Impact of Insecticide Treated Nets and Indoor residual Spraying on malaria case prevalence in Geita and Nyang'hwale districts of Tanzania.

By

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A dissertation submitted to the University of Zambia in partial fulfillment of the requirements of the degree of Masters of Science in One Health Analytical Epidemiology

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DECLARATION

I, Kiputa Gaudence Thobias, hereby state that the content of this dissertation is my own work and has not been submitted to another University or institution for any award or degree.

Student name: ……………………………………………………………………………..

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CERTIFICATE OF APPROVAL

This dissertation submitted by Kiputa Gaudence Thobias is approved as fulfillment part of the requirements for the award of the degree of Master of Science in One health Analytical Epidemiology at the University of Zambia

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ABSTRACT

A retrospective longitudinal study was conducted to assess the impact on malaria prevalence of ITNs combined with IRS in Geita district, IRS alone in Nyang'hwale district and to compare the two interventions between the two districts.

Malaria is a protozoan disease and one of the leading causes of illness and deaths in the world. Infection occurs after exposure to blood-feeding infective *Anopholes* mosquitoes. Malaria is predominant in the tropics and subtropics and it is reported that malaria kills a child every minute. In Tanzania, at least 40% of outpatient attendances are attributable to malaria. Geita and Nyang'hale districts are within Geita region where malaria prevalence is highest in Tanzania. Geita and Nyang'hwale districts of Tanzania have been controlling malaria transmission by using the combined intervention of insecticide-treated nets (ITNs) with indoor residual spraying (IRS) and IRS alone respectively.

District malaria surveillance data for five years (2011-2015) and two years (2013-2014) were collected and analyzed for Geita and Nyang'hwale districts, respectively. Results show that a total of 1,387,805 ITNs were distributed and 435,719 households sprayed between 2011 and 2015, however IRS coverage was uneven. There was evidence of malaria prevalence reduction, from 53% to 12%, in Geita district within the five years of intervention. The ITNs coverage was associated with a reduction in malaria prevalence while IRS was not. In Nyang'hwale district malaria cases increased from 103,788 cases in 2013 to 123,337 in 2014, and were accompanied by decreased households spraying from 49,554 to 41,632. The combined intervention reduced malaria prevalence in Geita district while an increase in malaria cases was observed in Nyang'hwale district where IRS alone was applied. Malaria prevalence difference between ITNs combined with IRS intervention and IRS intervention alone was 0.09 and prevalence ratio was 0.73. Only ITNs had a significant effect on malaria cases reduction ($p<0.001$). However, even at 100% ITN coverage, the estimated probability of finding malaria cases was not zero.

Therefore, based on this study, it can be concluded that ITNs were responsible for the observed reduction in malaria prevalence in the combined use of ITNs and IRS that both use pyrethroid insecticides under the prevailing field conditions in Geita district. The use of IRS either in the combined intervention in Geita district or alone in Nyang'hwale district had insignificant effects on malaria control.

DEDICATION

To my wife King Glory Apollo and my children Elisheba Kiputa, Mark Kiputa, Joshua Kiputa, Jediel Kiputa and Jeriel Kiputa who allowed me to leave them for the two years of study.

I owe you a lot!

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AIDS	:	Acquired Immunodeficiency Syndrome
CDC	:	Centre for Disease Control and Prevention
CS	:	Capsule Suspension
DDT	:	Diethyl-Dichloro-Trichloroethane
HIV	:	Human Immunodeficiency Virus
IRAC	:	Insecticide Resistance Action Committee
IRS	:	Indoor Residual Spraying
ITNs	:	Insecticide Treated Nets
PMI	:	President's Malaria Initiative
SC	:	Suspension Concentrate
WHO	:	World Health Organization

CHAPTER ONE

1.0 Introduction

1.1 Background

Parasites of the genus *Plasmodium* cause malaria in humans and the highest population at risk of malaria is in Africa (http://www.who.int/malaria/visual-refresh/en/). Based on WHO (2016) report 3.2 billion people are at risk of suffering from malaria worldwide. Illness and death in children under 5 years and pregnant women is largely attributable to malaria (Nwaorgu and Orajaka, 2011). It's reported that, worldwide 3,000 deaths per day are attributable to malaria (Erhabor *et al*, 2014)

According to Moyer *et al* (2012) malaria has been with humans for at least 50 000 years and the particularly dangerous species, *Plasmodium falciparum*, has been afflicting Africa for the past 6, 000 years. Despite progress in reducing the malaria burden over the past half decade, malaria remains a leading cause of morbidity and mortality in the developing world (Kim *et al*, 2012). On Tanzania Mainland, more than 40% of all outpatient attendances are attributable to malaria, resulting in an estimated 10 to 12 million clinical malaria cases annually and it is estimated that 60, 000–80, 000 malaria deaths occur annually in the Mainland (CDC, 2014a). Furthermore, 93% of the population on the mainland lives in high malaria transmission areas (PMI, 2014).

Malaria prevalence varies greatly by region. The prevalence is highest in Geita region (32%), Kigoma (26%), and Lindi (26%) and malaria is more common in Mainland Tanzania (10% prevalence) compared to Zanzibar (<1% prevalence) (United Republic of Tanzania, 2013a). In the countries where malaria is a problem, interventions to prevent and treat the disease are in progress. However, Insecticide Treated Nets are the primary means for malaria prevention worldwide (CDC, 2014b). Currently, ITNs and IRS have proved to be highly effective malaria control interventions being deployed in countries where malaria is endemic to achieve objectives on malaria control and elimination programs (Simon *et al*, 2013; Lines and Kleinschmidt, 2013). ITNs ownership based on household percentage in Sub-Saharan Africa rose from 3% to 53% in 2011 and IRS protected 153 million people worldwide (WHO, 2012a). In Africa the combination of ITNs and IRS has become a commonplace practice (Okumu and Moore, 2011). These interventions are being deployed to achieve World Health Assembly Roll Back Malaria and Millenium Development Targets (Kleinschmidt, *et al.*, 2009).

A total of 18.2 million free ITNs were distributed during the Tanzania Mainland's universal coverage campaign between September 2010 and October 2011 and a 2011/12 nationwide health survey showed that more than 90% of all households had one or more ITNs (CDC, 2014a). In Tanzania, IRS was indicated to provide the best intervention when combined with ITNs in the districts with higher numbers of malaria cases (Mboera *et al*, 2013). Geita and Nyang'hwale districts are among the areas in Tanzania where IRS has been implemented (htt://www.rti.org/files/TVCSP-Success-Geita–Tanzania; PMI, 2014). Research on whether the combined intervention help reduce malaria prevalence have been done in several districts. However, most of the research focused on malaria prevalence based on parasitological indices rather than on malaria cases prevalence (clinical cases and confirmed cases) (Mashauri *et al*, 2013; West *et al*, 2014). Apart from other areas of Tanzania, IRS has been carried out in malaria endemic areas around Lake Victoria (Mboera *et al*, 2013), Geita and Nyang'hwale districts inclusive. A randomized trial on the impact of combined IRS and ITNs and with IRS on malaria prevalence was performed in Mleba district (Kagera) and based on parasitological/haematological indices (parasitaemia/anaemia) (Mboera *et al* 2013; West *et al*, 2014). There is no study which has been done to assess the impact of IRS and ITNs on the prevalence of malaria cases (West *et al*, 2014). No research has been conducted in Geita and Nyang'hwale districts, whether based on parasitological indices or malaria cases, on the impact of IRS and ITNs on malaria prevalence. Therefore, conducting research on the impact of IRS and ITNs on malaria cases in Geita and Nyang'hwale districts, which are within the region with the highest malaria prevalence in Tanzania (32%) (United Republic of Tanzania, 2013a), was of great significance to fill the gap and add knowledge on impact of the combined intervention on malaria cases (clinical cases and confirmed cases) prevalence.

1.2 Statement of the problem and justification

Many researchers have investigated the impact of IRS on malaria prevalence based on parasitemia and/or haematological indices. In contrast, few researchers have compared the impact of IRS combined with ITNs on malaria cases (clinical cases and confirmed cases) prevalence. There is no information on whether both IRS (pyrethroids) and ITNs (pyrethroids) have significant effects in the combined intervention and which one between the two (IRS or ITNs) has greater impact on reported malaria cases.

In Tanzania, like in many other countries, IRS and ITNs are being used in combination to interrupt malaria transmission (Mboera *et al*, 2013). However, there is no research which has assessed the impact of IRS and ITNs on the prevalence of malaria cases (clinical cases and confirmed cases) (West *et al*, 2014). Geita and

Nyang’hwale districts are among the districts in Tanzania where IRS (lambda-cyahalothrin) combined with ITNs and IRS alone is being used to control malaria, respectively. But the impact of the two interventions on malaria cases has not been investigated in the districts (Geita and Nyang’wale Districts’ Health Departments). However, previous researches showed added benefits when IRS insecticide class used were organophosphates, organochlorine or carbamates (Kamuliwo *et al*, 2013; Simon *et al*, 2013; WHO, 2014a).

1.3 Objectives

1.3.1 Main objective

The main objective of this study was to assess the impact of ITNs and IRS on the prevalence of malaria cases (clinical cases and confirmed cases) in Geita and Nyang’hwale districts of Tanzania.

1.3.2 Specific objectives

To assess the impact of the combined interventions of IRS (pyrethroid) and ITNs on malaria cases prevalence in Geita district.

To predict malaria cases probabilities if the coverage rates of the intervention with greater effect in the combined intervention were 50%, 80% and 100%.

To assess the impact of IRS (lambda cyhalothrin) alone on malaria cases prevalence in Nyang’hwale district.

To compare the impact between IRS combined with ITNs in Geita district and IRS alone in Nyang’hwale district, on malaria cases prevalence

CHAPTER TWO

2.0 Literature review

Malaria in humans is caused by four major parasites-*Plasmodium vivax, P. malariae, P. ovale* and *P. falciparum*. *P. falciparum* malaria is the most deadly (WHO, 2007)

However, monkey malaria parasites are being reported to infect humans in the forest regions of South East Asia (WHO. 2015)

When malaria parasites are ingested by a mosquito, they undergo development within the mosquito before they become infectious to humans, the parasites are ingested as gametocytes, which develop into zygote, oocys and finally the sporozoites (Fig. 2.1) which are infective (CDC, 2015).

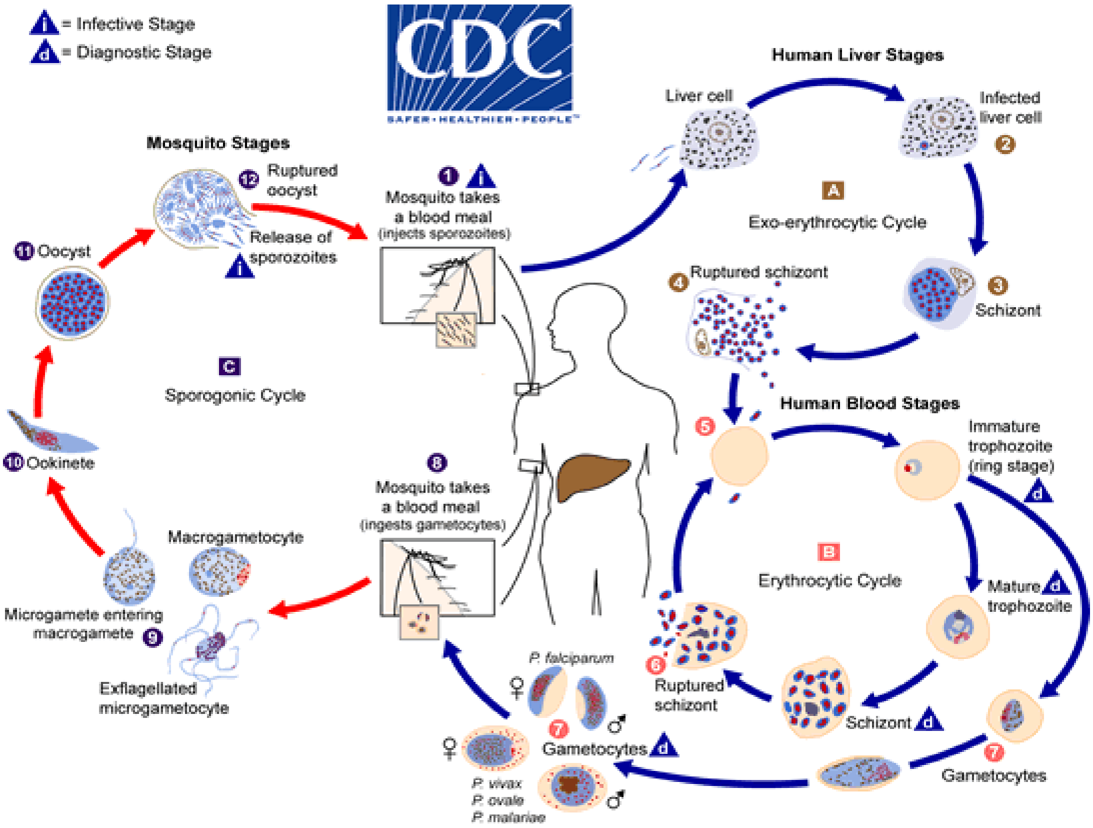

Figure 2.1: Plasmodium development in Anopholes and human (http://www.cdc.gov/malaria/about/biology/).

2.1 Malaria vector and parasite transmission

Almost all aquatic habitats can be used for mosquito breeding (Oyewole *et al*, 2009). However, river and oceans water which contain calcium, magnesium sulphate, nitrate and dissolved solids in high proportion and still, cool and clear water with suitable pH and temperature, are preferred by *Anopholes gambiae*, however, Anopholes larval survival is endangered by high water current and flooding due to reduced oxygen tension and physical harm (Oyewole *et al*, 2009).

Anophelines go through four stages in their life cycle: egg, larva, pupa, and adult (Fig. 2.2)

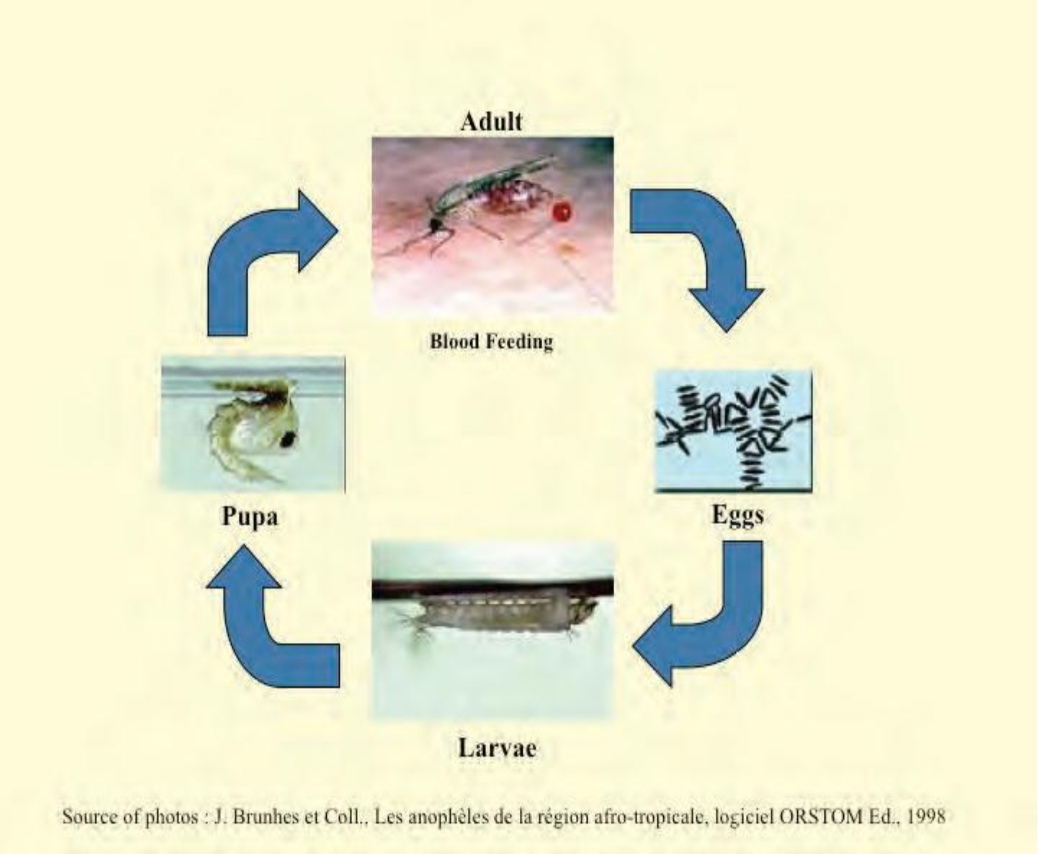

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Figure 1.2: Life cycle of *Anopholes* mosquito (WHO, 2013)

Like all other mosquitoes whereby the first three stages are aquatic, an adult female mosquito can live up to two weeks in nature and adult females lay 50-200 eggs per oviposition and it takes up to 2-3 weeks to hatch in colder climates (CDC, 2015). Anopholes mosquitoes resting indoors (endophagic) usually are found in dark places, regardless of the height from the floor (Harbison *et al*, 2006).

All malaria parasites are transmitted by the bite of an infective *Anopheles* mosquito, in rare cases, transmission occurs by blood transfusion, organ transplantation, needle sharing, or congenitally from mother to fetus (CDC, 2015). Malaria is solely transmitted by female mosquitoes of the genus *Anopholes,* which prefers feeding on humans or animals such as cattle. To suck blood efficiently the mosquito has a proboscis or long, sucking organ with six hair-like stylets or probes, two used for piercing the skin, two for sawing the wound open and third pair sucks out blood (Namuchimba, 2007). (Fig.2.3)

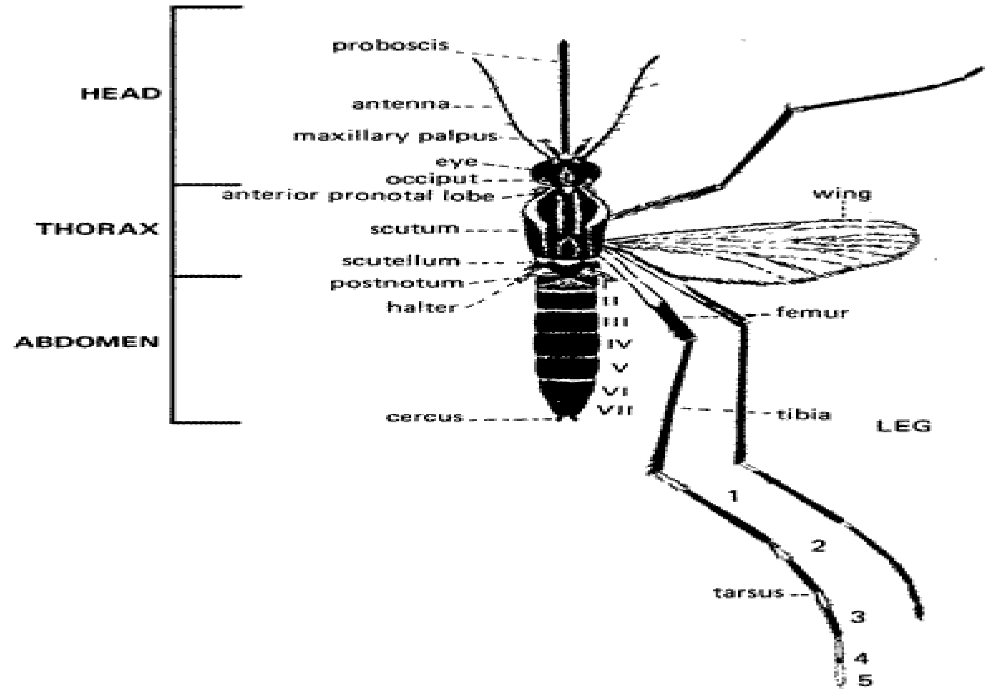


Figure 2.3: Body parts of a mosquito (CDC, 2015)

The sub-Saharan Africa bears most of the world malaria burden due to endemicity of three mosquito species that almost depend upon humans and cattle for blood meal which is important for egg development (Killeen *et al,* 2013). With exception of the Antarctica, *Anophelines* are found worldwide and are not only found in malaria endemic areas, but in areas where malaria has been eliminated (CDC, 2015). Although not all *Anopholes* mosquitoes feed on animal blood, *Anopholes gambiae* and *Anophles funestus* are blood feeders and therefore are the major malaria vectors in the world (CDC, 2015). *Anopholes* mosquitoes are further divided into two groups based on whether they feed indoor-endophagic or outdoor-exophagic (WHO,2013).

2.2 Effects of malaria parasite on human host

Malaria symptoms varies depending upon the type of malaria, whether uncomplicated or complicated. Uncomplicated malaria symptoms are nonspecific which includes headache, fatigue, abdominal discomfort, muscle and joint aches followed by fever, chills, anorexia, perspiration, vomiting and worsening malaise (WHO, 2015). Complicated malaria symptoms includes severe anaemia, metabolic acidosis, hypoglycaemia, coma, acute renal failure or acute pulmonary oedema and if untreated is fatal (WHO, 2015). Infants and young children, pregnant women and people living with HIV/AIDS are at the highest risk of suffering from malaria (Schantz-Dunn and Nawal, 2009).

2.2.1 Health effects

Exposure to malaria at early ages leads to poor educational attainment, worse mental and physical health outcomes which has bad effect in cognitive function, heart problems and high mortality in old age unlike the unexposed (Chang *et al*, 2011).

Additionally, children’s performance at school is adversely affected on when they are frequently attacked by malaria (Fernando *et al,* 2003). Clinical consequences of malaria infection during pregnancy include death of both the pregnant woman and the child (Okafor *et al*, 2012). Children and pregnant women suffer from renal and hepatic dysfunctions which are part of the pathological effects of malaria infection (Olusegun, 2015)

Malaria infection is associated with rapid HIV-1 replication and creates a good microenvironment for the spread of virus among the CD4 cells (Van geertruyden, 2014). In adults with advanced immunosuppression, due to HIV, there is increased risk of malaria infection and clinical malaria (WHO, 2004). Pregnant women that are HIV infected severely suffer from malaria (Olusi and Abe, 2014). Severe malaria is associated with increased viral load and decreased CD4+ cell count because malaria parasites infection promotes macrophages and CD4+ cells to activate viral transcription (Alemu *et al*, 2013). In a study by Sanyaolu *et al* (2013), a significantly higher number of malaria infected patients were HIV sero-positive.

2.2.2 Economic effects

Malaria has some effects on the output and income through health care and days lost without working by a person suffering from the disease.

Early deaths due to malaria decrease the quantity of labor available in production activities when it occurs, in subsequent periods and malaria morbidity results into reduced output by increasing the number of people who do not work and incapacitation (Asante and Asento-Okyere, 2003). In a study by Achoja (2011) in Nigeria, it was found out that the loss of income experienced by fishers was related to man days lost and malaria treatment cost. An adult male suffering from malaria causes economic loss in a household especially for males dealing with farm production (WHO, 2007). Barofsky *et al* (2011) in their study in Uganda, they found evidence that by eradicating malaria there was an increase in income levels

2.3 Interventions used to control and prevent malaria infection

2.3.1 Chemoprophylaxis

The development of resistance to drugs by malaria parasites and insecticides by malaria vector necessitated the idea of developing vaccine as the sole means for the disease eradication (Lorenz *et al*, 2014). However, apart from the currently most advanced vaccine candidate RTS,S/AS01, it has been concluded that the vaccine cannot help eradicate malaria and this is reported to be attributable to the sporozoites' surface protein, circumsporozoite protein (CSP) which is attributable to *Plasmodium's* highly advanced immune evasion abilities (Lorenz *et al*, 2014). The vaccine, RTS,S/AS01, was created in 1987 (http:www.who.in/immunization/research/development/malaria_vaccine_qa/en/). RST,S/AS01, has potential to become a complementary tool for malaria control which could be added to the other preventive and treatment methods (WHO, 2016). Repeated exposure to malaria parasite infection develops partial immunity in human, that is why non-exposed individuals, especially children suffer severe malaria in areas of high malaria transmission rate (Magombedzea et al, 2011). Therefore vaccine development has been unsuccessful due highly advanced immune evasion abilities of the *Plasmodium* parasite

2.3.2 Chemotherapy

Effective malaria treatment can be successful at early stages, but when delayed may lead to fatal consequences. (CDC, 2016). Malaria transmission can be reduced by chemotherapy through two mechanisms, which are early, effective treatment and reducing infectivity (WHO,2015). In the first mechanism gametocytaemia is reduced by asexual blood stages elimination and the latter either by direct effect on gametocytes or on parasite developmental stages in mosquito. (WHO,2015).
Choosing a drug for malaria prevention differ by country of travel and the list include Atovaquone-Proguanil, Chloroquine and Hydroxychloroquine Doxycycline, Mefloquine and Primaquine (CDC, 2016). However, expert advice is needed because no prophylactic medication can offer complete protection (Castelli *et al*, 2010).

Currently, Artemisinin-Combination Therapies is the first line antimalaria treatment, but malaria parasite has started becoming resistant to artemisinins which are the basis of ACT (Bianca, 2013). Additionally, opting to drug combination as means to avoid development of resistance to drugs by malaria parasite has led to side effects and multidrug resistance. (Wernsdorfer, 1986). A study in India by Goswami *et al* (2013) reported that replacing chloroquine to artemisin combination showed no difference in malaria prevalence.

Treatment of malaria aims at preventing further transmission of the infection to others and prevent the possibility of emergency of malaria drug resistance, however, there is a possibility of an increase in resistance due to wide spread use of antimalaria drugs , use of monotherapy and incomplete dosing(WHO, 2015).

Therefore the use of chemotherapy in controlling malaria has not been very successful because of the prolonged use of one type of drug and incomplete dosing, especially outpatients

2.3.3 Use of insecticides in blocking malaria transmission

Insecticide Treated Nets and Indoor Residual Spraying are among the major malaria control methods (Kleinschmidt *et al*, 2009). The effectiveness of the combined intervention to prevent malaria transmission depends upon the ability to repel or kill endophagic mosquitoes (Huho *et al*, 2013). There are four major classes of insecticides (Table 2.1) used in indoor residual spraying which are the pyrethroids, organochlorine, carbamates and organophosphates (Graham, 2011).

IRS is spraying of an insecticide on walls inside houses to interrupt malaria transmission by either killing or repelling adult female mosquitoes from entering houses (CDC, 2015). Apart from repellant effect and physical barrier provided by ITNs, which reduce human-mosquito contact at individual level, also kill mosquitoes (CDC, 2015).

Table 2.1 Chemical groups and the corresponding insecticide(s) used in IRS

	CHEMICAL GROUP	INSECTICIDE (S)
1	Pyrethroids	Alpha-Cypermethrin, Bifenthrin, Cyfluthrin Deltamethrin, Etofenprox, Lambda –Cyhalothrin
2	Organophosphates	Fenitrothion, Malathion and Pirimiphos methyl
3	Organochlorines	Dichlorodiphenyl Trichloroethane (DDT)
4	Carbamates	Bendiocarb and Propoxur

The four chemical groups have different modes of actions. Carbamate and organophosphate are acetyl cholinesterase inhibitors. Organaochlorines are gamma aminobutyric acid (GABA) - chloride gated channel antagonists. Pyrethroid and DDT are sodium channel modulators (http://www.irac.online.org). Full recommended long-lasting insecticidal nets are Alpha-cypermethrin, Permethrin and Deltamethrin treated (http;//www.who.int/whopes/quality/new specif/en/).

2.3.3.1 Impact of Indoor residual spraying (IRS) alone in malaria control

There was a reduction in parasitaemia in children when IRS was repeatedly applied in Pare Taveta region of Tanzania in 1955 and 1959 (Nankabirwa *et al*, 2014). This was confirmed in the assertion that IRS is effective when properly applied (Blumberg *et al*, 2014). A study to assess the impact of IRS with DDT, alphacypermethrin and deltamethrin in Madagascar, the use of IRS with DDT and pyrethroid greatly decreased the vector-human contact, and there was a marked reduction in the plasmodial index (Ratovonjato *et al*, 2014). A Meta-Analysis comparing the organochlorine, organophosphates and carbamates effectiveness in IRS, indicated that use of DDT reduced malaria infection (Kim *et al,* 2012*).* In Muleba district north-western Tanzania, two rounds of IRS (lambdacyhalothrin) intervention reduced the malaria parasitological indices (Mashauri *et al*, 2013). It was further reported that in Tanzania over 60% and 55% reduction in the prevalence of parasitaemia and anaemia in children under five years of age were recorded respectively following two rounds of IRS with lambda-cyhalothrin (Kitau *et al*, 2014). Indoor residual spraying using deltamethrin in Malaysia reduced parasitaemia by 90%-100% (Rohani *et al*, 2006).

In a field study to evaluate lambda- cyhalothrin (ICON® 10 SC) in India, it was found that vector density, parity rates and malaria cases reduced considerably in the ICON® 10 SC-sprayed villages (Raghavendra *et al*, 2011). In southern Mozambique, there was a reduction in *P. falciparum* prevalence after the implementation of IRS associated with decrease in notified malaria cases (Sharp *et al,* 2007). Assessment of malaria control progress in Zambia showed that children in households protected by ITNs or IRS had lower rate of parasitaemia (Chizema-Kaweshia *et al*, 2010). In many studies it has been shown that when IRS was applied alone it reduced malaria prevalence.

2.3.3.2 Impact of Insecticide-treated nets (ITNs) alone in malaria control

In some areas ITNs alone have been deployed to control malaria transmission. A cross-sectional survey undertaken among school-age children in Somalia and Uganda suggested that nets use was associated with a 71% and 43% lower risk of *P. falciparum* infection respectively (Nankabirwa *et al*, 2014). It is further reported that the use of ITNs alone have shown to reduce the incidence of malaria cases by 50% in a variety of settings (Skarbinski *et al*, 2012). However, nets can provide protection against blood feeding mosquitoes even if they are not insecticidal because ITNs physically prevent bites by mosquitoes. (Okumu *et al*, 2013). Therefore even if the ITN insecticide becomes ineffective to mosquitoes, an ITN can still provide protection against malaria transmission.

2.3.3.3 Impact of Combining ITNs and IRS use on malaria control.

The effectiveness of the combined intervention to prevent malaria transmission depends upon the ability to repel or kill endophagic mosquitoes (Huho *et al*, 2013). Currently, for the purpose of resistance management World Health Organization recommends additive rotational spraying with non-pyrethroids in areas with ITNs (WHO, 2015a). The insecticides for ITNs (Olyset Nets) and IRS were permethrin (WHO, 2014c; Graham, 2011) and lambda cyhalothrin (http://www.rti.org/files/TVCSP-Success-Geita-Tanzania) respectively. In a study by West *et al* (2014) in Muleba district to investigate the impact of IRS (beniocarb- a carbamate) and ITNs, IRS when combined with ITNs proved to be effective against malaria infection than ITNs alone. Furthermore, it was reported that malaria transmission could be decreased where both ITNs and IRS are deployed in the same geographical area and malaria infection was two third lower than with neither intervention (West *et al,* 2015).

In contrast, in a similar study carried out in Benin to measure the impact of IRS (bendiocarb) and ITNs on clinical incidence of malaria in children under 6 years, it was concluded that there were no added benefits for reducing malaria morbidity, infection, and transmission when combining ITNs and IRS with a background of ITNs coverage (WHO, 2014d). Again, there was no evidence of reduced malaria parasite infection prevalence between the use of IRS combined with ITNs and ITNs alone when a cluster randomized trial was conducted in Sudan in 2012 (WHO, 2014d).

In a non-randomized prospective cohort study which was conducted in Western Kenya in 2008, lower infection incidence was observed where both interventions were deployed (WHO, 2014d). When assessing the impact of IRS combined with ITNs, on malaria parasitemia and anemia prevalence in children under five years of age by cross-sectional household survey, conducted in Malawi by using lambda cyhalothrin Icon® 10 CS (Skarbinski *et al*, 2012), the combined intervention had no association with the reduced infection rate. In a randomized controlled efficacy trial conducted in Gambian villages to investigate the impact of IRS (DDT) in areas with high coverage of ITNs, there were no additional benefits (Pinder *et al*, 2014).

A study in Zambia conducted by using national surveillance data for five years (2006-2011), IRS (pirimiphos methyl) and ITNs combined intervention reduced malaria cases (clinical cases and confirmed cases) and deaths due to malaria (Kamuliwo *et al*, 2013). A similar research performed in Botswana by using national surveillance data (2008-2012), where DDT was used for IRS, showed that malaria cases and deaths attributable to malaria reduced tremendously (Simon *et al*, 2013). Exophagic behavior enables malaria vectors evade insecticide treated nets and indoor residual spraying with insecticides by feeding outdoors (Killeen *et al*, 2013). Apart from the fact that ITNs and IRS provides useful protection, its protective efficacy is conferred to those who are inside houses but those who are actively outdoors are excluded (Mathania *et al*, 2016).

It is recommended to protect against outdoor feeding by using insecticide-treated clothing or repellents (WHO, 2014). Nearly a quarter of all mosquitoes bites in the evening and early hours of night, therefore application of repellents and proper clothing, during this period can provide protection against malaria transmission (Korgaonkar *et al*, 2012). Although ITNs and IRS remains the major means for malaria vector control, in many instances complete interruption of malaria transmission can’t be successful by these interventions alone (WHO, 2014e).

2.3.4 Other ways used to prevent malaria infection apart from ITNs and IRS.

There are other ways of preventing malaria infection apart from the use of ITNs and IRS. For example, repellents, mesh clothing and larvicides.

A mosquito repellent is a substance applied on skin, clothing, or other surfaces which deters mosquitoes from landing or crawling on that surface which reduces chances of being bitten by a mosquito and therefore reduced risk of malaria infection (Massachusetts public health fact sheet, 2014).

There are chemical mosquito repellents which are recommended for use, for example DEET (N, N-diethyl-m-toluamide) and plant based mosquito repellents, additionally, mesh clothing can be used Hats, shirts, pants, socks and jackets (Caroline, 2005). However, essential oils have been proposed as a suitable substitution of chemical repellent (Shooshtari *et al*, 2013). Repellents of plant origin do not pose hazards to humans and domestic animals, are easily biodegraded and presumed to be safer for human (Pattanayak and Dhal, 2015).

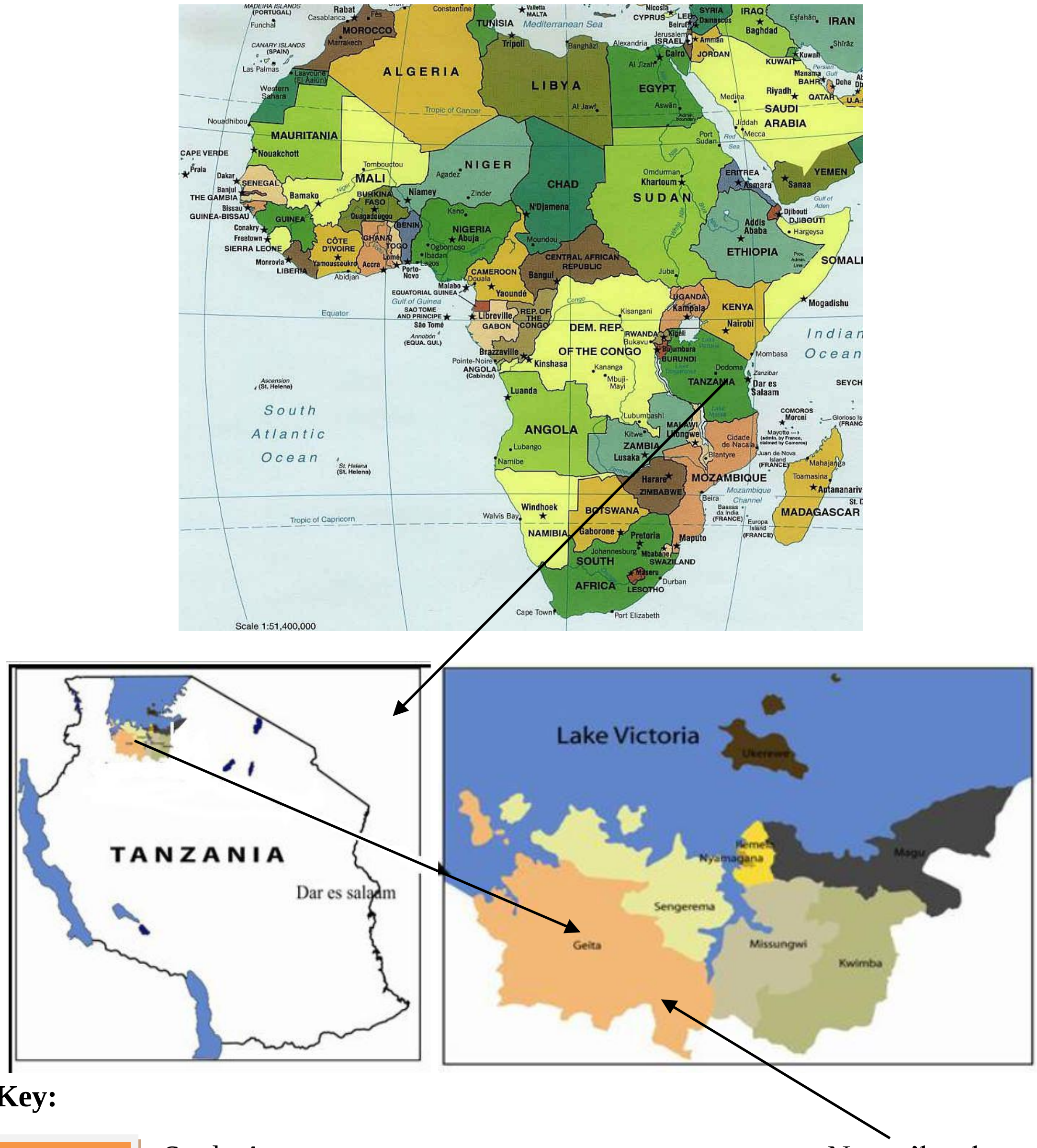
Larvicides are products which work by killing mosquito larvae and pupae before they can grow into adults and larvicides come in many forms, liquids, tablets, pellets, granules and briquettes (http:/www.cdc.gov/zika/pdfs/larvicides-factsheets.pdf). Larviciding is the application of chemicals to habitats to kill pre-adult mosquitoes, there are microbial and chemical larvicides (EPA, 2000).

CHAPTER THREE

3.0 Material and methods

3.1 Study area

The study was conducted in Geita and Nyang'hwale Districts, Geita region of Tanzania from October 2014 to October 2015. Geita region located in the Northern part of Tanzania lies between latitude 2° 15′ and 3° 48′ south of the equator and longitude 31° 15′ east of Greenwich. To the West and North bordered with Kagera region, South and South eastern by Shinyanga region and Mwanza region to the North. The region is also bound by Lake Victoria water (United Republic of Tanzania, 2013b). Geita region is a newly established region from Mwanza region and Nyang'hwale district from the former Geita district. The districts are among the five districts of Geita region of Tanzania. The region covers an area of about 21,879 square kilometers, with a population of 1,739,530 according to 2012 census (United Republic of Tanzania, 2012). Geita and Nyang'hwale districts have a population of 807,619 and 148,320 respectively as per 2012 census (United Republic of Tnzania, 2012). Geita district is located at 02°55′S 032°15′ while Nyang'hwale district is at 03°12′S 032°39' (Fig. 1). Geita district borders Shinyanga region in the South East, North and East- Mwanza region, North West- Kagera region, South-Bukombe and SouthWest-Chato district. Nyang'hwale district borders Sengerema in the North, East- Misungwi and Shinyanga rural, south-Kahama and West-Geita district. The main economic activities in the districts are agriculture, livestock production, small-scale mining and fisheries.



Key:

🟧 Study Area

🟦 Lakes

Figure 3.1: The map showing the study area, Geita and Nyang'hwale districts

NOTE: Nyang'hwale district is a newly formed district from Geita district. The map shows Geita district because the map for Nyang'hwale district is currently not available

3.2 Study design

A retrospective longitudinal study design was carried out to assess the impact of IRS and ITNs on malaria cases prevalence in the districts.

3.3 Data collection

3.3.1 Malaria morbidity

Annually aggregated district malaria cases data for 2011, 2012, 2013, 2014 and 2015 were obtained from the Districts' Health Departments. Malaria cases consisted of both clinically diagnosed cases and microscopically confirmed cases.

At health center level malaria cases are recorded in special forms called Health Information Management System forms. Data are compiled monthly at health center level into a report which is submitted to the district hospital each month. At the Districts' Health Departments there are designated persons, the Malaria Focal Persons, who compile malaria cases data for further use.

3.3.2 Population and housing data

Both population and housing data for 2011, 2012, 2013, 2014 and 2015 were obtained from the Districts' Planning, Monitoring and Statistics Departments. The data served as denominators for IRS and ITNs coverage rate~~s~~ calculation.

3.3.3 IRS and ITNs coverage

The IRS and ITNs coverage data were obtained from the Districts' Health Departments. The number of ITNs consisted of the ITNs distributed to children under the age of five through children welfare clinics, pregnant women through antenatal clinics and ITNs distributed freely door to door. Local leaders were required to register the names of people in every household. The nets were distributed depending on the number of people per household

Before distributing nets there were campaigns to encourage people to use their nets once they are provided. It is assumed that the ITNs life of use is three years and one ITN on average protects two persons (Kamuliwo *et al*, 2013).

3.4 Ethical considerations

This type of study is deemed not to be human subject~~s~~ research hence did not need human specimen and patient identifiers were not included in the data (Kamuliwo *et al*, 2013; Kigozi *et al*, 2012), and therefore, did not need ethical clearance.

3.5 Data analysis

To determine the association between the burden of malaria, being the total of both clinically diagnosed and confirmed cases and ITNs combined with IRS, a Logistic regression was used. A Stata Epidemiological table feature was used to compare the impact on malaria prevalence between the combined interventions (ITNs combined with IRS) in Geita district and IRS alone in Nyang'hwale district. The district coverage rates of ITNs were calculated as [ITNs distributed/Total population] x 100, while IRS coverage rates were calculated as [households sprayed/number of households in a given year] x 100. Below is the final fitted model used to calculate the estimated probability of malaria cases.

$$Estimated\ probability\ of\ malaria\ cases = \frac{e^{(2.5-3.0\ x\ ITNs\ coverage)}}{1+e^{(2.5-3.0\ x\ ITNs\ coverage)}}$$

Where e = 2.718281828 (a constant)

The data were cleaned in Microsoft Office Excel 2007 before analysis. All statistical analyses and graph production were performed by using STATA 12 (Stata Corporation, College Station, TX, USA).

At 95% confidence interval, a *p*-value less than 0.05 was statistically significant.

CHAPTER FOUR

4.0 Results

4.1 The number of confirmed malaria cases and clinically diagnosed malaria cases in Geita district (2011-215)

In both Geita and Nyang'hwale districts the confirmed cases are few compared to clinically diagnosed cases. In Geita district the number of confirmed cases (Fig.4.1) dropped nearly half from 2011 to 2012, 47,031 in 2011 to 24212 in 2012.

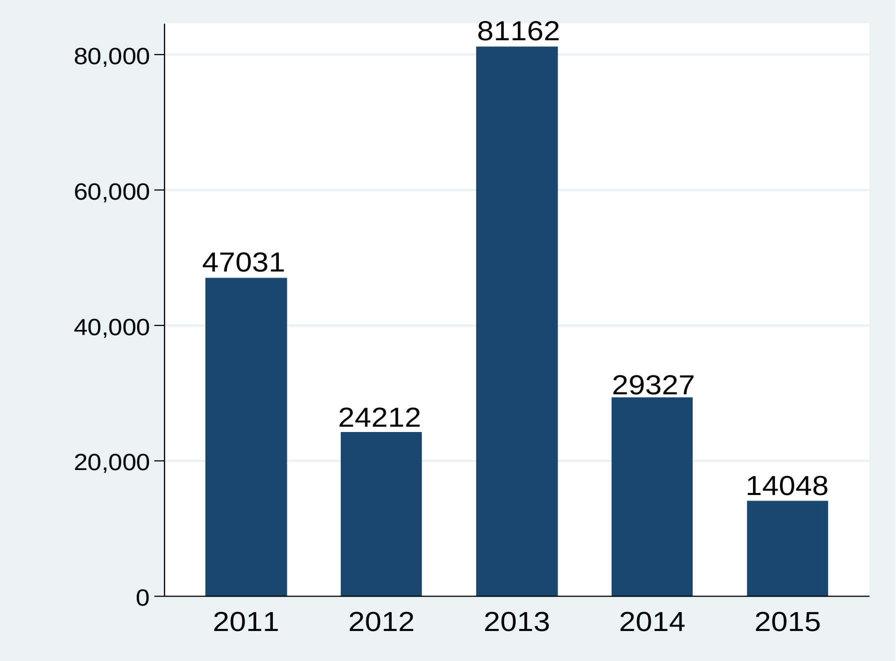


Figure 4.1: The number of confirmed malaria cases in Geita district (2011 - 2015)

However, there was a sharp rise in confirmed cases in 2013 followed by a sharp drop in 2014 up to 2015.

The clinically diagnosed cases decreased from 423280 (2011) to 113661(2015).

There is no year in which clinically diagnosed cases exceeded the cases in the preceding year (Fig.4.2).

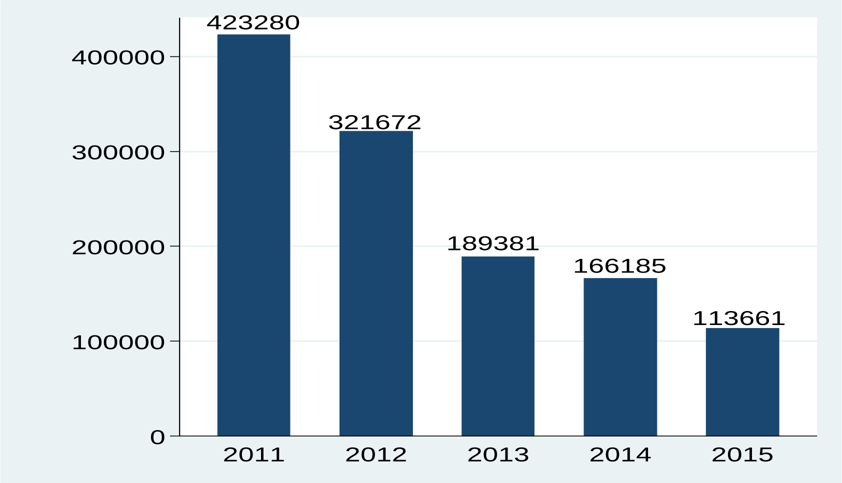


Figure 4.2: Clinically diagnosed malaria cases in Geita district (2011 - 2015)

4.2 The percentage of confirmed malaria cases and clinically diagnosed malaria cases in Geita district (2011-2015).

When confirmed cases are presented as percentage, the highest was in 2013 and the minimum was 7% in 2012. Clinically diagnosed cases percentages didn't vary very much from year to year. The highest was 93 in 2012 and the minimum 70 in 2013 (Fig. 4.3).

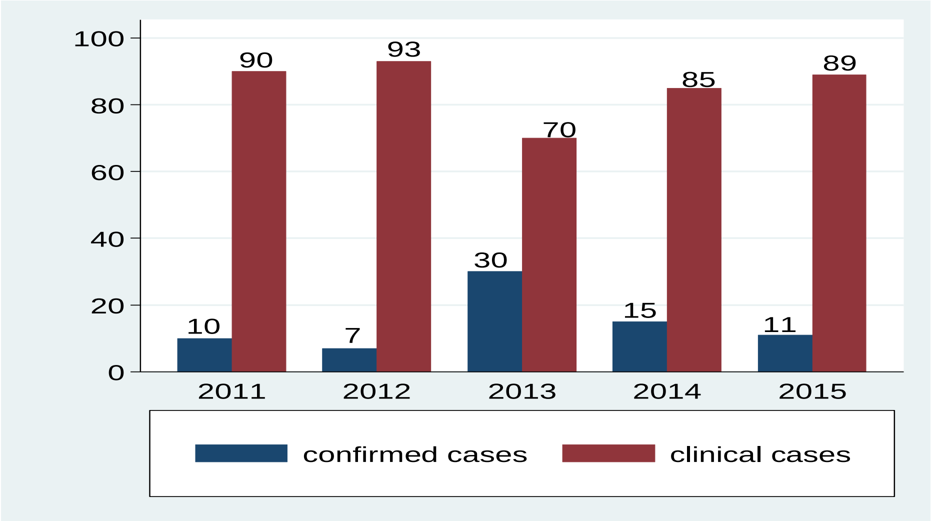


Figure 4.3: Percentage of confirmed malaria cases and clinically diagnosed cases in Geita district (2011 - 2015)

4.3 The number of confirmed malaria cases and clinically diagnosed malaria cases in Nyang’hwale district (2013-2014)

In Nyang’hwale district the confirmed cases decreased from 14,535 in 2013 to 11,113 in 2014. Clinically diagnosed cases increased from 89,258 in 2013 to 112,324 in 2014 (Fig. 4.4)

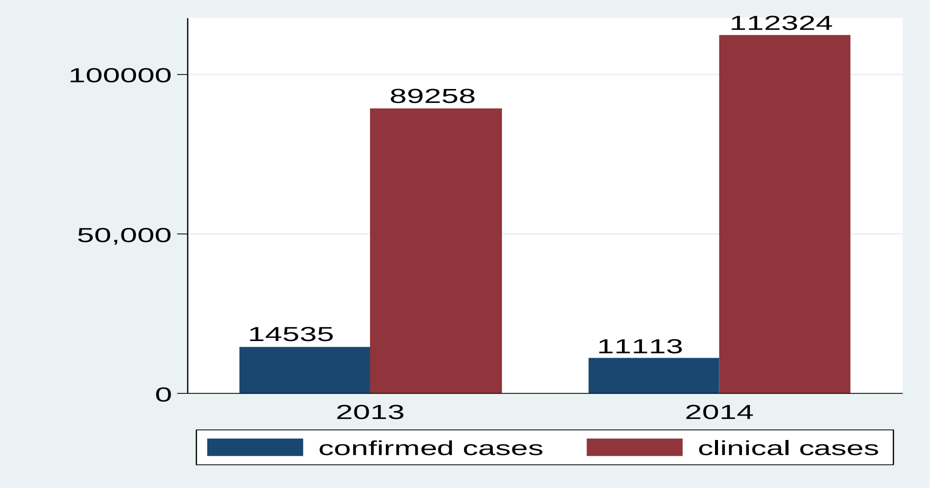


Figure 4.4: Number of confirmed malaria cases and clinically diagnosed cases in Nyang'hwale district (2013 - 2014)

4.4 Percentage of confirmed malaria cases and clinically diagnosed cases in Nyang’hwale district (2013-2014).

Percentage of confirmed cases decreased from 14 in 2013 to 9 in 2014, while percentage of clinically diagnosed increased from 86 in 2013 to 91 in 2014.

In Nyang’hwale the situation was different from Geita, the trend of clinical cases in 2014 was higher than the preceding year (Fig.4.5)

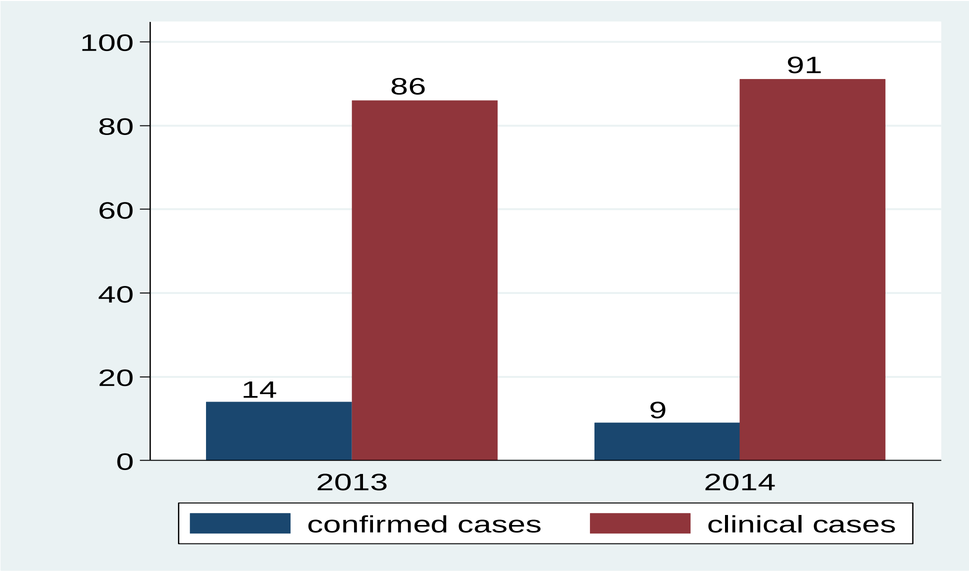


Figure 4.5: Percentage of confirmed malaria cases and clinically diagnosed cases in Nyang'hwale district (2013 - 2014)

4.5 The impact of ITNs combined with IRS in Geita district and IRS alone in Nyang’hwale district on malaria prevalence

There was a reduction in malaria prevalence in Geita district, where the combined intervention of ITN+IRS was used from 53% (470,311) prevalence in 2011 to 12% (127,709) prevalence in 2015. There was a sharp decline in malaria prevalence between 2011 and 2012. Reduction in malaria prevalence remained somehow constant from 2012 to 2015 despite the sharp increase in the number of ITNs distributed. However, there was an uneven IRS coverage from 2012 to 2015 (Fig.4.6 & 4.7).

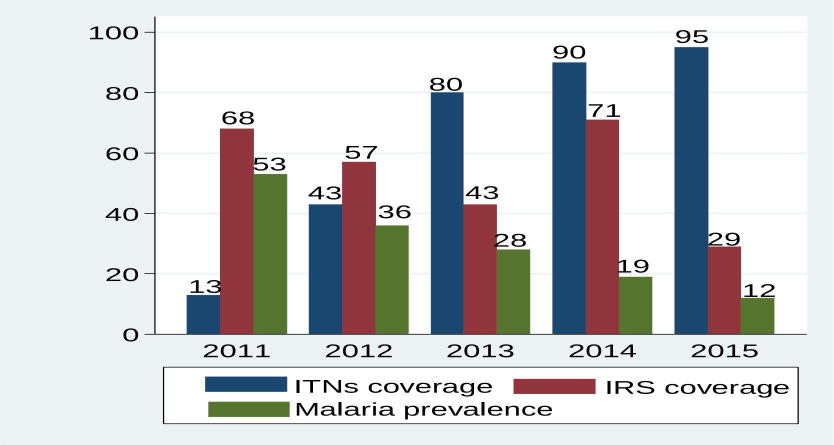


Figure 4.6: Malaria prevalence in Geita district (2011 - 2015)

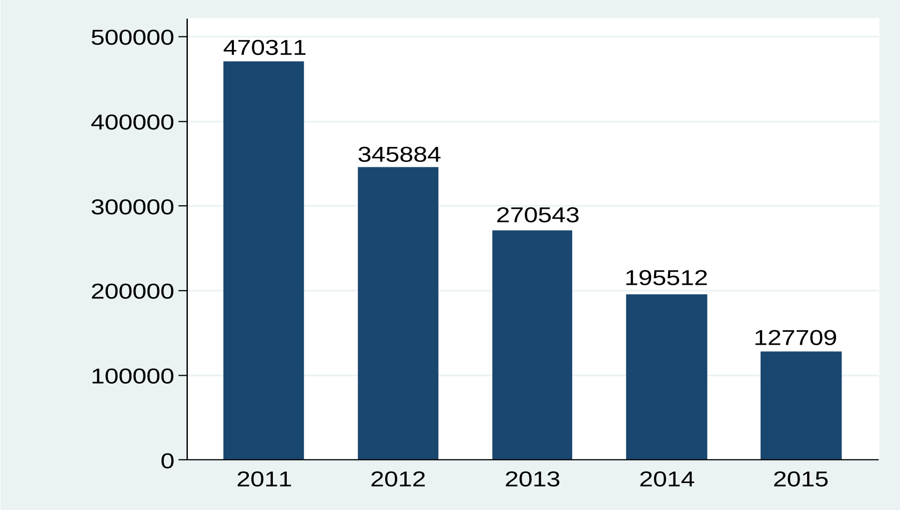


Figure 4.7: Malaria cases in Geita district (2011 - 2015)

On the other hand in Nyang'hwale district where only IRS was applied to control malaria transmission, malaria prevalence was 30% (103,788) and 34% (123,437), in 2013 and in 2014, respectively, while the number of households sprayed was 80% (49,554) in 2013 and 61% (41,632) in 2014 (Fig.4.8 & 4.9).

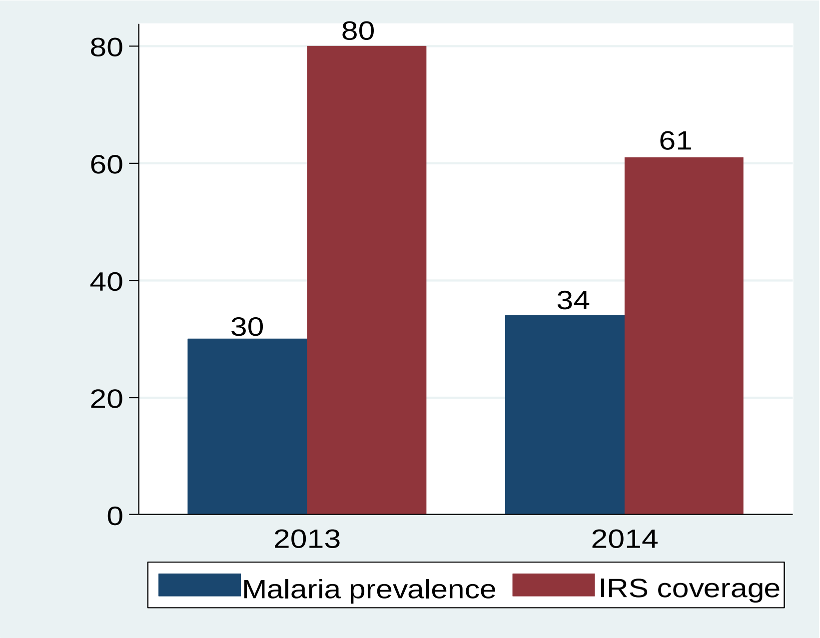


Figure 4.8: Malaria prevalence and households sprayed in Nyang'hwale district (2013 - 2014)

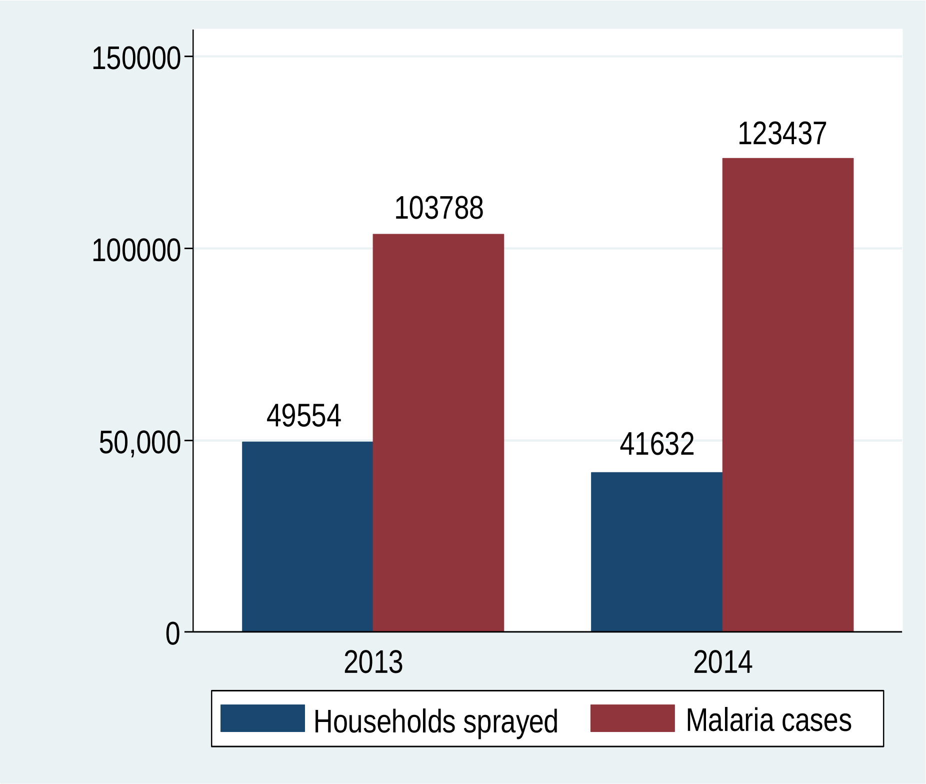


Figure 4.9: Malaria cases and households sprayed in Nyang'hwale district (2013 - 2014)

IRS in Nyang’hwale district was conducted in 2013 and 2014 only, therefore data for comparing malaria burden between Geita district (IRS combined with ITNs) and Nyang’hwale district (IRS only) were for the two years. The data from the districts, Geita and Nyang’hwale, were compared because they are neighboring districts and the two interventions were applied for the same period (2013 and 2014).

4 .6 Association between the interventions (IRS combined with ITNs) and malaria cases

The Logistic regression was performed to find out whether both ITNs and IRS were significant in the combined intervention and identify which between the two had greater effect on malaria cases. The odds and their corresponding odds ratios showed that malaria cases decreased from 2011 to 2015 (Table 4.1).

Table 4.1: The odds of malaria cases and their corresponding Odds Ratios for the five years (2011- 2015)

	Year				
	2011	**2012**	**2013**	**2014**	**2015**
Odds	1.15	0.57	0.38	0.24	0.14
Odds Ratio	1.00	0.50	0.33	0.21	0.12

ITNs were found to have significant association ($p<0.001$) with reduced malaria cases (Table 4.2).

Table 4.2: Association between malaria cases and IRS or ITNs in the combined intervention

	Variables			
	OR	**P-Value**	**[95% Confidence Interval]**	
IRS	1.34	0.134	(0.643	4.793)
ITNs	0.05	<0.001	(0.001	0.002)

If ITNs coverage were 50%, 80% and 100%, malaria cases probabilities would be 0.73, 0.52 and 0.34 respectively, therefore the probability of getting malaria reduced with an increase in ITNs coverage. It was further observed that there was a negative relationship (r = -0.53) between ITNs and malaria cases, meaning that as ITN coverage increased, malaria cases decreased. In addition, there was a very weak positive relationship (r = 0.16) between IRS and malaria cases, which was far from being a perfect association, a perfect association *r* is close or equal to +1 or -1. This implies that as IRS coverage changed there were no predictable changes on malaria cases (Table 4.3).

Table 1.3: Relationship between interventions and malaria cases

	Malaria cases	**IRS**	**ITN**
IRS	0.16	1.00	
ITNs	-0.53	0.20	1.00

4.7 Difference in malaria burden between Geita district (ITNs combined with IRS) and Nyang’hwale district (IRS only)

A Stata Epidemiological table feature was used to compare the impact of the two interventions on malaria prevalence between the two districts. A comparison between ITNs combined with IRS and IRS alone, revealed a prevalence difference of -0.09 (9%) (*p*<0.001) and the prevalence ratio was 0.73 (*p*<0.001) (Table 4.4).

Table 4.4: Difference in impact on malaria prevalence between ITNs combined with IRS and IRS alone

	ITNS + IRS	**IRS alone**	**P-Value**	**[95% Confidence Interval]**
Prevalence	0.23(23%)	0.32 (32%)		
	Point estimation			
Prevalence difference	-0.09		0.00	(-0.087 -0.085)
Prevalence ratio	0.73		0.00	(0.728 0.735)

CHAPTER FIVE

5.0 Discussion

In order to ensure universal access to malaria interventions, the distribution of ITNs which was implemented both under the voucher scheme and free door to door distribution started in 2004 in most parts of Tanzania (Ministry of Health and Social Welfare-Tanzania, 2013) and 90% of households had one or more ITNs based on 2011/2012 nationwide health survey. In Mwanza and the newly created Geita districts, an additional intervention of IRS has been conducted once a year since 2010 while IRS alone was conducted in Nyang'hwale district once a year from 2013 to 2014 (PMI, 2014).

This study was conducted to assess the impact of a combination of ITNs and IRS in Geita district, IRS alone in Nyang'hwale district and compared the impact of the two interventions between the two districts on the prevalence of malaria cases, (both clinical and confirmed cases), by using district surveillance data for five years (2011-2015) in Geita district and two years (2013 to 2014) in Nyang'hwale district. IRS insecticide in use was lambda cyhalothrin, a pyrethroid, (http://www.rti.org/files/TVCSP-Success-Geita-Tanzania).

In Nyang'hwale district where only IRS was conducted to control malaria vector population, there was an increase in malaria prevalence with a corresponding decline in IRS coverage (Fig.4.8). These results indirectly provide evidence that IRS with a pyrethroid insecticide lambda cyhalothrin had an impact on malaria prevalence recorded in Nyang'hwale district because the decrease in IRS coverage was followed by an increase in malaria prevalence. Similarly, IRS though with lambda cyhalothrin proved to be effective in reducing malaria transmission as indicated by earlier studies (Mashauri *et al,* 2013; Raghavendra *et al,* 2011).

Furthermore, in this study it was revealed that the combined intervention of ITNs (pyrethroid) and IRS (pyrethroid) resulted in reduction of malaria prevalence in Geita district (Fig.4.6). Likewise, the odds and their corresponding odds ratios showed that malaria cases decreased from 2011 to 2015 (Table 4.1). These findings are in accordance with those of other studies conducted in Zambia and Botswana (Kamuliwo *et al,* 2013; Simon *et al,* 2013) that reported reduction in malaria prevalence, although the IRS insecticides were pirimiphos methyl, an organophosphorous, and DDT, an organochlorine, respectively. The reduced malaria prevalence in Geita district may not all be attributed to the use of IRS and ITNs together.

There has been a rapid increase in house construction in the district and larger parts of these areas were marsh lands, also construction of roads in many areas of the district accompanied by proper drainage systems, clearing of vegetation for various activities, this has helped destroying mosquitoes breeding sites leading to decreased mosquito population. Hence, environmental changes are likely to have an impact on malaria morbidity and mortality, in this case due to reduction in mosquito population (Mboera *et al,* 2013; Simon *et al,* 2013). ITNs were increasingly distributed from 2012 to 2015, but change in malaria prevalence seemed to be constant. This may be due to ITNs distribution system. Ideally, ITNs are supposed to be distributed through a door to door channel but practically the ITNs are not distributed at once. Moreover, people are required to go to special centers to collect ITNs, which are distributed free of charge. Everyone is expected to collect the ITN(s) and the numbers of ITN(s) to be collected depend upon the size of a household. Individual pick up of ITNs leads to prolonged times to complete distribution of ITNs to the beneficiaries and therefore ITNs fail to provide the expected protection and hence reduced impact on reduction of malaria prevalence. ITNs were found to have significant effect in combination but not IRS (Table 4.2). This result may be due to increased ITNs coverage from 2011 to 2015 (Fig.4.6). These results are comparable to the study by Kamuliwo *et al* (2013) which reported significant association between ITNs and reduced malaria prevalence. Additionally, IRS protection is likely to be lower where ITNs coverage is at high levels (West *et al*, 2014; WHO, 2013; WHO, 2014a; WHO, 2014b). This is supported by a study which reported that there was no added benefit for combining ITNs and IRS in areas with a background of high ITN coverage (Corbel *et al*, 2012). Meanwhile, the association of ITNs with the reduced malaria prevalence in this study is contrary to a previous study which reported that IRS was associated with malaria prevalence reduction but ITNs were not (Simon *et al*, 2013). The difference in the findings between these two studies may be attributed to the different types of IRS insecticides, DDT in the study by Simon *et al* (2013) and lambda cyhalothrin in this study.

In Geita district where both ITNs and IRS were used together malaria prevalence was 9% less (Prevalence difference = 0.09) than in Nyang'hwale district where only IRS (pyrethroid) was applied (Table 4.4). These results show that the combined intervention had an added benefit compared to IRS alone, but the average IRS coverage for the two years 2013 and 2014 was 57% and 61% in Geita and Nyang'hwale, respectively. However, evidence of the effects of IRS and ITNs used together compared with one method alone, has revealed contradicting results (Kleinschmidt *et al*, 2009). In a similar study which compared the combined intervention to the use of IRS with pyrethroid alone in Burundi reported no additional benefit of combining the two interventions and it was suggested that the results may have been caused by high coverage of IRS which was 90% (Protopopoff *et al*, 2007). When the combination of ITNs and IRS provides no added benefit relative to one method alone, then implementing both is not economical (Hamel *et al*, 2011). The low IRS coverage in Nyang'hwale districts may have contributed to the added benefit in the combined intervention, because it is reported that in order to generate effective protection against malaria transmission, IRS coverage should at least be 80% (WHO, 2016). Again, a survey in Bioko Equatorial Guinea, which compared the combined intervention with IRS (bendiocarb-a carbamate) alone, in which IRS coverage was more than 80%, the combination showed added benefit in malaria control compared to IRS alone (Kleinschmidt *et al*, 2009). Based on these findings, the use of IRS below 80% coverage in Geita district was wastage of resources since IRS conferred no protection in the combination. Again, the continued use of lambda cyahalothrin, a pyrethroid, as IRS insecticide in Geita district may influence resistance development to pyrethroid by mosquitoes based on the findings that if the combination is necessary the IRS insecticide should be another class of insecticides but not pyrethroids (WHO, 2014b) in order to minimize the possible development of resistant mosquitoes. There is a risk of causing high selection pressure to malaria vectors for insecticide resistance due to massive use of pyrethroids (Kisinza *et al*,2011). The combined intervention has proved to have added benefit where IRS insecticide was bendiocarb, a carbamate (WHO, 2014a) and ITNs were pyrethroid treated. The added benefits of bendiocarb are due to the fact that it is highly toxic and thought to be quite effective at inhibiting mosquitoes feeding (Okumu *et al*, 2011). In this vein, a study by Kigozi *et al* (2012) showed that bendiocarb (carbamate) had the highest effect among the three classes of insecticides.

In this study, even at 100% ITNs coverage malaria cases couldn’t be reduced to zero. This may have been attributable to the behavior of malaria vector, some being endophagic and others exophagic (WHO, 2013). Therefore even if ITNs provides useful protection, only those under ITNs are protected but those outdoors are excluded (Mathania *et al*, 2016). Furthermore, according to Ferguson *et al* (2010) even at 100% ITNs coverage, malaria cases cannot be reduced to zero, because entomological inoculation rate (EIR), a measure of human exposure, is more than a thousand infectious bites per person per year .

Integrated vector control to minimize the development of resistance recommends the use of more than one control method at a time and when an insecticide of a particular mode of action is frequently used will lead to insecticide resistance (Insecticide Resistance Action Committee, 2011; Graham, 2011). If insecticides are to be used in both methods, it is important to use insecticides with different modes of action (Hemingway, 2014). A study by Pinder *et al* (2014), showed that there was no added benefit when ITNs (pyrethroid) combined with IRS (DDT) were used, this may have been due to the two having the same mode of action, sodium channel modulators (http://www.irac.online.org). In this study, although two different control methods were used in Geita district, the same class of insecticide was used in both interventions. The ITNs are pyrethroid treated and IRS (lambda cyahalothrin) is a pyrethroid. It’s advised to take great care when combining IRS and ITNs to avoid onset of resistance (WHO, 2012b). Furthermore, for the purpose of managing insecticide resistance, IRS with different mode of action from that of pyrethroids may be applied where there are ITNs (WHO, 2014a).

Currently, the high selection pressure for pyrethroid resistance is due the use of pyrethroids in all ITNs and in not less than 80% of IRS campaigns (Hemingway, 2014). There has been an increased use of wholly pyrethroids treated ITNs in recent years which has increased selection pressure for this group of insecticide (Insecticide Resistance Action Committee, 2011). Effective insecticide resistance management depends upon alternate, sequential or rotational use of insecticide with different mode of action (Insecticide Resistance Action Committee, 2016). This, coupled with the low IRS coverage in Geita district, has the possibility of increasing the development of resistance in mosquitoes and making malaria control less successful. The use of ITNs at high coverage for long time in this study before the introduction of IRS may have contributed to insignificancy of IRS which is in agreement with the study which reported that resistance to insecticides is at high levels where control activities are in progress and development of resistance to pyrethroids by mosquitoes has been found to be rapid in areas where the control interventions were ITNs (Brogdon and Mcllister, 1998). Currently, synthetic pyrethroids remain the only class of insecticide for insecticidal ITNs (Insecticide Resistance Action Committee, 2011). In Nyang'hwale district IRS with a pyrethroid appeared to have an impact on malaria prevalence reduction, this may have been attributed to the fact that there was no intervention which used pyrethroids before and therefore, mosquitoes were susceptible to lambda cyhalothrin, which is a pyrethroid. This is in agreement with the findings by a study by Kisinza *et al* (2011) that there is a risk of causing high selection pressure to malaria vectors for insecticide resistance due to massive use of pyrethroids.

Effectiveness of ITNs is estimated to remain for 3-5 years allowing selection for resistance to pyrethroids (Simon *et al*, 2013; Hemingway, 2014) and currently, in all

African countries malaria vectors are not fully susceptible to pyrethroids (Hemingway, 2014). In Geita district distribution of ITNs began in 2008, considering the life span of ITNs there is high possibility that mosquitoes have developed resistance to pyrethroids. Studies in Tanzania, Chad, Senegal, Mozambique and Malawi have revealed mosquito resistance to pyrethroids (Mboera *et al*, 2013). This suggests that where IRS lacks impact when combined with ITNs, insecticide resistance, apart from other factors, should be taken into account.

In many cases resistance is blamed for control failure, when in fact there may be other reasons why control is not being achieved some of which are poor application, insufficient coverage, incorrect dilution and incorrect frequency of application (IRAC, 2016). Both in Geita and Nyang'hwale districts the confirmed cases were few compared to clinically diagnosed cases. The aggregated malaria cases are compiled at the district hospital, but higher malaria cases come from health centers which are located in remote areas and most of the health centers lack diagnostic equipments such as microscopes and other reagents. The findings in this study are in agreement with previous studies done in other parts of Tanzania, Misago *et al* (2015) reported that in poor resource settings most febrile cases are attributed to malaria due to reliance on clinical diagnosis. Again, in febrile patients in endemic areas, malaria is the main diagnosis (Strom *et al*, 2013).

CHAPTER SIX

6.0 Conclusion and recommendations

6.1 Conclusion

It can be concluded from this study that malaria vector control by means of combined intervention in Geita district reduced malaria prevalence from 53% to 12% and the odds of malaria cases reduced from 1.12 to 0.14, while in Nyang’hwale district where IRS alone was applied there was an increase in malaria prevalence accompanied by a decline in IRS coverage. Furthermore, prevalence difference between ITNs combined with IRS and IRS alone was 0.09 and prevalence ratio was 0.73. The Logistic regression model showed that in the combined intervention, only ITNs had a significant effect and if ITNs coverage were 50%, 80% and 100%, estimated malaria cases probabilities would be 0.73, 0.52 and 0.34 respectively. Therefore, even at 100% ITN coverage, the estimated probability of finding malaria cases would not be zero.

6.2 Recommendations

Recommendations from this study are that:-

1. The combined interventions of ITNs and IRS using pyrethroids only, have no added benefits and should be avoided.
2. Since ITNs are pyrethroid treated, when a combined intervention is used, the IRS insecticide should be one with a mode of action that is different from that of pyrethroids

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