countries, infectious diseases remain one of the most important public health challenges. Visceral leishmaniasis, also known as Kala-azar, is a lethal vector-borne parasitic disease with an increasing number of cases. However, it remains one of the most neglected diseases in the world. It is the most severe form of leishmaniasis and is endemic in 75 countries. Around 95% of the patients live in seven countries: Brazil, Ethiopia, India, Kenya, Somalia, South Sudan, and causes about 20,000-40,000 deaths per year of which 50-70% are children. In Central

**Corresponding author: E-mail: sdoumbi@gmail.com;*

Africa, this pathology is little known and less documented, making it difficult to access information. We have performed this study to characterize the knowledge on the epidemiology of visceral leishmaniasis in Central Africa. We reviewed the literature on visceral leishmaniasis in Central Africa on the number of reported cases, identified parasites, reservoirs and vectors. The documents consulted came from WHO reports, publications of scientific journals, reports of research institutions and abstracts of scientific conferences consulted online on Pubmed and Google Scholar. The information covers the period from the first reporting of cases in each country until December 2020. The review of the situation of visceral leishmaniasis revealed that it is not a significant public health problem in Central Africa. However, a lot of work remains to be done especially surveillance and research in order to present the exact situation of the disease in this part of the continent. This work would include the underreporting of cases inherent to the weaknesses of the surveillance system in these countries, the clarification of the transmission dynamics of human visceral leishmaniasis, canine leishmaniasis, the identity of parasites and vectors.

Keywords: Visceral leishmaniasis; epidemiology; underestimation; Central Africa.

1. INTRODUCTION

Visceral leishmaniasis (VL) is the most severe form of leishmaniasis and is one of the 20 World Health Organization (WHO) neglected tropical diseases [1]. It is caused by *Leishmania,* an obligate intracellular parasite, transmitted by infected sand flies [2]. The parasite attacks the viscera, generally the spleen, liver, but also the bone marrow, hence the name visceral leishmaniasis. Widespread and endemic in 75 countries, 95% of the patients live in seven countries: Brazil, Ethiopia, India, Kenya, Somalia, South Sudan and Sudan. In 2017, 22,000 new cases of VL were reported worldwide with 570 deaths. Around 50 to 70% of patients were children [3]. No human vaccine against VL is currently available, other than a vaccine of lesser efficacy or being researched [4].

According to WHO, confirmed cases of VL decreased in the last decade from 60,000 to about 20,000 cases [5]. In underdeveloped countries, thousands of epidemiological data are unreported, resulting a huge underestimation of official data [6], either because these countries do not have standardized tools to collect VL data or do not report data to WHO.

In Africa, VL is endemic in many regions. However, a great number of cases of the disease is concentrated in the eastern part, which represents the second largest site in the world after the Indian subcontinent [7,8]. In this region, extensive clinical, epidemiological and ecological studies on the disease have been conducted. VL is caused by *Leishmania donovani* and the main vectors are *Phlebotomus orientalis* and *Phlebotomus martini*. Two epidemiological cycles are known, one anthroponotic with humans as reservoirs and the other zoonotic in which dogs and rodents are the animal reservoirs [9,10,11]. Numerous syntheses and reviews have improved the knowledge of the disease in terms of epidemiology [11-14].

In the Mediterranean region of Africa, VL represents a major public health problem and a mandatory reporting disease in some countries [15-17]. In the Maghreb as in southern Europe, VL is mostly pediatric, but in recent years, cases of immunocompromised adults have been recorded [18]. The disease is caused by *Leishmania infantum* and the reservoir of this parasite is the domestic dog. The main vectors are *Phlebotomus perniciosus, P. perfiliewi* and *P. longicuspis.*

In West Africa, VL is sporadic. In recent years, scientific study has led to a better understanding of the epidemiology of the disease in this region [19-22]. Two *Leishmania* species were suspected, namely *Leishmania donovani* for anthroponotic cycle and *Leishmania infantum* for zoonotic VL. However, the exact status of the parasite is not known except that of *Leishmania infantum* described in a child in Senegal [23]. Serological studies have detected dogs as reservoirs [24-25].

In Central Africa, VL is sporadic, under-reported and less documented. Contrary to other African WHO regions, no systematic review studies were carried out, which makes the information difficult to access for people interested in leishmaniasis in general and in VL in particular.

This article reviews the VL in the central part of Africa and is based on articles written from the first case reports until 2020. The purpose of this review is to summarize the current knowledge on VL and to point out the lack of scientific data on its distribution, vectors, causal agents and reservoirs in each of these countries. .

2. MATERIALS AND METHODS

This study is based on documentation about the distribution, vectors, parasites and reservoirs of VL in 9 Central African countries namely Angola, Cameroon, Central African Republic, Chad, Congo, Democratic Republic of Congo, Equatorial Guinea, Gabon and Sao Tome and Principe (Fig. 1). The data presented cover the period from the first reporting of cases in each country to 2020 and came from many sources: WHO reports, publications in scientific journals, reports from research institutions and abstracts of scientific conferences consulted online using databases such as Pubmed and Google Scholar. The searches included the following terms: "visceral leishmaniasis", "*Leishmania donovani*", "*Leishmania infantum*", "*sandfly*" and "Leishmania reservoirs". Published articles on cutaneous and mucocutaneous leishmaniasis were not included.

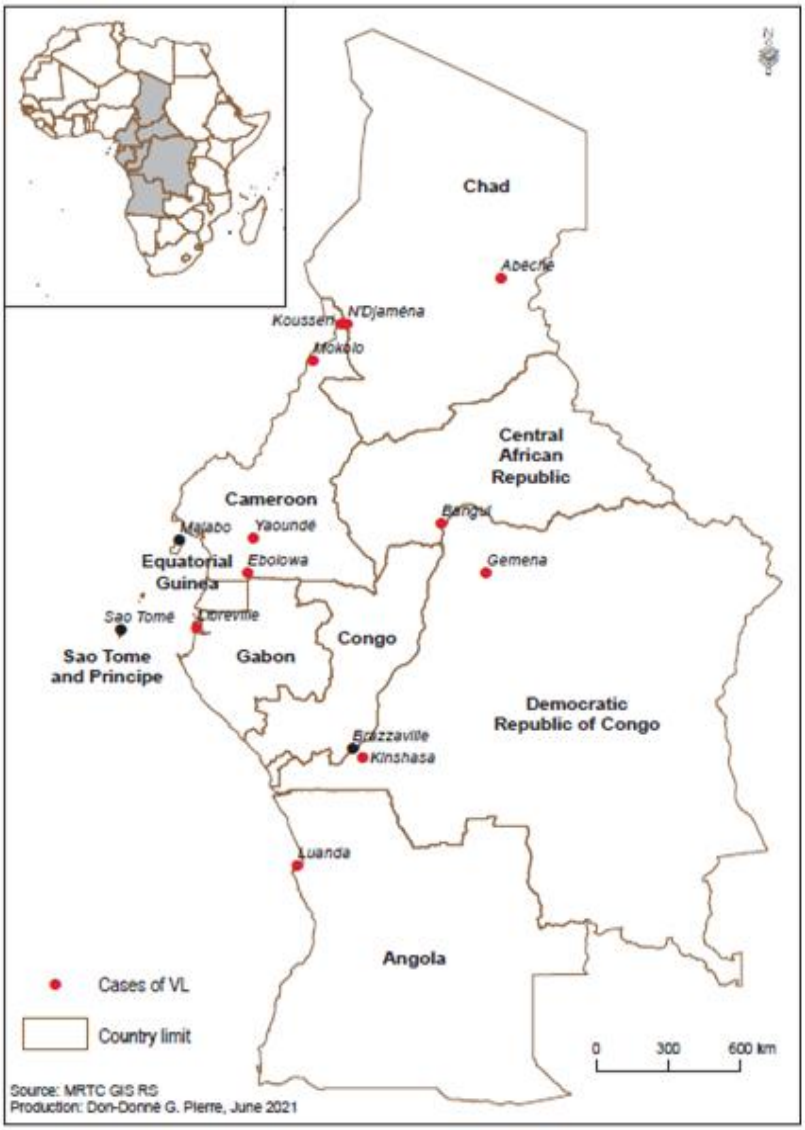

Fig. 1. Map of study areas. Source MRTC GIS-RS, Author MATHIAS Dolo March 2021

3. RESULTS

3.1 Angola

3.1.1 Distribution

The first case of VL was recorded in Angola in 1963 [26], however, cases are few and mostly diagnosed outside the country. In 1994, a 26-year-old man with no history of travel outside the country and typical symptoms of VL was diagnosed positive only three weeks after arriving in Spain [27]. Six years later in 2000, a 40-year-old immunocompromised immigrant in Germany was treated in a specialized center for VL infection [28]. On January 5, 2005, another Angolan immigrant aged 35 was admitted to the hospital in Pordenone, Italy, this time for recurrent complaints of fever, weight loss and back pain. He had lived successively in two endemic areas of VL in southern Italy (1991-2003) and then returned to Angola before coming back to Italy in 2004 where he lives in a non-endemic area. After treatment of a renal infection, other diagnoses had revealed the presence of *Leishmania* in a bone marrow puncture smear [29].

3.1.2 Vectors and causal agents

The *sand fly* fauna is not very diverse, in 1967, Abonnec revealed the presence of 15 species during a mapping of Angola's *sand fly* fauna [30]. However, the vector role was not shown in any of the species collected. Leishmania strains isolated from patients in Spain, Italy and dogs in Angola had been identified as *Leishmania infantum* [27,29,31]. In Germany the parasite has not been identified with certainty to its species, however, it is part of the *Leishmania donovani* complex [28].

3.1.3 Reservoirs

In 2014, Vilhena et al had examined the seroprevalence of anti-leishmanial antibodies with direct agglutination and polymerase chain reaction tests on 300 dogs from Luanda. A total of 2 (0.6%) dogs were infected with *Leishmania infantum* [31]. Another seroprevalence study in 102 cats in Luanda showed [32] that only dogs were animal reservoirs.

3.2 Cameroun

3.2.1 Distribution

In Cameroon, VL is historically known to be endemic in the north and far north of the country where the disease was generally sporadic and sometimes epidemic. It was first reported without biological confirmation in 1976 [33] in a woman from the north. It was not until ten years later, in 1986, that another case was parasitologically diagnosed in Yaoundé in a girl from Kousseri in the far north [34]. Other cases were reported in the same region during a prospective study which revealed that out of 120 people sampled, 46 had symptoms of VL and nine had been parasitologically and serologically confirmed [35]. A seroepidemiological survey, using an indirect immunofluorescent antibody test, was conducted in 2001 on 223 healthy students living in Kousseri, which revealed that 9 (4%) were seropositive for VL [36]. Cases of VL have also been reported outside the traditional homes of the country. These include pediatric cases in an 8-year-old boy from the East [37], a 4-year-old child in Yaoundé hospital [38] and three other cases from the South [35]. A total of 25 cases of VL were recorded in Cameroon during the 44 years from 1976 to 2020.

3.2.2 Vectors and causative agent

The first sand fly fauna composition in Cameroon was made in the 1950 [39,40] but it was not until 50 years later that further studies were carried out in the Mokolo area, where cases of cutaneous leishmaniasis were recorded to identify sand fly species involved in the transmission of leishmaniasis [41]. In Mokolo, the parasite was not identified with certainty to its species, however, the DNA of the *Leishmania donovani* complex was found in *Phlebotomus duboscqi* [42], traditional vector of cutaneous leishmaniasis to *Leishmania major* in West Africa [43].

3.2.3 Reservoirs

Not studied

3.3 Central African Republic

3.3.1 Description

Although the first case of VL has been known since 1949 in the Central African Republic [44], very little information is available on this pathology today. After a second parasitologically detected case in a child in the Bangui region, three more cases were observed in 1969 [45].

3.3.2 Vectors and causative agent

The *sand fly* fauna of the Central African Republic is very diverse. In 1983, Grépin

identified 33 species in a study of the geographical distribution of Central African sandflies [46]. Only two species of the genus *Phlebotomus* had been collected, but their role in the transmission of leishmaniasis in the Central African Republic was not demonstrated. An isoenzymatic analysis allowed the isolation of *Leishmania infantum* from a patient [44].

3.3.3 Reservoirs

Not studied

3.4 Chad

3.4.1 Description

In Chad, the incidence of VL is low despite endemicity in all neighboring countries, namely Libya to the north, Sudan to the east and west, Niger, Nigeria and Cameroon. Few data have been published to date on this disease, yet VL was first reported in 1966 [44]. From 1966 to 1973, 64 cases of VL were recorded in the registers of the central hospital of N'Djaména [44,47]. From 1973 to 2004, after an interruption of nearly 31 years in Marseille, a case of VL was diagnosed and reported in a 38-year-old French soldier returning from Chad after a two-month mission [48]. After this last case reported in Marseille, no study was published, making 65 VL cases reported in Chad since the first notification.

3.4.2 Vectors and causal agent

In Chad, the first notes mentioning sandflies date from 1928 [49]. In 1967, Lewis and Hitchcock reported that an inventory of sand fly fauna carried out in the areas of N'Djaména, Lake Chad, and Abéché had identified 15 species. *Phlebotomus orientalis*, vector of VL in Sudan, and *Phlebotomus duboscqi*, vector of cutaneous leishmaniasis in West Africa, made up the fauna [50]. The parasite has not been identified.

3.4.3 Reservoirs

Two dogs had been diagnosed positive in N'Djamena by the veterinary service, suggesting that dogs would be the most likely reservoir hosts for the infectious agent and sources of human infection [44].

3.5 Congo

3.5.1 Description

In present day no case of human VL have been reported in Congo but only three cases of canine leishmaniasis were notified in 1940 [51].

3.5.2 Vectors and causative agent

Numerous studies have been devoted to Congo sandflies, but their role in the transmission of VL has not been proven and the parasite is unknown [52,53,54].

3.5.3 Reservoirs

Three infected dogs were diagnosed in the Congo in which leishmaniases were found by scratching the skin [51].

3.6 Democratic Republic of Congo

3.6.1 Description

Very little data on VL in the Democratic Republic of Congo is available. Knowledge of the existence of the disease in this country dates back to 1968 by Prevot's note [55] and confirmed ten years later by a second indigenous case in the Gemena region in the Guinean savannah north of the equatorial forest in the north-west of the country [56]. Since then, no further cases have been reported.

3.6.2 Vectors and causative agent

Several surveys have been carried out in the Democratic Republic of Congo on sandflies, but their role in the transmission of VL has not been studied [57,58,59]. No information is available on the pathogen.

3.6.3 Reservoirs

Not studied

3.7 Equatorial Guinea

3.7.1 Description

Not described

3.7.2 Vectors and causal agent

No information available

3.7.3 Reservoirs

Not studied

3.8 Gabon

3.8.1 Description

In Gabon, since the first notification of an indigenous case of VL in 1920 [60], no further

mention has been made of this pathology until today.

3.8.2 Vectors and causative agent

Sandfly-vectors of VL have not been identified in Gabon as well as the parasites, however, many studies have been devoted to sandfly-vectors in this country [61,62,63,64].

3.8.3 Reservoirs

Not studied

3.9 Sao Tome and Principe

3.9.1 Description

Not described

3.9.2 Vectors and causative agent

No information available

3.9.3 Reservoirs

Not studied

4. DISCUSSION

4.1 Description

VL is one of the major public health problems in many parts of the world, however, in Central Africa it is poorly studied at the region. Our review shows that human visceral leishmaniasis is present in Central Africa in six countries: Chad, Cameroon, Central African Republic, Democratic Republic of Congo, Gabon and Angola (Table 1). Based on the WHO classification, we can say that no country in Central Africa is an endemic country because the full cycle of VL is not described in any of these countries [65]. The exact geographic extent of the disease is unknown. Countries such as the Central African Republic, Democratic Republic of Congo, Gabon, and Congo had been reporting for more than 50 years except Cameroon and Angola whose last cases were reported 20 years ago. Given the scarcity of data, steps need to be taken to improve existing surveillance systems or establish new ones where they do not exist based on standardized tools developed on the recommendation of WHO [66]. In Angola, most cases were reported in countries where diagnostic and management structures were developed [27,28,29], in Cameroon, an 8-year-old boy would have been saved if and only if diagnosis and treatment had followed from the patient's first contact with health facilities [37]. These weaknesses require support in diagnosis and care in these countries. In contrast to East African countries where epidemics are frequent, Central Africa is spared. With climate change [67], the increase in inter-state trafficking and cross-border transhumance of nomadic herders, VL will no longer be limited to a region or country, but will spread from country to country and cause epidemics in non-endemic areas [68]. Also, in Central African countries, access to chemotherapy for the treatment of VL is at the expense of patients' relatives or with the humanitarian assistance of the WHO. With the scarcity and age of data, surveillance and research must be encouraged and undertaken to know precisely where the outbreaks of VL and its forms in Central Africa are located.

4.2 Vectors and Causative Agent

Sand fly vectors of leishmaniasis have been studied in several Central African countries except two: Equatorial Guinea and Sao Tome and Principe. However, the main vectors of VL in East and North Africa, *Phlebotomus orientalis, Phlebotomus martini, Phlebotomus perniciosus, Phlebotomus perfiliewi and Phlebotomus longicuspis* have never been encountered except in Chad where *Phlebotomus orientalis* had been identified. Most of the studies were aimed at mapping *sandflies* unrelated to the parasites except in Mokolo in Cameroon [42]. Given that VL was reported in most of the Central African countries, we assume that there is at least one of the associated vector species that must also be present or at least one species whose vectorial potential is currently unknown (Table 2). Indeed, in Sudan, Elnaim and collaborators had demonstrated the vector role of *Phlebotomus rodhaini* [69] while the latter was rarely associated with any transmission of VL. In Central Africa, *Phlebotomus rodhaini* had been identified in several countries, namely Cameroon [41], Chad [50], Angola [30], Central African Republic [46], Congo [54] and Gabon [64]. It would be reasonable to assert in current contexts that *Phlebotomus rodhaini* would probably be one of the species that ensures the transmission of VL between humans and other reservoirs in Central Africa.

Table 1. Number of reported cases of VL in Central Africa since the first year of reporting

Countries	Year of first notification	Year of last notification	No. of Cases	Reference
Angola	1963	2004	4	Sabido et al, 1963 ; Jeminez et al, 1994 ; Harms, 2003 ; Beltrame, 2008
Cameroon	1976	2011	25	Kaptue et al, 1992 ; Dondji et al, 2001 ; Mbassi Awa et al, 2011 ; Mah et al, 2011
Central African Republic	1949	1969	5	Desjeux, 1991 ; Cagnard et Lindrec, 1969
Chad	1966	2004	65	Desjeux, 1991 ; Aubry, 2004
Congo	-	-	0	-
Democratic Republic of Congo	1968	1978	2	Prevot et al, 1968 ; Gigase et al, 1978
Equatorial Guinea	-	-	0	-
Gabon	1920	1920	1	Tournier, 1920
Sao Tome and Principe	-	-	0	-
Total cases			102	

Table 2. *Phlebotomus* species and transmission of VL in Central Africa

Countries	Known vectors	Suspected Vectors	Known parasites	Suspected parasites	Reservoirs	Visceral leishmaniasis cycle	Reference
Angola	Unknown	*Phlebotomus rodhaini*	*L. infantum*	Unknown	Dogs	Zoonotic	Abonnenc, 1967 ; Vilhena et al, 2014
Cameroon	Unknown	*Phlebotomus rodhaini Phlebotomus duboscqi*	*Complex L. donovani*	Unknown	Unknown	Unknown	Dondji et al, 2000 ; Tateng et al, 2018
Central African Republic	Unknown	*Phlebotomus rodhaini*	*L. infantum*	Unknown	Unknown	Unknown	Grépin, 1983 ; Cagnard et Lindrec, 1969
Chad	Unknown	*Phlebotomus orientalis, Phlebotomus duboscqi Phlebotomus rodhaini*	Unknown	Unknown	Dogs	Zoonotic	Lewis et Hitchcock, 1967 ; Desjeux, 1991
Congo	Unknown	*Phlebotomus rodhaini*	Unknown	Unknown	Dogs	Zoonotic	Trouillet et Vattier-Bernard, 1977 ; Malbrant, 1940
Democratic Republic of Congo	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Parrot et Wanson, 1938 ; Parrot et Wanson, 1939
Equatorial Guinea	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	
Gabon	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Galliard et Nitzulescu, 1931; Rahola et al, 2013
Sao Tome and Principe	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	

In Central Africa, the causative agent of VL had been mentioned in Angola, Cameroon and the Central African Republic. However, its identity remains somewhat unclear. *Leishmania infantum*, the causative agent of VL in the Mediterranean basin was isolated in two Angolans [27,29] and one child from the Central African Republic [44]. For Angola, it would seem that *Leishmania infantum* was introduced into Angola during the Portuguese colonization [27] as was the case of *Leishmania chagasi* in Latin America by the conquistadores [70]. Its presence in the Central African Republic would be the result of migration since its introduction via Angola, and similarly in other countries such as Gabon, Congo, and the Democratic Republic of Congo. The DNA of the *Leishmania donovani* complex was isolated from *Phlebotomus duboscqi*, a known vector of cutaneous leishmaniasis in Cameroon. Could it be *Leishmania infantum* or *Leishmania donovani*? The latter species had been suspected in Chad, neighbor of Sudan in East Africa, from which it originates before its migration, as well as *Homo Sapiens* [71]. Those species might have migrated with the Reservoirs and became responsible for VL cases in North Cameroon and other regions.

4.3 Reservoirs

In Central Africa, domestic dogs have been shown in three countries to be reservoirs that maintain the zoonotic cycle of VL. Two dogs had been diagnosed by PCR in Angola [31], three in Congo by microscopy [51] and two in Chad by clinical signs [44]. Considering the unsolved presence of *Leishmania donovani* in Central Africa despite the vicinity of several East African countries, it would not be risky to talk about anthroponotic VL in which man is the main reservoir.

5. CONCLUSION

This review of the situation of VL in Central Africa revealed that this pathology is poorly studied. However, in recently, VL has become a problem for the health authorities of some countries such as Chad, where an epidemic of VL is suspected in the second half of the year 2020 in the Borkou and Tibesti Regions on the border with Libya. This would be linked to the resurgence of locally acquired cases or cases of non-immune populations attracted by the gold panning practiced in these two regions. Much work remains to be done especially surveillance, sensitization of population and research to present the exact situation of VL in all the countries mentioned in this review including former outbreaks where the situation could change over time or areas likely to become outbreaks. This work would include underreporting of cases inherent to the weaknesses of the surveillance system in these countries, clarification of the dynamics of human and canine transmission of VL, the identity of parasites and vectors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

ACKNOWLEDGEMENTS

The study was funded by the "Organisation de Coordination pour la lutte contre les Endémies en Afrique Centrale" (OCEAC), on the basis of a financial cooperation between CEMAC and the Ministry of Economic Cooperation and Development (BMZ) of the Federal Republic of Germany, through the KfW (German Development Bank). We thank Fogarty International Center of the National Institutes of Health (NIH) for its support to the training through grant number D43TW008652.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Who. Neglected tropical diseases: Prevention, control, elimination and eradication. Sixty-sixth world health assembly (A66/20). Report by the Secretariat. 2013;8.
2. Ready PD. Epidemiology of visceral leishmaniasis. Clinical Epidemiology. 2014; 6:147-154.
3. WHO. Ending the neglect to attain the sustainable development goals: a road map for neglected tropical diseases 2021–2030 (No. WHO/UCN/NTD/2020.01). World Health Organization; 2020.

4. Jain K, Jain NK. "Vaccines for visceral leishmaniasis. A review," Journal of Immunological Methods. 2015;422:1–12.
5. WHO. Weekly Epidemiological Record, 2018 ;*93*(40) :521-540.
6. Guerin PJ, Olliaro P, Sundar S, Boelaert M, Croft SL, Desjeux P, Wasunna MK and Bryceson ADM. Visceral leishmaniasis: current status of control, diagnosis, and treatment, and a proposed research and development agenda. The Lancet infectious diseases. 2002; 2(8):494-501.
7. Alvar J, Vélez ID, Bern C, Herrero M, Desjeux P, Cano J et Boer Mden. Leishmaniasis control team. Leishmaniasis Worldwide and Global Estimates of Its Incidence. PLoS ONE. 2012;7(5):e35671. DOI:10.1371/journal.pone.0035671.
8. Leta S, Dao THT, Mesele F, Alemayehu G. Visceral Leishmaniasis in Ethiopia: An Evolving Disease. PLoS Negl Trop Dis. 2014;8(9): e3131.
DOI: 10.1371/journal. pntd.0003131.
9. Zijlstra EE, El-Hassa A. M. Leishmaniasis in Sudan. 3. Visceral leishmaniasis. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2001; 95(Supplement_1):S27-S58.
DOI : 10.1016/s0035-9203(01)90218-4.
10. Kassahun A, Sadlova J, Dvorak V, Kostalova T, Rohousova I, Frynta D, Votypka, J. Detection of Leishmania donovani and L. tropica in Ethiopian wild rodents. Acta tropica. 2015;145:39-44.
11. Al-Salem W, Herricks JR and Hotez PJ. A review of visceral leishmaniasis during the conflict in South Sudan and the consequences for East African countries. Parasites & Vectors. 2016;9:460 .
DOI 10.1186/s13071-016-1743-7.
12. Kolaczinski JH, Reithinger R, Worku DT, Ocheng A, Kasimiro J, Kabatereine N, & Brooker S. Risk factors of visceral leishmaniasis in East Africa: a case-control study in Pokot territory of Kenya and Uganda. International Journal of Epidemiology. 2008 37(2) :344-352.
13. Ngure PK, Kimutai A, Nganga ZW, Rukunga G, Tonui WK. A review of Leishmaniasis in Eastern Africa. Journal of Nanjing Medical University. 2009;23(2) :79-86.
14. Diro E, Lynen L, Ritmeijer K, Boelaert M, Hailu A and van Griensven J. Visceral Leishmaniasis and HIV Coinfection in East Africa. PLOS Negl Trop Dis. 2014;8(6): e2869.
DOI:10.1371/journal.pntd.0002869.
15. Aoun K, Jeddi F, Amri F, Ghrab J, Bouratbine A. Current epidemiological data on visceral leishmaniasis in Tunisia. Médecine et Maladies Infectieuses. 2009; Volume 39(10):775-779.
16. Adel A, Boughoufalah A, Saegerman C, De Deken R, Bouchene Z, Soukehal A, and Boelaert M. Epidemiology of Visceral Leishmaniasis in Algeria: An Update. PLoSONE. 2014;9(6): e99207.
DOI: 10.1371/journal.pone.0099207.
17. Hakkour M, Hmamouch A, El Alem MM, Rhalem A, Amarir F, Touzani M, Sadak A, Fellah H, Sebti F. New epidemiological aspects of visceraland cutaneous leishmaniasis in Taza,Morocco. Parasites & Vectors. 2016;9(1):1-9
DOI 10.1186/s13071-016-1910-x.
18. Monge-Maillo B, Norman FF, Cruz I, Alvar J, Lopez-Vélez R. Visceral Leishmaniasis and HIV Coinfection in the Mediterranean Region. PLoS Negl Trop Dis. 2014;8(8):e3021.
DOI:10.1371/journal.pntd.0003021.
19. Boakye DA, Wilson MD,, Kweku M. A review of leishmaniasis in West Africa. Ghana Medical Journal. 2005;39(3):94.
20. Kimutai A, Ngure PK, Tonui WK, Gicheru MM and Nyamwamu LB. Leishmaniasis in Northern and Western Africa: A review. Afr. J. Infect. Dis. 2009;3(1).
21. Tabbabi A. Review of Leishmaniasis in the Middle East and North Africa. African health Sciences. 2019;19(1):1329-1337. Available:https://dx.doi.org/10.4314/ahs.v19i1.4
22. Kone AK, Niaré DS, Piarroux M, Izri A, Marty P, Laurens MB, Piarroux R, Thera MA and Doumbo OK. Visceral Leishmaniasis in West Africa: Clinical Characteristics, Vectors, and Reservoirs. Journal of Parasitology Research; 2019. Available:https://doi.org/10.1155/2019/9282690.
23. Diatta BAD, Iallo M, Diadie S, Faye B, Ndiaye M, Hakim H, Dieng MT. Cutaneous leishmaniasis due to *leishmania infantum* associated with HIV. Annales de Dermatologie et de Vénéréologie. 2016; 143(10):625–628.
24. Adediran OA, Kolapo TU and Uwalaka EC. Seroprevalence of canine leishmaniasis in Kwara, Oyo and Ogun states of Nigeria. Journal of Parasitic Diseases. 2016;40(2): 510–514.

25. Sangaré I, Djibougou AD, Yaméogo BK, Drabo F, Diabaté A, Banuls A, Dabiré RK. First detection of *leishmania infantum* in domestic dogs from Burkina Faso (West Africa). Research Journal of Parasitology. 2016;12(1):27–32.
26. Sabido F, de Azevedo J F, Pinto MR. A case of kala-azar possibly contracted in Angola. Jornal da Sociedade das Ciencias Medicas de Lisboa. 1963;127:796-826.
27. Jimenez M, Puente S, Gutierrez-Solar B, Martinez P and Alvar J. Visceral leishmaniasis in Angola due to *Leishmania (Leishmania) infantum.* The American Journal of Tropical Medicine and hygiene. 1994;50(6):687-692.
28. Harms G, Schönian G and Feldmeier H. Leishmaniasis in Germany. Emerging Infectious Diseases. 2003;9(7):872.
29. Beltrame A, Arzese A, Camporese A, Rorato G, Crapis M, Tarabini-Castellani G, Boscutti G, Pizzolitto S, Calianno G, Matteelli A, Di Muccio T, Gramiccia M and Viale P. Acute renal failure due to visceral leishmaniasis by *Leishmania infantum* Successfully treated tith a single high dose of liposomal amphotericin B. Journal of Travel Medicine. 2008;15(5):358–360.
30. Abonnenc E. Les Phlébotomes de l'Angola (Diptera, Psychodidae), Office de la Recherche Scientifique et Technique Outre-Mer ; Bondy (Seine), Saint Denis, France. 1967;65.
31. Vilhena H, Granada S, Oliveira AC, Schallig HD, Nachum-Biala Y, Cardoso L and G Baneth. Serological and molecular survey of *Leishmania infection* in dogs from Luanda, Angola. Parasites & Vectors. 2014;7(1):1-4.
32. Lopes AP, Oliveira AC, Granada S, Rodrigues FT, Papadopoulos E, Schallig H, Dubey JP and Cardoso L. Antibodies to *Toxoplasma gondii* and *Leishmania spp*. in domestic cats from Luanda, Angola. Veterinary Parasitology. 2014;239:15–18.
33. Djibrilla KB. Existence d'un foyer de leishmaniose cutanée à Mokolo au Nord-Cameroun. Thèse de doctorat en médecine, Université de Yaoundé; 1976.
34. Deniau M, Mbede J, Obama Mt, Same-Ekobo A. Premier cas confirmé de leishmaniose viscérale au Cameroun. Bull Soc Fr Parasitol. 1986; 4:197-200.
35. Kaptue L, Zekeng L, Fomekong E, Nsangou A, Tagu Jp, Tchuela J. La leishmaniose viscérale au Cameroun. A propos de quelques observations et d'une prospection clinique dans la région de Kousseri, extrême-nord Camerounais. Bull Soc Pathol Exot. 1992;85(2):156-158.
36. Dondji B, Dereure J, Poste B, Same-Ekobo A, Dedet JP. Visceral leishmaniasis in Cameroon. Seroepidemiologic survey in the Kousseri region, north Cameroon. Bull. Soc. Pathol. Exot. 2001;94(5):418- 420.
37. Mbassi Awa HD, Pondy A, Njiki Kinkela M, Lebela J, Koki Ndombo PO. Leishmaniose viscérale : une observation pédiatrique en dehors des foyers traditionnels au Cameroun. Med Trop. 2011;71(6):618-620.
38. Mah EM, Chiabi A, Atangana P, Nguefack S, Mbassi Awa HD , Nzedjom C , Tietche F and Tetanye E. Disseminated leishmaniasis in a four-year-old child in Yaoundé, Cameroon. Turk J Pediatr. 2011; 53:(2).
39. Rageau J - Phlébotomes du Cameroun. *Bull Soc Pathol Exot*. 1953;44:793-800.
40. Rageau J, Adam JP. Note sur les phlébotomes d'Evodoula (Cameroun français). Bull Soc Pathol Exot. 1953; 46(4): 587-594.
41. Dondji B, Duhlinska DD, Same-Ekobo A. Species composition of the phlebotomine sandfly fauna (Diptera, Phlebotominae) in Mokolo region, Northern Cameroon. International Journal of Tropical Insect Science. 2000;20(3):221-226.
42. Tateng AN, Kirstein OD, Ngouateu OB, Krüger A, von Stebut E, Maurer M, Khan PV, Warburg A and Dondji B. First detection of *Leishmania donovani* in sand flies from Cameroon and its epidemiological implications. Trop Med Int Health. 2018;23 (9):1014-1021.
DOI: 10.1111/tmi.13123. Epub 2018 Jul 30.
43. Anderson JM, Samake S, Jaramillo-Gutierrez G, Sissoko I, Coulibaly CA, Traoré B. Kamhawi S. Seasonality and prevalence of Leishmania major infection in Phlebotomus duboscqi Neveu-Lemaire from two neighboring villages in central Mali. PLoS Negl Trop Dis. 2011;5(5): e1139.
44. Desjeux P. Information on the epidemiology and control of the leishmaniases by country or territory (No. WHO/LEISH/91.30. Unpublished). World Health Organization; 1991.
45. Cagnard V et Lindrec A. A case of visceral leishmaniasis in Bangui, Central African Republic. Medecine tropicale: revue du

Corps de santé colonial. 1969;29(4):531-535.
46. Grépin G. Phlébotomes (diptera-phlebotominae) de la République centrafricaine. Annales de Parasitologie Humaine et Comparée. 1983;58(1):85-90.
47. Sirol J, Vedy J, Barabe P, Cesari C and Berger P. Kala-Azar in the Republic of Chad. 6 year survey at the Central Hospital of N'Djamena (Fort-Lamy). Bulletin de la Societe de pathologie exotique et de ses filiales. 1976;69(3):232-237.
48. Aubry P. Leishmaniose viscérale au retour du Tchad: cas Clinique. Médecine Tropicale. Collections. Texte rédigé le; 2004.
49. Tubiana MJ. Jean Malval. Ma pratique médicale au Tchad (1926-1928). Journal des africanistes. 1994;64(1):122-123.
50. Lewis DJ and Hitchcock JC. Phlebotomine sandflies of Chad. Annals of Tropical Medicine & Parasitology. 1967;62(1):117-121.
51. Malbrant R. I. Canine Leishmaniasis In the French Congo. II. Canine Ancylostomiasis and the Formol-Gel Test. Bulletin de la Société de Pathologie Exotique. 1940;33: 12-14.
52. Trouillet J et Vattier-Bernard G. Les Phlébotomes (Diptera, Psychodidae) de la Likouala-République Populaire du Congo. Annales de parasitologie humaine et compare. 1988;63(6):455-461.
53. Vattier-Bernard G, Trouillet J. Phlébotomes du Mayombe congolais (Diptera, Psychodidae) Étude phénologique. Annales de Parasitologie Humaine et Comparée. 1983;58(4):391-401.
54. Trouillet J, Vattier-Bernard G. Présence en République Populaire du Congo de *Sergentomyia decipiens, Sergentomyia dissimillima, Sergentomyia tauffliebi, Sergentomyia wansoni* et *Sergentomyia squamipleuris*. Annales de parasitologie humaine et comparée. 1977;52(2) :195-203.
55. H, Parmentier R, Bounameaux Y. Case of visceral leishmaniasis in the Congo. Ann Soc Belges Med Trop Parasitol Mycol. 1968;48(4):421-7.
56. Gigase P, Moens F, Van Emelen J, Van Marck E, Van Mullem J. Autochtonous visceral leishmaniasis in Zaire. Ann Soc Belg Med Trop. 1978;58(3):235-240.
57. Parrot L et Schwetz L. Phlébotomes du Congo Belge. VI - Trois espèces et une variété nouvelles. Revue de Zoologie et de Botanique Africaines. 1937;24:221.
58. Parrot L et Wanson M. Phlébotomes du Congo Belge. VIII - Sur le mâle de *Phlebotomus gigas*. Revue de Zoologie et de Botanique Africaines. 1938;31:153-156.
59. Parrot L et Wanson M. Phlébotomus du Congo Belge. IX - *Phlebotomus* (*Prophelbotomus*) *mirabilis* n. sp. Revue de Zoologie et de Botanique Africaines. 1939; 32:149-153.
60. Tournier E. Note sur un cas de kala-azar infantile observé au Gabon. Bull Soc Pathol Exot Filiales. 1920;13:175-176.
61. Galliard H et Nitzulescu V. Contribution à l'étude des Phlébotomes du Gabon. Phlebotomus sanneri n. sp. Annales de Parasitologie Humaine et Comparée. 1931;9(3):233-246.
62. Rahola N, Depaquit J, Makanga BK, Paupy C. *Phlebotomus (Legeromyia) multihamatus* subg. nov., sp. nov. from Gabon (Diptera : Psychodidae). *Mem Inst Oswaldo Cruz*, Rio de Janeiro. 2013; 108(7):845-849.
63. Rahola N, Henni LH, Obame J, Ayala D, Makanga BK, Lehrter V, Izri A, Paupy C and Depaquit J. A molecular study of the genus Spelaeomyia (Diptera: Phlebotominae) with description of the male of *Spelaeomyia moucheti*. Parasites & Vectors. 2016;9(1):1-10.
DOI 10.1186/s13071-016-1656-5.
64. Obame-Nkoghe J, Rahola N, Ayala Diego, Yangari P, Jiolle D, Allene X, Bourgarel M, Maganga GD, Berthet N, Leroy EM and Paupy C. Exploring the diversity of blood-sucking Diptera in caves of Central Africa. Scientific Reports. 2017;7(1): 1-11.
DOI: 10.1038/s41598-017-00328-z.
65. Ruiz-Postigo JA, Grout L and Saurabh J. Global leishmaniasis surveillance, 2017-2018, and first report on 5 additional indicators. *Weekly* Epidemiological Record. 2020;95(25):265-280.
66. WHA60.13. Résolutions and Décisions: Control of leishmaniasis. The Sixtieth World Health Assembly. 2007; PP4.
67. Rocklöv J and Dubrow R. Climate change: an enduring challenge for vector-borne disease prevention and control. Nature immunology. 2020;21(5);479-483.
68. Sheik-Mohamed A and Velema JP. Where health care has no access: the nomadic populations of sub-Saharan Africa. Tropical Medicine and International Health.2020;4(10):695-707.

69. Elnaiem DEA, Hassan HK, Osman OF, Maingon RD, Killick-Kendrick R and Ward RD (2011). A possible role for *Phlebotomus (Anaphlebotomus) rodhaini* (Parrot, 1930) in transmission of *Leishmania donovani*. Parasites & vectors. 1999;4(1):1-6.

70. Van Eys GJ, Schoone GJ, Ligthart GS, Alvar J, Evans DA and Terpstra WJ. Identification of 'Old World' Leishmania by DNA recombinant probes. Molecular and biochemical parasitology. 1989;34(1):53-62.

71. Tuon FF, Neto VA, Amato VS. Leishmania: origin, evolution and future since the Precambrian. FEMS Immunol Med Microbiol. 2008;54:158–166.
DOI: 10.1111/j.1574-695X.2008.00455.x.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/69965