UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

PREDICTORS OF OUTCOMES FOR CHILDREN WITH SEVERE MALARIA ADMITTED AT MCHINJI DISTRICT HOSPITAL IN MALAWI

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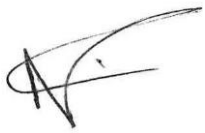
A research Report submitted to the faculty of Health Sciences, University of Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Public Health in the field of Rural Health

Johannesburg, June, 2017.

DECLARATION

I, Nedson G Fosiko, declare that this research report is my own work. It is being submitted for the degree of Masters in Public Health (Rural Health) at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this university or any other university.



Signed

On the **12th** day of **June 2017**

ABSTRACT

Introduction: Knowing the burden of severe malaria in children and the predictors of outcomes for children with severe malaria would help to put up interventions that would reduce the risk of poor outcomes and promote survival.

Aim: The aim of this study was to determine the predictors of outcomes for the children with severe malaria admitted at Mchinji district hospital, in Malawi.

Methods: This was a cross sectional study and 201 randomly sampled files of children admitted to Mchinji district hospital with severe malaria in 2013 and 2014 were reviewed. Univariate and multivariate logistic regression models were used to predict outcomes for the children with severe malaria.

Results: During the study period there were 2603(N) children admitted with severe malaria. A sample of 202 (n) files for children admitted with malaria was randomly selected, and 201(n) were included in the final analysis. The majority of the children were under the age of five years 155 (78.3%), 106 (53.5%) were male, with 147 (73.1%) being self-referrals and 54 (26.9%) health centre referrals. Fever was the most common presenting complaint, 177 (88.1%), while 76 (37.8%) had convulsions and 58 (28.9%) had vomiting. All patients were treated as per Malawi National Malaria Control Program treatment guidelines. The outcomes of the children were either discharged home alive, died, missing (referred to a specialised unit, or absconded from hospital). The case fatality rate was 7.5%. Of the children that died 11 (73.3%) were children under the age of five years and 9 (60%) were children referred from the health centre. Children who were referred from the health centres were more likely to die than children who were self referred by guardians from their homes [OR=4.84 1.63-14.35]

Conclusion and Recommendations: The study found that being referred from health centre, presenting with unconsciousness, long stay in hospital and receiving LA in the course of treatment are predictors of outcomes in children admitted with severe malaria. The predictors are a combination of patient and health systems factors that influence delay in accessing prompt treatment for malaria in general. Therefore, there is need to improve patient care right from home and in the hospital with special attention on the patient referral system. Further research on community and health system factors to improve the system for caring of children with malaria may be required.

DEDICATION

This is in recognition of the determination and support from

My wife Joyce

My children Peace and Wanga Fosiko

And the entire Fosiko family

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LIST OF ABBREVIATIONS

ACT	- Artemisinin Combined Therapies
CI	- Confidence Interval
DHO	- District Health Officer
Hb	- Haemoglobin
HMIS	- Health Management Information System
ICU	- Intensive Care Unit
iPT	- Intermittent Preventive Treatment
IRS	- Indoor Residual Spray
ITN	- Insecticide Treated Nets
LA	- Lumefantrine/ Artemether
LLITNs	- Long Lasting Insecticide Treated Nets
MIS	- Malaria Indicator Survey
MNMCP	- Malawi National Malaria Control Program
MoH	- Ministry of Health
MRDT	- Malaria Rapid Diagnostic Test
NMCP	- National Malaria Control Program
NTS	- Non-typhoidal Salmonella
OR	- Odds Ratio
QECH	- Queen Elizabeth Central Hospital
WHO	- World Health Organization

LIST OF DEFINITIONS

A Severe Malaria Case : Any child with a positive malaria test, needing hospital admission or had any of the following: high fever, convulsions, any impairment of consciousness, prostration, respiratory distress and abnormal bleeding, severe anaemia, any manifestation of shock like severe diarrhoea and vomiting with dehydration.

Self-Referral : Children brought to the hospital by their parents or guardians directly from home without passing through another health facility.

Health Centre Referral : Children who were brought to hospital after being sent by health worker from a primary health facility and may have received treatment prior to being sent to the district hospital.

CHAPTER ONE: INTRODUCTION

1.1 BACKGROUND INFORMATION

Malaria remains a major public health problem with 3.2 billion people at risk of the disease globally. In 2015, 212 million cases and 429, 000 deaths were attributed to malaria of which 90% of the cases and 92% of the deaths were registered in Africa (1). Additionally, malaria remains a major killer of children (1,2) and is more common in the rural areas (3).

Malaria is caused by a protozoan parasites called *Plasmodium* (*P. falciparum, P. vivax, P. ovale P. Malariae and P. knowlesi*) with *P. Falciparum* being the most common cause of severe disease especially in sub-Saharan Africa (1,4) . Malaria parasites are transmitted from one infected person to another person by a female *Anopheles* mosquito bite. Once a person is infected, it takes 10 to 15 days after the mosquito bite to develop malaria symptoms (4).

After a mosquito bite, the infective forms of malaria parasite (the sporozoites) travel to the liver to infect the liver cells (hepatocytes) and develop into approximately 30,000 development stage form of malaria parasites (merozoites) that are released in the bloodstream. This form of the parasites invade the red blood cells where they and schizoints then merozoite are released when the infected red blood cells rupture. Infected RBCs circulate containing ring-stage parasites, and a small proportion of merozoites will develop into male and female forms of the parasites (gametocytes) that infect mosquitoes, completing the parasite life cycle. The repeated cycles of red blood cell (RBC) invasion, replication and merozoite release will results in the exponential growth of the parasite population and lead to disease. The removal of infected RBCs by splenic macrophages or the uptake of free haemozoin results in the activation of innate immune receptors and storm of immunological compunds (cytokines). The circulating cytokines will cause paroxysms and induce the expression of adhesion molecules by endothelial cells, which mediate parasite sequestration. The sequestration of infected RBCs disrupts blood flow, promotes blood clots, injures cells of the blood vessels (endothilial cells) and ruptures vascular walls, leading to the release of vascular content and local tissue inflammation. These mechanisms affect different organs and contribute to the symptoms of malaria which are not specific to the disease. acute respiratory distress, cerebral malaria or placental malaria. Haemolysis of infected and bystander (uninfected) RBCs, uptake of altered RBCs by immunological cells of the spleen (splenic

macrophages) and cytokine-induced impairment of red blood cells production (erythropoiesis) cause anaemia. (5)

symptoms are similar to those of other viral, bacterial and parasitic diseases. They include fever, chills, abdominal discomfort, vomiting, loss of appetite, general body pains, difficult breathing, convulsions and coma (4). It is reported that children can progressive quickly to become very sick and suffer from severe disease if proper treatment is delayed (6).Malaria is diagnosed when malaria parasites are detected in a peripheral blood of a patient suspected to have malaria through microscopic examination of a blood film or a malaria antigen Rapid Diagnostic Test (MRDT) (6). A severe malaria case is when a patient is tested positive of malaria and has the following signs and symptoms: coma, recurrent convulsions, respiratory distress, shock and severe anaemia. It is a medical emergency that may necessitate intensive nursing care and careful clinical management (7). Those given ineffective treatment may end up with irreversible damage of vital organs and may die (8). In young children, death due to severe malaria exceeds 10% (8).

Malaria is preventable and curable. The World Health Organization (WHO) treatment guidelines recommend the use of artesiminin combination therapy and quinine for the treatment of malaria. The treatment and management of children with severe malaria require a lot of resources and organization, in terms of human resources, financial resources, medicines and equipment. This puts a lot of pressure on the health system, the family, and community. However, even after recovery, children treated for severe malaria may recover with different complications including epilepsy, loss of function of different parts of the body including hearing and visual loss (8) requiring further health care management.

Malaria is prevented by avoiding mosquito bites through the use of insecticide treated bed nets, applying insect repellents on exposed areas of the body and the use of indoor residual sprays (IRS) (10). There are also medicines available for chemoprevention of malaria but they are not 100% protective, they need to be combined with personal protective methods. An investigation of malaria vaccine is also showing promise in clinical trials and may be available in the near future (11).

The Malawi malaria indicator survey of 2014 reported approximately four million suspected cases of malaria causing about 40% of all hospital admissions of children less than five years

old (12). The Malawi Ministry of Health (MOH) National Malaria Control Program (NMCP) is responsible for the control of the disease in the country. The Malaria Strategic Plan of 2010-2015 aimed to reduce the malaria burden figures of 2010 by 50%, by 2015 (13) The unit has scaled up four malaria control strategies and these are: prompt treatment (within 24 hours of onset) of fevers in children, use of long lasting insecticide treated nets (LLITNs), indoor residual spray (IRS) and intermittent preventive treatment (iPT) of malaria to pregnant women (13). The Malawian malaria indicator survey of 2014 has since reflected that there is an increase in household ownership of ITN from 58% to 70% in 2010 to 2014 respectively (13) and 32% of children with fever received recommended anti-malarial medicine (Artimesinin Combination Therapy (ACT)) (13). However, the number of children with malaria admissions in Malawi has not decreased (14).

Mchinji district is one of the rural districts of Malawi and has a high malaria prevalence rate of 65.5% among the population (15) mostly affecting children. About 8% of under-five children malaria cases in the district are severe and require hospital treatment. In 2013 alone 1163 admitted cases of malaria were recorded of which 7.2% resulted in deaths (16).

1.2 PROBLEM STATEMENT

Children continue to die of malaria in Malawi (1,8,13). The children die when they develop severe disease. Children with severe malaria presents with a spectrum of syndromes (17) which also indicate the level of complications from the disease. These complications are resource demanding throughout the health system and can be influenced by a number of factors including socioeconomic status, age, immune status and access to health care. Delay to get proper care can occur at health facility level due to the following factor among others, incorrect diagnosis and treatment, lack of essential, poor health facility infrastructure and equipments to treat severe malaria and its complications. Any factors related to severe malaria can be used as a proxy to predict outcomes of those children with the disease condition. Knowing and understanding the predictors can help to put intervention that can save the children with severe malaria. Management of the children with severe malaria therefore, requires the capacity and ability of the health system to detect the severe cases of malaria to provide relevant care and ensure survival of the cases (17).

1.3 RESEARCH QUESTION

What are the predictors of outcomes for children with severe malaria admitted to Mchinji district hospital?

1.4 JUSTIFICATION

Identifying the risk factors of adverse outcome for severe malaria in children, would be used to predict deaths in children with severe malaria. Knowing predictors of outcomes for children with severe malaria would therefore, help to put up interventions that would reduce the risk of poor outcomes and promote survival. Therefore, this study was undertaken to establish the predictors of outcomes for children with severe malaria. The results will provide information for rapid and simple identification of the predictors of outcomes for children with severe malaria. This will strengthen best practices in clinical care of the children with severe malaria and optimize care to reduce mortality among hospitalized children (18). The information obtained from the study will strengthening the information education and communication (IEC) materials for malaria control. It will also inform management of severe malaria cases in children to reduce or prevent deaths. Hence this study will strengthen the strategy of case management and prompt treatment at all levels in the control of malaria in the district which is vital in the control of the disease. However these factors have not been established at Mchinji district.

1.5 LITERATURE REVIEW

Mortality due to malaria is persistently high in Africa and malaria trends to have not shown any decreasing trends in Malawi (13). This may be because of a number of reasons that include individual level factors, limited access to health care services, poor clinical case management and increased drug resistance. A number of studies have been done to establish clinical factors associated with fatal outcomes of malaria. The aims of most of these studies were to improve classification of severe malaria and help clinicians to avoid diagnostic delays and deaths by targeting resources to the sickest patients (19). This chapter reviews literature on the severe malaria burden, characteristics of children with severe malaria and factors associated with death in children with severe malaria.

1.5.1 Incidence and Burden of Malaria

Malaria has been known for more than 4000 years (20). Currently more than half the population of the world is at risk of malaria world wide affecting 95 countries and territories

of the world with 90% of the cases occurring in Africa. Thirteen countries in the subSaharan Africa account for 76% of malaria cases and 75% death globally (21). Currently the goal in all countries with malaria is to reduce levels of transmission remarkably and to reduce the numbers of malaria cases and deaths (22). Malaria distribution tends not to be evenly distributed even in places where the disease is prevalent (23). Despite generally increased coverage of malaria interventions in the world, studies have shown minimal changes in paediatric clinical malaria cases (14). The disease continues to be a major cause of admissions and hospital deaths in children aged 1–5 years, in many endemic areas (24,25).

It is reported that malaria is responsible for 34 percent of all outpatient visits and 40% 0f hospital deaths across all ages in Malawi. Malaria continues to be a major public health problem in the country and is a major cause of hospital admissions in children under the age of five years. More than 95% of the country is endemic to malaria and transimission is perennial (26). The disease is responsible for approximately 6.2 million presumed and confirmed cases reported annually from health facilities and by the community case management program (27). The 2014 malaria indicator Survey (MIS) reported a 33% microscopy malaria parisites prevalence in among children under five years country wide (28). In Malawi malaria accounts for 15-35% of total hospital deaths (29).

HIV co-infection has been shown to be associated with increased incidence of severe malaria and other co-morbidity carrying a higher case fatality rate (30). A study done in at Queen Elizabeth Central Hospital in Malawi found that 4.6% of children admitted with severe malaria to a malaria had a positive blood culture of which the majority had Non-typhoidal Salmonella bacteria species (NTS) isolates (58%) (31). Non-typhoidal salmonella (NTS) infections are a leading cause of sepsis and deaths in African children (32). In general 1-4% of children diagnosed with malaria are said to be severe enough to require hospital admission and parenteral antimalarial treatment (33) but very few (less than half) of the children who develop severe malaria are able to reach the health facility. Those that manage to reach the health facility have a case fatality rate of 20% in the hospital (34). Severe malaria cases are very difficult and costly to treat as they may need intensive care unit management. The actual average provider's cost for the management of malaria ranges between US$61.08 for a paediatric malaria inpatient with anaemia and US$74.29 for a case with neurological affection (35). The high cost of treatment includes transport costs and hospital cost and many poor families who are the most at risk may not afford the treatment resulting in poor access to

malaria treatment and deaths of children due to malaria. It is reported that a child dies of malaria somewhere in the world every minute (35).

1.5.2 Characteristics of Children with Severe Malaria

Children under five are at high risk of severe malaria regardless of the gender of the children (36). The risk of clinical malaria in children begins at around 4 months of age with infants becoming susceptible to severe disease and death (37). A study done in Nigeria found that age less than 11 years, duration of illness of less than 3 days and presence of fever were found to be at risk of developing severe malaria (38). Those children who live in the rural areas where there is poor access to health services are at high risk of developing severe malaria because of delayed and wrong treatment they receive (39,40). Studies done in Kenya and Togo demonstrated that 80% of the children with febrile illnesses were given antimalarial treatment at home which may be wrong antimalarials and ineffective treatment for the diseases (41,42,43). This result in children developing severe malaria and present to the health facility very sick following failure of treatment, also requiring referral to high levels of health care as primary health facility will fail to take care of the severely sick children. However, even after referral to high level facility, it is not uncommon that children with severe malaria are taken care of in basic facilities that do not have the required resources to manage the complications of severe malaria (44). In rural health settings where malaria is more prevalent, the health facilities mostly have inadequate clinicians and nurses, inadequate essential medicines, inadequate infrastructure and equipments to handle malaria cases especially severe cases with complications.

1.5.3 Clinical Features of Children with Severe Malaria

Studies done in Africa have shown that children with severe malaria presents with high fever, prostration, impaired conscious level, convulsions, anemia, poor nutrition and underlying chronic conditions (18). The Clinical presentation of the children with severe malaria and how they are managed determine the case fatality and survival rates for the children (45). The clinical presentation of children with malaria depend on the characteristics of the population, health seeking behavior and epidemiology of the disease (46). Studies have shown regional differences in proportions of clinical features and outcomes of children with severe malaria presenting to hospital (47). The clinical features of the disease are not specific for severe malaria. They can also be features of other diseases like bacterial, viral and parasitic

infection. Other diseases that can present like malaria include meningitis, sepsis, pneumonia, ear infections and gastrointestinal worm infestations (48).

1.5.4 Treatment and management of Severe malaria

Severe malaria is a critical condition and requires urgent treatment and management. It is treated according to WHO guidelines (See Appendix 6) with parenteral quinine, artesunate and any other artemisinin derivatives. In Malawi quinine and artesunate are used for the treatment of severe malaria. While the aim of treatment is to eradicate the parasites in the body, severe malaria treatment includes treatment of the complications of the disease. These may include treatment of dehydration, hypoglycaemia, convulsions, coma, anaemia, renal insufficiency and bleeding disorders associated with severe malaria (48).

1.5.5 Outcomes of Children with Severe Malaria

Severe malaria is an advanced staged of the disease and presents a medical emergency which require early intervention to prevent further complications and death (49). Otherwise it represents the end stage of improperly treated uncomplicated malaria (50). However, with proper treatment and clinical care most of the children with severe malaria are discharged from hospital alive. Those who survive severe malaria may remain with other complications especially in cerebral malaria. It is reported that approximately 10% of the children who survive cerebral malaria have neurological sequelae and may develop cognitive and motor functions deficit (51). Children with severe malaria may die if left untreated or when they have irreversible multiple organ failures. This may occur even with treatment. A study done in Tanzania found that children with multiple signs and symptoms of severe malaria on admission have higher risks of dying in hospital. (52). Another study in India demonstrated 89% survival rate and 11% case fatality rate of the children with malaria (53). Cerebral malaria, caused by *P falciparum*, has a mortality rate of 25%, even with the best treatment (48). Those that cannot be treated at lower health care facility need to be referred to high level of care like tertiary hospitals. Others may also abscond from hospital.

1.5.6 Factors Associated with Outcomes of Children with Severe Malaria

Many recent studies have identified factors associated with death in patients with severe malaria. These factors include coma, convulsions, respiratory distress hypoglycemia, retinal changes, acidosis and the presence of malarial pigment in peripheral blood neutrophils (54). In Mozambique, Bassat and colleagues found that malaria deaths depended on the presenting

characteristics. Their study showed that out of all the children dying with malaria, 55.0% presented with prostration, 41.1% with respiratory distress and 17.3% with severe anaemia (55). A study done in Malawi by Kazembe and colleagues found that age, referral status, distance from hospital and length of hospital stay for the admitted malaria cases were associated with unfavourable outcomes of severe malaria (46). Children receiving severe malaria treatment have a typical case fatality rate of 10-20% (17).

Children presenting at the hospital with severe malaria hold a lot of information required for the development and implementation of priority public health interventions and also guide national policies and treatment protocols for children with severe malaria (47). Analyzing data collected on admission of children with severe malaria would provide indicators of the predictors of outcomes in children with severe malaria. Hence the need for this study to generate information that would guide policy and best practices in clinical management of children with severe malaria being admitted to Mchinji district hospital and reduce deaths.

1.6 AIM OF THE STUDY

The aim of the study was to determine the factors associated with outcomes of children with severe malaria admitted at Mchinji district hospital, in Malawi.

1.6.1 Specific Objectives

i. To determine the proportion of children with severe malaria admitted at Mchinji district hospital in 2013 and 2014.

ii. To determine the outcomes of children admitted at Mchinji district hospital with severe malaria.

iii. To determine the predictors of outcomes of children with severe malaria admitted at Mchinji district hospital.

CHAPTER TWO: METHODS AND MATERIALS

2.1 INTRODUCTION

This chapter describes the study design, study setting, study population, study case selection, sample size, data collection, study variables and data analysis.

2.2 STUDY DESIGN

This was a cross sectional study of malaria cases among children aged between 4 months and 14 years admitted to Mchinji district hospital, in Malawi in 2013 and 2014. Hospital case files for malaria cases admitted between 2013 and 2014 were reviewed.

2.3 STUDY SETTING

The study was conducted at Mchinji district hospital in Malawi. The hospital serves as a referral hospital for 12 health centres and two community hospitals in the district. Mchinji district hospital also serves people from Mozambique and Zambia as the district borders with these two countries. The hospital is a 200 bed hospital of which 25 are paediatric beds. It has laboratory facility, X-ray equipment and an operating theatre for surgical cases but does not have an intensive care unit. All malaria cases that require admission are referred to this hospital for in-patient care and are considered severe malaria cases. The study utilised data collected and recorded in the patients hospital files.

2.4 STUDY POPULATION AND CASE SELECTION

The study population was all children aged between 4 months and 14 years admitted to Mchinji district hospital with severe malaria. A severe malaria case was any child with a positive malaria test needing hospital malaria treatment and had any of the following: high fever, convulsions, any impairment of consciousness, prostration, respiratory distress and abnormal bleeding, any manifestation of shock like severe diarrhoea and vomiting with dehydration (17). There were 2603 children admitted with confirmed diagnosis of malaria and 202 children were sampled. The simple systematic random sampling method was used where all the malaria cases were numbered 1 to 2603.

Sampling included children with severe malaria and those that had malaria and other conditions, including malnutrition, chronic diseases like diabetes, sickle cell anaemia, sepsis, meningitis, HIV disease, congenital cardiac diseases, trauma etc.

2.4.1 Exclusion Criteria

The study excluded the following patients:

1. Those treated for malaria but with unconfirmed malaria diagnosis
2. Those with missing files and insufficient information,

2.4.2 Sample Size

Epi-info was used to calculate the sample size of 133 from a population size (N) of 2603 children with severe malaria admitted to the hospital in two years, using a precision of plus or minus 5% for 10% prevalence of severe malaria cases. Below is the equation used for calculating the sample size as shown in the Table 2.1.

Sample size $\boldsymbol{n}$ **= [DEFF*Np(1-p)]/ [($d^2/Z^2_{1-\alpha/2}$*(N-1)+p*(1-p)]**

Table 2.1: Calculated Sample Sizes (n) for Various Precision Levels at 95% CI

Confidence Level %	Confidence limit	Sample Size (n)
1	9-11	1607
2	8-12	672
3	7-13	341
4	6-14	202
5	**5-15**	**133**

A sample size of 133 was calculated at the confidence interval of 95% as commonly used. However, the sample was increased to 202 to increase the power and precision of the study to estimate the indicators of the study while taking into consideration of the availability of the resources.

2.5 DATA COLLECTION

The data were collected by the investigator using hospital records review method at Mchinji district hospital. The malaria patient files were pulled out and data was extracted from them using a data extraction tool (see Appendix 3). These files contained demographic and clinical records of the patients which include name, age, residential place, gender, history of illness,

diagnosis, treatment given, date of admission, date of discharge and the outcome of treatment. The files were coded to maintain confidentiality. A pilot study was done on twenty randomly sampled patients' hospital ward files to explore and see data available in the files and the ease of further data extraction. However, data were not consistently recorded in the files and there was other missing data, especially residential and sociodemographic data for the guardians.

2.6 STUDY VARIABLES

2.6.1 Outcome Variables

The main outcome variables in the study were discharged home alive, died and unknown. Unknown outcome was when the child was referred to other specialized unit or where outcome was missing or absconded.

2.6.2 Exposure Variables

The exposure variables included demographic variables, Health system variables and clinical variables. These data were collected on clinical assessment at the hospital and included history of the malaria symptoms like fever, convulsions, unconsciousness, vomiting, diarrhoea, not eating, not able to sit, abnormal bleeding, etc. Vital signs including temperature, respiratory rate, pulse rate, blood pressure and blood glucose level were mostly completely missing. The diagnoses like epilepsy, malnutrition, diabetes, chronic cardiac diseases, HIV disease and childhood tumours were looked for as a sign of chronic diseases, however, these data were also not available. The data variables are shown in table 2.2 below.

Table 2.2: List of Data Variables Used

Data Variable	Description of Data Variable	Analysis Done
Gender	Categorical	Frequencies and proportions calculated
Age	Categorical	Frequencies and proportions calculated
Referral Status	Categorical	Frequencies, proportions calculated and inferential statistics
Day of Admission	Categorical	Frequencies, proportions and inferential statistics
Signs and Symptoms	Categorical	Frequencies, proportions and inferential statistics
Treatment Given	Categorical	Frequencies, proportions and inferential statistics
Duration of Hospital Stay	Continuous	Frequencies, proportions and inferential statistics
Outcome (Alive, dead, absconded, referred)	Categorical	Frequencies and proportions calculated Frequencies and inferential statistics

2.7 DATA MANAGEMENT

Data was collected using the data extraction tool (Appendix2) and verified to correct errors before entering the data into the Microsoft Excel program and cleaned for any errors. The data were then imported from the Excel into STATA Version 13 for analysis.

2.8 DATA ANALYSIS

Data analysis included calculation of frequencies of children with severe malaria by age, gender, referral status, presenting signs and symptoms, treatment given, and according to the outcomes of the cases as shown in the Table 2.3 below.

Table 2.3: Specific Objectives with Data Analysis Plan

Specific Objectives	Analysis Plan
To determine the proportion of children with severe malaria admitted to Mchinji district hospital and their sociodemographic characteristics.	Descriptive statistics (frequencies and percentages)
To determine the outcomes of children with severe malaria admitted to Mchinji district hospital.	Descriptive statistics (frequencies and percentages)
To determine the predictors of outcomes in children with severe malaria admitted to Mchinji district hospital	Inferential statistics (univariate and multivariate logistic regression using odds ratio and 95% confidence intervals)

2.8.1 Descriptive Statistics

Mean with standard deviation was calculated for continuous variables on assumption of normal distribution of the sample. Proportions were calculated for categorical variables like gender, malaria cases and the clinical syndromes of severe malaria. These were then presented as tables of percentages and frequencies.

2.8.2 Inferential Statistics

Difference in proportions for deaths due to malaria and outcomes were calculated with 95% Confidence Interval using Fisher's exact tests. Odds ratio and 95% confidence interval to identify factors associated with the outcomes of severe malaria were calculated using univariate and multivariate logistic regression. Statistically significant factors in univariate analysis were included in Multivariate logistic models to come up with the predictors of outcome for children with severe malaria.

2.9 ETHICAL CONSIDERATIONS

Ethical approval to conduct the study was obtained from Ethics committee of the University of Witwatersrand clearance certificate number M150637 and approval from Mchinji district health officer (DHO). Individual cases were given identification codes and data were kept confidential and accessed only by the principal investigator.

CHAPTER THREE: RESULTS

3.1 INTRODUCTION

This chapter presents the results of the study. It describes the sample studied and provides the flow of selected sample and malaria admissions, characteristics and clinical features, outcomes of children with severe malaria admitted between the 2013 and 2014 at the Mchinji district in Malawi. The chapter goes further to examine the factors associated with outcomes in children with severe malaria at Mchinji district hospital.

3.2 ADMISSIONS OF CHILDREN WITH SEVERE MALARIA

Details of the study population are summarised in Figure 3.1. Briefly, a total of 11,469 children were admitted at the hospital between 2013 and 2014. Of these 2603 (22.7%) were confirmed as severe malaria cases. Out of the 2603 children with confirmed severe malaria, the study randomly sampled 202 cases, however, data was analysed for 201 of the 202 sampled children because one of the children was excluded due to the extent of missing data. Socioeconomic data was missing in the files and was not included in the analysis. A total of 573 children admitted died of which 22.9% (131) were malaria related deaths.

Of the 201 cases analysed, 186 (92.5%) children were discharged alive, 15 (7.5%) children died. The final outcomes of 12 (6%) children were unknown (7 children were referred to other specialized centres and 5 absconded from hospital) see Figure 3.1.

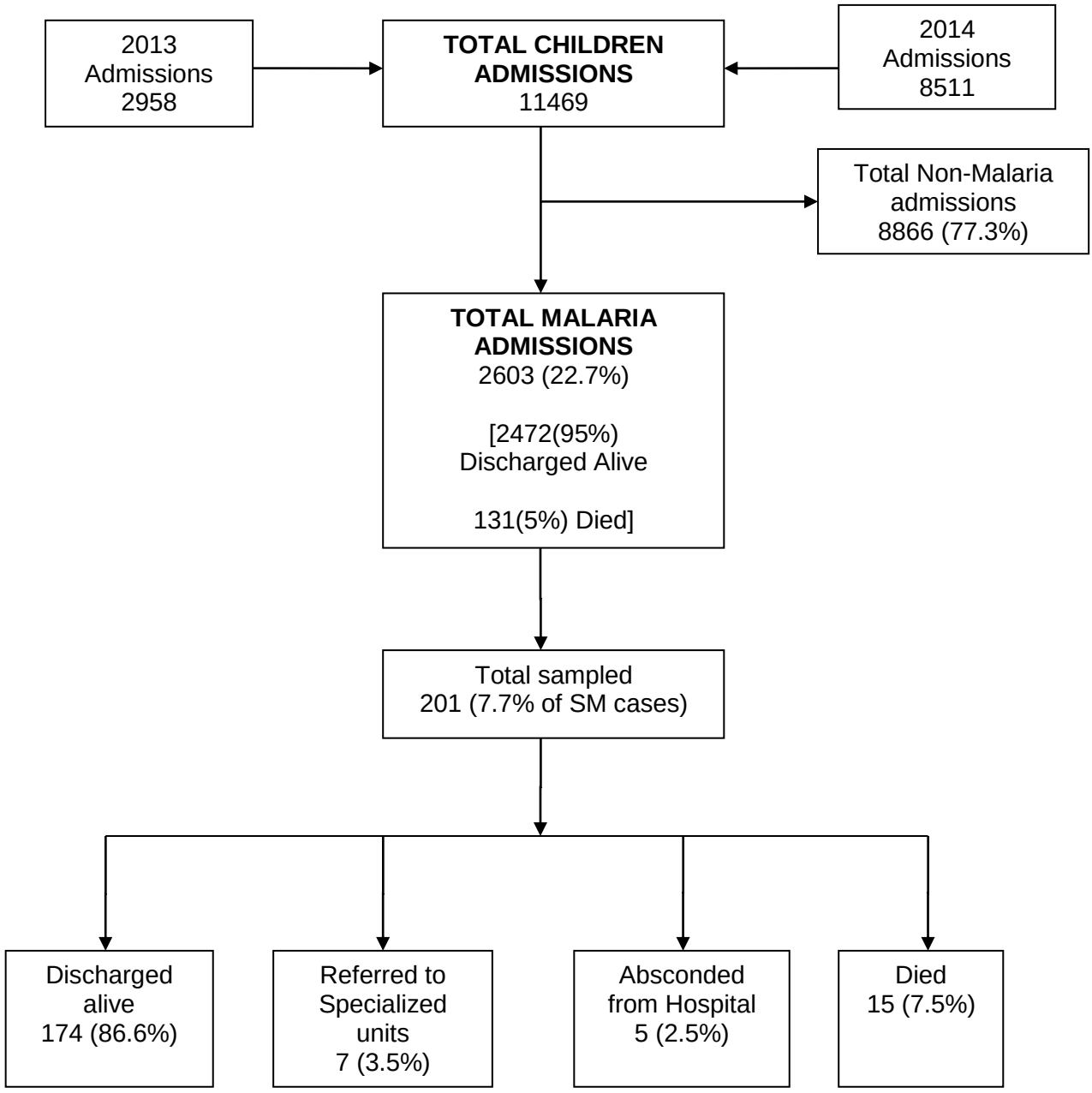

Figure 3.1: Flow Chart of Enrolled Participants

3.3 CHARACTERISTICS OF CHILDREN WITH SEVERE MALARIA ADMITTED TO MCHINJI DISTRICT HOSPITAL

3.3.1 Demographics of Children with Severe Malaria

The majority of the cases were males (53.5%) and those under the age of five years (78%). The sample had a mean age of 43.1 (CI:38.5-47.7) months with minimum age being 4 months and maximum age 144 months. The age for 4 children was missing. The mean weight of the children was 13.2 (CI:12.3-14.1) Kg with minimum being 5.7 Kgs and maximum 35 Kgs.

3.3.2 Clinical Presentation of Children with Severe Malaria

Children with severe malaria during the period under study presented with a wide range of clinical features. The majority 177 (88.1%) presented with fever followed by convulsions 76 (37.8%), vomiting 55 (27.4%) and unconsciousness 6 (3.0%). There were very few cases that presented with spontaneous bleeding (nose bleeding, bloody diarrhoea or urine) 9(4.5%), dehydration 8 (4.0%), jaundice 6 (3.0%) and splenomegaly 3 (1.5%). Data on vital signs especially respiratory rate, blood pressure, haemoglobin concentration (Hb) and history and signs of chronic diseases were mostly missing and were not included in the analysis.

3.3.3 Admission and Treatment of Children with Severe Malaria

The majority of the children, 147 (73.1%) were self-referrals straight from home by their guardians while 54 (26.9%) were referred through health facilities in the district. Those referred through health facilities came from 11 of the 13 health centres in the district and had received pre-referral treatment prior to admission at the district hospital.

Out of the sampled cases, 53 (26.4%) of the children were admitted over the weekend (Saturday and Sunday) and 148 (73.6%) were admitted during the working week days (Monday to Friday). Malaria was confirmed by malaria rapid diagnostic test (MRDT) in 87.1% of cases while 14.4 % were confirmed by microscopy. All the children were treated as per Malawi national malaria treatment guidelines which include quinine, Lumefantrine Artemether (LA) combination and paracetamol. However, 51 (25.4%) received malaria treatment only and 150 (74.6%) of the children were given malaria treatment plus other treatments mainly antibiotics implying covering them for bacterial infections and other conditions. Forty (19.9%) of the 201 children received blood transfusion.

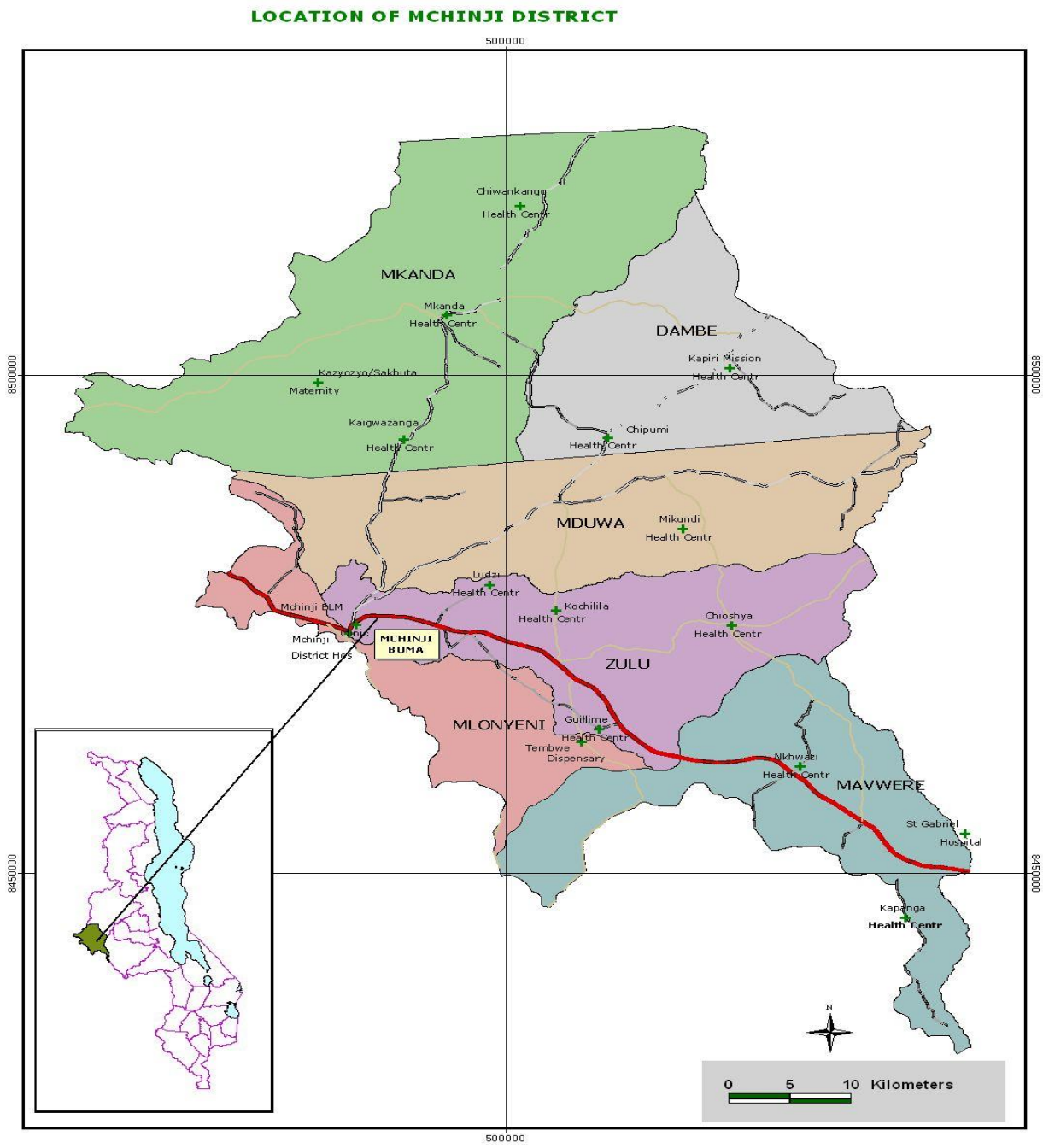

Figure 3.2: Map of Mchinji District Showing Health Facilities

3.3.4 Duration of Hospital Stay for Children with Severe Malaria

The duration of stay in the hospital varied from 1 day to 14 days, with mean duration of 3.8 days (95% CI 3.6-4.1 days). Almost half of the children 102 (50.8%) stayed in the hospital for a period of 1 to 3 days while 91 (45.3%) stayed for 4-7 days and 8 (3.9%) stayed for more than a week in the hospital. However, there was no difference in duration of stay between male 3.9 (95% CI:3.5-4.3) days and female 3.8 (95% CI:3.5-4.2) days with a p-value of 0.80. Data for chronic diseases and malnutrition were missing. See characteristics of Children with severe malaria admitted to Mchinji district hospital in the Table 3.1 below.

Table 3.1: Characteristics of Children with Severe Malaria

Characteristics	**Characteristic**	**Number (n/N)**	**Proportion (%)**
Gender	Males	106/198	53.5
	Females	92	46.5
Age Group	< 5 years old (3-60 months)	155/198	78.3
	>5 years old (61-144 months)	43	21.7
Referral Status	Health Centre Referral	54 /201	26.9
	Self-referral	147/201	73.1
Presenting Symptoms	Fever	177	88.1
	Convulsion	76	37.8%
	Unconsciousness	**6**	**3.0**
	Vomiting	58	28.9
	Diarrhoea, 32/201	21	10.4
	Difficult breathing	33	16.4
Treatment Given	Standard Malaria Treatment (SMRx)	51	25.4
	SMRx plus other Treatments	150	74.6
	Transfused with blood	40	20.3
Duration of Hospital Stay	1-3 days	102	50.8
	4-7 days	91	45.3
	8-14 days	8	3.9

3.4 OUTCOMES OF CHILDREN WITH SEVERE MALARIA

The outcomes of the children with severe malaria are shown in Table 3.2. In this study 86.6% of the children were discharged alive, 7.5% died, 3.5% were further referred to tertiary hospital and 2.5% absconded from hospital. Out of the 15 children that died, 6 (40%) were females and 9 (60%) were males of which 11 of those that died were children under the age of five and 4 were over the age of five. Out of the children that were referred from health centres 9 (16.7%) died and 6 (4.1%) of the self-referred patients died.

Table 3.2: Outcomes of Children with Severe Malaria

Characteristic (N)	**Outcome**				**P-Value**
	Alive	**Died**	**Referr**	**Abs**	
Female (92)	81 (88.0)	6 (6.5)	4 (4.4)	1 (1.0)	P=0.002
Male (106)	91 (85.8)	9 (8.9)	3 (2.9)	3 (2.9)	
Age group <5 (155) >5 (43)	 140(90.3) 32 (74.4)	 11 (7.1) 4 (9.3)	 1 (0.6) 6 (14.0)	 3 (1.9) 1 (2.3)	**P=0.001**
Self Referral (147)	132 (89.8)	6 (4.1)	4 (2.8)	5 (3.4)	P=0.012
HC Referral (54)	42 (77.7)	9 (16.7)	3 (9.3)	0 (0.0)	P=0.007
SMA (Hb =/<5.0 (29)	27 (93.1)	2 (6.9)	0 (0.)	0 (0.)	0.469
Std Rx (51)	49 (96.1)	2 (3.9)	0 (0.0)	1 (2.0)	0.417
Plus Other Rx (150)	137 (91.3)	13 (8.7)	0 (0.0)	0 (0.0)	0.364
Transfused (40)	39 (97.5)	1 (2.5)	0 (0.0)	0 (0.0)	0.312
Hospital days					
<4 days (102)	86 (84.3)	11 (10.8)	3 (2.9)	2 (2.0)	P=0.141
4 – 7 days (91)	82 (90.1)	2 (2.2)	4 (4.4)	3 (3.3)	
>7 days (8)	6 (75.0)	2 (25.0)	0 (0.0)	0 (0.0)	

3.5 FACTORS ASSOCIATED WITH OUTCOMES IN CHILDREN WITH SEVERE MALARIA AT MCHINJI DISTRICT HOSPITAL

The results of the analysis are shown in Table 3.3. In the univariate analysis, being referred from health centre, unconsciousness and duration of stay in hospital were associated with either dead or alive in children admitted with severe malaria. Receiving LA and paracetamol were associated with less chances of mortality. However, Gender, age, fever, convulsions, vomiting, diarrhoea, feeding problem, cough, difficult breathing, temperature, dehydration, blood transfusion and treatment options were not statistically significant.

In univarieate analysis, children referred from health centres were more than four times likely to die when compared to the self-referral group, OR: 4.84 (CI:1.63-14.35, p=0.004). Children who were reported unconscious were sixteen times likely to die than those who were not, with the OR 16.00 (CI 1.22-210.59, p=0.035) despite that the observed numbers were small and the wide confidence level. Children who stayed in hospital for 8 to 14 days were 2.76 times more susceptible to die when compared to those who stay for 1 to 3 days only, though not statistically significant (CI:0.47-15.37, p=0.247) as the numbers analysed are small. Children that stayed in hospital for 4 to 7 days were less likely to die when compared to children that stayed for a shorter duration of stay in hospital of 1 to 3 days. From both the univariable and multivariable models the reported OR suggest that the odds of dying is lower for 4-7 days compared to 1-3 days stay in hospital and higher for 8 days plus compared to 1-3 days. This suggests a U-shape of odds on risk of death, which may needs futher exploration and explaination.
In multivariate analysis children referred from health centres were eleven times more likely (OR:11.07, CI:1.16-105.79, p=0.037) to die than those who were self-referrals despite the small numbers analysed resulting in the wide confidence levels. Lumefantrine/Artemether (LA) administration maintained its protection to the children (OR:0.01, CI:0.01-0.08, p<0.001) in multivariate analysis.

Table 3.3: Factors Associated with Outcomes for Children with Severe Malaria

	Characteristic	**uOR (95% CI)**	**p-Value**	**aOR (95% CI)**	**p-Value**
Gender	Female	**1**		**1**	
	Male	1.40 (0.48-4.10)	0.537	0.68 (0.11-4.41)	0.687
Age Interval	3-60 months	**1**		**1**	
	61-144 months	1.33 (0.40-4.41)	0.638	1.02 (0.24-4.27)	0.975
Referral Status	Self-Referral	**1**		**1**	
	HC referral	**4.84 (1.63-14.35)**	**0.004**	**11.07 (1.16-105.79)**	**0.037**
Hospital Stay	1-3 days	**1**		**1**	
	4-7 days	**0.19 (0.04-0.86)**	**0.032**	**0.31 (0.04-2.38)**	**0.263**
	8-14 days	2.76 (0.49-15.37)	0.247	10.22 (0.85-123.33)	0.067
Treatment Options	Std malaria treatment	**1**			
	other treatment	2.32 (0.51-10.67)	0.278		

*uOR= Unadjusted Odds Ratio. aOR= Adjusted Odds Ratio

CHAPTER FOUR: Discussion

This chapter gives overview of the study findings. A detailed outline of the outcomes and the predictors of outcomes is then provided and explained. The outcomes in the study were: discharged home alive, death and unknown. The unknown outcomes were of those that were further referred to tertiary hospital and those children that absconded from the district hospital. The following factors were found to predict outcomes for the children with severe malaria: referral from health centre, duration of hospital stay, state of unconsciousness and being treated with LA. This chapter also goes on to discuss the limitations, conclusion and recommendations of the study.

4.1 OUTCOMES FOR CHILDREN WITH SEVERE MALARIA.

4.1.1 Discharged Alive

In this study the majority of the children (86.6%) were discharged alive and almost all of them stayed in the hospital for less than a week. This is similar to a study done in India that found 89% of the children with severe malaria being discharge alive after severe malaria treatment (53). This is not surprising because malaria is curable with prompt and proper antimalarial treatment and management of complications. All the children were treated according to the National Malaria Control Program treatment guidelines with almost three quarters receiving antibiotics on top of the malaria treatment. In Malawi severe malaria is treated with parenteral quinine and artesunate followed by oral LA for three days as soon as the patient is able to swallow and may be discharged. This is consistent with studies done to compare quinine and artesunate done in Africa and Asia (56). The majority of severe malaria patients treated with quinine or Artesunate are usually discharged from hospital after 4 to 8 days of treatment (56). The WHO and National Malaria treatment guidelines recommends that children with severe malaria should also be treated with antibiotics to cover for other infections associated with severe malaria when suspected. Studies have shown that severe malaria in children is associated with invasive bacterial infections and it is recommended to give antibiotic together with antimalaria treatment (57). This implies the majority of children may be coming to hospital with manageable complication and that the malaria treatment being given to the children may be effective enough to cure malaria and the recommended treatment protocols need to be encouraged and adhered to while monitoring for resistance.

4.1.2 Mortality

The study found that 7.5% of the children with severe malaria died in hospital while on treatment and the majority (73.3%) of those that died were children under the age of five years. This finding may not be surprising again because literature has recorded that in areas of endemic malaria, like Mchinji in Malawi, children under the age of five years are the most susceptible to severe malaria and death. The condition represents the severity of the disease which develops when treatment is delayed. Severe malaria patients die when they are not treated and when the extent of vital organ dysfunction is high. Children with severe malaria have high chances of dying within the first 2 days of admission regardless of treatment (56). In this study the majority (73.3%) of the children that died stayed in hospital for less than 4 days which is correlates with others studies. It may therefore, suggests delay in receiving effective treatment for uncomplicated malaria in the children and care may have been sort late. It has been reported in some studies that medical care is sort when the cases are very severe and near fatal (54,55). The case fatality rate in this study is consistent with previous studies of children with severe malaria done in Gabon, Kenya and Yemen that have reported case fatality rates varying from 1- 25% (58).

In this study it was further found that more than half (60%) of the children that died were referral cases from the health centres and had a case fatality rate of 16.7% compared to 4.1% for the self referrals. This suggests that children being referred form from the health centres were more sick with more complications than those that were not referred. Malaria in children progresses quickly to severe disease increasing the susceptibility for the children to die. Further delay to access treatment increases the risk. It is therefore essential to ensure quick interventions in children with severe malaria and that health facilities are well equipped or resourced to enable them to take care of children with severe malaria

4.1.3 Further referral and absconding

In our study some children (3.5%) were further referred to tertiary hospital probably for further supportive treatments like ventilation, dialysis and heamodynamic support or surgical interventions which require intensive care unit services not available in district hospitals in Malawi. However, the reasons for referral were missing. and the final outcomes of those referred to tertiary hospital were unknown. This suggests poor communication between Mchinji district hospital and the tertiary hospital where the children were referred to resulting

in no follow up and feedback between hospitals. A study done in Iran found that poor linkages in a patient referral system in three tier health care system in most places result in loss of information on referred patients (59). It was further found that 2% of the children absconded from hospital. While it is difficult to explain the reasons for absconding, it can be speculated that it is because of poor understanding of the children's condition by the guardians to tolerate treatment and hospital environment due to low literacy levels and cultural beliefs. Also guardians may not have been satisfied with quality of care and absconded to try other services elsewhere like traditional medicines. However, there is very little or no accurate evidence available in literature on patients who abscond from hospital (60)

4.2 PREDICTORS OF OUTCOMES FOR CHILDREN WITH SEVERE MALARIA

4.2.1 Referral from Primary Health Centre

In this study being referred from primary health centre was found to be an independent predictor of outcomes for children admitted with severe malaria. It was found that 60% of the children that died were referral cases from the health centres and had a case fatality rate of 16.7% compared to 4.1% for the self referrals. Children referred from health centres were more than eleven times likely to die in the hospital when compared to the self referral group. This is similar to findings by a study in Zomba, Malawi (46). Children being referred from the health centre to the district hospital may have been experiencing delays emerging from the health centres and community. These issues may be lack of resources and inefficiencies at the facilities due to lack of human resources (Clinicians and nurses), lack of essential medicines and equipments, and lack of availability of ambulances for transporting patients to the district hospital causing delay to prompt and effective treatment for children with severe malaria. Other studies have shown that children may also be presented at the health centre in already critically sick condition due to late presentation from home as a result of poor health seeking behaviour, cultural beliefs (61,62), poor access to health care, high costs of care including transport costs (63). Delays to treat children with severe malaria allows disease progression to further severe complications and deaths (64,65,66,67,68). Barriers to health care services promote malaria progression of diseases to very severe conditions increasing chances of death in children with severe malaria. Fever in malaria endemic places has been

used as a proxy for diagnosis of malaria presumptively (69). This means there is need to promote prompt treatment of fevers in children in Mchinji district.

Mchinji is a rural district in Malawi and has an average health centre catchment population of 33,137 with an average distance of 34Km from the primary health facilities to the district hospital with very poor road network and infrastructure (70). Rural health centres have challenges to deliver quality health services. It has been reported that often rural health facilities are challenged with inadequate human resources, stock-out of essential and effective drugs, lack of essential equipment and lack of quick access to ambulance support when needed (58,68,71,72,73,74,75). Such factors compound the problem of poor quality health care service delivery especially to those that are critically ill like children with severe malaria. Therefore, children with severe malaria and referred from the health centres may have severe complications due to delays in the health system and have high risk of dying in the district hospital. There is need to look into health systems strengthening for malaria control interventions both at community and health facility levels to prevent development of severe malaria and deaths in children. The Integrated management of childhood illnesses (IMCI) strategies in the district needs to be improved and strengthened to prevent childhood illnesses and deaths especially due to malaria. The IMCI promotes early identification of children with fever.....

4.2.2 Duration of hospital stay

The results of the study showed that the occurrence of deaths of children may take a U-shape, with more deaths occurring in the first days and longer days in hospital. Out of the fifteen children that died, eleven died within three days of hospital stay. Those children that stayed in the hospital for more than seven days were about three times more likely to die in the hospital compared to those that spent less than a week in hospital admission. Long hospital stay increases children's chances of catching hospital acquired infections (76) bringing severe complications and deaths in children with severe malaria. Severe malaria already poses bacterial infection risk in children. Hospital acquired infections are one of the leading cause of death in hospitalized patients and have a vicious cycle. The hospital acquired infections prolong hospital stay and prolonged hospital stay predisposes hospitalized patients to more hospital acquired infections creating a vicious cycle. These infections are difficult to treat due to resistances and have high case fatality rates (77). In this study most of the children were treated with antibiotics, 13 out of the 15 children who died were treated with antibiotics covering for bacterial infections which would be hospital-acquired. However, review by Jane

Crawley and colleagues noted that antibiotics treatment in children with severe malaria has less impact on reducing the current death rates for severe malaria children with other life threatening infections (78).

4.2.3 Unconscious state

State of unconsciousness on admission had high odds of dying. Children who were unconscious were 16 times more likely to die compared to those who were fully conscious on admission. There was a case fatality rate of 50% among children who presented on admission with unconscious state. Unconsciousness is one of the danger sign in sick children and may result from failure of multiple organs or physiological systems. Unconscious patients may have a collapsed airway, low blood sugars or electrolyte imbalances or brain damage making them critically sick. They may therefore, require resuscitation and intensive care services which are lacking at the health centres and district hospital in Malawi. This increases the chances of dying in children with severe malaria. Previous studies have reported unconsciousness (prostration or coma), convulsions, respiratory distress, severe anaemia as important clinical features related to outcomes of severe malaria in children (45,46,52,79). Therefore children with severe malaria presenting with unconsciousness must be given priority and maximum clinical care to ensure survival. Health system needs to be well equipped or resourced and coordinated to provide for proper care of unconscious children with severe malaria.

4.2.4 Treatment with Lumefantrine and Artemether (LA)

The study found that those children that were treated with LA were less likely to die in hospital. LA is treatment for uncomplicated malaria according to the Malawi National Malaria Control Program Treatment guidelines. In this study LA was given to children that had already improved and were out of clinical danger. It is therefore not surprising that use of LA predicated low chances of dying in children with severe malaria. However, this is encouraging as it implies effectiveness of treatment malaria in children that were given LA and it needs to be encouraged.

4.3 STUDY LIMITATIONS

Missing and incomplete medical records were a major short coming of this study. There were inconsistencies in the data being collected by different clinicians in the absence of standard prescribed admission forms and discharge notes. Factors such conscious levels, vital signs,

laboratory test results for classification and confirmation of other diagnoses other than malaria, socioeconomic and demographic data on the parent or guardian of the child were difficult to find or completely unavailable. The study was restricted only on hospital collected data, missing outcomes beyond the hospital for those that were referred and those that absconded resuting in small numbers of cases studied limiting the multivariate analysis. The study could not look into other predictors of outcomes of severe malaria associated with the home environment.

CHAPTER FIVE: CONCLUSION AND RECOMMANDATIONS

5. CONCLUSIONS AND RECOMMENDATIONS

Admission of children with severe malaria in Mchinji district suggests that there is still need to improve access to early diagnosis and treatment of malaria in the district. There is need to maintaining a high index of suspicion for severe malaria at all level. The intervention to prevent malaria related mortality remains early detection, treatment and referral where necessary to minimize complications and deaths. Delays in accessing proper treatment for uncomplicated malaria cases, incorrect diagnosis or treating children with ineffective treatments need to be minimized. This study demonstrated that the outcomes of children with severe malaria are not only related to clinical characteristics of the patients. They are also related to health system factors like, being referred from a primary health facility, long stay in hospital and being treated with LA during the course of treatment. These factors influence severity of complications in children with severe malaria. Therefore, the health system needs to be appropriately resourced to take care of severe malaria cases. There is need to investigate and address gaps in access and provision of prompt malaria treatment at community and health facility levels to minimise delays in management of children with malaria, specifically in the referral system and health seeking behaviour among the communities of Mchinji district.

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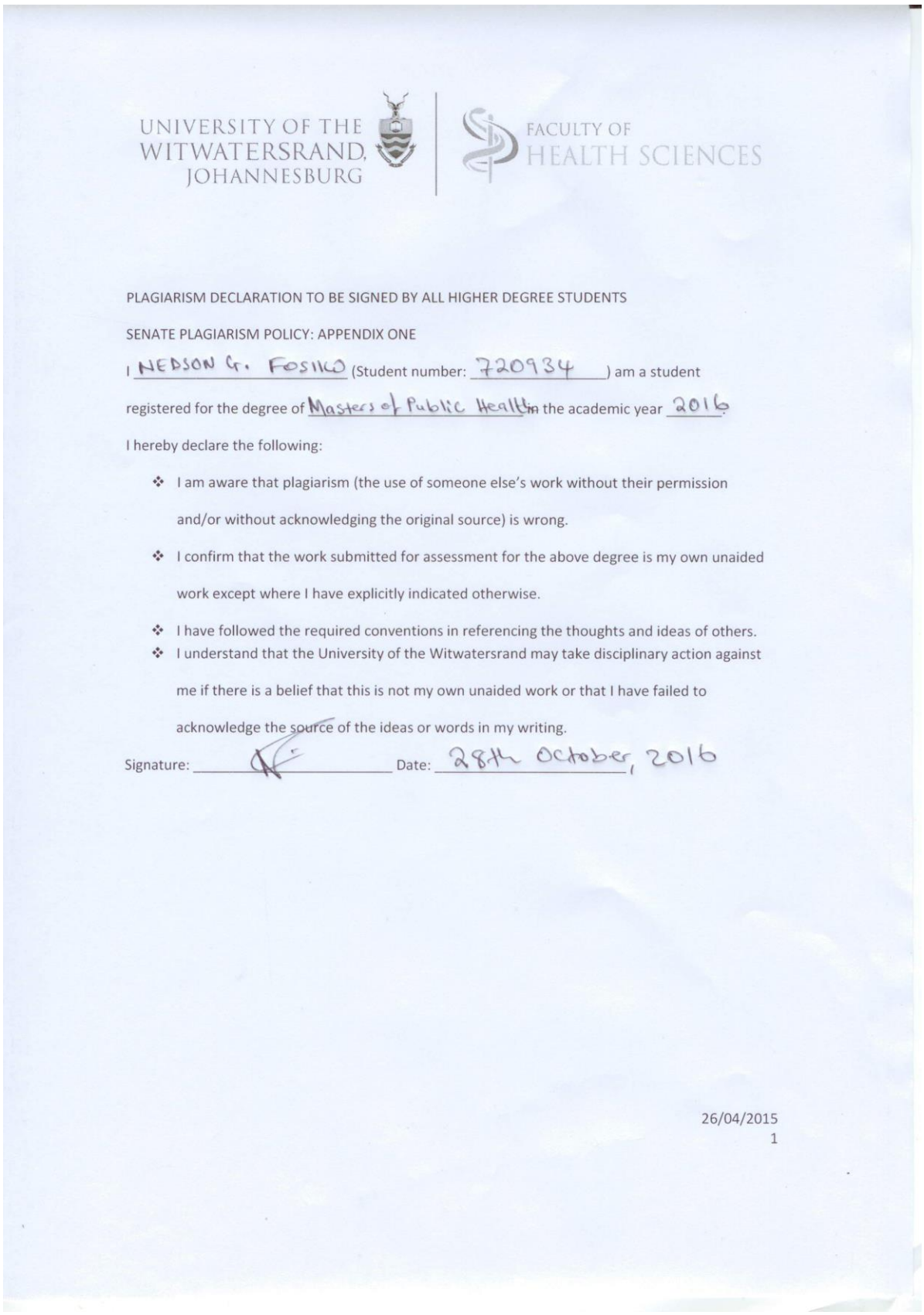
APPENDIX 1

- **PLAGIARISM DECLARATION REPORT**



UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG | FACULTY OF HEALTH SCIENCES

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I NEDSON G. FOSIKO (Student number: 720934) am a student registered for the degree of Masters of Public Health in the academic year 2016.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.

Signature: _____ Date: 28th October, 2016

26/04/2015
1

APPENDIX 2

- **HUMAN RESEARCH ETHICS CLEARANCE CERTIFICATE**

R14/49 Dr Nedson G Fosiko

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M150637

NAME: (Principal Investigator)	Dr Nedson G Fosiko
DEPARTMENT:	School of Public Health Mchinji District Hospital, Malawi
PROJECT TITLE:	Predictors of Outcomes of Severe Childhood Malaria Cases Admitted at MChinji District Hospital in Malawi
DATE CONSIDERED:	26/06/2015
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Aziza Mwisongo
APPROVED BY:	Professor P Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	29/06/2015

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDX 3

Telephone: 01 242 906
Fax : 01 242 262/235
e-mail : mchinjimoh@dho.com

All correspondences should be addressed to
The District Health Officer

In reply please quote Ref. No.
Ministry Of Health
Mchinji District Hospital
P.O. BOX 36
Mchinji
MALAWI.

26th February, 2015

Dear Dr. Nedson Fosiko,

PERMISSION TO CONDUCT A STUDY: PREDICTORS OF MORTALITY OF SEVERE CHILDHOOD MALARIA AT MCHINJI DISTRICT HOSPITAL.

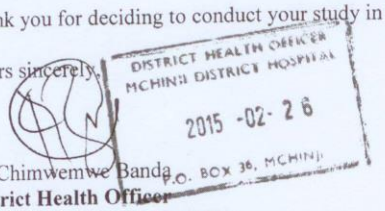
I have the pleasure to inform you that the district hospital management team has agreed that you conduct your study Predictors of Mortality of the severe Childhood Malaria at Mchinji District Hospital, Malawi using the patients' ward files for the children admitted to the hospital with severe malaria. This is upon approval by the Malawi research regulatory bodies.

The hospital management supports the study as it has benefits for the hospital as it will lead into improving the delivery of hospital services to the children admitted with malaria and also reduce mortality of the children admitted to our wards as close to 50% of the deaths on the children's ward are due to malaria and management would like to find means and ways of reducing these deaths. hence the relevance of your study to the hospital.

The hospital will ensure availability of the files for you to use in for the study and support with any other support that we can to ensure the success of the study.

Thank you for deciding to conduct your study in Mchinji and at Mchinji district hospital

Yours sincerely,



Dr. Chimwemwe Banda
District Health Officer
Mchinji District Health Office

APPENDIX 4

- **DATA COLLECTION FORM**

PREDICTORS OF OUTCOMES FOR SEVERE CHILDHOOD MALARIA CASES ADMITTED AT MCHINJI DISTRICT HOSPITAL IN MALAWI

Data Extraction Sheet (fill in accordingly)

Name of Data Collector		Date of data collection			Date of admission	
					Date of Discharge	
Patient Demographics						
Identity						
Village/ Town	Age	Gender	Weight	MUAC	Brought by	
Referred from						
Home	School	Health Centre	Rural Hospital	Other (Specify)		
Reason for referral						
Date, Day of the week and time						
Admission						
Discharge						
Duration of admission						
Outcome of admission						
Alive		Dead		Unknown	Other	
Presenting Complaint and duration on admission						
Fever	Convulsions	Unconsciousness	Vomiting	Not eating	Unable to sit	Shortness of breath
Cough	Not passing urine	Other				
Physical Examination						
Temperature	PR	RR	BP	Comma Scale/ Dehydration	Spontaneous Bleeding	Splenomegaly	Parasitaemia	Haemoglobin
Blood sugar								
Diarrhoea	Vomiting							
Diagnosis on admission								
Other Diagnosis (chronic heart disease, HIV disease, malnutrition, diabetes, etc						
Treatment given						

APPENDIX 5

- **WHO CRITERIA FOR SEVERE MALARIA**

One or more of the following clinical or laboratory features
Clinical Manifestations ▪ Prostration ▪ Impaired consciousness ▪ Respiratory distress (acidotic breathing) ▪ Multiple convulsions ▪ Circulatory collapse ▪ Pulmonary edema (radiological) ▪ Abnormal bleeding ▪ Jaundice ▪ Hemoglobinuria
Laboratory Test ▪ Severe anemia ▪ Hypoglycemia ▪ Acidosis ▪ Renal impairment ▪ Hyperlactatemia ▪ Hyperparasitemia

Taken from *WHO Guidelines for the Treatment of Malaria*. (WHO, Geneva Switzerland: 2006).

APPENDIX 6

- **WHO GUIDELINES FOR THE TREATMENT OF SEVERE MALARIA**

Summary of recommendations on the treatment of severe malaria
Severe malaria is a medical emergency. After rapid clinical assessment and confirmation of the diagnosis, full doses of parenteral antimalarial treatment should be started without delay with whichever effective antimalarial is first available.
Artesunate 2.4 mg/kg body weight (bw) i.v. or i.m. given on admission (time 3 0), then at 12 h and 24 h, then once a day is the recommended choice in low-transmission areas or outside malaria-endemic areas.
For children in high-transmission areas, the following antimalarial medicines are recommended as there is insufficient evidence to recommend any of these antimalarial medicines over another for severe malaria: ▪ Artesunate 2.4 mg/kg bw i.v. or i.m. given on admission (time 3 0), then at 12 h and 24 h, then once a day; ▪ Artemether 3.2 mg/kg bw i.m. given on admission then 1.6 mg/kg bw per day; ▪ Quinine 20 mg salt/kg bw on admission (i.v. infusion or divided i.m. injection), then 10 mg/kg bw every 8 h; infusion rate should not exceed 5 mg salt/kg bw per hour.
▪ Artesunate or artemisinin by rectal administration
▪ Artesunate or artemether i.m.
▪ Quinine i.m.
Use the parenteral antimalarial treatment locally available for severe malaria in full doses. Where available, AS is the first and artemether the second option in the second and third trimesters. In the first trimester, until more evidence becomes available, both artesunate and quinine may be considered as options.

Levels of evidence:

S - Formal systematic reviews, such as a Cochrane Review, including more than one randomized controlled trial;

T - Comparative trials without formal systematic review;

O - Observational studies (e.g., surveillance or pharmacological data);

E - Expert opinion/consensus.