UNIVERSITY OF ZIMBABWE

DEPARTMENT OF OBSTETRICS AND

GYNAECOLOGY

DISSERTATION FOR DR REUBEN BISHI

TITLE:

FETOMATERNALOUTCOMESOFPREGNANTWOMENADMITTEDWITHMALARIAATPARIRENYATWAHOSPITALANDINMASHONALANDEAST PROVINCE OF ZIMBABWE

DECLARATION

This dissertation is the original work of Dr Reuben Bishi. It has been prepared in accordance with the guidelines of Masters of Medicine in Obstetrics and Gynaecology of the University of Zimbabwe.

SIGNATURE OF CANDIDATE...... DATE...... DATE.....

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ABBREVIATIONS

PMTCT	Prevention of Mother to Child Transmission of HIV
HIV	Human Immunodeficiency Virus
ITN	Insecticide Treated Bed Nets
IPT	Intermittent Presumptive/Preventive Therapy
SP	Sulphadoxine and Pyrimethamine
ANC	Antenatal Care
Hb	Hemoglobin
HAART	Highly Active Antiretroviral Therapy
RDT	Rapid Diagnostic Test

ABSTRACT

TITLE: FETOMATERNAL OUTCOMES OF PREGNANT WOMEN ADMITTED WITH MALARIA AT PARIRENYATWA HOSPITAL AND IN MASHONALAND EAST PROVINCE OF ZIMBABWE

INTRODUCTION

There are 300million to 500million people who are infected with malaria worldwide every year and the disease kills about 3million yearly. 90% of the cases occur in Sub-Saharan Africa where HIV is also prevalent. Malaria is one of the major contributing factors to fetal and maternal morbidity and mortality causing severe anemia, cerebral malaria, renal failure, miscarriage, stillbirth and low birth weight. Zimbabwe has made significant achievements in reducing the incidence of malaria in the general population according to the data from the Ministry of Health and Child Welfare Department of Malaria Control but the disease burden remains high[**Figure 1**]. Malaria is the fifth leading cause of maternal mortality in Zimbabwe [6]. However, there is limited data on the impact of the disease on high risk groups like pregnant women in Zimbabwe.

This was done as a cross sectional descriptive survey to evaluate the effect of malaria on pregnant women and their fetuses.

OBJECTIVE

Main objective

1) To evaluate maternal and fetal outcomes of malaria in pregnancy

Other objectives

1) To assess factors which influence maternal and fetal outcomes.

METHOD

A cross sectional descriptive survey was done on pregnant women admitted with malaria over a period of 8 months (September 2011-April 2012).

An interviewer administered questionnaire was used to gather information on women admitted in the antenatal or labour ward with a diagnosis of malaria.

District hospitals (Mutoko, Murewa, Mudzi) in moderate to high seasonal malaria transmission located in Mashonaland East Province of Zimbabwe and one tertiary hospital, Parirenyatwa Hospital, were identified for the survey.

RESULTS

Of the 103 cases of malaria in pregnancy studied, there were 2(2%) maternal deaths, 6(6%) cases of severe anaemia and two cases of cerebral malaria. Maternal adverse outcome were influenced by booking status, human immunodeficiency virus(HIV) status, use of intermittent presumptive therapy(IPT), insecticide treated bed nets(ITNS) and late presentation to hospital. Ninety three cases were discharged from hospital without major complications.

There were 24(23%) live term babies, 10(10%) preterm deliveries, 10(10%) cases of low birth weight, 6(6%) stillbirths, 9(9%) miscarriages and two cases of threatened miscarriages. Fifty two percent of the participants were still pregnant when they were

discharged from hospital. There was under utilization of IPT (45%) and ITNs (45%) by participants.

CONCLUSION

Malaria infection had adverse effects on both mother and foetus. It was associated with maternal mortality and morbidity. Anaemia, cerebral malaria and maternal death were the main maternal complications encountered in this survey. Maternal adverse outcomes were influenced by booking status, HIV status, use of IPT, ITNS and time taken to present to hospital after onset of disease. There was significant fetal wastage (15%) resulting from miscarriages (9%) and stillbirths (6%). Malaria infection was also associated with low birth weight (28%) and preterm delivery (10%).

The survey also revealed that there was underutilization of prevention strategies (IPT and ITNs) by 45% of participants which was mainly due to failure to book or late booking for antenatal care (ANC). Case management was generally according to standard guidelines but participants were not adequately investigated in terms of other parameters such as complete blood count and renal function.

2) INTRODUCTION

2.1 BACKGROUND

"Of all infectious diseases, there is no doubt that malaria has caused the greatest harm to the greatest number...." (Laderman, 1975).

Malaria is an infectious disease caused by plasmodium parasite species (falciparum, vivax, malariae and ovale). In Zimbabwe, the majority of cases are due to plasmodium falciparum.

Malaria is transmitted by the female anopheles mosquito which is widely distributed in the tropics where the conditions are ideal for breeding. Malaria is an extremely climate sensitive tropical disease which makes it a grave concern because of global warming and climate change. A study which was done in the East African highlands from 1950 to 2002 has confirmed biological response of mosquito populations to warming. A half degree centigrade increase in temperature trend can translate into 30-100% increase in mosquito abundance[2].

Malaria which was once nearly eradicated is re-emerging as the world's number one killer infection. The disease now affects 300 million to 500 million and kills 3million people every year worldwide and 90% of the cases occur in sub-Saharan Africa. The situation is compounded by high prevalence of HIV in the same region [3]. Immune deficiency due to HIV infection makes humans more susceptible to malaria infection and on the other hand malaria fever has been noted to increase viral load by up to ten times[4].

Malaria is one of the major contributing factors to maternal morbidity and mortality because human immunity against the disease is reduced in pregnancy.

Malaria infection in pregnancy results in severe illness and maternal complications such as severe anemia, cerebral malaria, hemorrhage, renal failure and pulmonary edema.

The disease is more severe and more fatal in pregnancy with 13% mortality against 6.5% in non pregnant women[3].

According to WHO, 30 million women living in malaria endemic areas become pregnant each year and 80% of deaths due to malaria occur in pregnancy and children under 5 years[5].

The disease has adverse effects on the fetus with increased risk of stillbirth, preterm delivery, intrauterine growth restriction and low birth weight which are leading causes of perinatal mortality[5]. Congenital malaria is rare and occurs in 5% of the affected cases[5].

Fifty percent of approximately 12million people in Zimbabwe reside in areas that are endemic for malaria and the disease is responsible for 30% outpatient attendance. It is the third cause of mortality after HIV/AIDS and Tuberculosis in all age groups[1]

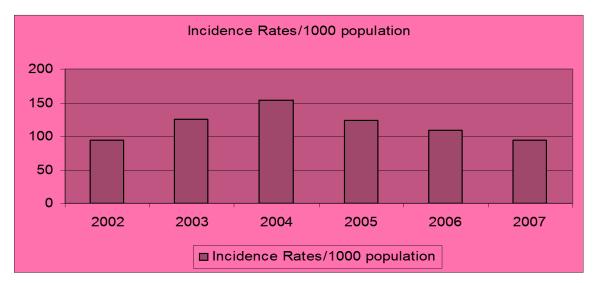


Figure 1: Trend of malaria incidence from 2002 to 2007(Zimbabwe Ministry of Health, Malaria Control Program

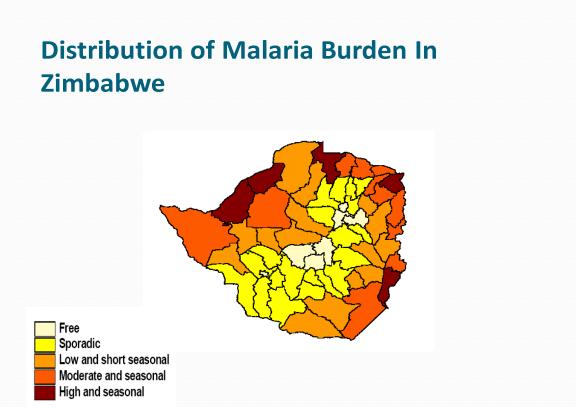


Figure 2: Distribution of malaria burden in Zimbabwe (Zimbabwe Ministry of Health, Malaria Control Program

The following are some of the key factors that influence general management and control of malaria:-

- drug resistance of the malaria parasite
- safety and appropriate use of different anti-malarial drugs during pregnancy
- high number of unbooked patients not monitored or followed up through antenatal facilities available
- Late presentation to hospital and delayed treatment of malaria cases
- climate change which has influenced geographical distribution of malaria
- role of HIV and transplacental transmission in patients with malaria in pregnancy

2.2 STUDY JUSTIFICATION

Malaria in pregnancy is particularly a serious condition that is life threatening to both mother and foetus. It is also associated with fatal complications if diagnosis and treatment are delayed. 90% of malaria cases occur in sub-Saharan Africa and Zimbabwe is one of the countries in this region. Despite significant achievements in reduction of malaria incidence among the general population in Zimbabwe as shown in **Figure 1** above, the disease burden remains high[1]. There is also limited data of the impact of the disease on high risk groups like pregnant women though its known to be the 5th leading cause of maternal mortality in the country[6]. The mortality is unacceptably high considering that malaria infection is preventable and can be treated in just 48hrs hence there is need to conduct regular surveys to assess the impact of intervention strategies targeted at prevention and control of malaria especially on high risk groups such as pregnant women.

2.3 OBJECTIVES OF THE STUDY

Main objective

1) To determine maternal and fetal outcomes of pregnant women infected with malaria.

Other objectives

2) To assess factors which influence maternal and fetal outcomes such as use of preventive measures (malaria prophylaxis and insecticide treated bed nets), antenatal care and case management.

2.4 LITERATURE REVIEW

Pathophysiology of malaria in pregnancy

Various hypotheses have been put forward to explain the pathophysiology of malaria in pregnancy. In pregnancy, there is general immune suppression due to reduced lymphoproliferative response and loss of cell mediated immunity resulting from elevated cortisol levels. This is designed to prevent fetal rejection but renders the pregnant woman susceptible to infection.

It has also been noted that primigravid women are more susceptible to malaria compared to multigravid women. Verhoff and co-workers found a prevalence of plasmodium falciparum malaria of 35.3% among primigravid and 13.6% in multigravid women in a study done in Malawi[7]. The explanation for this observation is thought to be due to the fact that the placenta is a new organ in primigravid women and allows parasites to bypass the existing host immunity and allows specific phenotypes to multiply. Multigravid women however develop placenta specific immunity thereby reducing susceptibility. Primigravid women therefore demonstrate high parasite load due to their immune inexperience with parasite subpopulations.

Pregnant women display type 2 cytokines and become susceptible to infections like malaria, tuberculosis (TB) and leishmaniasis which require type 1 responses for protection. Elevated levels of tumor necrosis factor alpha are associated with severe maternal anemia. Symptomatology of malaria and localized cytokine elevation contributes to adverse pregnancy outcomes.

Malaria parasites have high affinity for the dicidual cells of the placenta. The intervillous spaces may be filled with parasites and macrophages interfering with oxygen and nutrient transport to the fetus[8]. Villous hypertrophy and fibrinoid necrosis occur. These changes contribute to the complications experienced by the mother and the fetus.

Malaria in pregnancy and HIV infection

A multivariate analysis of data collected on pregnant women admitted during the rainy season of 2000 and 2001 in the obstetric division at St. Albert's Mission Hospital, Centinary District of Zimbabwe was done to determine the effects of malaria and HIV on pregnancy and neonatal outcome. The results showed that HIV infected women were more likely to develop malaria attacks during pregnancy than seronegative women. The study also revealed that malaria and HIV were associated with increased risk of stillbirth and preterm delivery[9].

Malaria and HIV were independently associated with increased risk of low birth weight, low APGAR and fetal growth restriction[9]. Dual infection was associated with increased maternal, perinatal and early infant death[9].

Complications of malaria in pregnancy

The physiological changes of pregnancy and the pathological changes due to malaria have a deleterious effect on each other.

Anaemia resulting from haemolysis of red blood cells and folate deficiency can be very severe and exacerbates the anaemia due to physiological changes of pregnancy. Anaemia increases the risk of placenta abruption, preterm labour, maternal death, low birth weight and miscarriages.

Malaria also causes pulmonary oedema which carries a very high mortality. A combination of hypercatabolisim, hyperinsulinaemia and starvation contributes to hypoglycemia which may be difficult to diagnose as symptoms are similar to those of malaria.

Immunosuppression which results from both malaria and pregnancy makes the infection more common and severe in pregnancy. Paroxysms of fever and relapses become more frequent.

Prenatal and perinatal mortality vary from 15%-70% [1]. In a systematic review of 117 studies published between 1948 and 2002, the link between malaria and perinatal mortality was explored. The outcome showed that the mean perinatal mortality rate was higher in malaria endemic countries (61.1/1000) than in non-endemic countries (25.8/1000) similarly fetal mortality rate was higher in endemic countries (40.1/1000) than in non-endemic countries (20.0/1000)[10].

Malaria in pregnancy causes spontaneous abortions, placental insufficiency resulting in intrauterine growth restriction, low birth weight, stillbirth and congenital malaria.

Acute renal failure could be prerenal due to unrecognized dehydration or renal due to severe parastaemia.

Diagnosis

There are no specific symptoms or signs and malaria infection may present with a flu-like illness. There are no clinical algorithms that permit accurate diagnosis by symptoms and signs. Guidelines by The Royal College of Obstetricians and Gynecologists recommended that any suspicion of malaria infection should be promptly confirmed by malaria blood film.

Microscopy and rapid diagnostic tests are the standard tools available. Microscopic examination of thin and thick blood films is the gold standard for diagnosis of malaria infection. It allows species identification and estimation of parastaemia. Rapid diagnostic tests which identify parasite antigen are less sensitive compared to blood films.

A study done in Malawi made a comparison of blood films and placental histology in diagnosing malaria infection at delivery revealed that placental histology was more sensitive (91%) than peripheral blood films(47%) or placental blood film(63%)[11]. Few women had microscopically detectable infection without a positive histology. Placental infection may be detected in the absence of peripheral blood parastaemia.

Prevention

Prevention has always been better than cure and remains the major tool in malaria control. A number of methods have been noted to be effective in preventing malaria infection. Protective measures such as use of insecticide repellants, protective clothing and minimizing nocturnal exposure were noted to be useful in pregnancy.

A research done on the decreasing burden of malaria in pregnancy in Malawian women and its relationship to use of intermittent preventive therapy or bed nets from 1997 to 2006 concluded that increased bed net coverage explains changes in parastaemia and birth weight among pregnant women better than sulfadoxine-pyrimethamine use. Sulfadoxine – pyrimethamine resistance may have contributed to its apparent loss of activity [12].

Chemoprophylaxis has also proved to be an important tool in malaria control. A number of drugs and in various combinations have been used for this purpose. The choice of drug is influenced by safety and patterns of drug resistance in that particular area. A case control study done on intermittent preventive treatment(IPT) in Bioko island, Equatorial guinea showed that one dose of IPT (sulphadoxine and pyrimethamine) during the first 26 weeks of pregnancy has been shown to decrease a woman's risk of malaria by 85% and anemia by 50%[13].

Proguanil and chloroquine have a long standing history of safe usage during pregnancy. Merfloquine is not safe in the first trimester but it can be used in the second and third trimester in regions of chloroquine resistance. Doxycycline is not recommended in pregnancy.

Insecticide spraying of mosquito breeding areas has shown significant success. Use of DDT, which is being phased out, was largely responsible for the historical success in malaria vector control in most parts of the world. The current malarial areas in South Africa are about one fifth of the size they were at the beginning of the 20th century because of the use of DDT. Alternatives to DDT are more expensive and more complicated to use.

Safety of antimalarials in pregnancy

Fear of potential toxicity of antimalarial drugs has limited their use in pregnancy. Animal toxicity studies have documented teratogenicity when these drugs are administered at high doses. However, there is no evidence to suggest that these drugs are teratogenic at standard doses except for tetracycline [14-16].

Primaquine is not recommended because of the potential risk of haemolytic effects on the feotus.

An increasing number of countries in sub-Saharan Africa are changing to artemisinins combination therapy as first line or second line treatment for malaria.

Studies on artemisinins combination therapy were identified via searches of MEDLINE, Cochrane, EMBASE and Current Contents databases (nine descriptive/case reports and five controlled trials). None of the studies found evidence for an association between the use of artemisinin compounds and increased risk of adverse pregnancy outcomes[16].

A review article by Shoklo Malaria Research Unit, Thailand, examined available information on the safety of antimalarials in pregnancy from both animal and human studies. The findings were that the antimalarials that can be used in pregnancy include chloroquine, amodiaquine, quinine, azithromycin, artemisinin derivatives, sulfadoxine–pyrimethamine, Merfloquine, dapsone-chloroproguanil and lumefantrine[17].

Drugs that should not be used in pregnancy include halofantrine, tetracycline and primaquine[17].

Drug resistance

Resistance has emerged to all classes of antimalarial drugs except the artemisinins and is responsible for a recent increase in malaria related mortality in Africa. Genetic basis of antimalarial drug resistance are rare events that occur spontaneously and thought to be independent of the drug used. They are mutations in the genes relating to the drug's parasite target or influx/efflux pumps that affect intraparasitic drug concentrations[18].

3 RESEARCH METHOD

Study Design

A cross-sectional descriptive survey was conducted at Parirenyatwa Hospital and three District Hospitals (Mudzi, Nyadire and Mutoko) in Mashonaland East Province of Zimbabwe.

Study Setting

The study was conducted at one tertiary hospital (Parirenyatwa Group of Hospitals) and three district hospitals (Mudzi, Nyadire and Mutoko) in Mashonaland East province of Zimbabwe. The district hospitals are in moderate to high seasonal malaria regions of Zimbabwe. Parirenyatwa Hospital is situated in a non-malaria zone and caters for cases that are referred from outside or those who develop the disease after traveling to malaria endemic areas.

Study Population

This study constituted all pregnant women admitted with malaria at the centres of the survey.

Inclusion Criteria

The study included pregnant woman who presented with malaria at the four study centres.

Exclusion Criteria

Those not willing to participate were excluded from the study.

Sample size

A proportion of 13% of pregnant women who present with malaria develop severe complications. Basing on this proportion, the following sample size is required, viz:-

$$n = \frac{(z^2 p(p-1))}{\Delta^2}$$
$$n = \frac{1.96^2 (0.13)(1-0.13)}{0.05^2}$$

Where z=1.96, *d*=0.05, p=13%

Sample size=174

Adjusting for 20% non-response rate=210

Data collection tools and design

A data collection form was used to gather information on pregnant women admitted to the antenatal ward, gynecology ward and labour ward with a diagnosis of malaria.

An interviewer-administered questionnaire was used to collect data. The questionnaire consisted of structured questions, scaled questions and response questions on the participant's demographic data, antenatal care, malaria prevention and prophylaxis, maternal and fetal outcome.

Study variables

Study variables included:-

- demographic data (place of residence, age, referring clinic or hospital)
- marital status
- parity
- booking status
- HIV status
- use of malaria prophylaxis and the number of doses of IPT taken during the course of pregnancy
- duration of illness prior to presentation
- method of diagnosis (clinical, slide positive, rapid malaria test)
- treatment modality (Oral or intravenous anti-malarial drugs)
- duration of hospital stay
- Maternal and fetal outcome (full recovery, partial recovery, other complications)

Pretesting the data collection tool

The data collection form was tested at Parirenyatwa hospital and necessary amendments were made.

Data capture processing (capturing process) and data quality control

Data was entered in EXCEL. Consistency and logic checks were done. The data was cleaned and coded for analysis.

Statistical Analysis

The participant's socio-demographic characteristics and measurements were done. Results were evaluated and further detail given through descriptive statistics. All statistical analysis was performed using Stata 12.0 (Stata Cooperation, College Station, Texas USA).

Permission to carry out the study

Permission was sought from the Joint Parirenyatwa Hospital and College of Health sciences Research Ethics Committee and Mashonaland East Provincial Medical Director.

Ethical considerations

The study was reviewed and approved by the Departmental Board of Obstetrics and Gynecology who took into consideration all ethical issues surrounding the study. The study was submitted to (the) Medical Research council of Zimbabwe and was approved. The purpose of the study was explained to all potential participants and a written informed consent was obtained.

4 RESULTS

SOCIO-DERMOGRAPHIC CHARACTERISTICS OF PARTICIPANTS

One hundred and three women who had malaria participated in the study. The majority of the women 96(93%) were married. Their median age was 25 (IQR: 20-30) years. These were admitted with malaria at the four institutions during the malaria peak season (Sept 2011-April 2012). The majority of the patients were unemployed 96(94%) with most 76(74%) having attained secondary level education. Most of those who had malaria came from malaria prone areas, 99(96%). The socio-demographic characteristics of the participants are as shown in **Table 1** below.

Table 1: Summary of patient demographics

Characteristic	Number of women
	n (%)
Hospital	
Parirenyatwa	13 (13)
Nyadire	47 (45)
Mutoko	16 (15)
Kotwa	27 (27)
Marital status	
Married	96 (93)
Single	1 (1)
Divorced	5 (5)
Widowed	1 (1)
Dccupation	
Unemployed	96 (94)
Employed	6 (6)
arity	
0	31 (30)
1	26 (25)
2	19 (19)
3	17 (16)
4	7 (7)
≥5	3 (3)
evel of Education	
None	1 (1)
Primary	24 (23)
Secondary	76 (74)
Tertiary	2 (2)
eligion	56 (54)
Christian	42 (41)
Apostolic sect	3 (3)
Traditionalist	2 (2)
None	
lesidence	99(96)
Malaria area	4(4)
Non-malaria area	

The participants had parity ranging from zero to six with an average of two children. Thirty one (30%) were primigravid women (figure 3).

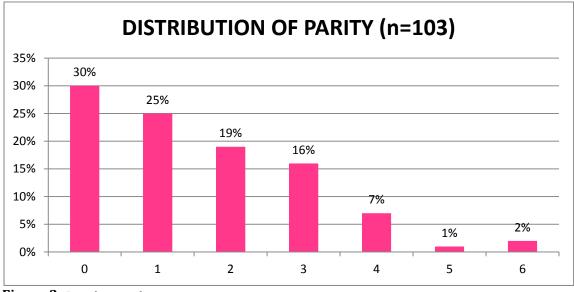


Figure 3: Distribution of parity

ANTENATAL CARE, DIAGNOSIS AND PREVENTION

A large proportion 38(37%) of participants were not booked for antenatal care. 65(63%) were registered for antenatal care. 19(18%) participants registered late in the third trimester (**Figure 4**).

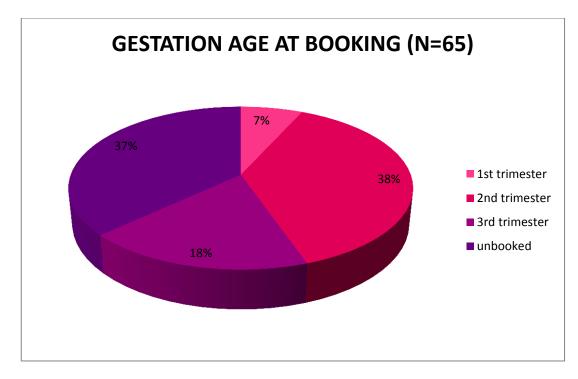


Figure 4: Gestation age at booking in trimesters

Figure 5 illustrates the gestation age distribution of participants on admission to hospital

with malaria. The majority of participants 73 (71%) had malaria in the third trimester.

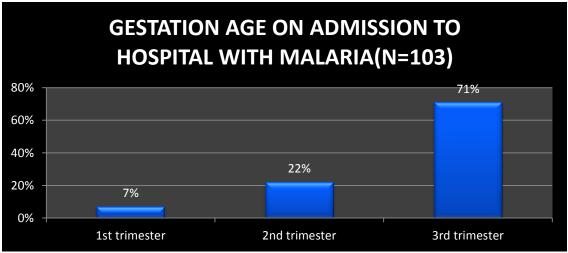


Figure 5: Gestation age on hospitalization with malaria.

65(64%) participants were HIV negative, 23(22%) were HIV positive and 15(14%) had unknown HIV status (**Figure 6**).

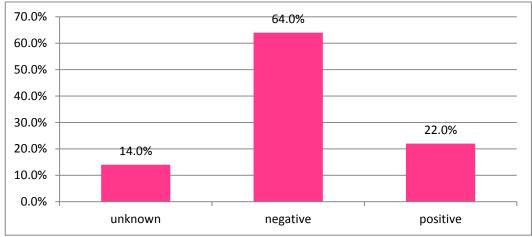


Figure 6: HIV status of participants

Of the 23 participants who were HIV positive, 12(57%) were on AZT prophylaxis for PMTCT, 4(17%) on HAART and 7(26%) were not on antiretroviral treatment or prophylaxis **Figure 7**. Four of the seven HIV positive participants who were not getting ARVs were not registered for antenatal care.

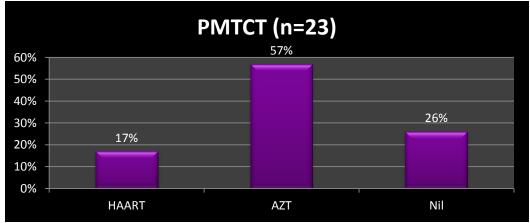


Figure 7: PMTCT management of participants.

Diagnosis

Seventy six participants (74%) presented to hospital within three days (median=3 days, range-1-15days) of onset of symptoms. A smaller number 4(4%), were admitted more than a week after onset of illness as shown in **Figure 8**.

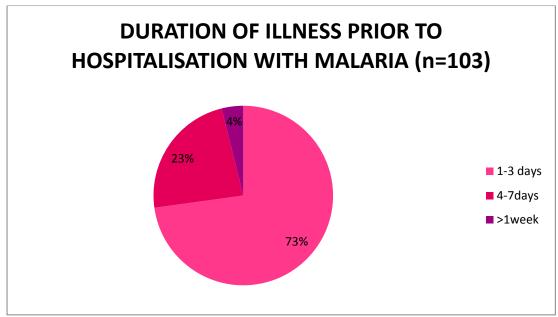


Figure 8: Duration of illness before admission to hospital with malaria

7(7%) of the 103 participants had been treated previously for malaria during the current pregnancy.

74(72%) participants had signs and symptoms of severe malaria such as respiratory distress, prostration, hypotension, jaundice, coca cola colored urine, convulsions and abnormal bleeding.

METHODS OF DIAGNOSIS

Rapid diagnostic test and blood slides were the main diagnostic tools used at the four study centers. Patients who were suspected to have malaria clinically were confirmed by rapid diagnostic tests or blood slides.

All participants who were recruited had a positive result for one or both tests. 58% (60) had slide positive malaria. Parasite density was recorded on 51(85%) slides (**figure 9**) as described below:

- 1+ 1-10 asexual parasites per 100 thick film fields
- 2+ 11-100 asexual parasites per 100 thick film fields
- 3+ 1-10 asexual parasites per single thick film field
- 4+ more than 10 asexual parasites per single thick film field

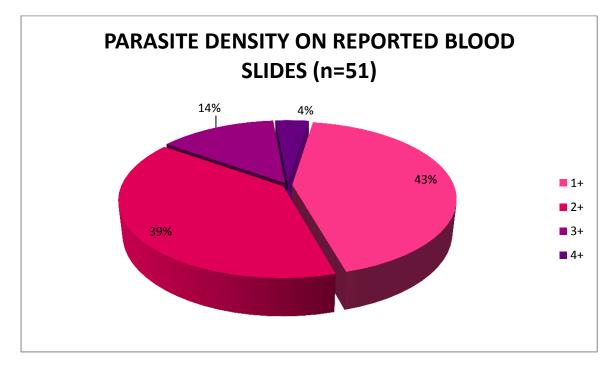


Figure 9: Parasite density on blood slides

OTHER LABORATORY INVESTIGATIONS

Thirty six(35%) participants had their hemoglobin checked and 31 of them had full blood count(FBC) while 5 had their hemoglobin checked with spencer hemoglobinometer. 23(63.9%) of those whose hemoglobin was checked were anaemic with hemoglobin less than 11g/dl (**figure 10**). The mean hemoglobin was 9.5g/dl.

Only 13(13%) of the participants had urea and electrolytes done and 4 of them had abnormally elevated urea and creatinine.

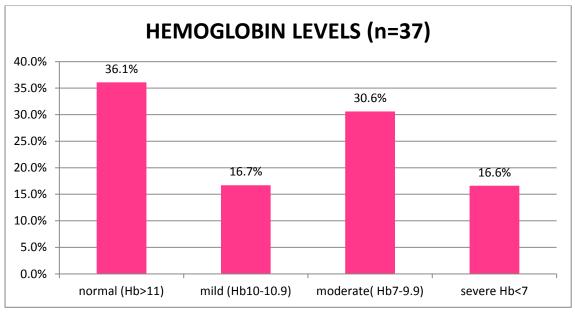
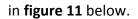


Figure 10: Haemoglobin level

30% of the participants who had FBC had thrombocytopenia less than 100x10⁵/ml as shown



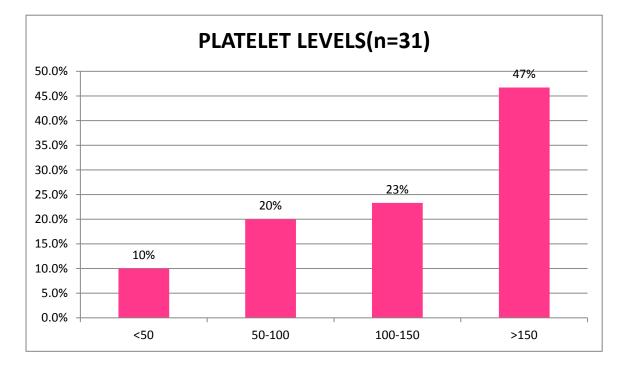


Figure 11: Platelet levels

Prevention

44(43%) participants received at least one dose of IPT. 11(11%) of the participants did not qualify for IPT according to the guidelines because their gestation age was below 16 weeks at the time of recruitment.

2(2%) participants were not given IPT because they were on cotrimoxazole prophylaxis for HIV (**figure 12**). Therefore, 46(45%) participants who required IPT did not get it.

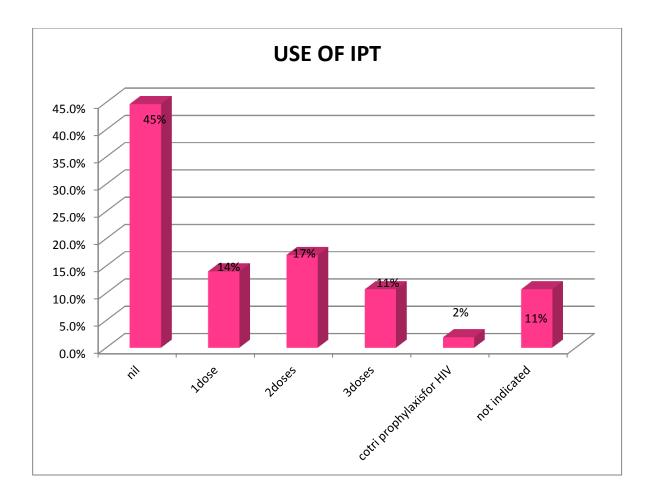


Figure 12: IPT use

25(55%) of those participants who were not given IPT were not registered for ANC.

21(45.7%) participants were booked for ANC and **figure 13** below shows the trimesters they were registered.

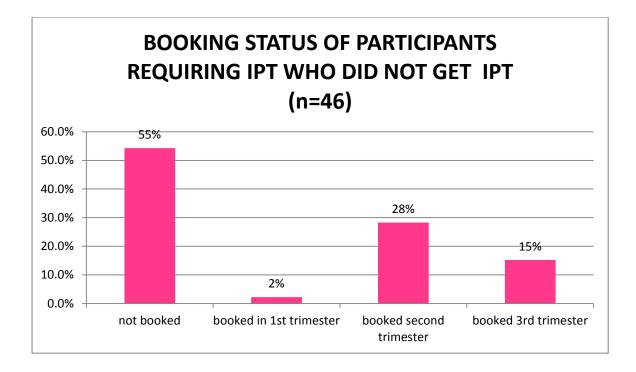


Figure 13: Booking status of participants who did not use IPT

A large proportion of participants 46(45%) never used insecticide treated bed nets and 32(31%) were using them but not all the time. Only 24% were using bed nets consistently



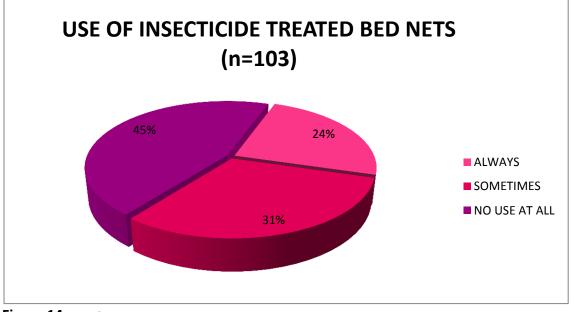


Figure 14: Use of ITNs

SUMMARY OF ANTENATAL CARE, DIAGNOSIS AND PREVENTIVE STRATEGIES

Characteristic	Number of women n (%)
	11 (70)
Booking status	
Booked	65(63)
Un-booked	38(37)
PT use	
None	46(45)
1 dose	15(15)
2 doses	18(17)
3 doses	11(11)
Not indicated	13(12)
Bed net use	
Always	25(24)
Sometimes	32(31)
Not at all	46(45)
Previous treatment	
No	96(93)
Yes	7(7)
HIV Status	
Negative	65(63)
Positive	23(22)
Not known	15(15)
HIV treatment	
HAART	4(18)
AZT	12(52)
None	7(30)

Table 2: Antenatal care, diagnosis and preventive strategies

TREATMENT

The majority of participants were treated with quinine. 43(42%) of the participants were treated with intravenous quinine (1-4days) and course completed with oral quinine. 37(36%) were given oral quinine only. 18(17%) were treated with co-artemether only (**figure 15**). Three participants who had anemia received two units of blood each. Hematinics (iron and folate) and antibiotics were also prescribed for most of the patients.

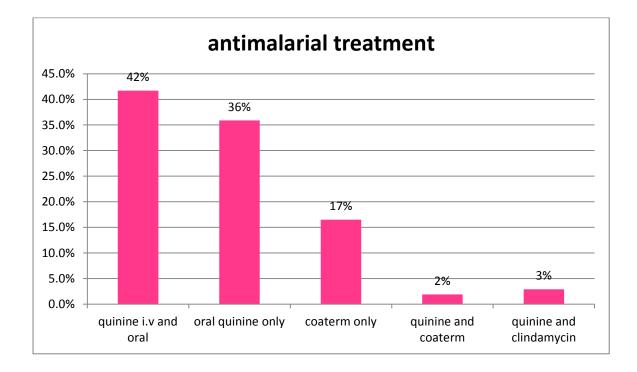


Figure 15: Antimalarial drugs used for treatment

MATERNAL OUTCOMES

95(92%) of the participants were discharged from hospital without severe complications. There were two maternal deaths. Two participants had cerebral malaria.

Four participants had severe anemia when they were discharged from hospital. **Table 3** below shows the characteristics of the participants classified according to their outcome.

Parameter	Discharge without major complications(n=93) n(%)	Maternal death(n=2) n(%)	Severe anaemia (n=6) n(%)	Cerebral malaria (n=2) n(%)
Booking status				
Booked	61(66)	1(50)	2(33)	1(50)
Un-booked	32(34)	1(50)	4(67)	1(50)
IPT use				
None	43(46)	2(100)	2(33)	2(100)
1 dose	15(16)	0(0)	0(0)	0(0)
2 doses	18(19)	0(0)	0(0)	0(0)
3 doses	11(12)	0(0)	0(0)	0(0)
Not indicated	6(7)	0(0)	4(66.7)	0(0)
Bed net use				
Always	24(26)	0(0)	0(0)	0(0)
Sometimes	30(32)	0(0)	0(0)	1(50)
Not at all	38(41)	2(100)	6(100)	1(50)
Previous treatment No				
Yes	83(89)	2(100)	6(100)	2(100)
103	10(11)	0(0)	0(0)	0(0)
Duration of illness				
prior to admission				
1-3	73(79)	0(0)	2(33)	0(0)
3-7	17(18)	0(0)	4(67)	1(50)
>7	3(3)	2(100)	0(00)	1(50)
Trimester				
1	5(5)	0(0)	2(33)	0(0)
2	21(23)	1(50)	2(33)	0(0)
3	67(72)	1(50)	2(33)	2(100)
Parasite density				
1+	22(24)	0(0)	1(17)	0(0)
2+	17(18)	0(0)	2(33)	2(100)
3+	6(7)	0(0)	3(50)	0(0)
4+	0(0)	1(50)	0(00)	0(0)
Not recorded	42(45)	1(50)	0(00)	0(0)
HIV Status				
Negative	61(66)	0(0)	3(50)	1(50)
Positive	17(18)	1(50)	3(50)	1(50)
Not known	15(16)	1(50)	0(0)	0(0)

TABLE 3: Maternal outcomes and their antenatal parameters

FETAL OUTCOMES

52(52%) of the participants were still pregnant when they were discharged from hospital.

Of the 51(48%) participants who had delivered at the time of discharge 6(6%) had stillbirth, 10(10%) preterm delivery, 9(9%) miscarriages and 24(23%) had live term babies (**figure 16**).

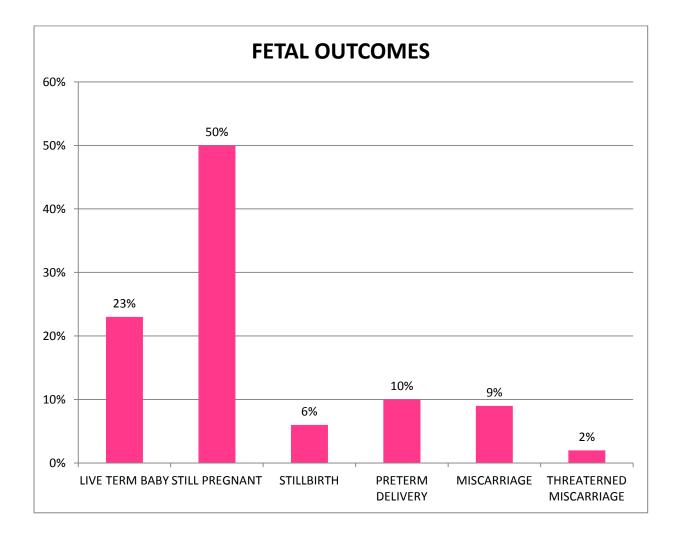


Figure 16: Fetal outcomes

12(30%) babies had low birth weight (<2500g) and average birth weight was 2739g (figure

17)

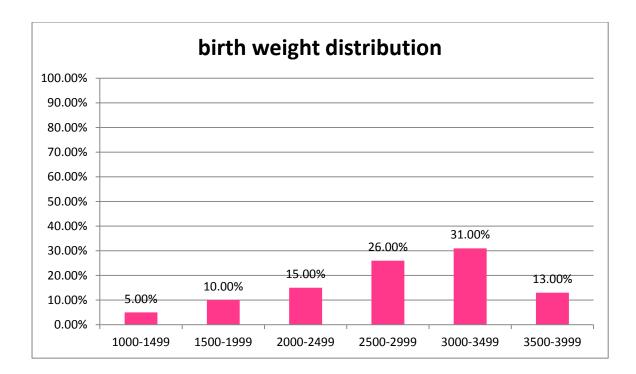


Figure 17: Birth weight

Characteristic	Normal term baby (n=24) n/%	Preterm delivery(n=10) n/%	Low birth weight (n=12)	Stillbirth(n=6)	Miscarriage(n=9) n/%	Threatened miscarriage(n=2) n/%
Booking status						
Booked	19(79)	6(60)	6(50)	4(67)	2(22)	0(0)
Un-booked	5(21)	4(40)	6(50)	2(33)	7(78)	2(100)
IPT use						
Non	9(38)	4(40)	7(58)	4(67)	4(44)	2(100)
1 dose	3(12)	1(10)	0(0)	1(17)	0(0)	0(0)
2 doses	4(17)	3(30)	3(25)	1(17)	0(0)	0(0)
3 doses	8(33)	2(20)	0(0)	0(0)	1(12)	0(0)
Not indicated						
	0(0)	0(0)	2(17)	0(0)	4(44)	0(0)
Bed net use						
Always	2(8)	3(30)	2(17)	1(17)	1(11)	0(0)
Sometimes	8(33)	4(40)	4(33)	3(50)	1(11)	2(100)
Not at all	15(63)	3(30)	6(50)	2(33)	7(78)	0(0)
Parasite						
dansity						
1+	4(17)	2(20)	2(17)	2(33)	2(22)	0(0)
2+	6(24)	4(40)	4(33)	0(0)	2(22)	0(0)
3+	3(13)	0(0)	0(0)	1(17)	0(0)	0(0)
4+	0(0)	0(0)	0(00	1(17)	0(0)	1(50)
Not recorded	11(46)	4(40)	6(50)	2(33)	5(56)	1(50)
HIV Status						
Negative	15(63)	4(40)	4(33)	2(33)	4(44)	1(50)
Positive	7(29)	6(60)	7(58)	3(50)	2(22)	1(50)
Not known	2(8)	0(0)	1(9)	1(17)	3(34)	0(0)
HIV treatment						
HAART	1(4)	2(20)	2(17)	0(0)	0(0)	1(50)
AZT	5(21)	0(0)	3(25)	3(50)	0(0)	0(0)
None	1(4)	4(40)	4(33)	3(50)	2(22)	0(0)
Negative/Status not known	17(71)	4(40)	3(25)	0(0)	7(78)	1(50)

TABLE 3: Fetal outcome and maternal antenatal parameters

BURDEN of MALARIA REQUIRING HOSPITALISATION

Table 1 below shows the burden of malaria in pregnancy among study centers.

	PARIRENYATWA	NYADIRE	Μυτοκο	MUDZI/KOTWA	TOTAL
PARTICIPANTS	12	47	28	16	103
TOTAL DELIVERIES	6212	378	1386	668	8644
INCIDENCE/1000DELIVERIES	2	124	19	24	12

TABLE 4: Burden of malaria in pregnancy requiring admission to hospital

LIMITATIONS OF THE STUDY

- Sample size could not be attained during the study period of 8months and this was due to the low incidence of malaria during the 2011-2012 malaria peak season.
- 2) The study did not exclude other co-morbidities such as pre-eclampsia which may also influence fetomaternal outcomes.

DISCUSSION

Total deliveries at the four study institutions during the period of study were 8644.

103 pregnant women who had malaria were recruited in the study. All the participants had acquired at least primary level education, however only 5.8% were formally employed. This demonstrated the high unemployment rate characteristic of the rural population of Zimbabwe. The majority of the women were housewives and households thrived on peasant farming. This could have a bearing on the capacity of the women to access healthcare services such as antenatal care. This is supported by a high proportion 38(37%) of the participants who were not booked for antenatal care compared to the national figure of 8.6 %[6].

The majority of the participants were resident in malaria prone regions of Zimbabwe. Only 4% were resident in malaria free regions. These 4(4%) developed malaria after travelling to regions with malaria and none of them took prophylaxis for malaria during travel.

The results demonstrated that Harare, the capital city of Zimbabwe, which is the main catchment area for Parirenyatwa Hospital largely remained malaria free. This is so because all 13 participants who were admitted at this hospital had malaria after travelling to places outside Harare or were referred from outside Harare with malaria.

Primigravid women formed the largest group among the study population 31(30%). This was consistent with studies which have shown that primigravid women are more susceptible to malaria[19],[20],[21, 22].

A significant proportion of participants booked late, 19(29%) booking in the third trimester.

The proportion of participants who were not booked together with those who booked late was high 57(55%). This compromised provision of antenatal care services and implementation of preventive measures to pregnant women at risk of malaria infection such as IPT. The participants who were not booked could not be given IPT and those who booked late missed some doses. Studies have shown evidence of significant benefit of IPT in reduction of malaria infection in pregnancy and associated complications.[13, 23]

Seventy three (70%) participants developed malaria in the third trimester. The majority of these participants could have been prevented from developing malaria if they had booked early and preventive measures implemented strictly.

The proportion of participants who had HIV infection 23(22%) was high compared to 16.% for women attending antenatal clinics countrywide according to the Zimbabwe Ministry of Health & Child Welfare's (MOHCW) PMTCT data base[24]. This was consistent with studies that showed increased susceptibility of HIV positive pregnant women to malaria compared to HIV negative[9].

Current recommendations to prevent malaria in African pregnant women rely on insecticide treated nets (ITNs) and intermittent preventive treatment (IPTp). In a randomised control trial done in Mozambique, SP showed 40% reduction (95% CI, 7.40-61.20]; p = 0.020) in the

incidence of clinical malaria during pregnancy, and reductions in the prevalence of peripheral parasitaemia (7.10% vs 15.15%) (p<0.001), and of actively infected placentas (7.04% vs 13.60%) (p = 0.002)[25]. However in this study, 44.6% of the participants developed malaria despite receiving at least one dose of IPT. This gives rise to questions on whether IPT with SP is still effective in our environment or the malaria parasite has developed resistance to it. 44.7% did not use IPT and this was largely because 54.3% of them were not registered for ANC.

The study has demonstrated underutilization of ITNs by participants which plays a complimentary role to ITP in prevention of malaria infection[12]. 45% of the participants never used ITNS during the course of their pregnancy up to the time they were admitted with malaria.

Rapid diagnostic test was the main diagnostic tool used by the four study centers. There were limitations in the use of blood slide (gold standard) which was done in 58% of the participants. This was because of shortage of skilled manpower and unavailability of reagents. Diagnosis using blood slides has advantages over RDT because parasite density can be estimated and the malaria species can be identified.

The same reason was responsible for unavailability of other laboratory investigations such as full blood count and urea and electrolytes which were done on a small proportion of participants 35.5%, and 12.6% respectively. The unavailability of such laboratory tests

especially in rural hospitals made it difficult to assess participants for other complications like renal failure.

Most of the participants were treated according to standard guidelines; however some patients who had severe anaemia did not receive transfusion because of non-availability of blood and related blood products.

Ninety five (92%) participants were discharged from hospital without major complications and 52% were still pregnant. Among the maternal adverse outcomes observed were 2 maternal deaths, 4 participants with severe anaemia and 2 with cerebral malaria. The majority of participants who were discharged without complications were booked for antenatal care (65%). More complications were observed in those not booked. Booking status of participants therefore could have an effect on maternal outcome.

None use of IPT was associated with adverse outcome. All participants who deceased and those who had cerebral malaria did not use IPT. The number of IPT doses taken was inversely proportional to the number of participants who were discharged without severe complications.

Participants who deceased did not use IPT and ITNs and presented to hospital more than a week after onset of illness. None use of ITNs was also associated with severe anaemia. None of the participants who had severe anaemia had used ITNs. Of those who were discharged

without complications, 41% did not use ITNs at all compared to 26% who consistently used ITNs.

Fetal losses due to miscarriage 9(%) and stillbirths 6(6%) was high. There were also a high proportion of preterm deliveries and low birth weight babies. Adverse fetal outcomes were high in participants who did not use IPT, ITNs, and HIV positive not on HAART or PMTCT prophylaxis.

CONCLUSION

Malaria infection has adverse effects on both mother and fetus. It was associated with maternal mortality (2%) and morbidity. Anaemia, cerebral malaria, and maternal death were the main maternal complications encountered in this study. Maternal adverse outcome was influenced by booking status, HIV status, use of IPT, ITNS and late presentation to hospital. There was high fetal wastage (15%) resulting from miscarriages (9%) and stillbirths (6%). Malaria infection was also associated with low birth weight (30%) and preterm delivery (10%).

The study also revealed that there was underutilization of prevention strategies (IPT and ITNs) by 45% of participants which was mainly due to failure to book for ANC or late booking. Case management was generally according to standard guidelines but participants were not adequately investigated in terms of other parameters such as blood count and renal function. This was mainly due to limited availability of laboratory services and skilled manpower.

RECOMMENDATIONS

- Provision of health education through accessible media to populations in malaria endemic regions emphasizing need for early booking of pregnancies for antenatal care and use of preventive measures during pregnancy.
- 2) Further research on the following;

a) Evaluation of SP as the drug of choice for IPT and the assessment of its efficacy,

b) The feasibility of using a combination of drugs for IPT,

c) Feasibility of using intermittent- screen and treatment method which involves screening patients at antenatal visits and treating those who test positive especially in malaria-prone areas,

d) Assessment of barriers that lead to low uptake of preventive measures currently available by population in malaria regions.

3) Provision of adequate laboratory facilities, equipment and skilled manpower especially for rural hospitals.

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APPENDIX

DATA COLLECTION FORM FOR STUDY ON PREGNANT WOMEN ADMITTED WITH MALARIA

Record number.....

Referring

institution.....

		CODING CATEGORIES	SKIP
			то
1	Age		
2	Parity		
3	Marital status	Married	
		Divorced	
		Single	
4	Age of partner		
5	Highest level of education		
6	Highest level of education attained by		
	partner		
7	Place of residence		
8	Occupation		
9	Occupation of partner	·····	
10	Religion	Christian	

		Apostolic sect
		Traditionalist
		Muslim
		other
11	Religion of partner	Christian
		Apostolic sect
		Traditionalist
		Muslim
		other
12	History of travel to a malaria area	Place
13	Intervaal between travel and onset of	Days
	symptoms	
14	Duration of stay	Days
Obst	tetrics	
15	Booking status	Booked
		Unbooked
16	Gravid	Weeks
17	Gestation at booking	Weeks
18	HIV Status	Negative
		Positive
		Unknown
19	РМТСТ	HAART
		AZT prophylaxis

		Single dose Nevirapine	
		None	
			I I
Mala	aria prevention		
20	Intermittent preventive therapy	1 st dose	
		2 nd dose	
		3 rd dose	
21	Prophylaxis during travel to a malaria		
	area		
22	Bed net use	Always	
		Sometimes	
		Not at all	
Con	dition on admission		
Con	dition on admission Duration of illness prior to admission	Days	
		Days	
23		Days Reduced consciousness	
23 24	Duration of illness prior to admission		
23 24	Duration of illness prior to admission	Reduced consciousness	
23 24	Duration of illness prior to admission	Reduced consciousness Hypotension	
23 24	Duration of illness prior to admission	Reduced consciousness Hypotension Respiratory distress	
23 24	Duration of illness prior to admission	Reduced consciousness Hypotension Respiratory distress Convulsions	

26	Previous treatment				
Met	hod of diagnosis and other lab	o investigations			
27	Clinical assessment with no				
	confirmatory test				
28	Paracheck	Negative			
		Positive			
29	Blood slide	Negative			
		Positive			
		% parastaemia			
30	FBC	WBC			
		НВ			
		MCV			
		Plt			
31	U&E	Urea (U)			
		Creatnine (Cr)			
		Sodium (Na)			
		Potassium (K)			
Trea	atment and duration				
32	Iv quinine	Duration			
33	Oral quinine	Duration			

34	Chloroquine and fansidar	Duration
35	Coarterm	Duration
36	Transfusion	Units
37	Other	Duration
	drugs	

Outcome

38	Maternal	Recovery without severe
		complications
		Paralysis
		Severe anaemia
		Renal failure
		Cerebral malaria
		Death
		Other
39	Foetal	Normal term baby
		Preterm delivery
		Birth weight
		Stillbirth
		Miscarriage
		Threatened miscarriage
		Still pregnant
40	Duration of hospital stay	

CLIENT INFORMED CONSENT

(ENGLISH/SHONA/NDEBELE)

NAME OF RESEARCHER: Dr Reuben Bishi

PHONE: 00263 773 474 951

PROJECT DESCRIPTION: <u>FETOMATERNAL OUTCOMES OF PREGNANT WOMEN</u> <u>ADMITTED WITH MALARIA AT PARIRENYATWA HOSPITAL AND IN MASHONALAND EAST</u> <u>PROVINCE OF ZIMBABWE</u>

Ongororo yechirwere chemalaria kumadzimai akazvitakura. Umhloliso womkhuhlane wemalaria kubomama abazithweleyo.

Your rights

Before you decide whether or not to volunteer for this study, you must understand its purpose, how it may help you, the risk to you, and what is expected of you. The process is called informed consent.

Kodzero dzenyu

Musati mabvuma kupinda muchirongwa ichi, munotarisirwa kutanga manzwisisa zvinangwa zvacho, zvachinokubatsirai uye njodzi dzamungasangana nadzo.

Ilungelo lakho

Ungakavumi ukungena kumhloliso lo, uyakuthazwa ukuqala uzwisise izizatho zakhona, ukuthi kuncedani njalo ingozi elingahlangana lazo.

Purpose of research

To determine the incidence of malaria in pregnancy, associated complications and evaluation of factors that influence patient outcome in the institutions of study.

The study also examines the quality of care offered to the patient.

Zvinangwa zvechirongwa ichi.

Ongororo iyi inotarisa huwandu hwechirwere chemalaria kumadzimai ane pamuviri, njodzi dzavanosangana nadzo uye zvimwe zvinorerutsa kana kuwedzera matambudziko anosangana nemadzimai aya.

Dzidzo iyi inoongororawo rubatsiro runopiwa madzimai aya kuti ndirwo runokodzera here muzwipatara zvichatariswa.

Izizatho zomhloliso lo

Umhloliso lo ukhangela ubunengi bomkhuhlane wemalaria kubomama abazithweleyo, ingozi abahlangana lazo njalo okunye okuyenza kubelula noma okwengezelela indubeko ehlangana labomama laba. Imfundiso le ikhangela uncendo oluphiwa omama laba ukuthi yilo olulingeneyo yini ezibhedleleni ezizakhangelwa.

Procedures involved in the study

Information will be collected from patient notes to fill a data collection form.

Patient interviews will also be contacted to fill information missing from the notes.

Nzira dzichashandiswa muongororo iyi.

Pane gwaro richashandiswa kuunganidza zvese zvichabvunzwa kana kutorerwa mumabhuku evarwere vanenge vasarudzwa kupinda muchirongwa ichi.

Indlela ezizasetshenziswa emboneni lo.

Kulencwadi ezasetshenziswa ukubuthanisa konke okuzabuzwa okunye kutholwa emabhukwini ezigulani eziyabe zikhethiwe ukungena kumhloliso lo.

Discomforts and risk

The research is not associated with any physical risks. There is also minimal discomfort which may be associated with interviews where necessary.

Zvimwe zvisingafadzi kana zvinokuvadza kumurwere

Ongororo iyi haina chinotarisirwa kukuvadza murwere kunze kwekuti vamwe varwere vanogona kusafarira kutorerwa nguva yavo vachibvunzwa mibvunzo.

Okunye okungathabisi noma okungalimaza isigulani

Umhloliso lowu awula okukhangelelwayo ukthi kungalimaza ogulayo ngaphandle kwezinye izigulani ezingakwanisa ukungathakazeleli ukuthathelwa isikhati sabo bebuzwa imibuzo.

Potential benefits

This study has no immediate or direct benefits to the patient but it is intended to improve prevention and management of malaria in pregnancy which will benefit the population at risk of getting the disease.

Mibairo ingapiwa varwere

Chirongwa ichi hachina mibairo ingapiwa kune vanenge vasarudza kupinda machiri asi tine tarisiro yekuti zvinenge zvawanikwa zvinokwanisa kubatsira mukudziirira, kurapa zvizere nekuderedza uwandu hwemadzimai akazvitakura anorasikirwa neupenyu nepamusana pechirwere chemalaria.

Imizuzo engaphiwa abagulayo

Umhloliso lo awula mizuzo engaphiwa kulabo abakhethiweyo ukungena,kodwa sikhangelele ukuthi loko esizakuthola kuzanceda ukhuvikela,ukwelapha okugcweleyo lokwehlisa ubunengi babomama abazithweleyo abalahlekelwa yimpilo ngenxa yomkhuhlane wemalaria.

Study withdrawal

You are free not to allow your information to be used in the study without any penalties.

Kubuda muchirongwa ichi

Muoziviswa kuti munekodzero yekusarudza kubuda muchirongwa ichi. Kubuda kwenyu hakuite kuti mutadze kupiwa rubatsiro rwamakakodzera pachipatara.

Ukuphuma kulo umhloliso

Liyaziswa ukuthi lilelungelo lokukhetha ukuphuma kumhloliso lo.Ukuphuma kwakho ak'wenzi ukuthi kuphambanise ukuphiwa kwako uncedo okufanele uluthole esibhedleleni.

Problems/Questions

Please feel free to ask questions about this research or consent.

Matambudziko kana mibvunzo

Makasununguka kutaura zvamusinganzwisisi kana mibvunzo yamunenge munayo.

Indubeko noma imibuzo

Ukhululekhile ukukhuluma ongakuzwisisiyo noma ukubuza imibuzo oyabe ulayo.

Authorisation

I have read this paper about the study or it was read to me. I understand the possible risks and benefits of this study. I know being in this study was voluntary. I chose to be in the study. I know I can stop being in the study and I will not lose any benefits entitled to me. I will get a copy of this consent form.

Mvumo

Ndaverenga nekunzwisisa maererano nechirongwa ichi. Ndanzwisisa matambudziko anotarisirwa kusangana nawo uye rubatsiro rwandingawana. Ndinoziva kuti

ndinokwanisa kubuda muchirongwa ichi pandinodira zvisingakanganisi kodzero yangu yekurapwa.

Imvumo

Ngibale ngazwisisa mayelana lomhloliso lo .Ngizwisisile indubeko ezikhangelelweyo ukuthi ngingahlangana lazo njalo loncedo engingaluthola.Ngiyakwazi ukuthi ngiyenelisa ukuphuma emhlolisweni lo lapho engifuna khona njalo kungaphambanisi ilungelo lami lokwelatshwa.

Client signature.....

Client name.....

Research signature.....

Witness signature.....