ADDIS ABABA UNIVERSITY

FACULTY OF LIFE SCIENCES

SCHOOL OF GRADUATE STUDIES

EFFICACY OF ALBENDAZOLE CURRENTLY IN USE AGAINST SOIL-TRANSMITTED HELMINTHIASIS AMONG SCHOOL CHILDREN IN WONDO GENET, SOUTHERN ETHIOPIA

A Thesis Submitted to the School of Graduate Studies of Addis Ababa University

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Biology/Biomedical Science

By

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List of Abbreviations and Acronyms

AAU	Addis Ababa University
AEs	Assessment of adverse effects
ALB	Albendazole
ANOVA	Analysis of variance
AR	Anthelminthic Resistance
BZ	Benzimidazole
CDC	Center for disease control
CR	Cure Rates
DALYs	Disability Adjusted Life Years
ERR	Egg reduction Rates
GM	Geometric mean
HIV	HUMAN IMUNO VIRUS
L3	Infective third-stage larvae
MBD	Mebendazole
STHs	Soil-transmitted helminths
WHO	World Health Organization

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ABSTRACT

The three major soil-transmitted helminths (STH), i.e., *Ascaris lumbricoides*, *Trichuris trichiura* and hookworm (*Necator americanus/Ancylostoma duodenale*) are among the most widespread parasites worldwide. Despite the global expansion of preventive anthelminthic treatment, the monitoring of anthelminthic efficacy is not a common phenomenon. The objective of this study was to assess the efficacy of a single 400 milligram dose of albendazole (manufactured by Khandeiwal Laboratories Pvt. Ltd) against the major STHs using a standardized protocol. In March 2011, fresh stool samples were collected from 298 students enrolled in one primary school located in Wondo Genet, Southern Ethiopia. Efficacy was assessed based on cure rate (CR) and the fecal egg count reduction (FECR) using quantitative Kato Katz technique. The prevalence of any STH infection among school children was 74.8%, showing that the community represents a high risk community. High CR of the drug was observed for *A. lumbricoides* (97%) and hookworm (95.3%). The efficacy of the drug was low (42.3%) for *T. trichiura*. The FECR was also very high for hookworm (93.3%) and *A. lumbricoides* (90%), but low for *T. trichiura* (25%). The findings suggest that 400 mg single dose of Albendazole is effective against hookworm and *A. lumbricoides* but a single-dose of ALB is unlikely to be satisfactory for *T. trichiura* parasite treatment. For this parasite a repeated dose regime of ALB for three consecutive days is likely to be more appropriate. Alternative drugs are mebendazole (single dose 500mg), pyrantel+oxantel (single dose 10mg/kg) and albendazole + ivermectin. This will have better effect in reducing prevalence and intensity of infection in school children due to the parasite.

Key words: *Helminths, Albendazole, Efficacy, Cure Rate, FECR*

1. INTRODUCTION

Helminth infections caused by soil-transmitted helminths (STHs) and schistosomes are among the most prevalent infections of humans living in areas of poverty in the developing world. The morbidity caused by STH and schistosomes is most commonly associated with infections of heavy intensity. Approximately 300 million people with heavy helminth infections suffer from severe morbidity that results in more than 150,000 deaths annually (Crompton, 1999 and Montresor *et al.*, 2002). In addition to their health effects, helminth infections also impair physical and mental growth in childhood, thwart educational advancement, and hinder economic development.

The four most common STHs are roundworm (*Ascaris lumbricoides*), whipworm (*Trichuris trichiura*,), and the anthropophilic hookworms (*Necator americanus* and *Ancylostoma duodenale*). De Silva et al. (2003) reported that, *A. lumbricoides* infects 1.221 billion people, *T. trichiura* 795 million, and hookworms 740 million. They are considered together because it is common for a single individual, especially a child living in a less developed country, to be chronically infected with all the three worms. Such children have malnutrition, growth stunting, intellectual retardation, and cognitive and educational deficits (WHO, 2005).

STHs are a group of parasitic nematode worms causing human infection through contact with parasite eggs or larvae that thrive in the warm and moist soil of the world's tropical and subtropical countries. As adult worms, the soil-transmitted helminths live for years in the human gastrointestinal tract. More than a billion people are infected with at least one species (WHO, 2005). Despite their educational, economic, and public-health importance (panel), STHs remain largely neglected by the medical and international community. This neglect stems from three features: first, the people most affected are the world's most impoverished, particularly those who live on less than US$2 per day; second, the infections cause chronic ill health and have insidious clinical presentation; and third, quantification of the effect of soil-transmitted helminth infections on economic development and education is difficult (Chan, 1997).

Studies have highlighted the profound effect of STH infections on school performance and attendance and future economic productivity (Bleakley, 2003). The infections might also increase host susceptibility to other important illnesses such as malaria, tuberculosis, and HIV infection (Fincham *et al.*, 2003).

1.1. Burden of Soil-transmitted Helminthiasis

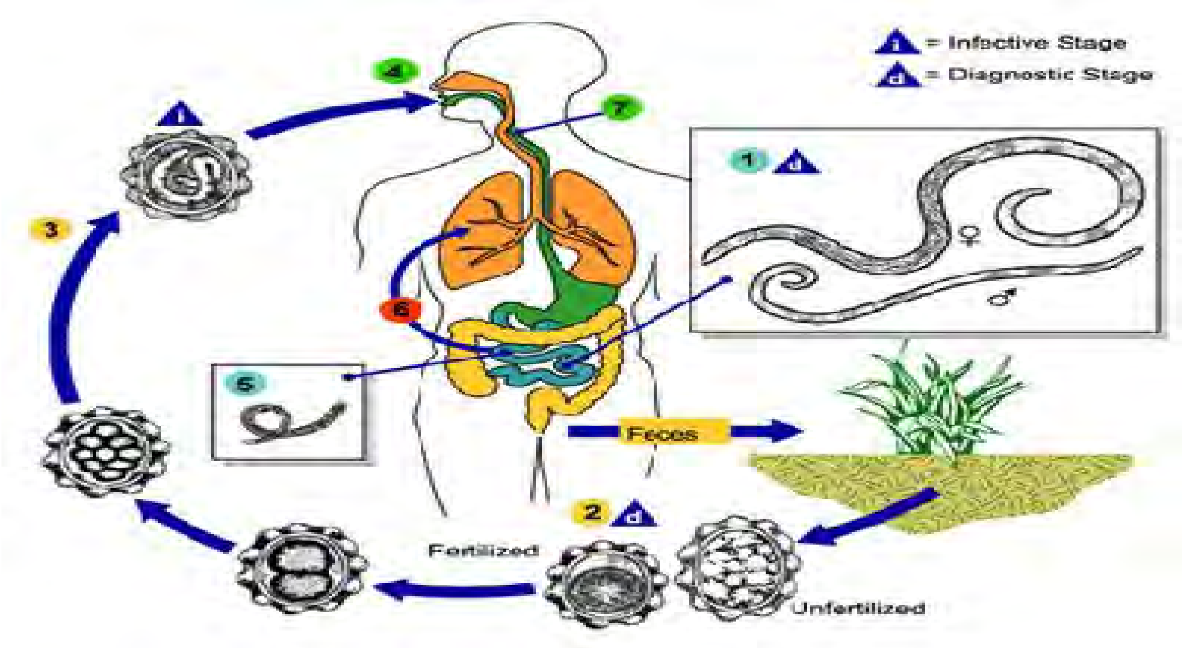
STH infections are among the most prevalent and widespread chronic human infections worldwide (Stoll, 1999). STHs are with the greatest public health burden occurring in developing countries, particularly in sub-Saharan Africa (Bethony *et al.*, 2006). The majority of these infections result from low standard of living, poor socioeconomic status, poor personal hygiene, and poor environmental sanitation (Bundy and Gutatt, 1996). STH infections are widely distributed in tropical and sub-tropical areas, especially in poor populations.

For all human soil-transmitted helminths studied to date, which so far includes *Ascaris*, *Trichuris*, both hookworms, *Enterobius*, and *Ternidens*, worm burdens exhibit a highly overdispersed distribution so that most individuals harbor just a few worms in their intestines while a few hosts harbor disproportionately large worm burdens (Bundy, 1995). These heavily infected individuals are simultaneously at highest risk of disease and the major source of environmental contamination (Bundy, 1995). In the case of *Ascaris* and *Trichuris* infections, overdispersed distributions also exhibit age dependency, with a peak in the childhoods, but with a subsequent decline among adults (Bundy, 1995).

Maximum prevalence of both *Ascaris* and *Trichuris* infections is usually attained before 5 years of age (Bundy, 1995). Numerous studies covering a diversity of geographic regions worldwide also indicate that for *Ascaris* and *Trichuris* infections maximum worm burdens occur in human populations at 5-10 years of age (Bundy, 1995). Although heavy hookworm infections occur in childhood, frequency and intensity commonly remain high in adulthood, even in elderly people (Bethony *et al.*, 2002).

1.2. Soil-transmitted Helminth Infections

Ascaris lumbricoides is the most common and important soil-transmitted helminth. This parasite is cosmopolitan and its distribution is largely determined by local habits in the disposal of faeces, because its eggs reach the soil in human faeces and so contaminate the human environment (Kightlinger *et al*., 1998). Its life cycle is presented in Figure 1.The parasite is one of the major public health problems in communities where the prevailing social environment is characterized by poverty, poor housing, inadequate sanitary practices and overcrowding (Chan, 1997 and Chan *et al*., 1994). *A. lumbricoides* have been shown to play a significant role in childhood malnutrition, which leads to growth retardation, cognitive impairment, and poor academic performance, resulting in a poorer quality of life and less ability to contribute to society (Drake *et al*., 2000).



1. Adult worm 2. Unfertlized egg 3. Fertelized egg become infective 4. Infective stage swallowed 5. Larvae hatch

Figure 1: Life cycle of *Ascaris lumbricoides* (source: CDC, 2009)

Infection with *T. trichiura* (trichuriasis) is the third most common helminth infections of humans (Peters and Pasvol, 2005). The distribution of trichuriasis is worldwide, being most abundant in the warm moist regions of the world. It is spread via fecal-oral transmission as shown in Figure 2 (life cycle of the parasite) and high prevalence occurs in areas with tropical weather and poor sanitation practices (Bethony *et al.*, 2006).The parasite commonly occurs together with *Ascaris lumbricoides* and likewise mainly affects children. Transmission may occur through the medium of food or water or directly from the hands of individuals. Children may be heavily infected and constitute important reservoirs.

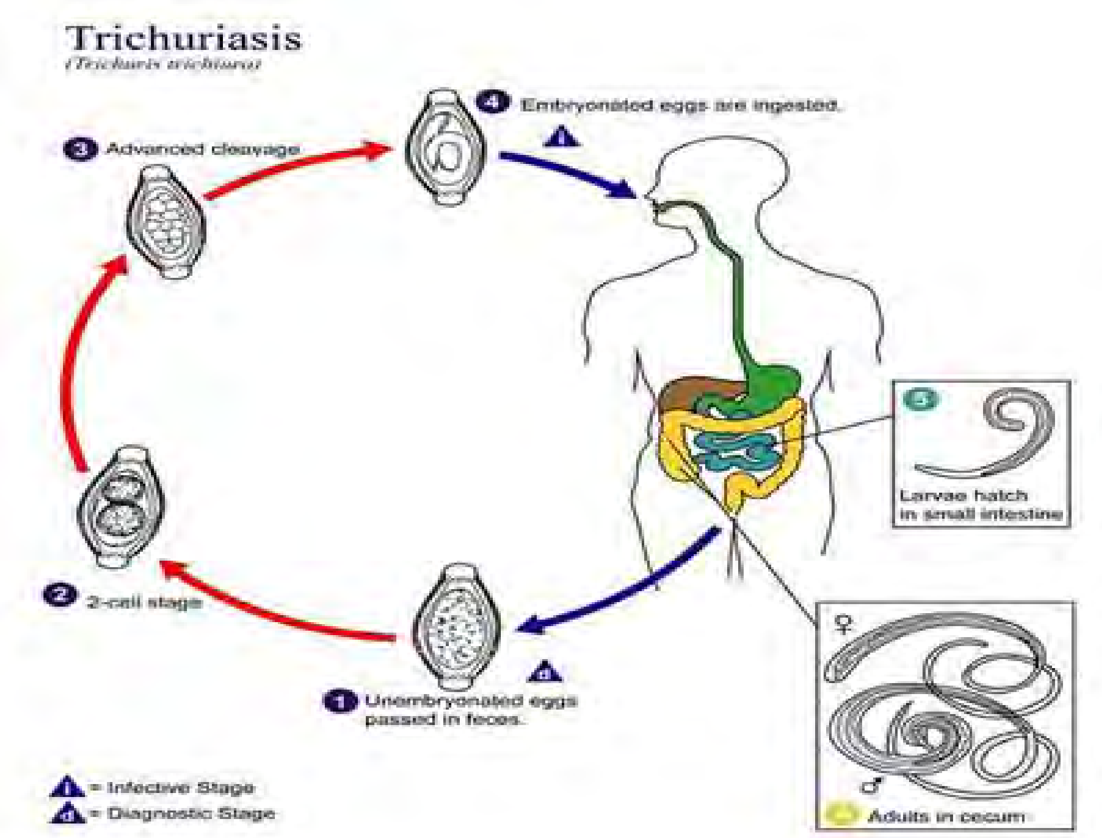


Figure 2: Life cycle of whipworms (source: CDC, 2009)

Hookworm infection in humans is caused by an infection with *Necator americanus* and *Ancylostoma duodenale* and is transmitted through contact with contaminated soil. The life cycle of the parasite is presented below, in Figure 3. It is one of the most common chronic infections (De Silva *et al.,* 2003). Hookworm infection is among the most important tropical diseases in humans. The use of disability-adjusted life years as a quantitative measure of the burden of disease reveals that this infection outranks African trypanosomiasis, dengue, chagas disease, schistosomiasis, and leprosy (Hotez *et al.*, 2003). The greatest number of hookworm cases occurs in Asia, followed by sub-Saharan Africa. In Ethiopia, *Necator americanus* is more common than *Ancylostoma duodenale*, and hookworm infections are most prevalent in communities located between 800 and 1200m altitude (Park, 2004). In most areas, older children have the greatest incidence and intensity of hookworm infection. In rural areas where fields are fertilized with night soil, older working adults may also be heavily infected.

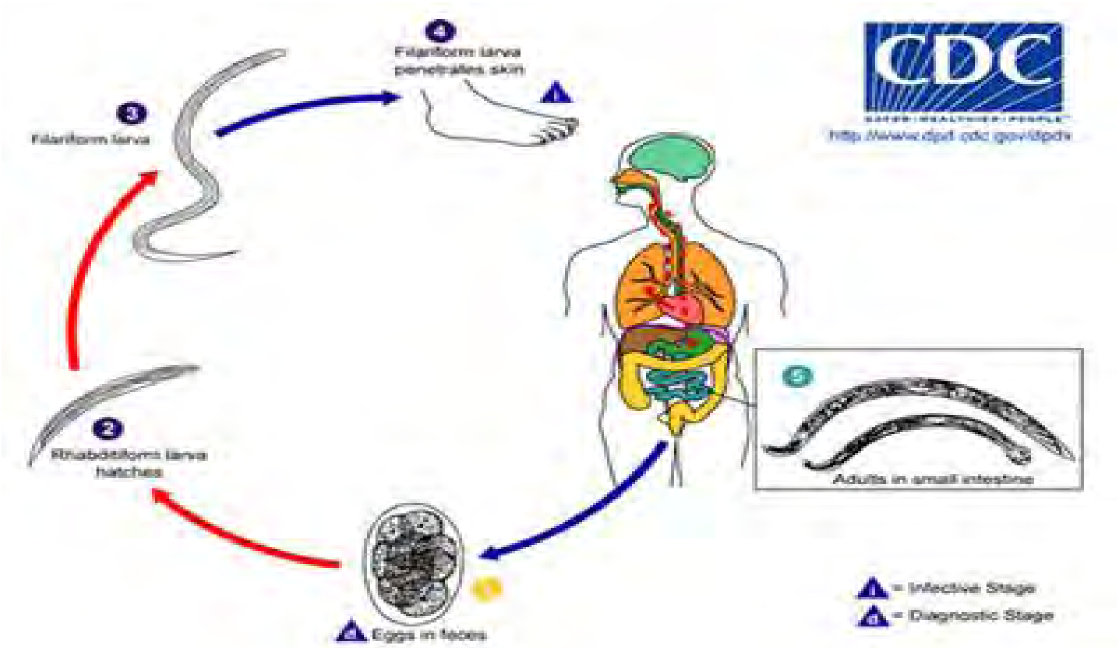


Figure 3: Life cycle of hookworm (source: CDC, 2009)

1.3. Soil-transmitted Helminth Infections in Ethiopia

Nineteen communities located in the southern part of the Ethiopian Rift Valley were surveyed for soil-transmitted helminth parasites of man Birrie *et al.*, 1994. Parasites encountered included *A. lumbricoides* (11.2%), *T. trichiura* (10.3%), hookworms (25.3%), *Taenia sp*. (8.1%), S*trongyloides sp*. (2.9%), *H. nana* (0.8%) and *Trichostrongylus sp* (0.3%) *F. hepatica* (0.1%) and *E. vermicularis* (0.1%). In some communities the prevalence of hookworms, *A. lumbricoides* and *T. trichiura* reached 70%, 66.6% and 60%, respectively. In a cross-sectional survey undertaken in 22 communities of 6 districts in the South Gondar Zone of the Amhara National Regional State, 2279 school children were examined for helminths(Jemaneh, 2000). The overall the prevalence rates were 28.9%, 9.5% and 12.9% for *A. lumbricoides*, *T. trichiura* and the hookworms, respectively.

In 1999 and 2002, a parasitological survey was made to determine the magnitude of soil-transmitted helminthiasis for Wondo Genet area, southern Ethiopia. The prevalence of infection for *Ascaris lumbricoides* and *Trichuris trichiura* among schoolchildren was 83.4% and 86.4%, respectively (Erko and Medhin, 2003). Legesse and Erko (2004) also reported high helminthiasis prevalence in primary school children in southeast of Lake Langano.

1.4. Impact of Soil-transmitted Helminths on Human Health

Soil-transmitted helminths are one of the world's most important causes of physical and intellectual growth retardation (Hotez *et al.*, 2006). The principal public health significance of STH infections lies in their chronic effects on health and nutrition. In addition to interferences in digestion and absorption of foods, *Ascaris lumbricoides* has been observed to decrease micronutrients and vitamin A absorption, probably by causing a structural abnormality of the mucosa in the small intestine. Hookworm infection is a recognized major contributor to gastrointestinal blood loss, iron and energy deficiencies, protein and zinc deficiencies and these thereby causing malnutrition and anemia which are most profound in women at childbearing age. Some 44 million pregnancies are currently complicated by maternal hookworm infections, placing both mothers and children at higher risk of death during pregnancy and delivery (Bundy *et al.*, 1995).

In the same way, *Trichuris trichiura* is now established to be associated with blood loss, malnutrition, and immunological disturbances (Stephenson *et al.,* 2000). STH infections rarely cause death. Instead, the burden of disease is related less to mortality than to the chronic and insidious effects on the hosts' health and nutritional status.

Helminths co-infection with HIV has an impact on health of HIV infected individuals.
Helminth infection leads to significant stimulation of the host immune response as these infections are characterized by the production of eggs, excretory products, and secretions. Helminth-infected individuals display increased levels of eosinophilia, increased IgE levels, and a Th2 immune bias (Kassu *et al.,* 2003). Immuno-regulation in response to helminth infection may suppress HIV-1-specific CD4+ and CD8+ proliferation and cytokine production which may compromise control of HIV-1 replication (Brown *et al.,* 2006). Immune activation may also result in increased cellular susceptibility to HIV-1 infection.

Immune activation is a major enhancing factor for HIV-1 viral replication and hence plasma HIV-1 viral load (VL), and so pre-existing immune activation in the host. Since people infected with helminths are immune-activated, they will be more prone to infection with HIV-1, and that once infected, they may have higher VL, and will therefore transmit the virus more easily and the infection will progress faster. Due to their dominant Th2 response, they will not develop potent HIV-1-specific cellular immune responses, which will be detrimental for the progression of the disease and for responding to vaccination against HIV-1 (Bentwich *et al.*, 1998).

1.5. Anthelminthics

In 2001, the World Health Assembly passed a resolution urging member states to control the morbidity of soil-transmitted helminth infections through large-scale use of anthelminthic drugs for school-aged children in less developed countries.

The most widely implemented method of controlling STH infections is through periodic administration of anthelminthics. Rather than aiming to achieve eradication, current control programs are focused on reducing infection intensity and transmission potential, primarily to reduce morbidity and avoid mortality associated with the disease (Albonico *et al.*, 2008). The four anthelminthics recommended by the WHO against soil-transmitted helminths are: mebendazole (MBD), albendazole (ALB), levamisole and pyrantel. While ivermectin is not recommended for the treatment of human STH, except for strongyloidiasis, it has activity against ascariasis, hookworm and trichuriasis albeit less than the 4 drugs listed above. However, in the new perspective of preventive chemotherapy this drug requires attention as it is used for onchocerciasis and in "combination treatment" for lymphatic filiariasis, and thus will have collateral effects in STH co-infection.

The benzimidazoles (BZ) – MBD and ALB - are the most frequently used anthelminthics to treat infections with STHs (Montresor *et al.*, 2002). While both show broad-spectrum anthelminthic activity, for hookworms a single dose of ALB is more effective than mebendazole (Bennett and Guyat, 2000).

Although both ALB and MBD are deemed broad-spectrum anthelminthic agents, important therapeutic differences affect their use in clinical practice. Both agents are effective against *Ascaris* in a single dose. However, in hookworm, a single dose of mebendazole has a low cure rate and albendazole is more effective (Albonico *et al.*, 2002). Conversely, a single dose of albendazole is not effective in many cases of trichuriasis (Adams *et al.*, 2004). For trichuriasis and hookworm infection, several doses of benzimidazole anthelminthic drugs are commonly needed. Another important difference between the two drugs is that mebendazole is poorly absorbed from the gastrointestinal tract so its therapeutic activity is largely confined to adult worms. Albendazole is better absorbed, especially when ingested with fatty meals, and the drug is metabolized in the liver to a sulphoxide derivative, which has a high volume of distribution in the tissues (Dayan *et al.*, 2003). For this reason, albendazole can be used for the treatment of disorders caused by tissue emigrating larvae such as visceral larva migrans caused by *Toxocara canis*.

A single oral dose of 400mg Albendazole is highly effective against *Ascaris lumbricoides* with cure rates (CR) and egg reduction rates (ERR) between 92% and 100%. The drug is effective against hookworms (CR 57%-95% and ERR 79%-99%) and has usually been shown to be more active than other anthelminthics against *Necator americanus* It is less effective against *Trichuris trichiura* with CR between 10%and 77% and ERR between 61% and 99 % **(**WHO, 1998). Treatment of *T. trichiura* with single oral doses of current anthelminthics is unsatisfactory; hence, new anthelminthics are urgently needed (Keiser and Utzinger, 2008; Olsen *et al.*, 2009**).** In Ethiopia, the respective cure rate and egg reduction rates of 83.9% and 96.3% were reported for *Ascaris lumbricoides* while the respective cure rate and egg reduction rates reported for hookworms were 84.2% and 95.0% **(**Adugna *et al.*, 2007**).** Benzimidazole anthelminthic drugs in the doses used to treat soil-transmitted helminth infections have shown systemic toxic effects such as: transient abdominal pain, diarrhea, nausea, dizziness, and headache.

The scale up of chemotherapy programs that is underway in various parts of Africa, Asia and South America, particularly targeting school children, is likely to exert increasing drug pressure on parasite populations, a circumstance that is likely to favor parasite genotypes that can resist anthelminthic drugs. Given the paucity of suitable alternative anthelminthics, it is imperative that monitoring programs are introduced to assess progress and detect any changes in therapeutic efficacy that may arise from the selection of worms carrying genes responsible for drug resistance.

The well documented occurrence of resistance to anthelminthics in nematode populations of livestock (Wolstenholm *et al.*, 2004) highlights the potential for frequent treatments used in chemotherapy programs to select drug resistant worms. Such an eventuality threatens the success of treatment programs in humans, both at individual and community levels (Albonico *et al.*, 2004). This indicates that, the possible development of anthelminthic resistance (AR) to currently available anthelminthics is a subject of significant interest.

Albendazole causes degenerative alterations in the tegument and intestinal cells of the worm by binding to the colchicine-sensitive site of tubulin, thus inhibiting its polymerization or assembly into microtubules. The loss of the cytoplasmic microtubules leads to impaired uptake of glucose by the larval and adult stages of the susceptible parasites, and depletes their glycogen stores. Degenerative changes in the endoplasmic reticulum, the mitochondria of the germinal layer, and the subsequent release of lysosomes result in decreased production of adenosine triphosphate

(ATP), which is the energy required for the survival of the helminth. Due to diminished energy production, the parasite is immobilized and eventually dies (WHO, 2002).

Albendazole also has been shown to inhibit the enzyme fumarate reductase, which is helminth-specific. This action may be considered secondary to the effect on the microtubules due to the decreased absorption of glucose. This action occurs in the presence of reduced amounts of nicotinamide-adenine dinucleotide in reduced form (NADH), which is a coenzyme involved in many cellular oxidation-reduction reactions. Albendazole also has larvicidal and ovicidal effects (WHO, 1996).

1.5.1. Anthelminthic Efficacy in Human Helminthiasis

There are a vast number of studies investigating the CRs and ERRs of (BZ) anthelminthics against human STHs, however, many of these are not directly comparable because several of these studies may have been confounded by methodological considerations (e.g. type of diagnostic tests, methods for determining the FEC/ERRs, treatment regimens, drug dosages, geographical location) (WHO, 2008).

The possible development of Anthelminthic Resistance (AR) to currently available anthelminthics is a subject of significant interest. In livestock, resistance to all three of the major anthelminthic classes used (BZ, imidothiazoles/ tetrahydropyrimidines and macrocyclic lactones) is widespread, and has been extensively studied (Wolstenholm *et al.*, 2004).

While it is possible that a similar situation observed for veterinary STHs might develop for human STHs, currently there is no conclusive data demonstrating that resistance alleles have been selected in human helminths, and that these alleles have spread in the parasite populations. Nevertheless, there are already worrying signs that anthelminthic efficacy may be declining, and unless the problem is taken seriously and appropriate measures implemented to prevent further decline in efficacy, in the next decade medical doctors may be facing similar problems to those currently being faced by veterinarians (Geerts and Gryseels, 2001).

1.5.2. Assessment of Drug Efficacy

Given the large differences in drug efficacies that have been seen within the same species in different geographical locations, it is important to understand the variability in normal drug response (i.e. before the start of mass chemotherapy) so that atypical responses can be identified. Therefore, it is important to have baseline data on drug efficacy before the beginning of the chemotherapy-based intervention. If AR is defined as a heritable change in a population of worms that enables them to survive drug treatments that are generally effective against the same species and stage of infection at the same dose rate (Coles and Kinoti, 1997) then it will be necessary to establish a change in drug efficacy over time. This will require longitudinal cohort studies over a number of treatments, with FEC conducted immediately before and after each round of treatment. However, if a drug efficacy trial is carried out on a sample of the population that will be subject to periodic treatment, it may be not necessary to repeat efficacy monitoring after each treatment round, especially if treatments are done two or three times/year.

1.5.3. Standard Method to Evaluate Efficacy

The current method of choice to determine the efficacy of an anthelminthic, in veterinary medicine, is to compare infection levels before and after treatment. Infection levels can be measured either by worm counts (method of choice) or Faecal Egg Counts (FEC). It is evident that for human STHs only FEC can be used as a measure of infection levels.

Whichever method is used to quantify the FEC, the uncertainty around this method of estimating parasite intensity should be acknowledged. Several reports have indicated a distinct density dependence effect on FEC in canine hookworms (Kopp et al., 2008). From Strongyloid infections in ruminants it is also known that the first signs of immunity development are reductions in worm length and worm fecundity, even before reductions of worm establishment are observed. Thus, in older animals low FEC are not always suggestive for light worm burdens and it may well be that this is also occurring for hookworms. For a good interpretation of FEC it is thus essential that information is available on the e.g. helminth species, age, gender, nutritional status, previous contacts with STH etc.

1.5.4. Mechanism of Anthelminthic Drug Resistance

Anthelminthic resistance has become a serious problem worldwide in helminth parasites of farm animals and horses. Understanding the mechanisms and genetics of anthelminthic resistance is important (a) to efforts to overcome resistance, (b) to efforts to slow the spread of resistance parasites, (c) to delay the development of resistance to new anthelminthic drugs, and (d) to better manage parasite control, including using anthelminthic combinations, with existing anthelminthics (Prichard, 2008).

Drug resistance can arise in a limited number of ways (i) a change in the molecular target, so that the drug no longer recognizes the target and is thus ineffective; (ii) a change in metabolism that inactivates or removes the drug, or that prevents its activation; (iii) a change in the distribution of the drug in the target organism that prevents the drug from accessing its site of action; or (iv) amplification of target genes to overcome drug action (Adrian *et al.,* 2004**).**

In principle, nematodes can employ a range of strategies to achieve a state of reduced susceptibility towards a given anthelminthic drug. These include the modification of drug target (e.g. binding site), increased target site numbers (e.g. neuronal receptors), increased drug efflux (e.g. through transmembrane pumps), increased metabolization or sequestration of the drug. In general, there are two types of mechanism of drug resistance: Specific resistance mechanisms, resistance associated changes in the drug target would generally be considered as specific mechanism of resistance, since only the respective drug class will be affected and unspecific resistance mechanism, play a role in benzimidazole resistance and macro cyclic lactones resistance (Geerts and Gryseels, 2001).

1.5.5. Drug Resistance in Nematodes

There are many chemotherapeutic trials in humans that show differing efficacies of the same drug. This is a cause for concern because it could indicate that natural tolerance to anthelminthic agents exists in some populations of nematodes and, with mass therapy, full resistance could develop rapidly. Two well-conducted trials on hookworms have given good evidence for benzimidazole resistance in *Necator americanus* in West Africa (De clercq *et al.,* 1997) and pyrantel resistance in *Ancylostoma duodenale* in Australia **(**Reynoldson *et al.,* 1997). Without new anthelminthics, hookworms could become difficult to treat. Also there have been two reports of failure in the treatment of human hookworm infection, involving mebendazole in Mali and Pyrantel in north-west Australia. In both studies, the anthelminthics were observed to be of low efficacy (WHO, 2002**).**

There are several factors which may influence the efficacy of anthelminthic drugs in human helminths as observed in the livestock. These include high treatment frequency, mono-drug regimes, targeting and timing of mass treatment and under dosing treatments (Geerts and Gryseels, 2000**).** Although the present importance of drug resistance in human helminths is not at all comparable with that in livestock, the dramatic and rapid spread of resistance to all major classes of veterinary anthelminthics should warn the medical world against the widespread use of anthelminthics for the control of helminths. In addition, generic versions of anthelminthic drugs are now available at low cost with the expiry of patents (WHO, 2002 and 2006). This is also a concern because drugs vary in their content of active ingredient, purity, disintegration, dissolution, and bioavailability, which affect therapeutic efficacy (WHO, 2002). Hence, the objective of this study is to assess the efficacy of albendazole currently in use against soil-transmitted helminths in Shesha Kekele School, Wondo Genet, Southern Ethiopia.

2. STATEMENT OF THE PROBLEM

Low economic standard, poor sanitation and ignorance of simple health promotion practices favor the wide distribution of intestinal helminthes in Ethiopia. Of all types of diseases in the country, helminthiasis is the second most common cause of outpatient morbidity next to malaria. Several studies in the country have also revealed that intestinal parasite infections are widely distributed with high prevalence rates. Children are the most affected group and serve both as source of infection and as victims, thus contributing to transmission of most parasitic infections within the community (Birrie and Erko, 1995**).**

National prevalence of hookworm is 16%, decreasing with altitude. National prevalence rates of *Ascaris lumbricoides* and *Trichuris trichiura* are 37 and 30%, respectively. No estimates of the national burden are available and, until recently, soil-transmitted helminths (STHs) were not specifically targeted for control (Tadesse *et al*., 2008). According to Erko and Medhin (2003), the prevalence of infection for *Ascaris lumbricoides* and *Trichuris trichiura* among schoolchildren in Wondo Genet area is 83.4% and 86.4%, respectively. The most prevalent soil-transmitted helminth in the area was *Trichuris trichiura*. Other rare helminths encountered were *Taenia* species, hookworms, *Enterobius vermicularis* and *Hymenolepis nana*, all occurring in less than 4% prevalence of infection. The heavy helminth burden among the schoolchildren calls for immediate intervention to reduce morbidity and transmission of helminthiasis in Wondo Genet.

By providing single-dose anthelminthics on a regular basis to entire populations or high-risk groups (such as schoolchildren and pregnant women), it is hoped to reduce both morbidity and transmission (Geerts and Gryseels, 2000**).** A single oral dose of 400mg Albendazole is highly effective against *Ascaris lumbricoides* with cure rates (CR) and egg reduction rates (ERR) between 92% and 100%. The drug is effective against hookworms (CR 57%-95% and ERR 79%-99%) and has usually been shown to be more active than other anthelminthics against *Necator americanus*. It is less effective against *Trichuris trichiura* with CR between 10%and 77% and ERR between 61% and 99 % **(**WHO, 1998). In Ethiopia, the respective cure rate and egg reduction rates of 83.9% and 96.3% were reported for *Ascaris lumbricoides* while the respective cure rate and egg reduction rates reported for hookworms were 84.2% and 95.0% **(**Adugna *et al.*, 2007**).** Also, it is highly effective against *Ascaris lumbricoides* infection, with cure rate of over 96% and egg reduction of over 99.8% and exhibited a cure rate and egg reduction rate of 13.9% and 63.4% against *Trichuris trichiura*, respectively (Legesse *et al.*, 2002).

However, many chemotherapeutic trials in humans reported that there have been differing efficacies of the same drug. The present efficacy study was, therefore, conducted in Wondo genet area, Southern Ethiopia, to determine the cure rate and fecal egg count reduction rate of albendazole (400 mg, manufactured by Khandeiwal Laboratories Pvt. Ltd) against soil-transmitted helminthiasis.

3. HYPOTHESIS

The World Health Organization has recommended mass drug administration for helminth infections. Virtually all of the important parasitic worm infections in humans can be treated with one of 5 anthelminthics currently in use: albendazole, mebendazole, diethylcarbamazine, ivermectin and praziquantel. Based on these considerations, albendazole will have high efficacy against soil-transmitted helminths in Wondo Genet, Southern Ethiopia

4. OBJECTIVES

4.1.1. General Objective

To assess the efficacy of albendazole currently in use against soil-transmitted helminths among school children in Shesha Kekele, Wondo Genet, southern Ethiopia

4.1.2. Specific Objectives

- To determine the cure and egg reduction rates of albendazole against soil-transmitted helminths
- To assess the side effects albendazole in the treatment of soil transmitted helminth infections
- To determine prevalence and intensity of STHs among school children in the study school.

5. MATERIALS AND METHODS

5.1. Study Area

The study was carried out in Wondo Genet, southern Ethiopia. Wondo Genet is a district located some 270 km south of Addis Ababa at an altitude of about 1800 m above sea level. According to the 2005.E.C censuses, the number of inhabitant was estimated at 5,792 (2,857 males and 2,935 females). Majority of the inhabitants of Wondo-Genet belong to the Sidama ethnic group who chiefly earn their living as farmers practicing settled mixed agriculture. Enset and maize are the principal food crops produced while sugar cane and chat *(Catha edulis)* are the principal cash crops of the area. Generally, agriculture, government employee and small scale trading are means by which the local people earn their living. According to Erko and Medhin (2003), hookworm, *Ascaris lumbricoides* and *Trichuris trichiura* are the three most prevalent intestinal helminths in the area.

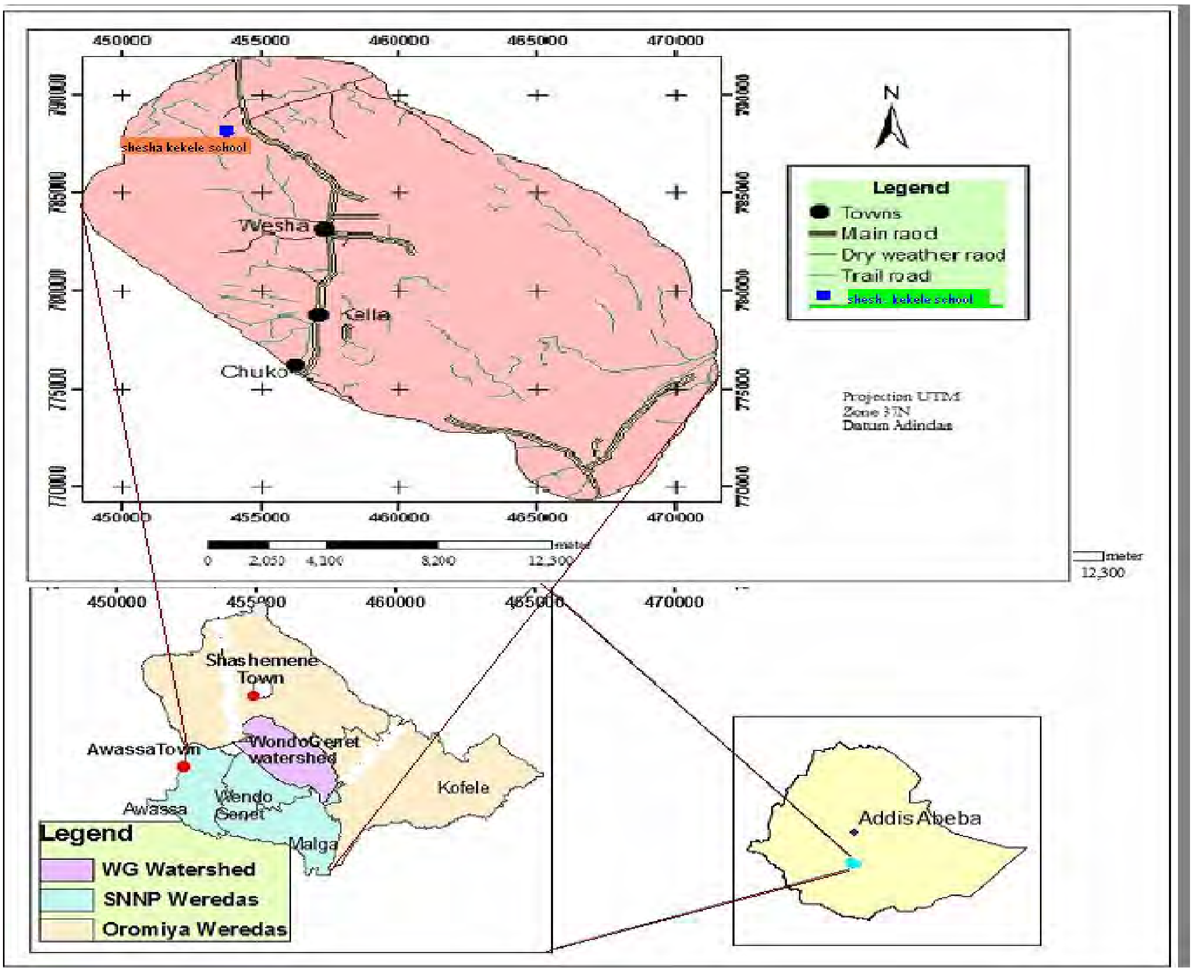


Figure 4: Map of the study area (Aklilu, 2010)

5.2. Study Population

School children were selected as the study population because school-age children typically have the highest intensity of worm infection. In addition, the most cost-effective way to deliver drugs regularly to children is through schools because schools offer a readily available, extensive and sustained infrastructure with a skilled workforce that is in close contact with the community (www.who.int/wormcontrol). Deworming has also an important impact on child development, physical fitness and working capacity. Its effect on growth and anemia is also improved by simultaneous treatment of intestinal parasites and the provision of adequate iron supplementation

(Richter, 2003**).** The data collected from this age group can be used to assess not only whether soil-transmitted helminthiasis threaten the health of school-age children, but also as a reference for evaluating the need for community intervention (Montresor *et al*., 1998). Hence, the study population consisted of 298 (155 males and 143 females) school children (5-16 years) enrolled in Shesha Kekele Primary Schools. The study was cross=sectional and the children were selected by simple random sampling**.**

5.3. Sample size Determination

The required sample was calculated using the following formula (Daniel, 1995):

$$n = \frac{Z^2 E (1 \quad E)}{d^2}$$

Where, n is the sample size

Z = Z statistic for 95% level of confidence

d = precision, and

E = expected efficacy of the albendazole drug

According to Legesse et al. (2002), the efficacy of a single dose of 400 mg albendazole was highly effective against *Ascaris lumbricoides* infection, with cure rate of over 96% and egg reduction of over 99.8%. However, the efficacy of the drug against *Trichuris trichiura* infection was 13.9% cure rate and 63.4% egg reduction rate. Also Legesse et al. (2004) reported that 400 mg single dose of albendazole have 92.5% high cure rate and 99.9% egg reduction rate against *A. lumbricoides*. It has 17.1% of cure rate and 69.8% egg reduction rate against *T. trichiura*. In other study, Albendazole showed a cure rate of 83.9% and egg reduction rate of 96.3% against *Ascaris lumbricoides* and a cure rate of 84.2% and egg reduction rate of 95% against hookworm infection (Adugna *et al.,* 2007). The expected efficacy was taken the lowest cure rate of *A. lumbricoides* from above reports, which is 83.9%, reported by Adugna et al. (2007) and estimation of effects with 95% confidence levels. Hence, based on the above formula the sample size (n) would be 206. Besides, the presence of excess material and to make allowance for non-response rate, 44.6 percent of the sample size was added to the normal sample (206 + 92= 298). Thus, a total of 298 schoolchildren (155 females and 143 males) were selected from Shesha Kekele, Primary school.

5.4. Stool Collection and Examination

After giving adequate instruction on how to provide stool samples, small pieces of plastic sheets were distributed to the selected children to provide sizeable fresh stool specimens of their own. Within 4 days a total of 298 children were invited to participate. For each specimen, two Kato-Katz slides were prepared using Kato technique employing a template delivering a plug of 41.7mg of stool and microscopically examined for eggs of intestinal helminthes (WHO, 1991). Egg count for hookworm was performed within one hour of stool collection and Kato slide preparation. The slides were examined for other helminths in the lab within one week of stool collection. Eggs per gram faeces (epg) were obtained when average of 2 slides egg counts multiplied by a conversation factor of 24.

The children who were found positive for at least one of the soil-transmitted helminth infections were treated with 400 mg single dose of Albendazole (manufactured by Khandeiwal Laboratories Pvt. Ltd). The Drug was swallowed with clean water and accompanied by a small food item. Before treatment all children were interviewed whether or not they received any anthelminthic drugs in the past three months and none of them reported to receive drug treatment during the period in question. Children attending grades 1–8 in Shesha Kekele School were eligible if they met all of the following inclusion criteria: written informed consent provided by parents or guardians, age of 5 years or older and sufficiently large stool sample to perform double Kato-Katz thick smears at baseline survey.

A follow-up stool examination (March, 2011) 21 days after ALB chemotherapy. The Kato-Katz stool examination used the same procedures as described above (2 smears/person).

5.5. Assessment of Post-treatment Signs and Symptoms

At 24 hour after treatment, sign and symptoms due to the treatment were assessed by a pretested questionnaire investigating side effects or any unusual reaction following Albendazole treatment. Children were interviewed by local nurse who were familiar with potential sign and symptoms resulting from anthelminthic treatment. The Questionnaire included: age, sex, and whether they had had headache, fever, diarrhea, stomachache, or vomiting/nausea immediately after taking the medication.

5.6. Efficacy Study

The timing of post-treatment examination that has been used in several recent efficacy trials for STH and recommended by WHO was three weeks. It was considered to be a time that (1) excludes new infection after treatment as it is as long as the minimum pre-patent period and (2) ensures that all live and dead eggs from worms present at the time of treatment have had time to be expelled (WHO, 2008). Therefore, in this study faecal samples were collected three weeks after the treatment. Drug efficacy was evaluated based on two parameters: percentage of individuals cured or cures rate, and percentage of egg reduction or egg reduction rate, as estimated by egg counts.

5.7. Statistical Analysis

The efficacy of the treatment for each of the three STH was evaluated based on the cure rate (CR) and the reduction in fecal egg counts (FECR). The outcome of the FECR was calculated using the following formula that is based on the mean (geometric mean) of the pre- and post-intervention fecal egg count (FEC)

$$\text{Egg count reduction} = \left(1 - \frac{\text{geometric mean of egg per gram after treatement}}{\text{geometric mean of egg per gram before treatement}}\right) \times 100\%$$

Cure rate after treatment was calculated as the percentages of individuals becoming parasitologically negative after treatment. The level of egg excretion intensity was calculated at the pre- and post-intervention survey.

The data was computerized using MS Excel 2003 and mean epg of the parasite was calculated using this window. Statistical analysis was done using SPSS window version-13 statistical package. T-test was used to test possible association of infection with gender and age group. P-value of less than 0.05 was considered statistically significant.

Table 1: Classes of intensity (epg) of soil-transmitted helminth infections

STH species	**Light intensity infections**	**Moderate intensity Infections**	**Heavy intensity infections**
A. lumbricoides	1-4,999	5,000-49,999	49,999
T. trichiura	1- 999	1,000- 9,999	9,999
Hookworms	1-1,999	2,000- 3,999	3,999

(Source: WHO, 2002)

5.8. Ethical Considerations

This study was reviewed and ethically approved by the Ethics Review Committee on Health Research, Faculty of Life Science, Department of Biology, Addis Ababa University. Permission to conduct the study was also obtained from Wondo Genet District Health Office, Educational Bureau, and School Principals.

The objective of the study was explained to school teachers and students at the time of baseline data collection. The stool sample was collected after obtaining written consent from parents/guardians and assent from children participated in the study. Positive individuals for STH and *S. mansoni* infections were treated with the standard dose of albendazole and praziquantel, respectively. The single-dose treatment of albendazole and praziquantel were administered under the supervision of local nurse.

5.9. Significance of the Study

Albendazole has a worldwide importance to treat soil-transmitted helminthiasis. It is one of the drugs that have unique broad-spectrum activity against STHs. The overall cure rates calculated from studies employing the recommended doses shows the following: 78% for hookworm in 68 studies: 92% for *A. duodenale* in 23 studies and 75% for *N. americanus* in 30 studies); *A. lumbricoides* (95% in 64 studies); *T. trichiura* (48% in 57 studies); *E. vermicularis* (98% in 27 studies); *S. stercoralis* (62% in 19 studies); *H. nana* (68% in 11 studies); and *Taenia* spp. (85% in 7 studies) (Horton, 2000). Reduced efficacy of this drug against helminths should be considered as an early warning to tackle the drug resistance problem. Therefore, it needs to be determined its efficacy in Wondo Genet, Southern Ethiopia.

6. RESULT

6.1. Pre- and post-treatment Prevalence of Helminth Infections

Of the total 298 stool specimens collected and examined using Kato-Katz, 88.3% (263) were found positive for one or more helminth infections (Table 3). Among these, 39.3% of the males and 35.6% of the females had STH infections, in which there was no significant association between gender and infection of the parasite ($P > 0.05$). The most prevalent parasites were *S. mansoni* (61%), hookworm (57.4%), *A. lumbricoides* (55.7%) and *T. trichiura* (52.3%). Other rare helminth infections (4.7%) encountered were *Taenia* spp., *Enterobius vermicularis*, *Trichostrongylus* and *Hymenolepis nana*.

The prevalence of any STH infection was found to be 29.2% among the children three weeks post-treatment, while the respective prevalence of hookworm, *A. lumbricoides*, and *T. trichiura* infections was 2.7 %(8), 1.7% (5), and 30.2% (90) (Table 3).

The prevalence of STH and schistosome infections increased with age until the age group 10-14 years (Figure 5). The prevalence of *S. mansoni* infection was relatively the highest for the age group 10-14 years, whereas the prevalence of *T. trichiura* infection was the lowest for all age groups. There was an association of infection found with age groups ($P < 0.05$).

The prevalence reduction rate for hookworm, *Ascaris* and *Trichuris* was 95.3%, 97% and 42.3%, respectively. Prevalence of rare helminths was reduced by 100%.

Table 2. Demographic characteristics of school children in Shesha kekele Primery school, Wondo Genet Southern Ethiopia, March, 2011.

	Age group			
	5-9 (n)	10-14 (n)	15-19 (n)	Total (n)
Mean age (yrs)	9.42	11.25	16.15	-
Male (n)	40	88	27	155
Female (n)	60	71	12	143

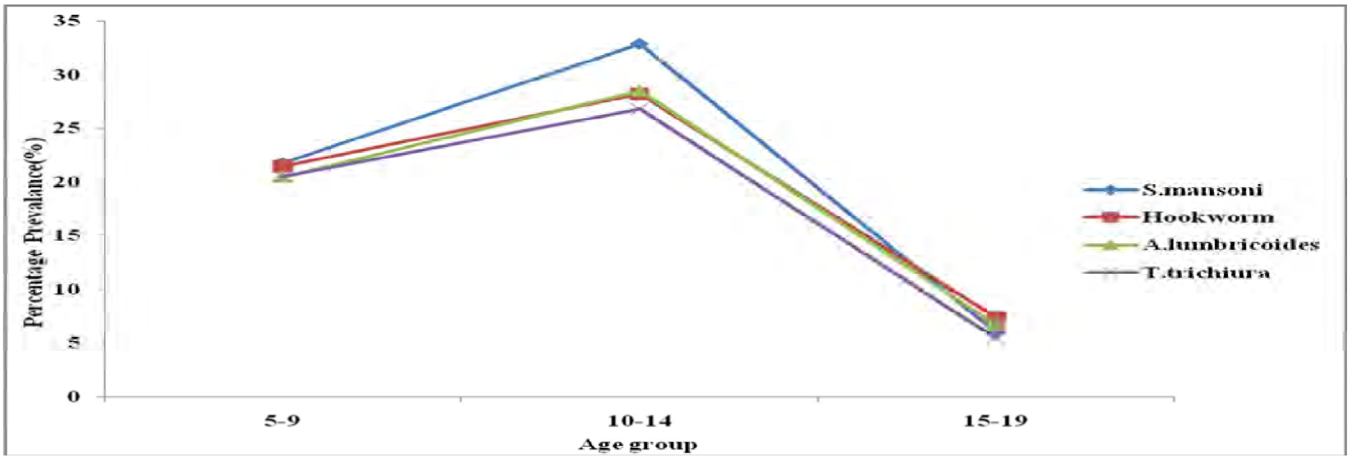


Figure 5. Pre-treatment prevalence of STHs and schistosomiasis among school children by age group in Shesha Kekele School, Wondo Genet, Southern Ethiopia, 2011.

The mean age with 5-9, 10-14 and 15-19 age groups was 9.42, 11.25 and 16.15, respectively, (Table 2).

6.1.1. Intensity of Infection

Proportion of classes of intensity of infections for the major STHs among school children are presented in Table 3. The proportions of light, moderate, and heavy infections for hookworm before treatment were 37.6 % (112), 10.1% (30), and 3.7 % (11), respectively, while the respective proportions of light and moderate infections for *A. lumbricoides* were 43.6 %(130) and 6 % (18), according to the interval shown in Table 1. Similarly, the proportions of light and moderate infections for *T. trichiura* were 40.9 % (122) and 3.7 % (11), respectively. Heavy infection was not observed in *Ascaris* and *Trichuris* infections based on table 1, categories of level of infection.

After the treatment, hookworm and *A. lumbricoides* had only light infections, whereas *T. trichiura* had 0.67 % moderate and 30.9 % light infections (Table 3).

Table 3. Pre- and post treatment intensity of infection for STHs among school children in Shesha Kekele School, Wondo Genet, Southern Ethiopia, March (2011).

Infection intensity	Percent (Number) infected					
	Hookworm		***A. lumbricoides***		***T. trichiura***	
	Pre-treatment	**Post-treatment**	**Pre-treatment**	**Post-treatment**	**Pre-treatment**	**Post-treatment**
Heavy	3.7(11)	0(0)	0(0)	0(0)	0	0
Moderate	10.1(30)	0(0)	6(18)	0(0)	3.7(11)	0.67(2)
Light	37.6(112)	1.34(4)	43.6(130)	1.34(4)	40.9(122)	30.9(92)

6.2. Cure Rate

Cure rate is defined as the children positive for parasitic infection pre-treatment but negative three weeks post-treatment. The overall Cure Rate (CR) observed for Albendazole was 97.1% for hookworm infection, 97% for *A. lumbricoides*, and 42.3% for *T. trichiura*. Albendazole produced the overall cure rate of 80.3% for any STH infection (Table 4).

Table 4. Efficacy of albendazole against STHs three weeks post treatment in school children in Shesha Kekele Primary School, Wondo Genet, Southern Ethiopia (March, 2011).

STHs	**% (Number) infected**		**PR (%)**	**CR (%)**	**Geometric mean(epg)**		**Egg reduction rate (%)**
	Pre-treatment	Post-treatment			Pre-treatment (%)	Post-treatment	
Hookworm	57.4 (171)	2.7 (8)	95.3	95.3	1102	73.8	93.3
Ascariasis	55.7 (166)	1.7 (5)	97	97	1170	121	90
Trichuriasis	52.3 (156)	30.2 (90)	42.3	42.3	147	110.9	25

6.3. Fecal Egg Reduction Rate

The number of children excreting eggs of hookworm, *Ascaris lumbricoides* and *Trichuris trichiura* pre and post- treatment, geometric mean egg count and the over all egg reduction rate are presented in Table 4. 400mg of single dose Albendazole had high efficacy against hookworm and *Ascaris* infections with egg reduction rates of 93.3% and 90%, respectively. However, Albendazole had low efficacy against *Trichuris* parasite with egg reduction rate of 25% as compared to *Ascaris* and hookworm parasites.

6.4. Post-treatment signs and symptoms

Out of 231 children interviewed about treatment-related signs and symptoms, 32.9% reported abdominal pain, 24.2% nausea, 13.85% headache, 12.98% fever, 8 % diarrhea, and 5.6% reported vomiting.

Table 5: Post-treatment signs and symptoms and their association with intensity of infection among school children in Shesha Kekele School, Wondo Genet, Southern Ethiopia (March, 2011).

Sign and symptoms	Hookworm %(n)			Ascariasis %(n)			Trichuriasis %(n)		
	Heavy	Moderate	Light	Heavy	Moderate	Light	Heavy	Moderate	Light
Head ache	11.8(2)	17.6(3)	70.6(12)	-	15.8(3)	84.2(16)	-	-	100(7)
Abdominal pain	4.8(2)	23.8(10)	71.4(30)	-	21.4(9)	78.6(33)	-	-	91.2(31)
Diarrhea	-	9.1(1)	90.9(10)	-	18.2(2)	81.8(9)	-	-	100(7)
Vomiting	-	33.3(2)	66.7(4)	-	33.3(2)	66.7(4)	-	-	87.5(7)
Fever	10.5(2)	10.5(2)	78.9(15)	-	10(2)	90(18)	-	7.1(1)	92.9(13)
Nausea	3.1(1)	12.5(4)	84.4(27)	-	9.1(3)	90.9(30)	-	7.7(2)	92.3(24)

Among children who reported headache, 11.8 %(2), 17.6 %(3) and 70.6 %(12) had heavy, moderate and light hookworm infections, respectively, where as 15.8 %(3) and 84.2 % (16) had moderate and light *Ascaris* infection, respectively. On the other hand, all who reported headache had light (100 %) *Trichuris* infection.

Those children who reported abdominal pain had 4.8 %(2), 23.8 %(10), and 71.4 %(30) had heavy, moderate and light hookworm infections, respectively. In *Ascaris* infection, 21.4 %(9) and 78.6 %(33) of abdominal pain was associated with moderate and light infections, respectively, while 8.8 %(3) and 91.2 %(31) of abdominal pain was associated with moderate and light hookworm infections, respectively.

Fever symptom was reported by children who had 10.5%(2) heavy, 10.5%(2) moderate and 78.9%(15) light hookworm infections, as well as 10%(2) moderate and 90%(18) light *Ascaris* infections. In addition, children who reported fever symptom had 7.1 %(1) moderate and 92.9 %(13) light *Trichuris* infection.

Nausea is one of the symptoms reported by the children who had 3.1%(1) heavy, 12.5%(4) moderate and 84.4%(27) light hookworm infections; 9.1%(3) moderate and 90.9%(30) light *Ascaris* infections;7.7%(2) moderate and 92.3%(24) light *Trichuris* infections.

7. DISCUSSION

The overall prevalence of helminth infections found in the present study (88.3%) among school children in Wendo Genet southern Ethiopia was relatively higher than that reported from other parts of Ethiopia (Legesse and Erko, 2004; Tadesse, 2005; Mengistu *et al.*, 2007). On the other hand, Roma and Worku (1997) reported higher overall prevalence (89%) of helminth infection than in the present report.

In the present study, hookworm was found to be the dominant STH, followed by *A. lumbricoides and T. trichiura*. The prevalence of hookworm infection (57.4 %) was comparatively higher than the prevalence of hookworm infection previously reported from other regions of Ethiopia (Mengistu *et al.*, 2007; Birrie *et al.*, 1994; Jemaneh, 2000), but slightly lower than the prevalence reported from Langano area (Legesse and Erko (2004).

The prevalence of *A. lumbricoides* and *T. trichiura* infections observed in the present study was 55.7% and 52.3%, respectively. This was higher than the prevalence t reported from different regions of Ethiopia (Birrie et al., 1994; Jemaneh, 2000; Legesse and Erko, 2004; Worku et al., 2009, but much lower than that reported in Wondo Genet, Southern Ethiopia (Erko and Medhin, 2003). Such variations in prevalence of helminth infections are attributable to several risk factors, including, poor personal hygiene, environmental sanitation, urbanization, human behavior, household clustering, occupation and climate.

The prevalence of STHs and *S mansoni* were increased from 5-9 to 10-14 years age group, as shown in figure 5, this may be due to the high exposure to environmental contamination with parasites egg or larva and the low immunity in children with this age group. However, the prevalence decreased after 10-14 years age group. After this point children may develop the immunity to protect such infections and the growth hormone may take a role to stimulate the immune system of children when their age increased.

Periodic monitoring of anthelminthic resistance is crucial to take timely measures in case of emerging resistant parasites to the existing drugs. Such studies are highly justified due to such factors as high treatment frequency, mono-drug regimes, targeting and timing of mass treatment and underdosing treatments have a potential to selection of anthelminthic drug resistance (Geerts and Gryseels, 2000). In addition, generic versions of anthelminthic drugs are available at low cost with the expiry of patents (WHO, 2002 and 2006). There is also a concern because drugs vary in their content of active ingredient, purity, disintegration, dissolution, and bioavailability, which affect therapeutic efficacy (WHO, 2002). In line with this, the efficacy of albendazole (Khandeiwal Laboratories Pvt. Ltd) was evaluated in the treatment of hookworm infection, ascariasis and trichuriasis at the dosages recommended by the manufacturer.

In this study, the overall cure rate (CR) produced by albendazole (ALB) was 95.3% for hookworm and 97% for *A. lumbricoides* infections. The results indicated that 400 mg of albendazole as a single dose was highly effective against *Ascaris lumbricoides* and hookworm infections. Several previous studies also reported high cure rates for *Ascaris* and hookworm infections using a single dose of ALB (Albonico *et al.,* 1994; Norhayati *et al.,* 1997; Ramalingam *et al*., 1983; Jongsuksuntigul *et al.*, 1993; Stephenson *et al*., 1990; Adugna *et al.,* 2007).

In previous studies in Ethiopia, a single dose of 400 mg albendazole (Smith Kline Beecham**)** produced a cure rate of over 92 % and egg reduction of over 99.8% against ascariasis (Legesse *et al.,* 2002 and Legesse *et al.,* 2004). Comparable to these previous reports, treatment of ascariasis with albendazole (manufactured by Khandeiwal Laboratories Pvt. Ltd) produced a cure rate of 97% and egg reduction rate of 90%. Cure rates obtained from this study was within the range of 85% to 100%, which have been reported previously (WHO, 1996). However, it is higher than the cure rates obtained elsewhere (Jagota, 1986 and Maisonneuve *et al*., 1984). The egg reduction rate obtained in this study was lower than the egg reduction rate reported by Jagota (1986) and Maisonneuve et al. (1984).

On the other hand, in the present study, 400 mg single dose of albendazole produced low egg reduction (25%) and cure (42.3%) rates in trichuriasis. Similar findings on the effect of ALB on trichuriasis have also been recorded in Bangladesh (Hall and Nahar, 1994), Guatemala (Watkins and Pollitt, 1996), and in Thailand (Sukontason *et al.,* 2000). The egg reduction rate of

25% obtained with a single dose of 400 mg albendazole for trichuriasis in the present study is lower than the previous report from Ethiopia by Legesse et al. 2002 and 2004, and much lower than the egg reduction rates ranging from 73.3 to 87% reported elsewhere (Albonico *et al*., 1994, Rossignol and Maisonneuve, 1983). Pre-treatment infection intensity and Environmental pollution by human faeces may contribute to low reduction in egg counts post the treatment in this study.

Cure rate of 42.3% observed in trichuriasis in this study is higher than the cure rates observed in previous studies in Ethiopia (Legesse *et al.*, 2002 and 2004), but it lies within ranges reported (10% to 67%) by WHO (1996). However, it is lower than cure rate reported by Jongsuksuntigul et al. (1993) and Jagota (1986). The low in cure rate of the drug in single dose against this parasite may be due to trichuris worm infect the lower bowel of the stomach so that the drug action with single dose of alb become unsatisfactory to cure and the parasite may be resistant to all anthelminthics and needs repeated treatment to cure infected individuals.

Treatment-related assessment of signs and symptoms revealed that the frequency of stomachache, nausea, fatigue, headache and fever was 32.9%, 24.2%, 14.72%, 13.85% and 12.98%, respectively. This agrees with treatment-related signs and symptoms reported in Southeastern Kenya (Jaoko *et al.*, 1996). Jaoko and his colleagues reported that the frequency of abdominal pain, headache, nausea, dizziness and fever was 36.3%, 35.3%, 13.1%, 9.7%, and 7.8%, respectively. Berhe et al. (1999) also reported that abdominal pain (86.9%), bloody and/or mucoid diarrhea (49.5%), dizziness (31.2%), and vomiting (24.9%) were the most common treatment related symptoms in northeastern part of Ethiopia.

ALB is said to cause few side effects when used for short-term therapy of STHs. Transient abdominal pain, diarrhea, nausea, dizziness, and headache occur occasionally (Urbani, 2003). There is no pharmacokinetic interaction and no synergistic effect with the treatment of ALB (Sirivichayakul *et al.*, 2001 and Pengsaa *et al.*, 2004). Generally, all the signs and symptoms reported by the children were transient and tolerable in this study.

8. CONCLUSIONS AND RECOMMENDATIONS

The results of the present study indicated that the therapeutic efficacy of 400 mg single dose albendazole (manufactured by Khandeiwal Laboratories Pvt. Ltd) was high in the treatment of *A. lumbricoides* and hookworm infections, but low in the treatment of *T. trichiura* infection.

As regards treatment related signs and symptoms, there are no single case of treatment-related severe sign and symptom was reported. In general, ALB had tolerable and transient side effects.

Treatment of *T. trichiura* with a single oral dose of ALB was unsatisfactory; hence, alternative drugs and/or alternative regimens should be sought for the treatment of *T. trichiura* infection. For this parasite a repeated dose regime of ALB on consecutive days is likely to be more appropriate. Alternative drugs are mebendazole (single dose 500mg), pyrantel+oxantel (single dose 10mg/kg) and albendazole + ivermectin.

The community in Wondo Genet area represents a high risk community for STHs. Hence, all school children enrolled and not enrolled should be treated twice a year until the prevalence falls below the level of public health importance (< 50%).

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10. APPENDICES

Appendix 1: Kato- Katz technique

Materials:

Spatula, previously soaked pre-soaked cellophane

Applicator sticks plastic sheet

Template with hole measuring 41.7g Microscope slides

Screen with specific mesh size forceps

Procedure

1. Put a screen over the sizeable stool specimen on the plastic sheet
2. Scrap the stool under the screen with spatula so that stool will be sieved out of the screen
3. collected the sieved stool with spatula and fill it in the holes of templates which each holes form approximately 41.7mg stool sample
4. Remove the template carefully so that the cylinder of feces is left on the slide.
5. Cover the slide with the stool with pre-soaked cellophane.
6. Gently slide over the sample with another slide so that the stool spread evenly.
7. Leave the prepared slide for at least 24 hrs to clear the smear.
8. Examine the slide with microscope for the presence of STH and schistosome egg.
9. Count the number of eggs encountered per each slide

Appendix 2: Questionnaire to Survey Post-treatment Related Signs and Symptoms

Questionnaire used to assess treatment related signs and symptoms among school children.

Put (P) for **yes** and (x) for **no** in the box below.

Sample no.	Abdominal pain	Diarrhea	Vomiting	Fatigue	Fever	Headache	Nausea
1							
2							
3							
4							
5							
6							
7							
8							
9							
10							
11							
12							
13							
14							
15							
16							
17							
18							
19							
20							
21							

Appendix 3: Written Consent Form of the Study

Here I am intending to assess the efficacy of the drug Albendazole which is the common drug widely used for the treatment of soil-transmitted helminth infections. For this, I need stool sample from your children which would be used only to detect the presence of Soil-transmitted helminth infections and to determine the treatment status of albendazole drug. It will be my pleasure, if you are volunteer to let the children participate in this particular study. I also want to inform you that there is no any health related risk in participating. If your children are found positive for soil-transmitted helminthiasis, they will receive standard drugs free of charge. The information in your records is strictly confidential. Your participation in this study is completely voluntary and you can refuse to participate or free to withdraw yourself from the study at any time. Refusal to participate will not result in loss of medical care provided or any other benefits. Do you understand what has been said to you? If not, you have the right to get proper explanation.

This consent form has been readout to me in my own language, and I understand the content and I am voluntarily consent to participate in the study.
Study Area ______________________________

Name ________________________ Signature ____________________ Date _______________

Wittiness Name _______________________ Signature ________________ Date____________

Investigator Name _____________________________ Signature ____________ Date_________

11. DECLARATION

I, the undersigned, declared that this thesis is my original work and has not been presented for a degree in any other university and that all sources of the material have been used dually acknowledged

Submitted by:

Fikresilasie Samuel	-----------------------	---------------------------------
	Signature	Date

Advisor:

Prof. Berhanu Erko	-----------------------	---------------------------------
	Signature	Date