ABSTRACT

Human Immunodeficiency Virus (HIV) and malaria pose major public health problems due to their high overlapping global geographic distribution and resultant high rates of co-infection. Sub-Saharan Africa bears the greatest burden of HIV (67%) and malaria (86%) infections. Malaria and HIV-1 are co-endemic in Kenya with more than 70% of the population at risk of acquiring malaria and 5.6% of the population living with HIV. Kisumu County in Western Kenya has a high prevalence of HIV (19.3%) and malaria (38%) compared to other parts of the country. HIV and malaria modulate an infant's immune response *in-utero*. In co-infected individuals, HIV related immunosuppression may lead to impaired control of parasitemia and increased risk of developing severe malaria. Moreover, severe malaria is thought to strongly predispose infants to other infectious diseases. However, the link between malarial infections and episodes of severe bacterial infections has not been investigated in this region of Kisumu Kenya. This longitudinal prospective case-control study examined the association between malarial infections and incidences of severe bacterial infections in infants with and without *in-utero* exposure to HIV. HIV Exposed Uninfected (HEU) refers to infants with *in-utero* exposure to HIV while HIV Unexposed Uninfected (HUU) refers to infants without *in-utero* exposure to HIV. Both groups were HIV negative. A total of 121 infants (HEU, n=63 and HUU, n=58) were recruited from the Chulaimbo sub-county Hospital in Kisumu County. Blood was collected by a certified phlebotomist from these infants at the ages of 6, 9, 12, 15, 18, 21, and 24 months. DNA was extracted from whole blood samples and *Plasmodium falciparum* parasitemia determined by Real-time PCR. The incidence of severe clinical infections was determined based on clinical data collected by the study team at all scheduled follow-up visits and voluntary sick visits. Chi-Square tests were used to compare the proportions of *Pf* positive samples in the HEU and the HUU infants and to determine differences in proportions of severe clinical infections at individual time points. Risk and odd ratios were used to determine the association between severe clinical infections and malaria in HIV exposed and unexposed infants. Student t-test was used to determine the difference in means at birth and 6-months of the anthropometric measures; weight (birth, p=0.1449; 6-months, p=0.5325), height (birth, **p=0.0236**; 6-months, p=0.1831) and head circumference (birth, p=0.6415; 6-months, p=0.1710) as well as the mean total malaria diagnosis (**p=0.0029**) between the two exposure groups. HUU infants had a greater proportion of "any-malaria" (**p=0.0004**) and total number of malaria episodes per infant (**p=0.0029**) than HEU infants. Maternal HIV status was not related to the outcome of severe clinical events (p=0.1295), with HEU infants having a lower but not statistically significant risk and odds of bacterial related severe clinical events outcome, than their HUU counterparts: diarrhea with severe dehydration (p=0.7817), severe pneumonia (p=0.3317) and severe malaria (p=0.0954) as determined by Pearson's Chi-square test between the two exposure groups. Thus, the data suggests that the likelihood of severe clinical bacterial infections is greater in HUU infants compared to HEU infants. The findings of this study may be attributed to the positive effects of healthcare interventions such as Cotrimoxazole prophylaxis treatment, insecticide treated bed net use, adherence to chemoprevention regimen by HEU infants and exclusive breastfeeding. This calls for a keen focus on HUU infants who are presumed to be healthier but seem to bear a greater burden of malaria infections and severe-bacterial clinical events. These findings are important for healthcare provision to both HEU and HUU infants residing in HIV and malaria co-endemic areas.