Original Research Article

Age and gender are differently associated with microfilaremic loiasis and *Mansonella perstans* infections in urban and rural provinces of Gabon, Central Africa

Comment [SN1]: Rewrite the title

Abstract

Background: Loiasis and blood mansonellosis are parasitic vector borne diseases, the most widespread in Gabon after malaria. Loiasis presents all characteristics of a Neglected Tropical Diseases with recent implication on excess mortality among hypermicrofilaremia patients and *Mansonella perstans* seems to interact with other pathogens. The present study aimed to determine the prevalence and sociodemographic risk factors for loiasis and blood mansonellosis in three provinces of Gabon with different levels of urbanization.

Methods: Participants were recruited in the province of Woleu-Ntem (rural area), Ngounié (rural area) and Estuaire (urban area). This cross-sectional study was conducted from December 2020 to April 2022. Sociodemographic data were collected, and venous blood was collected in an EDTA tube for detection of *Loa loa* and *Mansonella perstans* microfilariae by direct examination and leukoconcentration techniques.

Results: Globally, 2,132 participants were recruited: 1,342 in the Woleu-Ntem, 492 in the Estuaire and 298 in the Ngounié. Loiasis prevalence was 23.6% (n=503/2,132), 8.7% (n= 185/2,132) for *Mansonella perstans* infection and 2.4% (n=51/2,131) for co-infection in the study population. *L. loa* was found more frequently in Woleu-Ntem compared to Ngounié (OR : 1.9 [CI 95% : 1.4-2.8]; p< 0.01) and Estuaire (OR : 2.9 [CI 95% : 2.1-4.1]; p< 0.01). Regarding *M. perstans*, the risk of having microfilaremia was 14 and 7 times higher in Ngounié compared to Estuaire (OR : 14.7 [CI 95% : 7.9-29.8]) (p< 0.01) and Woleu-Ntem (OR : 7.3 [CI 95% : 5.2-10.3]) (p< 0.01). The microfilaremia geometric mean was significantly higher in the group of infected inhabitants from Ngounié sites (p< 0.01).No risk factors were found in Estuaire province for both filariasis. In Ngounié, participants older than 29 years old were less frequently infected by *L. loa* and *M. perstans* (p< 0.01). In Woleu-Ntem, men and the oldest people were more infected than their counterparts (p< 0.01).

Conclusions: Loiasis and blood mansonellosis burden are higher in rural settings, although also present in the Estuaire. Age and gender were differently associated with these blood filariasis carriage in the three provinces.

Keywords: Gabon, *Loa loa*, *Mansonella perstans*, urbanization, risk factors

Comment [SN2]: Please include specific references that compare sociodemographic risks with findings from other studies.

Background

Loiasis and blood mansonellosis are parasitic vector borne diseases, the most widespread in Gabon after malaria (1,2). These filariasis are mainly found in rural areas due to favorable forest environment for *Chrysops* sp. vector for *Loa* (*L.*) *loa* and *Culicoides* sp. for *Mansonella* (*M.*) *perstans* in Centra Africa (1,2). The specific symptoms of loiasis are Calabar swelling, crawling sensation and adult worm in eye; other symptoms such as pain, arthralgia, pruritus, as well as some rare serious ones like loss of vision, nephropathy, pulmonary inflammation due to its interference with cardiac complications are also described (3–5). Loiasis has shown a significant interest in public health in the control of river blindness. During mass drug administration (MDA) with ivermectin (IVM) for the elimination of onchocerciasis in coendemic areas, patients with *L. loa* hypermicrofilaremia can developed fatal severe adverse events (6–8). In the other side, in endemic settings, blood filariasis clinical symptoms are frequent reasons for outpatient consultations. Moreover, it was reported that hypermicrofilaremia was associated with a reduction of lifespan in Cameroon and Democratic Republic of Congo, neighbors countries of Gabon (9,10). Loiasis also impacts quality of life exposed populations (3).

Loiasis is considered as a common disease in Gabon; this endemic filariasis shares similar characteristic with Neglected Tropical Diseases (NTDs) such as soil-transmitted helminths. It is more frequent in rural areas were more than 60% of the community members can be infected, chronic carriage is also frequent and clinical symptoms are responsible for non negligible DALY'S, although not associated with death. Furthermore, there is no standardization of patient case management and no specific actions for loiasis control in endemic settings such as the Central Africa regional (11,12).

Although considered as non-pathogenic, *M. perstans* can interfere with other filariasis, causing cross-reactivity of rapid diagnostic tests and, consequently, false-positive results (13). In addition, *M. perstans* has been associated with high immunoglobulin E (IgE) levels, which correlate with exacerbated allergic symptoms in some infected individuals (14).

Recent data on the distribution of these two filariasis within the country are scarce (1,2,15–17). Previous local surveys were performed either in urban or rural settlements, either in onchocerciasis foci, either in a small population size (18,19). Moreover, socioeconomic disparities in urban and rural regions are known to influence the distribution of helminthic diseases that appear in the World Health Organization (WHO) NTD list. As loiasis and mansonellosis share some risk factors, including socioeconomic ones with these NTDs, their

prevalence could also be influenced by these risk factors or by community member seeking care behaviors (17,20,21). Thus, the present study aimed to determine the prevalence and sociodemographic risk factors for loiasis and blood mansonellosis in three provinces of Gabon with different levels of urbanization.

Methods

Study sites

This study was carried out in three of Gabon's nine provinces (Woleu-Ntem, Ngounié and Estuaire), with varying degrees of urbanization. In the Woleu-Ntem (northern province), the survey was performed in very remote rural communities, specifically in villages of the Ntem and Haut-Ntem departments, in the Ngounié (southern province), the survey was carried out in rural communities, more specifically in the Louétsi-Wano department. Finally, in the Estuaire province, the study was carried in the capital city, Libreville, more precisely in the Department of Parasitology-Mycology-Tropical Medicine (DPMTM) of the Faculty of Medicine at the Université des Sciences de la Santé. The DPMTM is the reference center for the diagnosis and management of filarial infections.

Study design

This cross-sectional study was conducted from December 2020 to April 2022. In Woleu-Ntem and Ngounié sites, a preliminary visit was organized to inform the local authorities and communities about the purpose, importance and procedures of the study. Awareness-raising campaigns were set up to facilitate the voluntary recruitment, ensuring that volunteers were fully informed of the study objective and procedures. In both provinces, the surveys were part of two projects (PHYLECOG project and OCEAC) in which the burden of endemic parasite carriage was assessed in the study sites. In Estuaire, outpatients and those who came for a biological testing for the diagnosis of blood filariasis at the DPMTM, were offered to participate in the study. Their oral consent to the subsequent use of their data for scientific purposes, was previously obtained.

Study population

Inclusion criteria and data collection

All participants who accepted to be tested for a filarial diagnosis in all the three sites, and who provided their informed consent were included. If the person was a minor, consent was sought

from their parents or legal guardians. For each participant, age, gender, location and the results of blood tests were reported on a dedicated case report from.

Sample size calculation

The required sample size for each site was calculated according to previously reported loiasis prevalence in the different sites (39.5%, 20.2% and 18.6% for Estuaire, Woleu-Ntem and Ngounié respectively) (2,15). The precision was fixed at 5% marginal error, and standard score at 95%. The minimum sample size determined were 280, 245 and 233 for Estuaire, Woleu-Ntem and Ngounié respectively.

Blood testing

Comment [SN3]: Include visual data related to the results of the blood analysis.

A volume of 7 ml venous blood sample was taken in an EDTA tube, between 10 am and 3 pm. In Libreville, the participants were directly sampled at the DPMTM. In Woleu-Ntem and Ngounié, samples were collected in the villages, stored in a refrigerated cooler, and transported to the field laboratory. The direct examination of 10 µL of blood and the leukoconcentration of 5 mL using the Ho Thi Sang and Petithory method allowed the detection and quantification of *L. loa* and *M. perstans* microfilaremia, as previously described (22). The Microfilarial density was expressed as the number of microfilariae per milliliter of blood (mf/mL). Hypermicrofilaremia was defined for a parasite density higher or equal than 8,000 mf/ml. *Mansonella perstans* and *Loa loa* were identified according to the microfilaria size, presence of sheath and nucleus size.

Ethical considerations

The study protocol was approved by the National Ethical Committee for the Scientific Research (CNER) under the reference number PROT No 0053/2022/CNER/P/SG for the Woleu-Nten sites, and under the reference number 0081/2019/SG/PR/CNR for Ngounié and Estuaire sites. An authorization was also obtained from the General Direction of Health as well as the village chiefs.

Statistical analysis

The data were double entered in Microsoft Excel® version 2016, with the involvement of an operator and a verifier to guarantee the integrity and accuracy of the information in each site. Then, the three data bases were merged and backups were preserved. Data analysis was then carried out using R software version 4.3.0. The quantitative variable “age” was transformed in

qualitative variable “age groups” as follows : less than 30 years old, between 30 and 60 years old and superior or equal to 60 years old. The qualitative data were presented in absolute values and percentages (95% confidence intervals). To determine the association between age groups, gender, provinces and *L. loa* and *M. perstans* infections and microfilaremia, the chi-square test was used. In the case of small numbers, the Fisher exact test was used. Microfilaremia and age were tested for normality using Karposi test. The *L. loa* and *M. perstans* microfilaremia was expressed in geometric mean and compared between the different provinces according to, age and gender using the Kruskal-Wallis test. A *p*-value below 0.05 was considered significant.

Results

Characteristics of the study population

The participant distribution according to age and gender is summarized in the Table 1. A total of 2,132 participants were recruited in the three study sites, 1,342 in the Woleu-Ntem, 492 in the Estuaire and 298 in the Ngounié. In all three sites, women predominated, the sex ratio was of 0.52 in the Estuaire, 0.76 in the Woleu-Ntem and 0.96 in the Ngounié province. The median age was 51 [2 ; 97] years old ; more than 90.0% of participants from Estuaire and Woleu-Ntem were over 30 years old (Table 1).

Table 1 : Characteristics of the study population in different localities

	Provinces					
	Estuaire		**Ngounié**		**Woleu-Ntem**	
Variables	**N**	**%**	**N**	**%**	**N**	**%**
Gender	**405**		**298**		**1341**	
Female	266	65.7	152	51.0	762	56.8
Male	139	34.3	146	49.0	579	43.2
Age (years)	**396**		**294**		**1330**	
<30	35	8.8	153	52.0	131	9.8
[30; 60[	182	46.0	85	28.9	719	54.1
≥60	179	45.2	56	19.1	480	36.1

Prevalence of filariasis and microfilaremia in the study sites

Overall, the prevalence of *L. loa* microfilaremia was 23.6% (n=503/2,132) in the whole study population. This prevalence showed a significant variability between the three provinces

(Table 2). It was found to be almost twice as high in Woleu-Ntem compared to Ngounié (OR : 1.9 [CI 95% : 1.4-2.8]) (p< 0.01). Participants from Woleu-Ntem were at 2.9 times at higher risk of being infected by *L. loa* compared to participants from Estuaire (OR : 2.9 [CI 95% : 2.1-4.1]) (p< 0.01) (Table 2). Regarding *M. perstans*, its global prevalence was 8.7% (n= 185/2,132). The risk of having *M. perstans* microfilaremia was 14 and 7 times higher in Ngounié compared to Estuaire (OR : 14.7 [CI 95% : 7.9-29.8]) (p< 0.01) and Woleu-Ntem (OR : 7.3 [CI 95% : 5.2-10.3]) (p< 0.01) (Table 2). Only 51 of 637 infected persons had dual *L. loa* + *M. perstans* coinfection, giving a global coinfection prevalence of 2.4% (n=51/2,131). Likewise, coinfection was also more frequent among the inhabitants of Ngounié (p< 0.01) (Table 2).

L. loa geometric mean microfilaremia was 321.7 mf/mL in the infected population. The microfilaremia ranged from 1 to 12,000 mf/mL in infected individuals from Estuaire, from 100 to 30,200 mf/ml in Ngounié and from 1 to 105,900 mf/mL in Woleu-Ntem. The geometric mean microfilaremia was significantly higher in the group of infected inhabitants from Ngounié sites (p< 0.01) (Table 2).

The *M. perstans* geometric mean parasitemia was 59.7 mf/mL. It was the highest at Ngounié province were the microfilaremia ranged from 100 to 105,900 mf/ml; this range was of 3 to 500 mf/ml in Woleu-Ntem and 1 to 5 mf/mL in Estuaire. *L. loa* hypermicrofilaremia was detected in 3.2% (n= 69/2,132) participants. Those living in Ngounié and Woleu-Ntem were 5 and 4 times at higher risk of having hypermicrofilaremia compared to those living in the Estuaire (OR : 5.2 [CI 95% : 1.2-35.5]; p< 0.01 for Ngounié and OR :4.2 [CI 95% : 1.2-25.9]; p<0.01 for Woleu-Ntem).

Table 2 : Prevalence of *Loa loa* and *Mansonella perstans* infections and microfilaremia in different localities

	Estuaire (N=492)		**Ngounié (N=298)**		**Woleu-Ntem (N=1342)**		***p*-value**
Prevalence	**n**	**% (95% CI*)**	**n**	**% (95% CI)**	**n**	**% (95% CI)**	
Loa loa							
Positive	51	10.4 (0.7-11.5)	46	15.4 (11.6-20.1)	406	30.2 (27.8-32.8)	<0.0001
Hypermicrofilaremia**	2	3.9 (7.9-13.5)	8	17.4 (8.3-31.9)	59	14.5 (11.3-18.4)	0.044
Mansonella perstans	12	2.4 (1.3-4.3)	107	35.9 (30.5-41.7)	66	4.9 (3.8-6.2)	<0.0001
***Loa loa* + *Mansonella perstans* coinfection**	3	0.6 (0.2-1.9)	23	7.7 (5.1-11.5)	25	1.9 (1.2 -2.8)	<0.0001

Microfilaremia		Gmean (mf/mL)		Gmean (mf/mL)		Gmean (mf/mL)	
Loa loa	51	204.4	46	969.7	406	300.5	0.056
Mansonella perstans	12	46.1	107	389.2	66	1.7	<0.0001

***** CI confidence interval

** Hypermicrofilaremia corresponding to ≥ 8000 mf/ml

Factors associated with *Loa loa* and *Mansonella perstans* single or co-infection

In the Estuaire province, nor age or gender were found associated with the presence of both filariasis. Participants older than 29 years old and living at Ngounié province were less frequently infected ($p< 0.01$) (Table 3). In Woleu-Ntem, men had more often a filariasis than Women ($p< 0.01$) (Table 3). Regarding the parasite species, age over 30 years old was associated with a higher rate of *L. loa* microfilaremia whereas participants older than 60 years old had a higher frequency of *M. perstans* infection (Table 3).

The *L. loa* and *M. perstans* parasite densities, were higher in older inhabitants from Ngounié (Table 3). Moreover, their geometric mean parasite density was twice higher than that of their younger counterparts (Table 3).

L. loa-infected participants from Ngounié were significantly youngers [mean age : 47.0 (±20.7) years] than those from Estuaire [mean age : 57.8 (±19.1) years] and from Woleu-Ntem [mean age : 54.9 (±16.1) years] ($p< 0.01$).

Table 3 : *Loa loa* and *Mansonella perstans* microfilaremia prevalence and parasite density in the three study sites by gender and age

	Provinces											
	Estuaire				Ngounié				Woleu-Ntem			
Variables	**% (95% CI*)**	***p*-value**	**Gmean**	***p*-value**	**% (95% CI)**	***p*-value**	**Gmean**	***p*-value**	**% (95% CI)**	***p*-value**	**Gmean**	***p*-value**
Loa loa												
Gender												
Male	12.2 (7.5-19.1)	0.90	166.8	0.5	17.8 (12.2-25.2)	0.34	1201.3	0.3	38.0 (34.0-42.1)	<0.0001	372.3	0.14
Female	11.3 (7.9-15.9)		217.2		13.2 (8.4-19.8)		734.0		24.4 (21.4-27.6)		233.3	
Age (years)												
< 30	8.6 (2.2-24.1)	0.20	303.8	0.4	5.2 (2.4-10.4)	<0.0001	1168.9	0.6	17.6 (11.7-25.4)	0.0009	286.3	0.8
[30; 60[	9.3 (5.7-14.8)		636.6		27.1 (18.3-38.0)		570.5		29.6 (26.3-33.1)		196.6	
≥ 60	15.1 (10.3-21.4)		158.0		23.2 (13.4-36.7)		1017.0		34.4 (30.2-38.8)		346.1	
Mansonella perstans												
Gender												
Male	2.1 (0.6-6.7)	1	100.0	1	39.0 (31.2-47.5)	0.32	384.5	0.6	7.2 (5.3-9.8)	0.0009	1.7	0.13
Female	2.6 (1.1-5.6)		49.3		32.9 (25.6-41.0)		394.6		3.1 (2.1-4.7)		1.49	
Age (years)												
< 30	0.0 (0.0-12.3)	0.35	217.2	0.8	24.2 (17.8-31.9)	0.0001	342.3	0.036	3.0 (1.0-8.1)	0.037	1.83	0.4
[30; 60[	1.6 (0.4-5.1)		N/A		50.6 (39.6-61.5)		314.2		3.9 (2.6-5.6)		1.0	
≥ 60	3.3 (1.4-7.5)		78.6		42.9 (30.0-56.7)		740.3		6.9 (4.8-9.6)		1.6	

***** CI confidence interval

** Gmean : geometric mean

Discussion

Comment [SN4]: Please reframe the discussion to reflect global insights and perspectives.

This study is the first describing the mapping and comparing *L. loa* and *M. perstans* microfilaremia in large populations of urban and rural settlements of Gabon. Not surprisingly, mansonellosis and loiasis were more prevalent in rural sites. This is in accordance with previous reports in Gabon (1,16).

In Estuaire, the rates of infection were the lowest, 10.4% and 2.4% respectively for loiasis and mansonellosis, similarly to prevalences recorded 8 years ago in the Estuaire (4.7% for loiasis and 1.1% for mansonellosis) and in the south of Gabon (4.8% for loiasis and 0.8% for mansonellosis) (16,23). Study design, sample size and techniques used for the parasitological diagnosis can explain this difference. In contrary, Bouyou and colleagues reported a prevalence four fold higher (39.5%) in the DPMTM (15). Thus, loiasis prevalence decreased between 2016 and 2021 in the capital city. Two major explanation can be raised. First, before 2020, the DPMTM was the single center historically recognized as the reference for filariasis diagnosis and case management. Outpatients who underwent a biological testing came from the nine provinces of the country. Secondly, in 2016, occult loiasis detected with serology was the most frequent form of loiasis, while indirect immunofluorescence was not performed in the present study (15). Thus, the burden of loiasis could be underestimated here. In another way, infected participants diagnosed at the DPMTM in 2021-2022 lived in the Estuaire. It is important to notice that the majority of them performe food crops or had weekly activities in their own plantations that are located in the suburban areas of Estuaire. These plantations are in savannah areas and burning is the main tool used to clean the land, fertilize the soil and prepare it for new planting, creating a favourable environment for *Chrysops* development. The frequent visits in rural provinces, from where some inhabitants of the Estuaire province come, would also explain the presence of *Loa loa* and *Mansonella* infected people in the capital city. Thus, although entomological data are lacking, there is a possible local transmission of loiasis in the Estuaire province.

Not surprisingly, the frequency of *L. loa* and/or *M. perstans* carriage was the highest in rural study sites. Indeed, the forest environment, as well as agriculture which is the main activity of adults in the villages, are recognized risk factors of these filariasis. Furthermore, rural communities have not easily access to heath structures. Even if they recognize the symptoms of loiasis, they usually consult traditional practitioners or treat themselves using plants or other traditional potions for symptomatic treatment (24). They remain chronically infected and maintain the transmission.

Differences in species prevalence were observed between Woleu-Ntem and Ngounié. *M. perstans* was highly prevalent in Ngounié while *L.loa* predominated in Woleu-Ntem. The geographical localizations and ecosystems would explain this observation. Indeed, in Ngounié, the alternate of tropical forest areas with swampy and open ground ones constitute the most favorable ecosystem for *Culicoides* sp. vector development (25). Whereas, the dense forest which predominates in Woleu-Ntem province, forces farmers to often burn the vegetation to allow a better cleaning, creating the most favourable condition for *Chrysops* sp. development and biting.

Age was differently associated with the rate of filariasis carriage according to the provinces. The mean age of *L. loa* carriers was significantly lower in Ngounié (47 years old) compared to Woleu-Ntem (55 years old) and Estuaire (58 years old) ($p< 0.01$). Akue and colleagues reported a positive correlation between microfilaremia and age, and an association with hunting activities which are preferably performed by order adults than the young population (2). Nevertheless, retired or older people represent the majority of the active populations in villages of Gabon, while the youngest ones work and live in the main cities. Thus, older adults of Woleu-Ntem are those who are responsible for the rest of the family livelihood. They practice hunting, fishing or agriculture. In contrary, in Ngounié province, several local and international agricultural companies that employed younger adults were established these last 10 years. Therefore, they are more likely exposed to fly bites and filariasis infection compared to the older community members.

The difference in filariasis infection rates between men and women, in Woleu-Ntem, may be due to the specific behavior of the local population. Agriculture, hunting and fishing are the main activities for daily subsistence in rural areas. Agriculture is practiced by both sexes, but mostly by women. Hunting and fishing, however, are predominantly male activities, especially hunting, which is more practiced than fishing and which is culturally considered an exclusively male activity in this region (17,26). Hunters can spend 10 to 15 days in the forest, that often means building wood fires for warmth or cooking in the night. This increases their exposition to insect bites, particularly by *Chrysop* sp. This vector is attracted by the smoke from wood fires (2,27). This gender heterogeneity was not observed in the Estuaire, the urban site, where hunting is only occasionally practiced and not by a large number of inhabitants, thus reducing the risk of infection.

This study has some limitations. First it was not performed in all the nine provinces of the country, thus the present data cannot be generalized to the whole population. Secondly,

specific geographical characteristic of the study sites as well as participants behaviours and daily activities that influence the exposition to the vectors were not assessed. Nevertheless, this is the first study that assessed human risk factors in different communities with a larger population sample.

Conclusion

Loiasis and blood mansonellosis burden are higher in rural settings, although also present in the Estuaire. Age and gender were differently associated with these blood filariasis carriage. Ecosystem, livelihood activities and the economical environment would also contribute to these différences and to the varying burden of these blood filariasis according to the settlements. Further investigations, including all these factors are needed to provide additional accurate data for a better knowledge of blood filariasis epidemiology.

List of abbreviations

CNER : National Ethical Committee for the Scientific Research

DPMTM : Department of Parasitology-Mycology-Tropical Medicine

EDTA : ethyldiaminetetraacetyl

IVM : ivermectin

L. loa : *Loa loa*

***M. perstans* :** *Mansonella perstans*

MDA : mass drug administration

NTDs : Neglected Tropical Diseases

Ethics approval and consent to participate

The study protocol was approved by the National Ethical Committee for the Scientific Research (CNER) under the reference number PROT No 0053/2022/CNER/P/SG for the Woleu-Nten sites, and under the reference number 0081/2019/SG/PR/CNR for Ngounié and

Estuaire sites. An authorization was also obtained from the General Direction of Health as well as the village chiefs.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

References

1. M'bondoukwé NP, Kendjo E, Mawili-Mboumba DP, Koumba Lengongo JV, Offouga Mbouoronde C, Nkoghe D, et al. Prevalence of and risk factors for malaria, filariasis, and intestinal parasites as single infections or co-infections in different settlements of Gabon, Central Africa. Infect Dis Poverty. 2018;7(1):1–17.
2. Akue JP, Nkoghe D, Padilla C, Moussavou G, Moukana H, Mbou RA, et al. Epidemiology of concomitant infection due to Loa loa and mansonella perstans in Gabon. PLoS Negl Trop Dis. 2011;5(10).
3. Veletzky L, Hergeth J, Stelzl DR, Mischlinger J, Manego RZ, Mombo-Ngoma G, et al. Burden of disease in Gabon caused by loiasis: a cross-sectional survey. Lancet Infect Dis. 2020;20(11):1339–46.
4. Ramharter M, Butler J, Mombo-Ngoma G, Nordmann T, Davi SD, Zoleko Manego R. The African eye worm: current understanding of the epidemiology, clinical disease, and treatment of loiasis. Lancet Infect Dis [Internet]. 2023;3099(23):1–14. Available from: http://dx.doi.org/10.1016/S1473-3099(23)00438-3

5. Buell KG, Whittaker C, Chesnais CB, Jewell PD, Pion SDS, Walker M, et al. Atypical Clinical Manifestations of Loiasis and Their Relevance for Endemic Populations. Open Forum Infect Dis. 2019;6(11):1–9.

6. Klion AD, Massougbodji A, Horton J, Ekoué S, Lanmasso T, Ahouissou NL, et al. Albendazole in Human Loiasis: Results of a Double-Blind, Placebo-Controlled Trial. J Infect Dis. 1993;168(1):202–6.

7. Pion SDS, Clarke P, Filipe JAN, Kamgno J, Gardon J, Basáñez MG, et al. Co-infection with Onchocerca volvulus and Loa loa microfilariae in central Cameroon: Are these two species interacting? Parasitology. 2006;132(6):843–54.

8. Chippaux JP, Boussinesq M, Gardon J, Gardon-Wendel N, Ernould JC. Severe adverse reaction risks during mass treatment with ivermectin in loiasis-endemic areas. Parasitol Today. 1996;12(11):448–50.

9. Hemilembolo MC, Niama AC, Campillo JT, Pion SD, Missamou F, Whittaker C, et al. Excess Mortality Associated with Loiasis: Confirmation by a New Retrospective Cohort Study Conducted in the Republic of Congo. Open Forum Infect Dis [Internet]. 2023;10(3):1–8. Available from: https://doi.org/10.1093/ofid/ofad103

10. Chesnais CB, Takougang I, Paguélé M, Pion SD, Boussinesq M. Excess mortality associated with loiasis: a retrospective population-based cohort study. Lancet Infect Dis. 2017;17(1):108–16.

11. Veletzky L, Hergeth J, Stelzl DR, Mischlinger J, Manego RZ, Mombo-Ngoma G, et al. Burden of disease in Gabon caused by loiasis: a cross-sectional survey. Vol. 20, The Lancet Infectious Diseases. 2020. p. 1339–46.

12. Metzger WG, Mordmüller B. Loa loa-does it deserve to be neglected? Lancet Infect Dis. 2014;14(4):353–7.

13. Wanji S, Amvongo-Adjia N, Koudou B, Njouendou AJ, Chounna Ndongmo PW, Kengne-Ouafo JA, et al. Cross-Reactivity of Filariais ICT Cards in Areas of Contrasting Endemicity of Loa loa and Mansonella perstans in Cameroon: Implications for Shrinking of the Lymphatic Filariasis Map in the Central African Region. PLoS Negl Trop Dis. 2015;9(11):1–20.

14. Bouyou-Akotet MK, Moussavou Boussougou MN, Ovono-Abessolo F, Owono-

Medang M, Kombila M. Influence of Mansonella perstans microfilaraemia on total IgE levels in Gabonese patients co-infected with Loa loa. Acta Trop [Internet]. 2014;131(1):11–5. Available from: http://dx.doi.org/10.1016/j.actatropica.2013.11.012

15. Bouyou Akotet MK, Owono-Medang M, Mawili-Mboumba DP, Moussavou-Boussougou MN, Nzenze Afène S, Kendjo E, et al. The relationship between microfilaraemic and amicrofilaraemic loiasis involving co-infection with Mansonella perstans and clinical symptoms in an exposed population from Gabon. J Helminthol. 2016;90(4):469–75.

16. M'Bondoukwé NP, Mawili-Mboumba DP, Koumba Lengongo JV, Ndong Ngomo JM, Bouyou-Akotet MK. Prévalences de la loaose et de la mansonellose microfilarémiques dans deux provinces du Gabon. Bull Médical d'Owendo. 2015;15(42):33–6.

17. Moutongo Mouandza R, Mourou JR, Moutombi Ditombi B, Roger Sibi Matotou H, Ekomi B, Bouyou-Akotet MK, et al. Sociodemographics, Clinical Factors, and Biological Factors Associated with Loiasis in Endemic Onchocerciasis Areas in Southern Gabon. Am J Trop Med Hyg. 2023;109(4):850–7.

18. Ella SN, Ogoussan K, Gass K, Hundley L, Diggle PJ, Johnson O, et al. An Integrated District Mapping Strategy for Loiasis to Enable Safe Mass Treatment for Onchocerciasis in Gabon. Am J Trop Med Hyg. 2022;106(2):732–9.

19. Id LV, Eberhardt KA, Hergeth J, Stelzl R, Manego RZ, Mombo-ngoma G, et al. Distinct loiasis infection states and associated clinical and hematological manifestations in patients from Gabon. 2022;1–15.

20. Silver ZA, Kaliappan SP, Samuel P, Venugopal S, Kang G, Sarkar R, et al. Geographical distribution of soil transmitted helminths and the effects of community type in South Asia and South East Asia – A systematic review. PLoS Negl Trop Dis. 2018;12(1):7–16.

21. Riaz M, Aslam N, Zainab R, Aziz-Ur-Rehman, Rasool G, Ullah MI, et al. Prevalence, risk factors, challenges, and the currently available diagnostic tools for the determination of helminths infections in human. Eur J Inflamm. 2020;18.

22. Ho Thi Sang, Petithory J. Techniques for the Concentration of Microfilariae from the Blood. Bull la Soc Pathol Exot. 1963;56(2):197–206.

23. Dieki R, Eyang Assengone ER, Nsi Emvo E, Akue JP. Profile of loiasis infection through clinical and laboratory diagnostics: the importance of biomarkers. Trans R Soc Trop Med Hyg. 2023;117(5):349–57.

24. Veletzky L, Schlicker V, Hergeth J, Stelzl DR, Zoleko Manego R, Mombo-Ngoma G, et al. Reported healthcare-seeking of loiasis patients and estimation of the associated monetary burden in Gabon: Data from a cross-sectional survey. PLoS Negl Trop Dis. 2024;18(8):e0012389.

25. Kershaw WE, Lavoipierre MMJ, Chalmers TA. Studies on the intake of microfilariae by their insect vectors, their survival, and their effect on the survival of their vectors. Ann Trop Med Parasitol. 1953;47(2):207–24.

26. Mengome MFA, Kono HN, Bivigou EA, M'bondoukwe NP, Ngomo JMN, Ditombi BM, et al. Prevalence of cardiometabolic risk factors according to urbanization level, gender and age, in apparently healthy adults living in Gabon, Central Africa. PLoS One. 2024;19(4 April):1–19.

27. Wanji S, Tendongfor N, Esum ME, Enyong P. Chrysops silacea biting densities and transmission potential in an endemic area of human loiasis in south-west Cameroon. Trop Med Int Heal. 2002;7(4):371–7.