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Malaria in pregnancy- A global health issue: A review

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ABSTRACT

Malaria in pregnancy (MIP) is an enormous public health problem particularly in malaria endemic areas such as Africa. MIP Results in abortion, premature labour, low birth weight, occasional still birth and neonatal death. It has severe consequences for a pregnant woman by considerably increasing the risk of maternal death and severe anaemia. It could also result in congenital malaria to unborn baby. Global strategies for combating MIP includes, roll back malaria and 'making pregnancy safer initiative' aimed at strengthening antenatal services and provide preventive measures, treatment, care and counselling to improve all aspect of health in pregnant women. The availability of insecticide treated nets, effective intermittent preventive treatment and effective case management of malaria illness, provides a unique opportunity that must be taken to protect the millions of African women who become pregnant each year and their babies.

KEYWORDS

Immunocompromised;
Primigravida;
Multigravida;
Perinatal morbidity;
Mortality;
Neonates.

INTRODUCTION

Malaria, a parasitic infection transmitted by mosquitoes, is one of the most devastating infectious disease, killing more than 1 million people annually. Pregnant women, children, and immunocompromised individuals have the highest morbidity and mortality, and Africa bears the heaviest burden. The World Health Organization defines malaria as a disease of poverty caused by poverty[32]. Mosquitoes are arthropod vectors of which the female anopheles species have been implicated in the transmission of malaria. Sub-Saharan Africa has the largest burden of malaria disease, with over 90% of the world's malaria-related deaths occurring in this region. Malaria is still a major contributor to high rate of the global infectious disease–related mortality and morbidity particularly in Africa, South-East Asia, Eastern Mediterranean Regions and parts of South America[42]. In the World Malaria Report (WMR) of 2009 the World Health Organization (WHO) estimated that 243 million cases of malaria occurred worldwide in 2008, and majority of the cases (85%) occurred in the African Region, followed by the South-East Asia (10%) and Eastern Mediterranean Regions (4%)[43]. A recent study from Mozambique that assigned cause of maternal death via autopsy examination found that up to 10% of maternal deaths were directly attributed to malarial infection and 13% were secondary to human immunodeficiency virus (HIV)/AIDS, which can be exacerbated by coexisting malarial infection[23]. This suggests that in parts of the world where malaria is endemic, it

may directly contribute to almost 25% of all maternal deaths.

Malaria in pregnancy (MIP) also contributes to significant perinatal morbidity and mortality. Infection is known to cause higher rates of miscarriage, intrauterine demise, premature delivery, low-birthweight neonates, and neonatal death. Owing to the endemicity and problems associated with malaria infection among pregnant women, it is now seen as a global health issue and treated as such. At global level, WHO is at the vanguard of combating malaria by having programs like 'making pregnancy safer initiative' aimed at strengthening antenatal services and provide preventive measures, treatment, care and counseling to improve all aspect of health in pregnant women and their new borne. While in year 2000 the first African summit on malaria was held in Abuja, Nigeria with African head of states committed to providing effective malaria intervention to at least 60 percent of pregnant women by 2005 and was later increased to 80%[39,44]. However, data from 2004 to 2009 suggests that, in spite of national policies for prevention and control of MIP (and the limitations and scarcity of available nationally representative survey data), insufficient progress has been made towards the targets for coverage of IPT (Intermittent preventive treatment) and ITN (Insecticide treated nets) use during pregnancy: 25% of pregnant women received at least one dose of IPT and, overall, coverage was lowest in areas of highest malaria transmission[11]. Roll Back Malaria is another international intervention program where, WHO partners with non governmental agencies and donors to meet the Abuja goal and reduce malaria in pregnant women. The availability of ITNs, effective IPT, effective case management of malaria treatment and a means of delivery through antenatal clinics, provides a unique opportunity that must be taken to protect the millions of African women who become pregnant each year and their babies.

However, for success to be achieved, women understanding of their vulnerability to malaria and other illnesses when pregnant is key to designing and promoting appropriate MIP intervention programs[29].

OVERVIEW AND CONSEQUENCES OF MALARIA INFECTION DURING PREGNANCY

Malaria in pregnancy (MIP) is an enormous public health problem particularly in malaria endemic areas in Africa[18]. Immunosuppression in pregnancy, particularly during the second half of pregnancy can lead to heavy parasitic infection of the placenta with subsequent haemolysis. Resulting in abortion, premature labour and occasionally still birth and neonatal death[39]. It has severe consequences for a pregnant woman and her unborn infant. An infant born to a mother with malaria is more likely to have low birth weight (LBW), which is the single greatest risk factor for death during the first months of life[19]. The risk of maternal death also increases considerably as a pregnant woman suffering from malaria is likely to develop severe maternal anaemia[40].

Pregnant women are 3 times more likely to suffer from severe diseases as a result of malarial infection compared with their non pregnant counterparts and have a mortality rate from severe disease that approaches 50%[32]. Likewise, malaria is about twelve times more common in pregnant women compared with non pregnant women[5]. In malaria endemic areas, it is estimated that at least 25% of pregnant women are infected with malaria, with the highest risk for infection and morbidity in primigravidas, adolescents, and those coinfected with HIV[32]. The effect of malaria infection during pregnancy is associated with maternal anemia. It has been estimated that approximately 26% of maternal anaemia cases are due to malaria during pregnancy. MIP is also known to directly and indirectly cause maternal mortality, but to what extent, is lessknown[8]. According to estimates, approximately 20% of the low birth weight (LBW defined as birth weight below 2500g) deliveries are a consequence of malaria during pregnancy. LBW, in turn, is associated with poor infant development and survival, and contributes to around 100,000 infant deaths: 11.4% of neonatal deaths and 5.7% of all infant deaths or 17 deaths per 1000 live births according to another estimate[8,40,44]. In addition, MIP is estimated to be responsible for 70% of intrauterine growth retardation cases (IUGR) and 36% of preterm deliveries.

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Placental malaria also increases the risk of stillbirth particularly during the third trimester of pregnancy[8]. It is believed that most of the indispositions in pregnancy results from 2 main factors: the immunocompromised state of pregnancy and placental sequestration of in infected erythrocytes.

Immunity diminishes significantly in pregnancy, particularly in primigravidas. A recent study of 300 women delivering in rural Ghana showed higher rates of anemia, clinical malaria, and placental burden of infection among primigravidas compared with multigravidas. The study also noted that babies born to mothers with placental malaria infection were more than twice as likely to be underweight at birth[26]. In pregnant women, additional sequestration of malaria infected erythrocytes occurs in the placenta. Pregnant women therefore suffer disproportionately from severe anemia as a result of infection. In Africa, it has been estimated that malaria is responsible for 25% of severe anemia during pregnancy. Women with severe anemia are at higher risk for morbidities such as congestive heart failure, fetal demise, and mortality associated with hemorrhage at the time of delivery.

Interestingly, the greatest degree of placental infestation is seen in women who have the highest level of immunity, leading to milder maternal symptoms and a disproportionate increase in fetal complications. It could be hypothesized, therefore, that although primigravidas may develop the clinical symptoms of malaria, women with higher immunity may not demonstrate symptoms, will not receive treatment, and will build a higher placental parasite burden. Fetal complications result from this placental inflammation, as well as maternal anemia, and manifest as stillbirth, intrauterine growth restriction, and low-birth-weight neonates. Low-birth-weight neonates, in turn, are at higher risk for neonatal and newborn death. Congenital malaria is a relatively rare complication in areas with endemic malaria; however, newborn parasitemia may present 2 to 3 months after delivery when maternal antibodies wear off[32]. MIP also put allot of life at risk. It is also estimated that in Africa, 30 million women living in malaria-endemic areas become pregnant each year. For these women, malaria is a threat both to themselves and to their babies, with up to 200 000 newborn deaths each year as a result of MIP[46].

CONGENITAL MALARIA

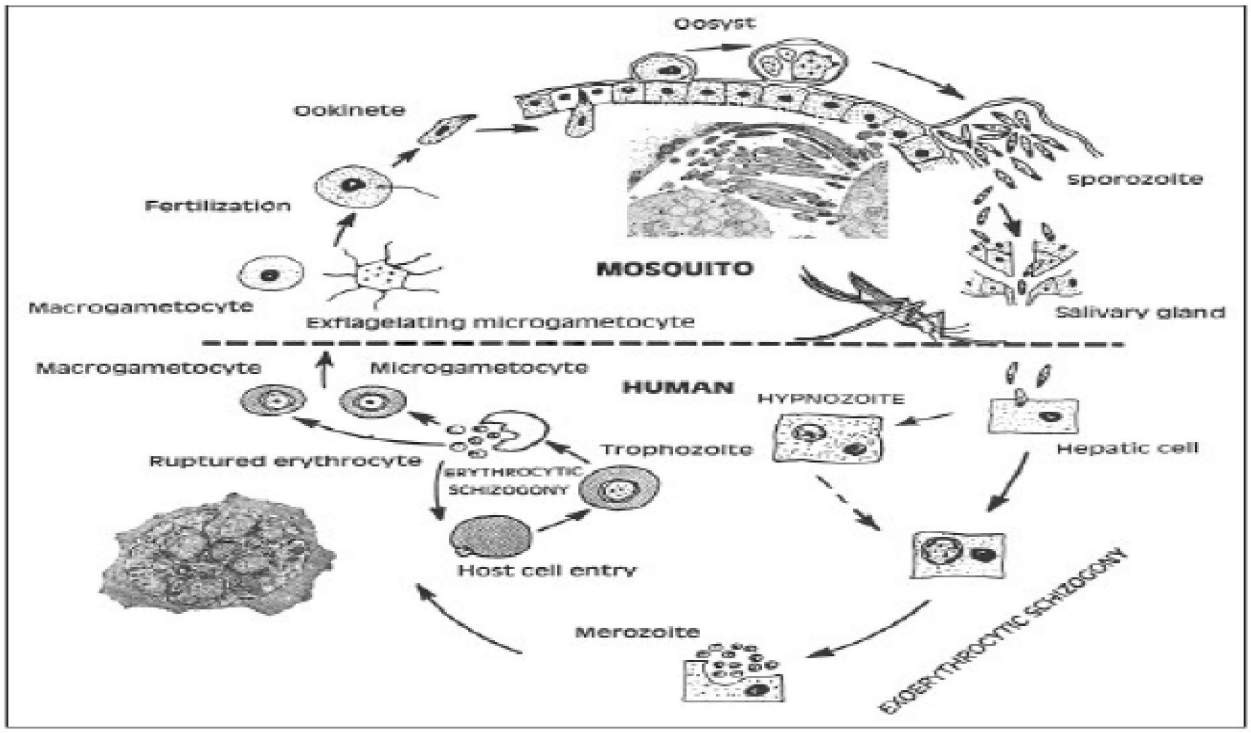

Figure 1

Congenital malaria is a public health concern globally. Congenital malaria is one resulting from the transplacental transmission of malaria parasites particularly P. *falciparum* from mother to fetus, is well described by some early reports[7]. However the precise definition of congenital malaria is still a subject that is not devoid of controversy debatable, but symptoms usually occur 10 to 30 days postpartum[6]. The disease can be observed in a day old baby or be delayed for weeks or months[14]. In 80% of the cases of congenital malaria, the most common clinical features include fever, anaemia and splenomegaly[31]. Some reports have noted that other signs and symptoms which could manifest are hepatomegaly, jaundice, regurgitation, loose stools, and poor feeding, and occasionally, drowsiness, restlessness, and cyanosis in children[7,14,31]. However, evidence from most of the cross-sectional studies conducted in parts of sub-Saharan Africa on congenital malaria within the last two decades (1990-2010) clearly indicates that congenital -sectional malaria is not as uncommon as previously thought. In fact, congenital malaria prevalence in majority of the cross studies within the last five years (2005-2010) ranged from 10.8% to as high as 54%.

EFFECT OF MATERNAL HIV INFECTION ON CONGENITAL MALARIA

The human immunodeficiency virus (HIV) infection has been described as a major factor that is contributing to worsen the burden of malaria in most endemic areas particularly in sub-Saharan Africa[1]. Evidence abound indicating that HIV infection interacts negatively with malaria, with each disease driving the progression and transmission of the other[12,28,37]. Some studies have demonstrated that HIV increases the risk of clinical and severe malaria, while malaria increases HIV replication in vitro and in vivo[712,28,37]. Both HIV infection and malaria are known to critically intersect in pregnancy and have serious consequences in pregnant women, their fetuses and their infants[35,36]. It is estimated that approximately 1million pregnancies per year are complicated by co-infection with malaria and HIV in subSaharan Africa[40,44]. However, whether the dual infection with malaria and HIV in pregnancy increases the risk of congenital malaria is yet to be unequivocally established, as studies examining these relationships are few and have inconsistent findings and a wide range of unanswered questions[30,35].

Nevertheless, in a recent report from Western Kenya, Perrault *et al*.[30] demonstrated that malaria and HIV co-infection in pregnancy increased placental parasite density and the rate of antenatal malaria transmission. The authors found that HIV serostatus was strongly correlated with cord blood infection, suggesting that HIV may impact congenital malaria primarily by allowing for higher parasite densities in the placenta. Reports from the 12th World AIDS Conference in Geneva also provided additional information from various researchers indicating that the presence of HIV may reduce a pregnant woman's ability to control the perinatal transmission of malaria[3]. Malarial infection in HIV-positive women is associated with higher levels of parasitemia, leading to a greater risk of severe anemia. Likewise, HIV viral load is increased, creating opportunity for infection and more severe disease[7].

GLOBAL STRATEGIES RELATED TO MALARIA IN PREGNANCY

The burden of (MIP) has been an invisible public health problem for a long time because of its asymptomatic nature and it has therefore received relatively little attention among international organizations. Only recently the vulnerability of pregnant women and severe consequences of the disease for pregnant women and their infants have been recognized and efforts have been made to develop effective prevention and control strategies to mitigate the impact of the disease. During the past ten years, there have been several global initiatives and summits to accelerate the control of malaria and efforts to build up partnership with maternal health programmes and malaria control in pregnancy through focused antenatal care (FANC) and the WHO Making Pregnancy Safer Programme[5,38].

Similarly,the MIP Consortium was therefore established to address the need for coordinated research on MIP. This global initiative, made up of 47

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institutions, is undertaking a five-year programme of research (2007–2012) to evaluate new and to improve existing interventions for the prevention and treatment of MIP (The Malaria in Pregnancy Consortium). Based on available evidences, WHO recommends a three way approach to the prevention and management of malaria during pregnancy[32]. These are;

- Insecticide-treated nets (ITNs)
- Intermittent preventive treatment (IPT)
- Effective case management of malarial illness.

Intermittent preventive treatment refers to the administration of 2 or more doses of chemoprophylaxis after 20s weeks of gestation in an attempt to reduce subclinical malarial load.

In a study comparing malarial chemoprophylaxis with no prophylaxis during pregnancy, Garner and Gülmezoglu[13] found a significant reduction in maternal anemia, parasitemia, and perinatal death, and a higher mean birth weight in the groups given IPT. More recent studies in Nigeria that examined specific IPT regimens found significant reductions in maternal anemia with the use of sulfadoxine-pyrimethamine as compared with chloroquine, pyrimethamine, or no prophylaxis. Sulfadoxine-pyrimethamine has been found safe in pregnancy when used intermittently as part of IPT[4,10].

Although the WHO currently recommends that all pregnant women living in malaria-endemic regions use insecticide-treated bed nets and IPTp-SP (intermittent preventive treatment in pregnancy with at least 2 doses of sulfadoxine-pyrimethamine), studies show poor uptake of both preventative efforts among pregnant women. A recent survey among postpartum women in rural Uganda, in which 88% had made more than 1 prenatal visit, found that only 31% of women used a bed net during pregnancy and only 36% had received 2 doses of IPTp- SP[21,29]. This indicates that as access to and utilization of antepartum care increase, there is still a role for improved administration of IPTp-SP and education regarding bed net use. It has been observed that, obtaining an ITN was also a motive for women in central Uganda delivering IPT in the community rather than at the ANC (Antenatal care) clinic improved uptake and increased awareness of the dangers of MIP[22] and, in eastern Sudan, bed net distribution through local committees and leaders authorities encouraged their use more than distribution through the ministry of health[15]. In Tanzania, a social marketing approach, using vouchers that pregnant women received as part of ANC and then exchanged for a subsidized bed net, has been tried. However, despite initial high voucher return rates, there have been mixed reports of awareness about the scheme, how to take part, and the intended recipients of the nets[34]. Additional constraints appear when there is concurrent use of IPT with antiretroviral medications for the treatment of HIV and prevention of vertical transmission secondary to limited knowledge surrounding the drug-drug interactions. In particular, review of the literature suggests increased risk of cutaneous and hepatic toxicity when IPT is used in conjunction with nevirapine, and increased risk of bone marrow suppression when used in conjunction with zidovudine, leading to unintended morbidity associated with treatment of the 2 diseases[29].

EFFECTIVE CASE MANAGEMENT OF MALARIA ILLNESS

Malaria treatment in pregnancy is a strive between preventing adverse drug effect and clearance of the parasites by clinicians. In 2006, the WHO recommended a combination of quinine and clindamycin for treatment of uncomplicated malaria in pregnancy. The most appropriate treatment however depends on gestational age, the malaria species and severity, local patterns of drug resistance and drug availability[33].

However, there is a risk of hypoglycemia with quinine use, as well as increasingly drug-resistant P.*falciparum*. More data currently support the use of artemisinin-based combination therapy, which appears safe and effective in pregnancy[27]. For severe malaria in pregnancy, WHO currently recommends treatment with either intravenous (IV) quinine or artesunate, or IV artesunate in the second and third trimesters. Not only should IV quinine be avoided in the second and third trimesters as it is associated with recurrent hypoglycemia, but evidence supports the superiority of artesunate over quinine in the non pregnant patient. In epidemic situ-

ations, if IV or intramuscular medication is unavailable, patients should receive artesunate suppositories and be transferred to a higher level facility[41].

CONCLUSION AND RECOMMENDATION

Malaria is a global health issue that is endemic in tropical Africa. Of which pregnant women due to their compromised immune status are the most vulnerable groups. This has negatively influenced Africa's human resources and impeded her annual economic growth. In view of this ugly menace, government and donor agencies have intensified efforts towards preventing, treating and possibly eradicating malaria from the planet earth. Some level of success is being achieved through the advocacy of the use of insecticide treated nets (ITNs) and intermittent preventive treatment (IPT) of World Health Organisation (WHO) for pregnant women. It is recommended that, existing programs should be developed upon, create more awareness and more research work should be done to possibly reduce or eradicate malaria in pregnancy.

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