Original Research Article

Comparative Study of Plasmodium falciparum and Plasmodium vivax Malaria in Pregnant and Non Pregnant Women in Visakhapatnam, Andhra Pradesh, India

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Abstract

Background: Pregnant women have a higher risk of malaria compared to non-pregnant women. It's associated with considerable maternal and perinatal morbidity and mortality in developing countries like India. Prevalence of malaria in pregnancy and non pregnant are ranging from 1.7 % to 20 % across India. The Slide Positivity Rate (SPR) for malaria parasite was 17 % for antenatal women in contrast to 8 % among febrile non-pregnant women. Aim: The present study is to compare the clinical features, severity, complications, treatment and outcome of Falciparum/vivax malaria in pregnant and non pregnant women. **Methods**: Pregnant and non Pregnant women who tested positive for malaria either by microscopy of peripheral blood smear or a quantitative buffy coat (QBC) testeach 100 were enrolled in the study. They were followed up till their delivery and discharge from hospital. Demographic, clinical and laboratory data was collected at enrolment, on event of complication and at delivery. **Results**: Malaria more common in primi gravida (64 %) and common in second trimester (68 %). Plasmodium falciparum most common causative agent in 60 (60 %) pregnant women and Plasmodium vivax is most common causative agent in 56 (56 %) non-pregnantwomen. Falciparum malaria are more common in primi gravida 40 % than Vivax malaria(16 %). Complications are more common in pregnancy (64 %) group and anemia was commonest complications in both groups. Low Birth weight(LBW) was observed in 46 %. Mortality is higher in pregnant women group (10 %). **Conclusion**: Malaria andi t's Complications were more common in pregnant women than non-pregnant. It's more common in primi gravida and in second trimester. Most common causative agent was Plasmodium falciparum in pregnant women and Plasmodiumvivax in non-pregnant women.

Keywords: Falciparum Malaria, Vivax Malaria, Pregnancy Complications, Anemia.

Introduction

Prevalence of malaria in pregnancy and non pregnant are ranging from 1.7 % to 20 % across India. The Slide Positivity Rate (SPR) for malaria parasite was 17 % for antenatal women in contrast to 8 % among febrile non-pregnant women[1-6]. The high prevalence of malaria in pregnant women attributed to multiple factors, including increased susceptibility to mosquito bites, immunological and hormonal changes related to pregnancy [1,7,8,9,10,11,12].

The Present study aimed to determine type of malaria infection in both febrile pregnant women and febrile non-pregnant women and to assess the outcome in both febrile pregnant women and febrile non-pregnant women.

Material & Methods

Subjects were diagnosed as out patients and inpatients in acute medical care unit, medical wards, obstetrics ward of a tertiary level private medical college GITAM Institute of Medical Science and Research (GIMSR), providing specialty and super specialty health care services Visakhapatnam, Andhra Pradesh, India. The present study was longitudinal comparative study. The study was conducted over a period of four years from November2015 to November 2019.

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Inclusion criteria

- Pregnant and non-pregnant women with either positive peripheral smear or a positive QBC test for malaria were included in this study.

Exclusion criteria

- Presence of other causes of fever; HIV positive; Co morbid diseases; not interested in participation of study

Total 200 cases of malaria occurring in female were taken into the study: Half of them (100) were pregnant and the other half (100) are non-pregnant. This study was done after approval by Institutional Ethics Committee of Medical College. Written Informed consent obtained from each participant prior to data collection and confidentiality of information was maintained during study.Detailed history was taken with special reference to presence of high-grade fever with chills and rigors.Checked presence of any complications like convulsions, coma,jaundice, decreased urinary output, bleeding manifestations, respiratory distress, anemia and pregnancy related complications. Complete physical examination was done. Presence of malaria was confirmed by positive bold smear or a quantitative buffy coat (QBC) test.The other investigations were done on all the patients: Haemogram with peripheral smear;fasting blood sugar; post prandial blood sugar; serum electrolytes; renal function tests; liver function tests; ECG; Coagulation profile; bleeding time, clotting time, prothrombin time; Ultra sound scan of abdomen and pelvis; urine examination. Newborns were weighed immediately after birth, standard newborn resuscitation measures were practiced. Response rate was 100 % and there was no subject lost to follow up.

Statistical Analysis

Data Management and Analysis- All clinical, demographic, and anthropometric information were carefully checked for correctness and inconsistencies were resolved before analysis. Data were entered in MS-Excel and analyzed by using SPSS V22. Using

kolmogorovsmirnov test normality was checked. Descriptive statistics was represented with percentages, Mean with SD. Chi-square test applied based on nature of the distribution. P<0.05 will be considered as statistically significant.

Observations and Results

Age: In pregnant study subjects, 84 (84 %) belonged to age group 16-25 years: the remaining 16 (16 %) belonged to age group 26-35 years. In non pregnant study subjects, 40 (40 %) belonged to age group 16-25 years, 40 (40 %) belonged to age group 26-35 years and remaining 20 (20 %) belonged to age group 36 years or above as shown in table 1.

Table 1: Age

Pregnant and non-pregnant women	Age-group in year's n (%)		
	16 - 25	26 - 35	36 - 45
Pregnant	84 (84 %)	16 (16 %)	0 (0.0 %)
Non-pregnant	40 (40 %)	40 (40 %)	20 (20 %)
Table 1. Distribution of Malaria cases based on age-group			

Trimester

Malaria more common in second trimester (68 %) next common in first trimester (24 %) and least common in third trimester (8 %) as shown in table 2.

Table 2: Distribution of Malaria Cases in Pregnant Subsample by Trimester

Trimester	Number
First trimester	24(24 %)
Second trimester	68 (68 %)
Third trimester	8 (8 %)
Total	**100**

Type of Malaria in Different Gravida

Falciparum malaria are more common in primi gravida 40 %, in second gravida 12 %& in multi gravida 8 %. Vivax malaria wasseen16 % in primi, 8 % in second& 4 % in multigravida.Mixed infectionwas 8 % in primi, 4 % in second& 0 % in multi gravida in graph 1.

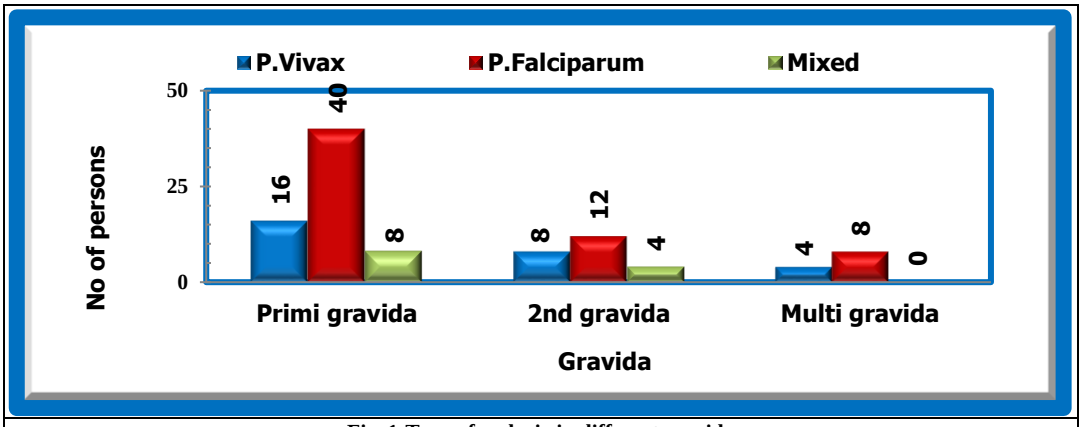

Fig. 1:Type of malaria in different gravida

Etiology of Malaria in Pregnant Women

Plasmodium falciparum most common causative agent in 60 (60 %): Plasmodium vivax in 28(28 %) and mixed infection in 12 (12 %).

Etiology of Malaria in Non-Pregnant Women

Plasmodium vivax is most common causative agent in 56 (56 %): Plasmodium falciparum in 40 (40 %) and had mixed infection in 4(4 %). The most common cause of malaria in pregnancy is P.falciparum (60 %) and in non-pregnant women is P.vivax (56 %) with a significant p value (0.01).

Complications: More common in pregnancy (64 %) than in non-pregnant (36 %) as shown in (Table 3) with a significant p value (0.001)

Table 3: Percentage of Complications in Pregnant and Non-Pregnant Women

Complications	Pregnant		Non Pregnant		P-Value
	Count	%	Count	%	
Present	64	64 %	36	36 %	**0.001***
Not present	36	36 %	64	64 %	
Total	100	100 %	100	100 %	
*P value =0.001 (Highly Significant)					

Table 4: Different Complications of Malaria in Pregnant and Non-Pregnant Women

	Pregnant	Non Pregnant
Total no of patients with complications	64	36
Hematological	64	36
Cerebral malaria	22	10
Jaundice	14	6
Convulsions	12	6
Renal complications	8	3
Hypoglycaemia	3	1
Shock	4	1
Hyperparasitaemia	20	4
Respiratory complications	3	1
Acidosis	4	2

Spontaneous bleeding	5	2
Still births	3	-
Abortions	5	-
Preterm deliveries	15	-
Low Birth Weight (LBW)	46	-
Intra uterine growth retardation (IUGR)	54	-
Neonatal deaths	3	-

Among complications hematological complications are common in pregnant group as shown in table 5.

Table 5:Hematological Complications in Pregnant Group

	Pregnant	Non Pregnant
Anemia	64	36
Severe Anemia	12	3
ModerateAnemia	35	21
Mild Anemia	17	12
Thrombocytopenia	6	2

Outcome

Percentage recovered from malaria is 90 % in pregnant and 97 %in non-pregnant women. Mortality is higher in pregnant women group (10 %) than non-pregnant women (3 %) which is statistically significant (P-value = 0.04).

Discussion

Malaria is the second most common cause of infectious disease-related death after tuberculosis in the world according to The World Health Organization (WHO) and its labeled as a disease of poverty. Every year large number of cases of Malaria infection due to P. falciparum and P. vivax in both pregnant and non-pregnant women are reported in India [1,4,5,11,12,13,20]. Mean parasite density for both parasitological types of malaria is significantly higher in pregnant women compared to non-pregnant women [1, 7, 8, 9, and 11]. All Pregnant women can be considered as a pertinent sentinel population for malaria.Twenty-five million pregnant women are currently at risk for malaria, and, malaria accounts for over 10,000 maternal and 200,000 neonatal deaths per year[20].Young women are more commonly parasitemic than older adults due to continuing development of malarial immunity [1,2,4,10,12]. In our study most of cases observed in Younger maternal age (≤25 years) about 84 % in pregnant and 40 % in non-pregnant groups.Malaria infection was more common in primigravida, falling progressively with increasing parity [1,2,4,9 ,13,14]. Sequestration of infected erythrocytes with P. falciparum in the placenta by expressing surface antigens, mainly variant surface antigen (VAR2CSA), that bind to specific receptors, mainly chondroitin sulphate A (CSA). The malaria risk decreases with increasing parity due to increase Levels of anti-VAR2CSA specific IgGs with parity [4,7,9,16,20]. This explains risk of malaria is higher in primigravidae by the non-recognition of these surface antigens by the immune system [4,7,22]. Recently sequestration of P. vivax in placenta also described[22]. In oustudy 64 % Malaria cases seen in primi gravida; 24 % in second gravida and 12 % in multi gravida. Falciparum malaria more common in primi gravid 40 %, in secondgravid 12 %& in multigravid 8 %. Vivax malaria produces 16 % in primi, 8 % in second& 4 % in multi Gravida. But in Naseem Saba et al study Plasmodium falciparum seen 59.70% in multigravida in [21].Normally the prevalence of malaria among pregnant women was highest early in the second trimester with a decline towards term due to changes in splenic function early in pregnancy[8,9,13]. In our study Malaria more common in second trimester (68 %) next common in first trimester (24 %) and least common in third trimester (8 %). But in another study P. falciparum prevalence was nearly the same in all trimesters and P. vivax prevalence in the second trimester was probably due to relapses [1]. It is due to pattern of malaria may vary in areas of different endemicity [1,4].Normally P. falciparum infection was common in pregnant women [4,6,7]. Prevalence of P. falciparum among pregnant women was about 67 % in the Singh N et al Jabalpur study[1], about 53 % in Hamer D.H et al Jharkhand study, [10] about 55 % Seal et al study,[2] about 85.4 % in Rakesh Romday et al Indore study, [9] about 88 % in another N Singh et al Jabalpurstudy, [13] in 76.75% Naseem Saba et al study [21] and about 62.4 % Nair LS et al Surat study [8]. Plasmodium vivax is also common in pregnant in Asia and the Americas[4,12] Its about 76.6 % in MousumiDatta et al Calcutta study study, [11] about 85 % in Mohammad Sohail et al Jharkhand study, [3] about 67.6 % in Valleesha N. Chandrashekar, et al Mangaluru study,[14] and 63.4 %. In Gowthami Palem et al study [5] In our study in pregnant women Plasmodium falciparum most common causative agent about 60 %: Plasmodium vivax 28 % and mixed infection 12 %. In non-pregnant women most malaria infections are caused by P vivax [1,9,12,17]. In our study also Plasmodium vivax is most common causative agent about 56 % Plasmodium falciparum in 40 % and had mixed infection in 4%. Differential geoparasitological distribution is probably responsible for this finding [1,4,11].

Malaria infection is associated with a broad spectrum of clinical manifestations [2,9,10,11,12,20]. All no immune individuals experience fever and other frequent symptoms include chills, sweats, headache, myalgias, fatigue, nausea, abdominal pain, vomiting, diarrhea, jaundice, and cough. Prevalence of Malaria amongst febrile pregnant women was around three times the prevalence in overall febrile population [24]. More atypical in presentation in pregnancy, malaria due to the hormonal, immunological and hematological changes of pregnancy. Asymptomatic plasmodial infections in pregnant women are very common even in low malaria transmission areas due to submicroscopic plasmodial infection [18]. In our study is fever, chills and sweating common symptoms in both pregnant and in non pregnant groups.Diagnosis of malaria done by smear for microscopy, quantitative buffy coat (QBC)test , rapid diagnostic tests (detecting circulating malaria antigens), Polymerase chain reaction (PCR), and placental histology. Recently several biological biomarkers could be used as indicators for identifying women at risk of placental infection complications, particularly when pre-eclampsia may occur [22].Severe malaria is more common in pregnancy (20- 80 %) mainly infected with falciparum and common in the second and third trimesters because of the lower immunity. Severe malaria was defined as a malaria attack associated with any of the following: cerebral malaria(10-30 %), severe anaemia (0-30 %), renal failure (0-20 %), pulmonary oedema(0-15%),hypoglycaemia(0-10%),shock(0-10%),spontaneous bleeding (0-10 %),repeated convulsions (0-15 %), acidosis(0-15%), Hyperparasitaemia (10-40 %) [1,2,3,9,1 1,13,14, 15,17]. In our study Complications are more common in pregnant group about (64 %) than in non-pregnant group (36 %). Majority also had one or more of other medical complications and these are in both groups-Hematological 64 %/36 %: cerebral malaria 22 %/10 %: jaundice 14 %/6 %: convulsions 12 %/6 %: renal 8 %/3 %: hypoglycaemia 3 %/1 %: shock 4 %/1 %: Hyperparasitaemia 20%/4 %; respiratory 3 %/1 %: acidosis 4 %/2 %: spontaneous bleeding 5 %/2 %.Anemia in malaria is multifactorial and causes are include obligatory destruction of red cells at merogony, accelerated destruction of non-parasitised , bone marrow dysfunction that can persist for weeks, shortened red cell survival and increased splenic clearance. Anaemia was present about 75 % of women attending antenatal clinics in India [1,8,9,14,20]. It was seen about 30-80 % in infection with malaria of both falciparum and vivax malaria but P.falciparum has a stronger effect than *P vivax* [1,2,4,5,8,9,10,14]. The risk of anaemia increase when Malaria infections in the first or second trimester of pregnancy. In our study anemia seenabout 64 % in pregnancy and 36 % in non-pregnancy group. We observed severe anemia (Hb<7 gm/dl) 12 %/3 %, moderate anemia (Hb 7-10 gm/dl)

35 %/21 %: mild anemia (Hb 10-<11gm/dl) 17 %/12 % in both groups. Thrombocytopenia observed about 6 % in pregnancy and 2 % in non-pregnancy group.

Placental malaria in pregnancy causes adverse perinatal outcomes[23].

Malaria increases Fetal complications like stillbirths (2-15 %), abortion (2-15 %), preterm labor (5-30 %), low birth weights (10-75 %), intra-uterine growth restriction (5-70 %) and intra-uterine fetal deaths (2- 35 %) particularly in primigravida, and this risk seems to be higher for infections in first or second trimester [1,2,4,5,8,12,14]. Both PfalciparumandPlasmodium vivax malaria cause but more seen with P falciparum. In our study stillbirths-3: abortions-5: preterm deliveries-15:low birth baby- 46:intra uterine growth retardatio-54: neonatal deaths- 3 observed.

8.Treatment: We follow World Health Organization (WHO) treatment guidelines[15,19,20,25]. For vivax malaria both in pregnant & non pregnant women treated with Chloroquine. For falciparum malaria both complicated and uncomplicated in 1st trimester pregnant treated with combination therapy like clindamycin with quinine .In 2nd and 3rd trimester pregnancy used artemisinin combination therapy artemether with lumefantrine. For falciparum malaria in non pregnant women artemisinin combination therapy artemether with lumefantrine used.In non pregnant Primaquine (15 mg/OD) was given for 14 days for vivax malaria to prevent relapse and 45mg/OD for 1 day was given for falciparum malaria to prevent recrudescence. Primaquine was not given in pregnancy and there were treated with 500mg Chloroquine once in week until the completion of lactation. Pregnancy management — an ultrasound examination should be performed to evaluate amniotic fluid volume, fetal size, and fetal well-being , as gestational-age appropriate during or after acute clinical malaria episode. Peripheral blood smears were negative for malaria parasites in all newborn babies.

9. Pregnant women have a three-times higher risk of Mortality (0-40%) than do non-pregnant women [1,2,11,12,13,23] due to severe malarial infection, and low immunity levles. Deaths are more in primigravida. Mortality in our study deaths are common in pregnant group about 10%.The limitation of our study unable to access the placental malaria.

10. Prevention. The most widely used to prevent malaria in pregnancy are insecticide-treated bed nets , including Long-Lasting Insecticidal Nets , intermittent preventive treatment in pregnancy and effective educational outreach programs [25].

Conclusion

Malaria is more common in pregnant women than non-pregnant women. It's common in primi gravida and in the second trimester of pregnancy. Most common causative agent was Plasmodium falciparum in pregnant women and Plasmodiumvivax in non-pregnant women. Treatment should be started immediately with the most readily available drug. Complications are more common and more severe in pregnancy group and anemia was commonest complications in both groups. There is a need for malaria diagnosis as part of antenatal care for all pregnant women to decrease the risk of complications residing in endemic areas.

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