Decrease on malaria clinical cases from 2017 to 2019 in Franceville, Southeast Gabon, Central Africa

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Abstract

Background. In Gabon, malaria remains a major public health problem. All malaria cases with axillary temperature ≥ 37.5°C with a parasites density ≥ 1200/µL are serious cases and must be treated as a medical emergency. Thus, early diagnosis is essential for successful treatment. Because of the impact of malaria on the population, the surveillance of malaria infections in hospitals is urgently needed. The aim of this study was to to assess of clinical cases of malaria in a private health structure in Franceville between 2017 and 2019.

Methods. For that, we conducted a retrospective study using data on malaria cases recorded in a private medical analysis laboratory in Franceville, southeast Gabon. Malaria was diagnosed in this laboratory using a Rapid Diagnostic Test and confirmed by microscopic analysis.

Results. Analysis of 2518 patient forms revealed an increase in malaria prevalence in Franceville between 2017-2019. The global clinical cases was 26.1% (658/2015). Children under 5 years (44.0%) and patients aged 5-14 years (40.1%) were more affected than patients aged ≥15 years (18.8%, P=0.0001). Malaria infection was also significantly dependent on season and gender. We observed at least three Plasmodium species and the predominant Plasmodium species was *P. falciparum* 80.0%, followed by *P. ovale* (19.5%) and *P. malariae* (17.8%).

Conclusion. Our study showed that malaria remains a public health priority for the population of Franceville and that the prevalence of clinical cases of malaria at the laboratory decrease between 2017 and 2019. Our results highlight the need for strategies to control malaria in Franceville, adapted to epidemiological contexts and environmental constraint.

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Background

Malaria is a life-threatening disease caused by parasites belonging to the genus *Plasmodium*.[1] Plasmodia are transmitted to people through the bites of infected female *Anopheles* mosquitoes.[2] In 2019, according to the World Health Organization (WHO), there were an estimated 229 million malaria cases and 409 000 deaths worldwide.[3] However, sub-Saharan African, and particularly the WHO African region, carried the global malaria burden with 94% of cases and deaths.[3-5] Thus, malaria is an obstacle slowing down economic prosperity in many tropical countries, particularly in Africa,[6] where it remains a major public health problem despite numerous efforts to combat this disease.[7]

In humans, malaria is caused by six *Plasmodium* species: *Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae, Plasmodium ovale-curtisi, Plasmodium ovale-wallikeri* and *Plasmodium knowlesi.*[8] *P. knowlesi*, although zoonotic, is an important pathogen in humans in several regions of South-East Asia.[9] Among these parasites, *P. falciparum* and *P. vivax* are far the most virulent in humans.[1] Relatively little effort has been dedicated to research on the other human malaria species.[1] Infections with species such as *P. vivax* with low parasitaemia can persist for long periods asymptomatically.[8] In recent years there has been a resurgence of *P. vivax* infections in Duffy-Negative Black African populations from central Africa.[10,11]

In Gabon, malaria remains a major public health problem. It is the main cause of medical consultations and hospitalizations. Gabon is in a hyperendemic area and malaria risk is present throughout the country.[5] Malaria transmission is perennial with a high transmission season from January to December with *Anopheles funestus* and *Anopheles gambiae* as the main vectors.

More than 90% of malaria cases are due to *P. falciparum*.[5] Moreover, multidrug resistant *P. falciparum* malaria is present in all malarial areas of Gabon. In 2018, according to WHO, malaria was responsible for 447 deaths in Gabon.[12] All malaria infections are serious illnesses and must be treated as a medical emergency. Thus, early diagnosis is essential for successful treatment.[13] A national antimalarial policy has been set up, based on artemisinin combination therapy (ACT), distribution of impregnated bed nets, and intermittent preventive treatment during pregnancy.[4,5] This antimalarial policy has led to a decline in the malaria burden in several urban areas of Gabon.[4] In Franceville in southeast, malaria prevalence dropped considerably from 69% in 2004 to 17.9% in 2010, followed by a minor recrudescence in 2012 (21.45%).[14-16] Thus, despite recent progress in malaria control, malaria is still present in Gabon.[15,17]

Because of the impact of malaria on the population, the surveillance of malaria infections in hospitals is urgently needed to understand the epidemiology and ecology of this disease across the country. Due to the absence of a national health information system in Gabon, data on malaria are mainly collected from public hospitals in large cities. The aim of this study was to determine trends of clinical cases of malaria in a private health structure in Franceville between 2017 and 2019. The prevalence of plasmodial species and the factors influencing the occurrence of malaria attacks were evaluated in a cross-sectional survey.

Materials and Methods

Ethical approvals

Ethics approval was obtained from the National Ethics Committee. This study was performed in strict accordance with the International Conference on Harmonisation's Guidelines for Good Clinical Practice, the Declaration of Helsinki, and applicable national and international standards. The Institutional Ethics Committee approved the study protocol. Consent was obtained directly from each participant or the participant's legal guardian under the age of 18 prior to their inclusion in this study. We used the telephone number contained in the patient records to contact all patients or patient representatives for consent.

Study area

The study was conducted at the Medical Analyses Laboratory at the Interdisciplinary Centre for Medical Research, in Franceville – CIRMF in the Haut-Ogooue province in southern Gabon. Franceville is the third largest town in Gabon. The Haut-Ogooue province receives 1100-2000 mm of annual rainfall and has an annual temperature of 15-29°C. There are two rainy seasons (September to mid-December and mid-February to May) and two dry seasons. In this town, malaria transmission is generally high year-round. The Medical Analyses Laboratory receives around 1000-1500 people for medical examination each year.

Study design and data collection

Three-year retrospective data (2017 to 2019) of febrile patients diagnosed for a malaria test were obtained from the database of the Medical Analyses Laboratory. Sociodemographic (sex, age, residence, civil and family situation) and laboratory data were collected from the patient registration book. In this laboratory, peripheral smear examination of a well-prepared and well-Giemsa-stained blood film is used to confirm the presence of the malaria parasite after an RDT (immunological test), following the WHO protocol. The source of the data was microscopically confirmed malaria cases screened by qualified and experienced medical laboratory technicians. Presence of malaria parasites was assessed using microscopic examination of Giemsa-stained smears (thin and thick smears). All slides were read at least twice by qualified and experienced medical laboratory technicians and any discrepancy resolved by a third reader. One hundred fields at 1000× magnification was examined before declaring a slide negative (limit of detection, approximately ≥2 parasites/µL as recommended by

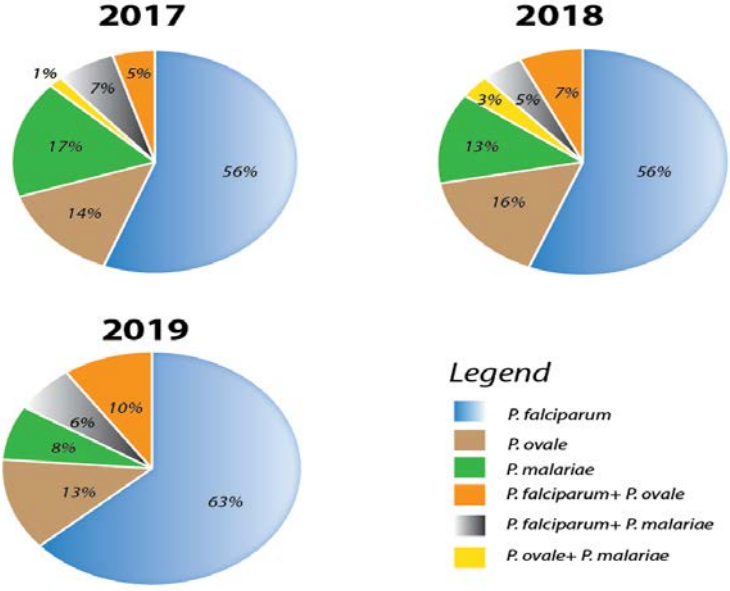

Figure 1. Diversity and prevalence of *Plasmodium* species by year. Pie charts for each year show the prevalence of each *Plasmodium* species and the prevalence of different mixed infections.

WHO). Clinical data defined a positive malaria case as a person with axillary temperature ≥37.5°C and with a parasite density ≥1200/µL. In Gabon, the staining techniques and blood film examination for malaria parasite detection are conducted according to a standard operating procedure in each hospital and health centre throughout the country. The study participants were all malaria-suspected individuals who had complained of febrile illness at the Medical Analyses Laboratory during the study period.

Data analyses

We collected data and first checked for completeness and consistencies. We performed bivariate analyses using a Chi-squared test with R software to test the influence of age, sex and season on malaria infection. The differences observed were considered significant at P<0.05.

Results

Prevalence and diversity of malaria infection

Retrospective analysis of the Medical Analyses Laboratory register indicated 2518 patients with suspected malaria were received for diagnosis between 2017 and 2019. Of these, 658 (26.1% [CI:24.42-27.85]) patients were infected with malaria parasites (Table 1). Two hundred and nineteen (219) confirmed malaria cases were recorded annually and cases varied monthly (Figure 1). The predominant *Plasmodium* species was *P. falciparum* 528/628 (80.0%), followed by *P. ovale* (128/658, 19.5%) and *P. malariae* (117/658, 17.8%) (Table 1 and Figure 2).

Approximatively, 20% (132/658) of individuals were infected with mixed infections. The most frequently observed association was *P. falciparum-P. ovale* (63/132) and the least frequently

Table 1. Diversity and prevalence of infection for each *Plasmodium* species and mixed infections between 2017 and 2019.

Year	Global prevalence	Prevalence by *Plasmodium* species			Mixed infection (frequency)		
	% (n/N)	*P. falciparum*	*P. ovale*	*P. malariae*	*Pf-Po*	*Pf-Pm*	*Pm-Po*
2017	29.92 (278/929)	22.61 (210/929)	5.71 (53/929)	6.89 (64/929)	1.94 (18/929)	2.69 (25/929)	0.65 (6/929)
2018	22.38 (167/746)	17.96 (134/746)	5.09 (38/746)	4.14 (31/746)	2.27 (17/746)	1.47 (11/746)	1.07 (8/746)
2019	25.27 (213/843)	21.82 (184/843)	4.39 (37/843)	2.61 (22/843)	3.32 (28/843)	2.01 (19/843)	-
Total	26.13 (658/2518)	20.96 (528/2518)	5.08 (128/2518)	4.64 (117/2518)	2.50 (63/2518)	2.18 (55/2518)	0.56 (14/2518)

Pm: P. malariae
Po: P. ovale
Pf: P. falciparum
n: cases number and N: total number

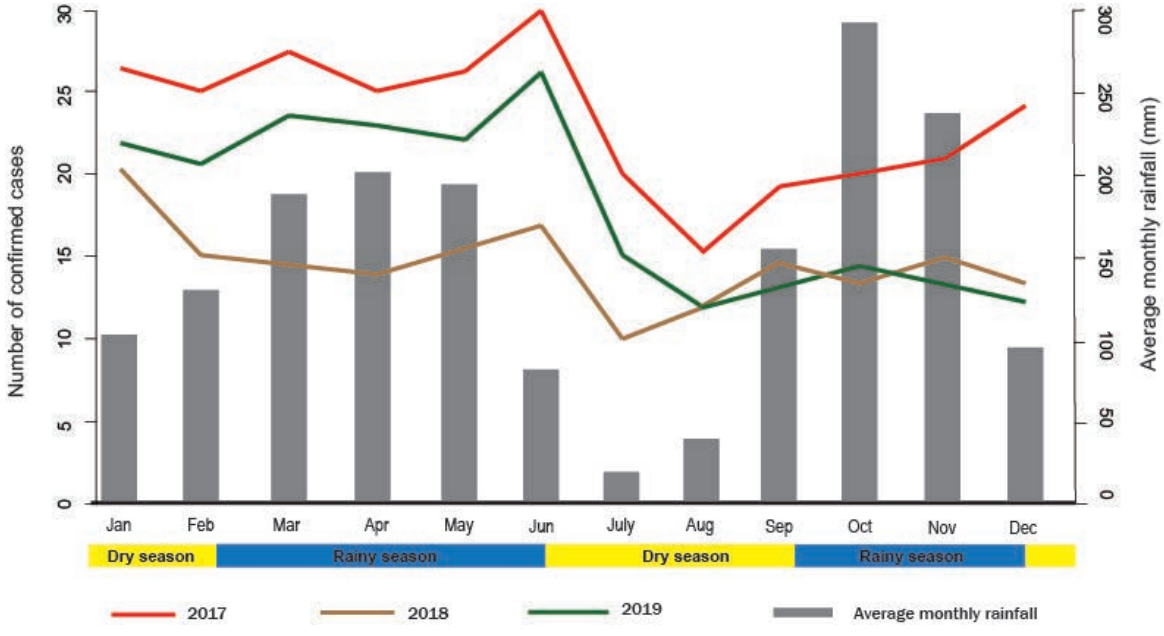

Figure 2. Monthly distribution of the mean malaria case number between 2017 and 2019 *vs* mean rainfall in Franceville.

observed was *P. ovale-P. malariae* (14/132) (Table 1). During this study, malaria cases declined from 2017 to 2019, although the number of cases remained high (>21%) (Table 1).

Factors influencing the infection

Malaria parasites were detected significantly more in men (56.3%) than women (43.7%) (P=0.0103; Table 2). Among patients with a positive slide for malaria from 2017-2019, children under five years (192/293, 44.0%) and patients aged 5-14 years old (204/498, 41.0%) were the most affected by malaria parasites, in comparison to patients ≥15 years (325/1727, 18.8%) (P=0.0001; Table 3). Malaria cases were significantly more common in rainy than dry seasons (P<0.001). The highest numbers of malaria cases were observed in the rainy season (mid-February-June), with a peak in June. However, we found a decrease in malaria cases during the dry season (July to September) in each year studied (Figure 2).

Multivariable analysis

Finally, a multivariate regression of the malaria risk attack including sex, season, age and year was carried out. It confirmed the effect of the season and the year of study on the risk of having a malaria clinical attack (Table 4). However, we also found that the number of observed clinical cases decreased between 2017 and 2019 with a higher prevalence in 2017 (Tables 1 and 4)

Table 2. Number of malaria cases recorded during 2017 and 2019 by gender.

Year	Number of malaria cases	Number of cases in men, n (%)	Number of cases in women, n (%)	X^2	d*f*	*p*	*S*	*M*+	*W*+
2017	278	165 59.35	113 40.65	6.10	1	< 0.001	+	+	-
2018	167	76 45.50	91 54.50	0.73	1	0.390	-	-	+
2019	213	129 60.57	84 39.43	5.95	1	0.015	+	+	-
Total	658	370 56.30	288 43.70	6.58	1	0.010	+	+	+

Table 3. The effects of season and age on malaria burden.

Factors	Variable	Number of individuals examined	Number of positive individuals	Percentage (%)	Comparison test *p*-value
Season	*Rainy*	1160	385	33.19	<0.001
	Dry	1358	273	20.10	
	Total	2518	658	26.13	
Age groups	< 5 y	293	129	44. 03	<0.0001
	5-14 y	498	204	40. 96	
	15+ y	1727	325	18. 82	
	Total	2518	658		

Table 4. Results of the multivariable regression analysis of the risk of clinical cases.

Fixed effects	Estimate	Std.Error	z value	*p*-value
Intercept	-1.33	0.18	-7.20	*5.88e-13***
Year[a]	-0.58	0.13	-4.27	*1.87e-05***
Sex[b]	-0.05	0.10	-0.53	0.59
Age	0.0008	0.002	0.30	0.76
Season[c]	0.189	0.19	-3.38	*0.048**

[a]Reference category: 2017. [b]Reference category: female. [c]Reference category: rainy season. *means different significance

Discussion

Malaria remains an important public health problem in Gabon. Each year this disease is one of the main causes of consultation or hospitalization in health facilities and leads to death across the country.[5,18,19] This study is the first retrospective survey of malaria conducted in South-East Gabon. It is very important to collect epidemiological data in the different regions at risk to implement appropriate health policies and control programs to fight against malaria.[17]

In the present study, the overall positivity rate of slides for malaria detection using a microscope was 26.1% (658/2518). However, a significant desrease in the number of clinical cases between 2017 and 2019 (Chi-square = 23.99 and p-value <0.001) in Franceville (Table 2). The infection rate is lower than in similar studies in Gabon.[4,20,21] The difference in prevalence observed could be due to the diagnostic methods used or variation in the ecological and climatological factors, which are important for the breeding of the *Anopheles* vector. However, despite the decline in malaria burden in many endemic areas of Gabon, such as Libreville and Melen,[19] we found a malaria prevalence of 26.1% in 2017-2019 in Franceville, which is higher than the level of infection of 17.9% previously reported in 2011 in a hospital in the same city.[14] Our results agree with recent studies conducted in Makokou and Port-Gentil, in which the authors also observed increasing malaria infection.[15,17] Thus, our observations are consistent with earlier results in Central Africa pointing to a patchy pattern of malaria transmission according to geographic location.[17]

The fluctuation in malaria infection rates between 2017 and 2019 could partly reflect poor application of malaria control methods by the populations or an ineffective malaria prevention policy by health authorities. This observation potentially reflects a general pattern of the resurgence of malaria.[15]

During our study, we observed that the predominant *Plasmodium* species detected was *P. falciparum* with ~80% of the overall occurrence, followed *P. ovale* with 19.5% and *P. malariea* 17.8%. This finding agrees with previous studies,[8,18,20] which reported circulation of these parasites and the predominance of *P. falciparum*.[5,20] In this study, 20% (132/658) of infections were a mixed infection of *P. falciparum* and *P. ovale*/*P. malariae* or *P. ovale* and *P. malariae*. This result is higher than in previous reports,[18,20] and indicates the co-existence of at least three *Plasmodium* species in Franceville, which may have an impact on local malaria epidemiology. It would be interesting to explore the interactions between different *Plasmodium* species, taking into account their positive or negative effects on human host and in particular on children.[22]

Among the factors affecting malaria transmission in Franceville in this study, seasonal variation played a central role, as we found higher *Plasmodium* infection rate in the rainy season than in the dry season. Our finding differs from a report in Libreville that found no association between malaria and seasons.[4] The discrepancy observed might be due to differences in ecological and environmental factors (season, climates and altitude) and community awareness of malaria transmission and control. The monthly distribution of malaria cases showed that the highest cases were reported in mid-February and June, with a peak in June during the transition from the rainy to the dry season. This suggests that the rainy season in Franceville creates a suitable environment for breeding in *Anopheles* mosquitoes. Our findings are consistent with a large study of malaria vectors in the Haut-Ogooué province that showed a seasonal influence in mosquito infection with a peak during the rainy season.[2,23] Conversely, the decrease in rainfall during the dry season (mid-June-mid October) leads to a decrease in suitable larval breeding sites for mosquitoes and, consequently, a decrease in malaria cases reported among patients.

In our study, malaria infection was reported in all age groups in Franceville. However, the most affected age groups were children under five years old with a global prevalence of 44.0%, followed by those 5-14 years-old with infection rate of 41.0%. Our observations agree with previous studies in Africa, and particularly in Gabon.[15,24] Indeed, as observed in other tropical areas, children under five years old were the majority of patients consulting for fever.[25] However, the prevalence of malaria cases found in children under 5 years of age in the present study was higher than observed in 2011 and 2016 in another hospital in same the city,[5,14] and in other cities such as Libreville.[26] This finding could reveal a recrudescence of malaria incidence in children due to parents abandoning prevention strategies or environmental change favourable to the parasite's expansion. In contrast, a reduction in malaria cases had been reported in children under 5 years in other Gabonese cities such as Libreville or Melen.[15] Our results support previous studies in children, which suggested delayed immunity acquisition in some regions of Gabon.[4,15] This result should alert the health authorities, because the majority of malaria cases in Gabon among children under 5 years are severe with possible neurological and hematological consequences.[19] Concerning the age group 5-14 years old, our results are consistent with studies conducted in urban areas of Senegal and Tanzania, where increased malaria risk was observed in different groups' age.[27]

We also found more male than female patients among all malaria cases. This agrees with previous studies conducted in the central Africa sub-region and more broadly in Africa.[28,29] The higher prevalence of malaria observed in men could be explained by their outside activities which expose them more to infectious mosquito bites compared to women who are at home more of the time and therefore less exposed to anopheline bites.[28,30]

Conclusions

This study showed that malaria remains a public health priority for the population of Franceville and that the prevalence of clinical cases of malaria increased between 2017 and 2019 and when compared to previous studies. Preventive measures should be reinforced with the population of Franceville to reduce the morbidity of an often-fatal disease when its clinical management is late or inappropriate.

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