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HIV-Malaria Co-infection and their immunohematological profiles

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ABSTRACT

Malaria and HIV are the two most important infectious diseases and have similar global distributions, with the majority of those infected individuals lived in countries with constrained resources like sub-Saharan Africa. In light of the epidemiological overlap and global importance of the two diseases, there is an urgent need for more research on a wide range of unanswered questions. This study is aimed to determine the prevalence of malaria among HIV positive individuals and effect of co-infection on immune-hematological profiles. A retrospective study was conducted on HIV positive adult individuals who had complain of febrile illness and gave blood for blood film examination at Gondar University Hospital. Data were analyzed using SPSS version 16 statistical package. Out of 377 patients who had acute febrile illness and presumed to have malaria and gave blood for blood film examination, 73 (19.4%) had confirmed malaria cases. High prevalence of plasmodium falciparum (72.6%) was detected compared to plasmodium vivax (27.4%). The mean CD4+ lymphocyte count of HIV-malaria co-infected patients was lower than HIV mono-infected patients. Similarly the mean hemoglobin value of HIV-malaria co-infected patients was lower than HIV mono-infected patients with P-value of 0.001. Nine (2.4%) of patients had sever anemia while 216 (57.3%) of patients had mild anemia. In multivariate analysis; sex (AOR = 2.6; 95% CI: 1.43-4.83), CD4+ count (AOR = 2.3; 95% CI: 1.13-4.77) and hemoglobin level (AOR = 8.3; 95% CI: 1.86-37.29) were found to be independently associated with HIV-malaria co-infection. HIV-malaria co-infections are found to be higher. Intervention strategies should give emphasis for females and patients with low CD4+ lymphocyte count. Further risk factors are needed to be investigated. Follow up studies are also needed to explore more on co-infections of these diseases and their public health speculation.

Key words: HIV, Malaria, Co-infections, Ethiopia.

INTRODUCTION

HIV/AIDS and malaria are among the most devastating diseases in many low-income countries, particularly in sub-Saharan Africa. The incidence of symptomatic malaria episodes, severe or uncomplicated, and the corresponding parasite density is higher in HIV infected individuals with lower CD4 count [1]. Majority of the malaria cases occurs throughout the tropical world where it remains one of the most prevalent infectious diseases with an estimated 300 million cases per year and approximately 90% of these cases occur in sub-Saharan Africa [2]. According to 2011 World Health Organization report, over 655,000 people died due to malaria in 2010 [3].

In Ethiopia, malaria is one of the most health problems top ranking in the list of common infectious diseases and three quarter of the total land mass of the country is regarded as malarious and about 68% of the total population is at risk of malaria infection [4]. Nowadays, malaria and HIV are the two most important infectious diseases and have similar global distributions, with the majority of those infected individuals lived in countries with constrained resources like sub-Saharan Africa, the Indian subcontinent, and Southeast Asia. Hence the rates of co-infection and geographical distribution is overlapping, interactions between the two diseases pose major public health problems and cause majority of deaths [5, 6].

Due to the overlapping distribution of HIV and malaria, there is a theoretical possibility of concomitant infection and the potential for immunological interactions between these two infections that farther results T-cell impairment and sever malarial anemia [7, 8].

Though malaria and HIV are known to be the most severe of all infections in Ethiopia [9], limited study has been done which evaluates the association between malaria and HIV particularly in the study area. So this study is aimed to determine the prevalence of malaria among HIV positive individuals and effect of co-infection on immune-hematological profiles that farther helps to develop joint intervention strategies for immediate and long-term benefits of the two diseases control program.

MATERIALS AND METHODS

Study design, period and setting

A retrospective study was conducted from July, 2011 to June, 2012 at Gondar University Hospital, Northwest Ethiopia. This university hospital serves more than 5 million populations surrounding it. It also provides inpatient and outpatient services, including care and treatment for HIV/AIDS patients. Patients being evaluated for ART initiation undergo a routine medical examination, including screening for febrile illness and other opportunistic infections.

Study population and data collection

The study participants were all ART naïve HIV positive adult individuals who had complain of febrile illness at Gondar University Hospital during the study period. Socio-demographic and clinical profiles of patients were collected using data collection format.

From patients who have clinical manifestations of febrile illness, blood sample from their finger was taken and both thick and thin smear was made. After the smear is air dried, the thick smear was stained by Geimsa stain which is used to detect the presence or absence of malaria parasite. But the thin smear was stained by Wright stain for the identification of the malaria species by using oil immersion objective microscope.

CD4 count and hemoglobin value was also collected from the patients' chart in HIV/AIDS clinic. The CD4 count was done by BD FACS count flow cytometry machine. The daily, weekly and monthly maintenance of the BD FACS count flow cytometry was done according to the instruments manual and quality control for both the reagent and the machine was done daily.

Data Analysis

Data were checked for completeness, cleaned manually and entered and analyzed using SPSS version 16 statistical package. Data were summarized using frequency tables. Bivaraite and multivariate logistic regression was done to identify different determinants of HIV-malaria co-infection. Statistical significance was declared at P-value <0 .05. Mean plus standard deviation with 95% confidence interval (CI) was also used for continuous variables and the difference in means was compared with independent-sample t-test.

Ethical Considerations

Ethical issues were approved by College of Medicine and Health sciences, University of Gondar. Data was collected after we got permission from College of Medicine and Health sciences, University of Gondar.

RESULTS

A total of 377 patients complained febrile illness and gave blood for blood film examination. Out of these, 264 (70%) were females and 315 (83.6%) were from urban and the rest were from rural areas. The mean age of patients was 33.5±9 years.

Malaria-HIV co-infection

Out of 377 patients who had acute febrile illness and presumed to have malaria and gave blood for blood film examination, 73 (19.4%) had confirmed malaria cases. The two deadly plasmodium species were confirmed with prevalence of 53 (72.6%) of *plasmodium falciparum* and 20 (27.4%) of *plasmodium vivax.* The majority of patients 270 (71.6%) were in WHO clinical stage of I followed by WHO clinical stage II 67 (17.8%) and WHO clinical stage III 40 (10.6%) [Table 1].

Table 1. Demographic and immunohematological profile of study participants at Gondar University Hospital, Northwest Ethiopia, 2012

Variables		Co-infection		Total (%)
		Yes (%) (malaria-HIV)	No (%) (HIV alone)	
Age	18-29	26 (32.6)	99 (35.6)	125 (33.2)
	30-39	25 (34.2)	130 (42.8)	155 (41.1)
	40-49	17 (23.3)	56 (18.4)	73 (19.4)
	50 and above	5 (6.8)	19 (6.2)	24 (6.4)
Sex	Male	31 (42.5)	82 (27)	113 (30)
	Female	42 (57.5)	222 (73)	264 (70)
Residence	Urban	59 (80.8)	256(84.2)	315 (83.6)
	Rural	14 (19.2)	48 (15.8)	62 (16.4)
WHO clinical stage	Stage I	49 (67.1)	221 (72.7)	270 (71.6)
	Stage II	12 (16.4)	55 (18.1)	67 (17.8)
	Stage III	12 (16.4)	28 (9.2)	40 (10.6)
CD4+ Lymphocyte count	<200Cells/mm3	25 (34.3)	109 (35.9)	134 (35.5)
	200-349Cells/mm3	35 (47.9)	101 (33.2)	136 (36.1)
	≥350 Cells/mm3	13 (17.8)	94 (30.9)	107 (28.4)
Hemoglobin level	>12g/dl	21 (28.8)	131 (43.1)	152 (40.3)
	8-12g/dl	48 (65.8)	168 (55.3)	216 (57.3)
	<8g/dl	4 (5.5)	5 (1.6)	9 (2.4)

Immunohematological profiles

The CD4+ lymphocyte count of study participants were determined and 134 (35.5%), 136 (36.1%) and107 (28.4%) of patients had CD4+ lymphocyte count of less than 200 cells/mm^3, CD4+ lymphocyte count of between 200 cells/mm3 and 350 cells/mm3 and CD4+ lymphocyte count of greater than or equal to 350 Cells/mm^3 respectively. The mean CD4+ lymphocyte count of HIV mono-infected participants was 293.5 ± 188.5 Cells/mm^3 and HIV-malaria co-infected patients had mean CD4+ lymphocyte count of 260.4±185.3 cells/mm^3 which is not statistically significant. The mean hemoglobin value of HIV mono-infected patients was 12.7± 2 g/dl and HIV-malaria co-infected patients had mean hemoglobin value of 11.8 ± 2.2 g/dl with P-value of 0.001. Nine (2.4%) of patients had sever anemia while 216 (57.3%) of patients had mild anemia [Table 1].

Predictors of malaria-HIV co-infection

In multivariate analysis; sex, CD4+ lymphocyte count and hemoglobin level were found to be independently associated with HIV-malaria co-infection. Females were 2.6 times (95% CI: 1.43-4.83) more likely to be co-infected compared to males. Individuals who had CD4+ lymphocyte count of <350Cells/mm^3 were 2.3 (95% CI: 1.13-4.77) times more likely to be co-infected than individuals who had CD4+ lymphocyte count of ≥350Cells/mm^3. Those who had hemoglobin level of <8 g/dl were 8.3 (95% CI: 1.86-37.29) times more likely to be co-infected than individuals who had hemoglobin level of >12g/dl [Table 2].

Table 2. Predictors of malaria-HIV co-infection among study participants at Gondar University Hospital, Northwest Ethiopia, 2012

Variables	Co-infection		OR (95%CI)		P value
	Yes (%) (malaria-HIV)	No (%) (HIV alone)	Crude	Adjusted	
age					
18-29	26 (32.6)	99 (35.6)	1		
30-39	25 (34.2)	130 (42.8)	0.73 (0.39-1.34)		
40-49	17 (23.3)	56 (18.4)	1.16 (0.58-2.31)		
50 and above	5 (6.8)	19 (6.2)	1.00 (0.34-2.94)		
sex					
Male	31 (42.5)	82 (27)	1	2.63 (1.43-4.83)*	.002
Female	42 (57.5)	222 (73)	1.99 (1.18-3.39)*		
Residence					
Urban	59 (80.8)	256(84.2)	1		
Rural	14 (19.2)	48 (15.8)	1.27 (0.65-2.45)		
WHO clinical stage					
Stage I	49 (67.1)	221 (72.7)	1		
Stage II	12 (16.4)	55 (18.1)	0.98 (0.49-1.97)		
Stage III	12 (16.4)	28 (9.2)	1.93 (0.92-4.07)		
CD4+ Lymphocyte count					
<200Cells/mm3	25 (34.3)	109 (35.9)	1.66 (0.80-3.42)	1.10 (0.50-2.44)	.021
200-349Cells/mm3	35 (47.9)	101 (33.2)	2.51 (1.25-5.02)*	2.33 (1.13-4.77)*	
≥350 Cells/mm3	13 (17.8)	94 (30.9)	1		
Hemoglobin level					
>12g/dl	21 (28.8)	131 (43.1)	1		
8-12g/dl	48 (65.8)	168 (55.3)	1.78 (1.02-3.12)*	2.44 (1.28-4.64)*	.004
<8g/dl	4 (5.5)	5 (1.6)	4.99 (1.24-20.10)*	8.32 (1.86-37.29)*	

DISCUSSION

Malaria and HIV are the most important infectious diseases in the tropics and their co-infection is expected to have comprehensive public health implications, particularly in countries with low resource setting [10]. In this study, the co-infection rate was found to be 19.4% which is comparable with Nigeria study (17.5%) found from blood donors [11]. In contrast, our result is lower than a study conducted in Cameroon (29.4%) [12] but higher than a finding in South Africa (10%) [13]. The difference could be due to the study design we used and the incidence of malaria in different settings.

High prevalence of *plasmodium falciparum* (72.6%) was detected compared to *plasmodium vivax* (27.4%). A study from Nigeria had also found high prevalence of *plasmodium falciparum* (93.3%) [14] but it was in contradiction to an Indian study [15]. This difference might be due to the geographical differences of the two diseases.

In multivariate analysis; sex, hemoglobin level and CD4+ count were found to be independently associated with HIV-malaria co-infection. Females were 2.6 times more likely to be co-infected compared to males which is supported by another study [11]. This could be due to high proportion of females who visited the clinic from the very beginning. Physiological immunosupression associated with pregnancy related events could also be the possible explanation. Anemia was diagnosed in more than half of the study patients and the co-infected patients were mainly affected than HIV mono-infected ones significantly (p-vale= 0.001). Of all, 2.4% of patients had severe anemia while 57.3% of patients had mild anemia. Those who had hemoglobin level of <8 g/dl were 8.3 times more likely to be co-infected than individuals who had hemoglobin level of >12g/dl. Research findings from Cameroon, Nigeria and Mozambique also revealed similar high prevalence of anemia in co-infected patients [12, 14, 16]. High prevalence of anemia in co-infected patients could be due to the hyperparasitaemic nature of *Plasmodium falciparum* (72.6%) as well as the double burden of both diseases [17].

Individuals who had CD4+ lymphocyte count of <350Cells/mm3 were 2.3 times more likely to be co-infected than individuals who had CD4+ lymphocyte count of ≥350Cells/mm3. CD4+ lymphocyte count was significantly associated with co-infection and it was supported by previous studies that a lower CD4 cell count predisposes to malaria infection [13, 18-20]. A study from Uganda also revealed that lower CD4+ T-cell count and risk of clinical manifestations of malaria is pronounced in co-infected patients [5]. Evidences from different literatures indicated that malaria infection and fever rates are increased in individuals with low CD4 counts. On the other hand, malaria

up-regulates HIV transcription transiently during acute episodes and increases the rate of CD4 decline, thus effective malaria control measures might con-tribute to reducing the spread of HIV and extending the life span of HIV-infected individuals living in malaria endemic areas as studies suggested [21].

The increasing number of HIV-malaria co-infected people creates particular interest in order to correctly understand and control both infections and their particular interactions. The combination of regular cotrimoxazole prophylaxis and use of insecticide-impregnated bed nets was associated with a reduction in the incidence of febrile episodes of malaria as studies indicated [22]. Their overlapping epidemiology as well their impact in clinical practice also needs to be continuously updated.

This study is a retrospective study hence follow up studies are needed to explore more on co-infections of these diseases and their public health speculation. We are unable to conclude whether lower hemoglobin value is due to HIV or malaria. We analyze only few variables found in the document hence further risk factors are also needed to be investigated.

CONCLUSION

HIV-malaria co-infections are found to be higher. Hemoglobin level, CD4+ lymphocyte count and sex were found to be independently associated with HIV-malaria co-infection. Intervention strategies should give emphasis for females and patients with low CD4+ lymphocyte count. Further risk factors are needed to be investigated. Follow up studies are also needed to explore more on co-infections of these diseases and their public health speculation.

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