

Does malaria during pregnancy affect the newborn?

Mohammad Yawar Yakoob¹, Asma Zakaria¹, Saima Naheed Waqar¹, Samiah Zafar¹, Ali Saeed Wahla¹, Sarah Kulsoom Zaidi¹, Arif R. Sarwari², Rahat N. Qureshi³, Amna Rehana Siddiqui¹

Departments of Community Health Sciences¹, Medicine² and Obstetrics and Gynaecology³, The Aga Khan University, Karachi.

Abstract

Objective: To investigate the effect of malarial infection during pregnancy on the newborn.

Methods: A retrospective cohort study was conducted at The Aga Khan University Hospital (AKUH), Karachi, using in-patient hospital records over an 11-year period from 1988 to 1999. The incidence of preterm delivery, low birth weight (LBW) and intrauterine growth retardation (IUGR) in 29 pregnant women with malaria, was compared with that in 66 selected pregnant women without malaria, who delivered at the AKUH during the same time period.

Results: Pregnant women with malaria had a 3.1 times greater risk of preterm labor ($p=0.14$). They were more likely to be anaemic compared to women without malaria ($RR=2.9$, 95% $CI=1.6-5.4$) and had a significantly lower mean haemoglobin level ($p=0.0001$). Maternal malaria was significantly associated with LBW babies ($p=0.001$). The mean birth weight of infants born to pregnant women with malaria was 461 g less ($p=0.0005$). No significant association was, however, found between malarial infection during pregnancy and IUGR ($p=0.33$).

Conclusion: Malarial infection during pregnancy is associated with poor maternal and fetal outcome. It is significantly associated with maternal anaemia and LBW infants. Appropriate measures must, therefore, be taken to prevent malaria during pregnancy, especially in endemic areas (JPMA 55;543:2005).

Introduction

Malaria is one of the most important health problems in many parts of the world, 40% of the world population is exposed to this illness.¹ It kills more than one million people a year.² The four species of malarial parasite (Plasmodium) affecting man are *P. falciparum*, *P. vivax*, *P. ovale* and *P. malariae*.³ *P. falciparum* causes more fulminant disease and complications like anaemia, black water fever, cerebral malaria, tropical splenomegaly syndrome and systemic shock (algid malaria).³ *P. vivax* infects only young erythrocytes and, therefore, causes milder disease.⁴ Infection with *P. ovale* and *P. malariae* is rare.³

Malaria is a major health problem in Pakistan today.⁵ It is a leading cause of preventable deaths in the country.⁶ The annual incidence of malaria in Pakistan was 62 per 100,000 population in 2001.⁶ Transmission of malaria in this country is seasonal, and mostly occurs after the July-August monsoon.⁷ Epidemics of malaria have also occurred periodically in Pakistan, major ones being in Punjab in 1975⁸ and in N.W.F.P. in 1989-90.⁹

Pregnant women are at a greater risk of acquiring malaria due to depression of cell-mediated immunity.^{4,10} Malaria in pregnancy can lead to death of the mother, abortion of the foetus or a still birth.¹¹ Low birth weight has also been described as one of the effects of malaria on the foetus.¹ The consequences of malaria in pregnancy have been widely evaluated in sub Saharan Africa, which is a stable endemic area for the disease.¹²⁻¹⁵ A few studies^{16,17} on this topic

have, however, been carried out in the Indian subcontinent, which is an unstable area for malarial transmission.⁹ This study was conducted to identify the effects of malaria during pregnancy on the mother and the newborn in our region.

Patients and Methods

A retrospective cohort study was conducted at AKUH, a 654-bed tertiary care referral centre in Karachi. The in-patient hospital records drawn over an 11-year period (from 1988 to 1999) identified 70 women admitted with the primary diagnosis of malaria during pregnancy. Thirty-five of these women delivered elsewhere and their delivery records were not accessible. Records of two more women were not found at the time of data collection. Four women with malaria had an abortion (termination of pregnancy before 20 weeks of gestation) and were also excluded from the study. The final number of women in the malaria exposed group was, therefore, 29. All women had malaria diagnosed on the basis of peripheral thick blood smear and delivered singleton live infants. Sixty-six women who had uneventful deliveries at AKUH during the same time period were selected to serve as the unexposed group.

Data was collected through a structured questionnaire which documented age of the mother, gravida status and haemoglobin level at delivery. Maternal records were also used to note the gestational age at delivery and the birth weight of the newborn.

Anaemia was defined as haemoglobin (Hb) of less

than 10 g/dL. Women who had Hb less than 7 g/dL were considered severely anaemic.

Delivery occurring before 37 completed weeks of gestation was considered preterm.

Low birth weight was defined as weight less than 2500 g at birth. Babies who had birth weight less than 10th percentile of expected weight at that particular gestational age were considered IUGR (intrauterine growth retardation).

Statistical Analysis was done by using Epi Info version 6.0. Student's t-test was used to compare means. Proportions were compared using Chi-square test (Yates corrected value was used where applicable). A p-value less than 0.05 was considered statistically significant.

Results

Maternal Characteristics

The exposed group consisted of 29 women who had malaria during pregnancy and delivered at the AKUH. Twenty-one women (72.4%) had infection with *P.falciparum*, while 8 (27.6%) had *P.vivax* on peripheral blood smear. The mean age of women in the exposed (25.9±5.1 years, range = 17-42) and the unexposed group (25.6±4.6 yrs, range = 17-39) was similar (p=0.91). Fifteen women (51.7%) in the malaria exposed group were primigravida, compared to 28 (42.4%) in the unexposed group (p=0.54). Women with malaria were 2.7 times more likely to have preterm delivery than women without malaria (RR=2.7, 95% CI = 0.9-8.2, p= 0.14) (Figure 1).

Malaria infected mothers were significantly more likely to be anaemic than uninfected mothers (RR = 2.9, 95% CI = 1.6-5.4, p=0.0015) (Figure 2). The mean Hb level at delivery in the exposed group (9.5±1.8 g/dL, range = 5.7-12.6) was significantly lower than in the unexposed

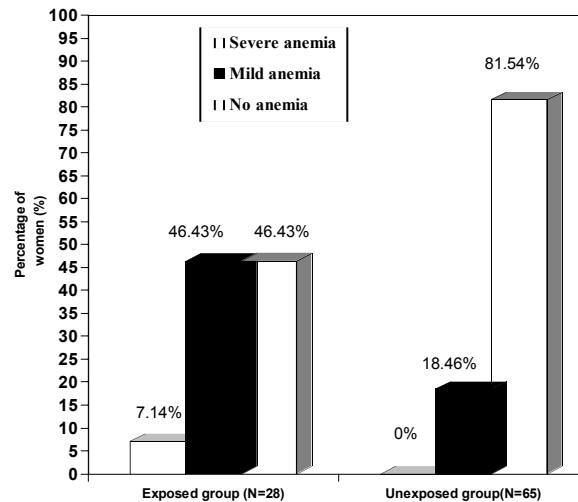


Figure 2. The percentage of women with severe (Hb < 7 g/dL), mild (7 ≤ Hb < 10 g/dL) and no anaemia (Hb ≥ 10 g/dL) in the two groups.

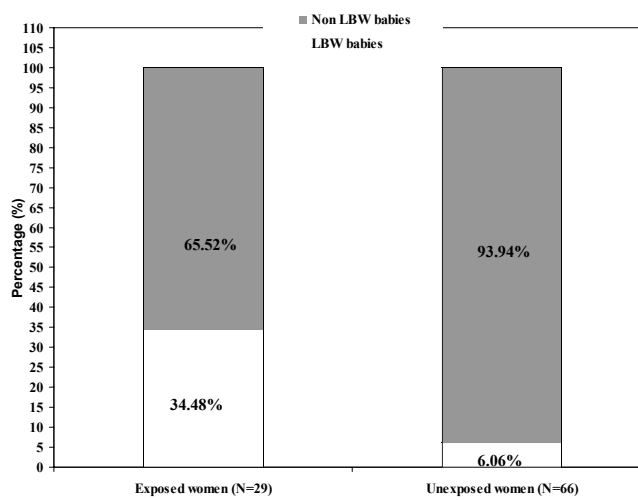


Figure 3. Percentage of low birth weight babies in the exposed and unexposed women.

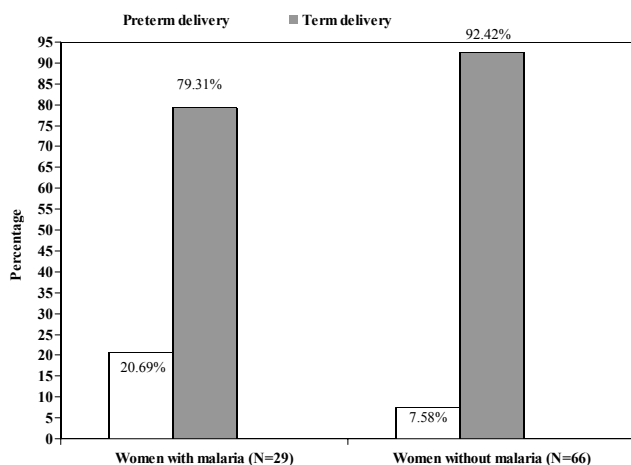


Figure 1. Percentage of term and preterm deliveries in pregnant women with and without malaria.

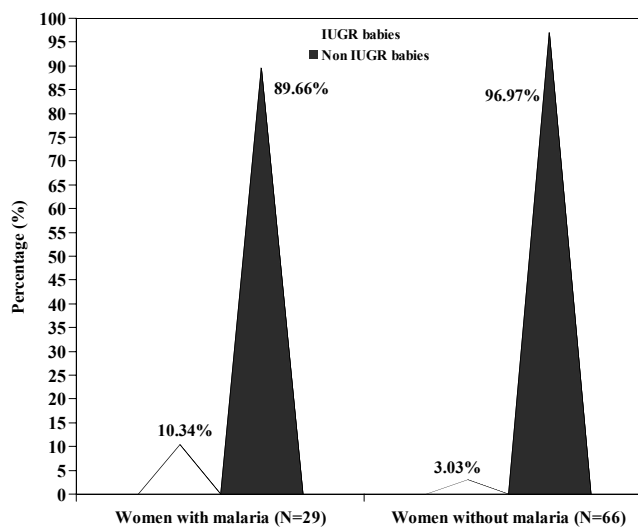


Figure 4. Proportion of babies with IUGR born to women with and without malaria.

(11.2±1.2 g/dL, range = 9.1-14.0) (p=0.0001). The Hb level was not available for one woman each in both groups.

Newborn Characteristics

Low birth weight was significantly more common in women with malaria (RR = 5.7, 95% CI = 1.9-16.7, p=0.001) (Figure 3). The mean birth weight of infants born to exposed mothers was 2611.9 g (SD = 605.5, range = 1500-3800), compared to 3072.8 g (SD = 423.8, range = 2100-3900) in infants of unexposed mothers. The difference in means was statistically significant (p=0.0005). Infected mothers were 3.4 times more likely to have IUGR babies than uninfected mothers (RR = 3.4, 95% CI = 0.6-19.4) (Figure 4). This association, however, did not achieve statistical significance (p=0.33).

Discussion

This study yielded some important information regarding the effect of malaria on the mother and the baby. Women with malaria during pregnancy were more likely to have preterm delivery (PTD). This association, however, was not statistically significant. This is similar to results of a study from Malawi in which maternal parasitemia and/or clinical malaria antenatally was not significantly associated with PTD.¹³

In our study, anaemia was significantly more common in infected compared to uninfected mothers. This is in agreement with results of some studies from sub-Saharan Africa¹⁴ and India.^{16,17} Other studies have reported significant association of malaria with anaemia only in primigravid mothers.¹⁸ Our data, however, was not analyzed for primi- and multigravida separately.

Malaria may cause anaemia by haemolysis of parasitized red blood cells and suppression of haematopoiesis.¹⁹ Anaemia in pregnancy, however, has multiple causes like iron deficiency, folate deficiency, poor nutrition and haemoglobinopathies.^{20,21} In our study, these factors were not controlled for and so it is difficult to evaluate the contribution of malarial infection to anaemia in our exposed women.

The difference in mean Hb level (1.63 g/dL) in the two groups in our study was significant. A study on pregnant women with and without malaria in Lao PDR found a significant difference in mean Hb level of 1.84g/dL.²² Other investigators have failed to find any significant difference in mean Hb levels of the two groups.²³

Our study showed a significant association between malaria during pregnancy and the birth weight. This is in agreement with other studies on this topic.^{15,17,24-27} Although, the difference in mean birth weight of 461 grams in our study is higher than other studies. The deficits in mean birth weight of singleton neonates of malaria infected

mothers from Sierra Leone²⁴ and India¹⁷ were 123 g, 264.7 g and 350g respectively.

Different hypotheses have been proposed for low birth weight in infected mothers. The malarial parasite can infest the placenta, leading to placental thickening and fibrin deposition, which impairs the transport of oxygen and nutrients to the foetus.⁴ Maternal anaemia, age and pre-pregnancy nutritional status can also result in low birth weight babies.¹ In our study, we were unable to control these factors. Our findings are, therefore, limited by potential confounding.

We did not find a significant association between malarial infection and IUGR. This is in contrast to a study which reported a significant association between parasitemia and/or clinical malaria antenatally and IUGR (OR = 5.13, 95% CI = 1.4-19.4).¹³ We had a small number of IUGR babies in both the groups, which may have decreased the power of our study to detect an association.

Maternal anaemia and low birth weight are leading contributors to maternal and newborn mortality respectively.¹¹ Our study shows a significant relationship between malaria during pregnancy and maternal anaemia as well as low birth weight in neonates. Efforts need to be made to prevent malaria during pregnancy either by chemoprophylaxis or use of bed nets. This is likely to have a favourable effect on child and mother survival in areas highly endemic for malaria.

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References

1. Alecrim WD, Espinosa FE, Alecrim MG. Plasmodium falciparum in the pregnant patient. *Infect Dis Clin North Am* 2000;14:83-95.
2. Sachs J, Malaney P. The economic and social burden of malaria. *Nature* 2002;415:680-5.
3. Zaman V, Keong LA, editors. *Handbook of Medical Parasitology*, Third Edition. Singapore: KC Ang Publishing Pte Ltd, 1995, pp. 61-7.
4. Silver HM. Malarial infection during pregnancy. *Infect Dis Clin North Am* 1997;11:99-107.
5. Shariff KM (editor). *Pakistan Almanac 2001-2002. Essential data on Pakistan*. Karachi: Royal Book Company, 2002, p. 210.
6. The Government of Pakistan. *Economic Survey 2001-2002*. Islamabad: Finance Division, Government of Pakistan 2002: 156. (<http://www.finance.gov.pk>)
7. Rowland M, Rab MA, Freeman T, Durrani N, Rehman N. Afghan refugees and the temporal and spatial distribution of malaria in Pakistan. *Soc Sci Med* 2002;55:2061-72.
8. Zulueta JD, Mujtaba SM, Shah IH. Malaria control and long-term periodicity of the disease in Pakistan. *Trans R Soc Trop Med Hyg* 1980;74:624-32.
9. Kazmi JH, Pandit K. Disease and dislocation: the impact of refugee movements on the geography of malaria in NWFP, Pakistan. *Soc Sci Med* 2001;52:1043-55.

10. Fievet N, Cot M, Chougnet C, Maubert B, Bickii J, Dubois B, et al. Malaria and pregnancy in Cameroonian primigravidae: humoral and cellular immune responses to *Plasmodium falciparum* blood-stage antigens. *Am J Trop Med Hyg* 1995;53:612-17.
 11. Greenwood B, Mutabingwa T. Malaria in 2002. *Nature* 2002;415:670-2.
 12. Steketee RW, Wirima JJ, Slutsker L, Heymann DL, Breman JG. The problem of malaria and malaria control in pregnancy in sub-Saharan Africa. *Am J Trop Med Hyg* 1996;55:2-7.
 13. Sullivan AD, Nyirenda T, Cullinan T, Taylor T, Harlow SD, James SA, et al. Malaria infection during pregnancy: intrauterine growth retardation and preterm delivery in Malawi. *J Infect Dis* 1999;179:1580-3.
 14. Ndyomugenyi R, Magnussen P. Anaemia in pregnancy: *Plasmodium falciparum* infection is an important cause in primigravidae in Hoima district, western Uganda. *Ann Trop Med Parasitol* 1999;93:457-65.
 15. Matteelli A, Donato F, Shein A, Muchi JA, Abass AK, Mariani M, et al. Malarial infection and birthweight in urban Zanzibar, Tanzania. *Ann Trop Med Parasitol* 1996;90:125-34.
 16. Singh N, Saxena A, Chand SK, Valecha N, Sharma VP. Studies on malaria during pregnancy in a tribal area of central India (Madhya Pradesh). *Southeast Asian J Trop Med Public Health* 1998;29:10-17.
 17. Singh N, Shukla MM, Sharma VP. Epidemiology of malaria in pregnancy in central India. *Bull World Health Organ* 1999;77:567-72.
 18. Shulman CE, Graham WJ, Jilo H, Lowe BS, New L, Obiero J, et al. Malaria is an important cause of anaemia in primigravidae: evidence from a district hospital in coastal Kenya. *Trans R Soc Trop Med Hyg* 1996;90:535-9.
 19. Miller LH, Baruch DI, Marsh K, Doumbo OK. The pathogenic basis of malaria. *Nature* 2002;415:673-9.
 20. Huddle JM, Gibson RS, Cullinan TR. The impact of malarial infection and diet on the anaemia status of rural pregnant Malawian women. *Eur J Clin Nutr* 1999;53:792-801.
 21. Fleming AF. Tropical obstetrics and gynaecology. 1. Anaemia in pregnancy in tropical Africa. *Trans R Soc Trop Med Hyg* 1989;83:441-8.
 22. Sychareun V, Phengsavanh A, Kityivoilaphanh B, Prabouasone K, Viriyavejakul P, Krudsood S, et al. A study of anaemia in pregnant women with *Plasmodium falciparum* at district hospitals in Vientiane, Lao PDR. *Southeast Asian J Trop Med Public Health* 2000;31 Suppl 1:91-8.
 23. Matteelli A, Donato F, Shein A, Muchi JA, Leopardi O, Astori L, et al. Malaria and anaemia in pregnant women in urban Zanzibar, Tanzania. *Ann Trop Med Parasitol* 1994;88:475-83.
 24. Morgan HG. Placental malaria and low birthweight neonates in urban Sierra Leone. *Ann Trop Med Parasitol* 1994;88:575-80.
 25. Singh N, Mehra RK, Srivastava N. Malaria during pregnancy and infancy, in an area of intense malaria transmission in central India. *Ann Trop Med Parasitol* 2001;95:19-29.
 26. Steketee RW, Wirima JJ, Hightower AW, Slutsker L, Heymann DL, Breman JG. The effect of malaria and malaria prevention in pregnancy on offspring birthweight, prematurity, and intrauterine growth retardation in rural Malawi. *Am J Trop Med Hyg* 1996;55(Suppl. 1):33-41.
 27. Guyatt HL, Snow RW. Malaria in pregnancy as an indirect cause of infant mortality in sub-Saharan Africa. *Trans R Soc Trop Med Hyg* 2001;95:569-76.
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