

## MALARIA IN PREGNANCY: A REVIEW

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### ABSTRACT

**Background:** Malaria remains highly endemic in many countries in sub-Saharan Africa. Pregnant women, more than other adults have been shown to have higher risks of contracting the disease. Malaria in pregnancy is associated with numerous adverse pregnancy outcomes and it remains a major public health challenge in this region.

**Materials and Methods:** A detailed literature search was conducted in Google scholar; PubMed and the Cochrane library to identify 74 articles relevant to understanding of malaria in pregnancy. Forty seven of these were original research papers (eighteen from Nigeria; seven from Burkina Faso; five from Ghana; three from Angola; two each from Cameroon, Thailand, India, and Malawi; and one each from Benin Republic, Gabon, Zambia, Kenya, Uganda, and the United Kingdom), while the remaining twenty seven comprised of systematic reviews, and reports of the WHO, CDC and the Nigerian Federal Ministry of Health.

**Result:** Malaria in pregnancy is associated with adverse pregnancy outcomes such as: low birth weight; abortions; pre-term delivery and maternal anaemia. Even though pregnant women are more vulnerable to malaria infection compared to other adults by virtue of their pregnancy state alone, some pregnant women are more vulnerable than others by virtue of their socio-demographic and obstetric characteristics. Placental infection seems to be the central point for the pathogenesis of these adverse outcomes associated with malaria infection during pregnancy.

**Conclusion:** Malaria in pregnancy remains a serious public health problem in malaria endemic regions. Wide spread adoption of insecticide treated nets and intermittent preventive treatment with suphadoxine-pyrimethamine have a strong potential of drastically reducing the presently observed undesirable effects of malaria in pregnancy.

**Keywords:** Malaria in pregnancy, associated factors, pathogenesis, prevention, treatment.

## 1.0 Introduction

According to the Centres for Disease Control (CDC), malaria is the second leading cause of infectious disease-related deaths after tuberculosis (CDC, 2007). The World Health Organisation (WHO) reports that an estimated twenty five million pregnancies are believed to occur annually in malaria-endemic regions of sub-Saharan Africa (WHO, 2004). Pregnant women have been reported to attract twice the number of anopheles mosquitoes compared to their non-pregnant counter parts (Lindsay et al., 2000). According to the Nigerian Federal Ministry of Health (FMOH), malaria in pregnancy accounts for 11% of maternal mortality in Nigeria (FMOH, 2005). It has dire consequences not only to the pregnant woman herself but also on the outcome of her pregnancy. It could also lead to complications like: early pregnancy loss (Butler et al., 1997); anaemia (Okafor et al., 2012); intra-uterine growth retardation, low birth weight, preterm delivery and infant mortality (Steketee et al., 2001). An estimated 75,000 to 200,000 infant deaths yearly have been attributed to malaria in pregnancy (Steketee et al., 2001). The aim of this study is to determine based on literature review, the enormity, pathogenesis, associated factors, as well as treatment and prevention of malaria in pregnancy.

## 2.0 Materials and Methods

A detailed literature search was conducted in Google scholar; PubMed and the Cochrane library. Search terms included: malaria in pregnancy; associated factors; pathogenesis; prevention and treatment. To determine suitability for inclusion, the titles and abstracts of the resulting articles were screened. Articles published from the year 2000 onwards were given preference however, a few very relevant articles published earlier were also included.

## 3.0 Result

A total of 74 published articles were selected for inclusion into this study. Forty seven of which were original research papers (eighteen from Nigeria; seven from Burkina Faso; five from Ghana; three from Angola; two each from Cameroon, Thailand, India, and Malawi; and one each from Benin Republic, Gabon, Zambia, Kenya, Uganda, and the United Kingdom), while the remaining twenty seven comprised of systematic reviews, and reports of the WHO, CDC and the Nigerian Federal Ministry of Health.

## 4.0 Discussion

### 4.1 Epidemiology of Malaria in Pregnancy

The prevalence of malaria in pregnancy has been varying in endemic areas. In countries like Nigeria, the prevalence seems to be consistently high all over the country. Of all adults groups, the prevalence of malaria has been highest among pregnant women, which has been

attributed to immunological and hormonal changes in their body (Samak, 2004). Prevalences as high as 48.1% (Isa et al., 2015); 54% (Nduka et al., 2006) and 72% (Adefioye et al., 2007) have been reported in Nigeria. In Ghana, 19.7 (Ofori et al., 2009), 47% (Clerk et al., 2009), 12.6% (Tay et al., 2013), 10.6% (Völker et al., 2017). In Burkina Faso, a prevalence of 18.1% has been reported (Cisse et al., 2014). In Angola, among pregnant women attending antenatal care centres, prevalence of 19.4% (Valente et al., 2011), 10.9% (Campos et al., 2012), and 9.6% (Sousa-Figueiredo et al., 2012) have been reported. Among pregnant women in the largest public hospital of Gabon the prevalence was 34.4% (Bouyou-Akolet et al., 2003). In Sanga-Maritime Division, Cameroun, the prevalence was 22.9% (Tonga et al., 2013), and 25.8% in Burkina Fasso (Tiono et al., 2009).

## **4.2 Factors Associated With Malaria in Pregnancy**

Even though pregnant women have been identified as a high risk group for malaria infection (Carrington, 2011), there are certain factors which make certain groups of pregnant women more vulnerable than others

### **4.2.1 Socio-demographic Factors**

The socio-demographic indicators used in most studies include: age; educational level; income and employment. However, the results for each of these factors have not always been consistent. A study among pregnant women in Burkina Faso reported a higher risk among those with no formal education when compared to those with some formal education (OR=1.9; 95% CI: 1.2-3.2) but there was no significant difference between age groups (Cisse et al., 2014). Among pregnant women at a health centre in Sudan, age and parity were not significantly associated with malaria infection (Adam et al., 2005). Another study in the South-west of Nigeria revealed, young maternal age less than 20 years to be associated with higher odds (OR=2.61; 95% CI: 1.13-6.03) of having malaria but there was no association with level of education (Agomo & Oyibo, 2013). Another study in North-western Nigeria had however shown lower prevalence of malaria with increasing level of education (Fana et al., 2015).

The only major risk factor for placental malaria after adjusting for relevant co-variables among pregnant women in Yaoundé was age less than 25 years (Tako et al., 2005). Among women from ante-natal care and delivery units in India, higher prevalence was also reported among those with informal education though this was not statistically significant (Sohail et al. 2015). In Sanga-Maritime, Cameroun, those pregnant women who earned less than 28,000 FCFA were more likely to have malaria compared to those who earned that amount or more (OR=3.9; 95% CI: 1.3-11.5). There was no difference between age groups and levels of education (Tonga et al., 2013). The risk of malaria in pregnancy has also been reported to be higher among women who did not attend ante-natal care (Coulibaly et al., 2007). The link between poverty and malaria still remains unclear. However, there is an important socio-economic differential in access to malaria interventions which is likely to make the poor more vulnerable (Worrall et al., 2005). Pregnant women residing in the peripheral areas, were also reported to be twice more likely to have malaria compared to those residing in the city centre (OR=2.0; 95% CI: 1.1-3.5) (Valente et al., 2011)

#### 4.2.2 Obstetric and Gynaecological Factors

In Koupela district, Burkina Faso higher risk ratios were reported for placental malaria among primigravidae (RR: 2.3; 95% CI: 1.6-3.3) and secundigravidae (RR=1.8; 95% CI: 1.2-2.7) when compared with multigravid women (Sirima et al., 2003). Similar findings were observed in Boromo district, Burkina Faso where primigravidae had a higher risk of malaria compared to multigravidae, but this risk declined with increasing gestational age (Coulibaly et al., 2007). Also in the same country, with reference to multi-gravidae, primigravidae (OR=2.1; 95% CI: 1.2-3.8) and secundigravidae (OR=5; 95% CI: 2.5-9.8) had higher risks of having malaria. However, there was no difference in risk for gestational age (Cisse et al., 2014). With regards to gestational age, another cross-sectional study among pregnant women at ANC centres and delivery units in India also revealed a greater than four folds risk for malaria among those in their first or second pregnancies compared to those in the third or more pregnancy (OR=4.23; 95% CI: 2.15-8.42). Also women of age less than 20 years were also at greater risk compared to older women (OR=2.47; 95% CI: 1.17-10.63) (Sohail et al., 2015).

In a sub-urban area in south-western Nigeria, the prevalence of malaria in pregnancy was higher among primigravidae and those in the lower age groups (Bolaji et al., 2014). Among pregnant women in Lagos, Gravity was not associated with any risk of having malaria (Agomo & Oyibo., 2013). Among pregnant women in Sudan, being in the third trimester was associated with a higher risk of malaria infection (OR=1.58; 95% CI: 1.02-2.4) (Adam et al., 2005). Multi-gravidity and being in the second trimester showed higher proportions of malaria, but these were not significant (Isa et al., 2015).

Three or more ante-natal care visits was associated with lower odds of having malaria in pregnancy compared to those who only had one or no visit at all. Those who had only two visits did not show any significant difference from those who had less number of visits (Sirima et al., 2006). A case control study in Zambia revealed that those who booked before their twenty first week (OR=0.51; 95% CI: 0.33-0.78) were less likely to be cases compared to those who booked at a later date; while those who received their last dose of intermittent preventive treatment with Fansidar before 36 weeks of gestation (OR=4.46; 95% CI: 2.58-7.71) and those with HIV infection (OR=1.7; 95% CI: 1.02-2.5) were more likely to be cases compared to those who received their last dose of SP after 36 weeks and those without HIV infection respectively (Gertrude et al., 2010).

#### 4.3 Complications of Malaria

Placental parasitaemia leads to impairment of foetal nutrition, resulting in low birth weight which in turn leads to impaired development and even survival (Steketee and Parise, 1996). Also, a rare complication which is also often neglected is congenital malaria. A prospective study in the North central of Nigeria among near term pregnant women with a prevalence of 13.82% malaria parasitaemia, revealed that 2.63% of their new born babies had congenital malaria (Omalu et al., 2012). In a prospective cohort study among pregnant women in Uganda, malaria within two weeks of delivery was associated with a twofold greater risk of having a stillbirth (OR=2.15; 95% CI: 1.04-4.46) (De Beaudrap et al., 2013).

In a region of low malaria transmission, malaria infection within the week before delivery was associated with an increased odds of infant mortality within one to three months of age (OR=4.0; 95% CI: 1.2-13.7) (Luxemburger et al., 2001). Among pregnant women in an area of seasonal malaria in Thailand, infection within the first trimester was associated with a

higher odds of miscarriage, which was higher for symptomatic (OR=3.99; 95% CI: 3.10-5.13) than for asymptomatic patients (OR=2.70; 95% CI: 2.04-3.59) (McGready et al., 2012). Among women who delivered in a district hospital in Kenya, there were significantly higher risks of severe anaemia and low birth weight as a result of malaria in pregnancy for women of all parities (Shulman et al., 2001). In a secondary health facility in Ibadan, the mean birth weight of neonates born to mothers with peripheral parasitaemia and placental parasitaemia were 138g and 122g respectively lower than those of their counterparts without malaria parasitaemia (Falade et al., 2010).

A cohort study among pregnant women with malaria parasitaemia in a Teaching Hospital in Pakistan showed that 14% had spontaneous abortion, 30% developed puerperal pyrexia, 6% had pre-term labour; and 9% of their babies died within the neonatal period (Saba et al., 2008). A systematic review in which studies from Nigeria were included, revealed a higher perinatal mortality rate in malaria endemic countries (50.5%/1,000; 95% CI: 35.5-65.5) compared to non-endemic countries (30.0/1,000; 95% CI: 25.7 – 34.3) (Geertruyden et al., 2004).

#### **4.4 Maternal Anaemia and Malaria in Pregnancy**

A haemoglobin concentration below 11 g/dl during pregnancy has been classified as anaemia by the World Health Organisation (WHO, 2001). In many African countries, a lower cut-off point of 10 g/dl is used (Abudu, 2004). In cases where haemoglobin concentration is not available, a haematocrit level of below 30% has been used to define anaemia in pregnancy (Ogbeide et al., 1994). The most common complication of *P.falciparum* infection is anaemia; and it is estimated that about 200,000 to 500,000 pregnant women in sub-Saharan Africa develop severe anemia (Steketee et al., 2001). In Nigeria, the weighted relative risk of maternal mortality from severe anaemia was 3.51 (95% CI: 2.05-6.0) (Brabin et al., 2001). Malaria in pregnancy was associated with a significantly lower mean haemoglobin concentration among pregnant women in Sudan [(9.4g/dl; 95% CI: 9.1-9.7) versus (10.7; 95% CI: 10.6-10.8);  $p<0.05$ ] (Adam et al., 2005). A higher odds of moderate or severe anaemia has been reported among primigravidae (OR=1.97; 95% CI: 1.52-2.56) and multigravidae (OR=1.45; 95% CI: 1.20-1.76) with malaria infection (Rogerson et al., 2000).

Even asymptomatic malaria had a positive correlation with anaemia among pregnant women in Ouagadougou, Burkina Faso (Douamba et al., 2012). Malarial anaemia is majorly microcytic hypochromic; but when parasitaemia is low, anemia is basically haemolytic and with high parasitaemia it is both haemolytic with inflammatory features (Ahiboh et al., 2008). Even sub-microscopic malaria infection was associated with a higher risk of maternal anaemia (Mockenhaupt et al., 2002). Intervillous infiltration by monocytes is believed to be the pathway through which malaria infection in pregnancy causes anaemia (Rogerson et al., 2003). Studies have revealed the possibility of a multi-factorial aetiology for maternal anaemia with diet also playing an important role (VanderJagt et al., 2007)

#### **4.5 Pathogenesis of Malaria in Pregnancy**

The female anopheles mosquito is responsible for transmitting the malaria parasite. Transfusion-transmitted malaria has also been reported (Owusu-Ofori et al., 2010). Infection starts following injection of sporozoites into the blood stream by infected mosquito during a blood meal. These sporozoites move to the liver where they multiply within the hepatocytes forming pre-erythrocytic schizonts which discharge merozoites into the blood stream. These

merozoites invade erythrocytes within which they undergo a ring stage during which they are basically dormant; then a trophozoite stage during which they are highly active and consume most of the erythrocyte's cytoplasm. They then undergo 4-5 rounds of binary division during a schizont stage, producing new merozoites which burst and infect new erythrocytes, and the cycle continues. In pregnant women, parasite infected red blood cells sequester in the intervillous spaces of the placenta binding to chondroitin sulphate A (Duffy, 2007) leading to pregnancy-associated malaria (Costa et al., 2006). This is followed by macrophage infiltration and the production of pro-inflammatory cytokines (Duffy, 2005). Immunity is developed with continuous exposures through the development of antibodies that block the adhesion of infected red blood cells to the placenta (Nunes and Scherf, 2007)

#### **4.6. Clinical Features of Malaria in Pregnancy**

Individuals with high level of parasitaemia may remain asymptomatic (Umaru and Uyaiabasi, 2015). In uncomplicated malaria, the initial symptoms are non-specific similar to a flu-like illness. Malaise, loss of appetite, dizziness, lassitude, desire to stretch limbs, myalgia, nausea, vomiting are usually experienced about two days prior to fever which is the hallmark of malaria (Warrel., 1993). For *P. falciparum* infection, the fever is initially irregular, but later becomes intermittent or continuous. Other features could include jaundice, rapid pulse (more than 120 beats /minute), increased respiratory rate and low blood pressure (systolic: 90-100mmHg) (Taylor & Strickland., 2000). Spontaneous post-partum clearance of *P.falciparum* parasitaemia was reported among pregnant women in Benin Republic and it has been suggested that since the placenta is the privileged site for sequestration of parasites, its presence is likely to facilitate persistent parasitaemia while its elimination would likely lead to rapid clearance (Bottero et al., 2011)

#### **4.7 Management of Malaria in pregnancy**

##### **4.7.1 Diagnosis of Malaria in Pregnancy**

Blood film microscopy is considered the gold standard for diagnosing malaria (Warhurst and Williams., 1996; Wongsrichanalai et al., 2007). Various forms of the parasite ranging from ring forms to gametocytes could be visualized in the red blood cells after staining (Warhurst and Williams., 1996). There are broadly two types of microscopy: thick blood and thin blood microscopy. The thick blood film microscopy is basically for parasite detection while the thin blood film microscopy can also be used for parasite density count. The threshold for detection of malaria parasite by thick blood film microscopy has been estimated to be between 4 to 20 parasites/mcl of blood (Payne., 1988; Dowling & Shute., 1966).

Another method is the rapid diagnostic test (RDT). There are presently several commercially available rapid diagnostic test kits which include Parasight F, Parachef P<sub>f</sub>, KAT<sup>TM</sup>-Quick (Wongsrichanalai et al., 2007). These kits however all work through the same principle which is detecting the parasites' antigen (protein) in the person's blood. Some are specific for *P. falciparum* while others can detect other species too. One of the popular parasite proteins for this is the Histidine rich protein 2 (HRP-2) which is specific for *P. falciparum*. Another is parasite lactate dehydrogenase (pLDH) (Wongsrichanalai et al., 2007). Each of these proteins has their own merits and demerits. For purposes of monitoring treatment, the HRP-2 may not be the best as these proteins may remain in the blood weeks after successful treatment (Moody et al., 2000). The pLDH on the other hand is also produced by the gametocyte forms

and may remain positive as such even after clearing off the asexual forms (Miller et al., 2001).

#### **4.7.2 Treatment of Malaria in Pregnancy**

The World Health Organisation (WHO) recommends treatment of uncomplicated *P. falciparum* malaria in the first trimester of pregnancy with quinine + clindamycin; while in the second and third trimesters, the use of one of the artemisinin-based combination therapies (ACTs) is recommended for three days (WHO, 2015). It is worth noting that a very high prevalence of anti-malaria resistance has been reported among pregnant women (Aliyu et al., 2017), and an increasing resistance to intermittent preventive treatment against malaria given during pregnancy is also on the increase (Ruizendaal et al., 2017).

#### **4.8 Prevention of Malaria in Pregnancy**

For protection against malaria during pregnancy, the WHO recommends for pregnant women in Sub-Saharan Africa, the use of Intermittent Preventive therapy with Sulphadoxime-pyrimethamine (IPT-SP); sleeping under insecticide treated nets (ITN); and prompt case management of malaria and anaemia (WHO, 2004).

The WHO recommends intermittent preventive therapy with at least two doses of sulphadoxine-pyrimethamine (WHO, 2004). The first dose is to be given during the second trimester; doses should be given at least one month apart; can be given on an empty stomach or with food; should be directly observed by a health worker; should not be taken concomitantly with daily folic acid supplementation; and should not be given to those receiving co-trimoxazole prophylaxis (WHO, 2012).

A systematic review of four studies comparing 2-doses of IPT-SP with case management or placebo in the first or second trimester of pregnancy revealed a lower risk with IPT-SP for placental malaria (RR=0.48; 95% CI: 0.35-0.68); anaemia (RR=0.90; 95% CI: 0.81-0.99) and low birth weight (RR=0.71; 95% CI: 0.55-0.92) (Kulie et al., 2007). Another systematic review of 14 cluster randomized and 8 individually randomized controlled trials showed that in areas of stable malaria, IPT-SP and ITN had a pooled protective efficacy of 35% in reducing low birth weight in the first or second trimester (Eisele et al., 2011). Pregnant women could also benefit from other preventive measures such as: insecticide spraying; environmental management and other personal behaviours and products.

## **5.0 Conclusion and recommendation**

Malaria in pregnancy is major public health problem in sub-Saharan Africa. It is associated with numerous adverse consequences to both the pregnant woman and foetus. Prevention remains the best option for averting these complications and as such, efforts should be intensified to promote the adoption of these preventive measures while more effective strategies should be researched into.

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## Declaration

The authors declare that there is no conflict of interest.

## Authors' contribution

Author 1: literature search and writing of manuscript.

Author 2: supervision and review of manuscript.

Author 3: supervision and review of manuscript.

## References

- Abudu, O. O. (2004). Anaemia in pregnancy. In: A. Agboola (Eds), *Textbook of Obstetrics and Gynaecology for Medical Students (72-78)*. Ibadan: Heinemann Educational Books (Nigeria) Plc.
- Adam, I., Khamis, A. H., & Elbashir, M. I. (2005). Prevalence and risk factors for *Plasmodium falciparum* malaria in pregnant women of eastern Sudan. *Malaria Journal* 4: 18.
- Adefioye, A. O., Adeyeba, A. O. Hassan, W. O., & Oyeniran, O. A. (2007). Prevalence of Malaria Parasite Infection among Pregnant Women in Osogbo, Southwest, Nigeria. *American-Eurasian Journal of Scientific Research* 2(1): 43-45.
- Agomo, C. O., & Oyibo, W. A. (2013). Factors associated with risk of malaria infection among pregnant women in Lagos, Nigeria. *Infectious Diseases of Poverty* 2: 19.
- Ahiboh, H., Oga, A. S., Yapi, H. F., Kouakou, G., Boua, G. D., Edjeme, N., & Monnet, D. (2008). Anémie, métabolisme du fer et protéines de la réaction inflammatoire au cours du paludisme (Abidjan, Côte d'Ivoire). *Bulletin de la Societe de Pathologie Exotique* 101(1): 25-28.
- Aliyu, M. M., Nasir, I. A., Umar, Y. A., Vanstawa, A. P., Medugu, J. T., Emeribe, A. U., & Amadu, D. O. (2017). Prevalence, risk factors, and antimalarial resistance patterns of falciparum plasmodiasis among pregnant women in Kaduna metropolis, Nigeria. *Tzu-Chi Medical Journal* 29(2): 98-103.



- Bolaji, R. E. Clem, D., Goerge, O. E., & Adesuwa, P. S. (2014). The occurrence of malaria disease in pregnant women Nigeria. *African Journal of Pregnancy and Childbirth* 2(1): 021-022.
- Bottero, J., Briand, V., Agbowai, C, Doritchamou, J., Massougbdji, A., & Cot, M. (2011). Short Report: Spontaneous Postpartum Clearance of *Plasmodium falciparum* Parasitemia in Pregnant Women, Benin. *American Journal of Tropical Medicine and Hygiene* 84(2): 267-269.
- Bouyou-Akotet, M. K., Nzenze-Afene, S., Ngoungou, E. B., Kendjo, E., Owono-Medang, M., Lekana-Douki, J., Obono-Obiang, G., Mounanga, M. & Kombila, M. (2010). Burden of Malaria during Pregnancy at the Time of IPTp/SP Implementation in Gabon. *American Journal of Tropical Medicine and Hygiene* 82(2): 202-209.
- Brabin, B. J., Hakimi, M., & Pelletier, D. (2001). An Analysis of Anemia and Pregnancy-Related Maternal Mortality. *Journal of Nutrition* 131: 604S–615S.
- Bulter, D. (1997). Time to Put Malaria Control on the Global Agenda. *Nature* 386: 535-541.
- Campos, P. A., Valente, B., Campos, R. B., Gonçalves, L., Rosário, V. E., Varandas, L. & Silveira, H. (2012). *Plasmodium falciparum* infection in pregnant women attending antenatal care in Luanda, Angola. *Revista da Sociedade Brasileira de Medicina Tropical* 45(3): 369-374.
- Carrington, A. (2001). Malaria: Its Human Impact, Challenges, and Control Strategies in Nigeria. *Harvard Health Policy Review: Current Issue* 2(2): 1-3.
- Centers for Disease Control and Prevention Web site, authors. Malaria facts. [Accessed August 1, 2009]. <http://www.cdc.gov/malaria/facts.htm>. Updated April 11, 2007.
- Cisse, M., Sangare, I., Lougue, G., Bamba, S., Bayane, D. & Guiguemde, R. T. (2014). Prevalence and risk factors for *Plasmodium falciparum* malaria in pregnant women attending antenatal clinic in Bobo-Dioulasso (Burkina Faso). *Bio Med Central Infectious Diseases* 14: 631.
- Clerk, C. A., Bruce, J., Greenwood, B., Chandramohan, D. (2009). The epidemiology of malaria among pregnant women attending antenatal clinics in an area with intense and highly seasonal malaria transmission in northern Ghana. *Tropical Medicine and International Health* 14 (6): 688–695.
- Costa, F. T., Avril, M., Nogueira, P. A. & Gysin, J. (2006). Cytoadhesion of *Plasmodium falciparum*-infected erythrocytes and the infected placenta: a two-way pathway. *Brazilian Journal of Medical Biology Resource* 39(12): 1525-36
- Coulibaly, S. O., Gies, S. and D'Alessandro, U. (2007). Malaria Burden among Pregnant Women Living in the Rural District of Boromo, Burkina Faso. *American Journal of Tropical Medicine and Hygiene* 77(6): 56–60.

- De Beudrap, P., Turyakira, e., White, L. J., Nabasumba, C., Tumwebaze, B., Muehlenbachs, A., Guérin, P. J., Boum, Y., McGready, R. M., & Piola, P. (2013). Impact of malaria during pregnancy on pregnancy outcomes in a Ugandan prospective cohort with intensive malaria screening and prompt treatment. *Malaria Journal* 12: 139.
- Douamba, Z., Bisseye, C., Djigma, F. W., Compaor'é, T. R., Bazie, J. T., Pietra, V., Nikiema, J., & Simpoire, J. (2012). Asymptomatic Malaria Correlates with Anaemia in Pregnant Women at Ouagadougou, Burkina Faso. *Journal of Biomedicine and Biotechnology* Article ID 198317, 6 pages.
- Dowling, M. A. C., & Shute, G. T. (1966). A comparative study of thick and thin blood films in the diagnosis of scanty malaria parasitaemia. *Bulletin of the World Health Organization* 34(2): 249-267.
- Duffy, P. E. (2007). Plasmodium in the placenta: parasites, parity, protection, prevention and possibly preeclampsia. *Parasitology* 134(Pt 13): 1877-1881.
- Duffy, P. E., & Fried, M. (2005). Malaria in the pregnant woman. *Curr Top Microbiol Immunol* 295: 169-200.
- Eisele, T. P., Larsen, D., & Steketee, R. W. (2011). Protective efficacy of interventions for preventing malaria mortality in children in Plasmodium falciparum endemic areas. *International Journal of Epidemiology* 39: i88–i101.
- Falade, C. O. Yusuf, B. O., Fadero, F. F., Mokuolu, O. A., Hamer, D. H., & Salako, L. A. (2007). Intermittent preventive treatment with sulphadoxine-pyrimethamine is effective in preventing maternal and placental malaria in Ibadan, south-western Nigeria. *Malaria Journal* 6:88.
- Fana, S. A., Bunza, M. D. A., Anka, S. A., Imam, A. U. and Nataala, S. U. (2015). Prevalence and risk factors associated with malaria infection among pregnant women in a semi-urban community of north-western Nigeria. *Infectious Diseases of Poverty* 4: 24.
- Federal Ministry of Health (2005). National antimalarial treatment guidelines. Federal Ministry of Health, Abuja.
- Geertruyden, J. V., Thomas, F., Ehart, A. & Alessandro, U. (2004). The Contribution of Malaria in Pregnancy to Perinatal Mortality. *American Journal of Tropical Medicine and Hygiene* 71(2): 35–40.
- Gertrude, K. N. (2010). *Effectiveness of Intermittent Preventive Treatment of full course of Sulphadoxine-pyrimethamine in clearance of placental malaria Parasites in pregnancy in Kafue district.* (Unpublished master dissertation). University of Zambia, Zambia.
- Isa, M.A., Mustapha, A., Bello, H.S., Gulani, I.A., Aisha, M.A., & Hyelabari, I. (2015). Prevalence of Malaria Parasite Infection among Pregnant Women Attending Ante-Natal Clinic in State Specialist Hospital. *The Journal of Applied Sciences Research*. 2(1): 13-19.

- Kuile, O. F., van Eijk, A. M. & Filler, S. J. (2007). Effect of Sulfadoxine-Pyrimethamine Resistance on the Efficacy of Intermittent Preventive Therapy for Malaria Control during Pregnancy: A Systematic Review. *Journal of American Medical Association* 297(23): 2603-2616.
- Lindsay, S., Ansell, J., Selman, C., Cox, V., Hamilton, K., & Walraven, G. (2000). Effect of pregnancy on exposure to malaria mosquitoes. *Lancet*. 355(9219): 1972-1975.
- Luxemburger, C., McGready, R., Kham, A., Morison, L., Cho, T., Chongsuphajaisiddhi, T., White, N. J., & Nosten, F. (2001). Effects of Malaria during Pregnancy on Infant Mortality in an Area of Low Malaria Transmission. *American Journal of Epidemiology* 154: 459-465.
- McGready, R., Lee, S., Wiladphaingern, J., Ashley, E., Rijken, M., Boel, M., & Nosten, F. (2012). Adverse effects of falciparum and vivax malaria and the safety of antimalarial treatment in early pregnancy: a population-based study. *The Lancet Infectious Diseases* 12(5): 388-396.
- Miller, R. S., McDaniel, P., & Wongsrichanalai, C. (2001). Following the course of malaria treatment by detecting parasite lactate dehydrogenase enzyme. *British Journal of Haematology* 113: 558-559.
- Mockenhaupt, F. P., Ulmen, U., von Gaertner, C., Bedu-Addo, G. & Bienzle, U. (2002). Diagnosis of Placental Malaria. *Journal of Clinical Microbiology* 40(1): 306-308.
- Moody, A., Hunt-Cooke, A., Gabbett, E. & Chiodini, P. (2000). Performance of the OptiMAL malaria antigen capture dipstick for malaria diagnosis and treatment monitoring at the Hospital for Tropical Diseases, London. *British Journal of Haematology* 109: 891–894.
- Nduka, F. O., Egbu, A. Okafor, C. & Nwaugo, V. O (2006). Prevalence of Malaria Parasites and Anaemia in Pregnant Women in Aba and Okigwe Town of Southeast Nigeria. *Animal Research International* 3(3): 508-512.
- Nunes, M. C. & Scherf, A. (2007). Plasmodium falciparum during pregnancy: a puzzling parasite tissue adhesion tropism. *Parasitology* 134(Pt 13): 1863-9.
- Ogbeide, O., Wagabtsoma, V., & Orhue, A. (1994). Anaemia in pregnancy. *East African Medical Journal* 71: 671-673.
- Okafor, I. M., Mbah, M. & Usanga, E. A. (2012). The Impact of Anaemia and Malaria Parasite Infection in Pregnant Women. Nigerian Perspective. *Journal of Dental and Medical Sciences* 1(1): 34-38.
- Omalu, I. C. J., Mgbemena, C., Mgbemena, A., Ayanwale, V., Olayemi, I. K., Lateef, I. & Chukwuemeka, V. I. (2012). Prevalence of Congenital Malaria in Minna, North Central Nigeria. *Journal of Tropical Medicine* Article ID 274142, doi:10.1155/2012/274142.

- Owusu-Ofori, A. K., Parry, C. & Bates, I. (2010). Transfusion-Transmitted Malaria in Countries Where Malaria is Endemic: A Review of the Literature from Sub-Saharan Africa. *Clinical Infectious Diseases* 51(10): 1192-1198.
- Payne, D. (1988). Use and limitations of light microscopy for diagnosing malaria at the primary health care level. *Bulletin of the World Health Organization* 66(5): 621-626.
- Rogerson, S. J., Pollina, E., Getachew, A., Tadesse, E., Lema, V. M., & Molyneux, M. E. (2003). Placental Monocyte Infiltrates in Response to *Plasmodium falciparum* malaria Infection and their Association with Adverse Pregnancy Outcomes. *American Journal of Tropical Medicine and Hygiene* 68(1): 115–119.
- Rogerson, S. J., Van den broek, N. R., qongwane, E. C. C., Mhango, C. G., & Molyneux, M. E. (2000). Malaria and anemia in antenatal women in Blantyre, Malawi: A twelve-month survey. *American Journal of Tropical Medicine and Hygiene* 62(3): 335-340.
- Ruizendaal, E., Tahita, M. C., Geskus, E. C., Versteeg, I., Scott, S., d'Alessandro, U., Lompo, P., Derra, K., Traore- Coulibaly, M., de Jong, M. D., Schallig, H. D. F. H., Tinto, H., Mens, P F. (2017). Increase in the prevalence of mutations associated with sulfadoxine–pyrimethamine resistance in *Plasmodium falciparum* isolates collected from early to late pregnancy in Nanoro, Burkina Faso. *Malaria Journal* 16:179.
- Saba, N., Sultana, A. & Mahsud, I. (2008). Outcome and Complications of Malaria in Pregnancy. *Gomal Journal of Medical Sciences* 6(2): 98-101.
- Samak, A.C. (2004) Malaria in Pregnancy: An Overview. *McGill Journal of Medicine* 8: 66-71.
- Shulman, C. E., Marshall, T., Dorman, E. K., Bulmer, J. N., Cutts, F., Peshu, N. & Marsh, K. (2001). Malaria in pregnancy: adverse effects on haemoglobin levels and birthweight in primigravidae and multigravidae. *Tropical Medicine and International Health* 6(10): 770-778.
- Sirima, S. B., Cotte, A., Konaté, A., Moran, A. C., Asamoah, K., Bougouma, E. C., Diarra, A., Ouédraogo, A., Parise, M. E. & Newman, R. D. (2006). Malaria Prevention during pregnancy: assessing the disease burden one year after implementing a program of intermittent preventive treatment in koupéla district, Burkina Faso. *American Journal of Tropical Medical Hygiene* 75(2): 205–211.
- Sirima, S. B., Sawadogo, R., Moran, A. C., Konate, A., Diarra, A., Yameogo, M., Parise, M. E. & Newman, R. D. (2003). Failure of a Chloroquine Chemoprophylaxis Program to Adequately Prevent Malaria during Pregnancy in Koupe´la District, Burkina Faso. *Clinical Infectious Diseases* 36: 1374–82.
- Steketee, R. W., Nahlen, B. L. Parise, M. E. & Menendez, C. (2001). The Burden of Malaria in Pregnancy in Malaria-Endemic Areas. *Am. J. Trop. Med. Hyg* 64(1,2): 28–35.

- Steketee R.W. & Parise M. (1996). The problem of malaria control in pregnancy in Sub-Saharan Africa. *American Journal of Tropical Medical Hygiene* 55: 2-7.
- Sohail, M., Shakee, S., Kumari, S., Bharti, A., Zahid, F., Anwar, S., Singh, K. P., Islam, M., Sharma, A. K., Lata, S., Ali, V., Adak, T., Das, P. & Raziuddin, M. (2015). Prevalence of Malaria Infection and Risk Factors Associated with Anaemia among Pregnant Women in Semiurban Community of Hazaribag, Jharkhand, India. Hindawi Publishing Corporation. *BioMed Research International* Article ID 740512.
- Sousa-Figueiredo, J. C., Gamboa, D., Pedro, J. M., Fançony, C., Langa, A. J., Soares Magalhães, R. J. et al. (2012) Epidemiology of Malaria, Schistosomiasis, Geohelminths, Anemia and Malnutrition in the Context of a Demographic Surveillance System in Northern Angola. *PLoS ONE* 7(4): e33189.
- Ofori, M., Ansah, E., Agyepong, I., Ofori-Adjei, D., Hviid, L., & Akanmori, B. (2009). Pregnancy-Associated Malaria in a Rural Community of Ghana. *Ghana Medical Journal*, 43(1): 13–18.
- Tako, E. A., Zhou, A., Lohoue, J., Leke, R., Taylor, D. W. & Leke, R. F. G. (2005). Risk factors for placental malaria and its effect on pregnancy outcome in Yaounde, Cameroon. *American Journal of Tropical Medical Hygiene* 72(3): 236–242.
- Tay, S. C. K., Agboli, E., Abruquah, H. A. & Walana, W. (2013). Malaria and Anaemia in Pregnant and Non-Pregnant Women of Child-Bearing Age at the University Hospital, Kumasi, Ghana. *Open Journal of Medical Microbiology* 3: 193-200.
- Taylor & Strickland (2000) as cited in Bartoloni, A., & Zammarchi, L. (2012). Clinical Aspects of Uncomplicated and Severe Malaria. *Mediterranean Journal of Haematology and Infectious Diseases*, 4(1): e2012026.
- Tiono, A. B., Ouedraogo, A., Bougouma, E. C., Diarra, A., Konate, A. T., Nebie, I. & Sirima, S. B. (2009). Placental malaria and low birth weight in pregnant women living in a rural area of Burkina Faso following the use of three preventive treatment regimens. *Malaria Journal* 8: 224.
- Tonga, C., Kimbi, H. K., Anchang-Kimbi, J. K., Nyabeyeu, H. N., Bissemou, Z. B. et al. (2013) Malaria Risk Factors in Women on Intermittent Preventive Treatment at Delivery and Their Effects on Pregnancy Outcome in Sanaga-Maritime, Cameroon. *PLoS ONE* 8(6): e65876. doi:10.1371/journal.pone.0065876.
- Umaru, M. L. & Uyaiabasi, G. N. (2015). Prevalence of Malaria in Patients Attending the General Hospital Makarfi, Makarfi Kaduna – State, North-Western Nigeria. *American Journal of Infectious Diseases and Microbiology* 3(1): 1-5.
- Valente, B., Campos, P. A., do Rosa´rio, E. E., Varandas, L. & Silveira, H. (2011). Prevalence and risk factors of Plasmodium falciparum infections in pregnant women of Luanda, Angola. *Tropical Medicine and International Health* volume 16 (10): 1206–1214.

- VanderJagt, D. J., Brock, H. S., Melah, G. S., El-Nafaty, A. U., Crossey, M. J. & Glew, R. H. (2007). Nutritional Factors Associated with Anaemia in Pregnant Women in Northern Nigeria. *Journal of Health Population and Nutrition* 25(1): 75-81.
- Völker, F., Cooper, P., Bader, O., Uy, A., Zimmermann, O., Lugert, R., Groß, U. (2017). Prevalence of pregnancy-relevant infections in a rural setting of Ghana. *BMC Pregnancy and Childbirth* (2017) 17:172.
- Warhurst, D. C. & Williams, J. E. (1996). Laboratory diagnosis of malaria. *Journal of Clinical Pathology* 49: 533-538.
- Warrel et al., 1993 as cited in Bartoloni, A. & Zammarchi, L. (2012). Clinical Aspects of Uncomplicated and Severe Malaria. *Mediterranean Journal of Hematology and Infectious Diseases*, 4(1), e2012026.
- WHO (2001). Iron Deficiency Anaemia: Assessment, Prevention, and Control. Geneva, World Health Organization, 2001
- WHO (2012). Intermittent Preventive Treatment of malaria in pregnancy using Sulfadoxine-Pyrimethamine (IPTp-SP). Updated WHO Policy Recommendation.
- WHO (2015). Guidelines for the Treatment of Malaria. Geneva, World Health Organisation.
- WHO (2004). A Strategic framework for malaria prevention and control during pregnancy in the African region. Congo Brazzaville: WHO Regional Office for Africa; 2004. Volume 01.
- Wongsrichanalai, C., Barcus, M. J., Muth, S., Sutamihardja, A., & Wernsdorfer, W. H. (2007). A Review of Malaria Diagnostic Tools: Microscopy and Rapid Diagnostic Test (RDT). *American Journal of Tropical Medical Hygiene* 77(Suppl 6): 119-127.
- Worrall, E., Morel, C., Yeung, S., Borghi, J., Webster, J., Hill, J., Wiseman, V., Mills, A. (2007). The economics of malaria in pregnancy—a review of the evidence and research priorities. *The Lancet Infectious Diseases* 7(2): 156 – 168.