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RANDOMISED TRIAL OF ALTERNATIVE MALARIA CHEMOPROPHYLAXIS STRATEGIES AMONG PREGNANT WOMEN IN KIGOMA, TANZANIA: I. RATIONALE AND DESIGN
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RANDOMISED TRIAL OF ALTERNATIVE MALARIA CHEMOPROPHYLAXIS STRATEGIES AMONG PREGNANT WOMEN IN KIGOMA,TANZANIA: I. RATIONALE AND DESIGN

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ABSTRACT

Objective: **The objective of the study was to assess the effectiveness of alternative strategies of malaria chemoprophylaxis on the reduction of malaria episodes and prevalence of parasitaemia among pregnant women in Kigoma urban district in western Tanzania.**
Design: **Randomised antimalarial prophylactic trial.**
Setting: **The study was conducted in an urban maternal and child health (MCH) clinic in Kigoma town.**
Subjects: **All pregnant women attending antenatal care services at Kigoma urban MCH clinic were eligible. Informed consent was sought from each pregnant woman for participation in the study.**
Intervention measures: **The intervention measures were intermittent and continuous malaria chemoprophylaxis using chloroquine and proguanil.**
Main outcome measures: **Reduction of malaria episodes and parasitaemia and haemoglobin levels among participating pregnant women in Kigoma urban district.**
Results: **Baseline data indicates that the overall mean haemoglobin concentrations among the primigravidae and multigravidae women were similar within the intervention and comparison groups (F-test *(df= 5,* N = 701) = 1.27, P = 0.27). Similarly, no significant difference was observed in the prevalence of malaria parasitaemia within the primigravidae intervention and comparison groups ($\chi 2$ test *(df=5,* N = 701) = *5.4, P = 0.4).* Hence, the process of randomisation produced comparable intervention and comparison groups with balanced characteristics. Specific results of the baseline studies are presented in the companion paper.**
Conclusion: **We conclude that the process of randomisation resulted in comparable intervention and comparison groups. As malaria is a common cause of considerable morbidity and mortality among pregnant women in Tanzania, the present study provided useful data for improving reproductive health in Kigoma region, western Tanzania.**

INTRODUCTION

The Tanzanian Ministry of Health estimates that malaria in Tanzania accounts for 4-5% of all deaths occurring among patients admitted in hospitals. The very high mortality rate attributable to malaria suggests the public health importance of the disease in Tanzania. The clinical effects of malaria among the highly vulnerable groups such as pregnant women and young children have been well documented in several studies(1-6). The studies have indicated that malaria in pregnancy is often associated with increased risk of severe anaemia, abortion, intrauterine foetal death and low birth weight. 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 has been recommended throughout the course of pregnancy (1, 7). However, since the severity of malaria has been shown to decrease with increasing number of pregnancies(3-4), there is a need to evaluate novel approaches for protecting pregnant women from the ill effects of malaria taking into account the documented differences in malaria immunity.

Studies conducted in Tanzania have shown that chloroquine is still a useful drug for treating malaria among pregnant women(8) and that proguanil (Paludrine®) is a better malaria chemoprophylactic drug as compared with chloroquine(9). In recognition of the health benefits of malaria chemoprophylaxis among pregnant women(5,7,9-12), the Tanzanian Ministry of Health recommends continuous weekly chloroquine

chemoprophylaxis for all pregnant women regardless of maternal age, gravidity or parity. This policy suggests the need for research programmes for evaluation of alternative strategies for protecting pregnant women against malaria. The present research project envisaged to test three alternative approaches of protecting pregnant women against malaria within the existing primary health care delivery system in Kigoma urban district. The ultimate aim of the project was to determine a simplified and cost-effective chemoprophylaxis method that might be recommended to the Ministry of Health for possible change in the current guidelines on malaria prophylaxis among pregnant women in Tanzania. Furthermore, the results of this research programme might be useful within the primary health care delivery system taking into account the socio-economic constraints obtainining in a poor resource country like Tanzania. In this paper, we present the rationale and study design used in evaluating the proposed alternative strategies of malaria prophylaxis among pregnant women in an area assumed to have low incidence of chloroquine resistant *P. falciparum* malaria. The study was implemented in Kigoma urban district in western Tanzania from September 1992 to January 1995.

Rationale and hypothesis of the study: There is no doubt that for a pregnant woman, malaria poses a greater hazard than any of the prophylactic drugs currently advocated. This means that to improve reproductive health, administration of malaria chemoprophylaxis to pregnant women throughout the course of their pregnancy and the first month of the puerperium is extremely important. However, the strategies need to take into account the proven differences in malaria severity among pregnant women(3). Primigravidae are more susceptible to severe form of malaria compared to multigravidae. Proguanil (Paludrine®) is undoubtedly a very effective prophylactic drug(9,10) but the cost of procuring proguanil in private pharmacies is beyond the financial ability of many pregnant women in Tanzania. Furthermore, the potential risk of encouraging the emergency and spread of parasite resistance to proguanil preclude wider use of proguanil among pregnant women while maintenance of compliance with continuous chemoprophylaxis using chloroquine may be a major problem(13).

These problems have lead to a number of research questions such as whether continuous malaria chemoprophylaxis provides an additional benefit in semi-immune multigravidae if chemotherapy is readily available, that is to say, giving treatment only when the pregnant women become ill with malaria. It appears that protection of pregnant women against malaria would be simplified by adopting intermittent chemoprophylaxis for all pregnant women if intermittent chemoprophylaxis gives similar protection as continuous chemoprophylaxis. Although intermittent prophylaxis may not be necessarily cheap, it is an attractive novel approach for increasing compliance while at the same time reducing drug pressure on malaria parasites in Tanzania. Three intervention strategies were evaluated using a cohort of 360 primigravidae and a similar number of multigravidae using different interventions (Table 1). Therefore, the aim of the study was to determine whether the three intervention strategies had different effect on malaria protection among pregnant women in Kigoma urban district in western Tanzania.

MATERIALS AND METHODS

Study site and population: Kigoma urban district was selected for the study in order to minimise the likelihood of interaction of *P.falciparum* resistance with the proposed interventions. Presence of high level of malaria resistance to chloroquine could potentially interfere with the evaluation of the effectiveness of the proposed chemoprophylaxis regimens. This was borne out of the fact that occurrence of chloroquine resistant *P.falciparum* malaria decreases with increasing distance as one moves away from Dar es Salaam to the western part of Tanzania(14). The research was conducted at an urban antenatal care clinic which serves a catchment population of approximately 85,000 people in Kigoma/Ujiji town(15). Kigoma town is located on the shores of Lake Tanganyika about 1300 kilometres west of Dar es Salaam while Lake Tanganyika is formed within the western part of the Great East African River Valley. Kigoma town is the main transit port for cargo and passenger vessels run by the Tanzania Railways Corporation to neighbouring countries of Burundi and the Democratic Republic of Congo (formerly Zaire). Kigoma/Ujiji township is surrounded by several fresh water bodies including valleys around Luiche river which drains into Lake Tanganyika. The mean annual rainfall for the Kigoma region is approximately 1000 millimetres with dry season running from July to September and has a high relative humidity. Consequently malaria transmission in Kigoma region occurs throughout the year.

According to the Regional Annual Health Report of 1989, malaria accounted for 10-15% of all outpatient attendances and 46% of all admissions in Kigoma region(16). This figure places malaria among the top ten causes of ill health in Kigoma region. At the present time there is no specific malaria control programme being undertaken in Kigoma region except for the chemotherapy which is routinely given to patients suffering from clinical malaria. Provision of malaria treatment is within the framework of the World Health Organisation tactical variant number II for malaria control(7).

Desc*ription of the treatment arms:* Primigravidae group 1 (P1) and multigravidae group 1 (M1) received the gold standard for malaria chemoprophylaxis using 100 mg of Paludrine® daily while primigravidae group 2 (P2) and multigravidae group 2 (M2) received a full course of intermittent supervised periodic malaria treatment using chloroquine at pre-determined time periods (Table 1). The rationale for this being that sometimes pregnant women forget to take the drugs on weekly basis which often leads to increased risk of developing malaria. Since the total dose of chloroquine (1200 mg) taken in four weeks for continuous malaria chemoprophylaxis is approximately equal to curative dose of malaria administered in three days at one-month interval, intermittent chemotherapy may improve compliance and could offer better protection than continuous chloroquine chemoprophylaxis. The standard 300 mg of chloroquine base taken weekly was used for group 3 primigravidae (P3) as recommended by the Tanzanian Ministry of Health while the semi-immune multigravidae group 3 (M3) received an initial curative dose of chloroquine treatment and thereafter were treated for malaria if they developed clinical malaria in the course of their pregnancy (Table 1). The reason for evaluating

the protective efficacy of chemotherapy in multigravidae group 3 (M3) was that if chemotherapy alone in semi-immune multigravidae is as effective as continuous chemoprophylaxis, then protection of multigravidae will be simplified through the provision of effective supervised periodic malaria treatment for multigravidae. In addition to the strategies being tested, all the study participants (primigravidae and multigravidae) were given folic acid and ferrous sulphate tablets in accordance with the Tanzanian Ministry of Health policy on prevention of anaemia in pregnancy. It was assumed that supplementation with folic acid and ferrous sulphate tablets would not have any interaction with the anti-malarial drugs except for the recently reported risk of increasing malaria incidence in the supplementation group(17-19).

Eligibility criteria: Eligibility for enrolment of pregnant women into the study included permanent residence in Kigoma town 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) of gestation. For the purpose of this study, a pregnant woman was defined as any woman who had missed her menstrual periods for three months or more and had in addition, other signs of pregnancy such as breast enlargement. The cut-off point of 24 weeks of gestation for inclusion into the study was determined through history given by the pregnant women (last date of menstrual period) and physical examination. The categorisation of pregnant women having their first and second pregnancies into one group was based on the assumption that in Tanzania the majority of women having their first and second pregnancies do not differ significantly in terms of age and other obstetric parameters.

Table 1

Regimens evaluated for malaria prophylaxis among pregnant women in Kigoma urban district, western Tanzania.

Group	Chemoprophylaxis regimens
Primigravidae (gravidae 1 & 2)	
Continuous prophylaxis* with proguanil (Group P1)	*First visit:* Curative dose of chloroquine (1500 mg CQ base in 3 days), and thereafter a daily dose of 100 mg proguanil until 4 weeks after delivery.
Intermittent prophylaxis with chloroquine (Group P2)	*First visit:* Curative dose of chloroquine (1500 mg CQ base in 3 days), and thereafter curative doses of CQ at 20, 24, 28, 32, and 36 weeks of gestation.
Continuous prophylaxis with chloroquine (Group P3)	*First visit:* Curative dose of chloroquine (1500 mg CQ base in 3 days), and thereafter 300 mg weekly until 4 weeks after delivery
Multigravidae (gravidae 3 or more).	
Continuous prophylaxis* with proguanil (Group M1)	*First visit:* Curative dose of chloroquine (1500 mg CQ base in 3 days) thereafter, daily doses of praguanil 100 mg until 4 weeks after delivery.
Intermittent prophylaxis with chloroquine (Group M2)	*First visit:* Curative dose of chloroquine (1500 mg CQ base in 3 days) thereafter curative doses of CQ at 20, 24, 28, 32, and 36 weeks of gestation.
Chemotherapy only with chloroquine (Group M3)	*First visit:* Curative dose of chloroquine (1500 mg CQ base in 3 days) thereafter treatment when ill with a positive malaria blood slide.

CQ = Chloroquine; *This regimen was assumed to be the gold standard for malaria chemoprophylaxis

Randomisation: Two senior 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. The researchers were given one-week training workshop on how to carry out specific components of the study including the process of randomisation and follow up. The anti malarial prophylactic regimens used were written on cards which were placed inside special envelopes prepared for the study. The envelopes were identifiable only by P or M series written on them (P standing for primigravidae and M for multigravidae). In order to ensure balanced allocation to the regimens, equal number of cards for each regimen in the P and M series were prepared, that is, 120 cards for each regimen to make a total of 360 cards for P series and similar number of cards

for M series. The envelopes were placed in two separate boxes, one box for P and another for M series.

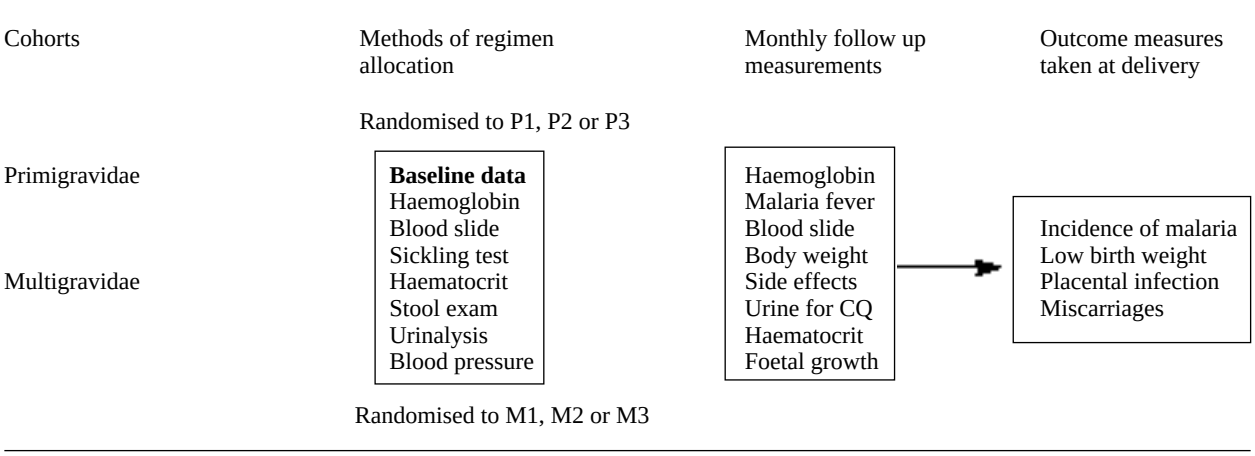
The objectives and study procedures were fully described to the women before asking for their verbal informed consent for participation in the study. The details included description of measurements to be taken during the study and anticipated benefits to the study participants. In addition, all the women were informed that they had the liberty to refuse participation in the study and that refusal to participate had no negative implications whatsoever on the quality of antenatal care services to those who refused to participate in the study. Allocation of the pregnant women to the various interventions was in accordance with the reported number of pregnancies for each woman. Therefore, any primigravida consenting to participate in the study was randomised to the chemoprophylaxis regimens denoted by P 1, P2, and P3 while multigravidae were randomised to regimens denoted by M1, M2 and M3. Pregnant women attending antenatal care at the selected urban maternal and child health (MCH) clinic in Kigoma town and who consented to participate in the study were enrolled into the study consecutively until a total sample size of 720 pregnant women was attained. Detailed analyses of the baseline data are presented in the companion paper. The senior nursing officers performed the process of randomisation by picking up one envelope from previously shuffled P or M series envelopes. Allocation of each subject to the appropriate chemoprophylaxis regimen was made after opening up the envelope and reading the chemoprophylaxis regimen written on the card. Each consenting participant underwent baseline studies immediately after randomisation was achieved. The baseline studies 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 (Figure 1). Sickle cell trait was tested at baseline in order to permit assessment of potential modifying effect of sickle cell trait on the occurrence of malaria parasitaemia during data analysis(20). 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.

Follow up studies: Pregnant women were followed up at monthly intervals up to two months of puerperium to determine the effect of the interventions on haemoglobin levels, birth weight, occurrence of malaria and other important parameters indicated in Figure 1. Any woman who became anaemic or developed malaria during the course of the study was offered treatment at the clinic or if complicated the patient was referred to Maweni Regional Hospital for appropriate management. The field team was responsible for follow up of all pregnant women who did not come to the clinic as advised on the their cards. The field team filled out a separate questionnaire for each woman who did not come for follow up and reasons for not coming for follow up. In addition, there was a separate follow up questionnaire designed to assess use of other preventive measures against malaria such as bednets, mosquito coils, and self-medication. These malaria preventive measures were closely monitored because they could potentially confound the effect of the proposed strategies on malaria protection. Similarly, other factors that may affect birth weight such as high blood pressure, twin pregnancy, and maternal workload were investigated. However, seasonal variation in malaria transmission was not assessed because the studies were running across all the seasons of the year.

The following measures were taken in order to ensure that the cohorts began at a known starting point. Firstly, baseline data on haemoglobin levels, haematocrit, malaria parasitaemia, and helminthic infestation were taken. Secondly, all women were treated for malaria using the standard chloroquine regimen recommended by the Tanzanian Ministry of Health to ensure that all women were free from any asymptomatic malaria infection. This was important in order to assess with reasonable certainty that any malaria episode occurring during the follow up period was due to new infections. Similarly, all pregnant women found to be infected with helminths were given appropriate treatment except antischistosomal treatment that is not normally recommended in pregnancy. The women were advised to come to the clinic for treatment any time they developed fever. Use of standby anti malarial 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. Any fever that responded well to the use of standby anti malarial drugs was interpreted to be due to malaria even if a subsequent blood test for malaria parasites was negative. Finally, all women were advised to deliver their babies in Maweni Regional Hospital in Kigoma. At delivery the field team was responsible for taking the following measurements: birth weight, placental smear for malaria parasites, and detection of congenital defects or malformations (Figure 1).

Figure 1

Follow up design and outcome variables among pregnant women in Kigoma urban district, western Tanzania



Ethical considerations: The project was reviewed and approved by the ethical committee of the Muhimbili University College of Health Sciences. There were no serious ethical problems because all the drugs used in the study are approved in Tanzania and there was no placebo group. The only issues to be considered involved the discomfort and inconveniences that could arise during the process of taking blood samples for estimation of haemoglobin levels, haematocrit and blood tests for malaria parasites as well as stool and urine examinations for helminths.

Sample size: The incidence of malaria among pregnant women in Kigoma was not known at the time of planning the study. To calculate sample size we used data reported from studies conducted in Kenya which had shown that the prevalence of malaria parasitaemia among pregnant women receiving chemoprophylaxis was 17.7% compared to 26.2% among those not receiving any form of chemoprophylaxis(21). The target of the study was to reduce the prevalence of malaria parasitaemia by more than 50%, that is, reducing the prevalence of parasitaemia from 26.2% to 10%. Using the statistical formula proposed by Fleiss(22) for calculating sample sizes in epidemiological studies with statistical power set at 80%, the number of pregnant women required for the study was estimated to be 670, that is, approximately 111 pregnant women for each of the six proposed intervention groups. However, the sample size was approximated to 720 pregnant women (about 120 pregnant women per intervention) in case a large proportion of the participants could decide to drop out of the study after enrolment.

Outcome measures: The primary outcome measure of interest was the occurrence of malaria among the women receiving the various chloroquine regimens as compared to the women receiving proguanil. Additional endpoints were abortion, low birth weight, and placental malaria parasitation (Figure 1). Proguanil regimen was used as the gold standard for malaria prophylaxis in pregnant women and the other chemoprophylaxis regimens as comparison groups in order to avoid the ethical problem of using placebo group. Use of placebo group was not acceptable as it would have denied some pregnant women a proven protective measure against malaria. The comparison regimens were considered effective if they reduced the incidence of malaria episodes and of placental infection at a similar level as proguanil malaria prophylaxis regimen. Although folic acid and ferrous sulphate were given to prevent anaemia, the incidence and prevalence of anaemia in pregnancy as well as the incidence of low birth weight babies were also assessed.

Data management: All completed questionnaire forms were checked for inconsistencies and illogical data. Data were entered into a computer using statistical package for social sciences (SPSS) version 5.0 while data analysis was conducted using SPSS version 8 for Windows. Open-ended variables were coded before data entry. Statistical data analysis was performed using one-way analysis of variance (ANOVA) and Chi-squared test for contingency tables. Results were considered significant if $P \leq = 0.05$. All P-values presented in this paper are two-sided.

RESULTS

Comparability of the intervention and comparison groups. Table 2 presents the distribution of malaria parasitaemia and mean haemoglobin (Hb) concentrations among the study groups. As can be seen in Table 2, there was no significant difference in the overall prevalence proportions of malaria parasitaemia between primigravidae and multigravidae groups (9.8% versus 9.0%; $\chi 2$ (df = 1, n = 701) = 0.81, P = 0.4). Likewise, there was no significant difference in the observed prevalence proportions of malaria parasitaemia within primigravidae intervention and comparison groups ($\chi 2$ *(df* = 2, N = 391) = 0.67, P = 0.70). Similar observations were seen among multigravidae intervention and comparison groups ($\chi 2$ (df = 2, N = 310)= 4.79, P = 0.1).

Table 2

Malaria parasitaemia and mean haemoglobin concentrations among the intervention and comparison groups in Kigoma urban district, Western Tanzania

	Malaria parasitaemia			Haemoglobin levels (g/dl)		
Predictor	Sample size	N	(%)*	P-value	Range	Mean (95% CI)**
Total series	**701**	**65**	**9.3**		**5.9 - 14.9**	**10.1(9.9-10.2)**
Intervention groups						
Primigravidae groups						
Proguanil prophylaxis(Pl)	135	15	11.1	P = 0.7	5.9-14.0	9.9 (9.6-10.3)
Intermittent CQ prophylaxis(P2)	131	11	8.4		6.3 - 13.0	9.9 (9.6-10.3)
Chloroquine prophylaxis(P3)	125	11	8.8		5.9 - 14.5	10.2 (9.8-10.4)
Total	**391**	**27**	**9.8**		**5.9 - 14.5**	**10.0 (9.8 -10.2)**
Multigravidae groups						
Proguanil prophylaxis (Ml)	103	13	12.6	P = 0.1	6.3 -13.5	10.0 (9.7 - 10.3)
Intermittent CQ prophylaxis (M2)	99	4	4.0		5.9 -14.1	10.2 (9.9 -10.6)
Chemotherapy when ill (M3)	108	11	10.2		5.9-14.9	10.4 (10.1-10.7)
Total	**310**	**28**	**9.0**		**5.9-14.9**	**10.2 (10.0-10.4)**

CQ= Chloroquine; *Overall rates corrected $\chi 2$ (df = 1, N = 701) = 0.81, P = 0.4; **F-test (df = 5, N = 701) = 1.27, P = 0.27.

The overall mean haemoglobin concentrations among the primigravidae and multigravidae women were also comparable within the intervention and comparison groups (F-test (df = 5, N = 701) =1.27, P = 0.27). According to Table 2, the overall mean haemoglobin concentration was 10.1 g/dl (range 5.9-14.9 g/dl) while the observed Hb concentration among primigravidae women was 10.0 g/dl (range 5.9 - 14.5 g/dl) and 10.2 g/dl (range 5.9-14.9 g/dl) for multigravidae women.

DISCUSSION

Epidemiological studies conducted in malaria holoendemic areas have demonstrated that malaria chemoprophylaxis is significantly associated with reduced incidence of severe anaemia and that of low birth weight babies(3,5,23-25). Reduction in the incidence of low birth weight babies may be due to the prevention of placental dysfunction which is often associated with placental malaria parasitisation (2,24). On the other hand, observations from malaria vaccine trial conducted among Tanzanian children in Ifakara district appear to be inconclusive(26) and it may take several years before the safety and efficacy of the new malaria vaccine is accepted for use among pregnant women. Therefore, prevention of malaria among pregnant women is still largely dependent upon chemoprophylaxis until such time that a cheap and effective vaccine will be available for use in poor resource countries like Tanzania. Consequently, evaluation of potentially new cost-effective interventions against malaria particularly among vulnerable populations is still important. The present study focused on evaluation of malaria chemoprophylaxis among pregnant women using a randomised trial design so as to generate data that will be useful for improving reproductive health in Tanzania. According to the data presented in this paper, randomisation of the study subjects to the intervention and comparison groups produced comparable groups with balanced characteristics. Therefore, the objectives of randomisation were achieved.

Nevertheless, it is important to appreciate the difficulties implicit in the design and conduct of malaria chemoprophylaxis field trials in an environment with diverse ecological and socio-economic settings. The existence of *P. falciparum* malaria resistance in most areas of Tanzania may result in the failure to demonstrate protective efficacy of any particular malaria chemoprophylactic drug. Furthermore, there may be problems in the ascertainment of compliance with the recommended dosage of anti malarial drugs among pregnant women. Studies conducted in Dar es Salaam showed that because of high incidence of chloroquine associated side effects, it was difficult for the pregnant women to comply with the recommended dose of chloroquine chemoprophylaxis(16). Therefore, failure to comply with the recommended dosage of chloroquine prophylaxis may result in poor protective effect among the defaulters. However, in the present study compliance was monitored through testing for chloroquine metabolites in urine at each follow up visit at the MCH clinic in Kigoma town. Therefore, it is highly unlikely that the participating women did not comply with the recommended dose for malaria prophylaxis. However, no attempt was made to perform any biochemical tests to monitor compliance rates among pregnant women who were receiving proguanil regimen. This was omitted because there were no reports indicating that proguanil had high non-compliance rates similar to chloroquine.

A further difficulty in any prospective follow up study is the likelihood of some participants choosing to drop out of the study. One of the problems associated with high attrition rates among the study participants is the reduction in the statistical power of the study to detect the difference in the trial groups. A more serious problem associated with high attrition rate is bias which may occur if those lost for follow up have different characteristics from those still remaining in the study. However, occurrence of high attrition rate was very unlikely because enrolment was based on permanent residence in Kigoma/ Ujiji town and the surrounding neighbourhoods. Moreover, the use of a randomised study design ensured that any losses to follow up could probably occur in all the groups and therefore give unbiased results.

Another likely problem in this study was the possibility of mixing the effect of the chemoprophylactic regimens being tested with the effect that might accrue from concurrent utilisation of other proven malaria preventive measures. The potential confounding factors include the differential use of bednets, mosquito coils, and insecticides among the trial groups. However, the process of randomisation may have corrected for any differential utilisation of any malaria preventive measures. Therefore, the results are very unlikely to be biased. Finally, recent studies indicate that supplementation with folic acid and ferrous sulphate tablets increases the incidence of malaria and other infectious diseases among those receiving supplementation(17-19). It is felt that this had no effect on impact evaluation because all the groups were given supplementation and any increase in the incidence of malaria would therefore occur in all the groups under investigation.

In conclusion, the results from this study will provide useful information for formulating policies towards improving reproductive health in Tanzania. During data analysis, careful adjustment for potential confounding factors were made in order to improve quality of the data. The interpretation of a positive result are straightforward and include implications for changes in malaria chemoprophylaxis policies while a negative result indicate continued use of and strengthening of the existing malaria prophylaxis regimens in Tanzania.

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