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Original Research Article

Impact of malaria infection on renal and liver functions in patients living with HIV/AIDS on HAART in Douala, Cameroon

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Abstract: Malaria and HIV (Human immunodeficiency virus) infection are known overlap in Sub-Saharan Africa countries. Thus, it is likely in this context that the burden inflicted by these both diseases is more important. This study was designed to determine the prevalence of malaria and its impact on renal and hepatic profiles in people living with HIV (PLWHIV) on HAART (Highly active antiretroviral therapy) and living in Douala. Between August 2015 and March 2016 a prospective and cross-sectional study was carried out at the District hospital of Deido in the town of Douala. Questionnaire form was used to document sociodemographic, clinic and biological data of participants. Blood samples were collected by venipuncture into tubes for biological analyses. These allowed to performed thick blood films for malaria diagnosis. Sera were obtained and used to measure transaminases and creatinine levels. A total of 723 patients were included in the study. The mean age of the population was 39.49 ± 11.17 years old. The malaria prevalence was 16.7% (95%CI = 14.2% - 19.6%). AST (aspartate aminotransferase) and ALT (alanine aminotransferase) were higher in malaria positive patients on average. In addition, the difference was statistically significant for ALT (p-value = 0.0403). In addition, creatinine levels were lower in malaria positive patients compared to their negative counterparts. Renal and liver functions were both further impaired in malaria positive patients especially ALT which is more specific of liver function. This study outlines the need for appraising the measurement of transaminases and creatinine especially in PLWHIV during their management.
Keywords: HIV/AIDS, Malaria, Co-infection, transaminases, Creatinine, Douala

INTRODUCTION:

Malaria is a vector-borne disease cause by a parasite protozoan belonging to *Plasmodium* genus. To date, five plasmodial species can infect humans in which they induce disease. Plasmodium falciparum is the most dangerous specie because responsible for about all cases of morbidity and mortality [1]. An estimated 214 million and 438,000 of cases and deaths were due to malaria in 2014. Africa stills the most burdened continent concentrating 80% and 90% of all cases morbidity and mortality respectively. Children less than five years old and pregnant women are the social groups the most at risk [1]. Beside malaria, human immunodeficiency virus (HIV) infection is also leading public health problem through the world and in Africa especially. Indeed, it was responsible for 35.3 million of cases in 2012 of which 24.7 million in sub-Saharan Africa accounting for 72% of all cases of infection worldwide [2].

Malaria and HIV share some risk factors such as poverty. Thus, it is common to report some cases of co-infections with these both diseases. In addition, many studies pointed out mutual interactions between the protozoan and the virus during their life cycle. HIV infection can increase the risk of getting malaria infection by enhancing the susceptibility to infection and decreasing the therapeutic and preventive efficacy of antimalarial drugs [3]. Conversely, others studies reported an increasing in viral load during malaria episodes even though a few weeks following an effective treatment. This viral load has been found positively correlated with parasite density. Besides, malaria parasites increase the production of TNF-α

which boost the ability of infected cells to elicit more viral particles [3-5].

These diseases have been showed induce deleterious effects such as anemia each in humans, which is a main cause of morbidity and mortality in groups at risk as children, women and immunocompromised persons [1]. On the other hand, HIV infection and/or its therapy can induce severe adverse effects on others organs such as liver and kidney in which it is responsible for mild functional alteration and liver and renal injury at worse [6-7]. In the context where co-infections with malaria and HIV are common, it is probable that function of these both organs is more deeply impaired. Unfortunately, little studies have addressed the issue in Cameroon. To the best to our knowledge, there are no data on the topic in the town of Douala, main business capital of Cameroon, and where the burden of these both diseases is still worrying.

Thus, this study was designed to determine the prevalence of malaria and its impact on renal and hepatic profiles in people living with HIV (PLWHIV) living in Douala.

MATERIAL AND METHODS:

This study took place in the town of Douala (Littoral Region, Cameroon). Douala is located 3°48'N, 10°08'E, near the Atlantic coast, within the Congo-Guinean phytogeographical zone characterized by a typical equatorial climate with two rainy seasons extending from March to June and from September to November (Antonio-Nkondjio *et al.*, 2012). These environment conditions are propitious for creation of breeding sites malaria vectors. Douala is a port city where many worse behaviors (liquors consumption, prostitution) significantly increase the risk of sexually-transmitted diseases (STDs). Douala is the main business one of the country and is ranked sixth (5.5%) in terms of HIV prevalence rate [8]. Participants were recruited at the district hospital of Deido which greets people coming from all parts of Cameroon owing to its strategic location and sustainable and constant supply with CD4 cells reagents and antiretroviral drugs for management of people living with HIV (PLWHIV).

The study population was consisted of individuals aged 5-49 years old of both sexes living with HIV and under HAART regimen. They were recruited in a convenient way and therefore a total of 723 patients were included in the study. Any patient who did not meet any of these abovementioned criteria were excluded from the study.

This cross-sectional and prospective study was carried out between August 2015 and March 2016. Participants included in the study were HIV-infected, attending at the district hospital of Deido for routine control and willing to participate in the study. Prior to their inclusion, they were given information, education and communication on malaria and HIV infection. Thereafter, an informed consent form was signed by each participant following explanation of objectives of the study to them. Approval of parents or guardians of children was also sought. A structured questionnaire was used to collect socio-demographic, clinic and biological data. Blood samples were collected and transported to the Laboratory of the district hospital of Deido for parasitological analyses. Investigative methods included a questionnaire approach, clinical and parasitological analyses. Patients or their parents/guardians were interviewed for 10-15 minutes upon obtaining informed consent forms. A structured questionnaire was used to document patients' information about sociodemographic, clinic and biological data.

Five milliliters (5 mL) were collected from each participant by venipuncture into sterile plastic syringes. Blood samples were then transferred into EDTA (2 mL) and dry (3 mL) tubes for all performing hematological, parasitological and biological analyses respectively. All tubes were labeled with the patients' barcode and pathology number. Blood contained in dry tubes was centrifuged at 3000 rpm for 3-5 minutes and sera obtained were tested for HIV presence and determination of transaminases and creatinine levels.

Thick blood films were performed using the protocol previously described by Cheesbrough (2004). Briefly, thick smears that were air-dried for 30 minutes, was stained with 10% Giemsa for 20 minutes. Thereafter, stained slides were allowed to air dry and stored not more than one day until microscopic examination. Microscopy was used for identification of malaria parasites by a senior. Thick blood films were considered positive when asexual forms (trophozoites and schizonts) and or gametocytes were present in the blood film. Slides were declared negative after observing at least 100 high power fields without detecting any parasites. In order to ensure quality assurance of parasitological data, thick smears-based results were classified as valid (positive or negative slides) and invalid (not read slides) as outlined in literature [9].

Measurement of creatinine was done following a method described by the 2002 International Federation of Clinical Chemistry (IFFC) protocol. Sera sample previously stored were retrieved from in freezer and left at room temperature. About 1000 µL of working solution were aliquoted into test-tubes corresponding to the number of samples. Thereafter, about 100 µL of sera was added with reagent as recommended by the protocol. Absorbance were read at

510 nm wavelength using the spectrophotometer Screen Master Plus® (HOSPITEX DIAGGNOSTICS Ltd). There was no incubation period during this laboratory activity as readings of absorbance and concentrations were made in a kinetic way [6-7].

Measurement of transaminases was done following a method described by the 2002 International Federation of Clinical Chemistry (IFFC) protocol which was previously by our research team in Douala and Yaoundé [6-7]. Commercial kits produced by HOSPITEX DIAGNOSTICS Ltd were used. The test was performed using the monoreagent procedure. Briefly, the working reagent was prepared by mixing 4 volumes of reagent one (R1) in 1 volume of reagent 2 (R2). R1 and R2 were gently mixed and stored far from light sources at 2-8°C. The spectrophotometer was calibrated for transaminases measurement and readings made at 340 nm wavelength. A series of labeled test tubes, i.e. Blank, normal control and patients from 1, 2….n^{th} according to the number of samples to be analyzed. The preparation was mixed and the first reading of absorbance was executed after 90 seconds. Incubating at 37°C, 3 other readings were performed at 60 seconds interval [6-7]. The change in absorbance per minute was then calculated. The activities were obtained from the following calculations:

340nm: Activity (U/L) = change in absorbance/ min. x 1769.

Normal values for ALT (SGPT) at 37°C: Women up to 34U/L. Men up to 45U/L. Normal values for AST (SGOT): Women up to 31U/L and Men up to 35U/L).

This study was carried out in conformance with the guidelines for human experimental models in clinical research as stated by the Cameroon Ministry of Public Health and the Helsinki declaration. Besides, the ethical and administrative clearances for this study were sought. The aim and objectives of the study were explained to them in the language they understood best (French or English), and their questions were answered. Only individuals who signed an informed consent form for their participation were enrolled. Participation in the study was strictly voluntary and patients were free to decline answering any question or totally withdraw if they so wished at any time. Furthermore, there was no difference in the malaria and HIV infection related care provided to persons who accepted to participate in the study and those who did not. All malaria positive patients were treated on the spot accordance to the national treatment guidelines.

All data were verified for consistency, coded, and keyed in an Excel sheet. Thereafter, statistical analyses were performed with SPPS 20.0 for Windows (SPSS, Chicago, IL, USA). Data were summarized in table as percentages with 95% confidence interval (95%CI) or mean ± standard deviation (sd) for qualitative and quantitative variables respectively where appropriate. Student's test was used to compare differences for normally-distributed variables. Chi-square test (χ^2) or Fisher's exact probability were computed to compare categorical variables. Significant levels were measured at 95% CI with significant differences recorded at *p-value* < 0.05.

RESULTS:

A total of 723 patients were included in the study. Majority of them were females (74.3%; p-value < 0.0001). The mean age was 39.49 ± 11.17 years old and this variable ranged between 4 and 74. In addition, patients aged 20-49 years old accounted for more than two thirds of the participants (79.7%, P-value < 0.0001), followed by more than 49 years (18.5%) and less than 19 years old (1.8%).

Malaria parasites were found in 121 individuals (16.7%; 95%CI: 14.2%-19.6%). Malaria prevalence was higher in females (12.9%) compared to their male counterparts (11.54%). Furthermore, malaria prevalence was higher in above 49 years old (13.43%) (p-value > 0.05) as summarized in Table 1.

Table 1: Malaria prevalence with regard to gender and age

Variables	Negative	Positive	Total	Chi-square	P-value
Gender					
Female	471 (87.06%)	70 (12.94%)	**541**	0.246	0.622
Male	161 (88.46%)	21 (11.54%)	**182**		
Age groups (years)					
[0 - 19]	13 (100%)	0 (0%)	**13**	1.963	0.375
[20 - 49]	503 (87.33%)	73 (12.67%)	**576**		
> 49	116 (86.57%)	18 (13.43%)	**134**		

Data are presented as frequency (percentage). Independent chi square was used to compare proportions. P-value < 0.05 was considered as significant.

As depicted in Table 2, AST and ALT were higher in malaria positive patients on average. In addition, the difference was statistically significant for ALT (p-value = 0.0403). Besides, proportion of people

with increased ASAT higher in patients tested positive for malaria infection compared to their negative counterparts (55.37% versus 50.00%) although no significant difference was found (Table 3).

Creatinine levels were lower in malaria positive patients compared to their negative counterparts (0.940 ± 0.250mg/dL and 0.987 ± 0.360 mg/dL respectively, p-value = 0.1647). Furthermore, as depicted in Table 3, the fraction of patients with decreased creatinine was higher in positive malaria patients (1.65%) although none difference was found (P-value = 0.5849).

Table 2: Mean values of transaminases with respect to malaria diagnosis

Transaminases	Negative (n = 602)	Positive (n = 121)	P-value
AST (UI/L)	34.375 ± 18.410	38.950 ± 36.126	0.0403*
ALT (UI/L)	28.284 ± 16.100	31.347 ± 28.790	0.1027

Data are presented as mean ± standard deviation; AST = Aspartate aminotransferase; ALT = Alanine aminotransferase; Unpaired Student's test was used to compare means between two groups; *: significant

Table 3: Fraction of participants presenting increased transaminases and creatinine with respect to malaria diagnosis

Transaminases	Categories	Negative (n=602)	Positive (n=121)	P-value
AST (UI/L)	Normal (n = 355)	301 (50.0%)	54 (44.63%)	0.3191
	Elevated (n = 368)	301 (50.0%)	67 (55.37%)	
ALT (UI/L)	Normal (n = 160)	133 (22.09%)	27 (22.31%)	0.9574
	Elevated (n = 563)	469 (77.91%)	94 (77.69%)	
Creatinine (mg/dL)	Low	5 (0.83)	2 (1.65)	0.5819
	Normal	558 (92.69)	113 (93.39)	
	Elevated	39 (6.48)	6 (4.96)	

Data are presented as frequency (percentage). AST = Aspartate aminotransferase; ALT = Alanine aminotransferase; Independent chi square was used to compare proportions. P-value < 0.05 was considered as significant.

DISCUSSION:

Thus, this study aimed at determining the prevalence of malaria and its impact on renal and hepatic profiles in people living with HIV (PLWHIV) on HAART and living in Douala.

Most of participants were females (74.83 %) and the difference was significant (p < 0.0001). This is in line with many reports about the existence of a sex-related risk of HIV infection across the world along with Cameroon where the same trend was reported over the territory in 2011 following a nationwide demographic survey [9]. Besides, some authors have also pointed out women were more vulnerable to HIV infection [10-11].

The malaria prevalence was 16.7% in the participants. This value is lower than that found by many reports [12-14]. These authors found 31.76%, 24.0% and 74.3% respectively. Conversely, our value is higher than the 11.75% found by Iroezindu et al. in Ghana [13]. Differences in sample size, study design, study period, study area along with genetic background and behavioral patterns of individuals can explained the discrepancies observed.

Creatinine levels were lower in malaria positive patients compared to their negative counterparts (0.940 ± 0.250mg/dL and 0.987 ± 0.360 mg/dL respectively, p-value = 0.1647). Furthermore, the fraction of patients with decreased creatinine was higher in positive malaria patients (1.65%). In a case report, it was pointed out malaria had elicited impairment in renal function in a 50 years old man before his death [15]. Besides, others studies reported malaria-induced severe adverse effects on others organs such as spleen [16].

AST and ALT were higher in malaria positive patients on average. In addition, the difference was statistically significant for ALT (p-value = 0.0403). Besides, proportion of people with increased ASAT higher in patients tested positive for malaria infection compared to their negative counterparts (55.37% versus 50.00%). This finding emphasizes the occurrence of dysfunction in the participants which is due to a destruction of hepatocytes. This destruction can be induced by virus infection, others pathogens, immune response, liquors ingestion and drugs [17]. Viral cause can likely explained one part of our results since transaminases were found increased in individuals infected with HIV only (Table 3). Liquors ingestion and immune response were not looked for in this study and therefore it was impracticable to confirm or infirm this assumption. All patients were HIV infected, thus the virus- and treatment-related assumption can be

excluded from explnations. Thus, others pathogens such malaria might fairly explained this increasing in transaminases levels in this study. However, it is needed to carry out further studies taking into account beverages consumption and immune response in order to confirm our findings.

CONCLUSION:

This study was designed to determine the prevalence of malaria and its impact on renal and hepatic profiles in people living with HIV (PLWHIV) on HAART and living in Douala. Renal and liver functions were both further impaired in malaria positive patients especially ALT which is more specific of liver function than AST. Thus, the risk of liver malignancies is higher in these patients. This study outlines the need for appraising the measurement of transaminases especially in PLWHIV during their management. This kind of studies will have to be carried out at larger scope in Douala and other regions of Cameroon.

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