

STUDY OF CEREBRAL MALARIA IN PREGNANCY IN A TERTIARY CARE HOSPITAL OF EASTERN ODISHA

Bidyut Prava Das¹, Ratnadeep Ganguly²

¹Associate Professor, Department of Pathology, S.C.B. Medical College and Hospital, Cuttack.

²Postgraduate Student, Department of Pathology, S.C.B. Medical College and Hospital, Cuttack.

ABSTRACT

BACKGROUND

The present work aimed at the clinical mode of presentation, degree of parasitaemia, complications and prognostic trends of pregnant women in cerebral malaria. Evaluation of mortality in different trimesters, varied complications and comparison with nonpregnant women was done.

MATERIALS AND METHODS

Thirty three pregnant women with cerebral malaria were studied. Twenty nonpregnant such cases of reproductive age group admitted to Department of Medicine, S.C.B. Medical College, Cuttack, Odisha, were taken as control. The cases were taken in random order.

RESULTS

Maximum numbers of cases (45.45%) were primigravidae in second trimester of pregnancy. They exhibited higher incidence of anaemia and parasitaemia (2-10%), resulting in abortion and premature labour.

CONCLUSION

All the cases of cerebral malaria were found to be anaemic, but the severity of anaemia was more pronounced in primi (21%) as compared to multigravidae (6.4%). High parasitaemia associated with leucocytosis (27.27%) resulted in poor prognosis. Hypoglycaemia (15.15%), high level of urea, creatinine and alteration in parameters of liver function test further complicated the scenario leading to multiorgan failure. Recovery in cases of primigravidae was prolonged as compared to multigravidae.

KEYWORDS

Cerebral Malaria, Parasitaemia, MOF (Multiorgan Failure) ARDS (Adult Respiratory Distress Syndrome).

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BACKGROUND

Cerebral malaria has emerged to be the most dreaded complication of falciparum malaria claiming heavy toll of mortality nowadays. It has been widely recognised that falciparum malaria can seriously jeopardise the outcome of pregnancy. They demonstrate a higher density of parasitaemia in comparison to nonpregnant women both in endemic and hyperendemic areas.¹ In nonimmune cerebral and other forms of severe falciparum malaria are common in pregnancy. Pregnant women are likely to have 2-10 times higher mortality than nonpregnant woman.² Hospital-based studies reveal primigravidae have higher clinical severity than multigravidae.

MATERIALS AND METHODS

All pregnant patients admitted during period from June 1998 to January 2000 into the Medicine Ward of S.C.B. Medical

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Corresponding Author:

Dr. Bidyut Prava Das,

Associate Professor, Department of Pathology,

SCB Medical College, Cuttack- 753007, Odisha, India.

E-mail: drbidyutpravadas24@gmail.com

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College, Cuttack, Odisha, with severe and altered sensorium were selected for the study. Out of 70 such cases, 33 came out to be cerebral malaria as per the WHO criteria. The cases were taken in random order. After a detailed history taking and meticulous physical examination, thick and thin blood smears were drawn. Using Leishman's stain, they were vigilantly examined for the asexual form of Plasmodium falciparum. Simultaneously, blood samples were taken for routine estimation of haemoglobin, differential count, total leucocyte count, different biochemical examination and blood culture wherever required. Twenty such nonpregnant patients of reproductive age group (20-45 yrs.) were taken as control.

Procedure

In thin smear, parasite density was calculated by counting at least 1000 red cells and expressing the number of parasitised red cells as a percentage. When Plasmodium falciparum was not detected after 100 oil emersion fields, the smear was considered negative. In all cases, detailed haematological parameters like haemoglobin estimation, total leucocyte count, differential count, total platelet count, packed cell volume and total red blood cell count was carried out. Biochemical analysis like blood urea, serum creatinine, serum bilirubin, serum ALT, serum AST and serum alkaline phosphatase was also done in addition to routine

examination of stool and urine. The statistical significance of data was determined by applying 't-test and Chi-square test'.

RESULTS

A total number of cases 53 (cases- 33, control- 20) were included in the study. Amongst them, maximum numbers of cases (45.45%) were primigravidae in second trimester of pregnancy. The distribution of cases in relation to haemoglobin level in control and study group has been depicted in Table 1 and parasitaemia in Table 2. They exhibited higher incidence of anaemia and parasitaemia (2-10%) resulting in abortion and premature labour. All the cases of cerebral malaria were found to be anaemic, but the severity of anaemia was more pronounced in primi (21%) as compared to multigravidae (6.4%). High parasitaemia associated with leucocytosis (27.27%) resulted in poor prognosis. Hypoglycaemia (15.15%), high level of urea, creatinine and alteration in parameters of liver function test further complicated the scenario leading to multiorgan failure. Recovery in cases of primigravidae was prolonged as compared to multigravidae. The comparison of parasitaemia and parity has been shown in Table 3.

Hb in gm Percentage	Control (n=20)	Cases (n=33)
<5	2 (10%)	16 (48.48%)
5-8	14 (70%)	12 (36.36%)
8-10	2 (10%)	4 (12-12%)
>10	2 (10%)	1 (3.03%)

Table 1. Distribution of Cases in Relation to Haemoglobin Level in Control and Study Group

The difference in mean haemoglobin level in control and study group is 1-40 gm%, which is statistically significant. (t-2.5 and P<0.02) indicating a lower level of haemoglobin in the study group, 48.48% of cases in study group have <5 gm% of haemoglobin as compared to 10% of control group.

Parasitaemia in Percentage	Case (n=33)	Control (n=20)	x ²	df	P
<2	4 (12.12%)	15 (75%)	-	-	-
2-5	13 (39.39)	2 (10%)	-	-	-
5-10	10 (30.3%)	2 (10%)	21.83	4	<0.001
10-50	4 (12.12)	1 (55%)	-	-	-
>50	2 (6.6%)	-	-	-	-

Table 2. Parasitaemia in the Sample Studied

Maximum numbers of pregnant cases have parasitaemia in the range of 2-10%. But, in control group, it is less than 2%, which is statistically significant P<0.001. Parasitaemia in none of the cases of control group exceeds 50%.

Parasitaemia in Percentage	Primipara (n=20)	Multipara (n=13)	x ²	df	P
<2	5 (25%)	3 (23.76)	-	-	-
2-5	4 (20%)	5 (38.76%)	-	-	-
5-10	7 (35%)	3 (23.76%)	1.9	4	NS
10-50	3 (15%)	1 (7.69)	-	-	-
>50	1 (5%)	1 (7.69)	-	-	-

Table 3. Comparison of Parasitaemia between Primigravidae and Multigravidae

Parasitaemia in most of the primigravidae were found to be 5-10% and maximum no multigravidae had 2-5% parasitaemia.

Out of 33 cases with cerebral malaria, 20 (60.60) succumbed to it. The number of deaths in control group was found to be 6 (30%). Statistically, this difference is highly significant (P<0.05). When the mortality was compared between primigravidae and multigravidae, it was observed that out of 20 primigravidae cases, 14 died (70%) and 13 multigravidae cases 6 (51%) died even after best treatment facility provided at the tertiary hospital.

DISCUSSION

The major finding in the current study is that most of the cases with cerebral malaria are primigravidae (45-45%) in second trimester of pregnancy (48-48%). They presented with profound anaemia, icterus, Adult Respiratory Distress Syndrome (ARDS), convulsion and oliguria suggesting higher clinical severity. Premature labour was a more frequent event in primigravidae (60%) than multigravidae (15.38%).^{2,3,4} Stillbirth and abortion occurred in 10% and 20% cases respectively in primi, whereas it was 15.38% in multigravidae for both.

In our study, high parasitaemia (2-10%) was observed in 69.69% of patients and particularly the primi claiming (5-10%). It peaks around 13th to 16th weeks of gestation.

In malaria endemic zone, the exacerbation of parasitaemia during pregnancy was thought to be consequence of altered humoral and cell-mediated immunity and immune suppression.⁵ Prior to pregnancy, women living in endemic region acquire a degree of immunity to malaria. Once pregnant, new uteroplacental vasculature is generated. This issue has no previous exposure to malaria and thus immunologically naive and help in parasite replication, but this is unable to explain the increased susceptibility of primigravidae compared to multigravidae.

Evidence for mechanism to explain parasite binding within the placenta has been observed recently. Parasites isolated from pregnant women and from their placental cytoadhered to Chondroitin Sulphate A (CSA). This ligand is present at a high concentration on the surface of the syncytiotrophoblast, which covers the placental villi and is equivalent with the endothelium in the maternal vascular compartment of the placenta. The parasites isolated from the nonpregnant women and from men in the same geographical area do not express binding to CSA. This raises the possibility that a clone of parasites capable of binding to CSA is selected during pregnancy. Incubation with sera from multigravidae inhibits the binding of these parasites to CSA in vitro providing a possible explanation for why multigravid are less susceptible to malarial infection than primigravidae.⁶

All the cases of cerebral malaria were found to be anaemic and the severity was more in primigravidae.^{2,6} In most of these patient's, haemoglobin level remained in the range of 5-8 gm%. The mechanism of the anaemia is multifactorial and complex involving haemolysis, inappropriate bone marrow response and immune destruction of the parasitised erythrocytes as well as

sensitised red cells.^{7,8} The degree of anaemia is proportional the magnitude of parasitaemia.^{1,3} Preexisting iron deficiency anaemia might be an aggravating factor for rapidly developing anaemia leading to severe complication in cerebral malaria.

High parasitaemia associated with polymorphonuclear leucocytosis >12,000/cmm affected the prognosis adversely.^{1,9,10} Leukemoid reaction along with peripheral monocyte showing visible malaria pigment was observed in few cases. Leucocytosis & basophilia was observed in a single case with poor prognosis.^{9,10} Negative blood and urine culture ruled out the possibility of any bacterial infection in cases of leucocytosis.

Hyperparasitaemia associated with hypoglycaemia and lactic acidosis lead to the development of complications.⁶ High value of urea, creatinine and alteration in parameters of liver function tests further complicated the scenario resulting in multiorgan failure.⁷

The mortality rate of pregnant patients with cerebral malaria in our study group is about 60% (control 30%), and in primigravidae, it was found to be 70% in comparison to 51% in multigravidae. It bears a very significant statistical value ($P < 0.01$). High parasite density has contributed to severe anaemia particularly in primigravidae.^{11,3,6} Besides coexistence of iron deficiency anaemia and malaria, relative lack of immunity and increased incidence of all pregnancy-related complications further aggravated the severity reflecting a high mortality trend in these patients.

There is an urgent need to target malaria control strategies for primigravidae in 1st trimester of pregnancy. Women in endemic zone suffer from repeated attacks of malaria, but they either neglect themselves or receive inadequate treatment. Hence, during antenatal period besides routine investigations, weekly antenatal screening for malaria is required. Regular haemoglobin estimation is recommended to treat anaemia so as to prevent complications in the event of falciparum malaria.

In areas of high transmission zone, examination of peripheral parasitaemia is not a sensitive way of screening for malaria infection as it will miss many women with placental and asymptomatic infection.⁶ In such zones, effective antimalarial prophylaxis or intermittent preventive treatment is recommended. It increases haemoglobin level and birth weight of babies.^{6,10} Chemoprophylaxis using chloroquine in suppressive dose is recommended for pregnant women in malarious area to avoid adverse effect of malaria during pregnancy.

Lastly, in tertiary care hospital, effort should be made to find out strain polymorphism and drug resistance pattern of the parasite by using Polymerase Chain Reaction (PCR) technique and to administer appropriate drug. Cooperation of physicians, obstetrician and pathologist is essential for management of such cases and to carry on further research in this field.

CONCLUSION

Cerebral malaria in pregnancy is a significant health problem in Odisha. Pregnant women in the stable transmission zone

are supposed to have immunity. But probably, the immunity declines during pregnancy due to altered physiology, lack of proper nutrition and pre-existing anaemia particularly in primigravidae. Hence, they contribute an important high-risk group for cerebral malaria, which leads to abortion, stillbirth, premature labour and other adverse outcome of pregnancy. Life-threatening malarial attacks with high parasitaemia further adversely influence the prognosis leading to high mortality in pregnant women in comparison to the nonpregnant women. Prompt treatment of clinical episodes of falciparum malaria in pregnancy assume greater clinical importance, particularly in under nourished primigravidae with anaemia, even in stable transmission region like Odisha. Chemoprophylaxis in such situation may be considered carefully as the drugs used have narrow margin of safety and possible noncompliance of drug intake due to lack of adequate monitoring personnel. Plasmodium falciparum is observed to show different genetic polymorphic strain and drug resistance pattern in polymerase reaction amplification. Further study in this respect is warranted to identify the genetic basis for vaccine and appropriate drug therapy.

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