View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by AJOL - African Journals Online

J. Afr. Ass. Physiol. Sci. 7 (1): 53-58, July 2019

Journal of African Association of Physiological Sciences

Official Publication of the African Association of Physiological Sciences

http://www.jaaps.aapsnet.org

Research Article

Co-infection of *Plasmodium falciparum* and HIV among pregnant women in Edo State, Nigeria

F.O. Akinbo[1], T.A. Olowookere[1], M.O. Oriakhi[2]

[1]Department of Medical Laboratory Science, University of Benin, Benin City, Nigeria and [2]Department of Obstetrics and Gynaecology, Central Hospital, Benin City, Nigeria

Keywords:
Edo State, HIV, pregnancy, P. falciparum Co-infection

ABSTRACT

Background: *P. falciparum* and HIV diseases affect the poorest group of a population that are made vulnerable by the lack of access to quality education, information and health facilities, all of which are characteristic of sub-Saharan Africa. This study was conducted to determine the co-infection of *P. falciparum* and HIV among pregnant women in Edo State, Nigeria. **Methods:** A total of 459 HIV infected pregnant women attending antenatal clinics at the Central Hospital Benin City, were enrolled. The age of participants ranged from 20 – 48 years. Blood specimens were collected from participants and analysed for HIV and *P. falciparum* detection, full blood count and $CD4^+$ T cells count estimation. Chi squared (X^2) was used for frequency data whereas odd ratio (OR) was analysed for each potential risk factor. **Results:** An overall prevalence of 27.2% of *P. falciparum* infection among HIV infected pregnant women in Edo State, Nigeria was observed. HIV infected pregnant women that are 20-29 years age group, those single, primary school leavers, traders, first trimester, primiparous, use of insecticide-treated bed nets, rainy season and anaemia significantly affected the prevalence of *P. falciparum* infection (P<0.0.0001). **Conclusion:** The administration of intermittent preventive treatment (IPT) as early as possible during pregnancy, use of insecticide-treated bed nets and effective and prompt malaria management are advocated.

© Copyright 2019 *African Association of Physiological Sciences* -ISSN: 2315-9987. All rights reserved

INTRODUCTION

Malaria and HIV infections are among the most important public health problems worldwide (UNAIDS, 2012). Malaria is prevalent in resource-poor settings, particularly occasioned by poverty, caused by inadequate sewage treatment, poor hygiene and substandard housing (Gallup and Sachs, 2001). Malaria remains one of the challenging infections affecting the lives of many HIV infected pregnant women in sub-Saharan Africa (WHO, 2004). It is estimated that about 24 million pregnant women are affected by *P. falciparum* yearly, majority of which are from sub-Saharan Africa and about 1 million are co-infection with HIV (Steketee *et al.*, 2001; WHO, 2004). HIV infection constitutes the leading cause of death among women of reproductive age and as such is considered an important maternal problem worldwide (Tang and Nour, 2010). HIV infected pregnant women are at increased risk of maternal anaemia, adverse pregnancy outcomes including low birth weights, stillbirths, infant morbidity and high mortality (Braddick *et al*., 1990; Robbins *et al*., 2007; Naniche *et al*., 2009; Zaba *et al*., 2013).

It has been reported that HIV infected pregnant women have an increased susceptibility to malaria (van Eijk *et al*., 2003). The co-infection of malaria and HIV infection have been reported to cause more than 4 million deaths annually (WHO, 2003). HIV and malaria epidemics overlap in sub-Saharan Africa (Meshnick *et al*., 2006). *P. falciparum* and HIV diseases affect the poorest group of a population that are made vulnerable by the lack of access to quality education, information and health facilities, all of which are characteristics of sub-Saharan Africa (Kwenti, 2018). These two diseases interactions are particularly significant in pregnant women as they form one of the most vulnerable population groups in sub-Saharan Africa (Uneke and Ogbonna, 2009). The interactions between the two diseases are bidirectional

*Address for correspondence:
Email: fredrick.akinbo@uniben.edu
Tel: +2348033796874

with each disease exacerbating the other (Gonzalez *et al*., 2012; Gonzalez and Naniche, 2015).

In Nigeria, both diseases are still serious life-threatening problems among pregnant women. *P. falciparum* and HIV are among the leading causes of morbidity in pregnancy where modest effects of one infection on the other could lead to a substantial negative impact on the health of pregnant women and the neonates (Corbett *et al*., 2002). Without a timely intervention, it is estimated that approximately 25 – 45 % of the HIV infected women will transmit infection to their children (Dabis and Ekpini, 2002). Information is lacking on the co-infection of *P. falciparum* and HIV among pregnant women in Edo State, Nigeria. As such pregnant women and their foetuses are exposed to the risk of malaria and HIV infections as both diseases overlap in Edo State. Against this background, this study was conducted to determine the co-infection of *P. falciparum* and HIV among pregnant women in Edo State, Nigeria.

METHODS

Study area

The study was conducted at the Central Hospital, Benin City, Edo State, a secondary referral health institution and a centre for HIV/AIDS management.

Study population

This study was conducted between November 2018 and June 2019 at the Central Hospital, Benin City, Edo State. A total of 459 HIV infected pregnant women attending antenatal clinics at the Central Hospital, Benin City were enrolled in this study. HIV infected pregnant women on HAART attending antenatal care clinics, those that were 20 years and above and those that consented to participate in the study were enrolled. Pregnant women that were less than 20 years and those with life-threatening medical and obstetrical conditions and those not on HAART were excluded from this study. The agents used in the HAART regimen for HIV infected patients consist of zidovudine, lamividine and nevirapine. A well- structured questionnaire bothering on biodata and sociodemographic characteristics was administered to each participant. Informed consent was obtained from study participants prior to specimen collection. The protocol for this study was approved by the Ethics and Research Committee of the Ministry of Health, Benin City, Edo State.

Collection of specimens

About 5 ml of venous blood was obtained from each participant and dispensed into ethylene diamine tetra acetic acid containers.

About 5 ml of venous blood was obtained from each participant and dispensed into ethylene diamine tetra acetic acid containers.

Processing of specimens

Pregnant women were screened for HIV using the Determine HIV 1/2 rapid immunoassay test strip. Positive cases were confirmed using the trinity Unigold HIV 1/2 kit (CDC, 2014).

Thick and thin blood films were made from each blood specimen, allowed to air-dry and stained in 1:10 dilution of Giemsa stain for 30 min. The stained blood films were rinsed in buffer solution and allowed to air dry. The stained thick films were examined for malaria parasites detection whereas the thin blood film was used for speciation by light microscopy. A total of 200 high power fields per blood film were examined (Cheesbrough, 2000).

The blood samples were analysed for full blood count using an auto-analyser Sysmex Kx-21 (Sysmex Corporation, Kobe, Japan). Anaemia was determined using haemoglobin concentration <11g/dl for pregnant women (Beutler and Waalen, 2006).

$CD4^+$ T cells counts were determined using the flow cytometry (Partec, Gmbh, Germany). Briefly, 20µL of monoclonal antibodies were added and incubated in the dark for 15 min at room temperature after which 800µL of buffer was added. The tube containing the mixture was plugged to the flow cytometer for counting and the value of $CD4^+$T cells obtained from a programmed monitor connected to the flow cytometer.

Data analysis

The data obtained were analysed using Chi squared (X^2) test in comparing the frequency data while the odd ratios (OR) were calculated for potential risk factors at 0.05 significance level. The statistical package used in the data analyses was INSTAT® (GraphPad software Inc, La Jolla, CA, USA).

RESULTS

Out of the 459 HIV infected pregnant women attending antenatal clinics at the Central Hospital, Benin City, 125 (27.2%) had *P. falciparum* infection. Age significantly affected the prevalence of *P. falciparum* infection among HIV infected pregnant women (P=0.0183) with the 20-29 years age group having the highest prevalence (31.1%). Marital status strongly affected *P. falciparum* infection among HIV infected pregnant women (P=0.0050) where single HIV infected pregnant women had the highest prevalence (44.3%). HIV infected pregnant women who are primary school leavers presented with the highest prevalence of *P. falciparum* (49.3%) followed by those with tertiary education

(20.7%) and the least was those with secondary education (17.6%). In addition, educational status significantly affected the prevalence of *P. falciparum* infection among HIV infected pregnant women. Traders were significantly more prone to *P. falciparum* infection among HIV pregnant women (P<0.0001). HIV infected pregnant women in their first trimester were more likely to be infected with *P. falciparum* (P<0.0001). Primiparous HIV infected pregnant women were more prone to malaria infection (P<0.0001) with a 1 to 4-fold risk of acquisition. Participants that used insecticide treated bed nets had significantly lower prevalence of *P. falciparum* infection (P=0.0021). Seasonal variation significantly affected the prevalence of *P. falciparum* infection among HIV infected pregnant women (P<0.0001) with the rainy season recording higher prevalence (45.5%) than the dry season (14.4%) (Table 1).

Table 1: Relationship between demographic characteristics and co-infection of *P. falciparum* and HIV among pregnant women

Characteristic	No. Tested	No. infected (%)	OR	95% CI	P value
Age (year)					
20-29	305	95(31.1)			0.0183
30-39.	124	22(17.7)			
40 & Above	30	8(26.6)			
Marital status					
Single	70	31(44.3)			0.0050
Married	351	83(23.6)			
Divorced.	23	6(26.1)			
Widowed.	15	5(33.3)			
Educational status					
Primary	146	69(47.3)			<0.0001
Secondary	284	50(17.6)			
Tertiary	29	6(20.7)			
Occupational status					
Trader	84	40(47.6)			<0.0001
Civil servant	91	9(9.9)			
Artisan	192	59(30.7)			
Business woman	92	17(18.5)			
Gestational age					
First trimester	138	56(40.6.)			<0.0001
Second trimester	192	49(25.5)			
Third trimester	129	20(15.5)			
Parity					
Primiparous	204	79(38.7)			<0.0001
Multiparous	255	46(18.0)			
Preventive measures					
Insecticide	67	23(34.3)			0.0021
Insecticide treated net.	189	5(18.5)			
Window netting	203	67(33.0)			
Seasonal variation					
Rainy season	189	86(45.5)	4.945	3.172, 7.710	<0.0001
Dry season	270	39(14.4)			

OR=Odd ratio; CI=Confidence interval; * *P*<0.05

There was a strong association between anaemia and *P. falciparum* infection among HIV infected pregnant women (OR=4.738; 95% CI= 2.851, 7.875; P<0.0001). $CD4^+$ T cells less than 200cells/μL did not strongly associate with the prevalence of *P. falciparum* infection among HIV infected pregnant women (P=0.9081) (Table 2).

DISCUSSION

Human immunodeficiency virus and malaria infections represent the most important health problems in sub-Saharan Africa, where these infections overlap and co-infection is rampant (Abu-Raddad *et al*., 2006). Co-infection with malaria and HIV presents specific complications for pregnant women and foetal development. The interactions between these two diseases during pregnancy are complex (Guyatt and Snow, 2004) thus, putting the life of the pregnant women and their unborn babies at risk of medical and poor obstetrical conditions and threatening antiretroviral and antimalarial treatments effectiveness. To our knowledge, this is the first study on the co-infection of *P. falciparum* and HIV among pregnant women in Edo State, Nigeria.

An overall prevalence of 27.2% of *P. falciparum* infection was observed among HIV infected pregnant women in Edo State. The prevalence of 27.2% reported in our study is lower than the 33.4% observed by Houmsou *et al*. (2014) in Benue State, Central Nigeria, the 47.7% reported by Sanyaolu *et al*. (2013) in Lagos, South West Nigeria and 49.83% recorded by Johnbull *et al*. (2014) in Enugu, South East Nigeria. In areas with stable malaria transmission such as our study area, HIV has been reported to increase the risk of malaria infection and clinical malaria in adults, especially those with advanced immunosuppression (Berg *et al*., 2014). The difference in our work and that of other studies may be attributed to geographical locations and the efforts of the MTCT unit at caring for HIV-infected pregnant women and ensuring compliance in taking their medications.

Table 2: Effect of anaemia and $CD4^+$ T cell counts on the co-infection of *P. falciparum* and HIV in pregnant Women; **P*<0.05

Parameter	No. Tested	No. infected (%)	OR	95% CI	P value
Anaemia					
<11g/dl	269	103(38.3).	4.738.	2.851, 7.875	<0.0001
>11g/dl	90	22(11.6)			
CD4 Count					
<200 cells/μL.	131	35(26.7)	0.9641.	106, 1.522	0.9081
>200	328.	27.4(27.4)			

Age has been reported as a co-factor in disease progression, and the immunity to malaria and HIV infection has been observed to be age-dependent (Schwartz *et al*., 2001). In this study, age significantly affected the prevalence of *P. falciparum* infection

among HIV infected pregnant women (P=0.0183) with the 20-29 years age group having the highest prevalence (31.1%). This finding is in contrast to that observed by Houmsou *et al*. (2014) that did not find an association between malarial infection in HIV infected pregnant women in Benue State, Nigeria.

Being single strongly associated with *P. falciparum* infection among HIV infected pregnant women (P=0.0050). This finding is at variance with the report of Houmsou *et al*. (2014) that observed increased malaria infection among divorcees. The reason for the difference may be due to the fact that singles are more likely to engage in several occupations that may expose them to mosquito bites.

In this study, educational status significantly impacted on the prevalence of *P. falciparum* infection (P<0.0001) where those with primary school education presented with the highest prevalence (47.3%).

Traders were observed to be more likely to acquire *P. falciparum* infection among HIV infected pregnant women (P<0.0001). This is because they are exposed to the bite of mosquitoes as they carry out their activities mostly around breeding mosquito sites. This may explain the reason for this finding.

HIV infected pregnant women who are in their first trimesters were found to be at risk in acquiring *P. falciparum* (P<0.0001) when compared with other trimesters which imply that most of the women enrolled in our study are at risk of adverse pregnancy outcomes. This finding is in tandem with the previous study of Houmsou *et al.* (2014) that observed that HIV infected pregnant women in their first trimester are more likely to be infected with *P. falciparum*. It has been observed that pregnant women in their first trimester are unlikely yet to be administered sulphadoxine-pyrimethamine used as the intermittent preventive treatment (IPT) that are usually given only to women at their second and third trimesters (Houmsou *et al.*, 2014).

First pregnancy is believed to be the most critical as women develop pregnancy-specific immunity against placental parasites over successive pregnancies resulting from repeated exposure (Flateau *et al*., 2011). Albeit, available information suggest that women who are infected with HIV have the same low level of immunity to malaria in subsequent pregnancies as they do in their first pregnancy and are twice as susceptible to clinical malaria, which increases the risk of adverse outcomes (Brenthinger *et al*., 2006; Flateau *et al*., 2011). In our study, primiparous HIV infected pregnant women are at 1 to 4 -fold increased risk of acquiring *P. falciparum* infection when compared with their multiparous counterparts (OR=2.871; 95% CI= 1.876, 4.396; P<0.0001).

Generally, the use of insecticide treated bed net is a recognized effective way of preventing malaria infection (Akinbo *et al.,* 2014). HIV infected pregnant women that used insecticide treated bed nets had significantly the least prevalence of *P. falciparum* infection (18.5%; P=0.0021) compared with other preventive measures. The World Health Organization recommends a three-pronged approach for malaria control during pregnancy in sub-Saharan Africa: intermittent preventive treatment (IPT), insecticide treated bed nets and effective case management of malaria illness (WHO, 2012). Thus, HIV infected pregnant women be issued and encouraged to use insecticide treated bed nets in order to reduce the adverse pregnancy outcomes occasioned by *P. falciparum* infection.

Parasite transmission and development are regarded to be influenced by climatic conditions particularly within the temperature range of 25-30^{o}C (Egbendewe-Mondzozo *et al*., 2011). There is a direct influence of temperature and rainfall on the number and productivity of breeding sites, ultimately the vector density (Afrane *et al*., 2012). This study observed *P. falciparum* infection peaked during rainy season among HIV infected pregnant women (P<0.0001). Rainy season has been reported to provide ecological changes favouring the breeding of the mosquito vectors which enhance the transmission of malaria (Erhabor *et al.,* 2014).

HIV infected pregnant women with malaria had a 2 to 7-fold higher risk of developing anaemia (OR= 4.738; 95% CI= 2.851, 7.875; P<0.0001). This observation agrees with previous reports of Johnbull *et al*. (2014) and Houmsou *et al*. (2014). The cause of anaemia in pregnancy is multifactorial and may include haemodilution infections particularly HIV and malaria, inadequate erythropoiesis (Agan *et al*., 2010). Both HIV and malaria are known causes of maternal anaemia (Moses et al., 1998; Guyatt and Snow, 2001). In addition, the presence of zidovudine among the HAART regimen used by our subjects and antibodies to HAART agents have been reported to be associated with anaemia (Moyle, 2002). The risk of anaemia secondary to malaria and HIV infection could be reduced through prompt, effective treatment and follow up during pregnancy in order to increase the chances of delivering a healthy infant. Adequate information about nutritional diet could also play a big role in reducing adverse pregnancy outcomes necessitated by anaemia.

It has been reported that independently, HIV and malaria interact with the host immune system to bring about complex activation of immune cells, which causes dysfunctional levels of cytokine and antibody production (Hochman and Kim, 2009). Furthermore, $CD4^{+}$ T cells play a major part in the development and

maintenance of antimalaria immunity, but HIV interferes with immunity (Troye-Blomberg and Berzins, 2008) by widespread lymphoid necrosis throughout the lymph nodes, spleen, and gut mucosae, hyperactivation of $CD4^+$ and $CD\ 8^+$ effector cells to secrete cytokines, HIV induced downregulation of $CD4^+$ T cells, decreases in $CD8^+$ T-cells counts, and upregulation of parasitemia, consequently leading to fatal malaria and a rapid progression to AIDS (Ryan-Payseur *et al.*, 2011). Surprisingly, $CD4^+$ T-cells count did not strongly associate with co-infection of malaria and HIV among pregnant women in this study (OR= 0.9641; 95% CI = 0.6106, 1.522; P=0.9081). The low malarial infection observed in those with $CD4^+$ T cell counts greater than 200 cells/μL could be the reconstitution of their immune system due to highly active antiretroviral therapy (HAART) or recently infected pregnant women that still have strong immune system. This may explain the reason for our finding.

CONCLUSION

This study reveals a prevalence of 27.2% of *P. falciparum* infection among HIV infected pregnant women in Edo State, Nigeria. HIV infected pregnant women that are 20-29 years age group, those single, primary school leavers, traders, first trimester, primiparous, those that use insecticide treated bed nets and rainy season significantly affected the prevalence of *P. falciparum* infection in this study (P<0.0001). In addition, anaemia strongly associated with *P. falciparum* infection among HIV infected pregnant women (P<0.0001). The administration of intermittent preventive treatment as early as possible during pregnancy, use of insecticide-treated bed nets and effective and prompt malaria management are advocated.

ACKNOWLEDGEMENTS

Authors acknowledge the participants used in this study for their cooperation and the Hospital Management Board for allowing us to use their laboratories.

REFERENCES

Abu-Raddad LJ, Patnaik P, Kublin JG. (2006) Dual infection with HIV and malaria fuels the spread of both diseases in sub-Saharan Africa. *Science*. 314(5805): 1603-1606.

Afrane YA, Lawson BW, Brenya R, Kruppa T, Yan G. (2012). The ecology of mosquitoes in an irrigated vegetable farm in Kumasi, Ghana: abundance, productivity and survivorship. *Parasit Vectors*. 5: 233.

Agan TU, Ekabua JE, Iklaki CU, Oyo-Ita A, Ibanga I. (2010). Prevalence of asymptomatic malaria parasitaemia. *Asian pacific journal of tropical medicine*. 2:1–5.

Akinbo FO, Osanyinbi BI, Omoregie R, Ande ABA (2014). Asymptomatic Malaria among pregnant women in Edo State. *Journal of Medicine and Biomedical Research*. 13(1): 61-69.

Braddick MR, Kreiss JK, Embree JB, Datta P, Ndinya-Achola JO, Pamba H, Maitha G, Roberts PL, Quinn TC, Holmes KK. (1990) Impact of maternal HIV infection on obstetrical and early neonatal outcome. *AIDS*. 4(10): 1001-1005.

Berg A, Patel S, Aukrust P, David C, Gonca M, Berg ES, Dalen I, Langeland N. (2014) Increased severity and mortality in adult co-infected with malaria and HIV in Maputo, Mozambique: a prospective cross-sectional study. *PloS One*. 9(2): e88257.

Beutler E, Waalen J. (2006) The definition of anemia: What is the lower limit of normal of the blood hemoglobin concentration? Blood. 107: 1747–1750.

Brentlinger PE, Behrens CB, Micek MA. (2006) Challenges in the concurrent management of malaria and HIV in pregnancy in sub-Saharan Africa. *Lancet Infect Dis.* 6(2): 100-111.

CDC (2014) Laboratory testing for the diagnosis of HIV infection: Updated Recommendations.

Cheesbrough M. (2000) Medical Laboratory Manual for Countries Part 2. Cambridge University Press. Cambridge. UK. 2nd edition. 2000.

Corbett EL, Steketee RW, ter Kuile FO, Latif AS, Kamali A, Hayes RJ. (2002) HIV-1/AIDS and the control of other infectious diseases in Africa. *Lancet*. 359: 2177-2187.

Dabis F, Ekpini ER. (2002) HIV-1/AIDS and maternal and child health in Africa. *Lancet*. 359: 2097-2104.

Egbendewe-Mondzozo A, Musumba M, McCarl BA, Wu X. (2011) Climate change and vector-borne diseases: an economic impact analysis of malaria in Africa. Intern J Environ Res Public Health. 8: 913-930.

Erhabor O, Mohammed HJ, Ahmed HM, Ezimah ACU. (2014) Effect of Plasmodium Parasitaemia on some Haematological Parameters in Children Living in Sokoto, North Western, Nigeria. *Intern J Clin Med Res.* 1(22): 57-64.

Flateau C, Le Loup G, Pialoux G. (2011) Consequences of HIV infection on malaria and therapeutic implications: a systemic review. *Lancet Infect Dis*. 11(7): 541-546.

Gallup JK, Sachs JD (2001) The economic burden of malaria. *Am J Trop Med Hyg*. 64(1): 85-96.

Gonzalez R, Ataide R, Naniche D, Menendez C, Mayor A. (2012) HIV and malaria interactions:where do we stand? *Expert Rev Anti Infect Ther*. 10(2): 152-165.

Gonzalez R, Naniche D. (2015) HIV and malaria interaction in the pregnant women. Springer Sci. doi 10.1007/978-1-4614-8757-967-1.

Hochman S, Kim K. (2009) The impact of HIV and malaria coinfection: what is known and suggested venues for further study. Interdiscip Perspect *Infect Dis.* 2009: 617-954.

Guyatt HL, Snow RW. (2001) The epidemiology and burden of *Plasmodium falciparum* -related anaemia among pregnant women in sub-Saharan Africa. *Am J Trop Med Hyg.* 64: 36-44.

Guyatt HL, Snow RW. (2004) Impact of malaria during pregnancy on low birth weight in sub-Saharan Africa. *Clin Microbiol Rev.* 17(4): 760-769.

Houmsou RS, Wama BE, Elkanah SO, Garba LC, Hile TD, Bingbeng JB, Kela SL, Amuta EU (2014) Malarial infection in HIV infected pregnant women attending a rural antenatal clinic in Nigeria. *Adv Epidemiol*. doi.org/10.1155/2014/6994213.

Johnbull OS, Uche AP, Kesiena AJ, Francis FA, Oyemocho A, Obianwu IM, Akabueze J. (2014). Prevalence and risk factors of malaria in HIV-infected pregnant women on antiretroviral therapy in Enugu, South East Nigeria. *J AIDs Clin Res*. 5: 321-326.

Kwenti TE. (2018) Malaria and HIV coinfection in sub-Saharan Africa:prevalence, impact, and treatment strategies. *Res Rep Trop Med*. 9: 123-136.

Meshnick SR, Nwapasa V, Rogerson SJ (2006). Protecting pregnant women from malaria in areas of high HIV infection prevalence. *J Infect Dis*. 194: 273-275.

Moses A, Nelson J, Bagby GC Jr. (1998) The influence of human immunodeficiency virus-1on hematopoiesis. *Blood.* 91: 1479-1495.

Moyle G. (2002) Anaemia in persons with HIV infection: Prognostic marker and contributor to morbidity. *AIDS Rev.* 4: 13-20.

Naniche D, Bardaji A, Lahuerta M, Berenguera A, Mandomando I, Sanz S, Aponte JJ, Sigauque B, Alonso PL, Menendez C. (2009) Impact of maternal human immunodeficiency virus infection on birth outcomes and infant survival in rural Mozambique. *Am J Trop Med Hyg.* 80(5): 870-876.

Rollins NC, Coovadia HM, Bland RM, Coutsoudis A, Bennish ML, Patel D, Newell ML (2007) Pregnancy outcomes in HIV-infected and uninfected women in rural and urban South Africa. *J Acquir Immune Defic Syndr*. 44(3): 321-328.

Ryan-Payseur B, Ali Z, Huang D, Chen CY, Yan L, Wang RC, Collins WE, Wang Y, Chen ZW (2011). Virus infection stages and distinct TH1 or Th17/Th22 T-cell responses in malaria/SHIV coinfection correlate with different outcomes of disease. *J Infect Dis*. 204(9): 1450-1462.

Sanyaolu AO, Fagbenro-Beyioku AF, Oyibo WA, Badaru OS, Onyeabor OS, Nnameka CI. (2013) Malaria and HIV co-infection and their effect on haemoglobin levels from three healthcare institutions in Lagos, South West Nigeria. *Afr Health Sci.* 13(2): 295-300.

Schwartz E, Sadetzki S, Murad H, Raveh D. (2001) Age as a risk factor for severe *Plasmodium falciparum* malaria in non-immune patients. *Clin Infect Dis.* 33: 1774-1777.

Steketee RW, Nahlen BL, Parise ME, Menendez C. (2001) The burden of malaria in pregnancy in malaria-endemic areas. *Am J Trop Med Hyg*. 64: 28-35.

Tang J, Nour NM (2010) HIV and pregnancy in resource-poor settings. *Rev Obstet Gynae.* 3(2): 66-71.

Troye-Blomberg M, Berzins K. (2008) Immune interactions in malaria co-infections with other endemic infectious diseases: implications for the development of improved disease interventions. *Microbes Infect.* 10(9): 948-952.

UNAIDS. (2012) Global report: UNAIDS report on the global AIDS epidemic. 2012. Geneva. WHO UNAIDS/JC2417E.

Uneke CJ, Ogbonna A. (2009) Malaria and HIV co-infection in pregnancy in sub-Saharan Africa: Impact of treatment using antimalarial and antiretroviral agents. *Trans R Soc Trop Med Hyg.* 109(8): 761-767.

Van Eijk AM, Ayisi JG, ter Kuile FO, Misore AO, Otieno JA, Rosen DH, Kager PA, Steketee RW, Nahlen BL. (2003) HIV increases the risk of malaria in women of all gravidities in Kisumu, Kenya. AIDS. 17(4): 595-603.

WHO. (2003) The African Malaria Report 2003. Geneva. 2003; World Health Organization.

WHO. (2004) Malaria and HIV/AIDS interactions and their implications for public health policy. Report of a technical consultation. 23-25 June 2004. Geneva. 2004; World Health Organization.

WHO. (2012) Intermittent Preventive Treatment of malaria in pregnancy using Sulfadoxine-Pyrimethamine. Updated WHO Policy Recommendations. WHO; 2012. Geneva.

Zaba B, Calvert C, Martson M, Isingo R, Nakiyingi-Miiro, J, Lutalo T, Crampin A, Robertson L, Herbst K, Newell ML, Todd J, Byass P, Boerma T, Ronsmans C. (2013) Effect of HIV infection on pregnancy-related mortality in sub-Saharan Africa: secondary analyses of pooled community-based data from the network for Analyzing Longitudinal Population-based HIV/AIDS data on Africa. *Lancet.* 20381(9879): 1763-1771.