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Spectrum of vivax malaria in pregnancy and its outcome: a hospital-based study

Kailash Chandra Nayak, Mahesh Pal Khatri, Bal Kishan Gupta, Parmendra Sirohi, Vinita Choudhary, Surendra Kumar Verma & Sanjay Beniwal

Department of Medicine, S.P. Medical College, Bikaner, India

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It has been recognized for nearly a century that pregnant women are especially prone to severe malaria. Studies from various countries of Asia regarding impact of unstable malaria in pregnant women have shown it to be an important cause of maternal death[1,2], but in India only a limited number of hospital-based studies have been carried out regarding the consequences of malaria infection in pregnant women[3–5]. Considering the severity of the problem, we planned to undertake an in-depth prospective study on impact of *Plasmodium vivax* malaria in pregnancy and its outcome in comparison to non-pregnant female patients residing in the same environment and community. These observations are of immense clinical significance and are essential for the theme presented in implementation of global malaria control programme.

This study was conducted on pregnant and non-pregnant female patients suffering from *P. vivax* malaria (confirmed by demonstration of asexual phase of parasite in peripheral blood smear) admitted in classified malaria wards of PBM Hospital, Bikaner (Rajasthan), India during 2006–08. Smear positive cases of only *P. vivax* infection were included in the study. Rapid card test for malaria (OptiMal test) was also performed in every case. Patients with *P. falciparum* infection were not included in the study. Thorough clinical and biochemical examinations were done in all patients, which included complete blood counts, liver function tests, blood urea, serum creatinine and urine analysis. Other investigations like widal test, blood culture, Australia Antigen (HBsAg) (Positive HBsAg cases were not included) and brucella antibody titre were performed to rule out other causes of fever[1]. Fundus and CSF examinations were done in patients of suspected cerebral malaria.

All pregnant patients were subjected to regular obstetric checkup in antenatal clinic and cases were followed-up till delivery. Sonography of abdomen was done in all the pregnant patients and weight of the fetus and placenta were recorded. Cord blood smear and fetal blood smear were also taken to see the evidence of malaria parasite. The Institutional Ethical Committee of S.P. Medical College, Bikaner approved the study. All the patients with uncomplicated malaria and pernicious syndromes were treated according to WHO guidelines[1]. Mortality and morbidity trends were statistically compared in pregnant and non-pregnant females by applying chi-square test.

The study was conducted on 169 female patients of *P. vivax* malaria, which included 25 pregnant females and 144 non-pregnant females. There was no history of prior hospitalization and treatment in both the groups. Duration of fever was 1 to 11 days in both the groups with mean 5.3 days in pregnant and 5.76 days in non-pregnant women and the difference was not statistically significant ($p > 0.05$). The incidence of malaria in pregnancy was found to be more in primigravida and second gravida (18/25) as compared to multigravida (7/25). Highest incidence of infection was observed during 14–28 wk of gestation (13/25) followed by the period >28 wk (9/25) and least in period of <14 wk (3/25) of gestation. We

Table 1. Incidence of various pernicious syndromes observed among pregnant and non-pregnant groups

Pernicious syndrome	Pregnant n = 25 (%)	Non-pregnant n =144 (%)	Odds ratio	Risk ratio	Chi-square	p-value
Severe anemia (Hb <5 g%)	15 (60)	40 (27.7)	3.9	2.16	8.66	0.002
Hepatic failure (S. bilirubin >3 mg%)	3 (12)	11 (7.6)	1.64	1.57	–	0.342
Renal failure (S. creat. >3 mg%)	2 (8)	5 (3.4)	2.41	2.3	–	0.276
Hypoglycemia (Blood glucose <40 mg%)	1 (4)	4 (2.7)	1.45	1.44	–	0.556
Thrombocytopenia (Platelet count <100000)	14 (56)	28 (19.4)	8.9	4.48	–	0.000005
ARDS	1 (4)	4 (2.7)	1.45	1.44	–	0.556
Multiorgan dysfunction	1 (4)	5 (3.4)	1.158	1.152	–	0.623

observed high incidence of all pernicious syndromes of malaria infection in pregnant females in comparison to non-pregnant patients. The results of statistical analysis are shown in Table 1. Out of 25 pregnant females, severe anemia was found in 15, hepatic dysfunction in three, renal failure in two, hypoglycemia in one, acute respiratory distress syndrome (ARDS) in one, multiorgan dysfunction in one and thrombocytopenia in 14 cases and in comparison to 144 non-pregnant females where severe anemia was found in 40 (27.77%), hepatic dysfunction in 11 (7.63%), renal failure in five (3.47%), hypoglycemia in four (2.77%), ARDS in four (2.77%), multiorgan dysfunction in five (3.47%) and thrombocytopenia in 28 (19.44%) cases.

The outcome of pregnancy was worse in primiparous women as compared to multiparous. Normal pregnancy continued in only two out of 10 primiparous and nine out of 15 multiparous pregnant women. Other complications of pregnancy, i.e. preterm live birth was reported in four, intrauterine death in one, stillbirth in two and abortion in one case were reported in primiparous group and preterm live birth was reported in four, intrauterine death in one and abortion in one case was reported in multiparous group. Majority of fetus (20) were born with low birth weight of <2.5 kg. Two fetus were aborted which were having birth weight <500 g. Out of 25 placenta examined, 18 had weight between 200 and 400 g, two patients who aborted had placental weight < 200 g and only five had weight >400 g[6].

Pregnant women are especially prone to develop severe and complicated malaria[1,2]. The incidence of severity of infection and pregnancy related complications varies according to the level of acquired immunity of pregnant women against the infections and the parity[7]. In our study, the susceptibility to malaria infection was found to be high in first and second pregnancies (18 cases). Similar results were reported in India which indicate primigravida are associated with more clinical severity than multigravida in the areas where transmission rate of malaria is high[3,4]. In highly endemic areas the peak level of *P. vivax* parasitaemia occurs between 9 and 16 wk of gestation and then decreases progressively until delivery. In our study, 13 patients were having 14–28 wk of gestation at the time of infection. This shows a greater incidence of malaria infection during second trimester and is in accordance with earlier studies[3,4]. The mechanism of increased susceptibility to malarial infection during pregnancy has not been elucidated but increased cortisol level, depressed cell mediated immunity, altered immune functions of spleen, immune evasion by parasite and interactions between malaria parasite and human nutritional status are believed to play an important role[7,8].

Pregnancy is associated with severe *P. vivax* malaria

and increased prevalence of various pernicious syndromes. Multiple organ failure was more common in pregnant females and associated with grave prognosis. Severe anemia (Hb <5 g%) was more commonly seen amongst pregnant group as compared to non-pregnant females. The mechanism of anemia is multifactorial and complex involving hemolysis and inappropriate bone-marrow response[3].

Thrombocytopenia (platelet <100,000/µl) is an important complication of *P. vivax* malaria which is more pronounced during pregnancy. Severe thrombocytopenia (platelets <50,000/µl) may be associated with bleeding tendency and it was observed in five pregnant patients as compared to only 10 non-pregnant patients in our study. Similar observations were reported by other workers[8].

Various authors from India[9,10] have described hypoglycemia in severe malaria. The incidence of hypoglycemia (blood glucose <40 mg%) is also increased during pregnancy. The possible mechanism for hypoglycemia in our patients included increased glucose consumption by host and the parasite[11], glycogen depletion and impaired gluconeogenesis[12,13].

Malaria leads to significant impact on development of fetus and placenta and outcome of pregnancy in areas of unstable transmission. In our study, preterm live births were seen in eight patients while the incidence of low birth weight babies was seen in 20 cases. Placental malaria is a significant cause of pregnancy related complications in the form of abortions, stillbirths, premature deliveries and low birth weight babies. Several investigators have demonstrated an association between placental infection and low birth weight. The biologic mechanism by which placental malaria infection leads to low birth weight is not fully established[5,8].

Limited data are available regarding spontaneous abortion as a complication of malaria infection. In our study, two patients had abortion, although various authors from other parts of the world have reported that malaria is not an important cause of spontaneous abortion in highly endemic areas[8]. As most of the reports are from highly endemic areas and have failed to document a direct association between maternal malaria and abortions, it seems that the evidence of abortions varies inversely with immunity of mother[9].

Malaria during pregnancy results in increased perinatal wastage in the form of maternal deaths and fetal wastage. Pregnant women are likely to have 2–10 fold higher mortality than non-pregnant women and few studies in India have also shown high incidence of maternal deaths in cases of malaria[3,4] but we have not observed any maternal death in our study which may be because of small number of cases, early recognition and management of the disease.

Thus, our study shows that *P. vivax* malaria infection has an adverse effect on progress and outcome of pregnancy. Therefore, early diagnosis and proper initiation of therapy can reduce the risk of serious maternal and fetal complications. As the chances of acquiring malaria infection are increased during pregnancy, measures should be taken to protect pregnant women from hazards of malaria infection.

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Corresponding author: Dr B.K. Gupta, Prem Kutir, Opp. DRM Office, Hospital Road, Bikaner–334 003, India.
E-mail: bkgbkn@rediffmail.com

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