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Low birth weight and maternal malaria

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ABSTRACT

Objectives: To explore the factors influencing low birth weight (LBW) in pregnancy with malaria

Methods: It is a prospective cohort study conducted in Thaton District Hospital, Mon State, Myanmar during the study period from July 1998 to June 2000. Ninety-six pairs of mother and baby in exposed group (pregnant women with malaria) and 301 pairs of mother and baby in unexposed group (pregnant women without malaria) were included. The following variables; age, parity, migratory status, season at delivery, history of malaria, haemoglobin level on admission, antenatal care, clinical severity, species of Plasmodia, parasite density (count/μ L), trimester at malaria attack occurred were analyzed for Crude cumulative incidence relative risk (CIR) and Mantel Haenszel weighted relative risk for LBW.

Results: CIR of low birth weight was 2.89 in mother with malaria. CIR increased to four times (CIR = 4.4) and seven times (CIR = 7.48) in uncomplicated malaria and complicated malaria respectively. Infection during the third trimester had significant increase in risk. The history of previous malaria, maternal anaemia and presence or absence of antenatal care had about two times increase in CIR. Maternal anaemia and presence or absence of antenatal care also had effect modification on LBW. Age, parity, season at delivery modified the effect of malaria on LBW although they had no significant association.

Conclusions: Prompt and effective presumptive treatment of clinical episodes of malaria, prevention and correction of anaemia during antenatal care are the most important steps to reduce the LBW rate in malaria endemic areas like Thaton District.

Key word: Maternal malaria, Low Birth Weight

INTRODUCTION

Malarial infection during pregnancy is a major public health problem in tropical and subtropical regions throughout the world including Myanmar. Pregnant women are the main group of adults at risk for malaria. Maternal malaria is not only the major cause of more than 3.5 million low-birth-weight infants born each year in sub-Saharan Africa but also it is preventable cause[1]. In the area of unstable transmission like India, Malaysia and the Thai-Myanmar border, both primigravida and multigravidae were reported to be more or less equally prone to severe attacks of malaria, probably because of the absence of sufficient pre-existing immunity in both[2,3,4]. Myanmar is one of the malaria endemic areas. Mon state is a long coastal State with hilly, foothill areas and plains situated in the east and northern sectors of the state and low land area in the west. Moderate and high-risk areas consist of foothill, forest clear plantation, some plains and costal areas. Urban areas of some townships are known to be malaria free. It has a stable transmission with some seasonal fluctuation. Proportion of malaria cases showed increasing trend since 1994. It may be related to the mobilization of people to and from border areas.

12.3% of overall parasite prevalence rate at antenatal booking visit with *P. falciparum* in 62.71% of cases, *P. vivax* in 33.9% and mixed infection in 3.39% and 29.6% of parasitaemia rate at delivery and 6.2% of symptomatic malaria in puerperium after hospital

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delivery at Thaton District Hospital (TDH) were reported[7]. Migrant (OR=4.01, 95% CI=1.53–10.52), history of malaria (OR=5.89, 95% CI=3.39–10.25), no antenatal care (OR=2.54, 95% CI=1.32–4.89) or antenatal care without malaria screening (OR=2.00, 95% CI=1.204–3.326), anaemia (OR=2.03, 95% CI= 1.288–3.192) and delivery in winter season (OR=5.53, 95% CI=2.96–10.57) were reported to be significant factors influencing the susceptibility to malaria during pregnancy in TDH[7]. Overall case fatality was reported to be 8.13% and highest case fatality rate (36.4%) was found in puerperial malaria cases admitted after home delivery. 12.1% over all fetal loss, 3.13% neonatal parasitaemia rate, 1.04% neonatal malaria rate, 4.17% of cord blood parasitaemia rate and 7.29% positive placenta smear rate were reported[7]. Women with severe anaemia (Hb ≤7 Gm%) were at 10 times increased risk to have fetal loss and 7 times higher to have maternal death. The severity of malaria and anaemia were reported to be most important influencing factors on maternal and fetal outcome in pregnancy with malaria[7].

Since more than a hundred years ago, an effect of malaria during pregnancy on birth weight had been proposed[12]. Birth weight differences between babies of the mothers infected or non-infected at delivery are variable but in all studies lower mean birth weights were reported to be associated with placental malaria. Significant differences in mean birth weight values have been reported only for primigravidae[13,14,15].

In sub-Saharan Africa, it is the infants who are most likely to die as a consequence of maternal malaria in that region. This risk of low birth weights in maternal malaria is as a result of intra-uterine growth retardation or prematurity. The mechanism of impaired fetal growth associated with maternal malaria is likely to be multifactorial but includes the contribution of malaria to severe maternal anaemia as well as the ability of *P. falciparum* parasite to remain sequestered in the placental transfer of nutrients[8]. Placental sequestration does not explain all the effects of malaria on the fetus. The mean reduction in birth weight observed in hyperendemic Africa is comparable to that in areas with low endemicity in South-East Asia, suggesting that the number of parasites sequestered and the frequency of infection during pregnancy are not the sole determining factors for intrauterine growth retardation. Furthermore, *P. vivax*, which is not known to result in sequestration, though it does not lead to red cell agglutinations called rosettes, also causes a reduction in birth weight. IUGR even occurs if there has only been a single *P. vivax* infection during pregnancy and even if there is no evidence of placental infection at birth[11].

The incidence of premature labour is significantly increased in non- immune mothers or those with a low level of acquired immunity[12,13,14]. Wickramasuriya (1937) reported a high risk of preterm delivery (54.5%) during the Ceylon epidemic of 1935[15]. Under conditions of year round transmission in Papua New Guinea, premature labour (less than 37 weeks gestation) occurred in less than 10% of women[16]. The rate was increased in primigravidae who were severely anaemic (Hb% < 8 g/dL) at booking, compared to those not severely anaemic (17% vs 9%)[16]. Low birth weight rate was 250/1000 total births among pregnant women with malaria in TDH[7].

Therefore it is important to determine factors influencing and modifying the effect of maternal malaria on low birth weight. It may be useful in preventing LBW in malaria endemic areas.

OBJECTIVES

To explore the factors influencing low birth weight (LBW) in pregnancy with maternal malaria

METHODS

It is a prospective cohort study. Pregnant women who attended antenatal clinic of Maternal and Child Health Centre and Thaton District Hospital (TDH), Mon State, Myanmar with or without malaria infection during pregnancy and who can be followed up to the time delivery in TDH during the study period from July 1998 to June 2000 were studied.

Sample size was calculated as follows. It was assumed that LBW occurs in about 100/1000 of total birth without maternal malaria and 250/1000 of total birth with maternal malaria[17]. The level of significance was set at 0.05; up to 20% of the participants are expected to drop out. To detect the assumed level of LBW with a statistical power of 0.90 the required sample size for each group was calculated using following formula[18].

$$N = 1/(1-f) \times [2 \times (Z_\alpha + Z_\beta)^2 \times p \times (1-p) / (p_0 - p_1)^2]$$
$$= 138 \text{ per group}$$

Where $p_0 = 0.10$, $p_1 = 0.25$, $p = (p_0 + p_1) / 2 = (0.10 + 0.25) / 2 = 0.175$, $1-p = 0.825$, $\alpha = 0.05$, $\beta = 0.10$, power $= 1- \beta = 0.90$, $Z_\alpha = 1.65$ ($\alpha = 0.05$), $Z_\beta = 1.28$ ($\beta = 0.10$), $f = 0.20$

After exclusion of cases with medical diseases apart from anaemia and obstetric complication, 149 pregnant women with malaria infection and 301 cases without malaria could be followed up. Six cases who miscarried and six cases of maternal death were excluded. 41 cases were lost to follow up. In the final analysis , 96 pairs of women and their babies with malaria infection in pregnancy were included in **exposed**

group and another 301 pairs without malaria infection in pregnancy were included in **unexposed group**. Outcome variable of interest was low birth weight. The following variables; age, parity, migratory status, season at delivery, history of malaria, haemoglobin level on admission, antenatal care, clinical severity, species of Plasmodia, parasite density (count/μL), trimester at malaria attack occurred were analyzed for crude cumulative incidence relative risk (CIR) and Mantel Haenszel weighted relative risk for LBW. Confounding factors and effect modifiers on LBW were studied.

RESULTS

The background characteristics of the exposed group and unexposed group of study population are summarized in Table (1).

Table (2) shows distribution of selected characteristics of malaria infection status in two groups of study population with or without LBW and unadjusted relative risk and 95% confidence intervals indicating the effects of characteristics on LBW.

Low birth weight babies are about three times more likely to be born to mother with malaria infection during pregnancy (CIR = 2.89) than mother without malaria infection during pregnancy. Although there was no significant increase in risk of low birth weight in asymptomatic parasitaemic women, the relative risk of LBW increased to four times (RR = 4.4) and seven times (RR = 7.48) in women with uncomplicated malaria and in women with complicated malaria respectively.

Regarding species of plasmodium, although *P. vivax* infection had no significant increase risk of LBW, *P. falciparum* and mixed infections had significant increase risk of about three times (RR = 3.3 in *P. falciparum* group and RR = 2.76 in mixed infection group)

Regarding the trimester when malaria attack occurred, the first and second trimester infection had no significant association with low birth weight. Infection in third trimester and puerperium had significant increase in relative risk of LBW, about four times in women with third trimester infection and about three times in puerperium respectively. Women with recurrent attack of malaria also had significantly increased risk of about three times.

Table (3) shows distribution of selected characteristics of total study population with or without LBW and unadjusted relative risk and 95% confidence intervals indicating the effect of characteristics on LBW. Age, parity, migratory status, residence, season at delivery had no significant association with LBW. History of previous malaria, presence of antenatal care and maternal anaemia had significant association with LBW. All had about two-fold increase in relative risk.

The exposed group and unexposed group were layered by groups of above independent variables and crude cumulative incidence relative risk (CIR) and Mantel Haenszel weighted relative risk of selected variables were calculated with the help of epi-info to show their confounding effect on effect of malaria on Low Birth Weight. Table (4) shows the results. In this analysis, the criterion of a 5% change in the risk ratio is used to select confounders for adjustment. Age, parity, migratory status, season at the time of delivery, history of malaria, haemoglobin at the time of admission and presence of antenatal care are analyzed. The risk difference of are 2.77% in haemoglobin concentration group at the time of admission, 2% in history of malaria, 1% in presence or absence of antenatal care and season at the time of delivery respectively. All other variables are found to have risk difference of less than 1%. It means that all these variables have no confounding effect on effect of malaria on Low Birth Weight. But some factors modified the effect of malaria on LBW.

Effect modification is present when the relationship between exposure and outcome is different from various subgroups in the population. Effect modification is detected by stratifying data by the status or subgroups of the variable of interest, calculating a measure of association for each stratum, and looking for differences in the relative risks among strata.

Among three subgroups of age, older women (age ≥35 years) had the relative risk to have LBW (CIR = 8.5) about 3 to 4 times higher than younger age groups (CIR of 2.6 in 15–24 years group and CIR of 2.33 in 25–34 years age group). It means that maternal age appears to modify the effect of malaria on low birth weight; older women with malaria infection are about 8.5 times as likely to have a low birth weight baby than those without malaria.

Among the three parity groups, women with 4 child births and above group and women with 2–3 child births group with malaria infection during pregnancy are about 7.7 times (CIR = 7.7) and about 5.52 times (CIR = 5.52) as likely to have a low birth weight baby than those without malaria. Among the women with no childbirth or one-childbirth with malaria infection had about 2 times (CIR = 2.12) than those without malaria.

Migratory status and residence had no effect modification.

Regarding season at delivery, women who deliver during summer season are about 4 times higher as likely to have low birth weight baby than those without malaria. For those who delivered during rainy season and winter season, the risks are 3 times and 2 times respectively higher than those without malaria. Women with malaria infection during pregnancy with history of malaria are about 16 times (CIR = 16.4) higher than those without malaria. Women without history of malaria are only 1.5 times (CIR = 1.5) higher risk than those without malaria.

Anaemia also appears to modify the effect of malaria on low birth weight; anaemic women are at 3.5 times higher risk (CIR = 3.56) to have low birth weight baby than those without malaria. Among the non-anaemic women, however, malaria is associated with only 1.66 times higher risk (CIR = 1.66) of low birth weight. Women who do not receive antenatal care have about 0.87 (or 87%) higher risk of delivering a low birth weight baby than women who receive antenatal care. On stratifying the data on effect of malaria during pregnancy on low birth weight by antenatal care, it was observed to be an effect modifier because women who did not receive antenatal care with malaria are about 6.5 times higher risk than those without malaria. Women who received antenatal care with malaria were only about 2 times higher risk than without malaria in pregnancy. The risk difference between women who did not receive antenatal care and those who received antenatal care with malaria were about 4.31 (431%).

TABLE 1
Characteristic of the study population

Socio-demographic characteristics	Pregnant women with malaria N=96			Pregnant women without malaria N=301		
	LBW			LBW		
	Yes n_1 (%)	No n_2 (%)	Total n (%)	Yes n_1 (%)	No n_2 (%)	Total n (%)
Age group						
15–19	1 (4.17)	4 (5.56)	5 (5.21)	4 (15.38)	21 (7.63)	25 (8.31)
20–24	6 (25.00)	17 (23.61)	23 (23.96)	6 (23.08)	75 (27.27)	81 (26.91)
25–29	5 (20.83)	22 (30.56)	27 (28.13)	7 (26.92)	68 (24.72)	75 (24.92)
30–34	7 (29.17)	19 (26.39)	26 (27.08)	7 (26.92)	62 (22.54)	69 (22.92)
35–39	4 (16.67)	8 (11.11)	12 (12.50)	2 (7.69)	34 (12.36)	36 (11.96)
40–44	1 (4.17)	2 (2.78)	3 (3.13)	0 (0.00)	15 (5.45)	15 (4.98)
Total	24 (100.0)	72 (100.0)	96 (100)	26 (100.0)	275 (100.0)	301 (100)
Migratory status						
Native	22 (91.67)	66 (91.67)	88 (91.67)	25 (96.15)	266 (96.73)	291 (96.7)
Migrant	2 (8.33)	6 (8.33)	8 (8.33)	1 (3.85)	9 (3.27)	10 (3.3)
Total	24 (100.0)	72 (100.0)	96 (100.0)	26 (100.0)	275 (100.0)	301 (100)
Residence						
Urban	16 (66.67)	46 (63.89)	62 (54.58)	15 (57.67)	182 (66.18)	197 (65.5)
Rural	8 (33.33)	26 (36.11)	34 (35.41)	11 (42.32)	93 (33.82)	104 (34.5)
Total	24 (100.0)	72 (100.0)	96 (100.0)	26 (100.0)	275 (100.0)	301 (100)
Parity						
0	11 (45.8)	39 (41.17)	50 (52.08)	17 (65.38)	140 (50.91)	157 (52.2)
1	3 (22.5)	15 (20.83)	18 (18.75)	4 (15.38)	55 (20.00)	59 (19.6)
2	4 (16.67)	7 (9.72)	11 (11.46)	0 (0.00)	32 (11.64)	32 (10.63)
3	4 (16.67)	6 (8.33)	10 (10.42)	4 (15.38)	22 (8.03)	26 (8.64)
4	1 (4.17)	1 (1.39)	2 (2.08)	1 (3.85)	9 (3.27)	10 (3.32)
≥5	1 (4.17)	4 (5.56)	5 (5.21)	0 (0.00)	17 (6.18)	17 (5.56)
Total	24 (100.0)	72 (100.0)	96 (100.0)	26 (100.0)	275 (100.0)	301 (100)
History of previous malaria attacks						
Yes	15 (62.5)	17 (23.61)	32 (33.33)	1 (3.85)	34 (12.36)	35 (11.6)
No	9 (39.5)	55 (76.39)	64 (66.66)	25 (96.15)	241 (87.64)	266 (88.4)
Total	24 (100.0)	72 (100.0)	96 (100.0)	26 (100.0)	275 (100.0)	301 (100)

Continuation from table 1…

Socio-demographic characteristics	Pregnant women with malaria N=96			Pregnant women without malaria N=301		
	LBW			LBW		
	Yes n_1 (%)	No n_2 (%)	Total n (%)	Yes n_1 (%)	No n_2 (%)	Total n (%)
Antenatal care						
Yes	16 (66.67)	65 (90.28)	81 (84.38)	23 (88.46)	241 (87.64)	264 (87.7)
No	8 (33.33)	7 (9.92)	15 (15.62)	3 (11.54)	34 (12.36)	37 (12.29)
Total	24 (100.0)	72 (100.0)	96 (100.0)	26 (100.0)	275 (100.0)	301 (100)
Season at the time of delivery						
Summer	6 (25.00)	10 (13.89)	16 (16.66)	8 (30.77)	79 (28.73)	87 (28.9)
Rainy Season	9 (37.5)	23 (31.94)	32 (33.33)	11 (42.31)	128 (46.55)	139 (46.2)
Winter	9 (37.5)	39 (54.17)	48 (50.00)	7 (26.92)	68 (24.73)	75 (24.92)
Total	24 (100.0)	72 (100.0)	96 (100.0)	26 (100.0)	275 (100.0)	301 (100)
Trimester at the time of enrollment						
1st trimester	2 (8.33)	2 (2.78)	4 (4.16)	0 (0.00)	7 (2.55)	7 (2.33)
2nd trimester	4 (16.67)	21 (29.17)	25 (26.04)	12 (46.15)	106 (38.55)	118 (39.2)
3rd trimester	18 (75.00)	49 (68.05)	67 (69.79)	14 (53.85)	162 (58.90)	176 (58.5)
Total	24 (100.0)	72 (100.0)	96 (100.0)	26 (100.0)	275 (100.0)	301 (100)
Clinical Features						
No			26 (100.0)	275 (100.0)	301 (100)	
Asymptomatic	10 (41.71)	63 (87.50)	73 (76.04)			
Uncomplicated	5 (20.80)	6 (8.30)	11 (11.46)			
Complicated	9 (37.59)	3 (4.20)	12 (12.50)			
Total	24 (100.00)	72 (100.00)	96 (100.0)	26 (100.0)	275 (100.0)	301 (100)
MP result						
Negative			26 (100.0)	275 (100.0)	301 (100)	
P.falciparum	17 (70.80)	44 (61.10)	61 (63.54)			
P.vivax	6 (25.00)	21 (29.20)	27 (28.13)			
Mixed infection	1 (4.20)	7 (9.70)	8 (8.33)			
Total	24 (100.0)	72 (100.00)	96 (100.0)	26 (100.0)	275 (100.0)	301 (100)
Parasite density (count/μL)						
0			26 (100.0)	275 (100.0)	301 (100)	
<5000	11 (45.83)	51 (70.83)	62 (64.58)			
5000–10000	3 (12.51)	15 (20.83)	18 (18.75)			
>10000	10 (41.66)	6 (8.33)	16 (16.67)			
Total	24 (100.0)	72 (100.0)	96 (100.0)			
Hb g/dL on admission						
≥10 g/dL	6 (25.00)	38 (52.78)	44 (45.83)	15 (57.69)	168 (61.09)	183 (60.8)
<10 g/dL	18 (75.00)	34 (47.22)	52 (54.17)	11 (42.31)	107 (38.91)	118 (39.2)
Total	24 (100.00)	72 (100.00)	96 (100.0)	26 (100.0)	275 (100.0)	301 (100)

TABLE 2

Distribution of selected characteristics of malaria infection status in two groups of study population with or without LBW and unadjusted relative risk and 95% confidence intervals indicating the effect of characteristics on LBW

	LBW		Relative risk	95% CI	P value
	Yes	No			
Malaria infection					
No	26	275	1		
Yes	24	72	2.89	1.75–4.8	0.000
Clinical features					
No infection	26	275	1		
Asymptomatic	10	63	1.57	0.80–3.14	0.188
Uncomplicated malaria	5	6	5.26	2.50–11.08	0.000
Complicated malaria	9	3	8.68	5.31–14.20	0.000
Species of Plasmodia					
No	26	275	1		
P. falciparum	17	44	3.23	1.87–5.57	0.000
P. vivax	6	21	2.57	1.16–5.70	0.022
Mixed	1	7	1.45	0.22–9.39	0.702
Parasite density (count/μL) groups					
0	26	275	1		
<5000	11	51	2.05	1.09–3.93	0.030
5000–10000	3	15	1.93	0.64–5.78	0.217
>10000	10	6	7.24	4.27–12.27	0.000
Trimester at malaria attack occurred					
No	26	275	1		
First trimester	1	2	3.86	0.75–19.93	0.244
Second trimester	1	8	1.29	0.20–8.46	0.564
Third trimester	4	7	4.21	1.77–9.99	0.014
Puerperium	13	42	2.74	1.50–4.99	0.001
More than one trimester	5	13	3.22	1.40–7.38	0.007

TABLE 3

Distrubution of selected characteristics of total study population with or without LBW and unadjusted relative risk and 95% confidence intervals indicating the effect of characteristics on LBW

	LBW		Relative risk	95% CI	P value
	Yes	No			
Age groups					
15–24 yrs	17	117	1		
25–34 yrs	26	171	1.04	0.59–1.84	0.89
35–44 yrs	7	59	0.84	0.36–1.92	0.67
Parity groups					
0–1	35	249	1		
2–3	12	67	1.23	0.67–2.26	0.502
4+	3	31	0.72	0.23–2.20	0.780
Residence					
Native	49	332	1		
Migrant	3	15	1.3	0.45–3.76	0.71
Season at delivery					
Summer	13	88	1		
Rainy	20	151	0.91	0.47–1.75	0.77
Winter	16	107	1.01	0.51–2.00	0.97
History of malaria					
No	34	296	1		
Yes	16	51	2.32	1.36–3.95	0.002
Haemoglobin					
≥10g/dL	21	206	1		
<10g/dL	29	141	1.84	1.09–3.12	0.02
Antenatal care					
Yes	39	306	1		
No	11	41	1.87	1.01–3.42	0.045

TABLE 4

Crude cumulative incidence relative risk (CIR) and Mantel Haenszel weighted relative risk of selected variables to show their confounding effect on effect of malaria on Low Birth Weight

	Pregnant women With malaria		Pregnant women without malaria		RR	95% CI	P value
	LBW		LBW				
	Yes	No	Yes	No			
Age (years) groups							
15–24	7	21	10	96	2.65	1.11–6.33	0.028
25–34	12	4	14	130	2.33	1.15–4.71	0.018
35–44	5	10	2	49	8.50	1.83–39.47	0.005
Crude cumulative incidence relative risk for all strata = 2.89 Mantel Haenszel weighted relative risk = 2.88, 95% CI = 1.74–4.77							
Parity							
0–1	14	54	21	195	2.12	1.64–3.93	0.017
2–3	8	13	4	54	5.52	1.85–16.45	0.002
4–5+	2	5	1	26	7.71	0.81–73.33	0.101
Crude cumulative incidence relative risk for all strata = 2.89 Mantel Haenszel weighted relative risk = 2.87, 95% CI = 1.73–4.77							
Migratory status							
Migrant	2	6	1	9	2.5	0.27–22.86	0.412
Native	22	66	25	266	2.71	1.62–4.52	0.000
Crude cumulative incidence relative risk for all strata = 2.8 Mantel Haenszel weighted relative risk = 2.79, 95% CI = 1.96–3.98							
Residence							
Rural	8	26	11	93	2.22	0.98–5.07	0.037
Urban	16	46	15	182	3.39	1.78–6.45	0.001
Crude cumulative incidence relative risk for all strata = 2.89 Mantel Haenszel weighted relative risk = 2.89, 95% Ci = 2.02–4.13							
Season at the time of delivery							
Summer	6	10	8	79	4.08	1.63–10.18	0.002
Rainy	9	23	11	128	3.55	1.61–7.85	0-001
Winter	9	39	7	68	2.01	0.80–5.04	0.129
Crude cumulative incidence relative risk for all strata = 2.89 Mantel Haenszel weighted relative risk = 2.92, 95% CI = 2.50–4.18							
History of malaria							
Yes	15	17	1	34	16.4	2.30–117.3	0.000
No	9	55	25	241	1.5	0.73–3.05	0.270
Crude cumulative incidence relative risk for all strata = 2.89 Mantel Haenszel weighted relative risk = 2.83, 95% CI = 1.50–5.34							
Haemoglobin at the time of admission							
≥10g/dL	6	38	15	168	1.66	0.68–4.04	0.263
<10g/dL	18	34	11	107	3.56	1.81–6.98	0.000
Crude cumulative incidence relative risk for all strata = 2.87 Mantel Haenszel weighted relative risk = 2.79, 95% CI = 1.94–4.01							
Antenatal care							
Yes	16	65	23	241	2.27	1.26–4.08	0.006
No	8	7	3	34	6.58	2.02–21.48	0.000
Crude cumulative incidence relative risk for all strata = 2.894 Mantel Haenszel weighted relative risk = 2.86, 95% CI = 1.71–4.79							

DISCUSSION

History of previous malaria, presence or absence of antenatal care and maternal anaemia had significant association with low birth weight with relative risk of about 2 in all 3 variables and age, parity, season at the time of delivery had no significant association on LBW. All these factors had no confounding effect on LBW but these factors modified the effect of malaria on LBW.

Interaction of malaria and anaemia on low birth weight rate had been an area of interest in malaria research and the findings of present study in comparison with other studies are presented in table (5).

Malaria continues to be a global epidemic with devastating consequences. Each year Plasmodium falciparum, the most important malaria protozoan, infects between 200 and 400 million persons, causing 1–4 million deaths. Human malaria may be caused by any of four Plasmodium species: P. falciparum, P. vivax, P. malariae, and P. ovale. P. falciparum is distinguished by the absence of mature forms in the peripheral circulation. Instead, by adhering to the endothelial surface, the mature forms of infected red blood cells (IRBCs) sequester in the deep vascular beds of various tissues. Sequestration is believed to impart the severe consequences of infection, such as cerebral malaria[22].

By adulthood, individuals residing in malaria endemic areas gain immunity sufficient to reduce the frequency and severity of infection. During pregnancy, however, women suffer increased susceptibility to malaria infection compared to their nonpregnant counterparts; this susceptibility diminishes with successive pregnancies. A characteristic feature of maternal malaria is the accumulation of parasites within the placenta, sometimes in the absence of peripheral parasitemia. Recent work has elucidated the mechanism for sequestration within the placenta, and suggested a model to explain the susceptibility of pregnant women to infection[23]. Here we describe patterns of malaria parasite adhesion, and the tissue pathology which ensues from placental infection, to explain the phenomenon of maternal malaria.

The life cycle of Plasmodium parasites involves invertebrate and vertebrate hosts (Fig. 1). The parasite, in the form of a sporozoite, is transmitted at the time of a mosquito bite to the mammalian host. Following inoculation the sporozoite circulates briefly in the blood, rapidly entering the parenchymal cells of the liver, where it undergoes multiplication during a stage referred to as exoerythrocytic schizogony. Roughly 2 weeks after invasion, the hepatocyte ruptures, liberating thousands of uninucleate merozoites which attach to and enter red blood cells. The young stage within the red blood cell is known as the ring form. Over 48 h the ring develops into a trophozoite, multiplies to produce the multinucleate schizont, then causes the red blood cell to burst, releasing merozoites into the blood circulation to invade new erythrocytes. This repetitive cycle of invasion, asexual multiplication, and release is known as the erythrocytic cycle of schizogony.

TABLE 5

Maternal anaemia and low birth weight rate in malaria endemic and nonendemic areas

Source	Area (Survey years)	Birth weight <2500 Grams (%)		
		Severe anaemia	Not severe	No anaemia
Present study (July 1998–June 2000)	Thaton, Myanmar*	66.66 (Hb ≤7 g/dL)	14.29 (Hb >7 to <10 g/dL)	9.25 (Hb ≥10 g/dL)
Mc Gregor[19] (1963)	Kenya* (Mombasa)	42.0 (Hb ≤7.5 g/dL)	32.0 (Hb >7.5 to <8.8 g/dL)	12.7 (Hb ≥8.8 g/dL)
Brabin *et al*[16] (1990)	Papua New Guinea*	65‡ (Hb <8.0 g/dL) 11§ (Hb <8.00 g/dL)	27‡ (Hb 8–140 g/dL) 9.0§ (Hb 8–140 g/dL)	
Gosh *et al*[20] (1997)	India (South Delhi)†	23.9 (Hb <8.0 g/dL)	19.7 (Hb 8–10 g/dL)	18.2 (Hb >10 g/dL)
Kaltreider[21] (1976)	USA†	33.3 (Hb <8.0 g/dL)	18.1 (Hb 8–9.9 g/dL)	16.8 (Hb ≥10 g/dL)

* = Malaria endemic area, † = Malaria nonendemic area
‡ = Primigravida, § = Multigravida

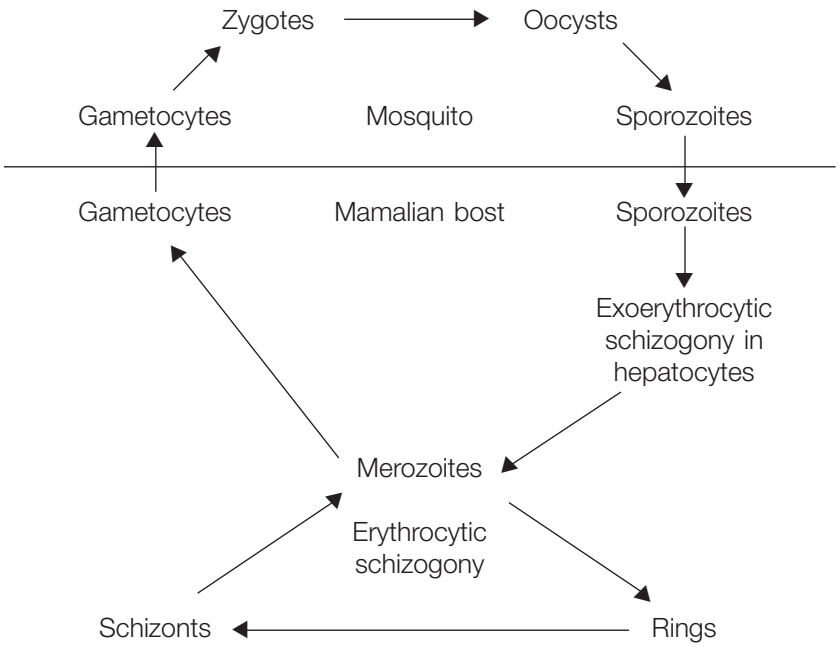

Fig. 1. Life cycle of the Plasmodium parasite

In a poorly understood process, some invading parasites develop into the sexual forms, called macrogametocytes and microgametocytes.When taken up in the bloodmeal of a female anopheline mosquito, these forms emerge as a macro- and microgamete, fuse to form a zygote, then successively develop into an ookinete and an oocyst. The oocyst, lodged under the basal lamina of the external wall of the mosquito midgut, enlarges over 10–14 days until it contains hundreds of sporozoites. Upon rupture of the oocyst wall the liberated sporozoites migrate to the salivary gland of a female mosquito, poised to infect another host at the next bloodmeal[24].

Falciparum malaria during pregnancy has long been recognized as an important determinant of low birth weight[25,26]. The reduction in birth weight is usually more marked in primigravidae[25] but can extend to second and third gravidae in areas of low malaria transmission[27]. A recent study conducted in Thailand has shown that Plasmodium vivax malaria during pregnancy also reduces birth weight[28]. In most studies designed to investigate the relation between malaria during pregnancy and birth weight, potential confounding factors, such as socioeconomic status, maternal nutrition, and smoking, have not been taken into account. However, a number of randomized controlled trials of preventive antimalarial measures during pregnancy have confirmed this causal effect by showing that preventing malaria increases birth weight[29–31].

The major adverse effect of malaria in pregnancy on the mother is anemia. In malarious areas, malaria and anemia are likely to act together to reduce birth weight. Their independent effects are difficult to distinguish. In a study conducted in a highly malarious area of Papua New Guinea, severe maternal anemia was associated with low birth weight in primigravidae, whereas there was no obvious consistent association between parasite positivity and low birth weight[32]. However, a more recent study, conducted in the same country, which attempted to quantitate the separate effects of anemia- and malaria-attributable low birth weight, concluded that, in malarious areas, malaria was a more important risk factor for low birth weight than was anemia[33].

Until recently, the distinction between full-term and preterm low birth weight was difficult in the tropics. As a consequence, the relative contributions of malaria-associated intrauterine growth retardation and preterm delivery were not clearly established. Since the introduction of accurate methods for the estimation of gestational age, it has been suggested that the relative importance of these causes of low birth weight may depend on the level of malaria transmission and the timing of malaria infection during pregnancy. Premature birth results commonly from symptomatic malaria and is usual in severe malaria. It is therefore common in low-transmission areas, where acquired premunition is poor, and in epidemics[34–38]. However, in prospective studies conducted in a low-malaria-transmission setting in Thailand, infection with malaria (which was most often asymptomatic) was associated with low birth weight, resulting mainly from intrauterine growth retardation rather than preterm delivery[27,39,40]. In sub-Saharan Africa where malarial transmission is generally

much higher and maternal malaria is rarely associated with symptoms, two studies have demonstrated that there were different consequences on the newborn infant, depending on the timing of infection. Parasitemia in the antenatal period was associated with intrauterine growth retardation, whereas cord blood parasitemia, probably reflecting a recent active infection, was associated with premature birth[41,42]. In an area of much higher rates of transmission, chronic placental infection was associated with both mechanisms, and low birth weight resulting from premature birth was more common than usually thought[43].

Despite recommendations that malaria be controlled among pregnant women in endemic areas[44], malaria during pregnancy remains a significant cause of maternal and infant mortality and morbidity. Problems related to compliance with drug regimens and the use of partially effective antimalarials are some of the reasons that have led many countries to question, and in many cases abandon, malaria control for pregnant women.

The parity pattern of malaria susceptibility in highly endemic areas (whereby primigravidae and, to a lesser extent, secundigravidae are more affected than are other parities) has been well established[45]. The tendency of Plasmodium falciparum parasites to invade the placenta in semi-immune women also has been described[46]. Regardless of the level of endemicity the main effects of malaria during pregnancy are maternal anemia and reduced birth weight of the newborn[4,47,48].

Malaria is thought to reduce birth weight through a combination of systemic and local effects. First, malaria may affect birth weight through malaria-induced anemia. Second, malaria also may reduce birth weight through placental infection[49]. In this case, parasites either directly cause a mechanical compromise of placental circulation or indirectly interfere with placental functions and/or induce pathological lesions[9,10]. However, there is still no agreement on which are the main mechanisms that mediate reductions in birth weight in placental malaria.

Chronic infection of the placenta (with pigment and parasites) appears to be associated with a significant reduction in birth weight and with the risk of LBW, both through prematurity and IUGR. Chronically infected placentas were seen more frequently among primigravidae than among other parities, which suggests either an increased frequency of infections or an impaired ability to resolve them among first gravidae[25]. Meanwhile, acute infections were associated with a statistically significant lower risk of LBW as a result of IUGR and with a nonsignificant increase in the risk of LBW as a result of prematurity. This indicates that acute infections at the end of gestation may play a role in the induction of premature labor, and this indication is in keeping with early reports of abortions and preterm deliveries during malaria epidemics[34]. Chronic infections also were associated with a reduction in the length and head circumference of the babies, indicating a prolonged effect on fetal nutrition, which has been suggested in other studies[48,50]. Similarly, reduction in the body mass index may reflect the severity and duration of fetal malnutrition.

In conclusion, prompt and effective presumptive treatment of clinical episodes of malaria, prevention and correction of anaemia and prevention of severe anaemia during antenatal care are the most important steps to improve maternal and fetal outcomes including LBW in pregnancy with malaria. Pregnant women who are anaemic, elderly, and multiparous, with history of previous malarial attacks should be the target group for intervention to reduce LBW in malaria endemic area like Thaton, Myanmar. It may be of help in health planning for implementation of the intervention for control of malaria during pregnancy.

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