Cholesterolemia and Triglyceridemia changes in adult with malaria in a hypo-endemic malaria region, Butembo-DR Congo

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RESUME

Introduction : Le paludisme est une endémie parasitaire associée à un problème global de santé publique dans le monde. La recherche a révélé que les changements lipidiques se produisent fréquemment chez les patients atteints de paludisme. Cette étude visait à évaluer les changements lipidiques dans le sang chez les patients atteints de paludisme à Butembo, une région hypoendémique.

Méthodes. Cette étude transversale, menée dans les Services d'Interne et de Parasitologie de l'Hôpital Matanda, situé à Butembo, du 1er juillet 2020 au 2 novembre 2020 ; impliquait 100 patients diagnostiqués avec le paludisme. Des analyses biochimiques réalisées par trois techniciens de laboratoire ont été effectuées chez des patients atteints de paludisme positif à l'aide d'une goutte épaisse positive. Les espèces plasmodiales, la densité parasitaire, les triglycérides, le cholestérol total, le HDL-cholestérol, le LDL-cholestérol ont été évalués.

Résultats : La cholestérolémie et la HDLémie ont démontré un faible niveau chez 93 % et 61 % des participants, respectivement ; alors que 73% des cas ont montré une augmentation du taux de triglycérides dans le sang. Le profil de la lipidémie était indépendamment associé à la densité parasitaire chez les patients atteints de paludisme.

Conclusion. Bien que les modifications lipidiques dans le sang ne soient pas spécifiques dans le diagnostic du paludisme, cette étude a mis en évidence leur statut chez les patients atteints de paludisme. Par conséquent, la dyslipidémie pourrait être utilisée dans le dépistage du paludisme.

Mots clés : *Paludisme, cholestérol total, HDL, LDL, triglycérides, Butembo*

SUMMARY

Introduction: Malaria is a parasitic endemic associated with a global public health problem in the world. Research has revealed that lipid changes occur commonly among patients affected with malaria. This study aimed to assess lipid changes in blood among patients with malaria in Butembo, a hypoendemic region.

Methods: This cross-sectional study, conducted in the Departments of Internal and Parasitology of Matanda Hospital, located in Butembo, from July 1st, 2020, to November 2, 2020; involved 100 patients diagnosed with malaria. Biochemical analyses carried out by three lab technicians were performed among patients who had positive malaria using positive thick film. Plasmodial species, the parasite density, the triglycerides, the total cholesterol, the HDL-cholesterol, the LDL-cholesterol were assessed.

Results: Cholesteroleamia and HDLemia demonstrated a low level in 93% and in 61% of participants respectively; whereas 73% of cases showed an increased level of triglycerides in the blood. Lipidemia profile was independently associated with parasite density among patients with malaria.

Conclusion: Although the lipid changes in the blood are not specific in the diagnosis of malaria, this study highlighted their status among patients with malaria. Further researches should be conducted to determine their impact on malaria outcomes. Therefore, dyslipidemia could be used in malaria screening.

Key words: *Malaria, total cholesterol, HDL, LDL, triglycerides, Butembo*

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Malaria is a parasitic endemic associated with a global public health concern over the world [1]. During the last decades, studies have reported an increase in mortality rate among patients affected with malaria, from 429,000 deaths among 212 million cases in 2015 [2] to 435,000 deaths in 219 million people in 2017 [3]. Despite the global efforts committed to improving the prevention, diagnosis and treatment of malaria; six African countries, had demonstrated the burden of more than half of malaria cases over the world in 2018; they are Nigeria (25%), the Democratic Republic of Congo (DRC) (12%), Uganda (5%), and Côte d'Ivoire, Mozambique and Niger (4% each) [4].

Research has revealed that lipid changes occur commonly among patients affected with malaria. Although these changes are not specifics for the establishment of malaria diagnosis, their presence might be suggestive of malaria in patients living in endemic or hypo-endemic areas and presenting clinical signs [5,6]. Previous studies concluded that patients living in endemic regions who showed lipidemia changes were found also with malaria [7]. However, few studies centered on the correlation between the parasite density and the lipid changes during malaria infection are available. Moreover, biochemical disturbances during malaria are not sufficiently documented in DRC. Therefore, this study is aimed at assessing lipid changes in blood among patients with severe malaria and to determine the role of dyslipidemia in screening malaria.

METHODS

This was a facility cross-sectional study using a quantitative design, conducted in the Departments of Internal and Parasitology of Matanda Hospital, located in Butembo (DRC), from July 1st, 2020, to November 2nd, 2020. Matanda hospital, a tertiary health facility, was chosen based on its importance in the treatment of patients with several illnesses including malaria, via its geographical location regarding the two health zone found in Butembo City, namely Butembo and Katwa. A consecutive and purpose sampling process was performed. The minimum size of our study used the following formula [8]:

$N = t^2 \times p\,(1 - p) / m^2$

Where N = sample size, t = 95% confidence interval (standard value of 1.96), p = estimated prevalence of malaria in areas with a mountain climate which is 3% according to the national program against malaria implemented in DRC, 2018 version [9], m = 5% margin of error (typical value of 0.05). The desired sample was 44. To avoid the effect of refusal rate, this sample was increased to 50 participants enrolled from Internal Medicine and 50 recruited from the Parasitology department.

To achieve our objectives, we worked on 100 subjects. Inclusion criteria were patients with fever, who presented at the internal medicine and parasitology department, whose malaria rapid diagnostic revealed malaria, who did not take any anti-malaria drug within one prior to admissions and who consent to participate. Exclusions were patients with a chronic illness including diabetes mellitus, hypertension, dyslipidemia or HIV; those who had sepsis or have taken an antibiotic drug or anti-lipid drugs two weeks prior to this study.

Four research assistants were trained for the data collection. A medical officer conducted the clinical assessment of potential through an in-depth interview. Participants who presented with fever were approached and were provided details regarding the objectives of the study. For those who consented, malaria rapid test was taken; and those with positive test were approached, and benefited for in an in-depth interview consisting of data collection addressing of socio-demographic and clinical characteristics.

Included participants were conducted to the department of parasitology where biochemical analyses carried out by two lab technicians were performed including the plasmodial species, the parasite density, the triglycerides, the total cholesterol, the HDL-cholesterol, the LDL-cholesterol.

Three milliliters of venous blood were taken for each participant and placed in a tube containing ethylene-diamine-tetra-acetic acid (E DTA) as an anticoagulant for biochemical examinations on a photometer machine. Biological confirmation of malaria was made on the thick film and the blood smear. The thick drop was stained with 10% Giemsa for 10 minutes. Slides were examined under the 100X immersion objective independently by three trained laboratory technicians to determine the parasite density. Indeed, each laboratory technician counts the asexual forms of the parasite for 200 white blood cells on the blood smear carried out for each case of malaria. The result obtained was the average of the numbers found by each of them. The following formula was applied:

Parasite / µL = Parasites counted / 200 × NGB counted [6]

The parasite density was described as low when the figure obtained had less than 1000 parasite / µL; moderate for values ranging from 1000 to 4999 parasite / µL and finally high for values greater than 5000 parasite / µL [12]. The quality control of our slides was also carried out at the parasitology laboratory of the university clinics of Kisangani.

Total, HDL and LDL cholesterols were assessed from the blood swear. For the total cholesterol, the usual values: considered for this study were ranged between 1.6 and 2.4 g / L, i.e. 4.1 and 6.2 mmol / L. HDL cholesterol called the good cholesterol had the values ranged between 0.35 and 0.75 g / L or 0.9 and 2 mmol / L. Lastly bad cholesterol named LDL cholesterol had the values ranged between 1.2 and 1.7g / L (3.1 to 4.4mmol / L). For the triglycerides, the usual values of triglycerides were ranged between 0.35 and 1.25 g / l, i.e. 0.4 and 1.4 mmol / L [10].

Statistical analyses were performed using SPSS software version 20.0. Univariate analyses were performed for nominal or categorical variables to determine the prevalence. Association between the parasite density and lipid changes was performed using bivariate logistic regression. Statistical significance was set at 0.05. The results were presented in tabular form using Microsoft Word 2016.

This study received approval from the internal medicine department and the ethics committee of the University of Kisangani. Permissions to conduct this study were received from the Executive Directors of Kisangani Teaching Hospital and Matanda Hospital, as well as the Chairman of Katwa health zone office. Data collection was conducted regarding the declaration of Helsinki. Written informed consent was obtained from each of them.

RESULTATS

The majority of participants were female (54%), aged between 21 and 40 years old and farmers (59%) (table I).

The mean cholesterol level of study participants was 117.7 ± 48.7 mg / dl. 93% of study participants had a level less than 200mg/dl. The low level of HDL cholesterol was recorded in 61% of cases. Hypertriglyceridemia i.e.≥ 150mg/dl was observed in 72% of cases (Table II).

Table I. Socio-demographic characteristics of participants

Variables	n	%
Age (years)		
> 40	20	20
21-40	58	58
18-20	22	22
Sex		
Female	54	54
Male	46	46
Occupation		
farmer	59	59
Trader	15	15
Student	13	13
Teachers	7	7
Others	6	6

The decrease in total cholesterol was observed in 9 2, 3% of cases, HypoHDLemia and hypertriglyceridemia were observed respectively in 61,5% and 74.7 % of participants with high parasitemia. Bivariate analysis revealed

that no association between parasitaemia and lipidemia has been demonstrated. Overall, all patients were infected with Plasmodium falciparum (100%) (table III).

Table II: Lipidemia profile of participants

Variables	n	%
Total cholesterolemia (mg/dl)		
Mean (SD)117.9 (48.7)		
<200	93	93
200-240	7	7
HDL- cholesterol mg/dl		
<40	61	61
≥40	39	39
Triglyceridemia mg/dl		
<150	28	28
≥150	72	72

Table III: Correlation between parasite density and lipid profile among patients with malaria.

Variables	Parasitemia		
	Low N=3	Medium N=6	High N=91
Total cholesterolemia (mg/dl)			
<200	3(100%)	6(100%)	84(92,3%)
200-240	0(0%)	0(0%)	7(7,7%)
HDL- cholesterol mg/dl			
<40	3(100%)	2(33,3%)	56(61,5%)
≥40	0(0%)	4(66,7%)	35(38,5%)
Triglyceridemia mg/dl			
<150	2(66,7%)	3(50%)	23(25,3%)
≥150	1(33,3%)	3(50%)	68(74,7%)

DISCUSSIONS

Findings of this study demonstrate that female patients were more likely affected than males with a sex ratio of 1.17. This sex ratio value is slightly lower than the findings of Nfor Omarine Nlinwe and Tang Bertilla Nange who reported a sex ratio of 1.38 for females [11]. The majority of participants were aged between 21 and 40 years old. This age group is mainly the most productive group of the population in African settings. Therefore, the displacement of communities across regions looking for fertile lands may explain the higher prevalence of malaria in the endemic marsh areas.

This study demonstrates that hypocholesterolemia was found in 93% of cases. These findings are similar to the study conducted by Chukuoka et al in Nigeria who reported a prevalence of 84% of malaria patients with hypocholesterolemia. However, our results are clearly higher than those reported by the series of Badiaga et al. [12] and Chagnon et al. in France [13] which were 40% and 45% respectively. Prior studies have already described the decrease in total cholesterol and HDL cholesterol. Indeed, the links between infection with fever and hypocholesterolemia were reported a long time ago. For instance, in 1960, Justin-Besançon et al. specified that two bacterial diseases on three altered cholesterol levels. Moreover, many authors have demonstrated important changes in lipid levels during a feverish or septic state. The association of hypocholesterolemia and hypertriglyceridemia is more frequently found during the acute phase of any infection, mostly the first three days of infection [14].

In addition, we found that hypoHDLemia was observed in 61% of cases.

HypoHDLemia can be explained by an inhibition, by the parasite or its products, of lecithin-cholesterol acyl transferase and lipoprotein lipase which participates in the development of HDLc [15]. The series of Al Omar et al. and Ozkaya G et al. demonstrated that patients infected with P. falciparum showed significantly low cholesterol levels compared to the group of healthy and normal controls [16-17]. They also found an inverse correlation between parasitaemia and cholesterol levels. The latter was considered to be a specific indicator (98%) of Plasmodium infection [18].

Results also revealed that hypertriglyceridemia occurred in 72% of cases. Our results diverge from those found by Chagnon et al., Y. Hansmann et al, Baptista et al who found hypertriglyceridemia respectively in 42.3%, 62% and 45.5% in patients with malaria [19]. The size of the samples and the locations of this study may justify this difference.

Hypertriglyceridemia can be explained by the reduction in the activity of lipoprotein lipase, in particular under the influence of

the tumor necrosis factor (TNF), and by a deficiency of the plasma compartment [19]. This hypertriglyceridemia has long been linked to the risk of cardiovascular accident, myocardial infarction, coronary artery disease and death in adults, independently of the other components of the lipid profile, hence the problem of this finding [20-21]. Ultimately, it seems that malaria has the peculiarity of lowering cholesterolemia more in a not insignificant number of cases than most other febrile infectious states, which could confer on such a finding a supplementary diagnostic value.

A study conducted in Saudi Arabia showed that there is a significant inverse correlation between parasitaemia and cholesterol levels in patients. The erythrocyte stages of Plasmodium have no lipids in reserve and are incapable of synthesizing fatty acids or cholesterol themselves de novo. They are forced to incorporate lipids from their environment into the host to meet the lipoprotein needs of schizogony [18]. Thus, we can explain the differences in lipid levels during malaria by the degree of parasitaemia, itself depending on many factors such as the epidemic face, the number of bites, the plasmodial species, the environment, the use of the insecticide-treated mosquito net. We did not find a significant difference between the degree of parasitaemia and the lipid profile. Few studies have addressing this topic in endemic regions for malaria during our research. However, hypercholesterolemia and hypertriglyceridemia have been observed in complicated and uncomplicated malaria and other acute infections [1, 18]. The magnitude of these changes appears to be related to the severity of malaria, but in a study conducted in Africa where malaria is endemic, it was found that between the severity of the malaria attack and its effects on lipoproteins density (HDL) and lowered cholesterol levels, the result was not too significant, although it was observed that the cholesterol levels of most Africans were lower than that of people living on other continents [16]. Indeed, certain studies stated indicate that weak parasitaemia of P. falciparum during malaria infection actually induces a significant change in lipid parameters [22]. Most of these studies were performed in hypo-endemic areas as is the case of our study. Al Omar, Eligail, Al-Ashban and Shah AH established, during their studies on the impact of malaria infection on the lipid profile, a significant relationship between the parasite density and changes in cholesterolemia among patients with malaria [16].

Findings of this study were similar to the results of numerous studies conducted in Saudi Arabia on the effect of P. falciparum malaria on blood cholesterol and platelets and in Nigeria on biochemical indices of severity in human malaria respectively [16]. These studies demonstrated a significant relationship between the parasite burden of malaria and cholesterol levels. Moreover, studies conducted in Sao Tome, an endemic region for malaria, demonstrated that cholesterol, triglycerides, HDLc and LDLc levels in the blood were significantly low in children infected with P. falciparum [23].

Nevertheless, these results contradict those published by Lathia T Joshi R, which found no relationship between malaria infection and blood cholesterol levels [24], as is the case for the results of our research.

Limitations of the study

The purposive sampling process could not allow the generalization of its findings. In addition, the sample size as well as the study design will not allow determining the cause-effect of the study.

CONCLUSION

This study reveals that malaria is associated with important lipidemia changes suggesting, malaria infection in patients living in endemic and hypo endemic regions. Total cholesterol, bad and good cholesterol demonstrated abnormal levels among patients with malaria due to P. falciparum. However, the findings revealed that lipidemia profile was independently associated with parasite density among patients with malaria.

Further researches should be conducted to determine their impact on malaria outcomes.

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