THE IMPACT OF IVERMECTIN MASS DRUG ADMINISTRATION ON THE LEVEL OF ENDEMICITY AND INTENSITY OF *ONCHOCERCA VOLVULUS* INFECTION IN THE ADANSI SOUTH DISTRICT OF GHANA

BY

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DECLARATION

I hereby declare that this submission is my own work towards the M.Phil and that, to the best of my knowledge, it contains no material previously published by another person nor material which has been accepted for the award of any other degree of the University, except where due acknowledgement has been made in the text.

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DEDICATION

I dedicate this thesis to the loving memory of my late, beloved brother Prince Sowah-Sixtus. May your soul rest in perfect eternal peace!

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ABSTRACT

Onchocerca volvulus infection remains a major public health problem with more than 120 million people estimated to be living in endemic areas, majority in sub-Saharan Africa. Clinical manifestations include severe dermatitis, visual impairment, and blindness. Ivermectin has been the main operational drug for the treatment and control of onchocerciasis. However reports have emerged about sub-optimal response to this drug in Ghana posing a challenge to the control of *O. volvulus* infection. In this study, the impact of ivermectin mass drug administration on the level of endemicity and intensity of *O. volvulus* infection was assessed. About 1223 volunteers from 19 hyperendemic communities in two sub-district areas, who had received 3 to 5 rounds of ivermectin were examined by palpation for onchocercal nodules. Out of the 1223 volunteers, 444 were assessed for microfilaria loads and the community microfilarial load (CMFL) for each of the study communities was determined. Level of endemicity was measured using onchocercal nodule and microfilarial prevalence while the intensity of infection was measured by CMFL, a reference index used by the OCP. At the end of the study, 41.8% of the 1223 volunteers were nodule positive. A significant difference was observed (p=0.0107) in the nodule prevalence between New Edubiase and Akrofuom sub-districts. Of the 444 volunteers, 54.5% were microfilaria positive. The microfilaria prevalence and community microfilarial load in the study communities ranged from 13.3% to 88.9% and 1.4mf/mg to 5.2mf/mg respectively. There was no significant difference in the microfilarial prevalence (p=1.000) and CMFL (p=0.3539) between the two study areas. The overall nodule and microfilarial prevalence in the study areas suggest that these areas are mesoendemic for *O. volvulus* infection and the intensity of infection as suggested by an average CMFL of 2.7mf/mg is below APOC's threshold of 5mf/s. This study has shown that 3 to 5 rounds of ivermectin treatment has significant impact on the level of endemicity and intensity of *O. volvulus* infection which means ivermectin still remains an effective tool for the control of onchocerciasis.

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LIST OF ABBREVIATIONS

APOC – Africa Programme for Onchocerciasis Control

CDC – Centre for Disease Control

CDD – Community-Directed Distributor

CDTI – Community-Directed Treatment with Ivermectin

CMFL – Community microfilarial load

GPELF – Global Programme for Elimination of Lymphatic Filariasis

IVM – Ivermectin

KCCR - Kumasi Centre for Collaborative Research in Tropical Medicine

MDA – Mass Drug Administration

mf – Microfilariae

mf/mg – Microfilariae per milligram

NTDCP – Neglected Tropical Disease Control Programme

NTD - Neglected Tropical Disease

OCP – Onchocerciasis Control Programme in West Africa

OEPA – Onchocerciasis Elimination Programme for the Americas

SIZ – Special Intervention Zone(s)

WHO – World Health Organization

CHAPTER ONE

INTRODUCTION

1.1 Background

Human onchocerciasis is a major public health problem in many parts of the world, with about 96% of all cases in Africa, mostly in the Western sub-Saharan region (Basáñez *et al*., 2006; WHO, 2011). Studies have estimated that over 37 million people are infected (Basáñez *et al*., 2006; Hoerauf, 2006; WHO, 2007). In 1995, the World Health Organization (WHO) Expert Committee on Onchocerciasis estimated that about 123 million people in over 34 countries in Africa, the Middle East, South America, and Central America were at risk of which 27 are in sub-Saharan Africa. Of the total at risk individuals, 18 million are infected of whom 500,000 were severely visually impaired. A further 270,000 were completely blind due to the disease (WHO, 2001).

The disease is a chronic, multisystemic disease caused by the filarial nematode parasite *Onchocerca volvulus*. Infection with this nematode is able to lead to severe dermatitis, visual impairment, and ultimately blindness (cited from Debrah *et al*., 2006). It is one of the leading infectious causes of blindness in the developing world second only to trachoma (Thylefors *et al*., 1995; WHO, 2001).

The third-stage infective larvae (L3) are transmitted by *Simulium spp* (blackfly). It is estimated that about 95% of onchocerciasis globally is transmitted by *Simulium damnosum* which is the major species in Africa (Crosskey, 1990; Crosskey and Howard, 2004). The vector transmits immature larval forms of the parasite from human to human and breeds along fast flowing rivers and streams (Blacklock, 1927; Duke, 1990; Opoku, 2000; WHO, 1995). For this reason, this disease is commonly known as river blindness. In the human body, the larva forms nodules in the subcutaneous tissue and matures into adult worms. Taylor and colleagues (2010) have indicated that the prevalence of infection and disease in a community is directly correlated to the proximity to riverine breeding sites of the blackflies with the highest burden of infection and disease in communities adjacent to rivers.

The prevalence of onchocerciasis is lowest in individuals aged between 0 to 10 years, and highest in those aged 20 – 30 years (Little *et al*., 2004a; Michael *et al*., 1996). The reason for the low prevalence in children aged between 0 to 10 years, who are mostly school pupils, is largely because of reduced exposure to bites from blackflies whose biting activity is greatest in the morning. Comparatively the disease is generally highly prevalent in men than women (Hailu *et al*., 2002). This trend has partially been attributed to increased exposure of blackfly bites in men, which are related to the occupational risk in farmers and fishermen (Little *et al*., 2004a).

A study by Little and colleagues (2004b) have shown that there is a direct association between microfilarial load and excess mortality among onchocerciasis patients. Within the onchocerciasis control programme cohort, blindness incidence has been shown to be associated with past microfilarial load in individuals surveyed (Little *et al*., 2004b). The infective larva of the parasite has the potential to develop into the adult filariae which has an average life expectancy of 10 years, during which period they produce millions of microfilariae (Habbema *et al*., 1990). The presence of these microfilariae in the skin of infected individuals is responsible for the physical manifestations of onchocerciasis. These manifestations include dermatitis, skin atrophy and inflammation of the eye, and over half of the infected people presenting with various skin diseases (Hoerauf *et al*., 2009; Thylefors *et al*., 1995; WHO, 1995).

Onchocerciasis also causes troublesome itching and skin changes. A multi-country study showed that over 30% of the population in endemic areas had onchocercal dermatitis (Hagan, 1998). In a survey of skin disease in 7 endemic sites in 5 African countries, 40 – 50% of adults reported troublesome itching (Murdoch *et al*., 2002). Murdoch and colleagues (1993) indicated that skin changes usually range from early reactive lesions such as acute papular onchodermatitis, chronic papular onchodermatitis and lichenified onchodermatitis ('Sowda') to late changes such as depigmentation and skin atrophy. Despite the high microfilarial loads in endemic areas, most patients present with subclinical or intermittent dermatitis corresponding to acute papular onchodermatitis, with little cellular attack against live microfilariae (Murdoch *et al*. 2002).

Due to the devastating effects of this disease and the detrimental effects on socioeconomic development, it is the aim of the world community to eliminate onchocerciasis as a public health problem (WHO, 1997). Efforts to eliminate onchocerciasis have evolved over the last 4 decades. The Onchocerciasis Control Programme in West Africa (OCP) was launched in 1974. This programme aimed at controlling the breeding of blackflies through aerial larviciding of fast flowing rivers and streams (Thylefors *et al*., 1995; WHO, 1995). The programme was undertaken in 11 endemic West African countries including Ghana until it officially ended in 2002 (Harlem, 2002).

At the end of the Onchocerciasis Control Programme in West Africa in 2002, all subsequent onchocerciasis control programmes were transferred to the participating countries (Borsboom *et al*., 2003), and it has almost entirely been based on periodic mass treatment using community-directed treatment with ivermectin (CDTI) (Remme, 1995). Current control programmes such as the African

Programme for Onchocerciasis Control (APOC) rely on community-based annual mass distribution of ivermectin, a highly effective microfilaricidal drug which reduces microfilaria loads in infected humans for several months thereby halting the transmission albeit transient by the insect vector (Molyneux *et al*., 2003; Remme, 1995).

In 1987, ivermectin (IVM) was registered for human use for the control of onchocerciasis (Thylefors and Lawrence, 2008) and later for lymphatic filariasis (Ottesen *et al*., 2008). The drug causes nematode paralysis by impairing neuromuscular function. Its primary effect is against microfilariae (mf) in the human body, which are the transmissible parasite stages of these diseases, often referred to as microfilaricidal effect. It also prevents the release of mf from the female worms' uteri and is called the embryostatic effect. The newly produced mf are blocked inside the uteri where they die and degenerate within four weeks post-ivermectin treatment (Schulz-Key, 1990). This effect is temporary and mf start progressively repopulating the skin and other tissues about three months after treatment (Basáñez *et al*., 2008).

Since the mid-1990's, IVM has been used extensively in mass drug administration campaigns across Africa by the Africa Programme for Onchocerciasis Control (APOC) [Amazigo, 2008], OCP in West Africa and the Global Program to Eliminate Lymphatic Filariasis (GPELF) [Coffeng *et al*., 2013]. Annually, more than 80 million people across the tropics are treated with IVM by MDA (MDP, 2009). Ivermectin mass drug administration has helped reduce transmission and mitigate the clinical manifestations of the infection (Awadzi *et al*., 1999; Goa *et al*., 1991).

A study by Alley and colleagues (1994) showed that a single treatment with ivermectin had a significant medium-term impact on microfilarial loads. In the same study it was observed that overall reduction of microfilarial loads observed between the base line survey and one year after the last treatment was 90% for the total population examined and over 93% for a cohort which received the drug at all 5 treatment rounds (Alley *et al*., 1994). Other studies have suggested that prolonged, high coverage of more than 80% of ivermectin treatment in endemic areas at 6 month intervals have a high probability of eliminating *O. volvulus* infection (Habbema *et al*., 1996; Plaisier *et al*., 1990; Winnen *et al*., 2002). This therefore suggests that ivermectin treatment has significant effect on the intensity and level of endemicity of *O. volvulus* infection.

1.2 Rationale

This infection is known to be endemic in 9 out of the 10 administrative regions of Ghana, except the Greater Accra region (Taylor *et al*., 2009). More than 3,200 communities in over 60 districts are affected with about 247 of these communities in Brong Ahafo and Ashanti regions been designated as Special Intervention Zones (SIZ). These designated areas are hyperendemic for onchocerciasis and are located in the Pru River basin that serves as foci of CDTI. About 3.4 million people are estimated to be at risk of onchocerciasis in Ghana (Taylor *et al*., 2009).

In 2006, high infectivity rates of 0.556 – 1.01 per 1000 parous flies were recorded from sites within the White Volta, Kulpawn, Anum and Pra River basins. Fly nuisance was significant in each of the surveyed sites (Taylor *et al*., 2009). This entomological and epidemiological survey indicated that fly infectivity levels and infection in humans required improved programme attention. A study conducted at the central region end of the Pra and Offin River recorded a CMFL range of 5 to 40.3mf/s which indicate *O. volvulus* infection remains a major public health problem along these rivers (Timmann *et al*., 2008).

A survey by Osei-Atweneboana and colleagues (2007), showed that despite 6 to 18 rounds of ivermectin treatment, microfilarial prevalence and community microfilarial load ranged from 2.2% to 51.8%, and 0.06 to 2.85mf/s respectively. Their results also suggested that the adult worms had not responded to the known suppressive effects of the multiple treatments of ivermectin previously administered. Several reports in Ghana have questioned the efficacy of ivermectin (Awadzi *et al*., 2004a; Osei-Atweneboana *et al*., 2007). However, a review of the impact of 10 – 12 years of IVM treatment in Cameroon revealed that IVM was very effective in controlling the public health aspect of the disease (Borsboom *et al*., 2003).

In Ghana, very little epidemiological studies have been done to assess the level of *O. volvulus* infection and impact of ivermectin MDA in the Akrofuom and New Edubiase sub-districts of the Adansi South District in the Ashanti region. These two sub-districts lie along the Ashanti region end of the Pra and Offin River basins and are largely composed of migrants from all the administrative regions of the country. These areas were known to be hyperendemic for onchocerciasis but very little data are available to help monitor the control of this infection.

This study examined the impact of ivermectin MDA on onchocerciasis in the Akrofuom and New Edubiase sub-districts of the Adansi South District in the Ashanti Region where IVM has been administered for the past three years. Using the prevalence of onchocercal nodules as described by Osei-Atweneboana *et al*. (2007) and the prevalence of microfilariae in the snip, the level of endemicity of *O. volvulus* infection was assessed. This study also sought to measure the public health importance and the intensity of *O. volvulus* infection using the community microfilaria load (CMFL), the reference index used in OCP.

1.3 Aim

The aim of the study was to assess the impact of ivermectin mass drug administration (MDA) on *O. volvulus* infection in Akrofuom and New Edubiase sub-districts of the Adansi South District in Ghana.

1.4 Specific Objectives

i. To assess the level of endemicity of *O. volvulus* infection by determining the prevalence of onchocercal nodules and microfilariae among the inhabitants in Akrofuom and New Edubiase sub-districts of Adansi South District.

ii. To assess the intensity of *O. volvulus* infection in the study areas using Community Microfilarial Load (CMFL), the reference index in OCP.

iii. To assess the impact of ivermectin mass drug administration on the intensity of *O. volvulus* and intestinal helminthic co-infections in Akrofuom and New Edubiase sub-district areas of Adansi South District in Ghana.

CHAPTER TWO

LITERATURE REVIEW

2.1 *Onchocerca volvulus* Infection

Onchocerca volvulus, one of the nine worldwide filarial nematode parasites in which humans are the definitive host, has been widely known for causing human onchocerciasis also known as river blindness. Onchocerciasis is an eye and skin infection, occurs through the bite of female blackflies of the genus *Simulium*, which bite during the day and are found near rapidly flowing rivers and streams.

The number of *O. volvulus* infections has been estimated to be more than 37 million worldwide (Basáñez *et al*., 2006; WHO, 2007) in 34 countries and are mostly in Africa. Endemicity of this infection extends latitudinally across the entire continent of Africa and into southwest Asia, with patchy foci in Yemen, and Oman in the Arabian Peninsula. Other countries in the Americas where infection occurs include Brazil, Venezuela, Mexico, Ecuador and Guatemala (Plate 1.1) [Thylefors, 2004].

In 1995, the World Health Organization Expert Committee on Onchocerciasis estimated that over 120 million people lived in areas where this infection was endemic (WHO, 1995). In 2001, it was estimated that 500,000 people and 270,000 people globally experienced secondary visual impairment and blindness, respectively (WHO, 2001). Nations with the highest historical prevalence of onchocerciasis included 11 sub-Saharan West African countries such as Ghana, Nigeria, Liberia, and parts of Mali. In these highly endemic areas, infection rates have been reported to be high as 80–100% among individuals aged 20 years with clinical manifestations peaking at 40 – 50 years of age (Duerr *et al*., 2011; Greene, 1992; WHO, 1995).

This infection often results in major socioeconomic liabilities, as working-aged adults are often the ones afflicted and debilitated leaving the young to care for the adults as well as to provide care for the family (Diemert, 2011; WHO, 1995). Research studies (Kirkwood *et al*., 1983; Prost, 1986; Prost and Vaugelade, 1981) have shown that hyperendemic regions are frequently depopulated due to a 3 to 4 folds increase in all-cause mortality compared to non-infected populations and decrease in average life expectancy by 7 – 12 years.

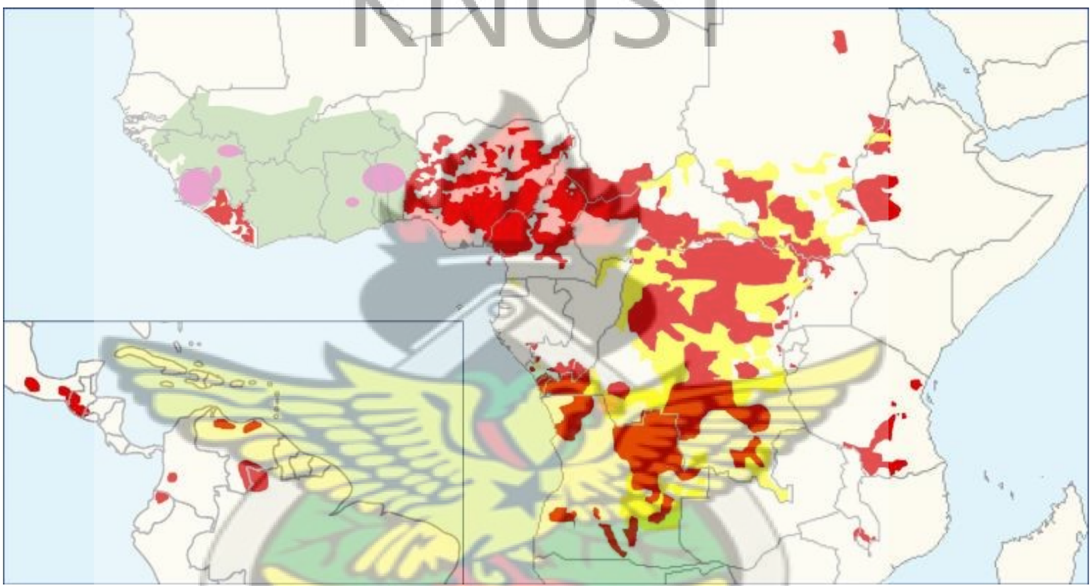

Plate 1.1: Global epidemiological distribution of *Onchocerca volvulus* infection (Source: Basáñez *et al*., 2006)

(Red, yellow, green and pink shaded denote -areas receiving ivermectin treatment, requiring further epidemiological surveys, covered by OCP in West Africa, Special Intervention Zones respectively).

Onchocerciasis has more than just an effect on the quality of life but also appears to shorten it. Little *et al*. (2004b), indicated an association between *O. volvulus* microfilarial load and all-cause mortality, claiming 5% of the deaths in the study's temporal and regional boundaries were attributable to this infection. It is one of the leading infectious causes of blindness in the world (WHO, 2001) second only to trachoma. Data have shown that patients with glaucoma in Ghana had a higher prevalence of onchocerciasis (mf positivity) [Egbert *et al*., 2005].

2.2 Life Cycle of *Onchocerca volvulus*

O. volvulus has a 5-stage life cycle, in which the blackfly (genus *Simulium*) acts as an obligate intermediate host (Blacklock 1927; Buttner *et al*., 1982). Evidence suggests that humans are the sole definite host, while no animal reservoirs have been found (Dozie *et al*., 2005; Krueger, 2006; Trpis, 2006)

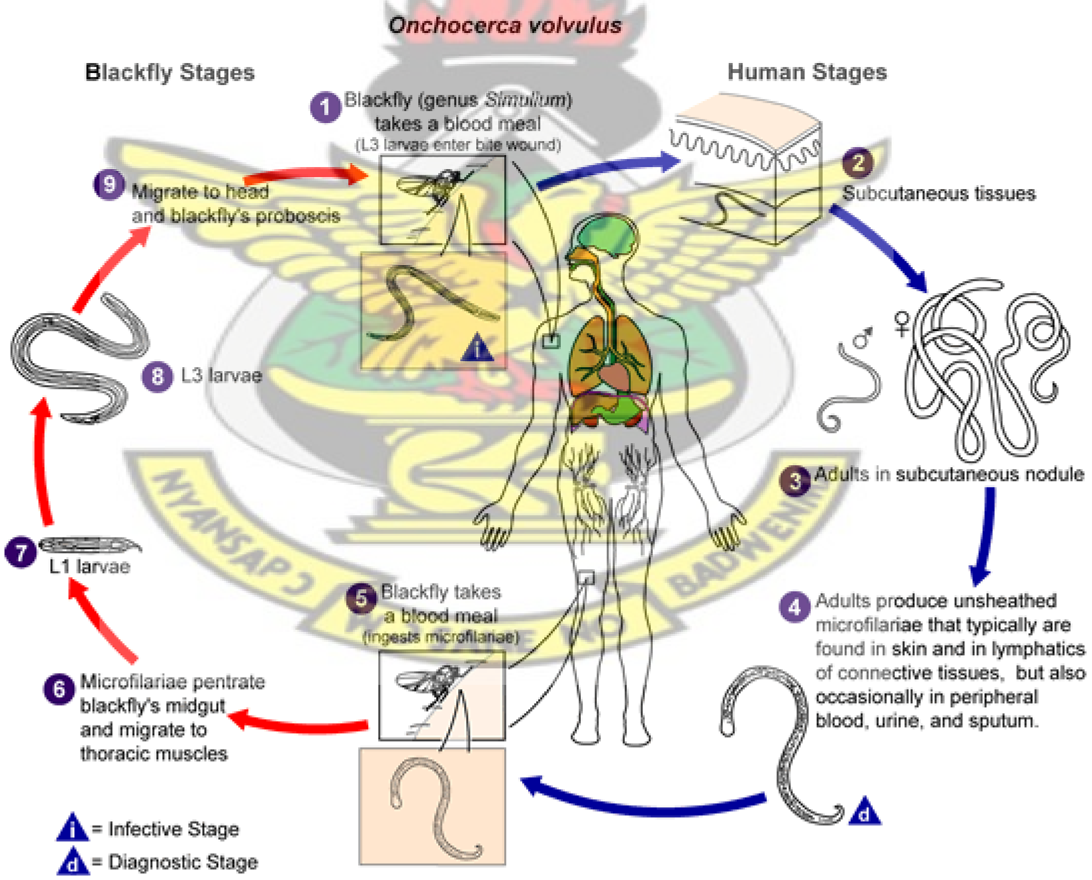

Figure 2.1: Diagrammatic Presentation of the Life Cycle of *Onchocerca volvulus*

(source: Centre for Disease Control (CDC), http://www.dpd.cdc.gov/dpdx)

Infection occurs when an infected blackfly introduces an *O. volvulus* stage 3 larvae (L3) into the human host during a blood meal. The female nematode develops to adulthood and permanently incarcerates itself in a fibrous capsule (nodules) in subcutaneous connective tissues, whereas male adults move freely throughout the skin and subcutaneous spaces. The female adult worms measure 33 – 50 cm in length and 270 – 400 µm in diameter, while males measure 19 – 42 mm by 130 – 210 µm. Within 10 to 12 months after initial infection, the female adult worms start producing microfilariae. During adulthood, the female worm sheds hundreds of thousands of unsheathed microfilariae with broad spatulate head and pointed tail free from nuclei measuring 220 – 360 µm by 5 – 9 µm (Little *et al*., 2004b) that can migrate through the skin of the human host, with particular affinity for the eyes. The inflammatory response against dying microfilariae over the years of repeated infection causes gradual blinding and eventual sclerosal opacification of the anterior eye by local inflammation and that of the posterior eye by autoimmune mechanisms (Hall and Pearlman, 1999). The microfilariae are occasionally found in peripheral blood, urine, and sputum but are typically found in the skin and lymphatics of connective tissues. The life cycle continues on uptake of microfilariae by the blackfly during a blood meal. After ingestion, the microfilariae penetrate the blackfly's midgut and migrate through the hemocoel to the thoracic flight muscles, where they develop into first-stage larvae and subsequently into third-stage infective larvae. The third-stage infective larvae migrate to the proboscis of the blackfly's feeding apparatus. They then enter another human host during a blood meal, thus completing the cycle.

Microfilariae persist in the human host for about 1 – 2 years, in contrast to the adult female worm life span, which ranges 2 – 15 years (Karam *et al*., 1987; Somorin, 1983). The reproductive life span of the adult averages 9 – 11 years, while the maximal production of offspring occurs during the first 5 years of the worm's reproductive life after which there is a linear decline (Buttner *et al*., 1982; Duke, 1993; Maso *et al*., 1987; Trpis, 2006)

2.3 Parasite, Vector and Host Dynamics of Onchocerciasis

Studies suggest that humans are the sole definite host of *O. volvulus* and no animal reservoirs have been found (Buttner *et al*., 1982; Krueger, 2006). The human host harbors various stages of the parasite. These include the infective (L3) larvae, the migrating and developing pre-adult forms, the adult male and female worms and the microfilariae (mf). Most of the adult worms are found in the subcutaneous onchocercal nodules (onchocercomata) in humans (Awadzi *et al*., 2004a). According to Gregory and Woolhouse (1993), it is typical for about 15% of individuals to serve as host to about 80% of helminth parasites in endemic human communities.

Epidemiological data show there are 2 forms of onchocerciasis in West Africa; onchocerciasis of the savanna regions and that of the forest zones (Bryceson *et al*., 1976; Duke and Anderson, 1972). Duke and Anderson (1972) have shown differences in pathogenicity in the savanna and forest strains of *O. volvulus.* Microfilariae taken from savanna patients produced worse keratitis after inoculation into the eyes of rabbits than did the microfilariae taken from patients in the forest zones (Duke and Anderson, 1972).

O. volvulus belongs to the family *Onchocercidae* and is the main causative parasite for onchocerciasis. Most filarial nematode parasites including *O. volvulus* contain an endosymbiont bacterium *Wolbachia*. *Wolbachia* has been demonstrated to be an essential endosymbionts for the parasite fertility and survival and its absence leads to disrupted or ceased larval development of *O. volvulus* (Saint Andre *et al*., 2002).

Simulium damnosum is the main vector in most parts of Africa and it is considered epidemiologically important in the transmission of onchocerciasis (Kutin *et al*., 2004; Opoku, 2000). In Latin America, *S. ochraceum*, *S. exiguum*, *S. metallicum*, and *S. guianense* are the main vectors in Mexico and Guatemala, Columbia and Ecuador, northern Venezuela, and southern Venezuela and Brazil respectively (Bradley *et al*., 2005; WHO, 2005). Evidence suggests the female blackflies belonging to the dipteran taxonomic family are the main vectors of human onchocerciasis in West Africa (Boakye *et al*., 1998). Their biting activities occur mostly in the morning and afternoon and are affected by factors such as light intensity, clouds, seasons, and temperature (Alverson and Noblet, 1976; Opoku, 2000; Saunders, 1976; Underhill, 1940). Opoku (2000) observed higher biting densities in the morning due to the stimulating effects of the morning sunlight after inactivity in the night and a general lull in biting activities in the afternoon due to high temperature conditions of about 32 ^{o}C.

According to the Basáñez *et al*. (2009) epidemiological patterns in vector-borne infections such as onchocerciasis are thought to be caused by the interactions between the parasites and the vectors. They suggested that the possible co-evolution of the *Onchocerca-Simulium* complex may give rise to local adaptations with the potential to stabilize the infection. Studies have also shown that the monthly onchocerciasis transmission potential, which is a basic index for assessing the infection transmission by the vectors, is comparatively higher in the rainy season than in the dry season (Cheke *et al*., 1992a; Opoku, 2000). Other scientists however oppose this observation and believe that the transmission potential is rather higher in the dry season than in the rainy season (Achukwi *et al*., 2000; Cheke *et al*., 1992b).

Models which have been adduced to explain the dynamics of transmission have found that a nonlinear relationship exists in terms of the dependence on densities of host, parasites and vector to drive transmission (Basáñez *et al*., 2006; Basáñez *et al*., 1994; Soumbey-Alley *et al*., 2004). Several studies suggest that, factors such as the intensity and seasonality of transmission, the *Onchocerca-Simulium* complex, the parasite distribution among hosts, the density-dependent processes operating upon the parasite's life cycle, and all these will control interventions and their coverage will determine the stability of the host-parasite interactions and our efforts to push this infection below transmission levels (Basáñez and Ricárdez-Esquinca, 2001; Churcher *et al*., 2005; Duerr *et al*., 2005).

2.4 Clinical Presentation of *O. volvulus* infection

Egbert and colleagues (2005) observed that in *O. volvulus* - infected people, clinical manifestations are highly variable and may either appear asymptomatic or symptomatic. Patients are asymptomatic in about 10% of cases. Symptoms of onchocerciasis usually indicate the stage of development of the parasite and the host's immunological response, and are mainly caused by the inflammatory response to dead or dying microfilariae (Hall and Pearlman, 1999). They do not appear until after the L3 larvae mature into adult worms.

The earliest symptoms are fever, arthralgia, and transient urticaria involving the trunk and face. Basáñez and colleagues (2006) also described onchocerciasis as a systemic disease. Systemic manifestations of onchocerciasis may include weight loss (reduced body mass index), musculoskeletal pain, inguinal hernias, and systemic embolization of microfilariae (Burnham, 2007; Kale, 1998; Murdoch *et al*., 2002; Richards *et al*., 1998).

Typically, dermatologic manifestations are the initial presenting symptoms; infected individuals with symptoms usually exhibit one or more of the three general manifestations: (i) onchocercal dermatitis, (ii) ocular onchocerciasis and/or (iii) subcutaneous bumps or nodules (onchocercomata), with the most severe presentation consisting of eye lesions that can progress to blindness (CDC, 2008; Hagan, 1998). Eye lesions occur after many years of repeated infection resulting in severe infection. They are usually not common amongst people under the age of 30 years (Hall and Pearlman, 1999). Epidemiological studies (Duke, 1981; Woodruff *et al*., 1977) have shown that there is high prevalence of blindness in the endemic communities in the western savanna woodlands of Africa, whereas cutaneous symptoms are more prevalent in the rainforest and in the East African highlands.

In patients with chronic disease, the cutaneous manifestations may be differentiated across a spectrum, from pruritic lichenification on one end to asymptomatic depigmentation, commonly referred to as “Leopard skin” on the other.

2.4.1 Onchocercal dermatitis

Onchocercal dermatitis is the most common symptom of the disease. A multi-country study showed that more than 30% of the population in endemic areas had onchocercal dermatitis (Hagan, 1998). Its initial manifestations can occur anywhere on the body and may include itching, scratching and alterations in skin pigmentation. Pruritus may be intermittent and mild, continuous and severe, or may be absent altogether. The most troubling symptom suffered by those affected is itching (Hagan, 1998). A survey of skin disease in 7 endemic sites in 5 African countries, 40 – 50% of adults reported troubled itching (Murdoch *et al*., 2002). Reactive onchocercal dermatitis and troublesome itching were common in all age-groups and were an important cause of stigma in most endemic communities (Hailu *et al*., 2002; Kale, 1998)

A papular rash may appear anywhere on the body. The papules may be small and densely packed or large and separated. The maculopapular rash is often associated with severe pruritus. Excess scratching often times lead to bleeding, ulceration, and secondary infection. A clinical classification system of onchocercal dermatitis was developed to standardize and facilitate the collection of data worldwide (Murdoch *et al*., 1993).

2.4.2 Acute papular onchodermatitis (APOD)

It is characterized by solid, scattered, pruritic papular rash. Vesicles or pustules at the apex may or may not be present. The obliteration of the skin creases due to edema also may or may not be present.

2.4.3 Chronic papular onchodermatitis (CPOD)

This also presents with a scattered, pruritic, hyperpigmented, and flat-topped papulomacular rash. The diameter of the papules is at least 3mm, with or without excoriations. In populations where onchodermatitis is endemic, the most common skin manifestation is chronic papular onchodermatitis (Hagan, 1998)

2.4.4 Lichenified onchodermatitis (LOD)

It is characterized by raised, discrete, pruritic, and hyperpigmented papulonodular plaques associated with lymphadenopathy. The lesions may be confluent, with or without the presence of excoriations.

2.4.5 Atrophy

This involves wrinkled and dry skin. Firmly pressing the edge of a finger along the skin reveals additional fine wrinkles. In patients younger than 50 years, atrophy is considered as a significant abnormality. In populations where onchodermatitis is endemic, the third most common skin manifestation is onchocercal atrophy (Hagan, 1998).

2.4.6 Depigmentation

It is also characterized by areas of incomplete pigment loss, with associated islands or spots of normally pigmented skin surrounding hair follicles. Leopard skin is similar, except that it is characterized by a complete loss of pigmentation, with islands or spots of normally pigmented skin around the follicles. It is a characteristic finding in older patients (Lazarov *et al*., 1997). It involves depigmentation of the pretibial areas of the lower extremities. This pattern is initially seen as discrete depigmented macules, with sparing of the hair follicles but later, macules become confluent, involving a large area of the anterior portions below the knee. This pattern can sometimes be seen in the groin or lower abdomen as well (Meyers *et al*., 1977; Vernick *et al*., 2000). In populations where onchodermatitis is endemic, the second most common skin manifestation is depigmentation (Hagan, 1998). Leopard skin is characteristically found in older people and it involves depigmentation of the pretibial areas of the lower extremities (Figure 2.2) [Kipp and Bamhuhiiga, 2002].

Figure 2.2: A volunteer with leopard skin presentation (Source: Author, 2013)

2.4.7 Other Skin Presentations

These include 'Sowda' and 'lizard skin'. Sowda is a severe form of dermatitis and is associated with an active delayed hypersensitivity response. They usually present with dark, thickened, intensely pruritic skin with papules. The regional lymph nodes are soft, nontender, and enlarged. Sowda is usually localized to a single lower extremity. Less common, more generalized form can involve both lower extremities and/or other parts of the body. They are usually amicrofilaridermic (Kale, 1998; Richard-Lenoble *et al*., 2001; Vernick *at al*., 2000). With lizard skin, there is generalized hyperpigmented and ashy appearance of the skin resulting from chronic onchodermatitis.

2.4.8 Onchocercomata

The infective larvae (L3) that survive in the human host molt within one week to form an L4 larva, which continue to develop into male and female adult worms within 1 – 3 months. These adult worms reside in the deep dermis and facial planes. Thick, fibrous, subcutaneous nodules called onchocercomas are formed as the result of the development of scar tissue around the adult worm. Onchocercoma is usually firm nodule in the subcutaneous tissue and usually contains 2 to 3 female adults and 1 to 2 male adults. The nodules vary in size from one to five centimeters in diameter and can cause discomfort, but are not usually painful (WHO, 2010). Dead worms may also calcify within the nodule. They are often surrounded by eosinophils and lymphocytes (Duke, 1993; Maso *et al*., 1987; Trpis, 2006)

These nodules are generally located over the bony prominences, and are easily palpable. In Africa, the nodules are often observed along the iliac crests, ribs, greater trochanters and ischial tuberosities (Figure 2.3) [Dozie *et al*., 2005]. Juxta-articular areas such as the knees, elbows, patella, and scalp, may also have nodules. Onchocerciasis in the Americas leads to fewer nodule formation with greater tendency to be located on the scalp, where the risk of ocular complications is generally higher than that located in other areas of the body. However, in Yemen onchocercomas are less common in onchocerciasis patients (Buttner *et al*., 1982).

A  B 

Figure 2.3: Nodules at the (A) right iliac crest region (B) left trochanter of a volunteer (nodule indicated by arrow head) [Source: Author, 2013]

2.4.9 Ocular onchocerciasis

Ocular manifestations of onchocerciasis are late, serious reactions that occur in about 5% of affected persons (Kale, 1998). Ocular onchocerciasis has been found in more than 1 million infected individuals (Kale, 1998). Variations exist in blindness rate in different geographical areas possibly attributed to biological variants (Kale, 1998; Murdoch *et al*., 2002; Stingl, 1997).

Onchocerciasis is more likely to lead to blindness in Africa than in the Latin America. It is estimated to be about 7 times less frequently blinding in the forest areas than in the savannah- nonforested areas. Cross-experimental infections had indicated strong local adaptation and heterologous incompactibility among the *Onchocerca-Simulium* complex to be responsible for the distinct distribution and severity of onchocercal blindness (Basáñez *et al*., 2009). Ocular onchocerciasis covers a wide spectrum ranging from mild symptoms such as itching, redness, photophobia, diffuse keratitis, and blurring of vision to more severe symptoms of corneal scarring, night blindness, intraocular inflammation, glaucoma, visual field loss and eventually blindness (Enk *et al*., 2003). Inflammatory reactions around microfilariae occurring in the eye have been shown to be responsible for ocular onchocerciasis (Egbert *et al*., 2005).

Ocular lesions which result from the migration of microfilariae to eye tissues and the inflammatory response invoked by their death, can involve all eye tissues except the lens, ranging from punctuate and sclerosing keratitis (anterior segment) to optic nerve atrophy (posterior segment) [Basáñez *et al*., 2006; Taylor *et al*., 2010; WHO, 2010]. Punctuate keratitis, which signifies initial involvement is transient and reversible with treatment, whereas long term infection results in sclerosing keratitis, iridocyclitis and inflammation in the anterior chamber and retinal epithelium (Egbert *et al*., 2005; Taylor *et al*., 2010). Lesions of the posterior segment may follow, including chorioretinitis, optic neuritis, and optic atrophy (Newland *et al*., 1991). Blindness may occur as a result of long-term exposure to the microfilariae (Burnham, 1998). Due to the devastating effect of *O. volvulus* infection in Africa and parts of the Americas, the world community aims to eliminate it as a public health problem (WHO, 1997).

2.5 Global Control of Onchocerciasis

Initial control efforts were implemented by Non-Governmental Oganizations (NGOs) and the Onchocerciasis Control Programme (OCP) in West Africa. The OCP was created in 1974 with a mandate to eliminate onchocerciasis in 7 countries in the Volta River Basin. These countries included Benin, Burkina Faso, Côte d'Ivoire, Ghana, Mali, Niger and Togo. The main intervention then was aerial larviciding directed against the blackfly aquatic stages. Weekly larviciding of the vector breeding grounds were implemented by OCP with the sole purpose of interrupting transmission. Towards the later period of OCP, ivermectin treatment was started. After 28 years of implementing OCP, it was estimated by Harlem (2002) that about 600,000 cases of blindness were prevented, 18 million children born in at-risk areas were freed from the risk of blindness, and 25 million hectares of land made safe for human resettlement.

In 1993, the Onchocerciasis Elimination Program for the Americas (OEPA) was established through regional partnership to eliminate all morbidity from onchocerciasis in foci of the 6 affected Latin American countries (Richards *et al*., 2004). Prior to OEPA, focal vector control was conducted in Guatemala with some degree of success (Ochoa *et al*., 1997). OEPA's strategy is currently based on biannual ivermectin mass treatment.

By 1995, ivermectin was considered efficacious and was made freely available to OCP countries. After the end of OCP in 2002, followed the establishment of multinational, multiagency partnerships such as the Africa Programme for Onchocerciasis Control (APOC) in 1995 to cover the remaining 19 African countries not covered under OCP (Blanks *et al*., 1998; Dull and Meredith, 1998; Etya´ale, 1998). The Onchocerciasis Control Programme has demonstrated that the prevalence and the intensity of infection with *O. volvulus* could be reduced to insignificant levels through vector control (Remme *et al*., 1990a). Both OEPA and APOC are exclusively concerned with supporting large scale ivermectin treatment programmes based on community distribution. Whereas the OEPA aims at eliminating the parasite altogether from most affected areas in Latin America, the

APOC seeks only to establish a sustainable community-directed drug distribution system in the countries concerned and thereby to eliminate serious onchocerciasis and eventually, to have a telling impact on transmission.

Control of other filarial infections including onchocerciasis, currently relies on mass drug administration (MDA) programmes based on the drug donation programmes from Mectizan® (Ivermectin) – Merck and Co. Inc® and Albendazole (GlaxoSmithKline®). Ivermectin alone is administered for control of onchocerciasis by MDA, while for lymphatic filariasis in Africa, the combination of IVM with albendazole is used and in Asia, where there are no onchocerciasis endemic areas, diethylcarbamazine citrate (DEC) is given alone or in combination with albendazole.

Studies have shown that these drugs are mainly microfilaricidal (Awadzi *et al*., 1999; Gyapong *et al*., 2005; Ottesen *at al*., 1997) and the strategies need to be sustained for extended periods to cover the reproductive lifespan of the long-lived adult worms. The drug must also be administered to a large population in order to interrupt transmission. Currently, programmes for onchocerciasis control (APOC and OEPA) together with lymphatic filariasis (GPELF) have been established to promote and sustain the application of MDA in affected communities (Dadzie *et al*., 2003; Molyneux *et al*., 2003).

2.6 Ivermectin and Onchocerciasis Control

Ivermectin is currently the sole drug approved by the World Health Organisation (WHO) for use in onchocerciasis control programmes (Awadzi *et al*., 2003; Boatin and Richards, 2006; Taylor *et al*., 2010; WHO, 2010). Ivermectin has contributed substantially towards the alleviation of suffering caused by onchocerciasis in 34 countries of Africa, the Eastern Mediterranean and Latin America (Dull and Meredith, 1998).

Ivermectin is an avermectin compound, which belongs to the macrocyclic lactones class of endectocides derived from the bacterium *Streptomyces avermitilis* (Geary, 2005). The mechanism by which ivermectin kills mf is not known with certainty, but the drug interferes with glutamate gated ion channels that can affect parasite contractility and release of immunomodulatory molecules by the parasite (Moreno *et al*., 2010). It acts by increasing the membrane permeability to chloride ions, mediating the paralysis of the nematodes and certain class of ectoparasites. Peak ivermectin serum concentrations are reached approximately 4 – 5 hours after administration. The half-life of IVM in various populations ranges from 12 to 56 hours (Kitzman *et al*., 2006).

Its primary effects have been against microfilariae (mf) in the human body, which are the transmissible parasite stages of the disease. Ivermectin has broad antiparasitic activity against nematodes (Enk, 2006). It is a potent microfilaricide which has also been shown to partially interrupt embryogenesis after frequent application (Awadzi *et al*., 1999; Osei-Atweneboana *et al*., 2007; Pfarr and Hoerauf, 2006). Studies show that annual ivermectin treatment is adequate to control onchocercal ocular disease even in populations with very high endemicity levels (Dadzie *et al*., 1991). Other studies have also shown that ivermectin is effective in alleviating dermatological symptoms associated with onchocerciasis (Whitworth *et al*., 1996). A Cochrane review asserts that mass treatment with ivermectin has been shown to effectively and significantly reduce infection rate in flies and humans (Ejere *et al*, 2012; Remme *et al*., 1990b; Taylor, 1990).

Pattern observed by Alley and colleagues (1994) in ivermectin use was that, there was a marked reduction of microfilarial loads shortly after each treatment followed by a steady repopulation of the skin until a subsequent treatment round. Their research also found out that even a single treatment with ivermectin had a significant medium-term impact on microfilarial loads, with microfilarial counts stabilized around 55% of pretreatment counts 2 to 4 years after a single treatment. Repopulation data of microfilariae from a study undertaken by Whitworth and colleagues (1996) suggested that adult female worms were still alive and fecund after repeated ivermectin treatment, strongly enforcing the need to continue treatment to cover the lifespan of the female worms (Enk, 2006).

Ivermectin is usually administered at a dose of 150 to 200 μg/kg of body weight. At recommended dose of 150μg/kg, it neither kills nor permanently sterilizes the adult worms (Awadzi *et al*., 1995), although it has been shown to impair the ability of the female worms to produce microfilariae (Duke *et al*., 1992; Klager *et al*., 1996; Plaiser *et al*., 1995). In an endemic area for lymphatic filariasis (LF), a meta-analysis of 748 patients showed that administration of ivermectin alone at a single dose induced nearly complete clearance of microfilariae from the blood of LF patients from the first day to 30 days post treatment followed by gradual recurrence of microfilaria and increase in intensity. Higher doses of IVM showed greater clearance effects and maintained lower mf levels for a longer time. The findings of the meta-analysis suggested that ivermectin given at a single dose of 200 μg/kg body weight or higher, had great potential for therapeutic strategies to control bancroftian filariasis (Cao *et al*., 1997).

Ivermectin is administered to all those aged 5 years or older, excluding pregnant women and those breastfeeding a child younger than one week old annually or bi-annually to reduce morbidity, disability and lower transmission (Boussinesq *et al*., 1997; Collins *et al*., 1992; Tielsch and Beeche, 2004).

Generally ivermectin is well tolerated, however there are a few adverse events associated with the drug which may appear 1 to 2 days after treatment. These adverse events usually correlate with an individual's microfilarial load, with high mf loads corresponding to substantial adverse events such as nausea, dizziness, pruritus, urticaria, dermatitis, fever, myalgia and oedematous swelling of the limbs and face (Taylor *et al*., 2010). A major difficulty however arises with ivermectin treatment of onchocerciasis in areas co-endemic for loasis (Boussinesq and Gardon, 1997; Taylor *et al*., 2010), especially since patients with high *Loa loa* microfilariae loads may develop encephalitis due to the rapid killing of the microfilariae (Boussinesq *et al*., 2001; Gardon *et al*., 1997). However *Loa loa* is not endemic in Ghana.

Despite successful mass drug administration and vector control, several studies have suggested that this infection was far from being eradicated with the emergence of reports of ivermectin suboptimal response in Ghana (Awadzi *et al*., 2004a; Awadzi *et al*., 2004b).

2.7 Current Status of Onchocerciasis in Ghana

Onchocerciasis has an estimated at-risk population of 3.4 million in Ghana. It affects 3204 communities in 66 districts in 9 out of 10 regions. Greater Accra Region is the only region that is not endemic for onchocerciasis. About 247 of these communities in Brong Ahafo and the Ashanti Regions have been designated as Special Intervention Zones (SIZ) because these areas are hyperendemic.

Ghana's SIZ areas include the Pru River basin covering a population of 85,000 with a prevalence of 7.8%. The Oti River basin and its tributaries in Togo cover a population of 185,000 and has a prevalence of 21.7%.

Since the devolution of the former Onchocerciasis Control Programme (OCP) and the inception of the SIZ program, the country has focused its package of intervention in areas identified as onchocerciasis transmission hot zones. These onchocerciasis transmission hot zones in Ghana include the Pra, Pru, Black Volta, the Oti and Asukawkaw River basins (APOC, 2010). In Ghana, these areas are marked as high priority zones for ivermectin MDA.

2.8 Ivermectin Distribution in Ghana

Ivermectin remains the principal drug of use under the onchocerciasis control programme in Ghana. Its distribution in Ghana started with the use of mobile teams in 1987. By 1988, the community directed treatment with ivermection (CDTI) was adopted for the MDA and remains the delivery approach. In Ghana, ivermectin treatment also started in lymphatic filariasis and onchocerciasis co-endemic areas in 2001 and has undergone a gradual upscaling to cover about 61 endemic districts by year 2005. It was estimated that over 3.4 million people were treated through CDTI from 2002 to 2007. This represented a coverage range from 48.4% to 79.1%.

It has been observed that there appears to be a declining uptake of treatment in these communities (APOC, 2010). However, data from the Ghana National Onchocerciasis Control Programme, indicates there has been a marked improvement both geographic and therapeutic coverage since 2006 to first round of ivermectin treatment in 2009.

Table 2.1 CDTI data for Ghana National Onchocerciasis Control Program since 2006 (source: APOC midterm evaluation report, 2010)

Year	Treatments		Coverage (%)	
	Persons	Communities	Therapeutic	Geographic
2006	1,269,341	1,963	65.4	88.9
2007	1,544,155	1,851	72.8	82.8
2008	1,835,162	3,244	71.8	97.9
2009 (1st round)	544,959	1,280	75.8	93.7

Since 2006 onchocerciasis control has been implemented in the context of the Neglected Tropical Diseases Control Programme (NTDCP), a 5 year programme designed to integrate and scale up delivery of preventive chemotherapy for 5 targeted neglected tropical diseases (NTDs) including onchocerciasis. Implementation of this programme started in April 2007 on a pilot basis in 5 regions of Ghana; Northern Region, Upper East Region, Upper West Region, Western Region and Brong Ahafo Region (GHS, 2008).

There have been joint programmes around the community-directed mass drug administration that have included lymphatic filariasis, schistosomiasis and vitamin A distribution. In 2007, the NTDCP took delivery of over 25.5 million ivermectin tablets and over 8 million tablets of Albendazole for distribution to endemic regions in Ghana (APOC, 2010).

Many control efforts have been implemented using ivermectin MDA by multiagencies to eliminate *O. volvulus* infection especially in Ghana. The aim of this study is to assess the impact of ivermectin mass drug administration (MDA) on *O.*

volvulus infection in Akrofuom and New Edubiase sub-district areas of Adansi South District in Ghana.

CHAPTER THREE

MATERIALS AND METHODS

3.1 Study Area and Population

The study was conducted in 19 onchocerciasis endemic communities in the Akrofuom and New Edubiase sub-districts, at the Adansi South District in the Ashanti Region of Ghana. According to the Neglected Tropical Disease Control Programme report, the population of the two sub-districts is 46,753 (NTDCP, 2012). The Adansi South District is one of the 27 districts in the Ashanti Region of Ghana, and the southern-most district in the Ashanti Region. The District shares borders with Central and Eastern Regions to the south and east respectively, and with Adansi North, Obuasi Municipal, Bosome Freho in the Ashanti Region to the North-East, North-West, and South-West respectively. The District capital is New Edubiase which is about 92 km from Kumasi on the main Kumasi-Bekwai-Cape Coast trunk road. It is bounded to the west by River Offin and the east by River Pra. It is worthy to note that there are also two confluences within the District, namely; the confluences of Rivers Offin and Pra and Birim and Pra respectively (MOFA, 2013).

The major occupation of the inhabitants of these communities is farming, mainly cocoa farming. The district is home to eight forest reserves which include ardwood lumber, a major asset to the district. Most of the communities lie very close to River Pra, one of the major rivers in Ghana and serves as one of the ideal breeding site for the vector, blackfly (*Simulium spp*), for *O. volvulus* infection.

The district is considered as hyper-endemic for this infection according to mapping carried out by the Onchocerciasis Control Programme (OCP) of the Ghana Health Service (GHS, unpublished data). According to the local Disease Control Officers in these two sub-districts, ivermectin MDA distribution started in 2009.

Most of the houses in these communities are made of mud, with bamboo and palm leaves used for roofing. A notable number of these houses however had Aluminium-roofing. The district is very diverse with different ethnic groups such as the Northerners, Krobos, Ewes, Fantis, Akwapims, Akims and the indigenous Adansi of Ashanti who reside there. These multi-ethnic settlers have come from near and far to engage in cocoa farming which is the principal economic activity in the District. The district is made up of two constituencies namely New Edubiase and Akrofuom Constituencies. The District covers an area of 889 sqkm; about 4% of the total area of Ashanti Region.

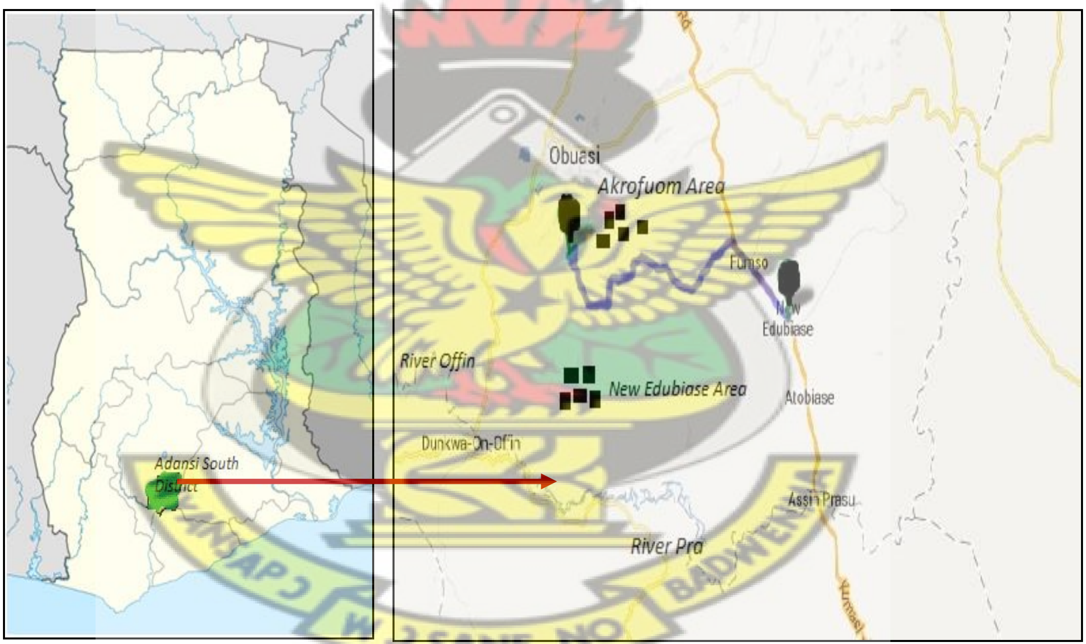

Plate 2.1 Map of Study Area: Adansi South District

3.2 Ethical Approval

This study was approved by the Committee on Human Research, Publication and Ethics (CHRPE) of the School of Medical Sciences of the Kwame Nkrumah University of Science and Technology (KNUST) and Komfo Anokye Teaching

Hospital (KATH), Kumasi, Ghana. The study conformed to the principles of the Helsinki Declaration of 1964 (as revised in 1983, 2000, and 2004).

Additional permission to conduct the study in the selected communities was sought from the Akrofuom and New Edubiase sub-district Health Directorates of the Adansi South District of the Ashanti Region in Ghana. Meetings were also held in all the participating communities with the chiefs, opinion leaders and inhabitants to explain the nature, purposes and procedures of the study in the local language (Twi), which was the most common language of communication among inhabitants and non-inhabitants of the participating communities. Written informed consent was obtained from all participants either by thumb-printing or signing.

3.3 Study Design

This study was an epidemiological assessment of the level of endemicity and intensity of *O. volvulus* infection and the impact of ivermectin treatment. It was conducted in 19 endemic communities in Akrofuom and New Edubiase sub-districts of the Adansi South District in the Ashanti Region of Ghana. Sampling was conducted from May, 2011 to October, 2012.

This study was conducted in two major phases. The first phase of the study involved the examination of all the volunteers in these communities for the presence of palpable onchocercal nodules (onchocercoma). This examination of the palpable onchocercal nodules was done by a highly skilled and experienced Medics/Scientist with over 10 years work experience in onchocerciasis research. Only volunteers who had satisfied the inclusion criteria were admitted into the study. Volunteers deemed eligible, based on the inclusion and exclusion criteria described in Section 3.3.1 and 3.3.2 were enrolled into the study. A total of 1,223 volunteers were enrolled.

The second phase of this study involved assessing the volunteers for microfilaria loads. In all 444 volunteers were selected into this phase of the study from all the 19 study communities. Skin snips (skin biopsies) were then taken from each volunteer to determine the microfilarial (mf) load in the skin.

3.3.1 Inclusion criteria for enrolment of volunteers

i. Living in the endemic area for onchocerciasis
ii. Volunteers of both sexes, at least 18 years old and older
iii. Willingness to participate in the study by signing or thumb-printing the Informed Consent Form (ICF)

3.3.2 Exclusion criteria for enrolment of volunteers

i. Volunteers under the age of 18 years old
ii. Psychiatric disease that affects the ability of the participant to understand and cooperate with the study protocol.

3.4 Study Procedure

3.4.1 Enrollment of study volunteers

In each community the purpose of the study was explained to the chief and elders, and their permission to proceed was secured. All volunteers were advised that participation was voluntary and all who were willing to participate in this study and met all the inclusion criteria were admitted into the study after signing or thumb-printing the Informed Consent Form (ICF). All participants in this study volunteered to participate and at no time were any of them persuaded to be included.

3.4.2 Examination for onchocercal nodules

Characteristics of onchocercal nodules were described to all volunteers as hard, mobile nodules favoring bony-prominences outside the inguinal and cervical regions. The presence of subcutaneous nodules was determined according to the standard World Health Organization (WHO) protocol (WHO, 1994) and prevalence determined as described by Osei-Atweneboana *et al.* (2007). Prior to the standardized physical assessment for nodules, participants were asked if they were aware of any nodules present. Each volunteer was examined for the presence of subcutaneous onchocercal nodules (onchocercoma). The body was systematically inspected following a standardized routine that gave particular attention to the bony prominences by palpation. This examination was done by Dr. Mrs. Linda Batsa-Debrah, a research biologist with more than 10 years research experience in onchocersiasis. She is a senior research scientist at the Kumasi Centre for Collaborative Research in Tropical Medicine (KCCR), KNUST in Kumasi, Ghana.

3.5 Parasitological Examinations and Analysis

3.5.1 Determination of skin microfilarial loads

Skin microfilarial loads of each volunteer were assessed to determine the prevalence of microfilaria and the intensity of *O. volvulus* infection. This was done using skin biopsies taken from the left and right buttocks to determine the microfilariae per milligram of skin. Although this procedure was invasive, it is currently considered the "golden standard" in detecting the presence of *O. volvulus* microfilariae in infected populations. According to Guzman *et al*. (2002), skin biopsies are a very specific method and as such are in line with the World Health Organization (WHO) strategy on the needs of surveillance methods to be highly specific despite concerns of low sensitivity.

3.5.2 Skin biopsy and microfilariae count

Holth-corneoscleral punches were used to take bloodless skin biopsies from each volunteer in the study. Two skin biopsies, one from the upper part of the right and left buttocks (iliac crest) were taken from each volunteer. This was done at least 8 months after the last ivermectin (MDA) intervention. Before the taking of the skin biopsy, the skin (left and right iliac crest regions) were disinfected and cleaned using 70% alcohol with swaps and allowed to dry. Using the Holth-corneoscleral punch, the skin biopsy was taken and each biopsy was immersed in 100µl of 0.9% NaCl solution in a separate well of a 96 well round bottom microtitre plate (Nunc, Roskilde, Denmark) and labeled with the volunteer's unique identification code number. The snipped area was dressed by covering with a sterile plaster. The punches were thoroughly sterilized using 10% Mucocit™ solution (1 in 10 dilution of stock solution with distilled water) for between 5 - 10 minutes according to the manufacturer's protocol.

The wells of the plates were then covered with adhesive tape to prevent evaporation and spilling of the contents during transportation from the field (village) to the laboratory at the New Edubiase Government Hospital at New Edubiase. The skin biopsies in the plates were incubated overnight at room temperature to allow the mf to emerge out of the skin into the saline solution.

During the microfilaria count, the solution in each well was thoroughly mixed and pipetted onto a glass slide for microscopic examination. Microfilariae were then counted using 10-fold magnification of a compound microscope (Axiostar Plus, Gottingen, Germany). Each skin biopsy was blotted to remove excess moisture and weighed using OHAUS Adventurer Pro analytical electronic balance (OHAUS, New Jersey, USA) and the number of mf from each biopsy determined as mf per milligram (mf/mg) of skin. The geometric mean of the mf from the two skin biopsies from each patient was calculated and used as a measure of intensity of infection.

3.5.3 Determination of community microfilarial load (CMFL)

Intensities of *O. volulus* infection in the communities were also assessed with community microfilaria load (CMFL), the reference index used in OCP, as the geometric mean of the individual microfilarial loads (including zero counts) in volunteers aged 20 years or older. This calculation was done using log (n+1) transformation, where n is the individual microfilaria load per snip (mf/mg) [Remme *et al.*, 1986].

3.5.4 Examination of stool samples for intestinal helminths

Each volunteer snipped was given a sterile, screw-capped stool container with an applicator and asked to provide fresh stool (faeces) sample no more than 10 millilitres (ml) in volume. All stool samples were examined within 12 hours of the same day of collection for infection with intestinal helminthes. The concentration technique for stool examination was used in the preparation and examination of each stool sample.

3.5.5 Concentration technique for stool examination

The concentration technique procedure was performed mainly to separate the parasites from fecal debris. The concentration procedure not only increases the number of parasite in the sediment but also unmasks them, making them more detectable. In this study, the Formol-Petrol Concentration Technique was used.

About 10ml of 10% v/v formol-saline was added to approximately 1 gram of freshly collected stool sample in a plastic, screw-capped lid container labeled with each volunteer's unique identification number. It was then thoroughly emulsified, looking for blood, mucous, pus and worms. A double layer of 400 μm mesh size surgical gauze was fitted into a funnel and the funnel placed on top of a new, correspondingly well-labeled 15 ml falcon centrifugation tube.

The stool-formol-saline suspension was poured through the surgical gauze filter into the falcon tube until 10ml mark was reached. The filter, together with the trapped lumpy residue, was removed from the funnel and discarded.

About 3ml of petrol was added to the filtered suspension in the falcon tube and shaken vigorously for about 30 seconds to mix well. The falcon tube containing the suspension mixture was centrifuged at 900g (600 rpm) for 3 minutes (Megafuge®, Thermo Scientific). After centrifuging, the fatty plug was loosened with an applicator stick and the supernatant poured off by quickly inverting the falcon tube and its content in a sink.

Each falcon tube was placed in a rack and the fluid on the sides of the tube was allowed to drain down to the sediment. The sediment at the bottom of the tube was mixed well and a drop was transferred onto a well-labeled glass microscope slide using a Pasteur pipette. A 22 X 22mm microscope coverslip was carefully placed onto the drop on the microscope slide such that no bubble formed under the preparation.

The whole area under the coverslip was then examined using the 10X and 40X objectives of a light compound microscope (Axiostar Plus, Gottingen, Germany) for the presence of ova and larvae of intestinal helminthes. Slides that were positive for ova and/or larvae of intestinal helminthes were recorded.

3.6 Statistical Analyses

Statistical analyses were done using Microsoft Excel® 2007, Stata® 11.0 and Minitab 16® software programmes. The raw data was entered using Microsoft Excel® while all the other statistics were done using Stata® 11.0 and Minitab 16®. Descriptive statistics were used to obtain general descriptive information such as the mean and standard deviation from the data. Paired t-test analysis was used to compare two proportions or groups. For non-parametric data sets, analyses were done using Mann-Whitney U test for unpaired data that were not normally distributed. A p-value less than 0.05 ($P < 0.05$) was considered statistically significant.

CHAPTER FOUR

RESULTS

4.1 Demographic Data of the Study Volunteers

A total of 1,223 volunteers from 19 villages were recruited for this study. All the volunteers were examined for the presence of onchocercal nodule (onchocercoma). Out of the 1,223 volunteers, 50.1% were males with a mean age of 39.6 years and age range of 18 to 87 years, and 49.9% were females with a mean age of 38 years and age range of 18 to 78 years. There was no significant difference between the mean ages for both sexes (p=0.188). The overall mean age was 38.8 years (Table 4.1).

Table 4.1: Demographic data of study volunteers

Gender of study volunteers	Number of volunteers	Age (mean±SD)/years
Male	613	39.6 ± 12.8
Female	610	38.0 ± 12.3
Total	1223	38.8 ± 12.6

Out of 1,223 volunteers, 444 (36.3%) were skin snipped for microfilarial load assessment. Of the 444 snipped volunteers, 250 (56.3%) were males with a mean age of 39.1 ±10.9 years and age range of 19 to 63 years, while 194 (43.7%) were females with a mean age of 39.9 ±10.1 years and age range of 18 to 60 years. There was no significant difference between the mean ages of both sexes (p=0.509). The overall mean age for this group was 39.5 ±10.5 years.

4.2 Nodule Prevalence Assessment

A total of 1,223 volunteers were recruited for nodule prevalence assessment in the 19 study communities.

Table 4.2: Nodule prevalence rates for *O. volvulus* in the 19 onchocerciasis-endemic study communities

	Nodule Presence status		
Study communities	**Total number of volunteers examined**	**Number with nodules (Nodule positive)**	**Prevalence (%)**
Akrofuom area, (n=14)			
Abusa	76	29	38.2
Adjeikrom	70	24	34.3
Adoosu	63	26	41.3
Akuapim	111	42	37.8
Alata	98	36	36.7
Amoakokrom	74	25	33.8
Betenase	121	50	41.3
Bredi	9	7	77.8
Essonkrom	73	28	38.4
Mensonso 1	111	28	25.2
Mensonso 2	80	25	31.3
Ofrikrom	16	9	56.3
Yadome	114	50	43.9
Yaw Owusukrom	73	43	58.9
Sub-total	1089	422	**(38.8)**
New Edubiase area, (n=5)			
Brodekor	13	9	69.2
Essonkrom	54	38	70.4
Aniapam	29	18	62.1
Otutu	17	9	52.9
Sonkowuah	21	15	71.4
Sub-total	134	89	**(66.4)**
Total	1223	511	**41.8**

Mann Whitney U test (p- value) between the two study areas p=*0.0107*

Table 4.2 represents the nodule prevalence assessment of the study population. Out of 1223 volunteers, palpable nodules (onchocercoma) were found in 511 volunteers representing an overall nodule prevalence of 41.8%. The prevalence in the study communities ranged from 25.2% to 77.8% (Table 4.2).

The overall results from the nodule palpation showed that Akrofuom sub-district area had a nodule prevalence of 38.8% while that of New Edubiase sub-district was 66.4%. Comparing the prevalence in the Akrofuom area to New Edubiase area showed that there was a significant difference between the two areas (Mann Whitney U test, p=0.0107). This indicates that inhabitants in the New Edubiase sub-district, which lies very close to the Pra River, had more palpable onchocercal nodules than those at Akrofuom sub-district.

Amongst the 14 study communities in the Akrofuom sub-district, Bredi was the smallest with a total of 9 volunteers largely due to its small size. Although Bredi had the lowest number of volunteers, it gave the highest prevalence of palpable nodules (77.8%). The largest study community in the area was Betenase where 121 volunteers turned up for nodule examination out of which 50 (41.3%) were found to be nodule positive (Table 4.2). Only one of the 14 study communities in the area had a nodule prevalence of more than 75% (Bredi) indicating hyper-endemicity, 12 communities had nodule prevalence of between 30-75%, indicating meso-endemicity and one community (Alata) had a nodule prevalence of less than 30% indicating hypo-endemicity as described by Vivas-Martinez and colleagues (2000).

In the New Edubiase area, all the communities had nodule prevalence between 30 - 75% indicating meso-endemicity, with the highest prevalence recorded in Sonkowuah (71.4%) and the lowest prevalence recorded in Otutu (52.9%) from Table 4.2.

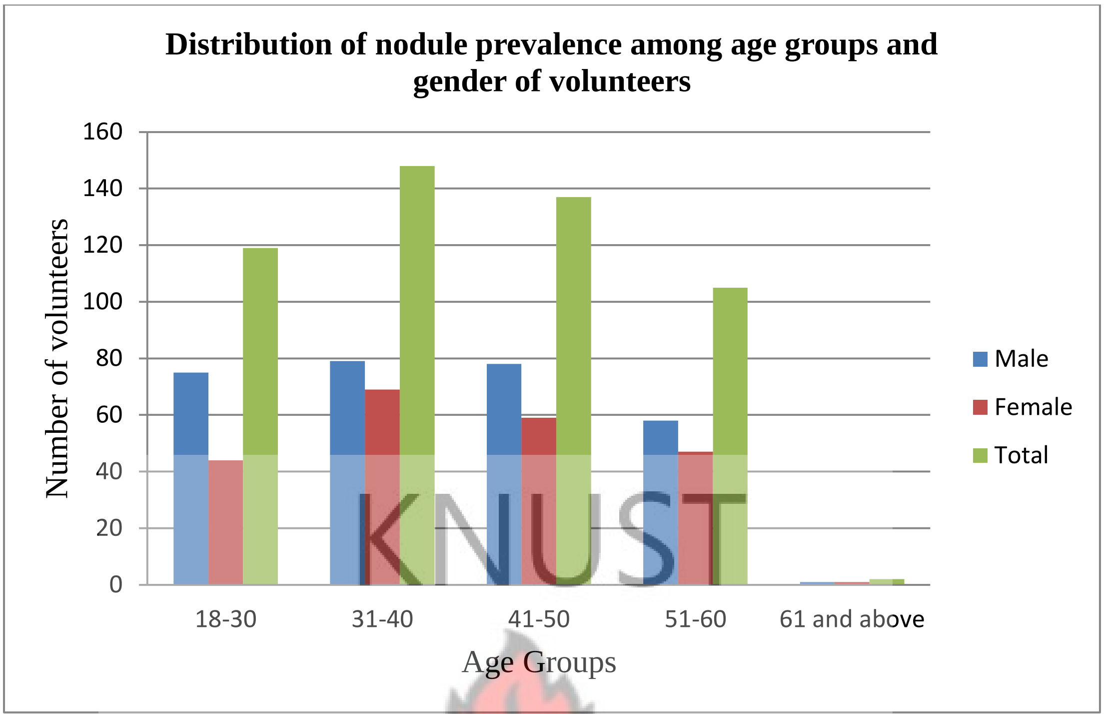

Figure 4.1: Histogram graph of prevalence of nodules among age groups and gender of volunteers

Figure 4.1 shows a histogram graph of age-group and gender-dependent assessment of onchocercal nodule prevalence. Out of 511 nodule positives, 291 (57%) were males while the remaining 220 (43%) were females. Comparatively, the result suggested that there was a higher prevalence of palpable onchocercal nodules among males than females but there was no significant difference between them (p=0.057). It also indicated that onchocercal nodules were present among all selected age groups with the highest prevalence among volunteers aged 31 to 40 years.

The histogram (Figure 4.1) showed that the prevalence of onchocercal nodules kept increasing with age in both males and females until the age of 40 years, where it began to decline with age increase. In males however, prevalence of onchocercal nodules plateaued between 40 to 50 years. There was no such observation in the female group.

4.3 Microfilarial Prevalence Assessment

For microfilarial loads assessment, 444 were selected from the 1,223 volunteers and snipped for microfilariae count. In the males, the microfilarial load range was 0 – 93.2 mf/mg while that of the females was 0 – 158.6 mf/mg of skin.

Table 4.3: Microfilarial status of volunteers and prevalence rates for *O. volvulus* in the study communities

Study communities	Total number of volunteers examined	number of volunteers with:		mf prevalence (%)
		No mf	mf	
Akrofuom sub-District				
Abusa	27	11	16	59.3
Adjeikrom	17	8	9	52.9
Adoosu	13	3	10	76.9
Akuapim	30	10	20	66.7
Alata	15	13	2	13.3
Amoakokrom	17	8	9	52.9
Betenase	51	19	32	62.7
Bredi	9	2	7	77.8
Essonkrom	18	2	16	88.9
Mensonso 1	28	18	10	35.7
Mensonso 2	12	4	8	66.7
Ofrikrom	16	9	7	43.7
Yadome	37	25	12	32.4
Yaw Owusukrom	22	12	10	45.5
Sub-total	312	144	168	**53.8**
New Edubiase sub-District				
Brodekor	13	6	7	53.8
Essonkrom	54	26	28	51.9
Aniapam	29	13	16	55.2
Otutu	16	5	11	68.7
Sonkowuah	20	8	12	60.0
Sub-total	132	58	74	56.1
Total	**444**	**202**	**242**	**54.5**

Mann Whitney U test (p- value) between the two study sub-districts p=1.*0000*

Tables 4.3 showed that out of 444 volunteers selected randomly for skin microfilarial load assessment, 242 of the study volunteers were microfilariae positive, giving an overall microfilarial prevalence of 54.5%. The prevalence however, varied greatly between the 19 study communities with a range of 13.3% to 88.9%. Alata had the lowest microfilarial prevalence of 13.3% while Essonkrom in the Akrofuom sub-district had the highest microfilarial prevalence of 88.9% (Table 4.3).

The Akrofuom sub-district had overall microfilarial prevalence of 53.8%, and New Edubiase sub-district had overall microfilarial prevalence of 56.1%. Although the prevalence in New Edubiase sub-district was relatively higher than Akrofuom sub-district, there was no significant difference between the two sub-district study areas (Mann Whitney U test, p=1.000). In all, only one community (Alata) had a microfilarial prevalence of less than 30% suggesting hypoendemicity, 15 communities had microfilarial prevalence between 30 - 75% indicating meso-endemicity and 3 communities had microfilarial prevalence of more than 75% indicating hyperendemicity as described by Vivas-Martinez and colleagues (2000).

Using nodule and microfilarial prevalence as parasitological indices to assess the degree of endemicity as described by Osei-Atweneboana *et al*. (2007), of the 19 study communities, Bredi had the highest endemicity level with a nodule and microfilarial prevalence of 77.8% and 77.8% respectively. The result also suggested that, although the two study sub-districts were classified as meso-endemic for *O. volvulus* infection, the level of endemicity in the New Edubiase sub-district was higher than Akrofuom sub-district.

4.4 Community Microfilarial Load Assessment

In all, microfilarial loads for 440 of the snipped volunteers were used to determine the community microfilarial load (CMFL) for the study communities. Four out of 444 volunteers were excluded due to the age limitation (Remme *et al*., 1986).

Table 4.4: Community microfilarial loads for the study communities

Study communities	Total number of volunteers examined	CMFL
Akrofuom area		
Abusa	27	2.3
Adjeikrom	17	1.8
Adoosu	11	4.3
Akuapim	30	3.0
Alata	15	1.4
Amoakokrom	17	2.3
Betenase	51	3.1
Bredi	9	2.5
Essonkrom	18	5.2
Mensonso 1	28	1.4
Mensonso 2	12	3.6
Ofrikrom	15	1.6
Yadome	36	1.5
Yaw Owusukrom	22	2.1
Sub-total	308	**2.4**
New Edubiase area		
Brodekor	13	1.7
Essonkrom	54	2.9
Aniapam	29	3.5
Otutu	16	4.1
Sonkowuah	20	3.0
Sub-total	132	**3.0**
Total	440	
Mann Whitney U test between the two study sub-districts		p = 0.3539

From Table 4.4, the CMFL of the 19 study communities ranged between 1.4 to 5.2 microfilariae per milligram (mf/mg). Both Alata and Mensonso 1 had the lowest CMFL of 1.4mf/mg, while Essonkrom in the Akrofuom sub-district had the highest CMFL of 5.2mf/mg. The Akrofuom sub-district recorded a CMFL range of 1.4 - 5.2 mf/mg with the lowest CMFL of 1.4mf/mg recorded at Alata and Mensonso 1, while Essonkrom had the highest of 5.2mf/mg. The overall CMFL of the Akrofuom area was 2.4mf/mg. In the New Edubiase sub-district, the CFML range was 1.7 – 4.1mf/mg. Brodekor had the lowest CMFL of 1.7mf/mg, while Otutu had the highest CMFL of 4.1mf/mg. The overall CMFL of the New Edubiase area was 3 mf/mg (Table 4.4).

There was no significant difference between the CMFL for New Edubiase and Akrofuom sub-districts (Mann Whitney U test, p=0.3539), which means that the intensity of infection in New Edubiase and Akrofuom were not too varied, both within the CMFL limit of 5 mf/mg (Table 4.4). Results from Tables 4.2, 4.3 and 4.4 showed that the New Edubiase sub-district, with a mean microfilarial prevalence of 56.1%, nodule prevalence of 66.4% and CMFL of 3.0mf/mg had a higher endemicity and intensity of *O. volvulus* infection than the Akrofuom sub-district (mean microfilarial prevalence of 53.8%, nodule prevalence of 38.8% and CMFL of 2.4mf/mg).

4.5 Microfilarial Load Densities in the Study Communities

Table 4.5: Variation of microfilarial load densities in the study communities (Percentage of number of volunteers in parenthesis)

Study communities	Total number of volunteers with mf	Number of volunteers with microfilariae per mg of snip of:					
		0.1-4.9	**5-9.9**	**10-29.9**	**30-49.9**	**50-79.9**	**≥80.0**
Akrofuom area							
Abusa	16	10(63%)	1(6%)	5(31%)	0	0	0
Adjeikrom	9	7(78%)	0	2(22%)	0	0	0
Adoosu	10	6(60%)	2(20%)	2(20%)	0	0	0
Akuapim	20	13(65%)	1(5%)	3(15%)	1(5%)	2(10%)	0
Alata	2	0	2(100%)	0	0	0	0
Amoakokrom	9	6(67%)	1(11%)	1(11%)	1(11%)	0	0
Betenase	32	13(41%)	5(16%)	9(28%)	4(12%)	0	1(3%)
Bredi	7	5(72%)	1(14%)	1(14%)	0	0	0
Essonkrom	16	6(38%)	5(31%)	5(31%)	0	0	0
Mensonso 1	10	8(80%)	2(20%)	0	0	0	0
Mensonso 2	8	5(63%)	0	2(25%)	0	1(12%)	0
Ofrikrom	7	6(86%)	1(14%)	0	0	0	0
Yadome	12	9(75%)	2(17%)	1(8%)	0	0	0
YawOwusukrom	10	5(50%)	2(20%)	2(20%)	1(10%)	0	0
New Edubiase area							
Brodekor	7	5(71%)	2(29%)	0	0	0	0
Essonkrom	28	12(43%)	5(18%)	5(18%)	3(11%)	0	3(10%)
Aniapam	16	6(38%)	1(6%)	6(38%)	1(6%)	2(12%)	0
Otutu	11	4(37%)	3(27%)	2(18%)	0	2(18%)	0
Sonkowuah	12	5(42%)	1(8%)	6(50%)	0	0	0
Total	**242**	**131**	**37**	**52**	**11**	**7**	**4**
	(100%)	(54%)	(15%)	(22%)	(4%)	(3%)	(2%)

Table 4.5 shows the variation of microfilarial load densities among the mf-positive volunteers in the study communities. Out of the 242 volunteers, 131(54%) had mf densities between 0.1 - 4.9 mf/mg and represent the largest group. Alata was the only community with no volunteer with mf within that density range. The 10 – 29.9 range was the second largest group with 52(22%). Only Betenase (in the Akrofruom area) and Essonkrom (in the New Edubiase area) had volunteers in the mf density range of ≥80.0 mf/mg, which was the smallest group with 4 (2%) volunteers. The microfilarial load densities recorded in New Edubiase were generally higher compared to Akrofuom area.

4.6 Comparison of Age and Sex of Microfilariae Positive Volunteers

Table 4.6: Age and gender-dependent assessment of microfilariae positive volunteers

		Prevalence of microfilariae by gender		
Age Group	**Total**	**Males (%)**	**Females (%)**	**Overall Prevalence (%)**
18 - 30	57	40 (70.2)	17 (29.8)	23.5
31 - 40	74	42 (56.8)	32 (43.2)	30.6
41 - 50	59	35 (59.3)	24 (40.7)	24.4
51 - 60	52	31 (59.6)	21 (40.4)	21.5
61 and above	0	0	0	0.0
	242	148 (**61.2**)	94 (**38.8**)	**100**

(Paired t-test for males against females, p = 0.042)

Table 4.6 shows the age-group and gender-dependent assessment of microfilariae positive volunteers. Among the microfilariae positive volunteers, 148 of them were males representing 61.2% and 94 (38.8%) were females. Comparatively, this infection was significantly higher in male than the female volunteers (p=0.042).

4.7 Comparison of Number of Nodules with Microfilarial Status

Table 4.7: Comparison of number of nodules with microfilarial status

Number of nodules	Total number of volunteers examined	Number of volunteers with:	
		No mf	mf
0	**132**(29.7%)	89(67.4%)	43(32.6%)
1	**125**(28.2%)	52(41.6%)	73(58.4%)
2	**91**(20.5%)	37(40.7%)	54(59.3%)
3	**57** (12.8%)	16(28.1%)	41(71.9%)
4	**20**(4.5%)	4(20%)	16(80%)
5	**7** (1.6%)	1(14.3%)	6(85.7%)
6	**5** (1.1%)	1(20%)	4(80%)
7	**3** (0.7%)	1(33.3%)	2(66.7%)
8	**1** (0.2%)	0	1(100%)
9	**2**(0.5%)	0	2(100%)
11	**1**(0.2%)	1(100%)	0
	444 (100%)	202	242

In Table 4.7, comparison was made between the numbers of palpable nodules found per volunteer to microfilarial status. Volunteers with no palpable nodules contributed to 29.7% of the total study population. Among those with no palpable nodule, 43 (32.6%) of them were found to have microfilariae. Volunteers with one palpable nodule contributed to 28.2% while volunteers with 2 palpable nodules were 20.5% of the total volunteers. Among volunteers with 1 nodule, 73 (58.4%) out of

125 were found to be microfilariae positive. In the volunteers with 2 nodules, 53 (58.2%) out of 91 were also microfilariae positive. Volunteers with 3 to 7 palpable nodules contributed to 20.5% of the total snipped population. Volunteers with 8 to 11 nodules per person only contributed to 0.9% of the total snipped population. There was one volunteer with 11 palpable nodules but had no microfilaria load. The general observation from Table 4.7 showed that the percentage of volunteers with microfilarial positivity increased with increasing number of nodules with exception of the only volunteer with 11 small palpable nodules.

4.8 Number of Rounds of Ivermectin against Microfilarial Status

Table 4.8: Comparison of number of rounds of ivermectin treatment against microfilarial status of volunteers

Rounds of IVM treatment	Total number of volunteers examined	Number of volunteers with:	
		No mf	mf
0	189(42.6%)	84(44%)	105(56%)
1	121(27.2%)	48(40%)	73(60%)
2	79(17.8%)	38(48%)	41(52%)
3	36(8.1%)	19(53%)	17(47%)
4	8(1.8%)	4(50%)	4(50%)
5	6(1.4%)	4(67%)	2(33%)
6	4(0.9%)	4(100%)	0
9	1(0.2%)	1(100%)	0

Table 4.8 shows the distribution of volunteers using the number of rounds of ivermectin treatment against microfilarial status in the communities. From this Table,

189 volunteers representing 42.6% had not taken ivermectin treatment before and had the highest number of volunteers with mf. Only one volunteer had taken 9 rounds of ivermectin treatment and had no microfilariae. From this table, it was observed as the number of rounds of ivermectin treatment increased, the percentage of volunteers with no mf increased. All volunteers with 6 – 9 rounds of IVM treatments had no mf.

4.9 Number of Rounds of Ivermectin against Microfilarial Load Densities

Table 4.9: Comparison of number of rounds of ivermectin treatment with microfilarial load densities

Rounds of IVM treatment	Total number of mf positives	Number of volunteers with microfilariae per snip (mf/mg) of:					
		0.1-4.9	**5-9.9**	**10-29.9**	**30-49.9**	**50-79.9**	**>80.0**
0	105	41(39%)	21(20%)	28(26.7%)	8(7.6%)	5(4.8%)	2(1.9%)
1	73	50(68.5%)	12(16.4%)	8(11%)	1(1.4%)	1(1.4%)	1(1.3%)
2	41	22(53.6%)	4(9.8%)	12(29.3%)	2(4.9%)	0	1(2.4%)
3	17	14(82.3%)	0	2(11.8%)	0	1(5.9%)	0
4	4	3(75%)	0	1(25%)	0	0	0
5	2	1(50%)	0	1(50%)	0	0	0
6	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0

Table 4.9 compares the number of rounds of ivermectin treatment with microfilarial load densities. Volunteers with 0 to 1 round of ivermectin treatment recorded microfilarial load densities in all the 6 mf density groups. However, volunteers with one round of IVM had 68.5% of them having mf density between 0.1 – 4.9 compared to those with no IVM treatment (39%). Volunteers with 2 rounds of ivermectin

treatment were found in all the groups except 50 -79.9 density group. Those with 3 rounds of ivermectin treatment were found in only 3 groups. Volunteers with 4 and 5 rounds of ivermectin treatment had members only in 0.1 – 4.9 and 10 – 29.9 density groups. Volunteers with 6 and 9 rounds of ivermectin had no representation in any of the mf density groups. Out of the four volunteers in the highest mf density group (≥80mf/mg), two of them had never taken ivermectin treatment while the remaining two have each had 1 and 2 treatment rounds. The density of mf declined as the treatment rounds increased.

4.10 Number of Rounds of Ivermectin against Microfilarial and Nodule Status

Table 4.10: Comparison of number of rounds of ivermectin treatment with microfilarial and nodule status

Rounds of Ivermectin	Total number of volunteers examined	mf-nodule- (endemic normals)	mf+nodule- (Mf positives only)	mf-nodule+ (Nodule positives only)	mf+nodule+
0	**189** (42.6%)	49 (25.9%)	24 (12.7%)	35 (18.5%)	81 (42.9%)
1	**121** (27.2%)	23 (19%)	14 (11.6%)	25 (20.7%)	59 (48.7%)
2	**79** (17.8%)	6 (7.6%)	3 (3.8%)	32 (40.5%)	38 (48.1%)
3	**36** (8.1%)	4 (11.1%)	1(2.8%)	15 (41.7%)	16 (44.4%)
4	**8** (1.8%)	2 (25%)	1(12.5%)	2 (25%)	3 (37.5%)
5	**6** (1.4%)	2 (33.3%)	0	2 (33.3%)	2 (33.3%)
6	**4** (0.9%)	3 (75%)	0	1 (25%)	0
9	**1** (0.2%)	0	0	1 (100%)	0
	444(100%)	**89** (20%)	**43** (9.7%)	**113** (25.5%)	**199** (44.8%)

From Table 4.10, the study volunteers were classified into four main groups according to microfilarial and nodule status. These groups were microfilaria-negative-nodule-negative (mf-nodule-) referred to as endemic normals (EN), microfilaria-positive-nodule-negative (mf+nodule-) referred to as mf-positives only, microfilaria-negative-nodule-positive (mf-nodule+) also referred to as nodule-positives only, and microfilaria-positive-nodule-positive (mf+nodule+). These groups were compared against the number of rounds of ivermectin treatment to observe the impact of ivermectin treatment on microfilaria and nodule status.

Among the 444 volunteers who were snipped for assessment of microfilarial load, 312 (70.3%) were nodule positive while 132 (29.7%) were nodule negative. Out of the 312 volunteers who were nodule positive, 199 (63.8%) were microfilariae positive. Among the 132 nodule-negative volunteers snipped, 43 (32.6%) were microfilariae positive.

The result from Table 4.10 showed that 89 out of 444 volunteers were mf-nodule-(EN) representing 20% of the study population. The majority, 49 (55%) in this group had never taken ivermectin treatment and only 3 volunteers had taken 6 rounds of ivermectin, the maximum intake in this group. The mf+nodule- group (mf-positives only) had 43 volunteers representing 9.7% of the study population. A total of 24 (55.8%) of this group had never taken ivermectin treatment and only one volunteer had taken 4 rounds of ivermectin treatment. There was no volunteer in this group who had taken 5 or more rounds of IVM. The mf-nodule+ also had 113 volunteers representing 25.5% of the study population. Thirty-five (31%) volunteers in this group had also never taken ivermectin. However the majority (69%) of them had taken between 1 to 9 rounds of treatment. The mf+nodule+ formed the largest group with 199 volunteers representing 44.8% of the entire population assessed. Out of this group, 81 (40.7%) had never taken ivermectin while 118 (59.3%), the majority have had 1 to 5 rounds of treatment. There was no representation in this group for those who had taken 6 or 9 rounds of IVM treatment (Table 4.10).

4.11 Demographic Characteristics of Ivermectin-naïve Volunteers

Table 4.11: Characteristics of ivermectin-naïve volunteers (non-compliance)

Variable	Frequency	Percentage
Sex		
males	112	59.3%
female	77	40.7%
Age-groups		
18-30	54	28.5%
31-40	58	30.7%
41-50	47	24.9%
51-60	30	15.9%

A total of 189 volunteers snipped had never taken ivermectin despite the effect of ongoing MDA. Table 4.11 showed that non-compliance among male volunteers (59.3%) was higher than in the females (40.7%). Among the various age groups, non-compliance was also shown to be higher among the younger age groups with the highest percentage in volunteers aged 31- 40 years (30.7%) [Table 4.11].

4.12 Prevalence of Intestinal Helminths

As part of this study, co-infection with intestinal helminths was also studied (Table 4.12). Co-infection with intestinal helminths was studied in 363 out of the 444 volunteers in the study who provided stool samples. In all 16 out of the 363 volunteers were found to be infected with intestinal helminths indicating a prevalence of 4.4%.

Table 4.12: Co-infection of intestinal helminths among the study volunteers

		Intestinal helminth (IH)		
Study communities	**Total number of volunteers examined**	**hookworm**	***S. stercoralis***	***Taenia spp***
Akrofuom area				
Abusa	22	1	0	0
Adjeikrom	17	0	0	0
Adoosu	12	0	0	0
Akuapim	28	1	1	0
Alata	13	1	0	0
Amoakokrom	16	2	0	0
Betenase	51	2	0	0
Bredi	7	0	0	0
Essonkrom	16	0	0	0
Mensonso 1	27	1	0	0
Mensonso 2	12	0	0	1
Ofrikrom	16	1	0	0
Yadome	35	2	0	0
YawOwusukrom	22	0	2	0
	294	**11**	3	**1**
New Edubiase area				
Brodekor	10	0	0	0
Essonkrom	33	0	1	0
Aniapam	12	0	0	0
Otutu	7	0	0	0
Sonkowuah	7	0	0	0
	69	**0**	**1**	**0**
Total	**363**	**11(3%)**	**4(1.1%)**	**1(0.3%)**

From the 16 infected volunteers, 11 of them had hookworm representing 3% of the studied population, four of them had *Strongyloides stercoralis* representing 1.1%, while one had *Taenia spp* representing 0.3%. All the cases of hookworm were recorded in the Akrofuom sub-district with no case in New Edubiase sub-district. Three (75%) out of 4 with *S. stercoralis* was observed in the Akrofuom sub-district with only one case (25%) observed in the New Edubiase sub-district. Only one case of *Taenia spp* infection was observed in the study occurring in the Akrofuom sub-district (Table 4.12). In all 15 of the 16 infection with intestinal helminthes occurred in the Akrofuom sub-district indicating an area intestinal helminth prevalence of 5.1%. The intestinal helminth prevalence in New Edubiase sub-district was 1.4%.

CHAPTER FIVE

DISCUSSION

5.1 Introduction

Onchocerca volvulus infection is a highly debilitating filarial disease and remains an important public health problem for many countries in Africa especially the sub-Saharan countries including Ghana (Basáñez *et al.*, 2006). As a result of the devasting effect of this infection, Merck & Co. Inc. in 1987 took an unprecedented decision to donate ivermectin (IVM) for as long as needed to eliminate this infection as a public health problem (Meredith and Dull, 1998). In Ghana, mass drug administration (MDA) of ivermectin started in 1987, and the ultimate intervention goal is to reduce the community microfilarial load (CMFL) to below 0.05 mf/mg by 2015 (GHS, 2008). In this study, the impact of ivermectin MDA on the level of endemicity and intensity of this infection was examined in the Akrofuom and New Edubiabe sub-districts of the Adansi South District in the Ashanti region where IVM has been administered for the past 3 and 5 years respectively.

Firstly the level of endemicity of *O. volvulus* infection is discussed using the prevalence of onchocercal nodules and microfilariae while the intensity of the infection is discussed using the community microfilarial load (CMFL) as described by Osei-Atweneboana *et al.* (2007). A nodule and microfilarial prevalence of more than 75% in this group would be indicative of hyperendemic status in the community, between 30 and 75% is indicative of mesoendemicity, and below 30% is hypoendemicity as described by Vivas-Martinez *et al.* (2000). For the assessment of infection, community microfilarial load (CMFL) exceeding 5mf/mg was used to indicate whether or not the infection is a significant public health problem in the communities (APOC, 2010).

5.2 Level of Endemicity of *O. volvulus* infection in the Study Communities

According to Basáñez and colleagues (2006), the true burden of onchocerciasis has largely been underestimated. In this study an attempt was made to establish the true level of endemicity of *O. volvulus* infection in these two sub-districts by determining the prevalence of onchocercal nodule and microfilariae. Out of a total of 1,223 volunteers assessed for onchocercal nodules, which has been shown to be a highly significant risk factor for all forms of onchocercal skin disease (Ozoh *et al*., 2011), 41.8% were found to be nodule positive. The nodule prevalence obtained for New Edubiase and Akrofuom sub-Districts were 66.4% and 38.8% respectively. Using the nodule prevalence assessment alone means that these areas are meso-endemic for *O. volvulus* infection.

The analysis from this present study showed significant geographical variation in patterns of nodule prevalence. The average nodule prevalence observed in the New Edubiase sub-district was significantly higher than that of the Akrofuom area. This indicates that most of the inhabitants in the New Edubiase sub-district developed more nodules compared to those in the Akrofuom sub-district which means this infection was more endemic in New Edubiase compared to Akrofuom sub-district. Both sub-districts are adjacent to each other and are located in the forest zone with New Edubiase being closer to the Pra River. The findings from this study also confirmed that this infection is more common in areas closest to rivers or streams that serves as breeding site of the blackflies with the highest burden of infection and disease in communities adjacent to rivers (Kayembe *et al*., 2003; Law *et al*., 1998; Taylor *et al*., 2010).

In this study, 47.5% and 36.1% of male and female volunteers respectively had palpable nodules. The result of this epidemiological survey further suggested that the prevalence of palpable nodule was higher in males than in females but there was no significant difference between both genders. Patterns of *O. volvulus* infection have been shown to vary markedly with locality, sex- and age-dependent exposure to the vector (Filipe *et al*., 2005). The reason for the lack of differences between males and females was that, both males and females in these communities are equally involved in farming and hence the levels of exposure to the blackfly bites are similar. In this study, almost all the male volunteers were continually engaged in farming irrespective of their age and thus explain for the higher prevalence among males compared to females because of increased exposure to blackfly bite in males. Opara and Fagbemi (2008) have also attributed this trend to different pattern in sex-dependent exposure to black flies' bites, with men being more exposed.

Nodule prevalence levels among the various age groups were not significantly different. However, it was observed that while the nodule prevalence in females declined sharply after age 40 years, in males there was a plateau phase between aged 40 to 50 years before it declined sharply (Figure 4.1). According to Filipe *et al*. (2005), host age- and sex-heterogeneous exposure largely explains for local-specific infection patterns. The reason for this observation was that males between 40 to 50 years continually engaged in active farming activity whiles in the females there was a reduction in active farming hence the reduced exposure to blackfly bite in females compared to their male counterparts as observed also by Opara and Fagbemi (2008). Additionally, most of the women by 40 years assume full roles of mothers and spend most of their time performing house chores leading to reduced exposure to fly bites. Immunological studies by Sahu *et al.* (2008) suggest

IgA which seems to be more produced in females compared to male plays a protective role in filarial infections.

The overall microfilarial prevalence of 54.5% and what was obtained in each of the sub-districts from this study also confirms that these study sub-districts are meso-endemic for this infection. The microfilarial assessement also showed that the infection was more endemic in New Edubiase than Akrofuom although there was no significant difference between the two areas. The change from hyperendemic status in 2009 (GHS, unpublished data) to a meso-endemic status could be due to the impact of ivermectin MDA since there was no antivectorial control done in these areas. Ivermectin had significantly reduced the endemicity level of *O. volvulus* infection after 3 to 5 rounds of MDA. In Nigeria, it has been reported that, IVM also significantly reduced the microfilarial prevalence from 69.3% to 39.3% after six years of MDA (Opara and Fagbemi, 2008). It is expected that with repeated rounds of MDA, this infection could be reduced to below transmissible levels.

Previous studies have indicated that onchocerciasis infection (using microfilariae) peaks in individuals aged 20-30 years and is more common among males (Hailu *et al*., 2002). This study also showed that the prevalence of microfilariae was higher among males, increased also with age in both sexes but however peaked in volunteers aged 31 to 40 years old. In this study, the difference in the peaking age group could be due to differences in patterns of exposure to blackfly bite and parasite acquisition, geographical location, occupational and immunological (acquired immunity) status of the locals (Filipe *et al*., 2005) and also the MDA. The present study also confirms studies done with protective immunity that age-intensity profiles would peak with age and decline subsequently, and peak infection intensities are higher in younger aged groups as transmission increases (Anderson and May, 1985; Woolhouse *et al*., 1991). It could also be influenced by the impact of the MDA with IVM.

5.3 Intensity of *O. volvulus* infection in the Study Communities

O. volvulus infection is considered an important public health problem when the community microfilarial load (CMFL), a measure of the intensity of the infection in the community exceeds 5mf/mg (APOC, 2010). In Ghana the ultimate intervention goal by 2015, is to reduce CMFL below 0.05mf/mg to completely eliminate this infection. It is established that high microfilarial load can negatively affect its host life expectancy (Little *et al*., 2004a). The CMFL obtained in 18 of the communities was within the recommended limit of less than 5mf/mg. This achievement could be due to the impact of the mass drug administration of ivermectin and as such with repeated rounds of MDA, this infection could soon be reduced to very low transmissible levels of 0.05mf/mg making this infection no longer a public health problem in these communities. After six years of ivermectin MDA in Nigeria, there was a significant reduction in CMFL from 7.11 to 2.31 (Opara and Fagbemi, 2008).

However, onchocerciasis still remains a public health problem in one of the communities (Essonkrom) at Akrofuom sub-district, with a CMFL of 5.2mf/mg, which was above the threshold set by APOC and was the highest observed CMFL in this study. Records showed that about 45% of the volunteers in Essonkrom had never taken IVM and the highest intake was 2 rounds largely accounting for the high observed CMFL. The situation in Essonkrom (microfilaria prevalence – 88.9% and CMFL – 5.2mf/mg) is alarming and suggests critical attention needs to be paid with the MDA to curb this infection. Using CMFL alone as an indicator, this study suggests that the burden of *O. volvulus* infection as an important public health problem may be declining. However the microfilaria prevalence in the study communities raises concern about possible transmission of this infection. There is therefore the need for ivermectin mass drug distribution to be sustained (WHO, 1998; Winnen *et al*., 2002).

A study conducted at the Central region end of the Pra and Offin River recorded a CMFL range of 5.0 to 40.3mf/s (Timmann *et al*., 2008). In this present study conducted in communities in the Ashanti region end of the Pra and Offin Rivers yielded a CMFL range of 1.4 to 5.2 mf/mg indicating that the intensity of *O. volvulus* infection is lower than the Central region end and this could be as a result of the successful implementation of the ivermectin MDA programme in the area.

In this present study, it was also observed that, as the number of palpable onchocercal nodules increased, there was accompanied increase in percentage of volunteers with microfilariae (Table 4.7). These nodules contained adult worms which produce millions of mf (Little *et al*., 2004b). Ivermectin treatment has been shown to have minimum effect on the life of the adult worm (Osei-Atweneboana *et al*., 2007) and as such to completely eliminate this infection there is also the need to develop a macrofilaricidal drug to complement the use of ivermectin as demonstrated by Debrah and colleagues (2006).

The overall finding from this study suggests the IVM mass drug administration may have reduced the intensity of *O. volvulus* infection in the two study areas. This observation suggests that ivermectin treatment is still effective as also suggested by Osei-Atweneboana *et al*. (2007) and could be the reason for the observed lower intensity of infection. It is therefore assuring that when the MDA programme is sustained with improved distribution, access and coverage, *O. volvulus* infection could be controlled below transmissible level target of 0.05mf/mg in Ghana (Awadzi *et al*., 1995; Dadzie *et al*., 2003; Enk, 2006; Ejere *et al*., 2012; WHO, 2010).

5.4 Impact of Ivermectin Mass Drug Administration

In order to interrupt the transmission of *O. volvulus* infection in these two study sub-districts, there must be low and declining levels of these observed epidemiological indices (nodule prevalence, microfilaria prevalence and CMFL) as outlined by Ghana Health Service strategic plan (GHS, 2008). Other studies have also asserted that, in order to achieve elimination of *O. volvulus* infection as a public health problem, ivermectin has to be applied annually for 10 to 20 years or more (Dadzie *et al*., 2003; WHO, 1997; WHO, 1995). According to Coffeng and colleagues (2013), the prospect of eliminating onchocerciasis from Africa by mass treatment with ivermectin has been rejuvenated following recent successes in certain foci in Mali, Nigeria and Senegal.

Findings from this present study shows that as the number of rounds of ivermectin intake increased the percentage of volunteers with no mf increased and intensities decreased (Tables 4.8 and 4.9). Similar observations have been made by other studies (Boatin *et al*., 1998; Osei-Atweneboana *et al*., 2007). This suggests that ivermectin treatment suppresses reproduction by the adult worms with its effect rising with increasing rounds of IVM treatment. After 3 to 4 rounds of ivermectin, there was complete microfilariae clearance in at least 50% of volunteers. Again after 5 rounds of ivermectin intake, there was complete clearance in 67% of volunteers. A significant observation in this study was that, there was complete microfilariae clearance in all volunteers with 6 to 9 rounds of ivermectin intake. The result from this study suggests that ivermectin still remains an effective microfilaricide.

Ivermectin is a broad spectrum anti-helminthic used currently for the treatment of human onchocerciasis. It has been shown that even a single dose of ivermectin is able to reduce the winding and coiling motility of microfilaria (Soboslay *et al*., 1987). Acoording to Basanez *et al*. (2008) a 99% efficacy of microfilaricidal effect was achieved after each IVM dose and a reduction in mf production by fertile worms. It was evident in this present study that after one round of IVM treatment, there was drastic decline in mf density (even after 8 months of last intake) compared to ivermectin-naïve volunteers. These observations indicate that ivermectin has an effect on motility of microfilariae of *O. volvulus* following administration to humans (Alley *et al*., 1994; Whitworth *et al*., 1996; Dadzie *et al*., 1991).

Since the introduction of ivermectin and its usage in onchocerciasis control in the Pru and Black Volta basins in 1987, there have been increasing enrollments of communities resulting in substantial reduction in transmission and parasite burden (Awadzi *et al*., 2004a; Boatin *et al*., 1998; Borsboom *et al*., 2003). According to the Disease Control Officers, communities at the Akrofuom sub-district were enrolled into the MDA programme in September 2010 and had since been administered at 6 months treatment intervals. Communities at New Edubiase sub-district were enrolled into the programme in September 2009 and had since been administered annually with exception of 2010 and 2012 where ivermectin was administered twice in those years. Before this study, there had been at least 3 and 5 rounds of ivermectin treatment in Akrofuom and New Edubiase sub-districts respectively.

The observed effect of ivermectin in this study is consistent with previous studies that were undertaken when ivermectin was introduced for onchocerciasis control (Awadzi *et al*., 2003; Burnham, 2007; Remme *et al*., 1990b). Repeated rounds of treatments showed that ivermectin is still a highly effective microfilaricide (Osei-Atweneboana *et al*., 2007). Among the ivermectin-naïve volunteers 56% were microfilaridermic, while 33% of volunteers were microfilaridermic even after 8 months of last treatment with low microfilarial load densities after 5 rounds of ivermectin. In volunteers with a minimum of 6 rounds of ivermectin, none had microfilariae. This result confirms the suggestion that repeated rounds of ivermectin is required to completely eliminate *O. volvulus* infection (Dadzie *et al*., 2003; WHO, 1997; WHO, 1995). It is therefore very important to sustain ivermectin MDA and increase coverage to ensure *O. volvulus* infection is completely eliminated as a public health problem.

According to the Neglected Tropical Disease Control Programme (NTDCP) report in 2012, New Edubiase and Akrofuom sub-districts recorded ivermectin coverage of 86.3% and 84.5% respectively. Contrary to the reported coverage, this study showed that about 42.6% of study volunteers remain ivermectin-naïve (non-compliance). Men and the young people are the most culpable (Table 4.11). A recent IVM compliance study reported that 6% had never taken IVM despite 8 rounds of MDA in Cameroon and Nigeria (Brieger *et al*., 2011). These ivermectin-naïve people remain an essential group for re-transmission of this infection. Two major reasons have been assigned to this difference between the coverage reported by NDTCP and what was observed in this study; systemic and personal reasons. Among the systemic reasons, the first one is that the NDTCP reports are based on the mode of drug distribution. The distribution of ivermectin is based on house-hold rather than individual treatment. As a result of this, although the drug may have been distributed, it did not follow that the treatments were taken by the individuals. Compared to the Polio Eradication Programme, the Direct Observed Treatment (DOT) have higher efficiency because it is based on individual treatment.

The second reason is with the selection of Community-Directed Distributors (CDD). The CDD personnels locally referred to as 'Organizers' in these communities are mostly non-health workers. As a result they are often unable to explain to the local folks the reasons and importance of taking the IVM treatment. With the introduction of the community-based health planning and service (CHPS) compounds, community health nurses can be deployed to implement CDTI.

The third challenge is with the allocation of CDDs to communities. In most of the small communities, no CDD is assigned to them. As a result they rely on the bigger communities for their drug supply. Most often it is difficult for the CDDs to effectively distribute the drugs limiting accessibility of the drugs to inhabitants in smaller communities. The efficiency of the MDA can be heightened when CDDs are assigned to every community irrespective of its size.

Personal reasons have also been given by the community folks, which include lack of understanding on why they need to take the ivermectin treatment. This challenge can be addressed by training well-informed CDDs. When well-informed CDDs are selected they will be able to comprehensively explain the need for the treatment.

Secondly, fear and rumours about developing adverse effects (AE) has been cited as one of the reasons. The mode of action of ivermectin is often not explained to them, as a result there is panic among those who have never taken ivermectin. There is the fear that taking the MDA drug will 'expose their hidden ailments'.

The third reason is the lack of interventions for AEs occurence. People who usually develop AEs after the first drug intake stay away from taking subsequent rounds of IVM treatment because of fear of developing AEs again. This can be addressed when community nurses are deployed as CDDs, in that way the community people can be well attended to when they develop AEs and this will reduce fallouts after initial treatment round.

Another challenge is the lack of understanding to why they must take the IVM treatment. Because the people do not understand the need to take the ivermectin treatment, they stay away from participating in the MDA treatment programme and there is no urgency among them to take the treatment. Education is essential in sensitizing them about the need for treatment.

Due to the observed impact of ivermectin treatment in this study, the target by Ghana Health Service to achieve a CMFL below 0.05mf/mg in 2015 in these areas may be far from reach. For these goals to be achieved sooner, stringent approaches and correction of some of these challenges must be implemented to ensure the inhabitants in the endemic areas get access to ivermectin MDA and really take the treatment as required.

5.5 Co-infection of *O. volvulus* with Intestinal Helminths

According to Njoo and colleagues (1993), onchocerciasis patients are more likely to be co-infected with other parasitic infections. Ivermectin as a microfilaricidal drug is also known to be an anti-helminthic and has been recommended for use in the treatment of helminthic infections such as *Strongyloides* (Boussinesq, 2005; Taticheff *et al*., 1994). It is active against various life-cycle stages of many but not all nematodes. It has also been suggested that annual and twice-annual treatments with ivermectin over a period of up to 17 years may have had a significant impact on *T. trichiura* infection (Moncayo *et al*., 2008).

Studies by Whitworth and colleagues (1991) showed that ivermectin had significant effect on *Ascaris lumbricoides* infection reducing its prevalence and intensity of infection for at least 3 months. Further studies have shown there is no significant protection although it may reduce the intensity of infection with other intestinal helminthes including *Schistosoma spp* and *Trichuris trichiura* (Behnke *et al*., 1994; Njoo *et al*., 1993; Taticheff *et al*., 1994). In this study, 3 types of helminthic co-infection were detected among the study volunteers which included 3% co-infection with hookworm, 1.1% with *S. stercoralis*, and 0.3% with *Taenia spp*.

The results in this study concerning hookworm infection, shows no significant difference between those who had taken the ivermectin treatment and ivermectin-naïve volunteers. Among the 11 volunteeers co-infected with hookworm, 5 were ivermectin-naïve, two had taken it once and one had taken it twice, while three had taken 3 rounds of IVM. The prevalence and intensity of hookworm infection was higher in ivermectin treated than ivermectin-naïve volunteers. This confirms that ivermectin may have no effect against hookworm infection as previously observed in other studies (Beach *et al*., 1999; Marti *et al*., 1996; Naquira *et al*., 1989).

It has been shown that ivermectin is highly effective against strongyloidiasis (Belizario *et al*., 2003; Marti *et al*., 1996). This study suggests that the low prevalence of *S. stercoralis* may be attributable to ivermectin mass drug administration. However, *S. stercoralis* infected people may require repeated doses to clear this infection since two out of the four infected volunteers had only taken 1 round of treatment with IVM. Those with one round of ivermectin however had very low intensity of infection and this could be due to the effect of the MDA drug on *S. stercoralis*.

The only volunteer with *Taenia spp* infection in this study had 3 rounds of ivermectin treatment. Little is known about the effect of ivermectin treatment on *Taenia spp* in humans. Research in dogs has shown that ivermectin had no effect against occasional infection with *Taenia spp* (Anderson and Robertson, 1982). This finding could suggest that ivermectin may not have any effect on *Taenia spp* in humans despite multiple ivermectin treatment.

CHAPTER SIX

CONCLUSION AND RECOMMENDATION

6.1 Conclusion

Ivermectin mass drug administration has contributed significantly towards the alleviation of suffering caused by *O. volvulus* infection in several countries. After 3 to 5 rounds of ivermectin treatment, communities previously considered hyperendemic can now be classified as mesoendemic. This means that the intensity of onchocerciasis, a public health problem at Akrofuom and New Edubiase sub-districts is declining as a result of the MDA and as such, these communities can be labeled as mesoendemic due to ivermectin MDA. This study also suggests that ivermectin-naïve, mf-infected individuals in the communities may serve as source of re-infection with *O. volvulus*. This study further suggests that ivermectin is still a potent microfilaricide and that for elimination of onchocerciasis by ivermectin mass treatment alone to be feasible, high coverage and compliance to treatment must be maintained for a long period of programme implementation. The observed impact of the six monthly treatments in Akrofuom is evidence enough that this semi-annual treatment could be implemented to quicken the rate of elimination.

6.2 Recommendations

It is therefore recommended that:

i. Since this study revealed that about 42.6% of study volunteers were still ivermectin-naïve despite a recorded coverage of over 80%, there is the need to develop a suitable strategy to ensure true maximum coverage is attained. For example community nurses can be deployed as CDDs and individual treatment strategy can be adopted.

ii. Direct Observed Treatment (DOT) can be adopted for the smaller communities to ensure people are actually taking the ivermectin treatment.

iii. Education on the essence of ivermectin MDA should be given to the inhabitants to enable them understand why they need to take the drug, why they develop AEs and what they must do when they develop AEs.

iv. Every community needs to be assigned a locally based CDD to ensure availability of the MDA drug.

v. Since most of the inhabitants only come to the communities during farming seasons, timetables for IVM distribution can be adjusted to capture a majority of the people during this season.

vi. Inhabitants living in communities where intestinal infections such as Taeniasis are common may require other forms of treatment such as praziquantel or niclosamide.

vii. Further studies should be conducted to provide more evidence on why onchocerciasis is less frequent in females (genetic or immunological studies).

viii. There is the need to develop a macrofilaricidal drug to help quicken the elimination of this infection.

ix. Further epidemiological surveys need to be conducted at periodic time-points to assess the efficacy of ivermectin MDA in onchocerciasis control.

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