CHAPTER ONE: INTRODUCTION

1.0 Background

It is estimated that 3.3 billion people were at risk of malaria in 2011, and people living in sub Saharan Africa at greatest risk. 80% of malaria cases and 90% of deaths occurred in sub Saharan Africa. The most severely affected were pregnant women and children under five years of age, (World Malaria Report 2012). Malaria is caused by a parasite called Plasmodium, which is transmitted via the bite of infected female anophelene mosquitoes. There are four parasite species that are known to cause Malaria in humans*: P. ovale, P. vivax, P.malariae* and *P.falciparum.* The most virulent of these, is the *P.falciparum* that accounts for 95% infections in Zambia. *P.malariae* accounts for about 3% of infections and *P.ovale* about 2%, whereas *P.vivax* infections are very rare (WHO 2012). In the past 10 years, tremendous progress has been recorded in the control of malaria. According to the WHO report of 2012, in Sub Saharan Africa the percentage of households owning at least one insecticide treated net (ITN) rose from 3% in 2000 to 53% in 2011 and remained at that in 2012. The coverage of indoor residual spraying (IRS) rose from 5% in 2005 to 11% in 2010. This was representative for the African region. Further, the procurement of rapid diagnostic tests (RDTs) and arteminisin-based combination therapies (ACTs) increased to 77% in 2011 from 68% in 2005. This resulted in the global decrease of Malaria mortality by about 25% between the periods 2000 to 2010. Despite the mortality decline recorded, Malaria transmission still occurs.

In Zambia, malaria epidemiology can be stratified into three categories; firstly, areas where malaria control activities has reduced transmission and parasite prevalence to less than 1%. Then second category represents areas where there is sustained malaria prevention and transmission and parasite prevalence is at or under 10%. This represents areas such as Central, Southern and Western Provinces. The last category represents areas where there has been recorded progress in malaria control and has been attained, but is not yet sustained and lapses in prevention coverage have led to the resurgence of malaria in children. This exceeds 20% at the peak of the transmission season and includes Eastern and Luapula provinces, (MoH 2010)

In African children complicated malaria manifests in two major ways, severe malarial anaemia (SMA) and cerebral malaria, (Brewester 1990). SMA is a severe complication that is as a result of infection with plasmodium falciparum. It is a major cause of morbidity and mortality in young Zambian children, (Biemba 2000). The mechanisms that lead to the development of severe

malarial anaemia, (SMA) remain unclear (Abdalla 1990), but the major causes are thought to be red cell destruction by the parasite or the hosts immune system.

1.1 Malaria Epidemiology

The mortality rate due to malaria has decreased by well over 25% worldwide for the period 2000 to 2010. This was due to the combined international effort to combat malaria. Africa, the greatest hit region recorded a 33% decline for the same period. The annual number of global deaths due to malaria further decreased from 810,000 to 660,000. However the transmission of malaria still continues. The Sub-Saharan African region was worst affected with 90% of deaths recorded, mainly for children under the age of 5 years, (World Malaria Report 2012).

1.2 Malaria Parasitology

In Africa, and Zambia included as well, most Malaria infections are due to *P. falciparum*. Differential species refer to the plasmodium infections other than *P. falciparum*, which are *P. ovale, P. vivax* and *P. malariae*. Studies have revealed the possible infection of humans with a fifth plasmodium parasite, Knowlesi that was previously known to only infect monkeys, (Chaturong 2008).

The prevalence of other plasmodium species is unknown or poorly recorded, in eastern and southern Africa, *P. vivax* represents around 10% of malaria infections, (Mendis 2001).

For Zambia, it is not known or not documented, the contribution of the other plasmodium species to malaria infections.

1.3 Severe Malaria in Zambia

Malaria is endemic in Zambia and the most affected are those in rural areas. Most of the disease is caused by *P. falciparum* and is transmitted by *Anopheles gambiae* (*An. gambiae*) complex and *Anopheles funestus* (*An. funestus*). Malaria transmission follows the rainfall season, transmission begins around September to November when the rain starts and peak malaria transmission occurs around May, June once the rain has stopped, (Masaninga 2012).

Malaria accounts for 40% of infant mortality deaths that are recorded in Zambia, (Rollback Malaria Report 2011). The current infant mortality rate is at 70 per 1,000 live births and 119/1000 live births for under five children. Furthermore, 15–20% of deaths in children under five years of age are due to Malaria, (WHO 2001). Malaria transmission is generally lower in urban compared to rural areas. This may be due to better health facilities that are easily accessible and lower vector

density and improved drainage in urban areas. Anemia due to *P. falciparum* infection remains a major health problem in endemic areas for young children and pregnant women.

Severe malarial anaemia remains a great burden for Zambia. Study done in Lunagwa district, a high malaria transmission area show that in areas of near universal coverage of ITNs it is expected that the association of severe anaemia in children with malaria parasite infection to decrease. This reveals that chronic malaria parasite infections remains a significant risk factor for severe anemia in children 6-59months, (Eisele 2011).

In another study done at Macha Mission Hospital, an area endemic for malaria, SMA was found in 9.7% of all pediatric patients for a period if three years. SMA accounted for 10.7% of pediatric deaths, (Biemba 2000). The studies suggest that children with SMA tend to have chronic malaria infection as suggest by (Abdalla 1980).

Malaria Intervention Programs

In 2007, the World Health Assembly passed a resolution targeted at the 75% reduction of Malaria by 2015. In order for Zambia to achieve the target, intervention programs were designed. Malaria in Zambia is increasingly localized, community intervention programs were designed.. Integrated methods were introduced to control malaria. The methods included effective diagnosis and treatment policies, intermittent preventive therapy (IPTp) for pregnant women, vector control, communication sensitization and social mobilization and surveillance and evaluation, (MOH 2010). Between 2007 and 2010, 6 million ITNs were distributed. These were initially targeted at vulnerable groups i.e. pregnant woman, children under five, the aged and chronically ill persons. Indoor residual spraying (IRS) was increased from 5 to 54 districts. This was about one million households targeting about five million people. To increase diagnosis of Malaria, over two million rapid diagnostic tests (RDTS) were distributed annually between 2008 and 2010 to health centers and at community level. Community health workers were and are still trained in the diagnosis and treatment of Malaria. Information, education and communication activities using multiple channels have been conducted nationwide, (MIS 2012).

1.4 Plasmodium Lifecycle and Infection

Infection with malaria begins with the bite of an infected anopheles female mosquito injecting sporozoites into the bloodstream of the victim. The parasite undergoes three distinct stages, the asexual; exoerythrocytic and erythrocytic (blood) stages. The third stage is the sexual reproductive stage (sporogony), which occurs in the invertebrate (mosquito). When an anopheles mosquito bites an individual, the sporozoites invade and develop in the liver parenchymal cells (hepatocytes). In the hepatocytes, the parasite undergoes asexual replication to produce merozoites; this stage is called the exoerythrocytic schizogony. When merozoites are released from infected hepatocytes, they invade the erythrocytes. They undergo a tropic stage and the trophozoite enlarge. Metabolism and ingestion of the host cytoplasm and the proteolysis of hemoglobin accompany this stage. When erythrocytes rupture, merozoites are released. Fevers associated with malaria are due to the rupture of the infected erythrocytes and repeated re-infection of erythrocytes. Infected erythrocytes may adhere to endothelial cells and sequester in vital organs such as lung, brain and the heart.

The parasite may undergo sexual forms transformation, called the macro or microgametocytes. The gametocytes form in the erythrocytes but only have one nucleus. When a mosquito ingests gametocytes, this triggers gametogenesis- the production of gametes, this is the stage that occurs in mosquitos. Microgametes will fertilize the macrogamete leading to a zygote. The zygote will develop into an ookinete. The ookinete then penetrates the gut epithelial cells and develops into an oocyst. The oocyst goes through multiple rounds of asexual reproduction, which results in the production of sporozoites. The sporozoites migrate and invade the salivary glands to complete the lifecycle, and cause infection when a human is bitten (adapted from Dr. Wiser's notes 2009).

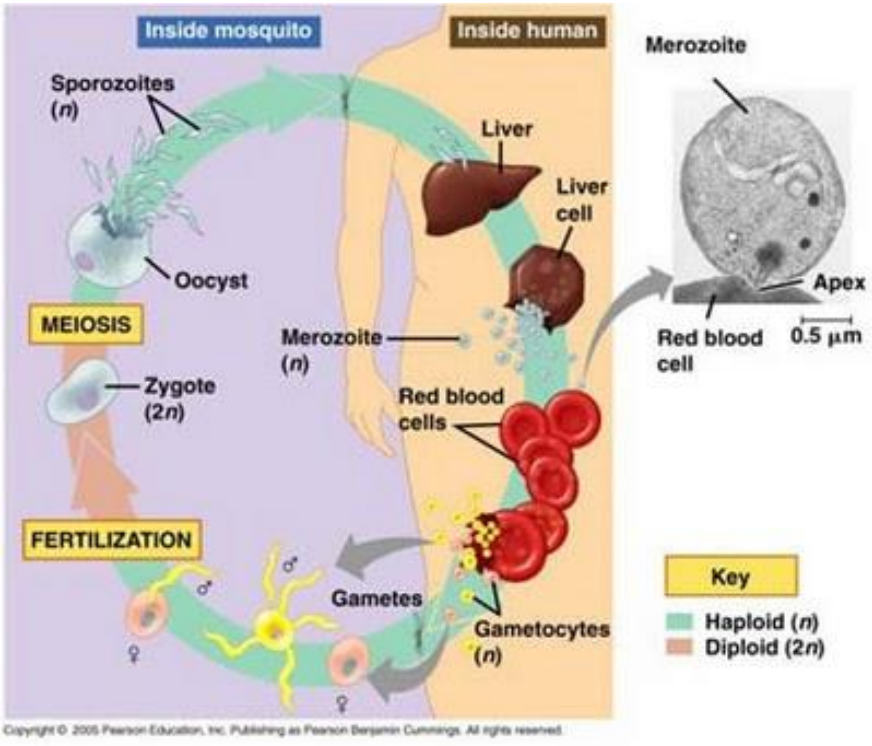

Fig. 1 -The life-cycle of *Plasmodium*
Source; Campbell *et al.* 2008

1.5 Severe Malarial Anemia

The handbook on the management of severe cases of malaria states that anemia is the leading cause of death in children infected with malaria. Most of the anemia in children under the age of five is caused by malaria. Generally, the more severe the infection with plasmodium the more profound the anemia. Severe anemia presents as a major public health concern for developing countries as it contributes up to 46% of inpatient paediatric fatalities in referral health facilities, (English cited in Perkins 2011). Studies that have been carried out in endemic areas of Africa show that 7.6 out of 1000 children are brought to hospital with severe malarial anemia. The case fatality rate for children between 0 and 4 years was 9.7%, (Reyburn 2005).

Pathophysiological processes (such as malnutrition and co-morbid infections) contribute to severe anaemia but the primary cause of SMA is the impaired and/or ineffective erythropoietic process. Hemolysis of red blood cells because of the presence of parasite will lead to low hemoglobin (Hb) levels in infant malaria. Parasite driven hemolysis results in the destruction of both parasitized and un-parasitized red blood cells. The impaired erythropoietic process results in loss of production of erythrocytes to replenish the depleted pool. This then results in the reduction of Hb, (Dormer 1983). Aside the hemolysis of red blood cells, impaired or ineffective erythropoietic process leads to SMA. Erythropoiesis is the process by which erythroid progenitors proliferate and differentiate into non-nucleated reticulocytes in the bone marrow. In an individual infected with plasmodium, this process is impaired/ ineffective which results in the reduction of the erythrocytes in circulation. The reduction in circulating erythrocytes results in lowered Hb leading to anaemia. The impaired erythropoiesis process in children with SMA is known to be caused by imbalance in the inflammatory mediators. As a way of controlling the parasitemia, the host releases pro and anti-inflammatory cytokines, chemokines and growth factors. In the event of unsuccessful control of parasitemia, damage to the host includes the suppression of the erythropoietic response. Observations show that persistent infection with childhood *P.falciparum* is associated with the suppression of the bone marrow. Table 1 below shows the physiological definition of anemia for children between 0-59months.

Table 1; Haemoglobin levels to diagnose anaemia at sea level (g/dl)*

Mild anemia	10-10.9 g/dl
Moderate	7.0-9.9 g/dl
Severe	0-7.0 g/dl

Adapted from reference Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity (Source: FAO & WHO 1992).

However, Malaria in under five children maybe co-morbid with other infections such as poor feeding leading to malnutrition as well as HIV infection, (Osterbauer 2012), this may prevent as a challenge in assessing Anemia thought to be caused by Malaria.

Risk Factors for Severe Malarial Anaemia

Host factors as well as other environmental and socio economic factors contribute to and determine the development of SMA. Reyburn (2005) showed that the peak age for severe malarial anemia was 1 for high transmission areas and 2-3 years for moderate to low transmission areas. Children remain at risk for infection with malaria because of their naïve immune system. SMA is not common or prevalent in children under the age of 1 year, this is because of elevated levels of fetal hemoglobin which is not favorable for parasite growth, (Falade 2007). Furthermore, infants that are breastfed are deficient in paraminobenzoic acid which the parasite thrives upon, (Giles 1957). Breastfeeding therefore has protective effects on infants.

SMA contributes 3-46% of in-patient pediatric fatalities in referral care facilities, (English 2004). The prevalence rates of anaemia in Zambia remain relatively high especially in the early years of childhood development (<5years). Results from a study done in Luangwa district, an area with stable *P.falciparum* transmission, showed that even with ITN coverage chronic malaria parasite remain as a risk factor for children between 6 and 59 months. Overall, the study results showed that 38.5% of children with severe anemia also had a malaria parasite infection, whereas 26.3% of children with a malaria parasite infection also had severe anemia. The results suggested that there was no difference in the prevalence of severe anemia in children who used an ITN and those that did not use. (Eisele 2001).

Socioeconomic status may play a role in the development of disease, and also the susceptibility to reinfection. In a study done in Gabon to assess the effect of socio economic factors, results revealed that socio economic factors had no significant influence on the severity of SMA. Socio economic status did not determine the time to first reinfection, (Luckner 1998).

Also, the degree of anaemia correlates with the severity of parasitemia, (Grobusch and Kremsner 2005).

Other risk factors for the development of SMA are parental education and type of accommodation. Anaemia was found to be significantly associated with the educational level of parents, the type of accommodation, health-seeking behavior and the child's nutritional status, (Kahigwa 2002).

Despite efforts to reduce anaemia and malaria infection, SMA remains a severe childhood burden for Sub Saharan Africa, (Brabin 2001).Anaemia if not carefully handled may lead to cognitive impairment and functioning, retarded growth and death. Severe Malarial Anemia presents as major public health concern for developing countries.

CHAPTER TWO: RESAERCH FOCUS

2.0 Statement of the Problem

The Malaria Indicator Survey (MIS) conducted in Zambia in 2012 found a national Malaria prevalence rate of 14.9% for children under the age of five; this was higher in rural areas compared to urban, with Luapula province recording the highest prevalence of 32.1%. The national prevalence rate of severe anaemia in 2012 was 6.8%, (MIS 2012). The anaemia prevalence was generally higher in provinces with higher parasitemia.

The prevalence rates of anaemia in Zambia remain relatively high especially in the early years of childhood development (<5years). Results from a study done in Luangwa district, suggested that there was no difference in the prevalence of severe anemia in children who used an ITN and those that did not use. (Eisele 2001).

Results of this study will provide greater clarity on the factors contributing to malaria associated anaemia, and the burden of malaria borne by under five children as well as estimate the societal cost of malarial anemia. Severe malaria is not only a threat to survival but also cognitive development as demonstrated by Fink 2013. Anaemia, if left untreated, has debilitating effects on children, especially early on in life. It may affect mental development and function which may lead to attention problems, delays in reading ability, poor school performance, and in very rare cases - stroke.

2.1 RATIONALE

In its aim to meet the Millennium Development Goal (MDGs) number 6 on Malaria, Zambia through the National Malaria Control Centre (NMCC) has allocated nearly $200 million into prevention and control programs. These programs include the distribution of Insecticide Treated Nets (ITNs), Indoor Residual Spraying (IRS), training of personnel in proper use of Rapid Diagnostic Tests (RDTs) and combination therapies. Unfortunately, a lot more needs to be done in complicated falciparum cases. Most cases of severe malarial anaemia may be comorbid with other infections making diagnosis difficult. This may lead to increased cases if morbidity and mortality in children under the age of five.

Results from this study will provide greater information and clarity on the factors associated with severe malarial anaemia and impact of malaria intervention strategies on the transmission of malaria.

Results will further identify which children under the age of five are most severely affected by severe malarial anaemia and will guide future intervention initiatives.

AIM & OBJECTIVES

2.2 Research Question

What are the factors associated with malarial-anemia and parasite density in Eastern, Luapula, Northern and Muchinga provinces?

General Objective

To investigate the prevalence of Anemia and its association with parasite density in under 5 year old children in communities with the highest parasitemia in Zambia.

Specific Objectives

1. To determine anemia prevalence in the four provinces,
2. To determine the socio demographic factors associated with malarial anemia in <5 year old children,
3. To determine the factors associated with malaria transmission in high parasitemia communities,
4. To assess the relationship between anemia, parasite density and fever,
5. To examine educational level of guardians and its association with anemia among children with malaria.

2.3 Conceptual Framework

A conceptual framework is a diagram or illustration that identifies the relationship between all relevant systems, components and any salient factors that may affect or influence an event or programme. To help understand an event or a disease a framework can be applied. Initially, conceptual frameworks were used in fertility studies.

In order to address the above objectives, the conceptual framework below adapted from Bongaart's model of the proximate determinants of fertility. It is expected that the progression of malaria to severe anemia is caused by host of interplaying factors.

Figure 1: Conceptual framework showing Proximate Determinants for Malaria

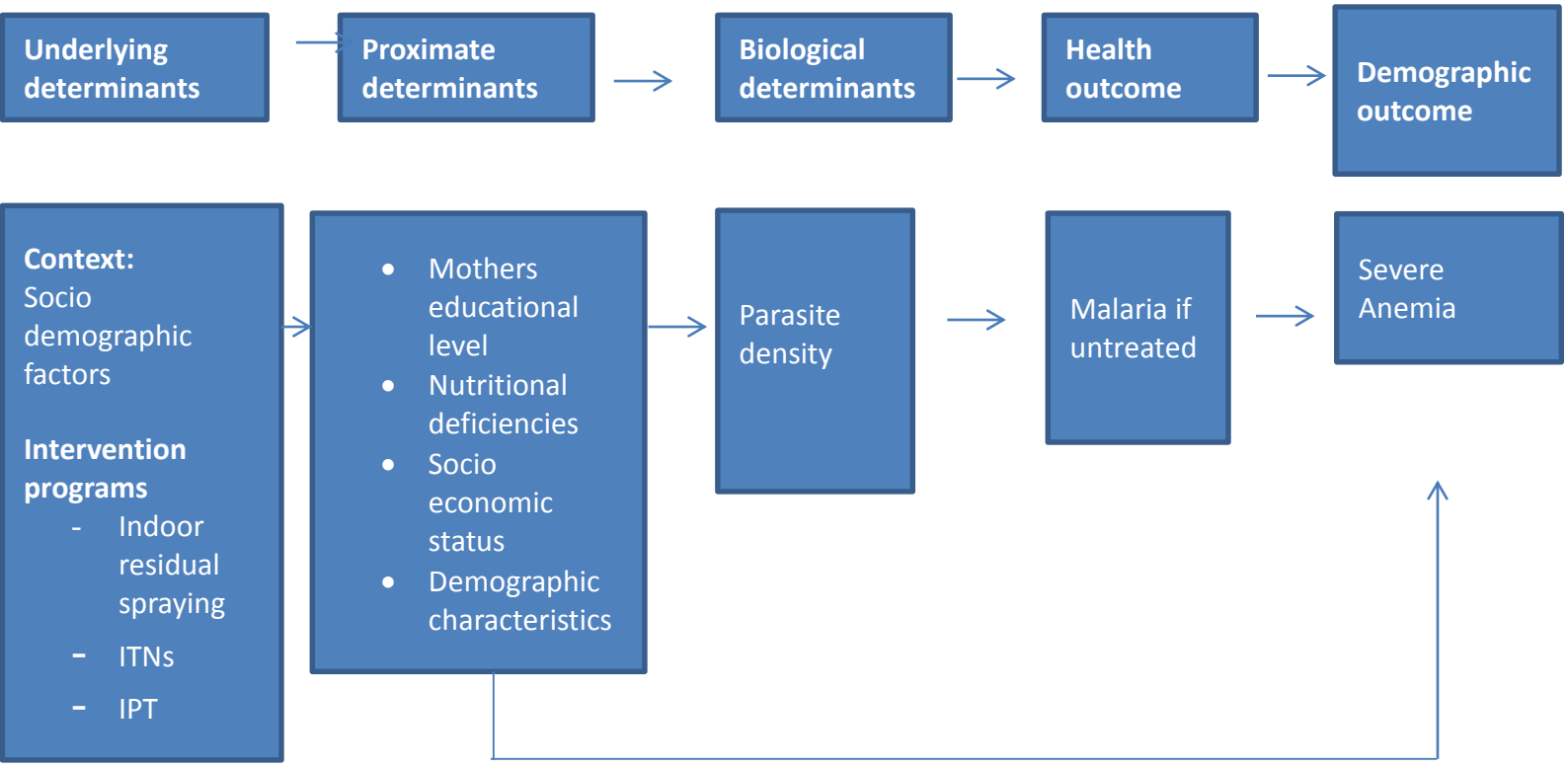

Figure 1 Conceptual Framework

CHAPTER THREE: Methods

3.1 Study setting and population

3.1.1 Study Setting

This study is based on data from the Malaria Indicator Survey (MIS) of 2012, a cross sectional nationally representative population based study. The survey covered household populations of Zambia with the aim of producing malaria estimates for the whole country, which included both urban and rural populations.

3.1.2 Study design

This research was secondary data analysis based a population based survey.

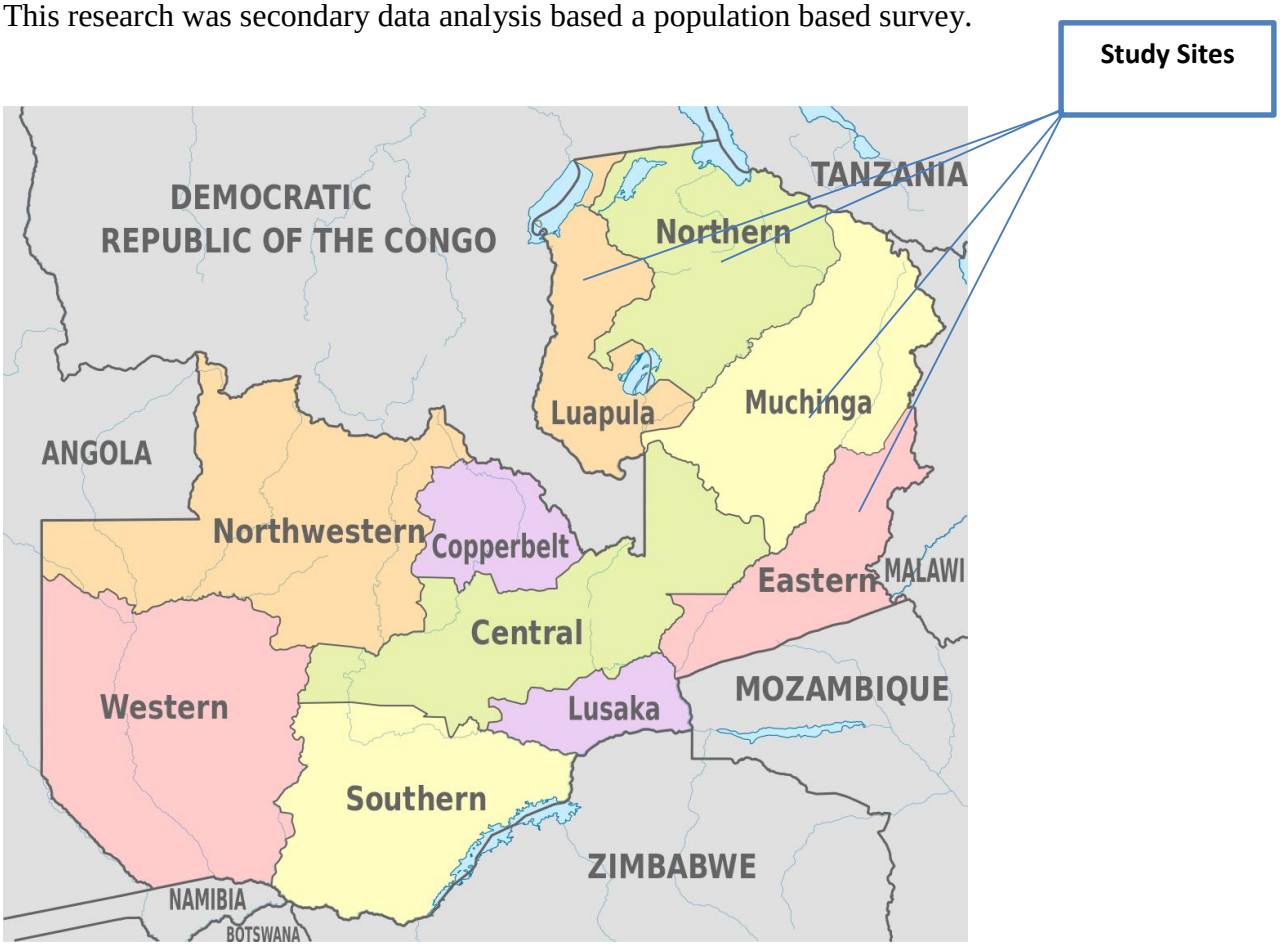

Figure 2; map of Zambia

Malaria Indicator Survey

The design for the survey was a representative probability sample. Zambia is administratively divided into 10 provinces which are sub-divided into districts. Each district is subdivided into constituencies and wards. For the survey, each ward was further divided into Census Supervisory Areas (CSAs) which were subdivided into Standard Enumeration Areas (SEAs).

The objective of the MIS of 2012 was to assess progress made towards achieving objectives set in the National Malaria Strategic Plan, 2006–2010. The survey further had the following specific objectives; firstly, to collect up-to-date information building on the experience of the MIS 2006, 2008 and 2012, on coverage of the core malaria interventions included in the NMSP 2006–2010. To assess malaria parasite prevalence among children under age five years, as well as to assess the status of Anaemia among the target populations (children ages 6 to 36 months). Further objectives were to assess disparities in malaria intervention coverage, and malaria parasite and Anaemia prevalence among the surveyed population by location and other background characteristics. Fifthly, to implement standardized, representative household survey methods, as well as to strengthen the capacity of the National Malaria Control Centre and local agencies involved in order to facilitate the implementation of surveys of this type in the future.

Two questionnaires were used in the Zambia MIS 2012: the household questionnaire and the women's questionnaire. The content of each was based on model questionnaires developed by the MEASURE Demographic Health Survey + programme and adopted and recommended for use by the Roll Back Malaria Monitoring Evaluation Reference Group Task Force on Household Surveys. The questionnaires had information on age, sex, education. The household questionnaire was used to identify women who were eligible to answer the individual questionnaire. Information on the wealth quintiles was based on data collected in the household questionnaire. Questions concerning the household's ownership of a number of items such as a television, bicycle and car; dwelling characteristics such as flooring material; type of drinking water source; toilet facilities; and other characteristics that are related to wealth status. Ownership of these assets were assigned a weight or factor score generated through principal components analysis. The resulting scores are standardized in relation to a standard normal distribution with a mean of zero and a standard deviation of one. These standardized scores were then used to create the break points that define wealth quintiles as: lowest, second, middle, fourth and highest.

The women's questionnaire was used to collect information from all women aged 15 to 49 years on background characteristics such as education level and economic status, reproductive and birth history, pregnancy status and knowledge on Malaria.

Anaemia Survey

A cross sectional survey was carried from four provinces (Luapula, Northern, Muchinga and Eastern). All samples from the four provinces were eligible provided they met the inclusion criteria. The data that was collected from the four provinces, Eastern, Muchinga, Northern and Luapula provinces that had anaemia readings was analyzed. The four provinces will be purposively sampled as these recorded the highest Malaria and highest Anaemia prevalence, the parameters of interest. Table 1 shows the variables that were measured.

2.8 Definition of Severe Anemia

For this study, severe anemia was defined as an Hb reading of <8g/dl. Severe malarial anaemia was defined as an Hb concentration of <8.0g/dl with a positive malaria slide.

Table 1; Operational Variable framework

Variable	Indicator	Measurement Scale
Dependent Variable		
Not Anaemic Severe Anaemia	Hb	Nominal
Independent Variables		
Socio Demographic Characteristics Residence Province Socio economic status	Residence	Nominal
Socio Demographic Of Mother; Age Educational Level	Age Never Primary Secondary Tertiary	Interval Ordinal
Parasite density	low moderate high	Ordinal
Fever	as recorded	Nominal
Intervention Programs: Any net (whether or not treated) ITN Indoor residual spraying,	yes/no	Nominal

Table 1: Operational Variable Framework

3.1.3 Sample Size for anaemia study

The confidence interval was set at 95%, the natonal prevalence of anaemia according to the MIS 2012 was 6.8%, and margin of error was set at 5%. The following formula was used to calculate the sample size.

$$\mathbf{n} = \frac{z^2 \times \mathbf{p(1-p)}}{\mathbf{m^2}}$$

n=required sample size
z = confidence level at 95% (standard value of 1.96)
p = estimated prevalence of Anaemia, which is 6.8%
m = margin of error at 5% (standard value of 0.05)

$n = [1.96^2 \times [0.068(1-0.068)]/0.05^2$

$n = (3.8416 \times 0.068 \times 0.9320)/0.025$

$n = 97.39$

Now adjusting for the design effect, where; **Deff** = 2, the design effect which is the measure of variability between clusters

$n_2 = 97.39 \times 2$

$n_2 = 194.78$

The taking into account the non-response set at 20%,

$n = n_2/r$

$n = 194.78/0.2$

$n = 973.9 \approx 974$

The minimum required sample size was 974 but all children (1990 in total) that met the inclusion criteria were included in the anaemia study.

3.1.4 Inclusion criteria for samples

Samples of children aged 0-60 months that were collected during the anaemia survey for Eastern, Luapula, Muchinga and Northern provinces whose data were complete.

3.1.5 Exclusion criteria for sample

Children, who had missing data for this study for example presence or absence of fever, Hb reading, information on ITN use, parasite density and other parental information. In addition, children whose blood slides were not readable were excluded from the study.

3.1.6 Laboratory methods

Blood slide samples that were collected in the field during the anaemia survey. Before being pricked, the child's finger was cleaned with an alcohol swab and then pricked with a disposable lancet. The first drop of blood was wiped from the finger, the second was used to prepare a thick blood smear, the third was placed in the HemoCue® photometer to determine the Hb level of the child, the 5 microliters of blood added to a rapid diagnostic test, (RDT) for malaria testing. The final drop was placed on filter paper that would be used for confirmation of diagnosis and parasite species if needed.

For this study, thick blood smear were examined to quantify the parasites. The analysis was done by two independent lab technicians, with the third as a verifier. The smear was placed under a microscope and then the technician quantified the malaria parasites.

3.2 Parasite Count

To estimate the parasite count in a 1µl of blood, the standard value for the white blood cell (WBC) was used, 8000 WBC/µl. The following formula was used to calculate the parasite count;

$$\frac{\text{Number of parasites counted} \times 8000}{\text{Number of leukocytes (200/500)}} = \text{parasites per µl}$$

3.3 Hemoglobin Results

Results for hemoglobin were obtained from the anaemia survey of the MIS of 2012, which were recorded in the field by use of hemocue machine.

3.4 Data Analysis

Data analysis was done using Stata® version 12, (College Station, Texas 77845 USA).
The complete MIS 2012 datasets was obtained from the National Malaria Control Centre. Parasite counts obtained from the lab were entered into excel and then exported to Stata®. Before data analysis was done, dataset of children and mother were merged. The first step was the bivariate analysis of the dependent variable and the independent variable to obtain p-values using the Pearson test of association. This was to identify the characteristics associated with malarial anemia, ($p<0.05$). Variables that had significant p-values ($p<0.05$) were entered into a logistic regression.

3.5 Ethical Consideration

The approval for this dissertation was obtained from ERES converge IRB. Permission to use data obtained from the National Malaria Control Centre to the use the MIS 2012 data. The study used secondary data and therefore presented no direct harm to participants.

When blood samples were used, unique identification numbers were used and all patient names were omitted. Confidentiality of identity was ensured at all times, by the use of unique identification numbers.

Participants from the MIS of 2012 signed consent forms and agreed for their slides to be stored at the National Malaria Control Centre and to be used to conduct future research.

CHAPTER FOUR: RESULTS

4.1 Socio-demographic characteristics of children under 5 years

A total of 1990 children under the age of five years were included in this study out of a total 3540 children who were captured in the 2012 Malaria indicator survey. As shown in table 1, 31.94% were from Eastern province, 23.56% from Luapula, 15.18 % from Muchinga and 29.30% from the Northern province of Zambia. The mean age was 2.45 years, with 33.8% of the children under the age of 1 year, 34.9% between the ages of one and 1-3 years and 31.8% between the age of 4 and 5 years. Of the 1990 children, 49% were male and the rest (51%) were female. Ninety six point three percent of the children lived in rural areas and 3.67% lived in urban areas. 49.10% were male and the female children were slightly more, (50.90%). The majority (83.97%) of children lived with their parents, while the rest (16.03%) of the children lived with other relatives (3.37%), brothers or sisters (0.45%), grandparents (11.56), were adopted (0.25%) or were not related at all (0.05%).

4.1.1 Social demographic characteristics of women (household heads)

In the MIS survey of 2012, 3,738 women were surveyed, but only 1590 were included in this study. Of these women, 43.77% were aged between 15 and 25 years, 30.69% were aged between 25 and 34 years. Of the 1590 women, 19.43% were aged between 35 and 44 years and 6.10% were between 45 and 49 years. The mean age for women was 28.3 years.

The educational status was distributed as follows; 27.80% had never been to school, 54.09% had attained primary school education, where as those who had gone as far as secondary school were 16.42. The remaining 1.70% had gone up to tertiary education.

Table 2; Background characteristics of children under 5 years for Eastern, Luapula, Muchinga and Northern provinces of Zambia.

Characteristics	n=1990	n%
Province		
Eastern	(636)	31.94
Luapula	(469)	23.56
Muchinga	(302)	15.18
Northern	(583)	29.30
Region		
Rural	(1,917)	96.33
Urban	(73)	3.67
Gender		
Male	(977)	49.10
Female	(1,013)	50.90
Relationship To Head of Household		
Wife/husband	(3)	0.15
Son/daughter	(1,671)	83.97
Son-in-law/ daughter-in-law	(2)	0.10
Grandchild	(230)	11.56
Parent-in-law	(2)	0.10
Brother/sister	(9)	0.45
Other Relative	(67)	3.37
Adopted/foster/step child	(5)	0.25
Not related	(1)	0.05
Age (in years children <5)		
<1	(673)	33.82
1-3	(694)	34.87
4-5	(623)	31.31
Wealth Quintile		
Poorest	(649)	32.61
Poor	(542)	27.24
Middle	(384)	19.30
Richer	(315)	15.83
Richest	(100)	5.03
Indoor residual spraying		
No	(1,623)	82.02
Yes	(356)	17.98
Missing 11		
Long Lasting Insecticide Net		
Yes	(649)	32.61
No	(1,341)	67.39
Background Characteristics of women, N=1590		
Age of women (in years)		
15-25	(696)	43.77
25-34	(488)	30.69
35-44	(309)	19.43
45-49	(97)	6.10
School level		
Never been	(442)	27.80

Primary	(860)	54.09
Secondary	(261)	16.42
Tertiary	(27)	1.70
Religion		
Catholic	(146)	9.18
Protestant	(414)	26.04
Muslim	(758)	47.67
Traditional	(3)	0.19
Other	(269)	16.92

4.2 Test for Association

Severe anaemia and Socio-demographic characteristics

Of the 1990 children included in the study, close to 60% of the children under 5 years recorded some form of anaemia (mild or moderate), Hb <11g/dl. Those that recorded severe anaemia were slightly over 10%.

Table 3 shows results chi square test of demographic characteristics with the hemoglobin reading. From table 2.1 the socio-demographic characteristics associated with the hemoglobin reading were, the region (p=0.018) and age of the child (p=0.005).

Table 3; Chi square test of severe anaemia results and social demographic characteristic n=1777, %

Socio-Demographic Characteristic	Hemoglobin Reading		
Province			
	Hb (>8g/dl)	**Hb(<8g/dl)**	**Total**
Eastern	28.47	3.32	31.79
Luapula	19.86	2.93	22.79
Muchinga	14.01	1.13	15.14
Northern	27.52	2.76	30.28
X^2 = 6.0905 P = 0.107			
Region			
Rural	86.21	10.07	96.29
Urban	3.66	0.06	3.71
X^2= 5.5875 P = 0.018			
Gender			
Male	44.12	5.01	49.13
Female	45.75	5.17	50.87
Total	89.87	10.13	100
X^2= 0.0080 P = 0.929			

Age(in years, children <5)			
<1	28.81	3.71	32.53
1-3	31.51	4.28	35.79
4-5	29.54	2.14	31.68
Total	89.87	10.13	100.00
X^2= 10.4351 P = 0.005			
Wealth quintile			
Poorest	28.53	3.83	32.36
Poor	24.14	2.87	27.01
Middle	17.84	1.91	19.75
Richer	14.74	1.24	15.98
Richest	4.61	0.28	4.90
Total	89.87	0.13	100.00
X^2= 5.6302 P = 0.229			
Background Characteristics of women, N=1590			
School level			
Never Been	20.86	3.03	23.89
Primary	54.31	7.58	61.89
Secondary	12.24	0.82	13.05
Tertiary	1.17	0.00	1.17
Total	88.58	11.42	100.00
X^2= 4.9250 P = 0.177			
Religion			
Catholic	25.06	2.45	27.51
Protestant	44.17	6.53	50.70
Muslim	0.23	0.00	0.23
Traditional	0.35	0.00	0.35
	18.76	2.45	21.21
Total	88.58	11.42	100.00
X^2 = 3.0388 P = 0.551			

Association between Malaria and Socio-demographic characteristics

Table 4 shows results of demographic characteristics with the malaria slide results. The socio demographic factors associated with the malaria slide result were, province ($p<0.001$), region ($p<0.001$), age ($p<0.001$), wealth quintile ($p<0.001$), any net present in household ($p=0.004$), IRS ($p<0.001$) children with fever 2weeks before ($p<0.001$).

Table 4; Chi square test of malaria slide results and social demographic characteristics n= 1777, %

	Malaria Slide result		
Socio-Demographic Characteristic			
Province			
	Positive (%)	Negative (%)	Total (%)
Eastern	10.80	22.97	33.77
Luapula	8.61	16.34	24.95
Muchinga	4.78	11.89	16.68
Northern	11.14	13.47	24.61
Total	35.34	64.66	100.00
$X^2 = 22.8259$ $p<0.001$			
Region			
	Positive	Negative	Total
Urban	0.48	2.94	3.42
Rural	34.68	61.72	96.58
Total	35.34	64.66	100.00
$X^2= 10.3157$ $p<0.001$			
Gender			
	Positive	Negative	Total
Male	17.02	31.78	48.80
Female	18.32	32.82	51.14
Total	35.34	64.66	100.00
$X^2 = 0.1316$ $P = 0.717$			
Age(in years)			
	Positive	Negative	Total
<1	7.72	24.33	32.06
1-3	14.08	22.69	36.77
4-5	13.53	17.63	31.67
Total	35.34	64.66	100.00
$X^2 = 41.0399$ $p<0.001$			
Wealth quintile			
	Positive	Negative	Total
Poorest	12.44	17.77	30.21
Poor	9.43	18.39	27.82
Middle	7.86	12.85	20.71
Richer	4.37	12.03	16.40
Richest	1.23	3.62	4.85
Total	35.34	64.66	100.00
$X^2= 18.8618$ $p<0.001$			

Malaria Intervention Initiatives			
	Positive	Negative	Total
Any Net			
Yes	12.17	16.69	28.84
No	23.17	47.98	71.16
Total	35.34	64.66	100.00
X^2= 12.1492 p<0.001			
	Positive	Negative	Total
LLIN*			
Yes	12.44	18.11	30.55
No	22.90	46.55	69.45
Total	35.34	64.66	100.00
X^2= 8.1458 P = 0.004			
	Positive	Negative	Total
IRS**			
No	30.24	50.93	81.47
Yes	5.02	13.81	18.83
Total	35.26	64.74	100
X^2 = 10.9767 p<0.001			
	Positive	Negative	Total
Fever2weeksbefore			
Yes	15.29	17.21	32.51
No	19.30	48.20	67.49
Total	34.59	65.41	100.00
X^2 = 41.2557 p<0.001			
IRS conducted by			
Gov.worker	30.28	50.58	80.86
Private	4.92	14.01	18.93
Other	0.14	0.00	0.14
Don't Know	0.00	0.07	0.07
Total	35.34	64.66	100
X^2= 17.0960 p<0.001			

IRS= Indoor Residual Spraying, LLITN*=Long Lasting Insecticide Treated Net,**

The Association between Parasite Density and Hemoglobin level

Table 5 shows that the hemoglobin level has a strong association with the parasite density, ($p<0.001$). As the parasite density increases, the proportion of SMA also increases.

Table 5; Parasite density * Malarial Anemia cross tabulation,

	Parasite count			
	Low	Moderate	High	Total
Hb8				
Hb (>8g/dl)	948	49	310	1307
Hb(<8g/dl)	59	6	81	146
Total	1007	55	391	1453
X^2 =68.8283 P<0.001				

Fever and Hemoglobin level

Table 6, is the test of association between Hb reading and children recorded with fever. It revealed that the hemoglobin reading has a strong association with children who had fever for 2 weeks 2 days before the survey was conducted, ($p<0.001$).

Table 6 Cross tabulation of children under 5 who had fever for 2weeks 2 days* malarial anemia

	Fever 2weeks 2 days		
	Yes	**No**	**Total**
Hb8			
Hb (>8g/dl)	1228	371	1597
Hb(<8g/dl)	109	71	180
Total	1335	442	1777
X^2 =22.7557 P<0.001			

Educational level of mother and Hemoglobin level

Table 7, is the test of association between Hb level of child and level of education the mother. It revealed that the hemoglobin reading was not associated to the school level the mother attained, (p=0.177).

Table 7 chi square test of school level of mother with Hemoglobin level

	School level of mother				
	Never been	**Primary**	**Secondary**	**Tertiary**	**Total**
Hb8					
Hb (>8g/dl)	179	466	105	10	760
Hb(<8g/dl)	26	65	7	0	98
Total	205	531	112	10	858
X^2= 4.93 P=0.177					

4.3 Relationship between severe Anemia & associated demographic characteristics

Results from table 8 revealed that those in urban areas were 0.133 times less likely to suffer from severe anemia compared to those in rural areas, (p=0.046). Furthermore, children aged 1-3 years were 1.044 times more likely to suffer from severe malarial anemia than those that were under the age of 1 year, association was not statistically significant (p=0.809). Children between the age of 4 and 5 years were 0.561 times less likely to suffer from severe malarial anemia compared to those under the under of 1 year, (p=0.007).

Table 8; logistic regression predicting odds of significant social demographic characteristics with children presenting with severe anemia, N=1777.

Characteristic	Odds ratio (95% CI)	P value
Region		
Rural	1	
Urban	0.1335(0.018-0.97)	0.04
Age (in years children <5)		
<1	1	
1-3	1.044 (0.73-1.48)	0.80
4-5	0.561 (0.37 -0.85)	0.001
Parasite count		
Low	1	
Moderate	2.118 (0.86-5.20)	0.10
High	4.419 (3.04-6.42)	0.00
Fever 2 weeks 2 days		
No	1	1
Yes	1.596 (1.10-2.31)	0.01

Relationship between Fever, Parasite Density and Severe Anaemia

Table 8 revealed that children with a moderate parasite were 2.118 more likely to suffer from severe anemia compared to those in the low parasite count category, association was not statistically significant (p=0.233). Furthermore, children in the high parasite count category were 4.419 times more likely to suffer from severe malarial anemia than those in the low parasite count category, significant at (p<0.001). Children who recorded fever for 2 weeks 2 days before the survey were 1.596 times more likely to suffer from severe malarial anemia compared to those that did not record fever for 2 weeks 2 days before the survey, significant at (p=0.014).

Factors associated with Malaria Transmission

Table 9 shows results based on positive malaria slides and socio demographic characteristics. Children living in Luapula province were 0.890 times less likely to suffer from malaria compared to children living in Eastern province, association was not statistically significant (p=0.493). Children living in Muchinga province were 1.169 times more likely to suffer from malaria compared to children living in Eastern province, (p=0.409). Children living in Northern province were 0.669 times less likely to suffer from malaria compared to children living in Eastern province, (p=0.01). Children living in urban areas were 2.53 times more likely to get malaria compared to those living in rural areas, (p=0.05).

Children aged between 1 and 3 years were 0.509 times less likely to suffer from malaria than those under the age of 1 year significant at (p<0.001). Children between the age of 4 and 5 years where 0.396 times less likely to suffer from malaria compared to their counterparts in the under 1 year category, (p<0.001).

Children in the poor wealth category where 1.361 times more likely to suffer from malaria than those in the poorest wealth category, (p=0.04). The middle wealth category had children who were 1.83 times more likely to suffer from malaria compared to the counterparts in the poorest wealth category, (p=0.63). The children in the rich category were 1.819 times more likely to suffer from malaria compared to children in the poorest wealth category significant at (p=0.04). The children in the richest category were 1.160 times more likely to suffer from malaria compared to children in the poorest wealth category, not statistically significant (p=0.668).

The children that lived in houses that had indoor residual spraying were 0.435 times less likely to suffer from malaria compared to children who lived in houses that did not have indoor residual spraying, (p=0.47).

The children that lived in houses that had no mosquito of any sort were 2.7 times more likely to suffer from malaria compared to children who lived in houses that had recorded a net in their home insignificant at (p=0.084). Also, children coming from homes that did not have long lasting insecticide nets were 0.4 times less likely to suffer from malaria compared children that lived in homes with long lasting insecticide nets. Children that did not record fever 2 weeks 2 days before were 0.5990 times less likely to suffer from malaria, significant at (p<0.001).

Table 9: logistic regression predicting odds of predictors of factors associated with malarial transmission, N=1452

Characteristic	Odds ratio	P value (95% CI)
Province		
Eastern	1	
Luapula	0.890(0.64-1.24)	0.49
Muchinga	1.169 (0.81-1.70)	0.40
Northern	0.669 (0.49-0.91)	0.01
Region		
Rural	1	
Urban	2.53 (1.00-6.426)	0.05
Age (in years children <5)		
<1	1	
1-3	0.50(0.39-0.68)	0.001
4-5	0.40 (0.30-0.53)	0.001
Wealth quintile		
Poorest	1	
Poor	1.36 (1.02-1.82)	0.04
Middle	1.08 (0.78-1.50)	0.64
Rich	1.82 (1.24-2.66)	0.001
Richer	1.16 (0.59-2.30)	0.67
IRS		
No	1	
Yes	0.44 (0.05-4.15)	0.50
Had any net		
Yes	1	
No	2.73 (0.88-8.48)	0.08
LLIN use		
Yes	1	
No	0.488 (0.16-1.50)	0.21
Child had Fever for 2weeks 2days		
No		
Yes	1	1
	0.60 (0.46-0.77)	0.001
Who sprayed		
Government	Dropped	Dropped
Private company		
Other		
Don't know		

CHAPTER FIVE

Discussion

Overall, severe anaemia due to malaria was found in 10.1% of the children included in the anaemia survey of 2012, for Eastern, Luapula, Northern and Muchinga provinces, this was similar to results obtained by Biemba, 2000 and Newton 1997. Eastern province was worst affected followed by Northern then Luapula province. Muchinga province was well off of the four provinces. SMA was more likely to occur in children in rural areas compared to those in urban areas. The occurrence of SMA was equal by gender. The socio demographic factors associated with severe malarial anaemia were the age, (1-3 years category) and the region (rural) of residence. The educational level of mothers had no significant relationship with severe malarial anaemia. Fever and parasite density were related to severe malarial anaemia. In relation to malaria, factors that were associated with its transmission were the province, region, age, wealth quintile, mosquito net use, IRS and fever.

The results revealed that children in urban areas were less likely to suffer from SMA than those in rural areas. The reasons for this were beyond the scope of this study. But it is reasonable to assume that children in urban areas are likely to be treated early by easy access and therefore do not suffer protracted hemolysis. Also, socio economic status is better and hence better nutritional status Biemba 2000 also noted that prolonged exposure to *P.falciparum* contributed to nutritional deficiency.

SMA varied across the age categories under 5 years; SMA was prominent in children in the age category between 1-3 years. The children aged between 4 and 5 years were less likely to suffer from SMA compared to those under the age of one year. Children under the age of 1 year had supplement from breast feeding and had less exposure compared to those between 1-3 years (who had been weaned off and were less likely to sleep under a mosquito net with their mothers.) the children aged between 4-5 years were exposed but had gained immunity and adapting to malaria. This reveals that SMA peaks in the age category 1-3 years and begins to drop as the children approach the age of 4 years and beyond. The strong independent associations between increasing parasite counts, Hb levels suggest a causal effect between *P.falciparum* and severe malaria. These results are consistent with those found by Biemba, 2000. It is then most likely that the hemolysis of parasitized red blood cells contributes to the onset of severe malarial anaemia. So, the higher the parasite count, the lower the Hb expected, (Grobusch and Kremsner 2005). Further assessment of clinical features like the nutritional status and weight would further help clarify this relationship. The results also suggest that children with SMA tend to have chronic malaria infections. (Biemba 2000 & Abdalla 1980).

There was no association between the educational level of the mother and the development of SMA. The whole northern and eastern region of the country is a hyper endemic area for malaria, with a prevalence of 35%. In an area such as this, whether one is educated or not the exposure is high and so is the risk of malaria equally high. The religion too had no effect on development of SMA. The wealth quintile revealed a clear dependent dose relationship though this was not significant.

In relation to malaria, factors that were associated with its transmission were the province, region, age, wealth quintile, mosquito net use, IRS, fever and who conducted the IRS. Overall malaria prevalence was 35.3%. The prevalence of malaria was equal by gender.

Children living in Luapula and Northern provinces were less likely to get malaria compared to those in Eastern province. Whereas, those in Muchinga were at a slightly higher risk than those in Eastern province. Furthermore, those living in urban areas were 2 times more likely to get malaria, these results were inconsistent with those obtained from children with SMA, (as those in urban areas were less likely to get SMA.) Even at independent regression analysis, results for province and malaria transmission remained the same.

The proportion of children that had malaria and used any net and IRS were less compared with those that did not. This result could suggest that intervention strategies provided protection against malaria, (that is mosquito net us and IRS). However, findings from logistic regression indicated that those that did not use LLIN were protected against malaria. The reasons for this could not be established from the study but it could be assumed that IRS provided protection against infection with *P.falciparum* for those that lived in households without LLIN. Furthermore more, the widespread continual use of LLINs leads to the development of vector resistance to insecticide. This resistance to insecticide could reduce the effectiveness of LLIN-based interventions. However, a study done in south west Benin, results showed that resistance of malaria vectors seemed to have not affected the impact of LLINs and that the use of LLINs was highly associated with reduced malaria prevalence irrespective of resistance, (Tokponnon 2014). Further research would help explain the findings of our study.

Who conducted the IRS had no impact on malaria transmission. An unexpected relationship was observed between transmission and wealth quintile, there was an increase in malaria transmission as the wealth quintile increased. The factor, fever 2 weeks before revealed no correlation with malaria positivity. A number of children carry parasites without typical manifestation of malaria symptoms, though, a fair amount of children who had fever turned out positive, not all fevers are attributed to malaria.

In studies conducted to examine whether malaria was a disease of the poor, results show that the use of income, expenditure or asset ownership to measure poverty directly failed to show any significant differences between poorer and less poor groups. Especially when studies when done individual or household level. Evidence is present for other measures of socio economic status, like occupation, housing type, rural location but these indicators are considered further off from the underlying causes of poverty. Interestingly, a link between poverty and seeking treatment has been discovered, poorer groups are more likely to self-treat and less likely to access health facilities. (Worall 2005 & Morris 2000). This could explain the higher likelihood of malaria transmission in other wealth quintile groups.

CHAPTER SIX

Study Limitation

This study involved the secondary analysis of data collected from the Zambia MIS 2012, and as such incompleteness of data and missing information was a problem. Datasets were already coded and this presented as challenge when doing analysis. We continually worked with originators of the datasets to ensure analysis was correctly interpreted. Furthermore, the survey did not capture information that would have been useful to this study, i.e. nutritional status and health history of children.

Conclusion

The study reveals that the burden of severe malarial anaemia is relatively high. Close to 60% of the children had some form of anaemia (mild to moderate), and close to 10% had severe malarial anemia. The major factors that were associated with SMA were the age of the child (1-3years), increasing parasite count and the residence (rural). The educational level of the mother had no association with SMA. Factors that were associated with malaria transmission were the province, region, age, wealth quintile, mosquito net use, IRS and fever. This may call for the prevention and control strategies targeted at the 1-3years age group, such as, sleeping under mosquito nets and prompt access to treatment as they are most vulnerable for SMA and malaria. Further malaria intervention strategies (IRS and mosquito net use) maybe continued.

Recommendations

From the results obtained from this study, the following recommendations are suggested, firstly, introducing prevention and control strategies for children aged between 1-3years as these were greatest affected by SMA. Secondly, health care providers/mothers to ensure the prompt treatment of malaria infections to prevent the progression to SMA, as well as consistently provide nutritional supplements. Thirdly evaluate the LLIN distribution program to ascertain its effectiveness in malaria prevention but to continue IRS programs particularly in the rural areas and the selected provinces. Fourthly, to evaluate the malaria control programs in urban areas and finally, continue with malaria awareness campaigns.

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APPENDICES

APPENDIX A; DATA EXTRACTION FORM

DISTRICT	WARD	TEAM SUPERVISOR	LAB TECH	CHILD UNIQUE ID	READER 1	READER2	AGRREGATED RESULTS

APPENDIX B; BUDGET FOR RESEARCH

Activity	**Quantity**	**Unit Cost (ZMK)**	**Total (ZMK)**
lab Research Assistants (3)	3 x 30days	100	9000
Stationary			2500
Printing			2500
Binding of proposal and Thesis			1500
ERES	-	-	500
External hard drive	1	350	350
Flash disk	1	150	150
Transport& Communication	-	-	2000
Communication	-	-	700
Publications	-	-	2000
Poster	-	-	800
Total			**22000**
Contingency (10%)			**2000**
Grand Total			**24000**

APPENDIX C; WORK PLAN

	Jan/Feb 2014	March 2014	April 2014	April 2014	May 2014	June 2014	July 2014
ACTIVITY							
Data collection							
Data entry							
Data Cleaning and Correction							
Data analysis							
Writing dissertation							
Submission of draft report							
Review of draft report based on comments							
Dissemination of findings							
Binding and submission of final findings							
Submission of final report/ Dissemination of findings							

SAMPLE QUESTIONNAIRE FROM SURVEY

ZAMBIA MALARIA INDICATOR SURVEY

MODEL HOUSEHOLD QUESTIONNAIRE

IDENTIFICATION[1]	
PLACE NAME _____	
NAME OF HOUSEHOLD HEAD _____	
CLUSTER NUMBER.....	–
HOUSEHOLD NUMBER.....	
REGION.....	
URBAN/RURAL (URBAN=1, RURAL=2).....	
LARGE CITY/SMALL CITY/TOWN/COUNTRYSIDE[2].....	
(LARGE CITY=1, SMALL CITY=2, TOWN=3, COUNTRYSIDE=4)	

INTERVIEWER VISITS				
	1	2	3	FINAL VISIT
DATE	_____	_____	_____	DAY / MONTH / YEAR
INTERVIEWER'S NAME	_____	_____	_____	NAME
RESULT*	_____	_____	_____	

INTERVIEWER VISITS				
				RESULT
NEXT VISIT: DATE TIME				TOTAL NO. OF VISITS

*RESULT CODES:

1	COMPLETED
2	NO HOUSEHOLD MEMBER AT HOME OR NO COMPETENT RESPONDENT AT HOME AT TIME OF VISIT
3	ENTIRE HOUSEHOLD ABSENT FOR EXTENDED PERIOD OF TIME
4	POSTPONED
5	REFUSED
6	DWELLING VACANT OR ADDRESS NOT A DWELLING
7	DWELLING DESTROYED
8	DWELLING NOT FOUND
9	OTHER _____ (SPECIFY)

TOTAL

PERSONS IN HOUSEHOLD

TOTAL ELIGIBLE WOMEN

LINE NUMBER OF RESPONDENT TO HOUSEHOLD QUESTIONNAIRE

SUPERVISOR	OFFICE EDITOR	KEYED BY
NAME _____ DATE _____		

[1] This section should be adapted for country-specific survey design