IAA Journal of Biological Sciences 10(1):96-103, 2023. ISSN: 2636-7254

Risk Factors for Malaria Infection among Pregnant Women in Nigeria

Ogenyi Franca C.

Department of Hospitality and Tourism, Nexus International University Uganda.

ABSTRACT

Malaria, a disease caused by an infected female Anopheles mosquito, is completely preventable, treatable and curable. The disease is considered not just a regional but global priority with a death toll of about 400,000 people globally every year. The most vulnerable group to malaria and its negative consequences are the pregnant women and children under the age of five years. In pregnancy, malaria predisposes expectant mothers to an increased risk of anaemia, spontaneous abortions, stillbirths, premature deliveries, intra-uterine growth retardation and low birth weight babies, and these are all important causes of infant mortality. Accordingly, malaria during pregnancy remains a serious public health problem. The aim of this study was to ascertain the occurrence of malaria and possible risk factors for malaria infection among pregnant women in Nigeria. Nigeria, with a population of over two million, is the most populous country in Africa and occupying seventh position in the world. In Nigeria, there are about 110 million clinically diagnosed malaria cases and 300,000 malaria-related childhood deaths annually. Malaria in Nigeria, which already overburdens the already weakened health system, adversely affects the social and economic sectors of the country. Pregnant women are among the most susceptible to malaria infection. Knowledge of their malaria infection status is an important yardstick to measure the effectiveness of any malaria control programme.

Keywords: Malaria, Pregnant women, Risk factor and Knowledge.

INTRODUCTION

Malaria infection during pregnancy is a major public health problem in tropical and subtropical regions throughout the world. The burden of malaria infection during pregnancy is caused mainly by Plasmodium falciparum, the most common malaria species in Africa [1] cited in [2]. Uneke [3] stated that a number of factors influence the prevalence of placental malaria in pregnant women, including maternal age, gravidity, use of prophylaxis, nutrition, host genetics, and level of antiparasite immunity, as well as parasite genetics and transmission rates. Different studies have been carried out to determine the prevalence of malaria parasite in pregnancy. Adefioye et al., [1] carried out a study to examine malaria parasite infection in pregnant women in relation to their behaviour and social pattern of living as they affect their exposure to malaria parasite infection. The study subjects consisted of 250 pregnant women who came for their ante-natal visit at Ladoke Akintola University of Technology Teaching Hospital, Osogbo [4, 5, 6, 7]. The women were of varying age ranging from 20-40 years and also of different status, the prevalence of malaria parasite in pregnant women according to age were as follows: Of the 250 samples examined, 180 (72%) had malaria parasite in their blood [8, 9, 10, 11, 12]. The age group 36-39 years recorded the highest prevalence rate of 88.2%, followed by age group 32-35 years 76% prevalence rate. According to educational status of the women, the illiterate pregnant women had the highest prevalence rate of 78.3%. The least prevalence rate was recorded among educated patients (54.4%) with 550 mean parasite density [13, 14, 15, 16, 17, 18].

According to the study conducted by Bassey et al [4] cited in Emenike [2] on the profile of malaria in pregnant women

attending antenatal clinics in rural community in Nigeria, out of the 1400 pregnant women they screened, 1035 (73.9%) had detectable p. falciparum in their peripheral blood sample. The highest malaria prevalence in their study was among primigravidae (55.8%) followed by those having second pregnancy (28.9%) and multigravidae (15.3%) respectively. The prevalence of p. falciparum among pregnant women was highest in the first trimester 41.3%, and showed decline to 30.0% and 28.7% in the second and third trimesters respectively [19, 20, 21, 22]. Consequently, this study aims to ascertain the occurrence of malaria and possible risk factors for malaria infection among pregnant women in Nigeria. Nigeria, with a population of over two million, is the most populous country in Africa and occupying seventh position in the world. In Nigeria, there are about 110 million clinically diagnosed malaria cases and 300,000 malaria-related childhood deaths annually [23, 24,25,26,27]. Malaria in Nigeria, which already overburdens the already weakened health system, adversely affects the social and economic sectors of the country. Pregnant women are among the most susceptible to malaria infection. Knowledge of their malaria infection status is an important yardstick to measure the effectiveness of any malaria control programme.

Maternal Risk Factors associated with Malaria

Maternal factors associated with the risk of malaria in pregnancy include maternal age, parity and gestational age. It is well established that younger women (primigravidae and multigravidae), particularly adolescents, are at higher risk of malaria infection than older women [5; 6] and this is independent of parity. Parity also affects the risk of malaria as primigravidae are at higher risk than multigravidae [6; 7] though less in low transmission settings, while in epidemic areas, the risk is not affected by parity [8]. Most of the available data on malaria relate to the second and third trimesters [9; 10]. The peak of malaria prevalence seems to occur during the second trimester [11]. Studies on malaria burden in the first trimester of pregnancy are scarce, but it is believed that the rates are similar to that of the second trimester. However, considering the difficulty of collecting this information (pregnant women start to attend the antenatal clinic after the first trimester), and of determining the gestational age with accuracy, it is unclear whether the risk starts to increase towards the end of the first trimester.

Effects of Malaria Infection

The effect of malaria infection during pregnancy will depend on the degree of acquired immunity, which in turn depends on the intensity of transmission.

Maternal Effects

Where transmission is stable, such as in most of sub-Saharan Africa, most infections are asymptomatic but increase substantially the risk of anaemia [12]. This occurs over a background of physiological anaemia of pregnancy due to increased blood volume. Both symptomatic and asymptomatic infections can cause anaemia. Severe anaemia is more often observed in stable transmission settings [13], and more in primigravidae than in multigravidae. Malaria infections in the first or second trimester of pregnancy increase the risk of anaemia, though one study reported an increased risk also for infections occurring in the third trimester [14]. Preventing malaria infection by intermittent preventive treatment during pregnancy (IPTp) reduces the risk of anaemia. Where malaria transmission is unstable, malaria can cause maternal anaemia [15], more in primigravidae than in multigravidae and for falciparum infections more than for vivax infections [15]. Nevertheless, severe anaemia is less common in these settings. In places where malaria transmission is stable, little is known on the importance of malaria infection as

a cause of miscarriage. Where malaria transmission is unstable, malaria as a cause of miscarriage seems more common, as the majority of infections evolve towards a clinical attack with fever, which may by itself determine miscarriage. Indeed, non malarial fevers also independently increase the risk of miscarriage. Maternal mortality associated to malaria is probably under-reported. Malaria was an important cause of maternal death in some studies, while in others it was not as frequent. For instance, the substantial reduction in maternal mortality observed in Thailand after the implementation of early detection and treatment of malaria suggests that malaria is an important contributor to maternal mortality [16]. When not a direct cause of death (severe malaria), malaria in pregnancy is often reported as co-morbidity, e.g. with eclampsia, in conditions associated with maternal mortality.

Perinatal Effects

Malaria increases the risk of low birth weight (LBW), [17] particularly in primigravidae, and this risk seems to be higher for infections in first or second trimester, though in one study this was true also for infections occurring late in pregnancy. In high malaria transmission settings, such an effect is due to intrauterine growth retardation (IUGR) rather than pre-term delivery, as most infections are asymptomatic. A meta-analysis of cross-sectional data in Africa, showed malaria prevention in pregnancy is associated with 21% (95% CI= 14-27) reduction in LBW. In unstable transmission settings, preterm deliveries, still births and neonatal deaths have been associated with malaria [15]. P.vivax infections are also associated with LBW, and this effect appears to be similar in all pregnancies. In women with a single infection of P.vivax or P.falciparum detected and treated in the first trimester, no significant effect on gestation or birth weight was observed compared to women who also attended in the first trimester but who never had malaria detected in pregnancy [16].

New Born and Infant Effects

Fewer studies on malaria in pregnant women have evaluated infant outcomes. Congenital malaria can occur in the neonatal period and can contribute to infant morbidity and mortality [18]. Placenta malaria, especially active infection has been linked to neonatal and infant mortality. A recent study in The Gambia has shown that malaria infection during pregnancy influences infant's growth, independently of LBW [19]. It also increases the risk of infant's death and perinatal mortality, by causing LBW [3]. This is confirmed by the reduction neonatal mortality, up to 60%, observed after the implementation of preventive interventions targeted to pregnant women, e.g. intermittent preventive treatment. In primi- and secundi-gravidae, malaria prevention with IPTp or insecticide-treated bed nets was significantly associated with a 18% decreased risk of neonatal mortality.

Pathophysiology

Pregnant women are at higher risk of contracting malaria than non-pregnant women. This increased susceptibility can be explained by the immunological changes induced by pregnancy, by hormonal factors, and by the higher attractiveness of pregnant women to mosquitoes [10]. In addition, P. falciparum –infected erythrocytes in pregnant women bind to specific receptors, i.e. chondroitin sulphate A (CSA), and sequester in the placenta. They rarely bind to the other two commonly described receptors in non-pregnant individuals, i.e. CD and the intracellular adhesion molecule (ICAM-1). In pregnancy, the parasite antigens expressed on infected erythrocytes are collectively known as variant surface antigen- pregnancy associated malaria (VSA PAM). They are different from those expressed

in non-pregnant individuals and in stable transmission settings are not recognised by the immune system, explaining the higher risk in primigravidae.64 The binding of the variant surface antigen (VAR2CSA) with chondroitin sulphate A has been implicated in the pathology of falciparum malaria in pregnancy [19]. The VAR2CSA belongs to the family of the erythrocyte membrane protein (PfEMP1), is encoded by the var2csa gene and its expression has been described in pregnant women with falciparum malaria. Levels of anti-VAR2CSA specific IgGs increase with parity, cannot be found in men and are associated with a favourable pregnancy outcome so that the malaria risk decreases with increasing parity. Besides the antibody responses to VSA PAM, cytokine responses such as Th1, Th2, interleukins, TNF and regulators, IFN gamma, and monocytes [20] have been observed in pregnant women with malaria. Rosetting, a phenomenon consisting of parasite-free erythrocytes surrounding parasite-infected erythrocytes and commonly observed in non-pregnant individuals, has been implicated in the pathogenesis of severe malaria but is uncommon in pregnant women with falciparum malaria. The sequestration of P. vivax in the placenta, though until recently thought not to occur, has been described [21], with the involvement of ICAM-1 and CSA as receptors. The effects of hormonal changes on pregnancy associated malaria have been described in few studies and are subject to debate. Increased cortisol levels have been associated with increased risk of malaria in pregnant women. The increased attractiveness of pregnant women to mosquitoes may be explained by physiological and behavioural changes occurring during pregnancy. Physiological changes include increased exhaled breath and increased abdominal temperature that may render pregnant women more easily detectable by mosquitoes. Behavioural changes are represented by the fact that pregnant women urinate twice as frequently as non- pregnant women, resulting in an increased exposure to mosquito bites at night because they have to leave the protection of their bed nets [11]. Malaria-associated placental changes have been described for stable and unstable transmission settings [16]. They include presence of parasites, inflammatory changes and hemozoin (pigment) deposition. Placental changes have been characterized into four levels, i.e. acute (parasites present, malaria pigment absent), chronic (parasites and malaria pigment present), past infection (no parasite but pigment present) and no infection (both parasites and malaria pigment absent) [22].

Clinical Presentation

Diagnosis

The diagnosis of malaria in pregnancy is essential to prevent its deleterious effects to the mother and the foetus. Unfortunately, the clinical signs of malaria in pregnant women are usually non specific, and where transmission is stable, most infections are asymptomatic. Therefore, suspected malaria cases should be confirmed by parasitological diagnosis [23], usually by microscopy and/or rapid diagnostic tests. Nevertheless, other methods such as PCR and placental histology can be also used, though the latter can be done only after delivery so that it cannot be used for the management of infections occurring during pregnancy. Microscopy is one of the most widely used methods for diagnosing malaria, including during pregnancy. It has some advantages such as the possibility of determining the parasite density and species. However, its major disadvantage, besides the need of a regular power supply, is its sensitivity, which cannot go below 10-15 parasites per μl. Therefore, a substantial proportion of infected pregnant women would not be detected because of extremely low parasite densities or of parasites sequestered in the placenta, though both conditions have deleterious effects

on the mother's and her offspring's health. Rapid diagnostic tests (RDT), detecting circulating malaria antigens can also be used. Generally, the sensitivity of RDTs for the diagnosis of malaria in pregnancy is lower than that of microscopy. However, the time needed for the diagnosis is shorter than for microscopy and the training required for their use is minimal. Although RDT can detect malaria antigens, they cannot estimate the parasite density. The sensitivity of RDT on peripheral blood using peripheral microscopy as a reference test is estimated at 81% (95% CI= 55-95), and the sensitivity of RDT on placental blood was 81% (95% CI= 62-92) using placental microscopy as the reference. PCR, which detects parasite DNA, can also be used for the diagnosis of malaria infection but is not readily available in health facilities. In stable transmission settings, the sensitivity of PCR was >80% when using microscopy as the reference [24]. PCR sensitivity has not been estimated against placental histology as reference test.

Severe Malaria

Severe malaria in pregnancy is more common in unstable transmission settings because of the lower immunity pregnant women have. Generally, women in the second and third trimesters of pregnancy are at a higher risk of developing severe malaria compared to non-pregnant adults. In low transmission settings, severe malaria in pregnancy is usually associated with pulmonary oedema, hypoglycaemia and severe anaemia. Mortality in pregnant women with severe malaria and treated with either artesunate and quinine varied between 9% and 12% [25].

Prevention and Treatment

Prevention

The most widely used interventions to prevent malaria in pregnancy are insecticide-treated bed nets (ITN), including Long-Lasting Insecticidal Nets (LLINs), and intermittent preventive treatment in pregnancy (IPTp). While ITNs have shown a substantial reduction in malaria morbidity and mortality in children (Leenstra, et al, 2003) in pregnant women, it has been associated with a decrease in maternal parasitaemia (38%), anaemia (41%) and LBW (28%), and 47% reduction in maternal anaemia. In one study, there was no evidence of a reduction in anaemia and parasitaemia. IPTp is the administration of therapeutic doses of an antimalarial, currently sulfadoxine-pyrimethamine (SP), at least twice during pregnancy, in the second and third trimester, irrespective of the presence of a malaria infection. The WHO recommends its use and many sub-Saharan African countries have included it in their malaria control program. In stable transmission settings, many trials have shown that SP given as IPTp is efficacious in preventing the adverse consequences of malaria during pregnancy [6]. However, SP resistance represents a major threat. A study in Benin has showed that, despite the presence of molecular markers of resistance, SP remained efficacious. This has been confirmed by a review reporting that IPTp with SP is effective up to a certain level of SP resistance. Nevertheless, finding an alternative to SP for IPTp is important. Mefloquine (MQ), thanks to its long elimination half-life, could be a good alternative to SP as it would provide a long post-treatment prophylactic period. Indeed, a trial in Benin showed that for IPTp MQ was as good as SP in preventing LBW. MQ was more efficacious than SP in preventing placental malaria, clinical malaria and maternal anaemia at delivery. However, MQ was less well tolerated than SP, potentially compromising its large scale use as IPTp. There is no evidence that one of the methods is better than the other [13] and the combined use appears tobe better than individual use. A different approach however, is systematic screening for malaria infections at regular intervals and treatment of the positive women, which may be more appropriate in settings

where malaria transmission is low and the risk of infection between antenatal visits is also low. Similarly, it is recommended that pregnant women with malaria are treated after parasitological confirmation of the diagnosis, reducing the unnecessary exposure to antimalarials of both the mother and the foetus.

REFERENCES

[1]. Agbor-Enoh ST, Achur RN, Valiyaveettil M, Leke R, Taylor DW, and Gowda DC. (2003). Chondroitin sulfate proteoglycan expression and binding of Plasmodium falciparum-infected erythrocytes in the human placenta during pregnancy. Infect Immun. 2003; 71(5): 2455-61

[2]. Asa OO, Onayade AA, Fatusi AO, Ijadunola KT, and Abiona TC. (2008). Efficacy of intermittent preventive treatment of malaria with sulphadoxine-pyrimethamine in preventing anaemia in pregnancy among Nigerian women. Matern Child Health J. 2008; 12(6): 692-8

[3]. Ayoola OO, Whatmore A, Balogun WO, Jarrett OO, Cruickshank JK, and Clayton PE, (2012). Maternal malaria status and metabolic profiles in pregnancy and in cord blood: relationships with birth size in Nigerian infants. Malar J.; 11:75

[4]. Bardaji A, Sigauque B, Sanz S, Maixenchs M, Ordi J, Aponte JJ, Mabunda S, Alonso PL, and Menendez C. (2011). Impact of malaria at the end of pregnancy on infant mortality and morbidity. J Infect Dis. 2011; 203(5): 691-9

[5]. Bouyou-Akotet MK, Ionete-Collard DE, Mabika-Manfoumbi M, Kendjo E, Matsiegui PB, Mavoungou E, and Kombila M. (2003). Prevalence of Plasmodium falciparum infection in pregnant women in Gabon. Malar J. 2003; 2: 18

[6]. Chotivanich K, Udomsangpetch R, Suwanarusk R, Pukrittayakamee S, Wilairatana P, Beeson JG, Day NP, and White NJ. (2012). Plasmodium vivax adherence to placental glycosaminoglycans. PLoS ONE. 2012; 7(4): e34509

[7]. Cottrell G, Mary JY, Barro D, and Cot M. (2007). The importance of the period of malarial infection during pregnancy on birth weight in tropical Africa. Am J Trop Med Hyg. 2007; 76(5): 849-54.

[8]. Dondorp A, Nosten F, Stepniewska K, Day N, and White N. (2005). Artesunate versus quinine for treatment of severe falciparum malaria: a randomised trial. Lancet. 2005; 366(9487): 717-25.

[9]. Hamer DH, Singh MP, Wylie BJ, Yeboah-Antwi K, Tuchman J, Desai M, Udhayakumar V, Gupta P, Brooks MI, Shukla MM, Awasthy K, Sabin L, MacLeod WB, Dash AP, and Singh N. (2009). Burden of malaria in pregnancy in Jharkhand State, India. Malar J.; 8:210.

[10]. Huynh BT, Fievet N, Gbaguidi G, Dechavanne S, Borgella S, Guezo-Mevo B, Massougbodji A, Ndam NT, Deloron P, and Cot M, (2011). Influence of the timing of malaria infection during pregnancy on birth weight and on maternal anemia in Benin. Am J Trop Med Hyg. 2011; 85(2): 214-20.

[11]. Ismail MR, Ordi J, Menendez C, Ventura PJ, Aponte JJ, Kahigwa E, Hirt R, Cardesa A, and Alonso PL (2000). Placental pathology in malaria: a histological, immunohistochemical, and quantitative study. Hum Pathol. 2000; 31(1):85-93.

[12]. Kattenberg JH, Ochodo EA, Boer KR, Schallig HD, Mens PF, and Leeflang MM. (2011). Systematic review and meta-analysis: rapid diagnostic tests versus placental histology, microscopy and PCR for malaria in pregnant women. Malar J. 2011; 10: 321.

[13]. McGready R, Boel M, Rijken MJ, Ashley EA, Cho T, Moo O, Paw MK, Pimanpanarak M, Hkirijareon L,

Carrara VI, Lwin KM, Phyo AP, Turner C, Chu CS, van Vugt M, Price RN, Luxemburger C, ter Kuile FO, Tan SO, Proux S, Singhasivanon P, White NJ, and Nosten FH. (2012). Effect of early detection and treatment on malaria related maternal mortality on the north-western border of Thailand 1986-2010. PLoS ONE. 2012;

[14]. Ndyomugyenyi R, Clarke SE, Hutchison CL, Hansen KS, and Magnussen P. (2011). Efficacy of malaria prevention during pregnancy in an area of low and unstable transmission: an individually-randomised placebo-controlled trial using intermittent preventive treatment and insecticide-treated nets in the Kabale Highlands, southwestern Uganda. Trans R Soc Trop Med Hyg. 2011; 105(11): 607-16

[15]. Newman RD, Hailemariam A, Jimma D, Degifie A, Kebede D, Rietveld AE, Nahlen BL, Barnwell JW, Steketee RW, and Parise ME. (2003). Burden of malaria during pregnancy in areas of stable and unstable transmission in Ethiopia during a nonepidemic year. J Infect Dis. 2003; 187(11): 1765-72.

[16]. Parekh FK, Davison BB, Gamboa D, Hernandez J, and Branch OH. (2010). Placental histopathologic changes associated with subclinical malaria infection and its impact on the fetal environment. Am J Trop Med Hyg. 2010; 83(5): 973-80.

[17]. Poespoprodjo JR, Fobia W, Kenangalem E, Lampah DA, Warikar N, Seal A, McGready R, Sugiarto P, Tjitra E, Anstey NM, and Price RN. (2008). Adverse pregnancy outcomes in an area where multidrug-resistant plasmodium vivax and Plasmodium falciparum infections are endemic. Clin Infect Dis. 2008; 46(9): 1374-81

[18]. Rantala AM, Taylor SM, Trottman PA, Luntamo M, Mbewe B, Maleta K, Kulmala T, Ashorn P, and Meshnick SR. (2010). Comparison of real-time PCR and microscopy for malaria parasite detection in Malawian pregnant women. Malar J.; 9:269.

[19]. Tuikue Ndam NG, Salanti A, Bertin G, Dahlback M, Fievet N, Turner L, Gaye A, Theander T, and Deloron P. (2005) High level of var2csa transcription by Plasmodium falciparum isolated from the placenta. J Infect Dis. 2005; 192(2): 331-5

[20]. Valea I, Tinto H, Drabo MK, Huybregts L, Sorgho H, Ouedraogo JB, Guiguemde RT, van Geertruyden JP, Kolsteren P, and D'Alessandro U. (2012). An analysis of timing and frequency of malaria infection during pregnancy in relation to the risk of low birth weight, anaemia and perinatal mortality in Burkina Faso. Malar J. 2012;11:71.

[21]. van Eijk AM, Ayisi JG, Slutsker L, Ter Kuile FO, Rosen DH, Otieno JA, Shi YP, Kager PA, Steketee RW, and Nahlen BL. (2007). Effect of haematinic supplementation and malaria prevention on maternal anaemia and malaria in western Kenya. Trop Med Int Health. 2007; 12(3): 342-52

[22]. WHO (2010). Guidelines for the treatment of malaria, Second edition. 2010: Geneva, Switzerland. p. 1-32

[23]. Wilson NO, Ceesay FK, Obed SA, Adjei AA, Gyasi RK, Rodney P, Ndjakani Y, Anderson WA, Lucchi NW, and Stiles JK. (2011). Intermittent preventive treatment with sulfadoxine-pyrimethamine against malaria and anemia in pregnant women. Am J Trop Med Hyg. 2011; 85(1): 12-21.

[24]. Ugwu, O. P.C., Nwodo, O.F.C., Joshua, P. E., Odo, C. E., Bawa, A., Ossai, E. C. and Adonu C. C. (2013). Anti-malaria and Hematological Analyses of Ethanol Extract of Moringa oleifera Leaf on Malaria Infected Mice. *International Journal*

*of Pharmacy and Biological Sciences,*3(1): 360-371.

[25]. Ugwu Okechukwu P.C., Nwodo, Okwesili F.C., Joshua, Parker E., Odo, Christian E. and Ossai .(2013). Effect of Ethanol Leaf Extract of Moringa oleifera on Lipid profile of malaria infected mice. *Research Journal of Pharmaceutical, Biological and Chemical Sciences*, 4(1): 1324-1332.

[26]. Ugwu O.F.C., Nwodo, PE Joshua, CE Odo, EC Ossai, B Aburbakar (2023). Ameliorative effects of ethanol leaf extract of Moringa oleifera on the liver and kidney markers of malaria infected mice. *International Journal of Life Sciences Biotechnology and Pharma Research,* 2(2): 43-52.

[27]. Enechi OC, CC Okpe, GN Ibe, KO Omeje, PC Ugwu Okechukwu (2016). Effect of Buchholzia coriacea methanol extract on haematological indices and liver function parameters in Plasmodium berghei-infected mice. Global Veterinaria 16 (1), 57-66.