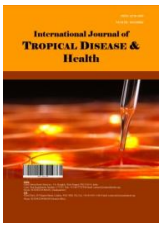

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Risk Factors for Placental Malaria and Birth Weight Outcome among Pregnant Women Attending Mawenzi Regional Referral Hospital, Moshi North Eastern Tanzania

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Authors' contributions

This work was carried out in collaboration between both authors. Author GAM collected the data and wrote the first draft of the manuscript. Author JOC conceived the study concept, analyzed the data and revised the manuscript. Both authors read and approved the final manuscript.

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ABSTRACT

Objective: This study aimed to determine the Prevalence and Risk Factors for Placental Malaria and its associated effects on Pregnancy Outcome among Pregnant Women in Mawenzi Regional Referral Hospital in Kilimanjaro Region.
Methodology: This was a hospital based cross-sectional study. We derived our study sample from previous survey of 700 pregnant women who attended labor ward at MRRH between 2018- 2019 in which we obtained study subjects by random sampling. The study included 350 subjects. We extracted data from the dataset using data extraction sheet and was analyzed using IBM SPSS software version 24. Chi–square was performed and we accepted an error of 5% level $P<0.05$ was the cut off for statistical significance.
Results: The prevalence of PM was 7.1% among the pregnant women in the study area. Primigravida had more cases of PM (11%) as compared to multigravida (2.7%). Pregnant women

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who had gestation age below 37 weeks attributed more cases of PM (9.6%) as compared to 6.7% of PM infections in pregnant women at gestation age of 37 weeks and above. Low birth-weight was estimated at 32% of all subjects who were identified with PM as compared to 6.2% of subjects without placental malaria and their difference was statistically significant (P<0.001). Gestational age of less than 37 weeks was associated with LBW with proportion of 21% among women with PM and it has strong statistical significance of P (<0.001). The use of bed nets was associated with PM among the non-user at 28% P (<0.001).

Conclusion: PM is still a major public health problem in low malaria endemic areas and the groups at risk are women who are Primigravida, women not using bed nets and women who gives birth at gestation age of <37 weeks. We recommend more studies on PM in low endemic.

Keywords: Low birth weight; placental malaria; Plasmodium falciparum; pregnancy.

1. INTRODUCTION

Placental malaria (PM) is a major health problem in malaria endemic countries, with adverse pregnancy outcomes including low birth weight babies, Preterm birth (PTB), and mortality. Globally, about 3.2 billion people are living with malaria while 80% are from Africa, Europe is malaria free while Asia, and Latin America are affected to lesser extent. Worldwide, it is estimated that 15% to 20% of all births are Low Birth Weight (LBW), representing more than 20 million births a year. In sub Saharan Africa alone, about 25% of pregnant women with malaria have evidence of placental parasitaemia during delivery [1,2]. Malaria in pregnancy accounts for 9% of all women with malaria in Tanzania [3,4]. In order for PM control to be effective, prevalence information need to be available. Placental malaria is a form of malaria caused by parasites that sequester in the sycytiotrophoblast region of the intervillous space of the placenta without necessarily manifesting any clinical symptoms [5,6]. The sequestration contributes to maternal morbidity, low birth weight, and preterm delivery [6,7].

There are five plasmodium species which are *P. ovale, P. vivax, P. malariae*, *P. knowlesi* and *P. falciparum*. Among the five plasmodium species, *P. falciparum* and *P. vivax* can infect pregnant women. *P. falciparum* is the most prevalent and fatal in African continent [8]. *P. vivax* is more common in many areas outside Africa, they can develop in lower temperatures, survive in high altitudes Compared *P. falciparum* [2]. Efforts to control PM have been part of the entire malaria control strategies. These strategies include the use of insecticide treated bed nets (ITNs), Intermittent Preventive Treatment (IPTp), Indoor residual spraying (IRS) programs and treatment of active infections. These strategies have had varied effectiveness due to different factors, such as development of resistance, coverage, acceptability of the strategies, climate change and vector mosquito feeding behaviors [2-4,8,9]. The use ITNs and SP are among the malaria preventive methods in Tanzania, given free of charge during ANC visits.

Among 66% of households having at least one ITN only 39% households own ITN for single individual which means one net is shared by three or more people. The coverage is lower than the one that was documented by the Tanzania Demographic Health survey report [3] where 56% of women slept under ITN with not more than two individuals in a net. According to TDHS only, 35% of all pregnant women received two doses of IPTp-SP while only 8% take ≤ 3 doses. In Kilimanjaro region 91% of pregnant women attend ANC clinic during their pregnancy and number of IPTp3+ is within 1%, 92% one dose and 37% two doses while ITN use was 59% [3]. The risk is among primigravida living in high endemic malaria while those living in low endemic all women are at higher risks [10].

In order for PM control to be effective, prevalence information need to be available. Most data available on the prevalence of PM are from high transmission areas whereas little is known on current situation of this public health issue [6,7]. With recently reported changing malaria patterns [11,12], resurgence and group shifts from under five to 5-15 years of age, it is urgent that fresh information is obtained on malaria prevalence, especially PM which is difficult to diagnose. Therefore, a study was carried out to determine prevalence and risk factors for placental malaria and its associated effects on pregnancy outcome among pregnant women in Mawenzi regional referral hospital in Kilimanjaro region.

2. MATERIALS AND METHODS

2.1 Study Site

The research was conducted in Mawenzi Regional Referral Hospital (MRRH) in Kilimanjaro region. MRRH is located in Moshi Municipality, providing health care to patients from six districts namely Moshi Rural, Moshi Urban, Rombo, Hai, Siha, Mwanga and Same. According to the National census 2012, Kilimanjaro region had a population of 793 140 males and 846,947 females [13]. The region is among the areas of low malaria transmission in Tanzania [4]. There are two rain seasons, the long-term rains and short-term rains which fall from March to May and November to December respectively. The persistence of water pools beyond the rain seasons serves as malarial vector breeding sites causing the area being malarial transmission throughout the year [14].

2.2 Study Design

The study was cross sectional hospital-based study conducted at Mawenzi Referral Regional Hospital (MRRH). It was a secondary analysis of the previous survey that was conducted among pregnant women who attended the MRRH between Sept 2017 and July 2018. The study included pregnant women who attended MRRH from 2018 to 2019. A minimum sample size of 125 women was estimated to provide a power of 95% with 5% precision as previously estimated by the Kish and Lisle formula [15]. To increase the statistical power, we recruited 350 study subjects using random sampling procedure. The primary endpoint of this study was placental malaria while low birth weight was secondary outcome of interest. In this case, low birth weight in this case refers to a birth weight below 2500 grams.

2.2.1 Demographic information

Data was collected using questionnaire by interviewing participating mothers in the labor ward. This involved mothers who were waiting to enter labor and the ones who were in latent phase of labor. Information regarding biographical, obstetrical and medical history of the participant during pregnancy recorded. Information on the new born was also recorded including infant birth weight. Gestational length was estimated based on the date of recorded last normal menstrual period (LNMP) or fundal height examination, when LNMP was unknown. All information of the participant from antenatal clinic card and medical registry was carefully reviewed by the principal investigator. This information included history of SP use, birth weights of infants and gravidity. Filling of all questions in the questionnaire were completed in the day of interview. Questionnaires completed by study assistants were reviewed in the evening roundup meeting to verify completeness and reliability of filled information.

2.2.2 Placental malaria determination

To determine placental malaria (parasitemia), placental blood samples were collected from the maternal side of the placenta by making an incision about 1.5 cm deep on the central maternal side by the pool-biopsy methods [16] and hence, about 4 cc of blood sample was collected from a small pool created in this incision after squeezing. Collected blood samples were used to prepare thick and thin blood smears on microscopic glass slides. Prepared smears were then stained with 5% Giemsa's stain for 30 minutes, fixed in absolute methanol for 5 seconds, dried for >45 minutes and examined by two independents experienced microscopists at 100X magnification guided by standard operating procedures (SOPs) up to 100 high power fields (HPFs). A slide negative after 100 HPFs was read by two experienced microscopists was declared negative. Discrepancy findings were reviewed by a third independent miscroscopist and results obtained were regarded as important. Hemoglobin was measured direct from the peripheral blood before the mother deliver.

2.3 Statistical Analysis

Following completion of data extraction from the dataset, we coded the data and entered them into IBM SPSS software version 24 for analysis. Before analysis the data were cleaned i.e. checked for the missing variables, outliers and unsound data. Categorical variables were summarized using cross tabulation to estimate different proportions, the primary outcome was proportion with placental malaria and secondary outcome was proportion with low birth weight. We summarized the variables in proportions to determine their associations using Chi square. A p-value of less than or equal to 0.05 was considered the cutoff for statistical significance.

3. RESULTS AND DISCUSSION

3.1 Social Demographic Characteristics of the Study Participants

Seventy two percent of all women were between 20 and 35 years of age while 20% were <20 years old. About one third (34.6%) of the women had attained no formal education, with only 10.6% of the participants having attained secondary education. About two-thirds (64.6%) of the women were married and 58.3% had given birth more than once (multigravida). Most women or 85.1%, were above 37 weeks of pregnancy and almost all (94.1%) of the women had used a bed net the previous 48 hours. The proportion of pregnant women who had placental malaria was 7.1%. The mean age (IQR) of the study participants was 23.89 (13-43; SD=6.8). The mean gestational age (weeks) was 37.6 (IQR=16-40; SD=1.8) (Table 1).

3.2 Factors Associated with Placental Malaria

Factors analyzed for association with PM were age of participant, education, gravidity, bed net use and gestation age. Only gestational age, gravidity and use of bed nets were associated with pregnancy malaria. Having had one pregnancy was associated with having pregnancy malaria (χ^2=13.0, p<0.001). Women who were in gestation age of lower than 37 weeks, were associated with having pregnancy malaria (χ^2=6.186, p<0.013) and women who used bed nets at home (χ^2=12.182, p<0.001) (Table 2).

3.3 Factors Associated with Low Birth Weight among Pregnant Women with PM

Low birth weight was estimated at 32% of all subjects who were identified with PM as compared to 6.2% of subjects without placental malaria and their difference was strongly significant (P<0.001), there was no statistical association among the use of SP and non. Gestational age of less than 37 weeks was associated with LBW with proportion of 21% among women with PM and it has strong significance of P (<0.001) (Table 3).

Table 1. Descriptive statistics of demographic information (n=350)

Variable	Frequency(n)	Proportion in %
Age group		
<20yrs	70	20
20-35yrs	252	72
>35yrs	28	8
Education level		
None	121	34.6
Primary	193	55.1
Secondary	36	10.3
Marital		
Married	225	64.6
Not married	125	35.7
Gravidity		
Multigravida	204	58.3
Primigravida	146	41.7
Bednet use		
No	18	5.1
Yes	332	94.1
Gestational age		
≥37wks	298	85.1
<37wks	52	14.9
SP use		
Completed	312	80.1
Did not complete	38	10.9
PM		
Yes	25	7.1
No	325	92.9

Table 2. Factors associated with placental malaria n=350

Variable	Pregnancy malaria		Total	χ^2 (p-value)
	No	Yes		
Age group				
<20yrs	65	5	70	0.289 (0.866)
20-35yrs	240	12	206	
>35yrs	25	3	28	
Education level				
None	115	6	121	0.587 (0.746)
Primary	182	11	193	
Secondary	33	3	36	
Gravidity				
Multigravida	218	6	224	13.004 (0.000)**
Primigravida	112	14	126	
Bed net use				
No	13	5	18	12.182 (0.000)**
Yes	312	20	332	
Gestational age				
>37wks	278	20	298	6.186 (0.013)*
≤37wks	47	5	52	

*[a]Fisher's Exact test; **p<0.001; *p<0.05*

Table 3. Associations of low birth weight with placental malaria: n =350

Variable	Low birth weight		Total	χ^2 (p-value)
	No	Yes		
PM				
No	305	20	325	21.070 (0.000)**
Yes	17	8	25	
Age group				
<20yrs	64	6	70	0.906 (0.636)
20-35yrs	188	18	206	
>35yrs	24	4	28	
Completed SP dose				
No	26	12	38	2.155(0.142)
Yes	301	11	312	
Gestational age				
≥37 weeks	281	17	298	44.916 (0.000)**
≤37	41	11	52	

**P<0.05, **P<0.01, [a]Fisher's Exact test*

4. CONCLUSION

The present study determined the prevalence and risk factors associated with placental malaria and association of low birth weight with PM among pregnant women attending Mawenzi Regional Hospital. Several studies have been carried out to assess the prevalence and risk factors of placental malaria in sub-Saharan Africa. In Tanzania, the prevalence of PM has been documented in few regions. The prevalence of PM among women who attended Mawenzi labour ward for delivery during the study period looks lower with the prevalence of the similar previous study conducted in Rufiji [6] where the prevalence of PM was 8%. The prevalence of PM observed in this study could be due to the fact that Kilimanjaro is an area of low malaria transmission while Rufiji is an area of moderate to high malaria transmission with prevalence of 20.8% [4].

The observed prevalence is also lower than that of the previous studies in Morogoro with similar malaria transmission intensity to Rufiji [10,17]. A previous study carried out in MRRH reported a lower prevalence of PM (2.3%) where one dose or more of SP had 60% protective efficacy

against placental malaria. In the same study, 89.1% of the pregnant women had taken ≥1 dose of SP which is similar to this study [10]. In this study, all women who had placental malaria reported to have used ITNs. The use of LLINs, treated with permethrin has been scaled-up in Tanzania, reaching universal coverage in 2011. The proportion of women who had used ITNs was 92%, similar to the findings of this study of women who reported to have used ITNs. In areas where ITN coverage is high, there is a community-level effect where everyone in communities is protected [4].

The prevalence of PM observed in this study is lower than prevalence rates reported elsewhere in sub-Saharan Africa, ranging from 9.5% to 37.1% [18-20]. However, the prevalence rates were obtained by placental blood smear microscopy. It should be pointed out that microscopy with placental blood is less sensitive than placental histology, this is because the parasites in the late stage of trophozoites adhere in the chondroitin sulfate A (CSA) glycosaminoglycan and present more features of *P. falciparum* infection. In a previous study by Desai and colleagues [8], histological analysis was done among three hundred and sixty placentae from pregnant women who had malaria infection where 69.6% of the placenta had parasitaemia.

A retrospective study conducted at KCMC between 2000 and 2011 revealed that 17% of pregnant women had malaria [21] which was almost two times higher compared to the prevalence reported in the current study. KCMC is a zonal referral hospital situated few kilometers from MRRH. Hospital, serving several regions of the northern zone. Therefore, malaria in pregnancy remains a public health problem in northern Tanzania.

According to the findings of this study, the likelihood of acquiring placental malaria infection was higher in primigravida than multigravida indicating that pregnancy specific immunity is acquired after exposure to malaria overtime in previous pregnancies [8]. The results from this study shows that only the primigravida were at higher risk of placental parasitemia. Another previous study shows that all women living in low endemic area are at higher risk due to lack of previous exposure and low immunity [22-24].

A pregnant woman at a gestational age of less than 37 weeks has higher probability of acquiring PM than pregnant woman at gestational age of at least 37 weeks. This is contrary to previous study by Menendez, 2000 which was conducted in Kilombero Tanzania among parturient mothers where 8% were preterm <37 GA among mothers with PM and the proportion was high among the primigravida than other parity groups.

Having PM was a strong risk factor associated with LBW ($p < 0.001$), these results are similar to previously reported findings [1,25,26]. Being among the risk factors for LBW and PM predisposes to neonatal mortality but malaria-induced low birth weight is estimated to be responsible for 3 to 17 deaths per 1000 live births. PM reduces BW through combination of systemic and local effects like induced anemia through placental infection thus interfere with placental functions. Our results show that babies born with GA less than 37 had LBW as supported by the study by Menendez [7] in which preterm babies born before week 37 of gestation had LBW.

PM is still a major public health problem in low malaria endemic areas and the groups at risk are women who are Primigravida, women who does not use bed nets and women who gives birth at gestation age of <37 weeks also LBW has been associated with PM. The determined prevalence presents the proportion of pregnant women at risk of PM and hence the adverse effects associated with PM to the fetus (LBW and premature or pre term birth).

CONSENT

All authors declare that written informed consent was obtained from the patient (or other approved parties) for publication of this paper.

ETHICAL APPROVAL

All authors hereby declare that "Principles of laboratory animal care" (NIH publication No. 85-23, revised 1985) were followed, as well as specific national laws where applicable. All experiments have been examined and approved by the appropriate ethics committee. Both authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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