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Review Article

Epidemiology and Risk Analysis of Malaria among Pregnant Women

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Abstract

Malaria remains a complex problem during the pregnancy, which threatens > 35 millions pregnant women every year. Malaria pathogenesis in pregnancy results in accumulation of infected RBCs in the intervillous spaces causing severe alterations leading to the reduced materno-foetal exchanges. In this article we have revisited the current evidences of clinical implications and overall burden of malaria in pregnancy. Many adverse aftermaths including, low birth weight, intrauterine growth retardation, preterm delivery, stillbirth and anemia were found associated with malaria in pregnant women. Despite of worldwide comprehensive control programmes for malaria in pregnancy, the disease control has been a daunting task everywhere. Socio cultural, economical, lack of awareness and various logistic problems compound the disease in developing countries. Thorough evidence based information and estimates, education and awareness and strengthening of prevention programmes are needed urgently to achieve success in malaria control in pregnancy.

Keywords: Malaria, Pregnancy, Infection, Prophylaxis

Introduction

Malaria is a serious parasitic disease of human population. It is transmitted by infected female Anopheline mosquitoes when they feed on humans for their oviposition and is responsible for millions of deaths every year around the world (1). Malaria as on today is among the major infectious diseases causing considerable deaths and can be assumed as prime etiological factor of slowed economic growth as a result of low production associated with mortality. Majority of malaria infections are caused by Plasmodium falciparum and present with high fever and convulsions, which may lead to coma and death. In addition to the parasite, thick density of vector mosquitoes manifolds the burden (2-4).

Malaria infections are common during pregnancy posing substantial risks to the mother, fetus and the newborn, which include severe anemia, placental parasitemia and intra-uterine growth retardation (5). These factors contribute to low birth weight and stillbirth, which are principal causes of infant mortality in the Africa (6). Primigravid, in particular, and secundigravid women are at higher risk for placental malaria than women with multiple prior pregnancies (7). The pregnant women experience more mosquito bites as compared to non pregnant women, which may be due to increased body surface and specific odors secretions during pregnancy (8, 9). Pregnant women are highly susceptible to malaria as compared to the adults, and both frequency and severity of disease are higher in pregnant women due to

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depressed cellular immunity during pregnancy (10, 11).

Until the early 20th century the problem of malaria in pregnancy was not described adequately however in the last few decades, many comprehensive studies have highlighted various issues of malaria in pregnancy and its effect on maternal and infant health (12). Despite comprehensive malaria control programme, control measures specifically aimed at malaria in pregnancy are not adequately available. The epidemiological data are scanty in order to develop effective policies to address this problem. In the present article, spectrum of malaria manifestation in pregnancy, its control measures and limitations has been reviewed and discussed. We have used data from relevant articles published between 1980-2010, which were searched on Google and Pubmed using malaria, pregnancy and related key words.

Pathogenesis of malaria in pregnancy

A characteristic infection of Plasmodium falciparum includes a process involving the accumulation of parasitized red blood corpuscles (RBC) in various organs and organ systems. Pregnant women have a large number of RBC accumulated in the intervillous spaces of placenta. Many studies have been carried out to explain the preference of malaria parasite proliferation in the placenta and accumulation of brown malarial pigment was found in almost all cases of infected placenta examined (13,14). This may show placental infection even in absence of peripheral parasitemia. The placental infection occurs by cytoadherence-sequestration mediated by adhesive interactions between ligands of parasite present on infected RBC's surface and host molecules (glycosaminoglycans chondroitin sulphate-A and hyaluronic acid) present on endothelium. This binding in placenta is the basis for higher susceptibility of primigravid women. Malaria infection during pregnancy may cause hepato-splenomegaly and megaloblastic changes in the bone marrow. Further during the labour and course of pregnancy falciparum malaria may cause pyrexia and heart attack to the mother, while intra uterine growth retardation (IUGR) and intra uterine death (IUD) of the developing fetus (10, 12). Placental infection acquired during the high transmission season may persist for a long time in the placenta itself. It causes the clogging of intervillous spaces with macrophages. The extent of clogging incurred due to infection is directly proportion to the severity of infection (12). Severe parasitization of placenta causes congenital anemia, premature delivery and stillbirth in the newborns which is primarily be due to the decrease in maternal blood output and exchanges between mother and fetus (15).

Malaria infection and control in pregnancy

Several epidemiological studies have been carried out but still a concrete strategy to decrease malaria in pregnant women is awaited. Two prospective hospital-based studies conducted in Chandigarh and Gujarat, India demonstrated that severity of clinical illness was significantly higher in pregnant patients for both Plasmodium vivax and P. falciparum (16-20). The pregnant woman affected by malaria experience maternal anemia, higher maternal death, intrauterine fetal death and severe peripartum complications like abortion, stillbirth, premature labour, low birth weight (LBW) (Table 1). The studies carried out in different parts of Africa have shown that > 25% of pregnant women have malaria infection at the time of delivery (10, 12). Malaria infections in most parts of Asia are very symptomatic (12) however in more endemic areas particularly in north eastern states, Orissa and some parts of West Bengal, where asymptomatic infections are common. Plasmodium falciparum infections may not result in fever and therefore remain undetected and untreated during pregnancy (21).

Meta-analyses of intervention trials suggest that successful prevention of these infections reduces the risk of severe maternal anemia by 38%, low birth weight by 43% and perinatal mortality by 27% among pregnant women (12).

The studies conducted in tribal villages in central India on pregnant women and infants revealed that 55 % pregnant women and 44 % infants investigated had malaria at some time during the study period (22, 23). A hospital based study in Tanzania showed that out of 413 women 91% slept under bed nets, still 43% were having fever. Malaria parasites were found in 8% of the placenta samples and parasite density was > 2,100 parasites/µl. This investigation has revealed that despite of using insecticide treated bed nets; malaria remains a problem in pregnancy. The delivery of intermittent preventive treatment in pregnancy could be useful at all levels of control implementation to attain maximum coverage at community level (5). Several investigations have shown that P. falciparum is responsible for the majority of malaria incidences (>75%) whereas the rest are contributed by P. vivax (16, 19, 20, 24). The infections due to P. vivax are generally ignored as compared to the P. falciparum in term of prevention and intermittent treatment. However, various studies have demonstrated that P. vivax malaria was associated with mild anemia and increased risk of low birth weight, which may be more pronounced in multigravidae than in primigravidae (25). The P. vivax infection, have not been found responsible for miscarriage, stillbirth and reduced duration of pregnancy in many investigations (20, 25). A report from Thai-Burmese border showed that the risk of severe malaria is reduced to >25% in both P. falciparum and P. vivax mixed infection as compared to P. falciparum alone (26). In the other studies, the multiplicity of the infection in placenta was associated with occurrence of low birth weight babies with some parasite genotypes were able to persist over several weeks (27). The infection multiplicity decreased significantly with an increasing number of pregnancies, and infection with multiple P. falciparum strains was significantly associated with anemia. The women infected with four or more strains have >2 times chance to be anemic than women harboring fewer strains (28).

The severity and timing of obtaining the infection plays a significant role in the intrauterine growth retardation (IGUR) and preterm delivery of pregnant women. A study carried out at Malawi has suggested that women who have parasitemia or clinical episode of malaria in the antenatal period were more than three times likely to deliver an IUGR infant than other women (29). Similarly the preterm delivery was found associated with cord parasitaemia (29).

Risk analysis

Malaria parasites infecting the pregnant women have distinct antigenic and adhesive properties than infecting the non pregnant women and other (30). Further the primigravidae mothers are likely to be more parasitaemic than multigravidae because antibodies are present in higher concentration in multigravidae (12, 24, 30). Adolescent mothers have more risk of acquiring malaria infection. Many studies have showed that the young primigravidae and multigravidae have greater risk of acquiring malaria and its adverse effects than older primigravidae and multigravidae (31-35). Therefore, in addition to the parity level immunity, which comes through consecutive pregnancies, the immunity associated with the age of mother also plays considerable role in reducing the malaria infection during pregnancy.

The risk of malaria infection in the first trimester as compared to the second trimester is very little, which may be due to changes in splenic function early in pregnancy (12, 36). However, the susceptibility in the first trimester should increase to explain the peak malaria prevalence in the second trimester. Some studies have demonstrated the risk in the early trimester but the results are not consistent every time (37-39). Recent study in Mozambique suggests that one-fifth of pregnant women with malaria symptoms are in their first trimester (12). Little information is available about the infection after delivery and the picture is still unclear, however some studies propose the increase in new and recurrent infections during first trimester

(37-39). In contrast, a few studies have shown a rapid clearance of peripheral parasitemia within two days post delivery (40). Therefore the chances of malaria infection depend upon the level of immunity present in the women at the time of becoming pregnant.

Peripheral malaria can also play a vital role in placental infection during pregnancy. Studies have proved that peripheral malaria may enhance the risk of placental malaria up to five times (41). However the chance of placental infection due to the peripheral malaria infection occurred in the beginning of pregnancy is much higher as compared to the malaria infection occurred toward end of pregnancy (3). This can be concluded due to the limited immunity at the beginning of pregnancy (12).

Limitations in health and communication

The prevention and control programmes in the areas of stable malaria transmission ensure the use of antimalarials and other intervention measures, still the malaria problem remains uncoverable. Several studies have revealed the importance of prophylaxis for malarial infection during pregnancy (41-43). However low prevention coverage, lack of personnel protective measures including insecticide treated bed nets (ITBN's), socio economic factors and resistance to antimalarials have posed a great challenge to the control programmes (18, 44, 45). World health organization (WHO) in malaria risk nations and National Vector Borne Disease Control Programme (NVBDCP) in India have clear guidelines towards prevention and treatment of malaria infection but these remain largely in the papers only due to several region specific problems namely, difficult terrain to reach the remote locations, resource scarcity, intentional underreporting of the cases due to various reasons, poverty and insurgency etc. There are information lacunae regarding the true burden of malaria infection which is very important for proper understanding and control of this serious health problem. Correct measurement on the direct or indirect measurement of malaria-associated maternal morbidity and mortality is an essential component to quantify the exact malaria burden in pregnancy. There are only a few systematic studies carried out in Asia and America which are insufficient to clarify the exact situation of malaria burden in pregnancy in these continents (12). The effective antenatal coverage is very inadequate and pregnant women mostly take care in the middle of second trimester or in the third trimester of pregnancy. The evaluation of the effect of antimalarial drug used for control purpose is difficult as there is widespread use of incomplete treatment course, leading to frequent recrudescent malaria infections with repeated production of gametocytes after infective mosquito bite (12, 36, 46).

The drug resistance problem in P. falciparum is threatening in many malaria endemic regions. Mefloquine and quinine have been found unable to produce satisfactory responses for the treatment of highly drug-resistant P. falciparum malaria in pregnancy, when used as single agents (47). Consequently, options for the treatment of pregnant woman are limited because of the unknown effects of antimalarials on the fetus (46). Socio-behavioural issues are also needed to be addressed in developing countries such as India, where people have strong religious and cultural values (48). Social and cultural barriers to the pregnant women limit the efficacy of any antimalarial intervention and success of control programmes. A study targeted on pregnant women from low socioeconomic groups in central India showed that >80 % did not accept chemoprophylaxis due to objections by family members (49). Therefore proper understanding of socio-cultural factors is important in tackling the problem of malaria among pregnant women.

Table 1: The overall effects of malaria during pregnancy (by studies)

Study (sample size)	Effects on mother		Effects on fetus		
	Peripheral parasitemia (%)	Level of anemia (%)	LBW (%)	PTD (%)	SB (%)
NOSTEN ET AL. 1991[50] (1358)	5.9	31.2	--	--	3.2
LUXEMBURGER ET AL. 1997[26] (1495)	--	77.2	16.0	11.0	2.7
NOSTEN ET AL. 1999[25] (9956)	6.4	77.3	18.7	--	--
MCGREADY ET AL. 2004[51] (204)	9.5	--	13.1	7.6	--
SINGH ET AL. 2005[46] (> 1000)	> 1.0	57.4	70.9	26.9	6.4
SINGH ET AL. 2005[52] (799)	6.1	--	--	--	--
RASHEED ET AL. 2008[53] (464)	--	41.37	--	--	--
HAMER ET AL 2009[54] (3104)	1.8	69.5	30.0	5.8	2.4

LBW- LOW BIRTH WEIGHT, PTD- PRETERM DELIVERY, SB- STILLBIRTH

Conclusion

The above issue illustrates the need for a greater degree of co-ordination and participation by the community with local organization and Govt. administration. Focus should be given on the reduction of parasite load by developing first rate surveillance in prevention and treatment programmes. Pregnant women must be tested for parasite infection on regular basis using rapid diagnostic kits on the spot itself and serious cases should be hospitalized without any delay. The community awareness can play a backbone role in malaria eradication as only personnel protective measures and malaria surveillance alone cannot assist effectively to fight with malaria. Better estimates and reporting of malaria maternal morbidity and mortality in pregnancy are also needed. Global risk maps will allow better estimation of potential impact and successful control of malaria in pregnancy. There is urgent need to stick the prevention guidelines and to provide medical service to the people living in remote areas in order to prevent the malaria related adverse effects and mortality upto considerable extent. The antimalarials which have been found effective and tested no side effects in pregnancy should be used in limit so as to check the resistance spread. Community based awareness and education programmes are essential to educate women about the benefits and risk associated with taking recommended chemoprophylaxis during the pregnancy.

Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc) have been completely observed by the authors.

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