J Obstet Gynecol Ind Vol. 54, No. 5 : September/October 2004 Pg 456-459

Observations On Malaria in Pregnancy

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OBJECTIVE – To make some observations about malaria in pregnancy especially in relation to the parasite type, drug sensitivity and complications. **METHODS** – The members of Medical Disorders in Pregnancy Committee of our Federation made these observation in different parts of India with an agreed proforma to have essential information by studying the records of a total of 215 pregnant women with malaria. **RESULTS** – Plasmodium falciparum infection was observed in 61%. Sixtyfour percent of the women in the study were primigravidas and Seventynine percent responded to chloroquine. Pregnancy complications were high in terms of miscarriage (32.05), preterm labor (47.44%), IUGR (12.82%) and IUFD (7.7%). Maternal complications were high and 8.4% mothers died due to complications of malaria. **CONCLUSION** – Malaria infection in pregnancy varies significanty according to the region of the country. Maternal complications are high specially with P. falciparum infection.

Key words : malaria during pregnancy, malaria

Introduction

According to WHO, malaria has resurged in 103 countries of the World affecting more than 1 billion people and is responsible for 1-3 million deaths each year[1]. Resurgence is observed predominantly in tropical countries[1,2]. Maternal mortality is high (15-50%) due to malaria in pregnancy when compared to that in the non-pregnant (10-20%). Deaths are mainly due to P. falciparum malaria[3]. Overall pregnancy complications are significantly high. Development of drug resistance has further intensified the problem.

Our aim was to study women with malaria infestation in pregnancy across the country. The type of parasite infestation, sensitivity of the parasite to drugs, severity of malaria in pregnancy and the severity of maternal complications due to malaria were studied.

Material and Methods

This study was conducted by the Committee for Medical Disorders in Pregnancy of the Federation of Obstetric and Gynecological Societies of India in the year 2001-2002. Across the country nine centres agreed to conduct the study. In each center, we had a principal investigator, who was a member of the committee. A proforma was prepared to gather the minimum but essential information as regards malaria in pregnancy. Keeping in mind the limitation of resources, the proforma was kept brief and short. This proforma was agreed upon by all the investigators before initiation of the study.

Table I. Investigators

Centre No.	Institution	Principal Investigator	No. of cases
1.	J N Medical College, Aligarh	Dr. Rajyashri Sharma	75
2.	Medical College, Amritsar	Dr. Madhu Nagpal	18
3.	Medical College, Baroda	Dr. Pankaj Desai	27
4.	M. K.C.G. Medical College, Berhampore	Dr. Gayetri Kar	64
5.	Nil Ratan Sircar Medical College, Calcutta	Dr. Hiralal Konar	8
6.	G.G.S Medical College, Faridkot	Dr. Manjeet Mohi	2
7.	Gauhati Medical College, Guvahati	Dr. Alakananda	10
8.	Regional Institute of Medical Sciences (RIMS), Imphal	Dr. Ranjit L Singh	6
9.	Kasturba Medical College, Manipal	Dr. Sia Sharma, Dr. Prahlad Kustogi	5

Paper received on 06/12/03 ; accepted on 12/08/04

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A total of 215 slide positive cases of malaria in pregnancy were recorded from the nine centres across the country over a period of one year. (Table I). A multivariate analysis of cases had been made to establish

the relationship of various demographic variables viz. geographic distribution, socioeconomic status, age and parity. Further analysis was also made to reveal the occurrence of malaria according to duration of gestation, parasite type, response to drug treatment, pregnancy complications and important maternal complications.

Results

A study of cumulative malaria epidemiological situation in India during the period 2000-2001 by the Directorate of National Anti-malarial Programme (WHO – 2001) revealed the statewise incidence of malaria[1]. Plasmodium falciparum infection is significantly high in Eastern (Orissa, Bihar), North Eastern (Meghalaya, Tripura, Assam, Mizoram, Manipur, Sikkim), Southern (Andhra Pradesh) and Central (Chhattisgarh) states. Deaths due to malaria during the period is significantly high in Orissa (46.3%) and North-Eastern states (58%).

The number of cases according to institutions and cities of the country in the present study are given in Table I. Majority viz., 46% were in the group with monthly income between Rs.1,000 and Rs.2,000; 19% were in the group with monthly income of more than Rs.2,000. Age group distribution revealed 43% were in the age group of 20-25 years and 33% in the age group of 26-30 years. Parity distribution showed that 64% were primigravidas. Distribution of malaria cases revealed that 32% were in the first , 36% in the second and 29% in the third trimester. In the postpartum phase fresh infection or recrudescence of malaria was observed in only 3% of cases.

A significant observation was the prevalence of plasmodium falciparum infection in the majority (61%). P. vivax was the causative agent in 32% cases. Mixed infection was observed in 7% of cases. Infection with plasmodium ovale accounted for one case of mixed infection with P. falciparum and not a single case of P. malaria was seen. Cases were grouped according to their response to chemotherapy. Chloroquine was used as a drug of first choice and 79% responsed to it, while 15% of the total cases required quinine and 6% required combined drug therapy as the parasitemia persisted following chloroquine therapy. In all such cases quinine was the second drug used to achieve the full therapeutic response.

Pregnancy complications observed were many and were significant, miscarriage (32.05%), preterm labor (47.44%), intrauterine growth restriction (12.8%) and intrauterine fetal death (7.69%) were observed. All these events mostly were in combination and led to high perinatal mortality. In one case malaria parasite was detected in the newborn.

Maternal complications were more serious. Significant maternal complications observed in the study were : anemia (38%), hypoglycemia (17%), convulsions (13%), jaundice (7.4%) acute renal failure (8%), adult respiratory distress syndrome (3%) and associated infection (2%). There were 18 (8.4%) maternal deaths due to malaria.

Discussion

There has been a gradual change in the trends of maternal deaths over the years. There is slight decline in direct causes of maternal deaths and increase in indirect causes. Medical disorders in pregnancy need to be properly understood and managed by the obstetric physician. Physiological alterations in pregnancy and the effect of pathology and the drugs on both the mother and the fetus need proper attention.

In India during the year 2000 and 2001 malaria infection was observed to be high by Konnar[4]. The states predominantly affected are : Orissa, Meghalaya, Mizoram, Assam, Tripura, Manipur, Andhra Pradesh and Chhattisgarh. During the same period, slide positivity rate (SPR) in India ranged from 0-17%. The overall mortality due to malaria was as high as 58% mainly in the Eastern and North-Eastern states.

Severity of malaria in pregnancy is high though pregnancy is not an immune deficient state[5,6]. The significant rise of maternal and perinatal mortality is due to the emergence of plasmodium falciparum infection (61% in our study) and also due to the development of resistance of the parasite to commonly used drug chloroquine.

Large number of cases were observed in center No.1 and 4 (Table I). Probably high altitude and/or low temperature may be the reason that vector transmission of parasite is low in some areas. The prevalence of the disease is inversely related to the environmental sanitation, personal protection and importantly, to the effectiveness of various control programmes[7]. Majority of the patients (81%) were in the income group with Rs.2,000 or less per month and 76% were in the age group between 20 and 30 years. Probably this is not a significant association as majority of women in this age group are in the child bearing age.

Sixty-four percent of women with malaria during pregnancy were primigravidas. Due to some unknown reasons severity of infection is high in primigravid women. Frequency of infection is high in late pregnancy[8]. In our study, 52% of the cases were beyond 24 weeks of gestation. Recurrent acute febrile attack with chill and rigor was the commonest presentation.

Convulsions followed by coma were observed in 13% cases. This is an uncommon but serious presentation. It is commonly due to cerebral malaria. In 61% of the cases, the causative agent was P. falciparum. Only one case of P. ovale (center No.8) having mixed infection with P. falciparium was observed. Rest of the mixed infections were with P. falciparum and P. vivax. Chloroquine was found effective in a vast majority (79%) of the cases. In all of the centres chloroquine was the drug of first choice. In center No.4, quinine was used as the drug of first choice after the physician found that the parasite was resistant to chloroquine, 6% cases received chloroquine as initial drug and subsequently they were treated with quinine to achieve the full therapeutic response. Chloroquine and quinine (in case of drug resistance) in therapeutic doses are found safe in pregnancy. However one has to weigh the benefits and risks while prescribing drugs for malaria in pregnancy[9]. Outcome of malaria in pregnancy may be fatal if left untreated. Experience of using other drugs in pregnancy like artemether, pyrimethamine, halofantine, atovaquone and meflaquine are limited[10,11].

One patient (center No.5) had repeated mixed infection (P. falciparum and P. vivax) at an interval of 6 weeks. She received chloroquine and quinine, and blood transfusion. She faced the pregnancy complications of pre-term labor, IUGR and still birth.

Hyperpyrexia may cause release of cylokines (ILs, TNF, leukotrienes) and chemical mediators. These initiate, the synthesis of prostaglandins and ultimately uterine contractions. Fetal complications e.g, IUGR, fetal distress and IUFD are directly related to the degree of maternal parasitemia and anemia. Congenital malaria is rare (>5%). Parasite may reach the fetal circulation when there is placental damage.

Maternal complications observed in this study were many and most were serious. They are directly related to the degree of parasitemia, vital organ dysfunction and the proportion of infected erythrocytes[12]. Mortality rises significantly when 3% or more erythrocytes are infected. Anemia was the major (38%) maternal complication. It is due to accelerated red cell destruction (hemolysis). There is excess demand of folic acid due to accelerated hemopoiesis. Convulsions and coma are uncommon but when present are serious in nature. Such cases need to be differentiated from eclampsia. Finding of raised blood pressure and proteinuria may be helpful. Unfortunately clinical findings are not a absolute guarantee to the diagnosis. Blood film examination and demonstration of parasites are essential to the diagnosis.

All the 31 cases of hypoglycemia were from center No. 4 where the infection was due to P. falciparum. It is due to increased glucose consumption by both the host and the parasite. Quinine also causes increased pancreatic insulin secretion. Hypoglycemia (plasma glucose < 40 mg/dL) is a poor prognostic indicator.

All the 14 cases of acute renal failure were observed in center No. 4 (12 cases) and center No.7 (2 cases). It is commonly due to blockade of renal microcirculation by the sequestrated erythrocyles. All these cases were due to P. falciparum infection. Renal failure is associated with high maternal mortality.

7.4% women developed jaundice. Majority of the cases were from center No. 4. Excessive hemolysis, hepatic cell damage and cholestasis are the important cau Hepatic dysfunction leads to hypoglycemia, metabo acidosis and increased maternal death.

Adult respiratory distress syndrome was observed in five cases. Patients suffered severe hypoxemia due to alveolar exudates. The exact etiology is not understood. Patients with vital organ dysfunction need intensive care management.

Eighteen i.e. 8.37% mothers died due to complications of malaria of whom 16 were from center No. 4 where P. falciparum was the main causative agent. All the medical complications like anemia, vital organ dysfunction (hepatic, renal, pulmonary), metaboli acidosis and electrolyte imbalance are associated with this infection leading to death.

Maternal complications were high specially w falciparum infection. Defection of high risk areas, ve control and personal protection are essential. Strategie at the community, state and national levels to prevent malaria need to be strengthened further. Obstetricians and the general practitioners need to be alert for early diagnosis and management for malaria in pregnancy.

Presumptive diagnosis and treatment of malaria are recommended in non-pregnant state. But the strategy in pregnancy is not clear. Antenatal chemoprophylaxis i recommended in certain areas where annual parasite index (API) is more than five . The new antimalarial, dapsona chlorproguanil (Lapdap) is yet to be tested in pregnancy for its safety[14].

Considering the severity of infection and the complications, presumptive diagnosis and treatment in pregnancy may have a place in certain regions in our country. However health awareness and personal protection have got no alternative.

Lastly, this study has marked limitations. Incidence of malaria during pregnancy was not studied at any center

and the management of malaria at various centers was not uniform. The study being restricted to few centers, it does not reflect a wider picture.

Acknowledgement

I thank the principle investigators mentioned in Table I for participating in the study. I also thank Mr. A Chakraborty for the statistical analysis and Mr Subir Pal for the preparation of the manuscript.

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