Malaria In Pregnancy

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INTRODUCTION

Malaria in pregnancy is an obstetric, social and medical problem of all over the world particularly in tropical and sub-tropical countries. Pregnant women with no previous immunity to malaria are two or three times more likely to develop severe disease as result of malaria infection than are non pregnant adults living in the same area. Pregnant women are especially prone to severe attacks of malaria which may cause abortion, premature labour and still birth. In most endemic areas pregnant women are the main adult risk group for malaria. The main burden of malaria infection during pregnancy results from infection with plasmodium falciparum. The impact of the other three human malaria parasites (P. vivax, P. malariae and P. ovale) is less clear.

PATHOPHYSIOLOGY

Malaria and pregnancy are mutually aggravating conditions. The physiological and the pathological changes due to malaria have a synergistic effect on the patient which causes life difficult for the mother, the child and the treating physician.

Pregnant women compared to non pregnant women are at an increased risk of malaria and the severity of clinical manifestation experienced by these women and their foeti depend on the level of pre-pregnancy immunity. Pregnant women are more susceptible to plasmodium falciparum infection with more frequent episode of clinical malaria, increased prevalence and density of parasitaemia during episode. The effect of infection on the pregnancy is dependent on pre-pregnancy immunity. This acquired anti-malarial immunity depends on intensity of transmission and the number of previous pregnancies among others. Studies have shown that prevalence of infection is highest in second gravida while others have reported a higher prevalence in primigravida and the density of parasitaemia is reported to be highest in the first trimester and primigravida could be at maximum risk in highly endemic area.

Loss of anti-malarial immunity is consistent with the pregnancy viz. reduced lymphoproliferative response. What is lost is cell mediated immunity, by which pregnant mother suffers. In pregnant women a change of balance of the local placental environment observed, which is consistent with large number of monocytes in infected placenta. While IFN-γ, IL-2 and TNF-α levels - hall marks of a type-1 cytokine response. Inflammatory cytokine account for the pathology of maternal malaria, associated with severe maternal anaemia, symptomatology of malaria and contributes to adverse pregnancy outcomes.

Placenta in Pregnancy

Placental parasitaemia in pregnant women leads to impairment of foetal nutrition and this contributes to low birth weight, a leading cause of poor infant development and survival. P. falciparum has the unique ability of cytoadhesion. Adhesion molecule - 1 may be involved in the development of severe malaria in adults. Chondroitin sulfate A and hyaluronic acid have been identified as a parasite attachment to placental cells. The putative ligand expressed by the malaria has been found to be antigenically conserved among global cases of maternal...
sub population of P. falciparum that do not bind to CD 36. The parasites sequentiate placental membrane, specifically the trophoblastic villi. Intervillous spaces are filled with parasites and macrophages which transport to the foetus. Villous hyprtrophy and fibrinoid necrosis of villi are also observed. All the placental tissues exhibit malarial pigments, which impede oxygen nutrient transfer and can cause general haemorrhge to the complications by both mother and child.

Manifestation of Malaria in Pregnancy

The symptoms of malaria during pregnancy differ with the intensity of malaria transmission and with the level of immunity acquired by the pregnant women. Since malaria transmission intensity may vary within the same country from areas of relatively stable transmission to areas of unstable or epidemic transmission. The clinical picture of malaria infection during pregnancy may range from asymptomatic to severe life threatening illness. Atypical manifestation of malaria are more common in pregnancy particularly in primigravida. Patient may have different pattern of fever from afebrile to continuous pyrexia. In the second half of pregnancy, there may be more frequent paroxysm of fever. Patient living in hyperendemic area may present with a severe anaemia without any definite pyrexia. Enlargement of the spleen may be variable in the course of pregnancy.

Complication of malaria in Pregnancy

In comparison to general population, risk of development of complications in pregnant women because of malaria is more. Particularly complications of malaria in pregnancy in women with low immunity are hyperpyrexia, hypoglycemia, severe haemolytic anaemia, cerebral malaria and pulmonary oedema.

1. Anaemia:

Anaemia due to malaria is more common in between 16-29 weeks of gestation. The cause of anaemia particularly in pregnant lady is because of haemolysis of parasitized blood and increased demand of blood during pregnancy. Anaemia increases perinatal mortality and morbidity and increased risk of post-partum haemorrhage.

2. Acute pulmonary oedema:

Acute pulmonary oedema may be the presenting symptoms of some cases of malaria in pregnancy in first trimester or it can develop in the second and third trimesters of pregnancy. It is aggravated by pre-existing anaemia and haemodynamic changes of pregnancy. Acute pulmonary oedema carries a very high mortality.

3. Hypoglycemia:

It is one of the complication of malaria more common in pregnant women because of increased demand of hypercatabolic state and infecting parasites. Increased response of pancreatic islet a secretory stimuli is also another cause. Hypoglycemia in these patients can remain asymptomatic, but it can be recurrent and therefore constant monitoring is needed.

4. Immuno suppression:

Hormonal changes of pregnancy reduce synthesis of immunoglobulins and decrease endothelial system function are the cause for immunosuppression in pregnancy. These make the pregnant women more prone for malaria.

Risk for the foetus

Malaria in pregnancy is one of the dreaded cause of fetal mortality and morbidity. Hypoglycemia, anaemia and other complications can all adversely affect the foetus. Falciparum malaria can cause problem for the foetus with mortality up to 15%. Spontaneous abortion, still birth, placental insufficiency and IUGR can also observed due to effect of malaria in pregnancy. Transplacental spread of malarial parasites result in congenital malaria in the first and second pregnancies in highly endemic areas.

Prevention and Management of malaria during pregnancy

WHO recommends a three - pronged approach to the prevention and Management of malaria during pregnancy:

- Insecticide - treated net (ITNs).
- Intermittent preventive treatment.
- Effective care management of malarial illness.

Insecticide - Treated Nets (ITNs)

ITNs kill and repel the mosquitoes that carry malaria, providing protection for both mother and newborns. In areas of stable transmission use of ITNs has been associated with lower prevalence of malaria infection and fewer premature death. A trial in the Gambia found that, during the rainy season in villages where ITNs were used, the prevalence of malaria infection among pregnant women was lower and fewer babies were classified as premature. Further evidence came from a recent study in a highly malarial areas of Kenya. During the first four pregnancies women who were protected by ITNs at night gave birth to 25% fewer premature or small - for gestational - age babies than women
who did not sleep under ITNs.

Intermittent Preventive Treatment (IPT)
For many years WHO recommended that pregnant women in malaria endemic areas should receive an initial anti malarial treatment on their first contact with antenatal check up, followed by weekly chemoprophylaxis (given at less than therapeutic dose) with an effective and safe anti malarial drug. In 2000 the WHO expert committee on malaria recommended the intermittent treatment with an effective, preferably one dose anti malarial drug, should be made available as a routine part of antenatal care to women in the first and second pregnancies in highly endemic areas. At present sulfadoxine-pyrimethamine (SP) given at therapeutic dose is the single dose anti malarial with the best over all effectiveness for prevention of malaria in pregnancy in areas with high transmission and low resistance to SP. Other anti malarial are being evaluated for potential use in IPT.

Management of Malarial Illness
Appropriate management should be available to all women with clinical cases of malaria. Diagnosis of malaria is typically based on the presence or recent history of a fever and whether the women lives in an area of stable or unstable transmission. Parasitological diagnosis of malaria is ideal if reliable light microscopy or rapid diagnostic tests are available. If this is not possible, the decision about whether to start treatment must be based on clinical picture (WHO 2006).

Management of malaria in pregnancy involves the three aspects, these are -
I) Treatment of malaria
II) Management of complications
III) Management of labour.

1. Treatment of Malaria:
   - Treatment should be initiated as early as possible.
   - Assess severity - general condition, temperature, BP, pulse, LFT, blood sugar, HB%, S. creatinine, Serum sodium, Serum potassium, Parasite count, urine out put chart.
   - Monitor maternal and fetal, vital parameters 2 hourly.

Malaria in pregnancy can cause sudden and dramatic complications. Therefore it is very much essential to look for any complications by regular monitoring of the patients-

- Choose drugs according to severity of the disease / Sensitivity Pattern of the parasites.
- Avoid over / under dosing of drugs.
- Avoid drugs that are contraindicated.
- Maintain adequate intake of calories.
- Avoid fluid over load / dehydration.

Anti malarials:
The recommended treatment in the first trimester of pregnancy is quinine. Chloroquine can be considered in mild form of the disease. According to current WHO guidelines Artemisinin Combination Therapy (ACT) can be given in second and third trimester of pregnancy. Quinine and Chloroquine can use in all trimester of pregnancy. It does not cause abortion in therapeutic dose. Uterine contraction is related to pyrexia and parasitemia. Mefloquine was used in some studies where its shows to be safe during pregnancy.

Contraindicated - Doxycycline, Primaquine, Tetracycline, Halofantrine.

2. Management of complications:
Hypoglycemia - 25% - 50% Dextrose 50-100 ml i.v. followed by 10% dextrose infusion can be considered. But fluid overload to be assessed and monitoring is essential. Blood sugar to be monitored every 4-6 hours in case of recurrent hypoglycemia.

Anaemia - Packed cell should be transfused if haemoglobin is < 7gm%.

Septicamic shock - Secondary bacterial infections is common in pregnancy associated with malaria. 3rd generation cephalosporine is useful in this situation.

ARDS - Monitoring of vital parameters, careful fluid management, oxygen supply, diuretics and ventilatory support if needed are essential according to patients clinical and laboratory parameters.

Renal failure - Renal failure could be pre-renal due to unrecognised dehydration, heavy parasitemia. Diuretics, careful fluid management and dialysis is the main treatment for this complication.

Exchange transfusion - Exchange transfusion is indicated in case of severe parasitemia.
3. Management of labour:
Severe malaria carries a very high mortality. Maternal and fetal distress may go unrecognized. Careful monitoring of maternal and fetal parameters is extremely important. Falciparum malaria induces uterine contractions, resulting in premature labour. Uterine contractions appear to be related to the height of the fever. Therefore all efforts should be made to rapidly control the body temperature by cold sponging, antipyretics like paracetamol. Careful fluid management is also very important. If the situation demands induction of labour may have to be considered. Fetal or maternal distress may indicate the need to shorten the second stage of labour. If need even caesarian section must be considered 20, 21.

P. Vivax in pregnancy
There are very few documented studies on P. vivax malaria in pregnancy. It affects more in primigravida than multigravida. Parasite densities may be associated with mild anemia and increased risk of low birth weight baby, abortion, still birth or a reduction of the duration of pregnancy19, 20,21. Recently it has been demonstrated in Thailand and India that infection with P. vivax is associated with lower haemoglobin levels and reduce birth with.

Treatment of vivax malaria in pregnancy
In recent years, increased attention has been drawn to severe malaria caused by P. vivax. Some cases have been reported in India and there is reason to fear that this problem will become more common in the coming years. Severe malaria caused by P. vivax should be treated like severe P. falciparum malaria. In pregnancy use of primaquine is contraindicated. Therefore to prevent the relapse of vivax malaria, chemoprophylaxis with chloroquine is recommended18, 19, 20.

Vaccine against malaria in pregnancy
Although a general malarial vaccine is a possibility, there is much hope for a vaccine against placental malaria. Studies about therapeutic use of monoclonal antibody is going on.23, 24

REFERENCES
15. WHO / Live at risk : Malaria in pregnancy. 2003/ 046 / En / 120 -140.