East African Medical Journal Vol. 77 No. 2 February 2000
RANDOMISED TRIAL OF ALTERNATIVE MALARIA CHEMOPROPHYLAXIS STRATEGIES AMONG PREGNANT WOMEN IN KIGOMA, TANZANIA: II. RESULTS FROM BASELINE STUDIES
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ABSTRACT

Objective: **To determine baseline data among pregnant women consenting to participate in a randomised trial of alternative strategies of malaria chemoprophylaxis in Kigoma urban district, western Tanzania.**
Design: **Cross-sectional study.**
Setting: **The study was conducted in an urban MCH clinic in Kigoma town in western Tanzania.**
Subjects: **All consenting pregnant women who fulfilled entry criteria were recruited into the study.**
Baseline studies: **Baseline data were collected prior to randomisation of women to antimalarial prophylactic regimens. Baseline measurements included examination for blood depleting parasitic infections (stool and urine examinations), haemoglobin levels, haematocrit, sickling test, and blood slide for malaria parasites.**
Results: **A total of 728 pregnant women consented to participate in the interview and of these 705 participated in baseline studies constituting a participation rate of 96.8%. The age of participating women ranged from 14 to 45 years with a mean age of 23.7 years (standard deviation [SD] = 5.4) while the mean number of pregnancies ranged from 1 to 13 with a mean of 3.2 (SD = 2.2). The prevalence of malaria parasitaemia among the pregnant women examined was 9.4% (N = 705) while the prevalence of anaemia (defined as Hb < 8.5 gdl^{-1}) was 12.4% (N = 579). No significant difference was observed in prevalence proportions of malaria parasitaemia in relation to age, parity, marital status and use of mosquito bednets. However the prevalence of anaemia among women in the age group 31-45 years was significantly lower than that observed among women in the age group 14-20 years (2.9% versus 18.9%; crude odds ratio [OR] = 0.13; 95% confidence interval [CI], 0.02-0.55). Sickle cell disease (HbAS) was found in 2.3% (N = 564) of the pregnant women examined.**
Conclusion: **It is concluded that the prevalence of malaria parasitaemia and anaemia was very high in this population suggesting the need for interventions directed at controlling these major causes of maternal morbidity and mortality in Tanzania.**

INTRODUCTION

A number of studies conducted in sub-Saharan Africa have indicated that malaria is a major public health problem, particularly among pregnant women(1-6). It has been reported that malaria in pregnancy is commonly associated with maternal anaemia, increased incidence of low birth weight, abortion and intrauterine foetal death(2,5). Malaria as a disease contributes significantly to the high maternal morbidity and mortality rates in sub-Saharan Africa(1) and it is estimated that malaria may account for up to 10% of all maternal deaths occurring among pregnant women admitted in hospitals in Tanzania(7). To alleviate the consequences of malaria on the health status of pregnant women and their unborn children, regular administration of safe and effective drugs against malaria have been recommended throughout the course of pregnancy(1,8). Hence, in recognition of the health benefits of malaria chemoprophylaxis among pregnant women(9-13), the Tanzanian Ministry of Health recommends continuous weekly chloroquine chemoprophylaxis for all pregnant women regardless of maternal age and parity.

Although malaria is the most important cause of anaemia in pregnancy, other causes of anaemia in pregnancy are also well recognised. Diseases associated with increased risk of anaemia among pregnant women include nutritional deficiencies and infection with blood depleting parasites such as hookworm, ascariasis and schistosomiasis(7). In addition, sickle cell disease might be an important cause of anaemia among pregnant women suggesting the need for assessing its prevalence among pregnant women in

Tanzania. Since use of mosquito coils and bednets may greatly influence occurrence of malaria and anaemia, it was important to assess them before evaluating the effectiveness of the proposed malaria chemoprophylaxis regimens on malaria parasitaemia and haemoglobin levels in pregnancy. Similarly, measuring the magnitude of other diseases associated with anaemia such as hookworm and other helminthic infections was considered important. In view of this we collected baseline data at enrolment of pregnant women into the study in order to determine the prevalence and effect of other causes of anaemia in pregnancy among the study population. In this paper we report baseline data for a randomised trial of alternative strategies of protecting pregnant women against malaria conducted in Kigoma urban district, western Tanzania.

MATERIALS AND METHODS

The characteristics of the study population and description of the treatment arms including eligibility criteria and the process of randomisation employed during the study are described in detail in the companion paper. The study was conducted at an urban antenatal care clinic which serves a population of approximately 85,000 people in Kigoma/Ujiji township in western Tanzania.

Eligibility for enrolment of pregnant women into the study included permanent residence in Kigoma/Ujiji township and the surrounding neighbourhoods. Exclusion criteria included history of allergic reaction to the drugs to be used in the study and pregnancy of more than 24 weeks (6 months). A pregnant woman was defined as any woman who had missed her menstrual period for three months or more and had other signs of pregnancy such as breast enlargement. The cut-off point of 24 weeks of gestation for inclusion into the study was determined by asking each consenting pregnant woman about her last date of normal menstrual period (LNMP) and by performing physical examination. The categorisation of pregnant women having their first and second pregnancies into one group was based on the assumption that women having their first and second pregnancies do not differ significantly in terms of age and other obstetric parameters.

Informed consent: Verbal informed consent was sought from all the women for participation into the baseline studies and subsequent follow up studies. Detailed description of the objectives of the study and methods of data collection were given before asking for verbal informed consent. All the women were told that they had full liberty to refuse participation in the study and that refusal had no negative implications whatsoever on the quality of antenatal care services to those who refused to participate.

Definition of malaria and anaemia: Malaria was diagnosed by measuring body temperature and microscopic examination of blood smear for malaria parasites. Any fever that responded well to the use of standby antimalarial drugs was considered to be a sufficient indicator for the diagnosis of clinical malaria even if a subsequent blood test for malaria parasites was negative. Anaemia was defined as haemoglobin concentration of less than 8.5 g per decilitre (gdl^{-1}).

Two senior female nursing officers and one senior medical laboratory technologist from Maweni Regional Hospital were recruited into the study as resident researchers responsible for data collection in Kigoma. Pregnant women attending antenatal care at the selected urban maternal and child health clinic in Kigoma/Ujiji town and who consented to participate in the study were enrolled into the study consecutively until a total sample size of 728 pregnant women was attained. Each consenting participant was interviewed using a questionnaire and those who subsequently agreed to participate in the trial underwent baseline studies which included estimation of haemoglobin levels and haematocrit, sickling test, blood slide for malaria parasites as well as testing for the presence of antimalarial metabolites in urine. All the tests were carried out at Maweni Regional Hospital in Kigoma by a senior medical laboratory technologist who was responsible for all the laboratory examinations needed for the study. Use of other malaria protective measures such as mosquito coils and bednets were assessed using a questionnaire at the beginning of the study.

All pregnant women found to have a positive blood slide for malaria parasites were treated using the standard chloroquine regimen recommended by the Tanzanian Ministry of Health. This ensured that all women were free from any asymptomatic malaria infection so that any malaria episode occurring during the follow up period would be considered to be due to new infections. Similarly, all pregnant women found to be infected with helminths were given appropriate treatment except for schistosomiasis which is not recommended in pregnancy. The women were advised to come to the clinic for treatment any time they developed fever. In addition, use of standby antimalarial drugs for self-medication was allowed provided the women reported to the clinic on the following day for a thorough check up and a blood test for malaria parasites. Finally, all pregnant women recruited into the study were advised to deliver their babies in Maweni Regional Hospital where birth weight and placental smear for malaria parasites were taken.

Statistical analysis: All questionnaire forms were reviewed for inconsistencies and missing data prior to computer data entry. Chi-squared ($\chi 2$) test for contingency tables was employed to analyse the relationships between number of pregnancies and other socio-demographic variables including use of malaria preventive measures such as bednets and mosquito coils. One way analysis of variance was used in comparing the group means in haemoglobin levels with 95% confidence intervals (95% CI) of the means. Bivariate odds ratios (OR) with 95% confidence intervals were used to assess the association between socio-demographic variables and prevalence of anaemia and malaria parasitaemia. All P-values presented in this paper are two-sided and values were considered significant if P was less than or equal to 0.05 ($P \leq 0.05$). Data entry was conducted using the data entry programme of the Statistical Package for Social Sciences (SPSS/PC+ for DOS Version 5) while statistical data analyses were performed using SPSS/PC+ Version 8.0 for Windows.

RESULTS

A total of 728 pregnant women consented to participate in the interview using a questionnaire and of these 705 pregnant women participated in the baseline studies constituting a participation rate of 96.8% (N = 728). The age of the participating pregnant women ranged from 14 to 45 years with mean age of 23.7 years and standard deviation (SD) of 5.4. The number of pregnancies ranged from one to 13 pregnancies with a mean of 3.2 (SD = 2.2). The distribution of the pregnant women according to sociodemographic variables are presented in Table 1. As can be seen in Table 1, the majority of primigravidae women were in the younger age groups while most of multigravidae women were in the older age groups.

Table 1

Distribution of the study population by age, parity, educational level and marital status in Kigoma urban district, western Tanzania.

Predictor	Number Studied	Intervention groups		P-value
		Primigravidae	Multigravidae	
	N	%(N)	%(N)	
Total	701	55.8 (391)	44.2 (310)	
Age group (years)				
14-20	257	93.0 (239)	7.0 (18)	0.001
21-25	214	54.7 (117)	45.3 (97)	
26-30	153	20.9 (32)	79.1 (121)	
31-45	77	3.9 (3)	96.1 (74)	
Unknown	4	–	–	
Marital status				
Married/cohabiting	644	53.4 (344)	46.6 (300)	0.001
Single/divorced/widowed	56	82.1 (46)	17.9 (10)	
Unknown	5			
Educational status				
No formal education	94	42.6 (40)	57.4 (54)	0.02
Primary education	538	57.4 (309)	42.6 (229)	
Secondary education	60	56.7 (34)	43.3 (26)	
Use of bednets				
Yes	317	51.4 (163)	48.6 (154)	0.04
No	384	59.4 (228)	40.6 (156)	
Use of mosquito coils				
Yes	311	57.6 (179)	42.4 (132)	0.4
No	390	54.4 (212)	45.6 (178)	
Sickle cell trait (HbAS)				
Yes	13	46.2 (6)	53.8 (7)	0.7
No	548	55.1(302)	44.9 (246)	
Missing cases	140	–	–	

Table 2

Prevalence of asymptomatic malaria infection among pregnant women in Kigoma

Predictor	Number examined	Prevalence (%) of malaria infection	Crude OR (95% Cl)
	N	% (N)	
Total series	705	9.4 (66)	
Age group (years)			
14-20	258	9.7 (25)	1.00
21-25	215	8.8 (19)	0.90 (0.46-1.76)
26-30	155	9.7 (15)	1.00 (0.48-2.05)
31-45	77	9.1 (7)	0.93 (0.33-2.34)
Gravidity			
Gravida 1-2	322	9.3 (30)	1.00
Gravida ≥ 3	317	9.5 (30)	1.02 (0.58-1.79)
Parity			
Para 0-1	162	11.7 (19)	1.00
Para ≥ 2	310	9.4 (29)	0.78 (0.40-1.50)
Marital status			
Married/cohabiting	647	9.4 (61)	1.00
Single/divorced/widowed	57	8.8 (5)	0.92 (0.28-2.42)
Educational status			
No formal education	95	9.5 (9)	1.00
Primary education	540	10.0 (54)	1.06 (0.48-2.20)
Secondary education	61	4.9 (3)	0.49 (0.08-2.10)
Use of bednet			
Yes	320	6.9 (22)	1.00
No	385	11.4 (44)	1.75 (0.99-3.09)
Use of mosquito coils			
Yes	312	9.0 (28)	1.00
No	393	9.7(38)	1.09(0.63-1.87)
Sickle cell trait (HbAS)			
Yes	13	30.8 (4)	1.00
No	551	10.3 (57)	0.26 (0.07-1.20)

Prevalence of asymptomatic malaria: Table 2 presents data on malaria infection among the women examined. As can be seen in Table 2, the overall prevalence proportion of malaria parasitaemia was 9.4% (N = 701) which was lower than the 21.3% reported from urban Zanzibar(15). According to Table 2, there was no significant difference observed in malaria parasitaemia in relation to age, parity, marital status and educational status. Similarly, lack of use of bednets and mosquito coils was not associated with increased risk of malaria parasitaemia in this population. Likewise, normal haemoglobin was not significantly associated with increased risk of malaria parasitaemia when compared to pregnant women with the sickle cell disease.

Prevalence of anaemia and sickle cell disease: Table 3 presents the prevalence of anaemia defined as haemoglobin level of less than 8.5 gdl^{-1} measured among the pregnant women enrolled into the study. The overall prevalence of anaemia among the pregnant women enrolled into the study was 12.4% (N = 579) with young women (14-20 years) having significantly higher prevalence rate (18.9% versus 2.9%) as compared to older women aged 31-45 (OR = 0.13, 95% CI, 0.02 - 0.55). High number of pregnancies (gravidity), parity, marital status and use of mosquito coils had no significant association with increased occurrence of anaemia in this population. However, women who reported not having used bednets were observed to have significantly higher prevalence of anaemia compared to those who reported having used bednets (OR = 1.79, 95% CI, 1.04-3.08). Sickle cell trait was not significantly associated with high prevalence of anaemia (7.7% versus 12%) as compared to women without sickle cell disease. The overall prevalence of helminthic infection in this population was high with ascariasis having the highest prevalence proportion. According to Table 3, being infected with blood depleting parasites was not significantly associated with increased risk of anaemia when compared to pregnant women having no parasitic infections.

Table 3

Prevalence of anaemia among pregnant women in Kigoma, Tanzania

Predictor	Number examined	Prevalence (%) of anaemia (Hb < 8.5 g/dl)	Crude OR (95%CI)
	N	% (N)	
Total series	579	12.4 (72)	
Age group (years)			
14-20	201	18.9 (38)	1.00
21-25	180	10.0 (18)	0.48 (0.25-0.90)
26-30	130	10.8 (14)	0.52 (0.25-1.04)
31-45	68	2.9 (2)	0.13 (0.02-0.55)
Gravidity			
Gravida 1-2	258	14.3 (37)	1.00
Gravida ≥3	266	9.0 (24)	0.59 (0.33-1.06)
Parity			
Para 0-1	131	9.9 (13)	1.00
Para ≥2	260	9.2 (24)	0.92 (0.43-1.99)
Marital status			
Married/cohabiting	530	12.5 (66)	1.00
Single/divorced/widowed	48	12.5 (6)	1.00(0.34-2.50)
Use of bednet			
Yes	281	9.3 (26)	1.00
No	298	15.4 (46)	1.79 (1.04-3.08)
Mosquito coils			
Yes	242	12.0 (29)	1.00
No	337	12.5 (42)	1.05 (0.61-1.79)
Sickle cell trait (HbAs)			
Yes	13	7.7 (1)	1.00
No	575	12.0 (69)	1.64 (0.23-70.95
Parasitic infections			
No infection	455	11.4 (52)	1.00
Hookworm	53	15.1 (8)	1.38 (0.57-3.25)
Ascaris	49	18.4 (9)	1.74 (0.70-3.92)
Others*	22	18.2 (4)	1.72 (0.41-5.50)

*Others include schistosomiasis, strongyloidiasis and trichuriasis.

Table 4

Prevalence of sickle cell trait among pregnant women in Kigoma

Predictor	Number examined	Prevalence (%) of sickle cell (HbAS)	Crude OR (95% Cl)
	N	% (N)	
Total series	564	2.3 (13)	
Age group (years)			
14-20	193	2.6 (5)	1.00
21-25	179	3.4 (6)	1.30 (0.32-5.50)
26-45	190	1.1 (2)	0.40 (0.04-2.49)
Gravidity			
Gravida 1-2	254	2.4 (6)	1.00
Gravida ≥ 3	258	2.3 (6)	0.98 (0.26-3.74)
Parity			
Para 0-1	310	2.3 (7)	1.00
Para ≥ 2	254	2.4 (6)	1.05 (0.29-3.69)
Marital status			
Married/cohabiting	519	2.1(11)	1.00
Single/divorced/widowed	45	4.4 (2)	2.15 (0.22-10.31)

Table 4 summarises the prevalence of sickle cell disease among the pregnant women enrolled into the study. As can be seen in the table, the overall prevalence of sickle cell trait was 2.3% (N = 564) among the women examined. The prevalence of sickle cell disease had no significant association with age, parity and marital status in this population.

DISCUSSION

The difference in the distribution of the intervention and comparison groups in relation to age, marital status and educational status was consistent with what was expected. Primigravidae were expected to be younger than multigravidae. However, the prevalence of malaria parasitaemia was significantly higher among young pregnant women when compared to pregnant women in the older age groups. This observation was consistent with what has been reported from other studies(5,16). On the other hand, the prevalence proportions of malaria parasitaemia were similar among women who reported having used bednets and those who stated that they had not used them. As the bednets used by the women were not treated with any insecticide, this observation was consistent with data reported from Papua New Guinea which had shown that untreated bednets were not adequate protection against malaria infection(17). Since several epidemiological studies have demonstrated very close association between malaria parasitaemia and increased incidence of low birth weight(9,18-21), the observed high prevalence of malaria parasitaemia in this population may indicate the likelihood of increased incidence of low birth weight babies in this population. Therefore, intervention studies are required to reduce the incidence of malaria parasitaemia in pregnancy which will ultimately lead to the reduction in the incidence of low birth weight babies. Malaria chemoprophylaxis using safe and effective drugs is among the recommended intervention measures against malaria in pregnancy. This recommendation is supported by recent data from Kenya which demonstrated that the incidence of malaria parasitaemia among pregnant women receiving malaria chemoprophylaxis was significantly lower as compared with women not on any form of malaria chemoprophylaxis(10,22).

An additional observation in the present study is the occurrence of asymptomatic malaria parasitaemia among the pregnant women. Asymptomatic malaria infection in pregnant women needs careful interpretation. It is plausible to state that the women who were detected to have malaria parasitaemia were in the process of developing malaria symptoms within the next few hours. Nevertheless it is possible also for some women to have continued being asymptomatic for sometime before developing malaria symptoms in which case further investigations may be needed to determine the significance of such asymptomatic malaria parasitaemia in pregnancy. Recent data from Zanzibar indicate that women with peripheral parasitaemia are more likely to deliver low birth weight babies than others(15). Therefore, women with asymptomatic malaria parasitaemia might be the ones who go on to develop malaria infection of the placenta which is commonly associated with high incidence of low birth weight. These data suggest that women should be routinely checked for malaria parasites at antenatal care clinics in order to detect women who may have asymptomatic malaria and who may be at an increased risk of giving birth to low birth weight babies.

The World Health Organisation definition for anaemia in pregnancy is haemoglobin concentration of 11.0 grammes or less per decilitre (Hb $\leq$ 11.0 gdl^{-1}) (23).

However, the Tanzanian definition of anaemia was used in this study because the majority of the pregnant women would have fallen into the anaemic group if the standard WHO definition of anaemia in pregnant women was used. Despite lowering the cut-off point for anaemia from 11.0 gdl^{-1} to 8.5 gdl^{-1}, the prevalence of anaemia in this population was still high. The prevalence of anaemia appeared to decrease with increasing maternal age suggesting that semi-immune multigravidae women may be protected against severe malaria which is often associated with anaemia. In addition, women who reported not having used bednets had significantly higher prevalence of anaemia than women who had used bednets. This observation suggests that use of untreated bednets may be protective against maternal anaemia even though occurrence of maternal anaemia is often associated with many factors including nutritional status of the pregnant women. Therefore, it is very unlikely that the high prevalence of anaemia in women who reported not having used bednets was solely due to failure to use bednets.

As infection with blood depleting parasites contributes greatly to the occurrence of anaemia and the prevalence of helminthic infections was high in this population, there is a need for instituting routine stool examinations for all pregnant women in Kigoma region, western Tanzania. This intervention measure which may be equally applicable to other regions with similar climatic conditions in Tanzania, could facilitate early diagnosis and treatment of worm infections before the pregnant women become severely anaemic.

In conclusion, it may be concluded that the prevalence of maternal malaria parasitaemia and anaemia are high among pregnant women in Kigoma urban district, western Tanzania. As malaria parasitaemia and anaemia are common causes of maternal morbidity and mortality in Tanzania, intervention measures should be instituted to control these conditions. Such measures might include promotion of wide use of impregnated bednets which have been proven to be very effective against malaria(24). In similar token, examination for blood depleting worm infections and deworming of those found to be infected should be part of the service provided routinely at antenatal care clinics.

ACKNOWLEDGEMENTS

We are grateful to Anna Fute and Kondo Rukinisha for data collection and the women who accepted to participate in this study. The valuable contributions of the Office of the Regional Medical Officer in Kigoma towards successful implementation of this project are highly acknowledged. We convey our thanks to the late Mr. Joseph B. Mtui for computer data entry. This project was supported by a research grant from the Commonwealth Regional Health Community Secretariat for East, Central and Southern Africa, Arusha, Tanzania.

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