Effect of HIV Infection on Anti-Malarial Treatment Outcome Among in Patients at the Moi Teaching and Referral Hospital

Article *in* International Journal of Advanced Research · January 2013

CITATIONS
0

READS
10

4 authors, including:

Joel Kirinyet
Moi University
4 PUBLICATIONS **4** CITATIONS
SEE PROFILE

Fabian Esamai
Moi University
203 PUBLICATIONS **5,977** CITATIONS
SEE PROFILE

ISSN NO. 2320-5407

Journal homepage: http://www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH

RESEARCH ARTICLE

Effect of HIV Infection on Anti-Malarial Treatment Outcome Among in Patients at the Moi Teaching and Referral Hospital, Eldoret, Kenya

***Kirinyet J. K.[1], Esamai, F. O.[1], Magambo, J. K[2]., Mkoji, G. M[3].**

1. Department of Child Health, School of Medicine, Moi University, P.O Box 4606 -30100, Eldoret, Kenya
2. Institute of Tropical Medicine and Infectious Diseases (ITROMID), Jomo Kenyatta University of Agriculture and Technology (JKUAT), Nairobi, Kenya.
3. Centre for Biotechnology Research and Development, Kenya Medical Research Institute.

Manuscript Info

Manuscript History:

Received: 30 April 2013
Final Accepted: 15 May 2013
Published Online: May 2013

Key words:
Effect, HIV Infection,
Anti-Malarial Treatment Outcome,
In-Patients, Moi Teaching,
Referral Hospital,
Eldoret, Kenya

Abstract

HIV/AIDS and malaria are both major public health and socio-economic problems in sub-Saharan Africa. HIV infection may, in particular, complicate the clinical picture of malaria or its management. In this paper, malaria parasitaemia and outcome of anti-malarial treatment is examined in relation to HIV infection in patients based on a study conducted at the Moi Teaching and Referral Hospital (MTRH) located in Eldoret, Kenya. One hundred consenting patients with malaria were recruited into the study, malaria parasitaemia levels, HIV status and CD4 counts were determined for each patient, and the outcome of anti-malarial drug treatment with quinine or artemisinin derivative drugs observed. Malaria parasitaemia was monitored for each patient after antimalarial drug administration, for up to 7 days. Regardless of patient age, malaria parasitaemia clearance in anti-malarial drug treated, HIV negative patients was 2-3 days, whereas in the HIV positive patients, parasitaemia did not clear even 7 days after initiating treatment. The delay in parasitaemia clearance was more evident in patients whose CD4 counts were below 200 cells /μL. Overall, nearly 88% of the HIV negative patients with malaria had cleared malaria parasitaemia by the end of the observation period, compared with only about 12% in the HIV negative patients, P=0.012, OR=5.33 (1.53-18.56). It was thus concluded that HIV infection may delay clearance of malaria parasitaemia in anti-malarial drug treated patients.

Introduction

Between 300-500 million persons suffer from malaria each year worldwide with some 3.2 billion people living in areas at risk of malaria transmission in 107 countries and territories, and approximately one million deaths result from the infection. The burden of disease occurs largely in the sub-Saharan Africa (CDC, 2004; WHO, 2005). The World Malaria Report of 2005 (WHO, 2005) has shown that over 80% of malaria deaths occur in Africa where around 66% of the population is thought to be at risk of malaria; in contrast, less than 15% of the global total of malaria deaths occur in Asia, including Eastern Europe (WHO/UNICEF, 2005). In the Americas, 14% of the population are at risk of malaria though the region sees only a tiny fraction of global malaria-related deaths (WHO/UNICEF, 2005).

The high prevalence of malaria in Africa could be due to the fact that the ecological climate of tropical Africa provides enabling conditions for its most common and efficient mosquito vector - *Anopheles gambiae* - to thrive together with aetiological agent, *P. Falciparum*, the most common and deadly species of malaria parasite (Francis *et al*., 1997a). This combination greatly increases the transmission of malaria infection and the associated risk of disease

***Corresponding author:** joelkirinyet@gmail.com, fesamai2007@gmail.com, jkmagambo@gmail.com*

and death. Further, poverty and lack of good-quality health care have hindered control and treatment efforts (WHO/UNICEF, 2005). Children, pregnant women, and non-immune individuals are the most vulnerable to malaria. In severe cases of cerebral malaria, surviving children are left with seizures, speech disorders or partially paralyzed (WHO/UNICEF, 2005). Even when the harm done to their minds and bodies is less evident, recurrent bouts of fever drain a child's capacity to learn (WHO/UNICEF, 2005). The population at risk of malaria is a function of the human population and malaria infection risk and endemicity. The most widely cited estimate of the global proportion of malaria morbidity and mortality borne by African region (AFRO) is 90%, with estimates ranging from 62 to 93%. The variation in these estimates has wide-ranging implications for policy and the strategic emphasis of the Roll Back Malaria Movement (Hay *et al*., 2004).

Based on the 1968 Lysenko malaria endemicity map and population distribution, falciparum and vivax malaria parasite rate values for prevalence index are as follows: population exposed to hypo-endemic (0·05); population exposed to meso-endemic (0·305); population exposed to hyper-endemic (0·63), and population exposed to holo-endemic (0·875). The product of the national prevalence and a *P. falciparum* index (the proportion of malaria cases reported nationally in 1993 that were due to *P. falciparum*) was used to create national falciparum prevalence (N*f*P). The results revealed that the scale of the problem in AFRO region ranks the highest (53% of global N*f*P) compared to South East Asian region (SEARO) countries (33% of global N*f*P) (Hay *et al*., 2004).

Mortality rates from *P. falciparum* infection are on average 9 per 1000 in the under-five populations among AFRO countries, and they range from 0.1-1 per 1000 and 0.01-0.1 per 1000 (in all age groups) in Myanmar (Burma) and Sri Lanka, respectively in SEARO. This order of magnitude difference in mortality risk means that most malaria mortality is in AFRO region (Hay *et al*., 2004).

In Kenya, malaria episodes account for 30% of all outpatient (OP) attendances and 19% of admissions to health facilities, being rated as the most important cause of death in children less than 5 years of age (DOMC, 2006). It is estimated that malaria causes 20% of all deaths in this age group. To combat malaria, the Kenyan Ministry of Health has prioritized and developed the National Malaria Strategy (NMS) 2001-2010 and the National Health Sector Strategic Plan II (2005-2010) with a view to laying emphasis on scaling up implementation of effective interventions. These interventions are aligned to the Abuja targets and the Millennium Development Goals (MDGs) that aims at reducing the morbidity and mortality due to malaria (DOMC, 2006). Falciparum malaria in high-altitude areas of western Kenya is best described as seasonal and meso-endemic (Hay *et al*., 2002).

The challenges facing the battle against malaria are overwhelming and have posed a serious obstacle to malaria control. These challenges range from drug resistance to high cost of anti-malarial drugs (Carrington, 2001). Chloroquine, the cheapest and most widely used anti-malarial drug, has lost its clinical effectiveness in most endemic areas (Mueller *et al*., 2004). But the next generation of anti-malarial drugs – artemisinin-based combination therapies (ACTs) – are highly effective and life saving but more expensive (WHO/UNICEF, 2005).

HIV/AIDS Infection

An estimated 38.6 million people worldwide were living with HIV by the end of 2005 (UNAIDS, 2006). In the same year, 4.1 million became newly infected with HIV and approximately 2.8 million lost their lives. Overall, the HIV incidence rate (the proportion of people with new HIV infection) is believed to have peaked in the late 1990s and to have stabilized subsequently, due, possibly to changes in behaviour and an increase in the use of preventive measures. The UNAIDS (2006) report further suggests that the decline in national HIV prevalence in two sub-Saharan African countries (Kenya and Zimbabwe), urban areas of Burkina Faso, West Africa and in Haiti in the Caribbean region, can be attributable to significant behavioural change, including increased condom use, fewer sexual partners and delayed sexual debut.

In the rest of sub-Saharan Africa, HIV/AIDS epidemics appear to be levelling off but at exceptionally high levels in most of southern Africa. The number of people living with HIV has continued to rise partly due to population growth and, more recently, due to the life-prolonging effects of anti-retroviral therapy. The African continent, however, remains the global epicentre of the AIDS pandemic with South Africa's AIDS epidemic being one of the worst in the world, showing no evidence of a decline (UNAIDS, 2006). There are no indications that HIV prevalence is declining elsewhere in southern Africa including in Botswana, Namibia and Swaziland (UNAIDS, 2006). In Swaziland, national adult HIV prevalence is estimated at 33.4% [21.2%–45.3%] in that country. HIV prevalence among pregnant women attending antenatal clinics rose from 4% in 1992, to exceptionally high infection levels of 43% in 2004. Botswana's epidemic is equally serious, with national adult HIV prevalence estimated at 24.1% [23.0%–

32.0%] in 2005. Lesotho's epidemic seems to be relatively stable at very high levels, with an estimated national adult HIV prevalence of 23.2% [21.9%–24.7%]. On the eastern coastline, a dynamic epidemic is underway in Mozambique, where the estimated national adult HIV prevalence is 16.1% [12.5%–20.0%]. HIV is spreading fastest in provinces linked by major transport routes to Malawi, South Africa and Zimbabwe (UNAIDS, 2006).

National adult HIV prevalence in the countries of North Africa is very low, and does not exceed 0.1%, except for Sudan (UNAIDS, 2006) but available data suggest that the epidemic is growing in several countries including Algeria, Libyan Arab Jamahiriya and Morocco. Across the northern African region, an estimated 64 000 people were newly infected with HIV in 2005, bringing the total number of people living with the virus in this region to some 440 000. Sudan accounts for 350 000 of those people infected with HIV/AIDS in the region (UNAIDS, 2006).

In the Eastern African region, some countries have shown real declines in HIV infection levels. For instance, Uganda's HIV infection prevalence fell from 13% in the early 1990s to 4.1% (2.8-6.6%) by the end of 2003 (Asamoah-Odei *et al*., 2004). Recent data suggests that Kenya could be on a similar path where data from antenatal clinics show median HIV prevalence falling from 13.6% (12.2-27.1%) in 1997-1998 to 9.4% (6.6-14.3%) in 2002. Data from Burundi also suggests a decline in HIV prevalence, though this is based on limited data from only six clinics (Asamoah-Odei *et al*., 2004). Asamoah-Odei's team have reported that Ethiopia's epidemic is most severe in urban areas, including in the capital city of Addis Ababa. However, the declining HIV trend among pregnant women in the capital (first detected in 1997) is continuing, with median prevalence dropping from 13.7% in 1997-1998 to 11.8% in 1999-2000, and has remained at about 12% since then (Asamoah-Odei *et al*., 2004).

The current national prevalence rate of HIV in Kenya as at the end of 2003 stands at 6.7% (KDHS, 2003), and in some groups such as pregnant women attending antenatal clinics, prevalence rate of as high as 25-30% have been observed (CDC, 2004).

Interactions Between Anti-malarial and ARV Drugs Used to Treat HIV Patients

Interactions between anti-malarial drugs and anti-retroviral drugs (ARVs) mostly involve protease inhibitors (PIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs). HIV PIs are potent inhibitors of cytochrome P_{450} enzyme inhibitor ketoconazole (a major pathway for drug metabolism), and NNRTIs are inducers and/or inhibitors of these enzymes. The anti-malarial drugs halofantrine, artemether, and/or lumefantrine (AL) should not be given to patients receiving PIs (or NNRTI delavirdine) because of excessive risk of toxicity. For patients receiving other NNRTIs (nevirapine or efapirenz) lower concentrations of lumefantrine and artemether may lead to increased risk of treatment failure (Lefevre *et al*., 2002). The use of quinidine (and thus, possibly quinine) is contraindicated because of potential cardiotoxicity among persons receiving a number of anti-retroviral agents, including nelfinavir and ritonavir (Viracept, 2002; Norvir, 2002).

The magnitude and clinical significance of these interactions needs further research. WHO recommends investigation on a potential interaction between quinine and NNRTI or with PI drugs used in the management of malaria in patients living with HIV-virus (WHO, 2005).

Effect of HIV on Malaria Treatment Outcomes

A Ugandan study has shown that adults with HIV infection exhibit a poorer response to anti-malarial therapy than HIV negative patients during the 28 days following treatment, and that treatment failure is due to higher frequency of new infections rather than recrudescence (Kamya *et al*., 2006). In Addis Ababa, Ethiopia, Birku *et al*. (2002) have reported that clearance of falciparum malaria after administration of artemisinin is delayed in patients with HIV co-infection. Adults also with advanced HIV may be at risk for failure of malaria treatment, especially with sulfa-based therapies (Slutsker, 2007).

Limitations of the Study

The limitation encountered in the study was the small number of HIV cases (n=17). This means that more comprehensive results could have been obtained. Despite this limitation, it is hoped that this paper will contribute to the existing pool of knowledge on the subject matter.

Material and Methods

The study was conducted in a hospital set-up at the Moi Teaching and Referral Hospital (MTRH), Eldoret, located in the Uasin Gishu District in the North of Rift Valley Province, Kenya. Eldoret town is situated at an altitude of 2300 metres above sea level and has a population of approximately 400,000, with an annual rainfall of 1140mm. It is situated about 360km North West of Nairobi, on the Uasin Gishu Plateau, punctuated with swamps of papyrus reeds, conditions that favour breeding of mosquito vectors. It is considered one of the malaria epidemic prone districts (Snow *et al*., 1998). In addition to malaria, the District has had its own share of the HIV epidemic. The MTRH has a bed capacity of 446. The hospital houses the School of Medicine of Moi University that, on average, receives about 150,000

referred patients who come from the North of the Rift Valley, Western and Nyanza Provinces for medical attention. About 123,000 of the referred patients receive laboratory services annually for various tests, and many are admitted for further care and management.

The study subjects comprised patients (males and females) two years and above that were recruited from among the clinical patients admitted to the wards for better management of various conditions. Recruitment of study patients was done at the medical wards (Paediatrics and Adult) among patients sent from Out-Patient Department presenting with febrile conditions among other ailments. A total of 1,344 in-patients were screened for malaria parasitaemia and 100 of them were recruited into the study after signing the informed consent form administered to them. All the study subjects were treated with anti-malarial drugs (either quinine I.V. or artemisinin derivatives I.M.) and given professional attention along with the other in-patients at their respective wards. Apart from the blood slide test, all the patients admitted to the study in the wards were screened to determine HIV-sero-status after counseling by trained AMPATH (Academic Model for the Prevention and Treatment of HIV/AIDS) personnel within the admitting wards. AMPATH Laboratories are jointly run by Moi University and MTRH. HIV-sero-positive results were made readily available in the patients' files only to professional medical personnel handling the patients. A 3ml venous blood sample from all HIV-infected patients was obtained for CD4 cell count at the AMPATH reference laboratory.

Only patients admitted to Paediatric and adult medical wards of MTRH, Eldoret, with symptoms of fever (temperature >38^{o}C) and/or diagnosed at the OP with malaria positive blood slide, aged ≥2 years and were willing (or their guardians or parents) to give a written consent to join the study were recruited. At the baseline, eligibility to the study was a positive blood slide with a minimum falciparum malaria parasitaemia of 1000/μℓ of blood (=25 trophozoites/200 white blood cells) and above. In addition, eligible subjects were required to accept to be screened for HIV. Any patient who declined to give consent on the above conditions or was considered too ill by admitting clinicians to have any meaningful monitoring of the response to anti-malarial treatment within the duration of confinement was excluded from the study.

Malaria Diagnosis

Pre-treatment and post-treatment blood samples were obtained from recruited subjects. Both thick and thin blood smears were prepared from each patient on day zero (D0). Thin blood films were fixed in absolute methanol for 2 minutes and the two smears (thick and thin) air-dried and stained with 10% standard buffered Giemsa stain (pH 7.2) for 10 minutes. Thick blood smears were scanned for the presence of malaria parasite under oil immersion objective x100 and scored accordingly per microlitre (μℓ) of blood. On the other hand, thin blood smears were similarly examined to confirm *Plasmodium falciparum* species. Malaria parasites were counted in all positive blood smears and reported per 200 white blood cells (WBC) counted. Parasite load was then calculated per microlitre (μℓ) of blood using the following mathematical formula (McKenzie *et al*., 2005),

$$\text{Malaria parasites per } \mu\ell \text{ blood} = \frac{\text{No. malaria parasites counted x 8 000}}{\text{200 WBC}}$$

An average of 8000 leucocytes per μℓ blood (range 4 000-11 000 leucocytes per μℓ blood) was used as the standard for the population under study. However, in spite of the inaccuracies as a result of the variations in the number of leucocytes between individuals in normal and greater variations in ill health, the above figure allows for reasonable comparisons between individuals' white blood cell values. Blood smears for parasitaemia change were consecutively taken at day zero (D0) pre-treatment, day one (D1), day two (D2), day three (D3), and day four (D4) after admission. Some patients were discharged home on the second or third day of admission to continue with the same treatment they had been started on (smears were not taken at home). Upon discharge, arrangements were made for patients to come back for a day seven blood slides re-check. Overall, there was 95% turn-up on day 7th for re-check. Change in parasitaemia levels after anti-malarial drug administration was calculated based on D7 parasitaemia rather than on D3 parasitaemia since 57% of the subjects had been discharged home by D2. Patients could not be kept longer in the wards by the clinicians due to cost of maintenance and congestion in wards. Fourteen subjects who remained parasitaemic on D7 were given artemisinin therapy before they were returned home to continue with treatment.

HIV Diagnosis

Blood samples for HIV screening were tested at admission in the wards by trained AMPATH personnel using two rapid test kits (Determine, Abboth, Abott Park, IL, USA; and Unigold Trinity Biotech, Wicklow, Ireland - immuno-chromatographic band and Unigold – spot colour change methods respectively). CD4 counts from

HIV-infected subjects were processed at AMPATH Laboratory using Flow Cytometric Method (BD FACSCount, Becton, Dickinson and Co, Franklin Lakes, NJ, and USA).

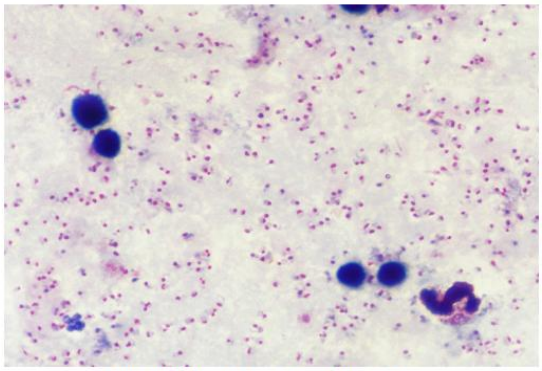
All the recruited subjects were treated with anti-malarial drugs (either quinine hydrochloride or artemisisnin derivatives) and monitored for seven days. The change in parasitaemia levels after anti-malarial drug administration was compared between HIV-positive and HIV-negative patients. A comparison was also made on the same subjects to determine their response to anti-malarial therapy. On HIV subjects, based on their CD4 levels (below or above 200 cells/µL), and whether or not they were receiving anti-retroviral drugs (ARVS), a comparison was made to determine the change in parasitaemia levels and response to anti-malarial therapy.

Data were entered into Microsoft Excel programme. The original hard written copy was safely kept for reference by the project's Principal Investigator (PI). No unauthorized persons were allowed access to the data. Only the clinicians who were handling the subjects in their respective wards were given copies of sample request form results to use for treating or monitoring subjects. Analysis of data was performed using SPSS (Statistical Package for Social Scientists) version 12.0 for Windows. Validation of data was done before analysis that involved descriptive statistics such as means, standard deviation, median and frequency distributions. Fisher's Exact Test was used to test for significant difference between HIV-positive and HIV-negative patients.

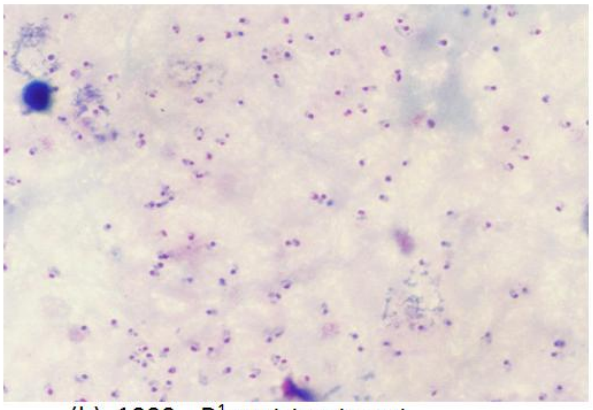
Results

Response to Anti-malarial Therapy

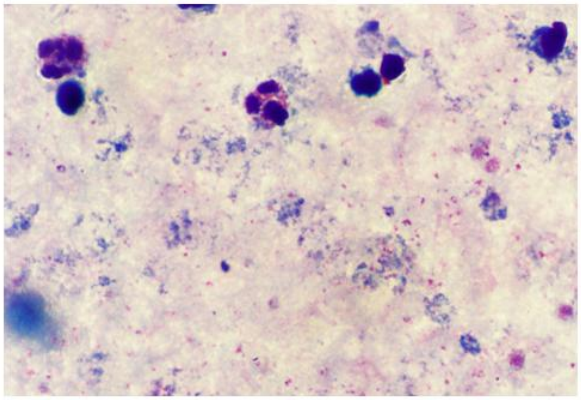
Figure 1(a-g) comprises studio-processed photographs of thick blood smears of one of the subjects showing parasitaemia clearance between pre-treatment and post-treatment period. The subject had been treated with quinine anti-malarial drug starting from day 0 (pday0) through day 7 (pday7) showing successful clearance of malaria parasitaemia on consecutive days of treatment.



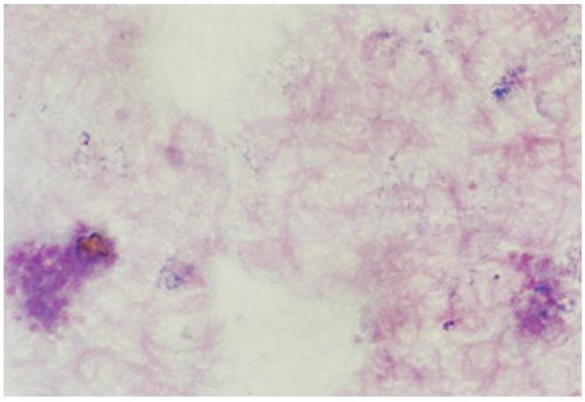
(a) x1000 D^{o} pre-treatment



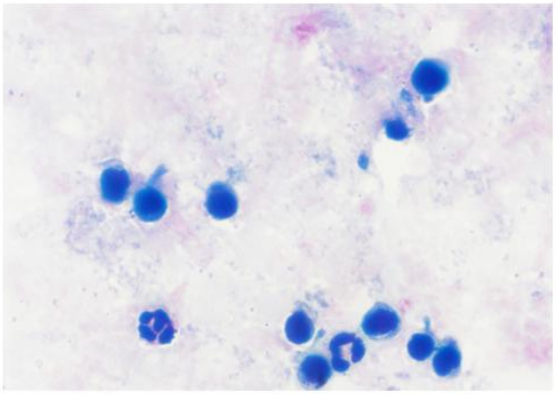
(b) x1000 D^{1} post-treatment



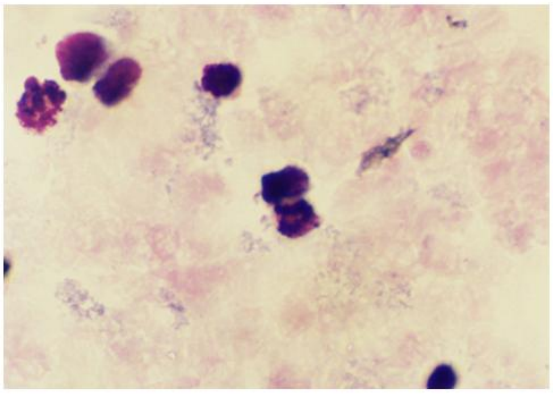
(c) x1000 D^{2} post-treatment



(d) x1000 D^{3} post-treatment



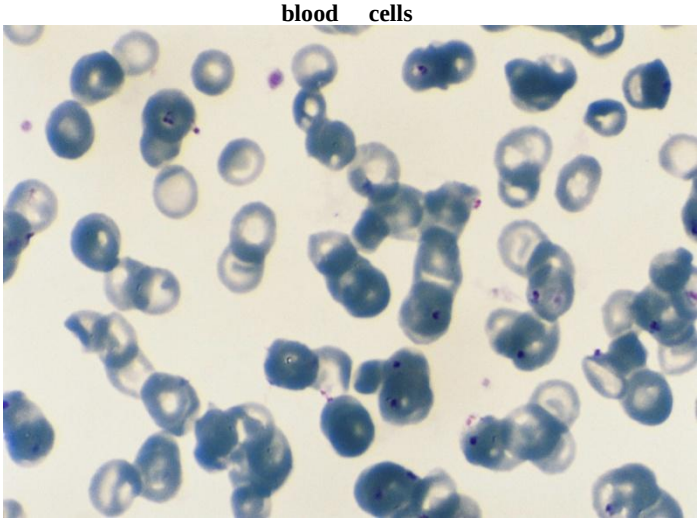
(e) x1000 D^{4} post-treatment



(f) x1000 D^7 post-treatment

Figure 1(a-f): Photo pictures of six blood slide samples taken from one of the subjects

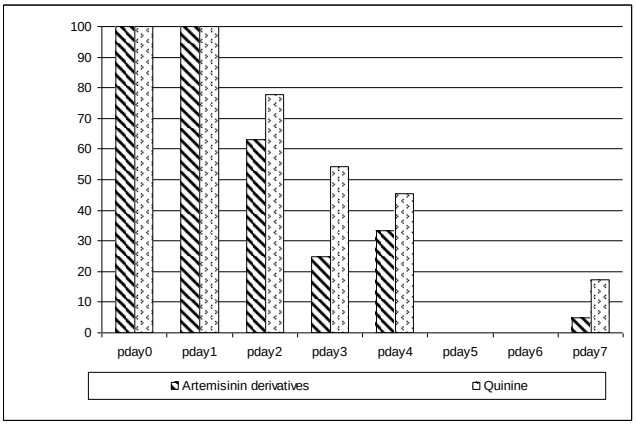
Figure 1(g): x1000 Thin blood film with parasitized red blood cells



Majority of the subjects (57%) under study (Figure 2) were discharged from the wards in their second or third day of admission after a positive clinical response to anti-malarial therapy. Upon discharge, study subjects were booked for blood slide re-check on the seventh day (pday7) of admission. Overall twenty subjects were treated with artemisinin derivatives while eighty others were treated with intravenous quinine dihydrochloride. Though the study shows Artemisinin derivatives to have superior action compared to quinine therapy, admittedly the number of artemisinin recipient (20) were very few for this analysis otherwise interesting results could have been realised. Of the 14 individuals who remained parasitaemic to day seven (pday7), thirteen of them had been treated with quinine.

Figure 2: Response to anti-malarial treatment (Artemisinin derivatives and Quinine)

Legend Pday - parasitaemia on day



Effects of Anti-malarial Chemotherapy in Children under 18 Years of Age

All the children treated with artemisinin derivatives, regardless of their HIV-status, had cleared malaria parasitaemia by day four (pday4) and no recrudescence was found on day seven (pday7). Some children treated with quinine dihydrochloride persisted with parasitaemia beyond day four (pday4) and on day seven (pday7) they still had not cleared malaria parasitaemia.

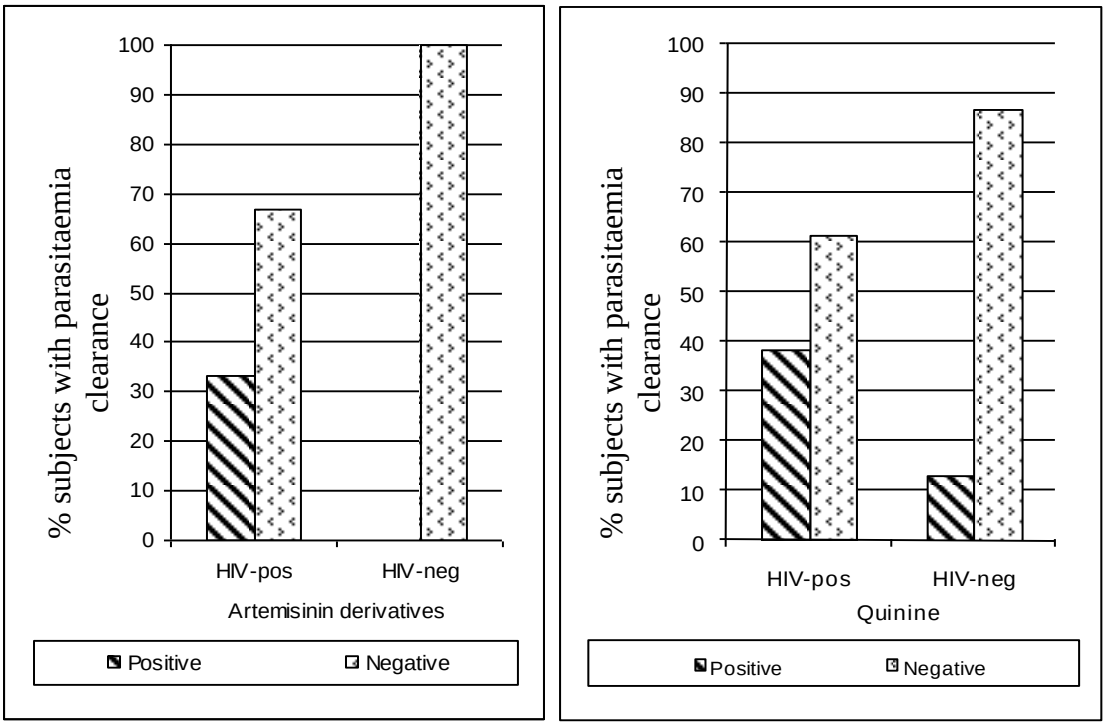
Effects of Anti-malarial Chemotherapy in Adults above 18 Years of Age

Among the adult participants, those that were treated with artemisinin derivatives (Larither) had cleared parasitaemia by day four (pday4) and became aparasitaemic to day seventh (pday7) regardless of their HIV-status except one who had failed to take treatment at home. Thirteen of the subjects treated with quinine were parasitaemic on day seventh (pday7), while 62 others were aparasitaemic (cured). Treatment was changed to artemisinin for all the cases resistant to quinine.

Change in Parasitaemia Levels after Anti-malarial Drug Administration

All the patients were treated with either artemisinin derivatives or quinine hydrochloride on admission (n=100) and were monitored up to day seven (Figure 3). Their parasitaemia levels were checked while in the wards, and comparison was made in relation to HIV-status and the effectiveness of each treatment group. Overall, 80 individuals were treated with quinine while 20 others were treated with artemisinin derivatives. Of the 13 HIV-positive individuals who were treated with quinine and lived up to day seventh, 5(38.5%) had remained parasitaemic while 8(61.5%) had been cured. Of the 62 HIV-negative individuals who were treated with quinine and lived

Figure 3: Effect of Artemisinin derivatives and Quinine therapy among subjects.



up to day seventh, 8(12.9%) had remained parasitaemic while 54(87.1%) had been cured (p=0.042). Of the four HIV-positive individuals who were treated with artemisinin derivatives and lived up to day seventh, 3(75%) were cured while 1(25%) remained parasitaemic due to non-compliance in taking treatment at home. All the sixteen HIV-negative individuals who were treated with artemisinin derivatives were cured of malaria infection.

Change in Parasitaemia Level after Anti-malarial Therapy Relative to CD4 Counts

HIV-positive participants (n=17) were compared on their response to anti-malarial treatment in relation to their CD4 count levels (Figure 4). It was found that individuals whose CD4 counts were above 200 cells/µL and had been treated with artemisinin derivatives had a much more malaria parasitaemia clearance (100%) than those whose CD4 counts fell below 200 cells/µL (about 50% clearance) (p=1.000). Among the quinine recipients, HIV-positive individuals whose CD4 counts were above 200 cells/µL had a better parasitaemia clearance (62%) compared to those whose CD4 counts were below 200 cells/µL (56%). The analysis could not show significance due to the small sample size.

Change in Parasitaemia Levels in those on ARVs and those not on ARV treatments

HIV-positive participants who were treated with quinine or artemisinin derivatives were compared on the basis of whether or not they were receiving anti-retroviral therapy (ARTs). It was observed in Figure 5 that malaria parasitaemia clearance activity was better among the HIV-positive subjects who were receiving ARVs and were treated with quinine anti-malarial drugs (71.4%) compared to those who had not been started on ARVs (28.6%), p=0.592. All the HIV-positive individuals (n=4) who were treated with artemisinin derivatives had cleared malaria parasitaemia by the seventh day regardless of whether they were receiving ARVs or not (p =0.333). The only one who remained parasitaemic by day seventh and had been treated with artemisinin derivates, had failed to take medicine at home upon discharge (non-compliance).

Figure 4: Effects of Artemisinin derivatives and Quinine therapy among HIV subjects.

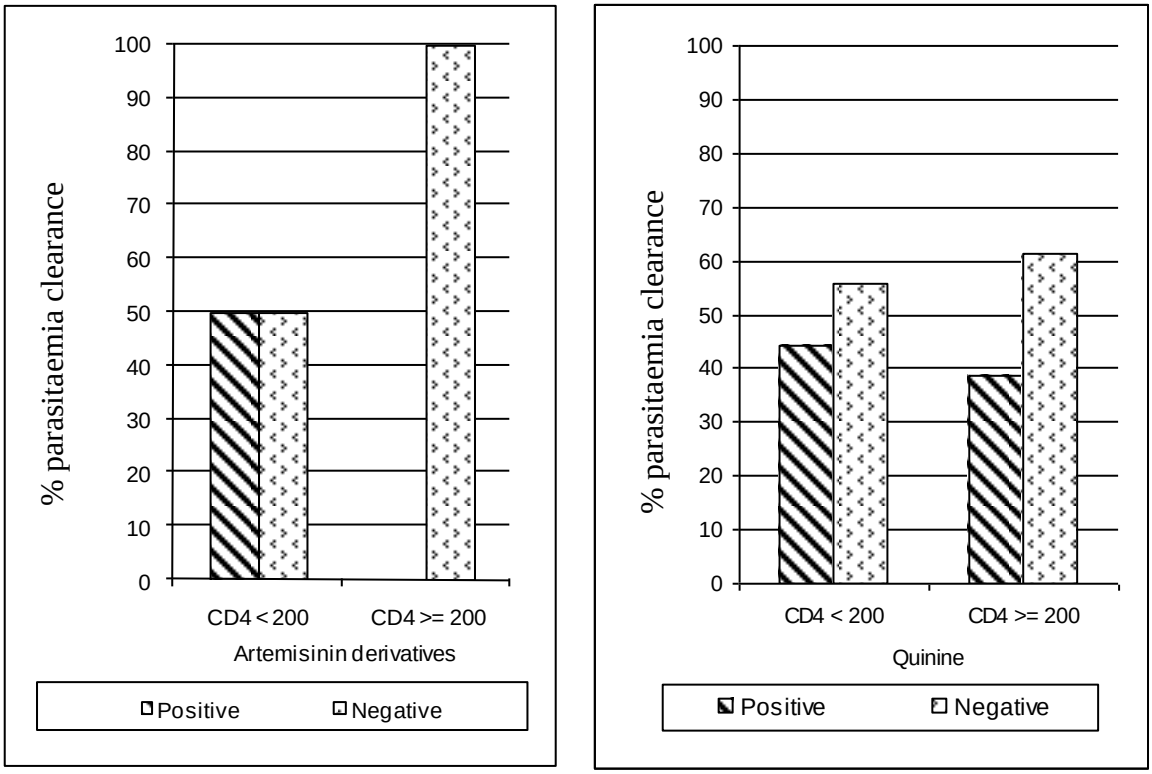
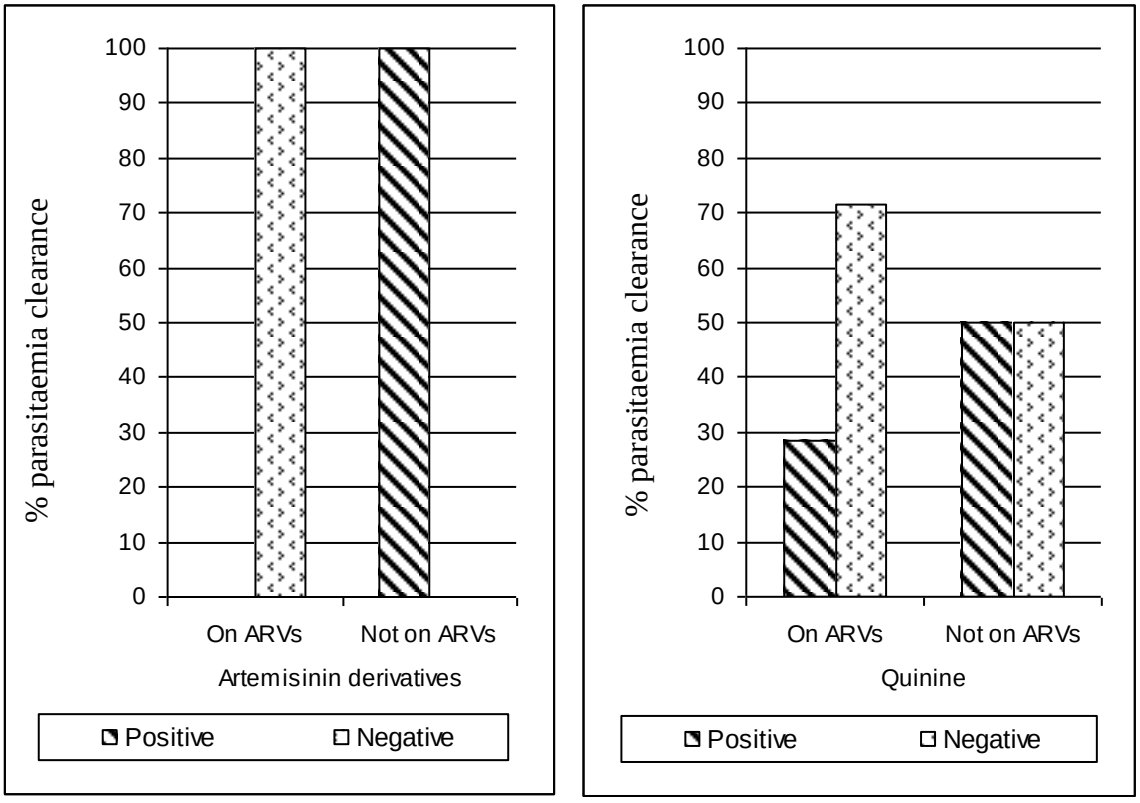


Figure 5: Effects of Anti-malarial drugs in ARV recipient subjects

Legend Positive - malaria not cleared
Negative - malaria cleared



DISCUSSION

After seven days treatment, the participants (n=100) were compared on their response to anti-malarial treatment. HIV-positive individuals (about 38%) had not cleared malaria parasitaemia by day seven compared to about 10% of HIV-negative individuals who were observed in the same period. There was a significant association between HIV sero-positive status with malaria (P=0.012), which was confirmed by the Odds ratio of 5.33(1.53-18.56), that implied that HIV-positive patients were 5.33 times likely to have malaria parasitaemia clearance prolonged than HIV-negative patients. It is suggested, therefore, that this delay in parasitaemia clearance may cause HIV disease progression due to continued production of cytokines (IL-6 and TNF-α) required for the HIV-1 RNA replication (Xiao *et al*., 1998; Piselli *et al*., 2002; Froebel *et al*., 2004; Rowland-Jones *et al*., 2002), causing some rise in viral load and a decrease in CD4 cells. This scenario may impact negatively on the response to anti-malarial treatment among HIV-infected individuals.

The poor response among HIV-positive individuals to anti-malarial therapy compares well with studies done elsewhere by Kamya *et al.* (2001), Birku *et al.* (2002), Patnaik *et al*. (2004), and Vangeertruyden *et al*. (2004). It appears, however, that HIV-positive individuals are better off with artemisinin derivatives therapy, as long as they do not have complicated malaria (CM).

Nine study subjects were started on ARV treatment by the time they were admitted for malaria management after they had been screened for HIV. Results show that the administration of ARVs to those whose CD4 cells count were below 200/µL appeared to have boosted the effect of anti-malarial quinine therapy than when quinine therapy was used alone. Although statistically not significant, it is assumed, in this scenario, that ARV therapy appears to have contained the replicative process of HIV-1 RNA; hence anti-malarial activity, boosted with improving cellular immunity, was able to clear malaria parasitaemia.

CONCLUSION AND RECOMMENDATIONS

A positive response to anti-malarial therapy has been shown by individuals with fairly active immune status as indicated by the strength of the CD4 cells count. Most of the HIV-negative subjects were able to clear parasitaemia by day 2 or day 3, but HIV-positive subjects remained parasitemic up to day seven as shown by anti-malarial treatment outcome. The study has also shown that artemisinin derivatives are not dependent on immune status but were capable of clearing about 100% of malaria parasitaemia compared to quinine hydrochloride (about 60%) that could take longer time to clear parasitaemia with moderate resistance.

Medical training institutions are urged to incorporate in their training curriculum the emerging association of the two infections (HIV and malaria) so as to strengthen feasible interventional measures, geared towards ameliorating the associated societies' sufferings and contribution to the realization of Millennium Development Goals (MDGs) in 2015.

Acknowledgment

This study wish to acknowledge with thanks the Institute of Tropical Medicine and Infectious Diseases together with Jomo Kenyatta University of Agriculture and Technology for availing their facilities for training towards the success of this work. Iam indebted to Moi University, my employer, for granting me a two-and-half year study period in Nairobi that enabled me complete this work. My gratitudes go to the Moi Teaching & Referral Hospital, headed by the then Director, Prof Haron Mengech for granting me permission to work with its patients during the study. Special thanks go to the nurses in wards 1-4, laboratory colleagues at the Department of Child Health & Paediatrics, Messrs, Kendagor and Kenduiywa for their assistance in laboratory work. Also to be thanked are Mr. Oludhe Henry,Ms Sarah Muyonga and AMPATTH colleagues for their assistance in CD4 counts. Finally, the KEMRI laboratory colleagues, Messrs Muniu and Mwangi for their assistance in data analysis at the Centre for Public Health Research, KEMRI Headquarters, Nairobi.

REFERENCES

Asamoah-Odei, F., Garcia-Calleja, J. M., & Boerma, J. T. (2004). HIV prevalence and trends in sub-Saharan Africa: no decline and large sub-region differences. *Lancet*, 364: 4-6.

Birku, Y., Mekonnen, E., Bjorkman, A., Wolday, D. (2002). Delayed clearance of *P. falciparum* in patients with human immunodeficiency virus co-infection treated with artemisinin. *Ethiop Med J*, 40: 17–26.

Centre for Disease Control (CDC), National Center for Infectious Diseases, Division of Parasitic Diseases (2004). *Geographic Distribution of Malaria*, April 23.

DOMC, Kenyan MoH (2006). *National Guidelines for Diagnosis, Treatment and Prevention of Malaria for health workers in Kenya*. DOMC, Kenyan MoH.

Francis, S. E., Banerjee, R., & Goldberg, D. E. (1997a). Biosynthesis and maturation of the malaria aspartic hemoglobinases plasmepsins I and II. *J. Biol. Chem.,* 272: 14961-14968.

Froebel, K., Howard, W., Schafer, J. R., Howie, F., Whitworth, J., Kaleebu, P., Brown, A. L., & Riley, E. (2004). Activation by malaria antigens renders mononuclear cells susceptible to HIV infection and re-activates replication of endogenous HIV in cells from HIV-infected adults. *Parasite Immunol,* 26: 213-217.

Hay, S. I., Simba, M., Busolo, M., Noor, A. M., Guyatt, H. L., Ochola S. A., & Snow, R. W. (2002). Defining and detecting malaria epidemics in the highlands of western Kenya. *Emerg Infect Dis*, 8: 555-562.

Hay, S. I., Guerra, C. A., Tatem, A. J., Noor, A. M., & Snow, R. W. (2004). The global distribution and population at risk of malaria: past, present, and future. *Lancet*, 4: 327-336.

Kamya M.R., Kigonya C.N., McFarland W. HIV infection may adversely affect clinical response to chloroquine therapy for uncomplicated malaria in children. AIDS, 2001; **15:**1187–1188.

Kamya, M. R., Gasasira, A. F., Yeka, A., Bakyaita, N., Nsobya, S. L., Damon, F., Rosenthal, P. J., Grant, D., & Havlir, D. (2006). Effect of HIV-1 Infection on Antimalarial Treatment Outcomes in Uganda: A Population-Based Study. *J Infect Dis*, 193: 9-15.

Kenya Demographic and Health Survey (KDHS) (2003). *Blood spots for estimation of HIV prevalence rates.* Author.

Lefevre, G., Carpenter, P., Souppart, C., Schmidli, H., McClean, M., & Typinski, D. (2002). Pharmacokinetics and electrocardiographics of artemether-lumefantrine (Riamet®) with concomitant administration of ketoconazole in healthy subjects. *Brit J Clin Pharm*, 54: 485-492.

McKenzie, F. E., Prudhomme, W. A., Magill, A. J., Forney, J. R., Permpanich, B., Lucas, C., Gasser, R. A., Wongsrichanalai, C. (2005). White blood cell counts and malaria. *J Infect Dis*, 192: 323-330.

Norvir, A. (2002). *Monographs from the Physicians Desk Reference*. Montvale, NJ: Medical Economics Company, Inc.

Patnaik P., Jere C., Miller W., Hoffman I., Wirima J., Pendame R., Meshnick S., Taylor T., Molyneux M., Kublin J. Incidence of malaria parasitaemia in a cohort of rural Malawian adults according to HIV sero-status, HIV-1 RNA concentration and CD4 count. J Trop Med Hyg 2004; **71**:456. (Abstract)

Piselli, T. L., Hoffman, I. F., Jere, C. S., Ballard, S. B., Molyneaux, M. E., Butera, S. T., Lawn, S. D. (2002). Immune activation and induction of HIV-1 replication within CD14 macrophages during acute *Plasmodium falciparum* malaria co-infection. *AIDS*, 16: 1503-1509.

Rowland-Jones S.L.,and Lohman B. Interactions between malaria and HIV infection an emerging public health problem? Microbes Infect 2002; **4**:1265-1270.

Slutsker, L. A., & Marston, B. J. (2007). HIV and malaria: interactions and implications. HIV infection and AIDS. *Curr Opin Infect Dis*, 20: 3-10.

UNAIDS (2006). *Overview of the Global AIDS Epidemic/2006 Report on the Global Epidemic*. UNAIDS.

Vangeertruyden, J. P., Mwananyanda, L., Chalwe, V., Moerman, F., Chilengi, R., Kestens, L., D'Alessandro, U. (2004). Higher risk of anti-malarial treatment failure in HIV-positive than in HIV-negative individuals with clinical malaria. *Am. J. Trop. Med. Hyg*, 71: 315. (Abstract). Viracept, A. (2002). *Monographs from the Physicians Desk Reference*. Montvale, N.J.: Medical Economics Company, Inc.

WHO (2005). *Malaria and HIV interaction and their implications for Public Health Policy*. WHO.

WHO/UNICEF (2005). *World Malaria Report: A 5 minute briefing on the World Malaria Report.* WHO and UNICEF.

Xiao, L., Owen, S. M., Rudolph, D. L., Lal, R. B., Lal, A. A. (1998). *P. falciparum* antigen-induced HIV-1 replication is mediated through induction of tumor necrosis factor-alpha. *J Infect Dis*, 177: 437-445.