Assessment of the impact of malaria on CD4+ T Cells and haemoglobin levels of HIV-malaria co-infected patients

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Abstract

Introduction: The human immunodeficiency virus (HIV) and malaria destroy important cells required for proper immunological and haematological functioning of the body. This research therefore aimed to assess the effect of malaria on CD4+ and haemoglobin (Hb) levels of HIV-malaria co-infected patients.

Methodology: The study was performed by sampling 220 adult HIV patients on highly active anti retroviral therapy (HAART) who routinely visited the Tema General Hospital in Ghana. Blood samples were obtained for both blood film microscopy identification of malaria parasites and analysis using rapid diagnostic test kits. A BD Facscount Analyzer was used in the quantification of CD4+ levels.

Results: Of the 220 patients sampled, 34 (15.5%) were HIV-malaria co-infected, all of whom (34; 100%) had CD4+ counts below the normal range, while 23 (12.9%) of the HIV mono-infected patients had normal CD4+ counts. Almost all HIV-malaria co-infected patients (33; 97.1%) had low Hb levels, whereas 79 (42.5%) of the HIV mono-infected patients had normal Hb. Malaria infection strongly correlated positively and significantly with both low CD4+ count ($\chi^2 = 0.828$, $P = 0.003$) and Hb ($\chi^2 = 0.817$, $P = 0.004$) levels.

Conclusion: Malaria co-infection with HIV decreases CD4+ T cells and Hb levels in patients. It is therefore recommended that HIV patients in malaria endemic areas should adhere to malaria preventive measures.

Key words: CD4+ T cells; Hb levels; HIV-malaria co-infection; highly active anti retroviral therapy (HAART)

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Introduction

Malaria and HIV-1 are two of the most common infections in sub-Saharan Africa and, to a lesser extent, in other developing countries. It is estimated that 38 million Africans are infected with HIV-1 [1], whereas 300 million to 500 million suffer from malaria each year [2]. Given the overlap of their geographic distribution and resultant rates of co-infection, interactions between the two diseases pose major public health problems. Together they accounted for over three million deaths in 2007 and millions more are adversely affected each year [3]. Quantitatively, the mean parasite density has been reported to be 12-fold higher in HIV-positive compared with HIV-negative patients [4]. Among HIV-positive persons, parasitemia is more common, lower CD4+ counts are associated with higher parasite densities, and clinical malaria is more common [5]. Clear evidence indicates an interaction between HIV-1 and malaria in pregnancy, causing more peripheral and placental parasitemia, higher parasite densities, more clinical malaria, more anaemia, and increased risks of adverse birth outcomes [6]. HIV-infected women remain susceptible to the effects of malaria whether or not they are pregnant. A study into the effects of malaria on the viral load in HIV patients noticed a significantly higher HIV-proviral load in patients with malaria than those without, and this remained higher for at least four weeks after treatment [7]. This increase in HIV load could lead to a decrease in CD4+ that suggests malaria causes faster progression of HIV infection. Agbede et al. [8] observed a significant decrease in CD4+ count of patients infected with malaria attending the highly active antiretroviral therapy (HAART) clinic of the University of Ilorin Teaching Hospital, Ilorin, Nigeria. A computer simulation modelling study estimated that HIV would increase the incidence of clinical malaria and malaria deaths across the continent by more than 5% [9]. Malaria is the single most important cause of morbidity and mortality in Ghana, especially in children under five years of age, pregnant women, and the poor [10]. In Ghana,
malaria accounts for 31.1% of all outpatient illnesses, 30.3% of all admissions, and 30.3% of deaths in children younger than five years old [11].

High prevalence of malaria is reported in several communities in Tema and other neighbouring towns, and HIV patients who live in these communities are at a high risk of becoming co-infected with malaria. Thus the objective of this study was to determine the effect of malaria on CD4+ and Hb levels of HIV-infected patients.

Methodology
Study area and design
The study was conducted in the Tema Municipality of Ghana and specifically at Tema General Hospital, the main and largest hospital in the municipality, which is also an HIV-designated centre. The study was undertaken over a six-month period with bi-weekly purposive sampling of HIV-infected patients visiting the clinic routinely for medical review and estimation of their CD4+ count to ascertain their responsiveness to HAART.

Ethical considerations
The study was approved by the Tema General Hospital and the Department of Laboratory Technology, University of Cape Coast. Informed consent was obtained from all study participants. All procedures followed were in accordance with the ethical standards of the Ghanaian Ministry of Health as well as the Helsinki Declaration of 1975 [12].

Patient selection criteria
The study targeted medically diagnosed HIV-positive patients on HAART between the ages of 18 and 65 years who were scheduled to visit the hospital at regular intervals (every three months) for routine medical review as well as immune system evaluation of their responsiveness to treatment based on estimation of their CD4+ count. A total of 220 HIV patients were sampled.

Patient exclusion criteria
Patients at the extremes of age, pregnant women, and those on chemotherapy were excluded from the study since they may naturally have a very weakened immune system. Additionally, patients not responding to HAART treatment from previous visits were also excluded.

Laboratory investigations
Study participants were enrolled after agreeing and signing an informed consent form. Blood was collected from participants into EDTA tubes. Thick and thin blood films were prepared and stained with Giemsa and observed under microscope to detect malarial parasites. Malaria positive samples were then confirmed with Rapid Diagnostic Test (RDT). Results were indicated as presence or absence of malaria parasite.

CD4+ lymphocyte counts were determined using the Becton Dickinson (BD) FACScount system (Becton, Dickinson and Company, CA, USA), while Hb was measured using a CELL-DYN 1800 automated haematological analyzer (Abbott Laboratories Diagnostics Division, Abbott Park, Il, USA).

Normal CD4+ count of ≥ 600 cells/µL and normal Hb values were 12-16g/dl for females and 13-18g/dl for males according to the Ghana Health Service Guidelines, Ministry of Health, Ghana [13].

Data analysis
Data was analysed using SPSS 16.0 software (IBM, Chicago, Il, USA). Descriptive analysis was performed while Pearson’s correlation was used to determine coefficients as well as double-tailed paired means comparison. P ≤ 0.05 was considered significant and P ≥ 0.05 not significant.

Results
Of the 220 patients sampled, 161 (73.2%) were adult females and 59 (26.8%) were adult males. The majority (186; 84.5%) had HIV infection only while 34 (15.5%) were HIV-P. falciparum malaria co-infected. None of the co-infected patients had a normal CD4 count (≥ 600) compared to 24 (12.9%) patients with HIV mono-infection. Only one (2.9%) co-infected patient had normal Hb, whereas 79 (42.5%) of the HIV mono-infected patients had normal Hb. None of the HIV mono-infected patients had severe anaemia compared with 6 (18.2%) of the HIV-malaria co-infected patients (Table 1).

Discussion
Results from the study revealed that out of the 220 patients sampled, 34 (15.5%) were co-infected with HIV and P. falciparum malaria. This concurs with works by Kublin et al. [14] who recorded 77 (21%) cases of malaria infection in 367 HIV patients in Malawi’s Thyolo District. We also observed that
all 34 (100%) patients who were co-infected with malaria had CD4 counts lower than the normal CD4 reference range (≥ 600), implying that they all had lowered immunity. Additionally, a significant number (91.2%) had very weakened immunity (CD4 < 200) compared with 38.7% in HIV mono-infected patients. *P. falciparum* has been shown to stimulate HIV-1 replication through the production of cytokines (interleukin-6 and tumor necrosis factor-alpha) by activated lymphocytes [15-16]. An important study from Malawi showed that HIV-1 plasma viral loads were significantly higher in patients with malaria infection than in those without, and these levels remained higher for up to 10 weeks after treatment [14], suggesting that malaria may speed the progression of HIV disease. These results agree with those observed in a study from Uganda that showed increased CD4 cell decline associated with episodes of malaria despite prompt treatment [17]. High HIV viral loads lead to a greater destruction of CD4 cells, resulting in lower immunity and a poor response to HIV treatments. Pearson correlation analysis of HIV-malaria co-infected patients and those with lowered CD4 count was strongly positive and significantly correlated ($\chi^2 = 0.828, P = 0.003$). This is confirmed by research findings which indicate that in sub-Saharan Africa, with an HIV prevalence of 8%, adult malaria secondary to HIV is 4% parasitaemia and 5% clinical malaria. In southern Africa, where the HIV prevalence is 30%, these rates increase to 20% and 30% [18].

The result of the haematological changes (Hb levels) in the patients showed that just one (2.9%) HIV-malaria co-infected patient had normal Hb values, whereas 79 (42.5%) of the HIV mono-infected patients had normal Hb. Additionally, of the anaemic patients, none of the HIV mono-infected patients were severely anaemic compared with six (18.2%) of the HIV-malaria co-infected patients. Clear evidence indicates an interaction between HIV-1 and malaria in pregnancy, causing more peripheral and placental parasitemia, higher parasite densities, more clinical malaria, more anaemia, and increased risks of adverse birth outcomes [6]. It has been observed that HIV-infected people in areas of malaria transmission have more frequent episodes of symptomatic parasitaemia and higher parasitaemias than those without HIV [19]. Increased parasitaemia leads to greater destruction of red blood cells causing anaemia in infected patients due to haemolysis (destruction of the red blood cells). A strong positive and significant association was observed ($\chi^2 = 0.817, P = 0.004$) between malaria-infected HIV patients and low Hb.

This study demonstrates that malaria infection in HIV leads to further reduction in immunological and haematological indices required for patients to manage the disease and stay healthy. Thus measures should be put in place to prevent or treat as early as possible any co-infection in HIV patients to ensure that all HIV patients on therapy will respond adequately to have a boosted immune system and high Hb levels.

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### References


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