HOST GENETICS AND EXPOSURE IN SUSCEPTIBILITY TO SOIL-TRANSMITTED HELMINTH INFECTIONS AMONG HOUSEHOLDS IN IGBO-ORA, NIGERIA

BY

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ABSTRACT

Soil-Transmitted Helminth (STH) infections remain one of the major health challenges in developing countries. Susceptibility factors such as host genetics and exposure play significant roles in determining human helminth infection. However information is scarce on the quantitative patterns of spatial and genetic determinants of susceptibility, which is required for the refinement of the ongoing control activities in Nigerian communities. This study was carried out to determine the relative contributions of host genetic factors and the presence of parasite in soil to the prevalence and intensity of STH infection among households in Igbo-Ora, Nigeria.

Igbo-Ora town was mapped into low, medium and high density areas using GIS-based household cross-sectional design. A pre-tested structured questionnaire was used to obtain demographic, risk factor and pedigree information from 508 participants from 239 randomly selected households. Stool samples were collected from the participants to assess the prevalence and intensity of STH infections using the Kato-Katz method. Also, 236 surface soil samples were collected around the selected houses to determine the presence of parasite in soil**.** Variance component analysis was used to assess the impact of genetic relatedness, that is, heritability (h^2), common shared household (C^2) and presence of parasite in the soil (E^2) on STH prevalence and intensity using Sequential Oligogenic Linkage Analysis Routine. Data were analysed using descriptive statistics and Chi-square at $\alpha_{0.05}$

The prevalence of hookworm was highest in high density areas (24.9%), while *Ascaris lumbricoides* was spatially clustered in the medium density areas of Igbo-Ora. Risk factors such as living in crowded room and mud houses were significantly associated with STH infection. The prevalence of STH infections was 18.5% (hookworm), 16.7% (*A. lumbricoides*), 3.0% *(Strongyloides stercoralis)* and 0.8% *(Trichuris trichiura)*. Prevalence was similar in male (28.2%) and female (28.1%) participants. Majority of STH infection (81.1%) were of low intensity, while 6.6% cases were moderate and 12.3% were heavy intensity in *Ascaris* and hookworm infections. The prevalence of parasite ova in soil was 24.1% (*Ascaris* sp), 3.6% (hookworm), 0.7% (*S. stercoralis*), 1.5% (*Taenia* sp) and 0.7% (*Schistosoma haematobium)*. Seven degrees of family genetic relationships resulting in 639 relative pairs from 296 individuals in 91 families were established. Heritability of *Ascaris*, and hookworm within the population was 22.7% and 1.1% and respectively. The common shared household had a greater impact (C^2 = 0.047, p = 0.023) on the prevalence of *Ascaris* infection, whereas genetic relatedness had a significantly higher effect (h^2= 0.25, p=0.023) on the intensity of *Ascaris* infection. The presence of parasite in the soil had greater and significant effect on both the prevalence and intensity (E^2=0.472, p=0.034) of hookworm infection.

Host genetics is an important susceptibility factor in the intensity of *Ascaris* infection, while exposure factors are more important in hookworm infection. These suggest the use of individual approach in soil-transmitted helminth infection control.

Keywords: Soil-transmitted helminth, Parasite prevalence, Host genetic factor, Common shared household

Word count: 475

CERTIFICATION

I certify that this thesis was written by OLUFUNKE ABIODUN OLUWATOBA, in the Department of Zoology, University of Ibadan, Ibadan.

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DEDICATION

I dedicate this work to my loving children; Gloria, Sharon, Beauty and Joshua. You are God's blessings in my life.

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CHAPTER ONE

INTRODUCTION

1.1 Background to the study

Soil Transmitted Helminth (STH) remains one of the major health challenges in the developing world. The important helminth includes *Ascaris lumbricoides*, *Trichuris trichiura*, *Strongyloides stercoralis* and the hookworms which are *Ancylostoma duodenale* and *Necator americanus.* These parasites belong to the class of parasitic nematode worms causing human intestinal infections. Man acquires these parasites by coming in contact with the eggs or larvae that thrive in the world's tropical and subtropical countries that are warm and moist. The adult worm can survive for many years in the human body. (Bethony *et al*., 2006). World Health Organisation (WHO) declared that over a billion people are infected with at least one species of STH (WHO 2012), thereby accounting for up to 40% of the global morbidity from infectious diseases. The global burden of infections with STH was estimated at 3.4 million disability adjusted life years (DALYs) by Global Disease Burden (GBD, 2015).

The greatest number of infections due to soil transmitted helminth occurs in the tropical and subtropical regions of Asia, especially China, India and Southeast Asia, as well as sub-Saharan Africa (WHO, 2012). Several studies have shown that significant helminth infection prevalence occurs within the population of people from Southeast Asia, South America and Sub-Sahara Africa, and having multiple helminth infection is a common phenomenon (Lili *et al.*, 2000; Guinard *et al*., 2000, Tchuente Tchuente *et al*., 2003, Raso *et al.*, 2004*).* Soil transmitted helminth remains a major cause of morbidity, and sometimes, mortality in developing tropical countries. In children according to WHO (2012), they are important cause of physical and intellectual growth retardation, likewise causing malnutrition, stunting, cognitive and educational deficit.

STHs remain largely neglected by the international and medical community, in spite of their economic, educational and public health importance, because the poor people of the world are the most affected. Bethony *et al.*, (2006) reported that it is difficult to quantify the effect of infection due to STH, especially as it affects education and economy, because it has insidious clinical presentation and causes chronic ill health. The unique effect of STH infection on school performance, attendance and future economic productivity have also been highlighted by other studies (Bleakley, 2003, Miguel and Kremer 2003). Multiple infections with STHs are commonly found in children, hence the need to diagnose each specie in order to estimate the prevalence and intensity of the infection. In determining the best control strategy for STHs, diagnosis thus becomes useful.

A resolution to control STH infection was passed by the World Health Assembly in 2001; countries which are highly affected were implored to participate in the said control through wider spread use of anthelminthic drug for school-aged children in under developed countries.

In Nigeria, despite the WHO resolution of large-scale deworming programme, there is no record of such a mass deworming programme. The survey carried out in 2011 by the Global Atlas for Helminth Infection was to develop the distribution map of STH infection prevalence in all the six geopolitical zones in Nigeria. Several small-scale deworming programmes that were done were as a result of one research programme or the other. In many communities in Nigeria, there have been records of high prevalence of STH infection, such as 71.5% prevalence seen in Benue State, North Central Nigeria (Jombo *et al*., 2007), 54.9% prevalence recorded in Ikenne, Ogun State (Ekpo *et al.* 2008); meanwhile, Kirwan *et al.*, (2009) recorded 50% prevalence in Ile-Ife, Western Nigeria, while Odu *et al*., (2011) in Port Harcourt Southern Nigeria, recorded 30.7% prevalence among preschool and school-aged children. In 2011, a total of 5.7 million (13.8%) school-aged children were predicted to be infected with STHs in Nigeria.

Oluwole *et al* (2015) in their nation-wide estimates of STH infection in Nigeria, using Bayesian geostatistical model, reported that hookworm, *A. lumbricoides*, and *T. trichiura* infections are endemic in 482 (86.8%), 305 (55.0%), and 55 (9.9%) out of 555 locations in Nigeria, respectively. Hookworm and *A. lumbricoides* infection co-exist in 16 out of 36 states, while the three species are co-endemic in 12 states. Overall, STHs are endemic in 20 of the 36 states of Nigeria, including the Federal Capital Territory of Abuja. They reported a prevalence range of 1.7% to 51.7% for hookworm in endemic locations, and prevalence range of 1.6% to 77.8% for *A. lumbricoides*, and 1.0% to 25.5% for *T. trichiura*. For hookworm, a model-based prediction of 0.7% to 51.0% prevalence range was reported, while it reported a range of 0.1% to 82.6% for *A. lumbricoides*, and 0.0% to 18.5% prevalence for *T. trichiura*. Their models therefore suggested that dense vegetation and land surface temperature during the day are necessary in order to discover the spatial distribution of STH infection in Nigeria. Adewale *et al.*, (2017) reported a prevalence of 34.8% among primary school pupils in Lagos. A recent systematic review and meta-analysis of the prevalence and distribution of STH infection among Nigeria children revealed an overall pooled prevalence estimate of 54.8% STH infection (Solomon 2018).

The idea of school based deworming programme has been lately debated as to its effectiveness in control of STH infection. Anderson *et al.,* (2013) concluded in their study that there is every possibility that school-age deworming will be of little benefit to the children. Also, that the treatment coverage and the frequency of treatment must be increased within this age-group before the desired benefits can be reflected in the larger community. Regular delivery of anthelmintic drugs is the mainstay for global soil-transmitted helminth control. Deworming campaigns are often targeted to school-aged children, who are at high risk of soil-transmitted-helminth-associated morbidity. However, findings from modelling studies suggest that deworming campaigns should be expanded community-wide for effective control of soil-transmitted helminth transmission. Results of this meta-analysis suggest that expanding deworming programmes community-wide is likely to reduce the prevalence of soil-transmitted helminths in the high-risk group of school-aged children, which could lead to improved morbidity outcomes (Clarke *et al.,* 2017).

Epidemiological studies revealed that in addition to exposure and household determinant, genetic factors account for an important proportion of variations in worm load (William-Blangero *et al*. 1999, 2012, Cuenco *et al* 2009, Quinell *et al*. 2010). And based on these, several facts have suggested that there is an important genetic influence defining the susceptibility to helminths infection. Holland *et al*. (2009) reported that helminths worm load in infected communities are over-dispersed with the majority of infection found within a few individuals.

Reports from other parts of the world have shown that these infections aggregate in families, likewise host genetic factor (relatedness) and domestic environmental factors have been shown to have significant involvement on susceptibility and infection intensity, but the facts about the aggregation in families and the involvement of host genetic factors in infection susceptibility are yet to be explored in this part of the world, that is, Nigeria. This study aims to investigate the impact of parasite contaminated soil and host genetic relatedness on the prevalence and intensity of Soil-Transmitted Helminth (STH) infection among household in Igbo-Ora, Oyo State, Nigeria.

1.2 Rationale

Environmental and socio-economic factors with human behaviour influences exposure to infection, while a range of known immunological, physiological or nutritional and unknown factors may affect susceptibility. This has been reported that in spite of increasing knowledge of environmental and household risk factors (Pullan *et al.*, 2008, Olsen *et al.*, 2001, Traub *et al.*, 2004, Raso *et al.*, 2006) and protective immune responses (Quinnell *et al.*, 2004, Hoffmann *et al.*, 2002) in helminth infection, few studies have addressed their relative contributions to predisposition (Holland, 2009).

In the recent years, school-based deworming programme have experienced increase in financial and technical support for school-based deworming, and quite a number of countries in sub-Saharan Africa implement this nationwide control. These however do not signal the end of epidemiological research, and detailed data on patterns and risk factors for infection are still required for the refinement of ongoing control activities. Nevertheless, only few epidemiological population-based studies of STH are available in Africa (Pullan *et al.*, 2010). Those few studies that exist typically report on age-related changes in infection prevalence and intensity, and demonstrate consistent increase with age, peaking in adults (Behnke *et al.*, 2000, Palmer and Bundy, 1995, Udonsi 1984a, b, Chandiwana *et al.*, 1989, Asaolu *et al.*, 1992) pronounced aggregation of high infection intensity within individuals who are at high risk (Behnke *et al.*, 2000, Palmer *et al.*, 1995), and villages (Asaolu *et al.*, 1992). Thus, Behnke *et al.*'s (2000) submission provides evidence for condition responsible for low or high intensity infection.

Investigations on spatial and genetic determinants of infection are few within African communities. A cohort study by Saathoff *et al.*, (2005), which involves primary school children of South Africa, demonstrated that within a small area, there is pronounced spatial clustering of infection. Thus, the infection was reported to have been strongly influenced by several environmental factors (Saathoff *et al.,* 2005). In the same vein, many studies outside Africa have reported that both family environment and host genetics play significant role in hookworm infection intensity (Breitling *et al.,* 2008, Quinnell *et al.,* 2010, Pullan *et al.,* 2009). A study on the genetic epidemiology investigation of hookworm in Zimbabwe, do not consider the effects of shared family household (William-Blangero *et al.,* 1997). Also, a study done by Pullan *et al.* (2010) in a rural community in Uganda suggested that exposure related factors play a greater role in hookworm and that host genetic factors is not a major determinant of infection. Till date, no study has investigated the role of host genetic relatedness in STH infection in Nigeria.

The significant role of human genetics in determining human helminth infection intensity has been reported, with heritability of up to 44% (Brooker *et al.*, 2006, Breitling *et al.*, 2008). Significant heritability in heavy or light infection is an indication that host genetics is an important factor for predisposition. However, Quinnell *et al.,* (2010) confirm the heritability of initial and reinfection intensity has heritable phenotypes, but the extent to which host genetics affect predisposition was not examined. Brooker *et al.*, (2006) in their study advocated for a scientific perspective that will integrate the use of spatial analysis with statistical methods that will measure the effect of environmental factors, genetic factor and household factor separately, for a better understanding of the determinants of infection. Two linkage scans study identified a Quantitative Trait Loci (QTL) on chromosome 13q33.3 which has been found to be associated with susceptibility to *A. lumbricoides*. This region harbours the gene Tumor Necrotic Factor Superfamily 13B (TNFSF13B gene) and it has been suggested to play an important role in antibody response to Ascaris. Also, information about the involvement of the gene in STH infection susceptibility is lacking in our environment. Therefore, this study sets out to conduct a population–based genetic epidemiological study of Soil-transmitted helminth infection in Igbo-Ora southwest Nigeria. This approach employed, firstly, negative binomial spatial modeling which investigated the spatial variation in the intensity of infection, taking into consideration the individual and household covariate.

Secondly, genetic variance component analysis was done using SOLAR a Unix software computer programme version 8.1.1.0. This is a genetic approach that takes into account genetic relationship among the selected individual households and between the different households as an aggregate of the entire communities and determine the relative contributions of host genetics (relatedness), domestic environmental factors, and other factors to the variation of infection intensity in the different density areas of Igbo-Ora, in southwestern Nigeria.

1.3 Objectives of the study

This study seeks to determine the effect of parasite contaminated soil around homes, host genetic relatedness and common shared household on the prevalence and intensity of Soil-Transmitted Helminth (STH) infection among household/communities in Igbo-Ora, Oyo State, Nigeria. Therefore, the specific objectives are:

1. to determine the prevalence, intensity, variability and associated risk factors of STH infection within the different communities in Igbo-Ora, Nigeria;
2. to determine the effect of house clustering density on prevalence of STH infection and spatial distribution of STH Infection in Igbo-Ora;
3. to determine the presence of STH in the domestic environment (soil) and its effect on human susceptibility; intensity of infection.
4. to determine the effect of genetic relatedness on heritability of STH infection within households in the community; and
5. to evaluate the contribution of host genetic relatedness, parasite contaminated soil in the domestic environment, common shared household, to the prevalence and intensity of STH infection.

1.4 Hypothesis:

Hypothesis

1. Prevalence and intensity of STH infection within and between households

   Ho: There is no relationship between the prevalence and intensity of STH within and between households in Igbo-Ora.

2. Familial aggregation of STH infection within households and domestic environment.

   Ho: There is no significant correlation between familial aggregation of STH infections within household and domestic environment.

3. Estimated contribution of addictive genetic (relatedness) effect and domestic environment.

   Ho: The estimated contribution of addictive genetic effect and domestic environment on the intensity of STH infection is zero.

CHAPTER TWO

LITERATURE REVIEW

2.1. The burden and Epidemiology of STH

Soil-Transmitted helminth infections have been reported by researchers from different parts of the world to cause significantly large burden on the poor nations of the world, especially on people living in rural or undeveloped urban settings. (Hotez 2007, 2008, Knopp *et al.*, 2008). Though Bethony *et al.*, (2006) reported estimates of death from Soil-transmitted helminth infection to vary widely from 12,000 to 135,000. Murray and Lopez (1996) submitted that the infections have been noted to cause more disability than death. Death and disability, therefore, are the main dimensions for estimating the burden resulting from STH infection with the worldwide burden of disease being typically assessed by disability-adjusted life years (DALYs). Hotez *et al.*, (2006), however, was more specific putting the burden of the DALYs around 39 million annually. According to Brooker (2010), the majority of DALYs were lost in Southeast Asia (47%) and sub-Saharan Africa (23%).

For Nigeria, the burden of STH infection estimates provided by Bundy *et al.*, (2000) was high in all class of people: preschool children, school-aged children and adult population. Although in Bundy's report, the highest prevalence was recorded in school-aged children, intensity of infection was however observed to be high among adults. Bundy and Brooker global and local estimates of STH burden reported above, underscore the importance of the disease with a potential worldwide scale of infection. More researchers, according to Bundy *et al.* (2000), have been giving recognition to the significance of helminthic infections, which Bundy noted to have dramatically increased with the upsurge of HIV infections. The factors that drive STH infection globally are similar from the submission of several authors in different parts of the world where researches on STH have been carried out. These causal pathways include environmental factors; Human behaviour; housing and human habitation pattern and rural-urban migration (Ulukanligil *et al.*, 2000). For instance in Nigeria, the endemic level of STH infection have mainly been blamed on unhygienic environmental situation, improper disposal of wastes, gross environmental pollution with agrochemical and industrial waste, domestic waste, plus steady contamination of surface and underground water (Oyerinde *et al.*, 1980, Fagbenro-Beyioku and Oyerinde 1987. Asaolu *et al.*, 1997, Jombo *et al* 2007, Egah and Akosu 2007, Ekpo *et al*. 2008). All these researchers found those factors listed above as contributing to environmental decay and ecosystem degradation, which are suitable conditions for high transmission and sustenance of many human diseases, especially parasitic diseases. Soil transmitted helminth infection are therefore diseases of the low or poor socio-economic conditions of human existence, particularly in area with poor sanitation whether rural communities or urban setting.

Humans become infected with STHs in two ways, firstly by the penetration of the infective third stage larvae of hookworms and *S. stercoralis* into the skin, and secondly by the ingestion of embryonated eggs in food or drink which has been feacally contaminated, as in the case of *A. lumbricoides* and *T. trichiura*, after which the larvae develop to adult worms and can survive in the human gastrointestinal tract for years. School age children have been identified as the most at risk of infection with STHs (Colley *et al.*, 2001; Dada-Adegbola *et al.*, 2005, Girum 2005) and early childhood infections have been reported to contribute significantly to debilitation (Colley *et al.*, 2001). These critical submissions have led researchers to prioritize school age children as target for epidemiological survey of STH and anti-helminthic treatment. Figure 2.1 shows the distribution of STH in Nigeria according to Global Atlas for Helminth Infection (GAHI) 2011 survey.

According to the map, the prevalence of <1% recorded in few areas of Nigeria may be due to several unreported reasons, while the prevalence of >1-10% are reported in virtually all the six geopolitical zones of Nigeria, but more in the northeast and southeastern part of the nation. The prevalence of >10-20 and >20-50 are reported mainly in the southwestern part of the nation, this may be due to the weather condition which is favourable to the survival of the ova of the parasite in the environment or availability of adequate facility for diagnosis or the availability of published data.

Several studies after the GAHI 2011 reports showed that the prevalence of STH within the nation remains as it was reported by GAHI. For instance, Babatunde *et al.*, (2013) reported a prevalence of 41.9% in Kwara State, while Dimejesi *et al.*, (2014) in their study of STH among pregnant women attending tertiary health facility for their antenatal clinic in Enugu, reported a prevalence of 32.4%. Likewise, Ibrahim *et al.*, (2015) reported a prevalence of 28.8% in a household study survey in a semi-urban community in the southwestern part of the nation. Aniwada *et al.*, (2016) reported a prevalence of 25.6% prevalence among primary school pupils in Enugu. Adewale *et al.*, (2017) reported a prevalence of 34.8% among primary school pupils in Lagos. A recent systematic review and meta-analysis of the prevalence and distribution of STH infection among Nigerian children revealed an overall pooled prevalence estimate of 54.8% STH infection (Solomon 2018). Oluwole *et al*., (2018) reported 34.6% prevalence for STH infection among primary school pupils in Ogun State.

2.2 Spatial distribution of Soil-transmitted helminth

In order to effectively control STH infection, there is a need for accurate description and understanding of the geographical distribution of infection. The use of geographical information systems, remote sensing and spatial statistics, in recent years, has greatly enhanced the ability to map the distribution of STHs (Brooker and Michael 2000, Brooker *et al.*, 2006). Many epidemiological studies have been done by examining the stool sample of the inhabitant. These results do not indicate the extent to which the residents are at the risk of parasitic infection but demonstrate the point prevalence of infection within the community sampled (Uga *et al*., 1997). The initial difficulty presented by the traditional cartography was one of the reasons for lack of information about the spatial patterns of infection. These difficulties have been dramatically resolved by the advent of the easy to use systems that will capture data, store it and analyse it, this include global positioning systems and geographical information systems (Hay *et al*., 2000).

Anderson and May (1991) reported marked heterogeneity in the pattern of parasite distribution within individuals, households and communities. The use of geographical information systems has now provided a novel understanding of ecology of infection. This has led to the development of low cost ways to identify target populations for treatment (Brooker and Micheal 2000, Raso *et al*., 2005, 2006). Saathoff *et al*., (2005) in their GIS-based studies in a cohort of South African primary school children demonstrated that within a smaller area, there is a pronounced spatial clustering of infection, which according to the authors was strongly influenced by several environmental factors. Studies done by Brooker *et al*., (2006) in Brazil and that of Pullan *et al*., (2008, 2010) in a rural community in Uganda reported households clustering of helminth infections. A random distribution was reported for hookworm infection by Raso *et al*., (2006) in a study done in a rural community of Cote d'Ivoire.

There is paucity of information on the spatial distribution of STH infection in Nigerian community.

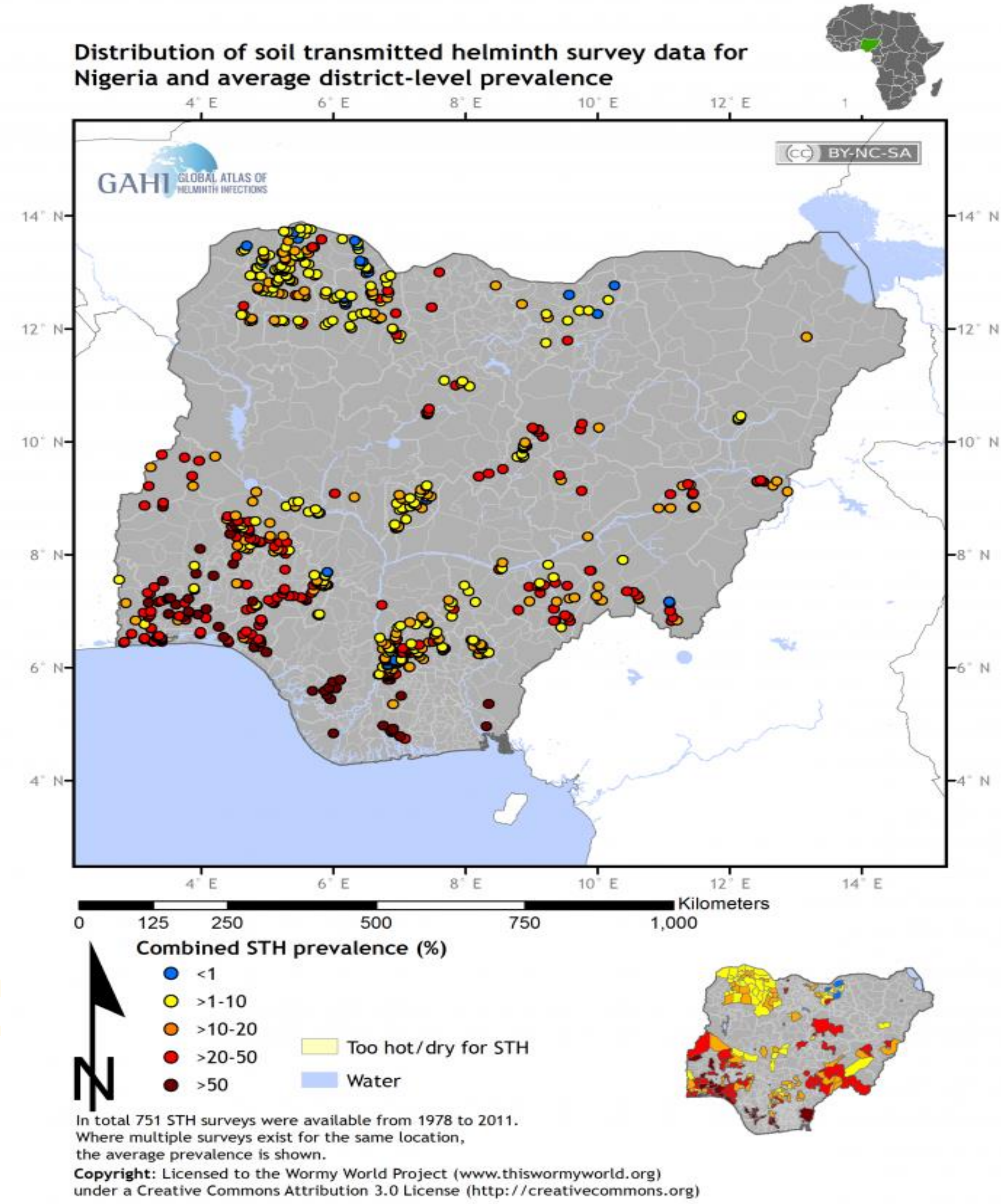


Fig. 2.1. Distribution of STH survey data for Nigeria and average district-level prevalence.

Source: Global Atlas for helminth Infection (GAHI 2012)

2.3 Pathogenesis of Soil-transmitted Helminth infections

In STH infections, the occurrence of the disease is directly correlated with the number of worms harboured in the host (Raso *et al.*, 2004). Pullan *et al.*, (2010) further clarified that the host worm load is what is described as infection intensity and which actually are the primary determinant of the transmission dynamics of soil-transmitted helminth infection and not the number of hosts infected. Thus, intensity of infection is the major indices used to describe STH infections, such that in the laboratory, quantitative egg counts, which is an indirect estimate of worm burden becomes the focus of analysis.

2.3.1 Ascaris lumbricoides: The roundworm

Ascaris is usually reported as the most common helminthic infection in developing nations (WHO 2012). Studies have demonstrated that in the majority of infected individuals, the adult worm presents minor or no symptoms, but in the case of heavy worm burden, intestinal obstruction, nausea, weight loss, and protein-energy malnutrition in children are common deleterious symptoms (Bethony *et al.*, 2006). In addition to symptoms relating to the intestinal phase of ascariasis, patients may also experience pulmonary symptoms when the worms migrate through the lungs. During this phase, patients may develop a low-grade fever, cough, eosinophilia, and/or pneumonia. An asthmatic reaction to the presence of the worms, which is allergic in nature, may also occur. According to the estimate provided by Bethony *et al* (2007), about 807-1221 million populations were infected with *A. lumbricoides* which is the most common roundworm infection. However, a more recent WHO estimates reported that over 1billion people are infected with roundworm (WHO, 2012), demonstrating the global increase in prevalence of roundworm infection and its continued global significance as a public health risk.

Infection occurs when the host ingests eggs found in stool-contaminated soil. In the duodenum, larvae are released and enter the circulation via the enteric mucosa. Once in the capillaries (venous, arterial or lymphatic), it reaches the liver via the portal vein and then the lungs within the first week. In the lungs, they damage the alveolar membrane and mature in the alveolus. Eventually, the larvae are expectorated and swallowed reentering the gastrointestinal tract. In the lumen of the small intestine, the larvae mature to adult worms in about 20 days. When the adult female and male worms are present, they copulate, and the female can produce approximately 200,000 eggs per day. They are later eliminated in the faeces to the soil. In the appropriate conditions of a moist, shady, and warm environment the eggs mature to infective form in two to eight weeks and remain viable for up to 17 months. They can be ingested and can restart the infective cycle (Sharma et al., 2017)

Patients infected with ascariasis can be asymptomatic, only showing long-term manifestations of growth retardation and malnutrition. If symptoms are present, abdominal pain, bloating, nausea, vomiting, anorexia, intermittent diarrhea are the most common manifestation. If the number of larvae passing through the lung is significant, pneumonitis and eosinophilia (also known as Loeffler syndrome) can be seen; symptoms include wheezing, dyspnea, cough, hemoptysis, and fever. In superinfection, adult worms can migrate to tubular structures like the biliary and pancreatic system causing cholecystitis, cholangitis, pancreatitis, small bowel obstruction, volvulus, appendicitis, and intussusception. Children are more susceptible to complications than adults. Jung *et al*., (2004) reported the case of acute interstitial nephritis in association with *A. lumbricoides* infection of a 48-year-old patient in Germany. Another case of a patient from the Ecuadorean Amazon region with limited access to drinking water, she presented to the emergency room with abdominal pain and a mass in the abdomen. After surgery, a mass with a perforation due to Ascaris was discovered. After discharge and due to lack of follow up and self-care, she became infected again, this time making her prognosis more complex and her clinical presentation more difficult (Molina *et al*., 2018). Another case of a 68-year-old Japanese man was presented with *Ascaris lumbricoides* discharge from his mouth. The infection was suspected to have occurred while the patient was in the Philippines. This *A. lumbricoides* migration occurred because a proton pump inhibitor was used and Billroth I resection had earlier been performed on the man, which reduced gastric acid secretion and increased gastric pH to 6.8; this made it easy for *A. lumbricoides* to migrate past the stomach to the mouth. The number of imported foods, of infected migrants and refugees, and of overseas travels is increasing, and these factors may lead to an increase in *A. lumbricoides* infection even in countries with a typically low incidence of such infections. Clinicians should bear in mind that parasitic infections may occur in non-endemic areas (Kobayashi and Tsuyuzaki 2018).

The prevalence of *A. lumbricoides* differs in many communities in Nigeria: Chijioke *et al.* (2011) reported a prevalence of 19.1% in their study done in Enugu, in the eastern part of Nigeria. Okeke and Ubachukwu (2015) reported the prevalence of 76.9% among schoolchildren in Ebonyi which represent the same eastern part of Nigeria. The reason for the differences observed may be as a result of many factors. Kirwan *et al.* (2009) in their study in Ile-Ife, Osun State, Southwest Nigeria reported *A. lumbricoides* (12.2%) has the dominant STH infection. Age, father's occupation and dog ownership were identified as the significant risk factors in the minimal adequate model for *A. lumbricoides*. The odds of being infected with *A. lumbricoides* increased as the children got older. Children aged 12-17 months and 18-25 months were 8.8 and 12.4 times, respectively, more likely to harbour Ascaris than those aged 7-11 months. The odds of harbouring Ascaris for children whose families owned a dog were 3.5 times that of children whose families did not own a dog. Children whose fathers were businessmen were 0.4 times less likely to be infected with Ascaris than those whose fathers were farmers. The findings from their study suggested that many of the young children, who are at a critical stage of development, are infected with Ascaris and that the prevalence of infection with this parasite increases with age.

Reports from other parts of the world showed similar prevalence as that of Nigeria: Galgamuwa *et al.* (2018) reported a prevalence of 38.4% for *A. lumbricoides* in their study among children in a tea plantation community in Sri Lanka. A prevalence of 60% and 72% was recorded for Ascaris and hookworm infection respectively in a cross-sectional survey done among school children in poor neighborhoods of Port Elizabeth, South Africa (Muller *et al.*, 2016).

***2.3.2 Ancylostoma duodenale & Necator americanus:* The hookworm**

Hookworm infection in developing countries remains one of the most important parasitic diseases of humans. Data published by Chan (1997) recorded that about 576-740 million people were infected worldwide with either of the two hookworm species resulting to as many as 22million disability-adjusted life-year lost every year. A more recent WHO estimates stated that 740 million people are infected with hookworm (WHO, 2012). Chan data though over a decade ago still fall within the margin of the

WHO recent estimates, justifying the increasing focus of researchers on hookworm infection in particular. There are two known species of hookworm which are *Necator americanus* and *Ancylostoma duodenale,* and there are two primary differences between the two organisms. First, the geographic distribution varies slightly with each organism. About 72.5 million people are infected with *A. duodenale* with the majority in Asia. About 400 million people are infected with *N. americanus* all over the world with one million living in the United States. *A. duodenale* which is also known as old world hookworm was seen in India, Southeast Asia, southern Europe, Japan and North Africa. *A. duodenale* causes a form of anaemia among the infected coal miners in Belgium and Great Britain and also in tunnel construction workers in Germany, Italy and Switzerland. Meanwhile, *Necator americanus,* commonly known as New world or American hookworm was believed to have been brought in to the Americas during the slave trade, it's found in the Caribbean, Central and South America. It has been found in China, India and Africa.

Secondly and more importantly for identification purposes, the adult worms of each have minor morphologic differences. The egg and larva stages, however, are basically indistinguishable. Adult hookworm lives in the jejunum with the anterior end attached to the mucosa. Morphologically, they have a sharply bent back head and a large buccal capsule, male have an expanded caudal bursa.

Thirdly, pathogenically, infection as a result of *Ancylostoma duodenale* is more serious and the adult worm is however larger than *N. americanus. A. duodenale* has two pairs of teeth on the ventral wall of its buccal cavity while *N. americanus* has a pair of cutting plate on the dorsal wall, a concave tooth on the medial wall and a pair of triangle-shaped lancets on the ventral wall of its buccal cavity.

According to Bethony *et al.,* (2006), the adult hookworm become haematophagous, feeding on blood in the human small intestine, resulting into chronic loss of blood, leading to iron deficiency anemia, particularly among children and pregnant women. The phase of getting infected with human hookworm can be said to be in three stages: (i) invasion of human via skin penetration (ii) migration/movement of the larva within the host and (iii) The establishment within the intestine.

i. **Invasion of the human skin through penetration**: Invasion begins with the penetration of human skin by the infective L3 larvae, although little damage is done to the superficial layer of the skin there is usually a granulomatous reaction which is as a result of the host cellular immune response during blood vessel penetration resulted in an urticarial condition usually known as ground itch.

ii. **The migration phase** is the time when the larvae move from the capillary beds into the lung then enters into the alveoli and migrate up to the bronchi and then to the throat where they are swallowed back into the intestine. When the intensity is high, that is, large numbers of worm are present, the migration of the worms produce severe bleeding, otherwise symptoms such as dry cough and sore throat may also be observed in the infected person. A phenomenon known as a stage of dormancy has been reported in *A. duodenale* infection in areas where re-infection is continual. This is a situation wherein the filariform larvae invade the skeletal musculature and remain dormant to resume development at a later time. It is known that dormancy can be caused by pregnancy and development resume at the onset of parturition. The larvae can be seen in breast milk, hence transmission of infection to breast feeding babies.

iii. **The establishment of the parasites within the intestine:** This is the most serious stage of hookworm infection. Once the parasite is established within its host, the young worm uses its teeth or buccal capsule to burrow into the mucosa and feed voraciously on the host blood. The anticoagulant properties in the salivary gland enable the parasite to feed to satisfaction without the blood getting clotted. The blood loss as a result of *A. duodenale* infection is ten times more than that of *N. americanus*. Iron deficiency anaemia with occasional abdominal pain, loss of appetite and craving to eat soil are some of the symptoms. In a situation of heavy worm load, other symptoms such as protein deficiency, delayed puberty, distended abdomen, dry skin and hair severe anaemia, stunted growth , mental dullness, cardiac failure and death, although rare, can be seen (Zeibig, 2013). The prevalence of hookworm infection differs from region to region. In Nigeria, Yaro *et al.*, (2018) reported the prevalence of 55.8% in Akwa Ibom and Kano States for hookworm infections. While Delta, Oyo and Benue States had prevalence of 38.08, 35.80 and 35.40%, respectively and another 22 states in Nigeria had prevalence of hookworm below 20.0%. Humphries *et al.,* (2011) carried out cross-sectional pilot study of hookworm infection among 292 subjects from 62 households in Kintampo North, Ghana. The overall prevalence of hookworm infection was 45%, peaking in those 11–20 years old (58.5%). In children, risk factors for hookworm infection included coinfection with malaria and increased serum immunoglobulin G reactivity to hookworm secretory antigens. Risk factors for infection in adults included poor nutritional status, not using a latrine, not wearing shoes, and occupation (farming). The most serious consequence of hookworm infection is anaemia, secondary to loss of iron and protein of gut (Hotez et al., 2010). It has been estimated that a single *A. duodenale* ingests about 150 µL blood per day, while *N. americanus* sucks about 30 µL (Midzi et al., 2010). In a situation where the worm burden is significantly high in an individual, infection is normally severe with iron deficiency anaemia, particularly in people with inadequate iron reserves or intake. In most developing countries, for instance, anaemia in pregnancy has been associated with worm infestation, especially hookworm (Hotez 2009). Prevalence and intensity of hookworm infection have been associated with age and sex (Verhagan *et al.,* 2013). Walana *et al.* (2014) reported considerable variation in the age-intensity profile of hookworm infestation in their study in Kumasi, Ghana. Their study revealed that infected individuals in age groups of <1, 1 to 9, 10 to 19, 20 to 29 and 30 to 39 years were in the proportion of 1.3%(2), 10.8%(17), 16.5% (26), 27.2% (43) and 23.4% (37) respectively. Their observation agrees with other existing findings that prevalence of hookworm is high among children (Rayan *et al.,* 2010, Mbae *et al.,* 2013, Osazuwa *et al.,* 2011). The high prevalence seen among individuals within the age of 10 to 39 years could be attributed to the fact that they are physically active and are more likely to be involved in activities such as farming which exposes them to the infection (Brooker *et al.,* 2007, Abu-Madi *et al.,* 2010). There are other reports that hookworm infection in the elderly could be relatively high (Lim *et al.,* 2009).

2.3.3 Trichuris trichiura: The whipworm

Trichuris trichiura, also known as the human whipworm, is a roundworm that causes trichuriasis in humans. It is referred to as the whipworm because it looks like a whip with wide handles at the posterior end. The whipworm has a narrow anterior esophagus and a thick posterior anus. The worms are usually pink and attach to the host via the slender anterior end. The size of these worms varies from 3 to 5 cm. The female is usually larger than the male (Truscott *et al*., 2015). The female worm can lay anywhere from 2000 to 10,000 eggs per day. The eggs are deposited in soil from human faeces. After 14 to 21 days, the eggs mature and enter an infective stage. If humans ingest the embryonated eggs, the eggs start to hatch in the human small intestine and utilise the intestinal microflora and nutrients to multiply and grow. The majority of larvae move to the ceacum, penetrate the mucosa and mature to adulthood. Infections involving a high-worm burden will typically involve distal parts of the large intestine (Truscott *et al*., 2015)

Trichuriasis is 1 of 3 well-documented soil-transmitted helminthiasis infections; the other 2 are ascariasis and hookworm infection. It is considered a neglected tropical disease by the World Health Organisation (WHO) and Centers for Disease Control and Prevention (CDC).

The egg of the whipworm is the infective stage, and favourable conditions for its maturation are warm and humid climate. This is why most of the disease burden is seen in tropical climates, specifically in Asia and less often, in Africa and South America. It is also found in rural parts of the southeast United States. It is estimated that worldwide there are between 450 million to 1 billion active cases with most diagnosed in children. It is thought that there is partial protective immunity that develops with age (Ranjan *et al*., 2015, William-Blangero *et al*., 2008).

Whipworm infection was estimated to affect about 1 billion people. Severe consequences, such as rectal prolapse and dysentery are associated with high worm load, with obvious and immediate influence on the health of infected individual (Stephenson *et al* 2000, Bethony *et al*., 2006). In contrast to the above data, a global prevalence of 795 million people was previously estimated by the World Health Organisation (WHO, 2012). The most common cause of trichuriasis is ingestion of infected eggs that are found in soil. This is often due to poor sanitary conditions, including open defecation and using human faeces as fertilizer. Some recent studies show that people with certain chromosome traits may be predisposed or have increased susceptibility to acquiring trichuriasis (Brooker *et al*., 2015).

A human host consumes infected eggs, typically while eating food. Once the embryonated eggs are ingested, the larvae hatch in the small intestine. From there, they migrate to the large intestine, where the anterior ends lodge within the mucosa. This leads to cell destruction and activation of the host immune system, recruiting eosinophils, lymphocytes and plasma cells. This causes the typical symptoms of rectal bleeding and abdominal pain. Most infections are of light intensity and therefore are asymptomatic. Characteristic symptoms such as weight loss nausea, bloody stools, pain in the lower abdomen, anemia and rectal prolapse can be seen in chronic infection as a result of *Trichuris trichiura*. Adult worms can be seen externally, embedded in the rectal mucosa in the case of rectal prolapse. Patients will typically reside in or have visited areas that are endemic to the whipworm. The patient will usually complain of abdominal pain, painful passage of stools, abdominal discomfort, and mucus discharge. Rectal prolapse is known to occur in a heavy infestation. Children may develop anemia, growth retardation, and even impaired cognitive development. The latter 2 are thought to be due to iron deficiency and poor nutrition secondary to worm burden and are not a direct cause of the infestation (Bansal *et al*., 2018, Shear *et al*., 2018).

Anemia results when the worms penetrate the intestinal wall, also some blood loss may be as a result of the worms ingesting host blood. Secondary bacterial infections are common feature of heavy infections, occasioned by the penetration of the mucosal lining by the worms, providing entry for pathogenic bacteria. The infection is usually associated with malnutrition and numerous studies have documented this in most of the developing worlds. Wilson *et al.* (1999) noted that children even with low worm loads manifest stunted growth. One of its most insidious effects reported in whipworm infection include Vitamin A deficiency and its debilitating effects on cognitive development (Stephenson *et al* 2000, Bethony *et al.*,2006) and deficiency in verbal fluency in children (Ezeamama, 2005). Ezeamama further cited the study conducted among Filipino children who were 7-18 years of age and that were carried out by Nokes *et al.* (1992) among Jamaica children 9-12 years of age as two evidential research reports that confirm the devastating influence of *Trichuris* *trichiura* on verbal fluency in children. These deficits in childhood growth and development occasioned by whipworm infection have long-term implication.

2.3.4 Strongyloides stercoralis: The threadworm

Strongylodiasis is best known in the developed world for the severe consequences of the hyperinfection syndromes linked to immunosuppression caused by diseases like lymphomas, leukemias, or the use of corticosteroids (Mejia and Nutman 2012). This is a small worm and in resource poor countries are associated with malnutrition. The most important presenting complaint of *S. stercoralis* infection reported is diarrhea, which in most cases is chronic. The infection may not show any symptom in normal immunocompetent individuals, but may be severe or fatal in individuals who are immunocompromised, especially in HIV and advanced tuberculosis patients, (Purtilo *et al*., 1974; Dada-Adegbola *et al*., 2010).

According to Krolewiecki *et al.* (2013), the principal features of *Strongyloides stercoralis* are: multiplication within the host which resulted in autoinfection, morbidity which may be acute or chronic, potential fatality, the main diagnostic stage is the larvae and the theraupeutic goal is cure. In immunocompetent host, the parasite usually infects the mucosa of the small intestine and persists as an asymptomatic but often chronic infection. Man gets infected with *S. stercoralis* through contact with the infective larvae in the soil rather than the larvae in contaminated water. Human cases of strongyloidiasis are currently estimated at about 100 million to 200 million worldwide. An estimated case of 21 million infections occur in Asia, while about 900,000 cases were reported in the former USSR, and 8.6 million cases in Africa, while 4 million in tropical America, 400,000 in North America, and about 100,000 cases in the Pacific islands. The free-living forms thrive best in warm, moist climates where sanitation is substandard. A reportedly high incidence of infection, among residents of mental institutions in the United States have been blamed on the prevalence of faeces with infective larvae or larvae capable of rapidly becoming infective combined with poor sanitation or personal hygiene. An 18% rate of infection was identified in a study among the mentally ill patients in New York City. The disease can be considered zoonotic because dogs and cats serve as reservoirs of infection for human infection (Bogitsh *et al.*, 2013).

Epidemiologic studies looking into the distribution of *S. stercoralis* in communities have shown prevalence peaks in adolescents, remaining stable in adults, with a similar distribution as hookworms. Some studies have shown no gender difference and others have found it more prevalent in males, possibly representing differential exposure (Becker *et al*., 2012, Steinmann *et al*., 2007, Krolewjecki *et al*., 2011). Findings of higher burden in the adult population challenge the current policies of focusing interventions (and also drug donations) in school-age and preschool-age children. WHO's guidelines offer a clear stepwise approach to the community based treatment of STH through anthelminthic therapy, with the 20% and 50% thresholds of combined prevalence for any of the major STH triggering the use of preventive chemotherapy interventions once or twice a year, respectively (WHO, 2006). While this strategy is in use around the world and delivering measurable benefits, there is room for further study of this strategy in order to provide scientific support to the expansion or modification of this approach. Among these unsolved areas is the definition of an appropriate prevalence threshold that should trigger community treatments for *S. stercoralis,* considering the particularities of the life cycle and treatment goals. The search for new diagnostic tools for *S. stercoralis* should not hamper the development of strategies for the implementation of control programs. The use of the available, albeit moderately sensitive, direct diagnostic tools in sentinel sites should allow predicting a good enough picture of the distribution of *S. stercoralis* that could justify a therapeutic intervention. More evidence and data are needed, however, to define such prevalence thresholds. Krolewjecki *et al*. (2013), in their write up, brought out the following key point about *S. stercoralis:* (i) Direct parasitological techniques for the diagnosis of *S. stercoralis* infections have suboptimal sensitivity, affecting adequate prevalence measurements, burden of disease estimations, and clinical trials design. (ii) The incorporation of *S. stercoralis* in the preventive chemotherapy strategy in place of other STH requires special adjustment in the drug regimens. Ivermectin is the drug of choice; albendazole and mebendazole have no significant activity in single drug regimens. (iii) The life cycle of *S. stercoralis*, which replicates within the human host, makes cure rather than lowering the worm burden, the appropriate theraupeutic goal. (iv) Although multiplex molecular-based diagnostics and optimal treatment regimens for *S. stercoralis* and STH burden, the appropriate therapeutic goal, Infections, should be pursued as a pressing need, their development should not delay the planning and implementation of strategies to control strongyloidiasis and STH with the existing tools.

2.4 Environmental risk factors predisposing to STH infection

Several studies (such as Asaolu *et al.*, 2002, Ugbomoiko *et al.*, 2008, Ilechukwu *et al.*, 2010, Mara *et al.*, 2010) carried out in Nigeria and around the whole world have reported the association of STH infections with environmental risk factors, such as lack of clean water, climate and season . The presence of refuse heaps, gutters and sewage unit in and around human dwellings, which pollute the environment contribute to the thriving condition for soil-transmitted helminth (Nwosu and Anya, 1980).

2.4.1. Temperature, climate and season

Soil-transmitted helminth infections are widely distributed throughout the tropics and subtropics, and climate is an important determinant of transmission of these infections. Adequate warmth and moisture are key features for each of the soil-transmitted helminth. *Ascaris lumbricoides* and *Trichuris trichiura* eggs survive drier climate better than the hookworm larvae. At low humidity (atmospheric saturation less than 80%) human ascaris ova do not embryonate (Brooker and Michael 2000). The viability of hookworm eggs and the survival of the larvae depends on whether egg-containing human faeces are deposited in an environment where the ambient temperatures are high enough and the soil conditions appropriate for larval development (Hotez, 2008). Chandler (1929) reported that the ambient temperatures of between 20 °C and 30 °C are optimal for the development of the larval in the soil, but that larval viability still continues even when temperatures rise into the low 40s. It has been discovered through the use of satellite mapping and remote sensing, that the environmental stages of hookworm have higher heat limits than other soil-transmitted helminth, such as *Ascaris lumbricoides* and *Trichuris trichiura*. This may be responsible for the observation that hookworm is endemic throughout most of Mali and southern Chad, in contrast to ascariasis and trichuriasis. On the other hand, hookworms exhibit a lower tolerance for cold temperatures than do either *Ascaris* or *Trichuris*, which explains why hookworms are seldom found at high altitudes. In Africa, the geographic range of temperatures and rainfall that make conditions suitable for hookworm larvae in the soil are similar to those conditions required for the *Anopheles* mosquito vector that transmits malaria. Thus, there is a high degree of geographic overlap and co-endemicity between hookworm and malaria in sub-Saharan Africa. Mabasso *et al.* (2003) discovered that summer temperatures in KwaZulu-Natal, South Africa, play a primary role in the transmission of hookworm infection, with cold temperatures serving as an effective means of regulating its inland and southward distribution. Bogitsh *et al*., (2013) reported that Ascaris and whipworm (Trichuris) are found in areas with dense shade, warm climate, heavy rainfall and poor sanitary conditions that are conducive to soil pollution. Children are more heavily infected than adults because they come into close physical contact with contaminated soil than adults. Stojčević *et al.* (2010), in their study on contamination of soil and sand with parasite elements as a risk factor for human health in public parks and playgrounds in Pula, Croatia, showed a higher contamination rate in December than in June. This correlates that the increase in the number of positive samples, as well as the increase in the number of helminth eggs found in December to be attributed to the very suitable environmental and climate conditions, with moderate temperature and sufficient soil humidity.

2.4.2 Availability of clean water:

The availability of clean water for domestic purposes is a key factor in reducing the rates of diarrhoea, ascariasis, schistosomiasis, and trachoma. The presence of sanitation facilities were also reported to decrease diarrhoea morbidity and mortality and the severity of hookworm infection (Esrey *et al.*, 1991).

Contrarily, Belyhun *et al.*, (2010) carried out a population-based study among mothers and their infant in a rural area of Southern Ethiopia and found out that the availability of piped water in the house compound was independently associated with increased risk of infant helminth infection, and the reason for this was suspected to arise from the poor quality of piped water. However, Bartram and Caincross (2010), in their article, suggested a five point summary about the importance of Hygiene, sanitation and water, which are: (1) that massive disease burden as a result of deficient hygiene, sanitation, and water supply can be largely preventable (2) that the costs of the interventions has a total benefits greater than the health benefits alone (3) that the ambition of international policy on drinking water and sanitation is inadequate; likewise, hygiene, sanitation, and water supply should be a development priority. (4) that hygiene, sanitation, and water supply continue to have health implications in the developed world. (5) that active involvement of health professionals in hygiene, sanitation, and water supply should be accelerated to consolidate progress for health.

Strunz *et al.*, (2014) conducted a review analysis on the association of improved Water, Sanitation and Hygiene (WASH) and the STH reduction; Water-related access and practices were generally associated with lower odds of STH infection. The meta-analyses examine the association of piped water access and use of treated water on STH infection. Using treated water (filtered or boiled) was associated with lower likelihood of having any STH infection (k=3, OR 0.46, 95% CI 0.36–0.60). The quality of evidence for the analysis was low, as all three studies used for the analyses were observational. The use of piped water was not associated with STH infection in general (k=5, OR 0.93, 95% CI 0.28–3.11). The quality of evidence for the pooled estimate was very low due to high heterogeneity (I^2=98.6%, 95% CI 98%–99%, Qp-value, 0.01) among the studies. The use of piped water was associated with reduced likelihood of *A. lumbricoides* infection (k=4, OR 0.40, 95% CI 0.39–0.41) and *T. trichiura* infection (k=3, OR 0.57, 95% CI 0.45–0.72). Evidence quality for these two meta-analyses was low, based on four studies and three studies respectively. They did not find a sufficient number of studies to conduct a similar meta-analysis for hookworm infection, although Nasr *et al*., (2013) found a significantly lower adjusted odds of infection (OR 0.59, 95% CI 0.34–0.91) for Malaysian children with access to piped water. Cundill *et al*. (2011) and Kounnavon *et al*. (2011) found no statistically significant associations between piped water access and hookworm infection.

In one study, examining storage of water, Quintero *et al*., (2012) found a significantly higher adjusted odds of *T. trichiura* infection for Venezuelan children and adults collecting water in ‘‘inappropriate’’ receptacles (OR 1.12, 95% CI 1.09–1.15) [69]. Belyhun *et al*., (2010) found a beneficial association of using an outside water pipe compared to an indoor tap for infection with any STH among Ethiopian infants (OR 0.21, 95% CI 0.09–0.51). Matthys *et al*., (2007) found that having a private well significantly increased the odds of hookworm infection for farming households in western Cote d'Ivoire (OR2.32, 95% CI 1.24–4.05). No evidence was found of an association between public or private water source and *S. stercoralis* infection (Hall *et al*., 1994). Having ‘‘inadequate water supply’’ in schools was strongly associated with increased infection with any STH among school children living on Pacific islands (OR 4.93, 95% CI 2.24–10.88) (Hughes *et al*., 2004).

2.4.3 Soil types:

The Ascaris eggs best survive with increases depth and in less permeable clay soils, (Crompton, 2001) and it prevents egg dispersal by water. Hookworm eggs hatch in soil and give rise to first-stage larvae, which molt to infective larval stage that penetrates the skin of man. Soil type is an important factor in that the developmental stages of soil transmitted helminth, this includes the ova that develops to the larval stage in the environment that is the soil. Clay soils have low permeability because their interstitial pores are small and therefore larval development is better in sandy soils rather than the clay soil. Hookworm mobility is greater and better in sandy soils than in clay soils. According to Mabasso *et al* 2003, the coastal areas in the developing world exhibit particularly high hookworm endemicity because they have sandy soil, and they are at low altitudes (and therefore high temperatures). Studies have shown that the occurrence of high hookworm prevalence at low altitudes was significantly associated with well-drained sandy soil types. Low hookworm prevalence at higher altitude was associated with poorly drained weakly developed soil types. Also, Mabasso *et al*. (2004) in another study found out that the particle size distribution of sand fractions, organic matter and clay content in the soil influence the survival of hookworm larvae and hence the parasite's transmission. Sandy soils, due to their geological characteristics, being formed by sand particles with diameters ranging from 0.02 to 2 mm, and with the ability to retain water between the spaces of soil particles, represent an important source of human infection by parasites. Helminth larval stages are notably aquatic, and a high humidity of the soil is essential for their survival. The development of eggs into embryos and in the viable larva stages are strongly influenced by the amount of sun to which the infected soil is exposed, the rate of evaporation, in addition to the rain pattern. Frequent rain throughout the year in places with sandy soil which are not directly exposed to sun and are protected from intense evaporation provides ideal conditions for rapid parasite development (Rocha *et al.*, 2011).

2.5 Human behaviour and socioeconomic factors:

Human behaviour and socio-economic factors are important predisposing factors to Soil-transmitted helminth infection (Girum 2005; Rukmanee, 2008). Several studies have highlighted hygienic practices such as hand washing habit and dirty fingernails, shoe wearing habit, proper sewage disposal and level of education as important and major contributory factors for STH infections (Ulukanligil 2001; Fatiregun and Oluwatoba 2008). Conditions that promote environmental decay include not well planned housing and human habitation patterns. This is because urbanisation in developing countries usually results from unplanned, uncontrolled and constant migration of people from rural areas to the urban centers in search of employment opportunities (Fashuyi 1983, Ozumba et al 2002). Furthermore, the combined factors of ecosystem degradation with socio-cultural and agricultural practices of the people create conditions favourable for high transmission and sustenance of many human diseases, especially parasitic diseases (Holland *et al.*, 1989, Kaliappan *et al.*, 2013).

2.5.1 Hygiene practices

Hygiene practices such as hand washing habit before eating and after the use of the toilet, dirty finger nails, and shoe wearing habit has been reported by various studies to be positively related to STH infections (Rukmanee 2008; Fatiregun and Oluwatoba 2008; Girum 2005). Mara *et al.* (2010) reported that out of human excreta, faeces are the most dangerous to health. According to their submission, one gram of fresh faeces from an infected person can contain around 106 viral pathogens, 106–108 bacterial pathogens, 104 protozoan cysts or oocysts, and 10–104 helminth eggs.

Bartram and Carincross (2010) compared intervention studies of hand washing with soap carried out in child-care centers in the United States and Australia with some developing countries and found similar reductions in diarrhoea of roughly 50%. Their observation further underscores the role of personal hygiene in the spread of STH infection. Three randomised controlled trials, two carried out in China and one in the Peruvian Amazon, found strong benefits for interventions that focused on promoting hygiene in schools (Xu *et al* ., 2001, Bieri *et al.*, 2013, Gyorkos *et al.*, 2013). Xu *et* *al*., (2001) assessed a randomized intervention that promoted handwashing with soap, both before eating and after defecation among 657 school children in three schools. All the infected children were treated at baseline. At the 1-year follow-up, *A. lumbricoides* prevalence for children in the experimental group had declined by 35.7% (pre-intervention prevalence, 68.3%; post-intervention cumulative infection rate, 43.9%) compared with an increase in the control group of 78% (pre-intervention, 41.4%; post-intervention, 73.7%); this was a statistically significant difference (p, 0.01). The study's primary limitation was that schools were the unit of randomization, with two primary schools becoming controls and the third receiving the intervention. With so few clusters, it is highly possible that confounding factors were not comparable between the control and experimental groups. Bieri *et al.* (2013) reported on a single-blind, unmatched, cluster-randomised intervention trial involving 1,718 children (aged 9–10) in 38 schools over the course of one school year. Schools were randomly assigned to a health-education package, which included an entertainment-education cartoon video, or to a control package, which only displayed a health-education poster. All participants were treated with albendazole at baseline. At follow-up at the end of the school year, knowledge about STH was significantly higher in the intervention group, and almost twice as many intervention children (63.3% versus 33.4%, p, 0.01) reported washing their hands after defecating. The incidence of STH infection (predominantly *T. trichiura* and *A. lumbricoides*) was also significantly improved in the experimental.

2.5.2 Occupation, housing system and family size

The spread, distribution and sustenance of various helminth infections may also be facilitated by the living conditions of the people in crowded or unhealthy situations (Udonsi and Amabibi, 1992). On many occasions, occupation has been used to determine the socioeconomic status of individuals and low-socio-economic condition is a risk factor for helminth infection (Hotez, 2008).

Housing system in terms of the structure and materials used for building, likewise the availability of toilet system in the house is another major determinant in STH infection within household. Holland *et al.*, (1988) in their study in Panama found houses made from wood and bamboo associate with significantly higher rates of Soil transmitted helminth infection than concrete houses.

Strunz *et al.*, (2014) discovered that sanitation access (availability or use of latrines) was associated with lower likelihood of infection with any STH (k=8, OR 0.66, 95% CI 0.57–0.76), T. trichiura (k=7, OR 0.61, 95% CI 0.50– 0.74), and *A. lumbricoides* (k=6, OR 0.62, 95% CI 0.44–0.88). The quality of evidence for these meta-analyses was low due to the observational nature of included studies. They did not find evidence that sanitation access was associated with hookworm infection (k=6, OR 0.80, 95% CI 0.61–1.06), which had very low evidence quality due to imprecision. They found limited evidence that use of shared or private sanitation facilities influenced odds of STH infection. Worrell *et al.*, (2013) found in Kenya that participants using toilets located outside of their household premises had significantly increased odds of infection with any STH. In contrast, another study found that sharing latrines with neighbouring households, compared with private latrine use, was associated with significantly lower odds of hookworm infection (Matthys *et al.*, 2007).

Another longitudinal study by Genser *et al*. (2006) in urban Brazil found that the major risk factors for diarrhoea in the first three years of life were low socioeconomic status, poor sanitation conditions, presence of intestinal parasites, and absence of prenatal examination. The study concluded that diarrhoeal disease rates could be substantially decreased by interventions designed to improve the sanitary and general living conditions of households. Adekunle *et al.* (1986) in their study of family influence on incidence of intestinal parasites among Nigerian children found ascaris prevalence and high worm burden to be higher among children from large family size and the order in which a child is born in large family also affects the likelihood of becoming infected.

2.6 Household clustering of infection

According to Anderson and May (1991), intestinal parasites are neither evenly nor randomly distributed among hosts, but tends to be aggregated in a few infected individuals in communities where the prevalence of infection is high. There are evidences of household clustering of infected individuals in most of the diseases as a result of helminth infection due to ascaris, trichuris, and strongyloides. This clustering can persist through time, as reported by Hotez *et al.* (2008) in their study of familial predisposition to heavy infection with *Ascaris lumbricoides* and *Trichuris trichiura* in Mexico. According to Ellis *et al.* (2007) individuals with high intensity of STH infection have been found to aggregate in families. Similarly, significant clustering both at a household and familial level was demonstrated in population endemic for *A. lumbricoides* in Nepal (William-Blangero *et al.*, 1999) and susceptibility to *T. trichiura* infection has also been shown to be common in families (Chan *et al.*, 1994). In Nigeria, where prevalence as high as 50% has been recorded among preschool children, the household aggregation of STH infection remains unexplored, most studies were carried out among school aged and preschool children. The study conducted by Asaolu *et al.* (1992) among all age groups in four different villages in Oyo State, recorded the significance of household size as an important factor influencing egg output. Hence, there is a need for this present study to look into the STH infections within and between households in southwestern Nigeria.

2.7 Host Genetic factors predisposing to STH infections

Helminth parasites are regarded as master manipulators of host immune response (Williams-Blangero *et al.*, 2012 Bethony *et al.*, 2006; Quinnell *et al.*, 2010). On helminth-host immunity relationship, Bentwich *et al.* (1995, 1999) have reported that the ability to mount an effective immune response to other infections, particularly HIV and tuberculosis is gravely impaired by helminth infections. Research reports on STH genome indicate Interleukin-10 as the most abundantly produced regulatory cytokine in soil-transmitted helminth infection (Jackson *et al*., 2004; Bethony *et al.*, 2006). The survival success of STH is attributed to their secretomes which interact with host tissues and maintain existence (Bethony *et al.*, 2006). Two key observations and implications emerge from these experts' findings above: The significance of host immune response to STH infection, implying a possible connection between individual genetic component and STH infection and secondly, the worm genetic effects. This points out the relative importance of both host genetic factors and worm genetic factors on disease distribution.

Several facts suggest that there is an important genetic influence defining the susceptibility to helminth infections. It is typical that worm loads are over-dispersed in the infected communities with 20% of the individuals harboring 80% of the parasites (Holland, 2009). Individual predisposition to get infected by heavy or light worm loads is maintained in treatment-reinfection studies (Hlaing *et al*., 1987), and aggregates in families (Chan *et al*., 1994). Epidemiological studies revealed than in addition to exposure and household determinants, genetic factors account for an important proportion of the variation in worm loads (William-Blangero *et al*., 1999, 2012, Cuenco *et al*., 2009, Quinnell *et al*., 2010).

Genetic factors have been also found to influence the levels of protective antibodies against helminths, as shown for the IgG levels to larval and adult worm antigens in humans infected by *W. bancrofti* (Cuenco *et al*., 2009). The heritability of circulating antibody levels against helminths (particularly IgG_1 and IgG_2) ranges between 70 and 80% depending upon time and isotype (Gasbarre *et al*.,1993), and gene expression analyses have found that many genes differentially expressed between resistant and susceptible animals are indeed implicated in antibody synthesis (Araujo *et al*., 2009). *A. lumbricoides* is very allergenic and, as explained earlier, induces in the host a type-2 skewed immune profile with several features that resemble the allergic response to non-parasitic allergens, including the synthesis of specific IgE (Fitzsimmons *et al.*, 2014). The role of this isotype in the resistance to *Ascaris* is controversial, but some studies have shown that worm loads and the proportion of re-infected children after treatment is significantly lower in individuals with the highest levels of anti-*Ascaris* IgE antibodies (Hagel *et al.*, 2008). In endemic populations, most of the infected individuals produce specific IgE to *Ascaris* without developing allergic symptoms, suggesting that the regulation of the antibody response to helminths is polygenic, and genetic loci influencing the strength and specificity of the IgE response to helminths do not necessarily confer susceptibility to allergic asthma or IgE sensitisation.

Researchers have largely been investigating diseases, including STH infection, from population-based approach, particularly with an important objective of finding out how the differences observed in susceptibility to many infectious diseases are greatly influenced by host genetic factors (Ellis *et al.*, 2007, Quinnel *et al.*, 2010, William-Blangero *et al.*, 2012, Kaliappan *et al.*, 2013). According to William-Blangero (2012), the host genetic factors that are found within a specified population is important in determining patterns of infection rather than host population structure. The identification of specific host genes responsible for susceptibility to infection or the phenotypic response to infection is most important in determining more effective intervention for assessment of the impact and control of STH in a population. The high density genetic markers that were used in identification of specific genes were specifically used to perform quantitative trait locus (QTL) which was used to track segments of DNA that are passed identical-by-descent across generations in order to co-localize them with phenotypic variations.

William-Blangero (2002) reported a strong evidence for two distinct loci influencing susceptibility to Ascaris infection. The strongest signal was found near the q terminus (13q32-q34) of chromosome 13, the observed logarithm of odd (LOD) score represent strong evidence that a gene in the area of chromosome 13 harbours an important quantitative trait locus influencing human host Ascaris burden. The second clear evidence for quantitative trait locus influencing susceptibility to Ascaris infection was on chromosome 1. On this chromosome, the LOD score exhibits a sharp peak at 1p32 with maximum value 3.01, genome-wide p-value 0.033. The peak is significant and provides clear evidence for a second locus influencing the Ascaris worm burden trait.

A further research in Nepal involving a genome scan of the Jirel tribe pedigree provided strong evidence for two distinct quantitative trait loci (QTL) influencing the susceptibility to *Ascaris* infection. The genes are on chromosomes 1 and 13 and there was an evidence for a third locus influencing *Ascaris* burden on chromosome 8. There are evidences that the latter quantitative trait locus was significantly less than the former two loci (Williams-Blangero *et al.* 2002). A subsequent genome scanning of the Jirel pedigree now in a higher number of host individuals, identified additional six and three chromosomal regions with evidence for QTLs influencing the intensity of and susceptibility to *Ascaris* infection and within the QTLs multiple immune-related genes were also identified. (Williams-Blangero *et al., 2008).*

The genome wide linkage analyses study done by William-Blangero *et al* (2008) in Eastern Nepal among the Jirel population, provide evidence for two quantitative trait loci (QTL) influencing susceptibility to whipworm infection, one located on chromosomes 9 (LOD score 3.35; genome wide P= .0138) and the other located on chromosome 18 (LOD score 3.29; genome wide P=.0159). The heritability (or familiality) of the whipworm egg count in this sample of individuals in the Jirel population is highly significant ($h^2 = 0.38 \pm 0.06$; P =6.5 x 10^{-17}). On chromosomes 9 is found the PDCD1LG1 which is also known as B7H1 genes, this gene are known to be involved in the stimulation of T cell response and have a particularly strong effect on the production of interleukin(IL) -10 (Dong *et al.*, 1999). Levels of IL-10 among other cytokines in humans, have been shown to be factors predictive of the susceptibility to whipworm infection (Jackson *et al.*, 2004).

Nevertheless and considering the overlap in biological pathways implicated in the immune responses to helminths and allergens, it has been hypothesised that some genetic variants influencing the IgE response to helminths may also predispose to develop IgE sensitisation with non-parasitic allergens (Muller *et al.*, 2007) or even predispose to allergic diseases (Hopkin 2009, Fumagalli *et al.*, 2010). Although the empirical evidence is limited, it can be noted that (i) the major histocompatibility complex (MHC) participate in determining susceptibility to helminthic infections (De Angelis *et al.*, 2012) (ii) some genetic variants are associated to both, susceptibility to helminthic infections and allergic sensitisation, as shown for the genes encoding for interleukin 13 (*IL13*), the signal transducer and activator of transcription 6 (*STAT6*), and chitotriosidase; and (iii) other genetic loci regulate the antibody response to helminths without predisposing to allergy.

Studies in humans and other mammals support the role of genetic factors in the predisposition to *Ascaris* (William-Blangero *et al.*, 1999, Nejsum *et al.*, 2009) but few genes have been identified so far (Mohler *et al.*, 2007, William-Blangero *et al.*, 2002, 2008, Peisong *et al.*, 2004,Acevedo *et al.*, 2009). The enhanced resistance to parasitic worms through genetic variation has been observed in Th2 immune signaling genes and some also contribute to allergic susceptibility. Peisong *et al.* (2004) found an association between a common genetic variant of the 3′-UTR regulatory elements of *STAT6* and *Ascaris* egg counts in China (Peisong *et al.*, 2004). In addition, a cross-population comparison between haplotypes in China and United Kingdom revealed a negative correlation between worm burden and expected risk of asthma (Mohler *et al.*, 2007). The 5q31 locus is another example of a common locus for the susceptibility to helminthic infection and allergic diseases. It contains genetic variants in the *IL13* gene associated with the worm burden of *Ascaris* in a Chinese population.

Genes encoding for human chitinases have been also identified as a potential link between ancestral responses to invertebrates and the susceptibility to allergic phenotypes. In humans, chitinases promote Th2 responses. The acidic mammalian chitinase (AMCase) is induced in epithelial cells and macrophages by an IL-13-mediated pathway and is expressed at high quantities in human asthma (Zhu *et al.*, 2004). Genetic polymorphisms in chitinase genes have been associated with asthma (Bierbaum *et al.*, 2005), and asthmatic children exhibited increased chitinase activity and increased YKL-40 levels in BALF (Goldman *et al.*, 2012). Genetic variants in the gene encoding chitotriosidase (*CHIT1*) have not only been associated with the response to filarial infection but also with asthma (Sinha *et al.*, 2014, Kim *et al.*, 2013).

Experiments using different strains of mice and rats demonstrated the MHC-restriction in the recognition of excretory-secretory products of *Ascaris* and the genetic control of the antibody response to its antigens (Kennedy 1989, Kennedy et al., 1990), however, the relationship between human MHC alleles and the specificity of the antibody response to *A. lumbricoides* is unknown. Linkage studies identified a quantitative trait locus (QTL) accounting for the variability in *Ascaris* egg counts and total IgE levels in chromosome 13q33-34 (William-Blangero *et al.*, 2002). A second linkage-based genome scan, including 1258 members of a single pedigree identified three potential QTLs influencing susceptibility to *A. lumbricoides* with genome-wide significance, localised on chromosomes 8, 11, and 13 (William-Blangero *et al* 2008). Of these regions, the 13q33 locus is of great interest because it contains the gene *TNFSF13B* encoding for the cytokine B cell activating factor (BAFF). They studied the role of common variants in the 13q33 locus on the IgE and IgG levels against *Ascaris* and the putative resistance marker ABA-1, and identified a region of 125 kb harbouring two polymorphisms significantly associated with antibody levels against *Ascaris* (Acevedo *et al.*, 2009). The effect of this variant was observed in both non-asthmatic and asthmatics, suggesting that participates in pathways implicated in antibody synthesis under physiological conditions and is not directly associated with allergic sensitisation and/or asthma. At this point, it is unclear if the association in

LIG4 is functionally related with this gene or resulted of the linkage disequilibrium with other variants. Furthermore, the polymorphism rs10508198 (3980G>C) in the *TNFSF13B* gene was associated to the specific IgG levels to *Ascaris*. The carriers of the wild-type genotype GG have the highest levels of specific IgG to *Ascaris* in both non-asthmatics and asthmatics, suggesting that *TNFSF13B* may regulate the strength of the antibody levels against *Ascaris*. There was no association between markers in the 13q33 locus and the IgE levels to House Dust Mites (HDM) or the presence of asthma (Acevedo *et al*., 2009).

In Nigeria, the data about the involvement of this human genetics in STH infection is lacking, hence there is need for the information about the heritability of STH among the Nigerian population.

2.8 Morbidity control through deworming programme

In the 1980s, several oral drugs developed and commonly used in veterinarian practices were found to be highly effective against human worm pathogens. These included praziquantel and albendazole (Hotez *et al*, 2004). This development, for the first time, allowed the systematic examination of the impact of these parasitic infections on more subtle aspects of morbidity, such as childhood growth stunting (Adams *et al*, 1994, McGarvey *et al* 1996, Olds *et al* 1999), delayed intellectual development (Nokes *et al*, 1992, Kimura *et al*, 1992), cognitive impairment (McGarvey *et al*, 1996), decreased function work capacity and anemia (Ezeamama *et al*, 2005, Friedman *et al*, 2005).

Through research, it became clear that a significant amount of morbidity induced by worms was based on a complex interaction between the host and the specific parasite. In children, for example, the growth stunting effect of parasites was most marked in early childhood or during the adolescent growth spurt; and it depended (to a large extent) on the baseline nutritional status of the population, i.e., populations which already had moderate to severe malnutrition, suffering disproportionately from the same degree of parasitic infection (Olds *et al*, 1996). Fortunately, growth stunting could often be reversed with curative chemotherapy, but it was critical to keep the child free of rapid reinfection (Olds *et al*, 1996). Cognitive impairment from parasitic infections was also most pronounced in the youngest children and could often be reversed rapidly, following parasitological cure.

Anemia was perhaps the most complex of the worm-induced morbidities. As one might expect, the impact of worms on anemia was greatest in populations who were already iron deficient and among women and growing children of both sexes. With infections, such as hookworm, anemia was principally driven by blood loss (Hotez *et al*, 2004). As a result, the development of anemia could be arrested with parasitological cure, but improvements in blood counts required iron supplementation (Hall, 2007).

It was also recognised that growing children had long-term detrimental effects of chronic parasitism that could be reversed if regularly "dewormed" (Cooper *et al*, 1995). The international health communities, specifically the World Health Organisation (WHO), began to look into the feasibility of deworming populations on a scale similar to childhood immunizations and distribution of oral rehydration fluid (WHO 2002a, 2002b, 2006). The evolving plan was to use a combination of anti-helminthic drugs to treat several parasitic infections, at the same time it was important to determine the most cost-effective way to deliver treatment, particularly to school-aged children. Such an approach also had to be both safe and effective. The WHO commissioned a double-blind placebo-controlled trial in four locations (two in Africa, two in Asia) using the identical protocol to make this determination (Cioli *et al*, 1995, Olds *et al* 1999). The study showed that the two most important drugs, albendazole and praziquantel, could be administered together and that the side effect profile was so low that they could be administered by school teachers and lay community health workers. This study and several additional ones were used to show that mass deworming could have a positive impact on growth stunting, anemia, and cognitive performance. As a result, the concept of deworming a significant percentage of the at-risk children of the world was brought to the international agenda in early 2000 (WHO 2002a 2002b).

Miguel and Kremer (2004) analyse the impact of deworming on children's health and education. They evaluated International Christelijk Steunfonds Africa's Primary School Deworming Project, which targeted children in 75 primary schools in the Busia region of Kenya with anti-STH and anti-schistosome treatment. Their evaluation results were inspiring: school-based deworming treatment kick-started a virtuous cycle of lower worm loads, improved growth, and fewer school absences among children. The Kenyan government and donors, impressed with their findings, seized the opportunity to incorporate school-based deworming into the new national school health policy. The government used a nationwide fecal survey and mapping exercise to identify high-burden areas and guide the design of the intervention. In 2009, school-based deworming went live at scale in Kenya.

Encouraging results from the Busia trial provided a strong basis for national scale-up. Researchers' analysis showed that one year after the intervention, children who received deworming children treatment were 44 percent less likely to have a moderate or severe worm infection. As a result, they were significantly taller, less likely to report being sick, and less likely to miss school than they would have been without treatment (Miguel and Kremer, 2004). By late 2014, four high-burden provinces saw dramatic reductions in infection, with STH prevalence falling to just 6 percent (Kenya Ministry of Education, Science and Technology, 2014 Report). These results have come at a remarkably low cost. In Kenya, it costs about US$0.56 per treated student per year. An analysis of Kenya's programme conducted for Millions Saved yielded a cost-effectiveness ratio of US$47.20 per DALY averted.

Kenya's efforts illustrate that delivering deworming drugs on a national scale necessitates a sophisticated programme that coordinates across schools, government ministries, and donors. It also shows that pairing decentralised delivery with measures to promote national accountability can work. And that public health intervention can impact more than health, reinforcing the need to look at synergistic gains in education, productivity, and growth. In Kenya, deworming's wide-ranging benefits changed the lives of millions of children for the better. But the programme is vulnerable given its reliance on donors, and the sustainability of the effort may be in question as Kenya faces funding battles for other disease priorities.

The use of anthelminthic drugs on a large scale for school-aged children in less developed countries was at the center of the 2010 resolution of the World Health Assembly. This led to the WHO 2010 resolution on achieving a 75% preventive chemotherapy coverage for pre-school and school-aged children by the end of that year yielded at the global level only 31% with 38% in India (WHO 2012). The reason for the decision was based on the facts that school-based studies have the tendency to improve compliance and further improve infrastructure. It has been reported that as few as ten roundworm can affect the growth of school-age children, and that moderate whipworm infections can cause retardation and anemia. In case of more severe infection, children infected with Trichuris dysentery syndrome show "catch-up growth" after treatment (Drake 2000). Several studies in Nigeria have demonstrated the efficacy, acceptability and cost-effectiveness of school-based control of Soil-Transmitted infections (Nworgu *et al.,* 1998, Ogbe *et al*., 2002, Kirwan *et al.,* 2009). Studies conducted among preschool aged children (Kirwan *et al.,* 2009) and other adult groups (Egwunyenga and Ataikiru 2005, Rukmanee 2008, Pullan *et al.,* 2010) show they harbour significant level of parasites that will allow the continual existence of the STH infection in the entire population; this will lead to reinfection after treatment. High rate of re-infection in endemic region despite several rounds of school-based deworming implies, therefore, that reduction of morbidity due to decrease worm burden is the purpose of deworming and not the reduction of prevalence. The severity, extent, and long-term consequences of morbidity are reduced following the WHO recommendation of regular administration of single-dose anthelminthic drugs. Amongst adults, prevalence and intensity of infection remains high (Kirwan *et al.,* 2009, Rukmanee 2008, Pullan *et al.,* 2010). Meanwhile, Ellis *et al*. (2007) in their study suggested that targeting "infected households" is an effective, practical and rapid method of identifying and treating helminth-infected adults in the community.

According to Katherine Parks (2017), Deworm the World has helped treat over 196 million children in Kenya, India, Ethiopia, Vietnam and Nigeria as at 2016, with some preliminary support introduced in Pakistan. Deworm the World's two biggest programmes are in Kenya and India. In Kenya, the Deworm the World Initiative has helped implement the government of Kenya's national deworming programme in schools since 2012. The collaborative project treated 6.41 million children in 16,708 schools in 2016. The programme served 83 percent of children in at-risk areas. Deworm the World's average cost of treating a child in Kenya is $0.71. India is the country with the most worm infections; 220 million children are at-risk of infection by STH. In India, the Deworm the World Initiative supported the government with the development and launch of National Deworming Day. National Deworming Day targets all children between one and 19 years old and is implemented in schools. In 2017, the government of India treated over 260 million children. Deworm the World's average cost of treating a child in India is $0.34. In 2016, 69 percent of at-risk children were treated for STH, a 6 percent increase from 2015. Coverage in African countries was 65 percent in 2016 (Katherine Parks, 2017).

2.9 New way forward: Target drugs or vaccine

The long-term use of anthelminthic drugs could promote drug resistance, thereby lowering the effectiveness against STH (Bethony *et al* 2006, William-Blangero *et al* 2008, Kirwan *et al* 2009). According to Bundy *et al* 1987 and other numerous studies, individuals are readily re-infected after receiving anthelminthic treatment, and it is an indication that acquired host immunity to infection is little (Bundy *et al* 1987, Bradley and Jackson 2004, Narain *et al* 2004). Helminth co-infections may also diminish the efficacy of future vaccines. It is generally accepted that vaccines for STHs would be the most ideal control agents as they would prevent re-infection, which anthelmintic drugs do not. However, there are no licensed vaccines (Noon and Aroian 2017). Currently, chemotherapy is delivered *via* mass drug administration (MDA), stirring grave concern for the strong selection of drug resistance, especially with limited efficacious anthelmintic drugs (Geerts and Gryseels, 2001). Immunity to STH infections does not develop upon clearance, and represents a vast issue for humans who are rapidly re-infected after chemotherapy (Bethony *et al.* 2006). Thus, vaccines would go a long way towards STH elimination.

An important distinction between STH infections in humans and livestock, ruminants in particular, is that in the latter, protective immunity often develops with age, but in the former, this is not the case. So, although the duration of vaccine-induced protection in livestock may only need to last long enough to protect younger animals, for humans this protection would need to last throughout their lifetime. Thus, developing vaccines for humans will likely be a much greater challenge than for livestock due to the high likelihood that repeated immunisations will be needed throughout life.

Bartsch *et al.* (2016) developed a target product profile (TPP) for a recombinant subunit vaccine against human hookworms and evaluated the vaccines economic and epidemiologic impact on hookworm infection in endemic Brazil. A modelled human hookworm vaccine administered in a single dose to infants (78% coverage rate) with an efficacy of 80% at preventing L3 maturation and providing at least 10 years of protection with a single booster at 15 years of age (78% compliance), and costing $1 per dose, was highly cost-effective and economically dominant compared with no intervention or annual MDA (Bartsch *et al.* 2016). Thus, a human STH vaccine with such a TPP should be ideal.

Many vaccine candidates for human parasite are undergoing clinical trials phases. Glutathione S-transferases (GSTs) play critical role in parasite-host interactions, and because it has demonstrated protective effect against some parasites, it has been targeted for pharmaceutical and vaccine purposes. For instance, a GST from schistosome is currently a leading vaccine candidate for human schistosomiasis. Parasite like hookworm which are blood- feeders need to maintain a cytotoxic-metabolic requirement balance and hence GST is a potential heme regulator. For hookworm Na-GST-1 adjuvanted with Alhydrogel has been shown to elicit protective immunity in two vaccine trials in a permissive hamster model (Zhan *et al* 2010). A recombinant bivalent subunit vaccine containing r*Na*-GST-1 expressed in *P. pastoris* and a catalytically inactive, but still immunogenic, r*Na*-APR-1 expressed in tobacco plants (used as an alternative to *P. pastoris* since expression was low) and formulated on Alhydrogel is currently in Phase I clinical trials for hookworm infection (Hotez *et al.* 2016). Clinical testing is also evaluating if including synthetic Toll-like receptor agonists glucopyranosyl lipid A (GLA) or CpG oligodeoxynucleotide will help achieve acceptable immunogenicity (Hotez *et al.* 2016). Surprisingly, to the best of our knowledge, there are no published results on the level of protection provided by the bivalent vaccine. Nevertheless, this vaccine is admittedly not expected to prevent hookworms from establishing infection within the small intestine (Hotez *et al.* 2010; Hotez *et al.* 2016), but the evidence does suggest that it will reduce clinicopathological parameters below threshold levels. Thus, although there are still many unanswered questions for this vaccine, there is cautious optimism for significant impact. There are no published studies for recombinant subunit vaccines for any Trichuris sp, vaccination of mice with adult *Trichuris muris* Excretory Secretory products resulted in almost complete protection against *T. muris* egg challenge, in association with a classical T_H2 response (Dixon *et al.* 2010)

The first study that tested recombinant subunit vaccines against *Strongyloides* spp. used a DNA vaccine approach against experimental *S. stercoralis* L3 infection in BALB/cJ mice (Kerepesi *et al.* 2005). *Strongloides stercoralis* deoxycholate-soluble L3 antigens tropomyosin (*Ss*-TMY-1), Na+-K+ ATPase (*Ss*-EAT-6) and galectin (*Ss*-LEC-5) were shown to be recognized by serum IgG isolated from human plasma obtained from exposed Haitian donors, and this serum was shown to passively transfer protection to BALB/cJ mice (Kerepesi *et al.* 2005). Currently, there are no published results for recombinant subunit vaccines against *A. lumbricoides*, while several studies have been published for *A. suum* and *B. schroederi*. Given the recent common ancestries between these ascarid species and *A. lumbricoides*, such studies are highly relevant to this most prevalent human STH (Noon and Aroian 2017).

In order to effectively control the prevalence and incidence of STH in Nigeria, there is a dire need for an improved understanding of the biological determinant of differential susceptibility to Soil transmitted helminth infection in Africa, particularly in Nigeria. The result of this study provides possibly the first step towards the identification of which factor, that is, human genetic factor or environmental factor, has greater influence on the differential susceptibility to Soil–transmitted helminth infection in Nigeria.

CHAPTER THREE

MATERIALS AND METHOD

3.1 Research Area

The study was conducted in Igbo-Ora, one of the most popular town in Ibarapa local government under Oyo State, southwestern Nigeria. Igbo-Ora lies in the savannah area of the country, having numerous small streams as one of its prominent geographical features. The town has three main rivers that pass through her; these are River Opeki, Ofiki and Ayin. Igbo-Ora is about 120km from Ibadan, the state capital; the majority of the people that make up the town are Yoruba. The climate consists of a cooler rainy season (April – October) and warm dry season (November – March). The majority of the men of the town are farmers and hunters by occupation, and the women are peasant farmers and retail traders. Igbo-Ora town was divided into six local communities, and each community has a traditional leader referred to as ‘Baale’ who are identified as Baba-aso of Igbole, Onisaganun of Saganun, Oludofin of Idofin, Olu of Ibeerekodo, Olu of Pako and the overall head, that is, the Kabiyesi is the Olu of Igbo-Ora.

3.2 House mapping

The town was geographically mapped, using Geographic Information System (GIS), into three density areas: Low density, medium density and high density areas, depending on the household clustering in each area. Seven clusters of house density was identified which comprise of 4 low, 2 medium and 1 high density areas. The GIS grid recorded a total of 88, 160 and 209 grids for the high, medium and low density areas respectively, out of which 30% of each was randomly selected for the study (Fig. 3.1). Each grid can have between 1-5 households, depending on the density of the area. All households within the randomly selected grid are eligible and were given a code number and individuals in those households were allotted a Personal Identification Code (PID). The longitude and latitude of each household participating in the study was determined using hand-held GeoExplorer Global Positioning System (GPS). A sufficient satellite reception was ensured by taking reading at a resolution of about 2m away from the front door or as near as possible. In all, an average of 10 readings of the co-ordinate was taken. Map was created using ArcGIS 10.3 (Environmental System Research Institute Inc., Redland, CA, USA).

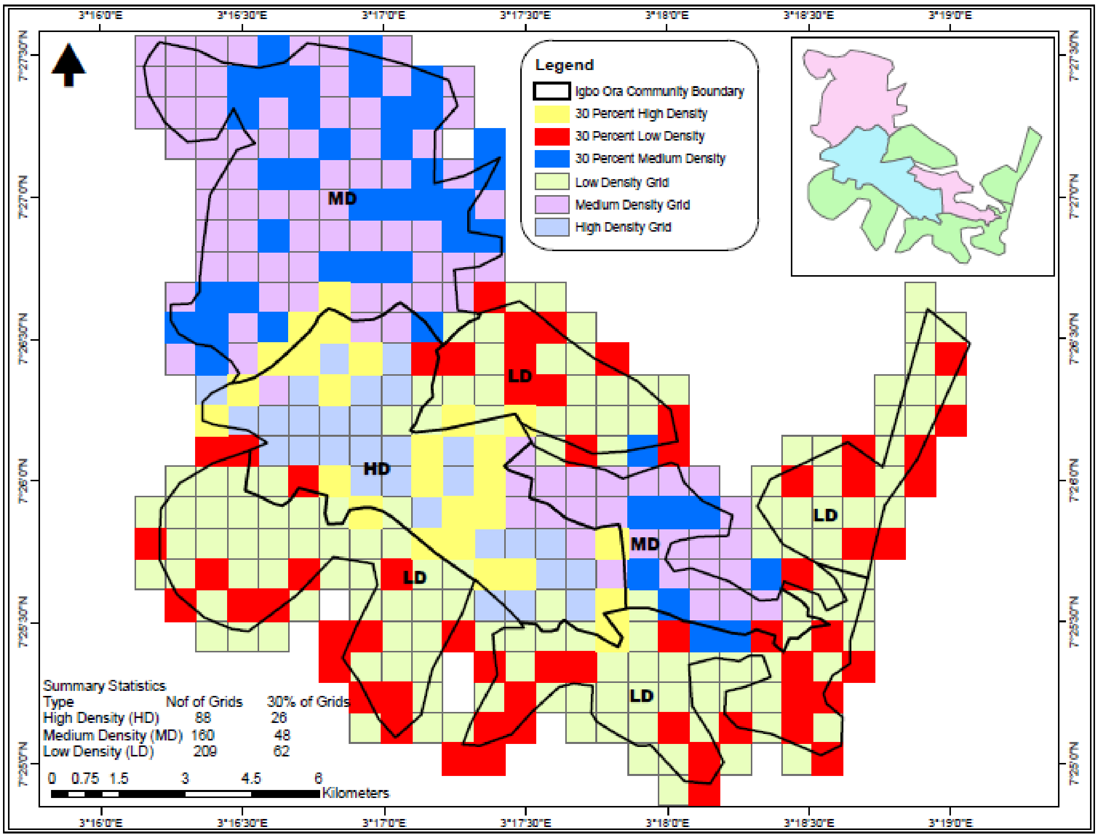


Fig. 3.1. A GIS map showing the sampling grid of Igbo-Ora according to house clustering of the community.

3.3 Questionnaire for collection of demographic, behavioural and observational data

Approval for the protocol was obtained from the Ethical Review Committee of the College of Medicine, University of Ibadan, Nigeria with approval number UI/EC/12/0267. (Appendix 1)

Inclusion criteria:

(i) The individual enrolled in this study must reside in the selected area over the last 2 years.

(ii) Consents of the members of the selected household were sought, and in case of minors, the parents or guardians gave consent on their behalf.

Exclusion criteria:

(i) The individual attending school or working outside the study area,

(ii) Received anthelminthic treatment within the last 1 year.

All individuals in the study were interviewed with a structured questionnaire. Demographic information for age, sex, education, occupation, past history of worm infection and treatment, availability of toilet facilities, shoe wearing habit with hand washing practices were obtained with the questionnaire and physical observation. (Appendix II)

3.4 Household survey for pedigree information

Information about relationships between all household members was provided by household heads during interview and this was further verified by asking close or related neighbours. All adult subjects and parents or guardians of minors gave their written or verbal consent (Appendix III). The pedigree data collection adopted the format designed by William-Blangero and Blangero (2006) and modified to suit the cultural ideology of the African race, especially the Yoruba norms about asking for information about relatedness. The collected information was recorded in a separate pedigree interview sheet for each household (Appendix IV). The family relationship was grouped as: First degree relative – parent offspring, second degree are siblings, third degree relative - grandparent/grandchild and fourth degree relative - cousins. Names of other first or second degree relatives living in other households within the study area were collected.

Individuals were assembled into a pedigree if they are related to or married to anyone in a pedigree. Pedigree was assembled and was virtualised using genetic pedigree software called PROGENY. The family information was coded into the pedigree file, while all other data were coded into the phenotype file in the SOLAR programme.

3.5 Soil analysis

Two soil samples were taken from two different locations at 20m distance from the entrance of each household according to Stojčeviić *et al*. (2010). At each site, 500g of top soil was taken with a small shovel in the area inside a square of 25 x 25cm and 10cm in depth. This was put inside a labeled plastic bag and taken to the laboratory (Stojčeviić *et al.* 2010). These samples were analysed in the laboratory using saturated $ZnSO_4$ solution in centrifugation floatation method as described by Cheesbrough (2000) and modified by Stojčeviić *et al*. 2010. 500g of the soil or sand sample was stirred and100g was placed in a cup and stirred again with 100mL water and sieved to remove larger particles. The homogenised solution was placed into sedimentation cups, filled with 500mL water and left overnight. After the supernatant was decanted, 20g of the sediment was re-suspended with 50mL water, placed in 2 centrifuge tubes and centrifuged at 1500 rpm for 5mins. Finally, the sediment was re-suspended in 15mL saturated $ZnSO_4$ solution and poured into centrifuge tubes which were filled to the brim and the coverslip was superimposed. The samples were centrifuged at 1500 rpm for 5mins, the coverslip was removed onto a microscopic slide and examined for the presence of parasites eggs under the microscope at x10 and x40 magnification. Pictures were taken by Optika Microscope Italy a digital binocular microscope 35ML).

3.6 Stool sample collection

After the administration of the pre-tested questionnaire, a wide mouth screw-capped 100 mL container pre-labelled with the participant PID was given to all subjects for the collection of their stool sample the next day. Uneducated participants were asked to give a mark or signs by which they could recognise each Child’s and ward’s sample bottles. Their ability to recognise their names was counter-checked. Each subject was instructed to scoop a thumb size stool sample using a provided scoop into the container. Parents and guardians were also instructed to monitor their children during the sample collection to ensure that they placed their stool samples into the right containers. All study subjects were asked to provide moderately large stool sample (at least 10g) so that both the wet preparation and Kato-Katz techniques could be performed (Katz *et al.,* 1972). A single stool sample collection was done contrary to the original design, because it was difficult to convince the participants against their cultural belief of giving away their stool samples for any purpose whether scientific research or not.

The presence of any parasite was determined by using normal saline wet preparation methods. This was necessary to identify parasite when the load is high and also to identify actively motile parasite such as *Strongyloides stercoralis*. Actively motile parasite such as *Strongyloides stercoralis* cannot be identified with Kato-katz concentration method adopted in this study and it can be missed out once the parasite dies. Kato-katz thick smear technique was used as the concentration method and the procedure was carried out for the stool sample collected, this method is appropriate in case of low parasite load. For the intensity of infection, quantification of ova/eggs per gram of faeces (epg), the ova was counted per gram of faeces. To make up for the impossibility of collecting two stool samples per participants, two slides were taken from each stool sample and were examined within 45 minutes of slide preparation.

3.6.1 Laboratory analysis

Wet Preparation

Two drops of normal saline was placed on a clean slide**,** **s**patula was used to pick a speck of faecal material. The faecal material was then mixed with the normal saline on the slide until it was dispersed**,** then a cover slip was gently placed on the slide with the smear in order to avoid bubble**,** the slide was placed on a microscope and viewed under x10 for general observation and x40 for confirmation.

Kato-Katz concentration method

A small mound of faecal material was positioned on a glass tiles, a cover screen was placed on top of the faecal material and some faeces were sieved through the screen. A flat-sided spatula was used to scrape the upper surface of the screen and the sieved faeces accumulate on the spatula. A template with holes was placed on the center of a microscope slide, the faeces from the spatula was added to the hole until it was completely filled and excess faeces was removed from the edge of the hole. The template was removed carefully from the slide, leaving mounted on it only the cylinder shaped faeces which was then covered with the already pre-soaked cellophane strip.

Another clean slide was used to firmly press the faecal sample with the cellophane strip; with mild pressure the faecal sample was evenly spread between the slide and the strip. The slide was gently removed without detaching the cellophane strip; the slides with faecal-smeared samples were placed on bench until water evaporated while glycerol in the strip cleared the faeces. For all, except hookworm eggs, slides were kept for at least one hour at ambient temperature prior to the examination under the microscope. The smears were systematically examined to report the number of each parasites species. These were later multiplied by 24 to give the number of the eggs per gram faeces and a quantitative variable scoring (light infection/low worm burden, moderate infection/medium worm burden and heavy infection/massive worm burden), following the standard procedure used by World Health Organisation (WHO, 2002) was created for each helminth.

3.7 Data analysis

All parasitological and questionnaire data were double-entered into an SPSS 15.0 database and STATA 12 (Stata Corp., TX USA) software and it was cross-checked. Bivariate analysis was calculated for all variables to determine what the strength of association between the exposure and the outcome variable might be. Odds ratio with 95% confidence interval and significance was at $p < 0.05$. Multivariate logistic regression was done using selected variables in relation to the presence of STH infection. Chi-square test $p < 0.05$ was significant.

Prevalence of infection was expressed in percentage, and intensity was measured by egg count per gram (EPG). The parasites isolated from each member of a particular household was grouped and treated as a single unit for spatial and genetic analysis.

Spatial analysis adopted a Bayesian geo-statistical approach which uses Moran index of Z-score at 2.3 and $p < 0.05$ level of significant, putting into consideration both spatial correlation and non-spatial clustering at a household-level which provided the spatial distribution of the infection in the community.

Variance components analysis was done by using a Unix-based software programme called Sequential Oligogenic linkage Analysis Routine (SOLAR). Family relationship information was recorded according to the file format requirements of the SOLAR 8.1.1 software package. The advantage of using SOLAR is its ability to incorporate covariate effects into the models to account for potential confounding factors and a Kullback-Leibler R-Squared value is estimated to indicate the effect size of the covariates in the model.

The family information was coded into the pedigree file, while all other data were coded into the phenotype file in the SOLAR programme. Models were developed that allowed the estimation of heritability (h^2) that is the proportion of variance in STH prevalence/intensity, attributable to genetic factors and the proportion of variance in prevalence/intensity, attributable to the effect of common shared household C^2. The software implement a maximum likelihood method which provides a log-likelihood estimate for each model.

The environmental model adopts the use of common shared households C^2 and the presence of parasite in the soil around household (e^2) as an additional factor, while host genetic factor also included the genetic relatedness.

The analysis of genetic factor was based on Genetic Variance Component Analysis (VCA) whereby the relative importance of genetic susceptibility, other domestic factors and (non- genetic) individual factors in determining infection intensity was assessed. Genetic variance component was used to define the contribution of genetics: the degree of relatedness and environmental influence on intensity of infection, which provided the overall estimate of the total cumulative effect of individual factors (the “addictive genetic” effect, or heritability) on overall variation.

CHAPTER FOUR

RESULTS

4.1 Socio-demographic factors of the participants.

The study population of 673 individuals from 239 households was recruited from four representative communities in Igbo-Ora. The communities were Igbole and Pako, representing the low density area; Isale-Oba in the medium density area; and Saganun in the high density area. A total of 508 consented individuals provided proper stool samples and complete demographic and behavioural information. Two hundred and thirteen (42%) were males and two hundred and ninety five (58%) were females. The age ranged from seven months to eighty six years, with the mean age of 22.8 (95% Cl 21.1-24.6). Table 4.1 showed that 10.2% of the sample population were children <1-5 years of age, while 44.3%, 18.1%, 14.6% and 12.8% were aged 6-15, 16-29, 20-49 and ≥50 years respectively.

More than 50% of the study participants were students while 3.1% of the participants were civil servants. The skilled workers were 5.9% which included professions such as hair dressers, fashion designers, mechanics, electricians and transporters. The unskilled workers were the petty traders and farmers which accounted for 18.3% and the unemployed were 9.8% of the study population.

Table 4.1 also showed the frequency of 68.7%, 27.4%, 3.1% and 0.8% for single, married, widowed and separated marital status of the participants.

The STH infection prevalence among the study participants showed that both male and female were equally infected with 28.2% prevalence in male and 28.1% in female participants. The highest infection prevalence of 34.5% was seen among the children in age group ≤1-5 years, while the age group 6-15 and 16-29 years had similar prevalence of 28.9% and 28.3% respectively. The lowest but not significantly different prevalence was seen among the age group ≥50 years.

STH infection in relation to occupation showed that participants who were civil servants had the lowest prevalence of STH infection with 18.7%, while the highest was seen among the skilled workers (33.3%), followed closely by the unskilled workers (30.1%). There was no significant association between the level of education of the participants and STH infection prevalence within the study population (Table 4.1).

4.2 Prevalence of STH infection in the sampled population

The overall prevalence of STH in the four communities sampled was 28.1%. This reflects the number of individuals infected with any one of the STH parasites. Cases of co-infection were counted once. The parasites identified were *Ascaris lumbricoides, Trichuris trichiura*, hookworm, and *Strongyloides stercoralis* (Fig. 4.1a, b, c &d). Figure 4.1c & d showed the adult worm passed out in faeces by one of the participants during the study. Hookworm infection was the predominant STH infection in the population sampled with 18.5%, followed by *Ascaris lumbricoides* with 16.7%, while *Strongyloides stercoralis* was 3.0% and *Trichuris trichiura* was 0.8% in the population from the four communities sampled. (Fig. 4.2)

4.2.1 Overall prevalence of multiple helminth infection in Igbo-Ora

The result in table 4.2 showed that multiple infections were observed in 36.4% of the infected population in double and triple helminth infections. Forty nine (94.2%) participants had double infections while 3 participants (5.8%) had triple helminth infections. *A. lumbricoides*/hookworm was 89.8% of the double helminth infections, while *A. lumbricoides* /*S. stercoralis*, hookworm/*S. stercoralis* were 4.1% each and *A. lumbricoides* /*T. trichiura* was 2.0%. Triple helminth infections were *A. lumbricoides*/hookworm/*S. stercoralis* with 66.7% prevalence, and *A. lumbricoides* /hookworm/*T. trichiura* was 33.3% of the triple helminth infections (Table 4.2).

4.3 Intensity of STH infection in the sampled population

The majority of the STH infections were of light intensity (table 3). Intensity was classified according to the WHO (2002) standard. For *A. lumbricoides;* 1 -4,999 ova were light intensity, 5,000 – 49,999 ova were moderate intensity, while >50,000 ova were heavy intensity. For *T. trichiura*: 1-999 ova for light intensity, 1,000-9,999 ova for moderate and ≥ 10,000 ova for heavy intensity. For hookworm: 1-1,999 ova as light intensity, 2,000-3,999 for moderate and ≥ 4,000 ova for heavy intensity. Few cases of moderate and heavy intensity were seen in *A. lumbricoides* and hookworm infections. In this study, intensity of *A. lumbricoides* and hookworm increases with age and both have two peaks of infection at different age groups (Fig 4.3)

Table 4.1. Demographic characteristics and STH infection among the study participants in Igbo-Ora (N=508)

Demographic factor	Number (%)	STH Infection Yes	Pearson Chi-square	P- value
Sex				
Male	213 (42%)	60 (28.2%)		
Female	295 (58%)	83 (28.1%)	0.0001	0.993
Age				

≤1-5	52 (10.2%)	18 (34.6%)		
6- 15	225 (44.3%)	65 (28.9%)		
16-29	92 (18.1%)	26 (28.3%)		
30- 49	74 (14.6%)	19 (25.7%)		
≥50	65 (12.8%)	15 (23.1%)	2.19	0.70
Occupation				
Student	319 (62.8%)	95 (29.8%)		
Civil Servant	16 (3.1%)	3 (18.7%)		
Skilled worker	30 (5.9%)	10 (33.3%)		
Unskilled worker	93 (18.3%)	28 (30.1%)		
Unemployed	50 (9.8%)	7 (14.0%)	6.64	0.16
Level of Education				
Primary	216 (42.5%)	58 (26.8%)		
Secondary	168 (33.1%)	56 (33.3%)		
Tertiary	34 (6.7%)	8 (23.5%)		
No formal education	90 (17.7%)	21 (23.3%)	3.80	0.28
Marital status				
Single	349 (68.7%)	104 (29.8%)		
Married	139 (27.4%)	31 (22.3%)		
Divorced	16 (3.2%)	7 (43.7%)		
Widowed	4 (0.8%)	1 (25.0%)	4.76	0.19

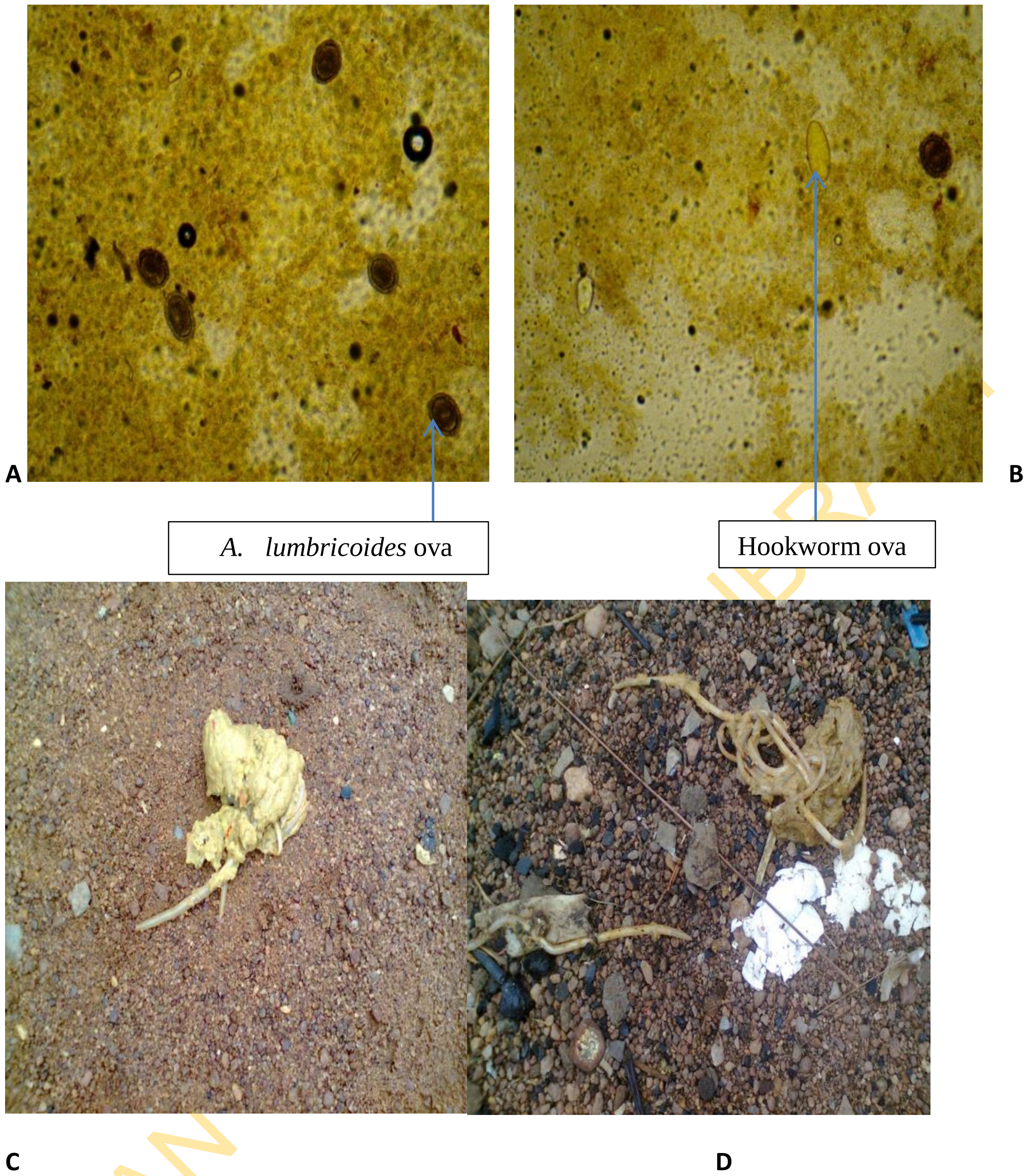


Fig. 4.1. Micrograph of ova and photograph of adult worm of STH parasite seen in participants stool sample.

A : Picture of Kato-Katz microscope slide showing ova of A. lumbricoides. PIN 369

B: Picture of Kato-Katz microscope slide showing ova of *A. lumbricoides* and hookworm.

PIN 404

C & D: Picture of large adult worm passed out with faeces by one of the participants. PIN 262

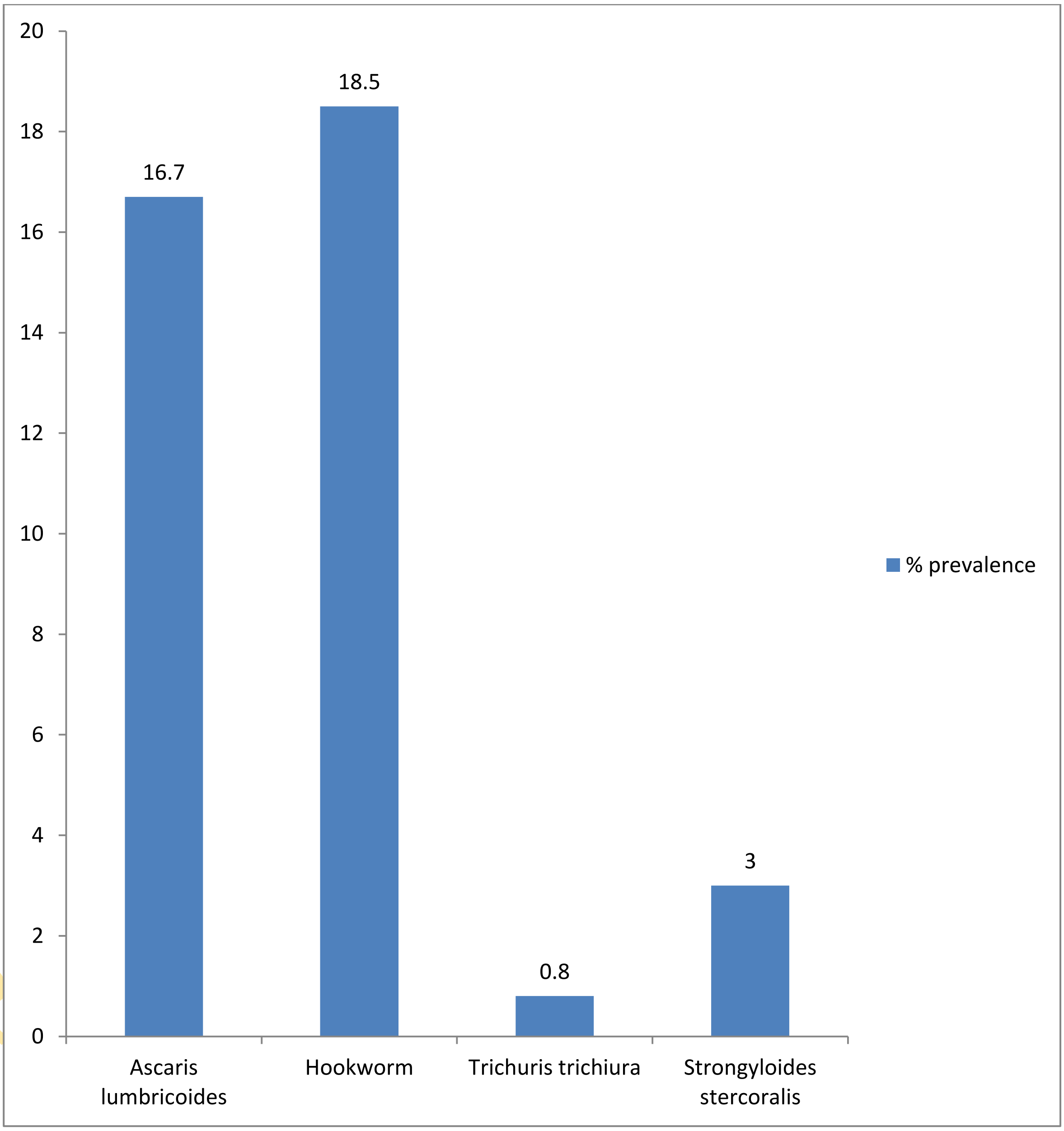
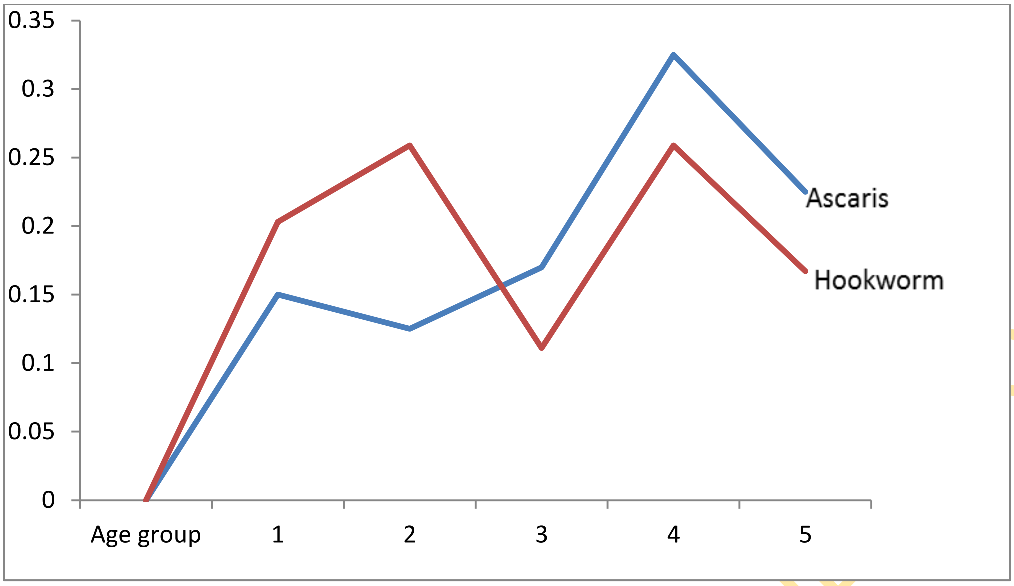


Fig 4.2: The prevalence of each STH parasite within the study population. N=508

Table 4.2: Overall prevalence of multiple helminth infection in the study population.

Multiple helminth infection Prevalence	No of infected individuals	(%)
Double helminth	**49**	**94.2%**
A. lumbricoides /hookworm	44	89.8%
A. lumbricoides /*S. stercoralis*	2	4.1%
A. lumbricoides /*T. trichiura*	1	2.0%
Hookworm/ *S. stercoralis*	2	4.1%
Triple helminth	**3**	**5.8%**
Asc/Hk/Strongy	2	66.7%
Asc/Hk/T. trichiura	1	33.3%
Total	52	36.4%

*Asc = *A. lumbricoides* Hk= hookworm Strongy= *S. stercoralis*



Age group: 1 =<1-5 years, 2 = 6- 15 years, 3 =16- 29 years, 4 = 30- 49 years, 5 = ≥50 years.

Fig. 4.3: The intensity of *A. lumbricoides* and hookworm infection in relation with age group

Table 4.3: Intensity of STH infection in the four GIS mapped community of Igbo-Ora

Infection	Intensity	Community			
		Pako (n)	Isale-Oba(n)	Igbole(n)	Saganun(n)
Ascaris	Light	16	10	23	17
	Moderate	1	-	1	2
	Heavy	2	4	1	9
Hookworm	Light	16	8	15	39
	Moderate	2	1	2	4
	Heavy	1	3	2	2
Strongyloides	Light	3	4	5	3
	Moderate	-	-	-	-
	Heavy	-	-	-	-
Trichuris	Light	2	-	1	-
	Moderate	-	-	-	-
	Heavy	-	-	-	-

Ascaris lumbricoides: 1-4,999 ova light intensity, Moderate intensity 5,000-49,999 ova, and heavy intensity ≥50,000 ova.

Hookworm: 1-1,999 ova is light intensity, 2,000-3,999 ova is moderate intensity and ≥4,000 ova is heavy intensity.

Trichuris trichiura: 1-999 ova light, 1,000-9,999 ova is moderate and ≥10,000 ova is heavy intensity.

4.4 Associated risk factors of STH infection within the infected population

The results from table 4.4 showed the STH infection and associated risk factors of infection in the 143 infected participants. The people living in mud houses are ≃2 times more likely to be infected with STH infection than those living in concrete houses (OR 1.69 95% CI 1.14- 2.49 $p< 0.05$). Likewise, those living in crowded room with more than four people in a room and not having toilet facility are 1.65 and 1.55 likely to be infected with STH infection (OR 1.65; 95% CI 1.12 – 2.44 $p=0.01$ and OR 1.55; 95% CI 1.04 – 2.30 $p=0.03$) respectively. Other factors such as past history of worm infection, defecating in bushes around homes, hand-washing before eating and after toilet, wearing of shoes and having dirty finger nails do not have significant association with STH infection in this study ($p>0.05$).

4.4.1 Multivariate logistic regression of risk factors of STH infection

The multivariate regression model of the associated risk factors for STH infection adjusted for the following variables: age, sex, occupation, hand washing after using the toilet, type of toilet facility, house type, living in crowded room, house density area and having access to toilet facilities (Table 4.5). The result showed that living in mud houses and overcrowded rooms with more than four individuals in a room are important risk factors of STH infection (OR 1.80; 95% CI 1.15 -2.81 $p =0.01$ and OR 1.65 95% CI 0.99 – 2.74 $p= 0.05$ respectively).

4.5 STH infection within households in Igbo-Ora

STH infection was found in 95 households out of the 239 households sampled. The number of participants ranged from 1 to 14 individuals per household. In 150 households, only one person from each household participated in the study. Overall, 39.7% of the households were infected with STH infection. Eighty-nine (89) households (35.7%) had two or more participants per household and STH infection was seen in 51(57.3%) out of the 89 households. Twenty-eight (28) out of 51 households had more than 50% of the household participants infected with STH within each household in the sample population. Forty-four (44) (that is, 29.3%) households out of the 150 households with one participant had STH infection.

Table 4.4: Bivariate analysis of risk factors associated with Soil-transmitted helminth infections within the infected population of Igbo-Ora, Nigeria. N=143

Risk factors	Prevalence of STH (%)	Odds ratio	95% Confidence Interval	P-value
Toilet access				
Yes	54 (23.4%)	1.0 (ref)		
No	89 (32.1%)	1.55	**1.04 -2.30**	**0.03**
Toilet type				
Water closet	26 (22.8%)	1.0 (ref)		
Pit latrine	27 (23.3%)	1.02	0.55 – 1.89	0.93
Bush around home	90 (32.7%)	1.62	0.97 - 2.68	0.061
Past history of worm				
Yes	93 (29.2%)	1.0 (ref.)		
No	50 (26.5%)	0.87	0.58 - 1.31	0.51
Treated for worm in the past				
Yes	28 (22.6%)	1.0 (ref.)		
No	115 (30.1%)	1.46	0.91 - 2.35	0.11
Living in overcrowded room				
≤4	64 (23.4%)	1.0 (ref.)		
>4	79 (33.6%)	1.65	**1.12 – 2.44**	**0.011**
House type				
Concrete	68 (23.5%)	1.0 (ref)		
Mud	75 (34.2%)	1.69	**1.14 – 2.49**	**0.008**
Hand washing before eating				
Yes	138 (28.9%)	1.0 (ref.)		
No	8 (27.4%)	0.88	0.54 – 1.46	0.57
Hand washing after toileting				
Yes	106 (27.0%)	1.0 (ref)		
No	37 (32.2%)	1.19	0.82 - 2.01	0.27
wear dirty finger nails				
Yes	54 (29.8%)	1.0 (ref)		
No	89 (27.2%)	0.87	0.59 -1.31	0.53
wear shoe regularly				
Yes	70 (28.9%)	1.0 (ref.)		
No	73 (27.4%)	0.99	0.63 -1.37	0.71
Community density				
Low density area	66 (46.1%)	1.0 (ref.)		
Medium density area	25 (17.5%)	0.69	0.41 - 1.19	0.41
High density area	52 (36.4 %)	0.93	0.61 – 1.44	0.61

Table 4.5: Multivariate logistic regression analysis of adjusted risk factor of STH infection in the study population

Variables	Odds Ratio	P>z	[95% Conf. interval)
Age group (years)			
<1 -5	1.00		
6--15	0.48	0.07	0.21 -1.06
16 -29	0.65	0.37	0.25 – 1.69
30 – 49	0.41	0.13	0.13 – 1.30
≥50	0.42	0.15	0.13 – 1.37
Sex			
Male	1.00		
Female	0.93	0.74	0.60 – 1.43
Occupation			
Student	1.00		
Civil servant	0.73	0.67	0.16 – 3.22
Skilled worker	1.21	0.75	0.39 – 3.76
Unskilled worker	0.96	0.93	0.37 – 2.47
Unemployed	0.22	0.01	0.08 – 0.63
Wash hand after using the toilet			
Yes	1.00		
No	0.71	0.24	0.40 – 1.26
Toilet type			
Water closet	1.00		
Pit latrine	0.75	0.39	0.39 – 1.45
Bush around the house	2.80	0.35	0.33 – 23.88
House density areas			
Low density	1.00		
Medium density	0.66	0.29	0.31 – 1.42
High density	1.03	0.92	0.63 – 1.67
Living in overcrowded room			
≤ 4	1.00		
>4	1.65	**0.05**	0.99 – 2.74
House type			
Concrete	1.00		
Mud	1.80	**0.01**	1.15 – 2.81
Have access to toilet facility			
Yes	1.00		
No	0.48	0.50	0.06 – 4.01

4.5.1 Households infection within each community

Table 4.6 showed the distribution of infected household per community. A total of 45, 52, 66, and 76 households were sampled in Saganun, Igbole, Pako, and Isale-Oba respectively. The highest number of STH infected household was found in Saganun, with 23 (51.1%) out of 45 households infected. Meanwhile, in Igbole, 22 (42.3%) out of 52 households were infected, Pako had 25 (37.9%) out of 66 participating households infected with STH, while 25 (32.9%) out of 76 households in Isale-Oba had STH infection.

4.6 The prevalence of specific STH parasite within the sampled communities in Igbo-Ora.

The prevalence of each soil-transmitted helminth infection in each of the community sampled showed that the triad of *A. lumbricoides, hookworm and S. stercoralis* was seen in all the four communities. *T. trichiura* was seen only in the two communities representing the low density communities, that is, Igbole and Pako, with 0.8% and 2.2% prevalence respectively. *A. lumbricoides* had the prevalence of 18.5, 21.5, 13.0 and 15.5% in Igbole, Pako, Isale-Oba and Saganun respectively. Meanwhile for hookworm, the prevalence of 13.8, 21.3, 11.1 and 24.9% was seen respectively. The prevalence of *S. stercoralis* was almost the same in three out four communities in Igbo-Ora. Figure 4.4 showed the flow chart of STH infection within each of the four communities with the error bar at 5% value.

The association between the community density and the prevalence of each STH parasite was analyzed, and it was found that there is a significant association with hookworm infection ($p<0.01$) while other STH parasite, that is *A. lumbricoides T. trichiura* and *S. stercoralis* do not have significant association with community density (Table 4.7).

4.6.1 Risk factors for hookworm infections

The significant association of hookworm infection with high density area, as shown in table 4.7 informed the decision to further investigate other associated risk factors for hookworm infection. Table 4.8 showed the bivariate and multivariate logistic regression analysis of hookworm infection with associated risk factors of STH infections. In the bivariate analysis, people who lived in high density area, in crowded rooms, mud houses and had no access to toilet facilities, had higher odds of acquiring hookworm infections OR 2.39 95% CI 1.23 -4.63; $p < 0.01$, OR 2.20 95% CI 1.39 – 3.49; $p<0.001$, OR 1.87 95% CI 1.19 – 2.94; $p<0.01$, and OR 1.64 95% CI 1.03 – 2.59; $p < 0.04$ respectively. Wearing of shoe was not significantly associated with an increased risk of hookworm infection in this study. In the multivariate analysis the variables tested and included in the model were; toilet access, overcrowding, house type, shoe wearing, density and toilet type.

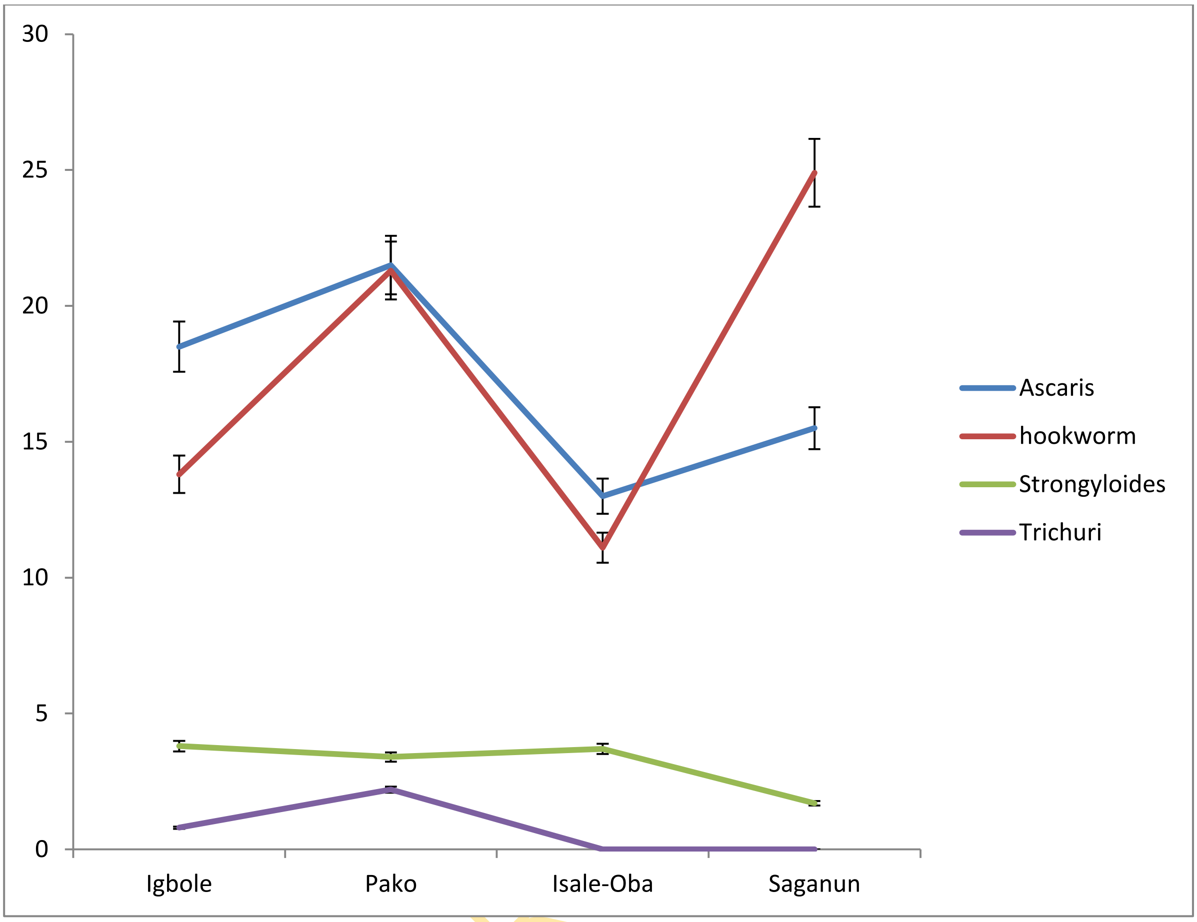


Fig 4.4: The prevalence of specific STH parasite within each of the four communities sampled in Igbo-Ora.

Table 4.6: Distribution of STH infection per household in the four communities

Density Area	Community	Infected households No (%)	Not infected households No (%)	Total No (%)
Low density	**Igbole**	**22 (42.3)**	**30 (57.7)**	**52 (100)**
	Pako	**25 (37.9)**	**41 (62.1)**	**66 (100)**
Medium density	**Isale-oba**	**25 (32.9)**	**51 (67.1)**	**76 (100)**
High density	**Saganun**	**23 (51.1)**	**22 (48.9)**	**45 (100)**
		95 (39.7)	**144 (60.3)**	**239 (100)**

Table 4.7: Association of community density areas and specific STH parasite in Igbo-Ora using Pearson chi-square.

STH parasite	Community density areas			Total	Pearson chi^2	p-value
	Low	Medium	High			
Ascaris lumbricoides	43 (19.6%)	14 (13.0%)	28 (15.5%)	85 (16.7%)	2.63	0.27
Hookworm	37 (17.0%)	12 (11.1%)	45 (24.9%)	94 (18.5%)	9.14	**0.01**
Strongyloides stercoralis	8 (3.6%)	4 (3.7%)	3 (1.7%)	15 (3.0%)	1.65	0.44
Trichuris trichiura	3 (1.4%)	0	0	3 (0.6%)	3.9	0.14

Table 4.8: Factors associated with hookworm infections by multivariate logistic regression analysis in the study population of Igbo-Ora.

Variables	Unadjusted OR (95% CI)	Sig.	Adjusted OR (95% CI)	Sig.
Density				
Low (Reference)	1.0		1.0	
Medium	1.99 (0.93 - 4.24)	0.07	0.91 (0.39 - 2.13)	
High	2.39 (1.23 - 4.63)	0.01	2.12 (1.23 - 3.65)	**0.01**
Shoewear				
Yes (Reference)	1.0		1.0	
No	1.16 (0.74 - 1.81)	0.52	0.62 (0.41 - 1.09)	0.12
Living in crowded room				
≤4 (Ref.)	**1.0**		1.0	
>4	2.20 (1.39 - 3.49)	0.001	2.19 (0.54 - 3.25)	**0.01**
Have access to toilet facility				
Yes (Ref.)	**1.0**		1.0	
No	1.64 (1.03 - 2.59)	0.04	11.6 (0.62 - 21.8)	0.1
House type				
Concrete (Ref.)	1.0		1.0	
Mud	1.87 (1.19 - 2.94)	0.01	1.67 (1.02 - 2.74)	**0.04**
Toilet type				
Water closet (Ref.)	**1.0**		1.0	
Pit latrine	1.99 (0.93 - 4.24)	0.07	1.39 (0.62 - 3.08)	0.41
Bush around the house	2.39 (1.23 - 4.63)	0.01	1.30 (0.09 - 18.7)	0.86

4.7 Prevalence and risk factors of infections in each of the community sampled

4.7.1 Pako Community

Pako community, according to the GIS mapping, was in the low density area of Igbo-Ora. The total population of participants from this community was 89. Forty three (48.3%) participants were males while forty six (51.3%) were females. The prevalence of infection was almost same for both sexes: 37.2% for male and 37.0% for female. Children between the ages of 11-15 years accounted for 71.9% of the participants in this community and had the highest prevalence of STH infection (42.2%). This was followed by a prevalence of 12.1% for the 6-10 years age group. Only 5 adults participated in the study; the reason for this was because the parents refused to take part in the study though allowed their children and wards to participate. Some parents collected the stool bottle only to return it empty without any sample. It was later discovered they held a meeting and agreed that only their children should participate in the study. The reason for this decision was best known to them (Table 4.9).

The prevalence of STH infection was 42.9% among those that had no toilet facilities in their home; while 28.6% prevalence was observed in those using water closet systems; and 34.6% prevalence in pit latrine users. However, the highest prevalence of 42.9% was seen in the category that defecated in bushes around their homes. Participants with more than four (4) people in a room had 41.5% prevalence for STH infection, while 25.0% prevalence was seen among those living in mud houses (Table 4.9).

All the participants reported hand washing practices, but when asked about the frequency of their hand washing practices, only 65 (73.0%) reported they washed their hands regularly and 24 (27.0%) reported they washed their hands occasionally, either before eating or after going to the toilet. Some 39.3% of the participants reported that they wear shoes while in the house but not into their rooms while 60.7% wore their shoes occasionally. The result from table 10 showed the prevalence of STH infection to be 35.4% among those that washed their hand regularly, while 31.9% prevalence of STH was seen in those that practised hand-washing after toilet the use of the toilet and 42.6% prevalence in those that wore shoe occasionally. The prevalence of STH infection was 38.2% among those with dirty finger nails and 38.9% in those with dirty house surroundings (Table 4.9).

Result in table 4.10 showed that the majority of the infections was light intensity in the community. The prevalence of *A. lumbricoides* and hookworm infection was the same, 21.3%; likewise similar intensity of infection was also seen for the two parasites. However, for *A. lumbricoides*, heavy worm load was observed in 10.5% of the infected individuals.

The overall prevalence of STH infection in Pako community was 37.1%. Multiple helminth infection prevalence was 27.3% in the infected population; double helminth infection was 66.7% of the multiple infections. *A. lumbricoides/* hookworm, *A. lumbricoides/T. trichiura,* and *A. lumbricoides/S. stercoralis* were double helminth infection with 11.1% prevalence each, while the prevalence for triple helminth infection with *A. lumbricoides/hookworm/T. trichiura* was also 11.1%. Figure 4.5 showed the bar chart presentation of STH infection intensity in Pako community.

Table 4.9: Risk factors and prevalence of soil-transmitted helminth infection in Pako community, Igbo-Ora.

Risk factors	**Intestinal helminth**				
	Yes No (%)	No No (%)	Total No (%)	x^2	P-value
Sex					
Male	16 (37.2%)	27 (62.8%)	43 (100%)		
Female	17 (37.0%)	29 (63.0%)	46 (100%)	1.0	0.58
Age group					
<1 – 5	0 (0%)	1 (100%)	1 (100%)		
6 – 10	4 (12.1%)	15 (78.9%)	19 (100%)		
11 – 15	27 (42.2%)	37 (57.8%)	64 (100%)		
16 – 25	1 (100%)	0 (0%)	1 (100%)		
26 – 40	0 (0%)	1 (100%)	1 (100%)		
41 – 50	1 (100%)	0 (0%)	1 (100%)		
51 – 70	0 (0%)	2 (100%)	2 (100%)		
>70	0 (0%)	0 (0%)	0 (0%)	8.56	0.20
House clustering					
≤ 4 living in a room	6 (25.0%)	18 (75.0%)	24 (100%)		
> living in a room	27 (41.5%)	38 (58.5%)	65 (100%)	2.05	0.11
House type					
Concrete	19 (31.7%)	41 (68.3%)	60 (100%)		
Mud	14 (48.3%)	15 (51.7%)	29 (100%)	2.31	0.10
Toilet Access					
Yes	15 (31.9%)	32 (69.1%)	47 (100%)		
No	18 (42.9%)	24 (57.1%)	42 (100%)	1.14	0.20
Toilet type					
Water closet	6 (28.6%)	15 (71.4%)	21 (100%)		
Pit latrine	9 (34.6%)	17 (65.4%)	26 (100%)		
Bush around house	18 (42.9%)	24 (57.1%)	42 (100%)	1.32	0.50
Hand washing habit					
Before eating					
Regularly	23 (35.4%)	42 (64.5%)	65 (100%)		
Sometimes	10 (41.7%)	14 (58.2%)	24 (100%)	0.30	0.38
After the use of toilet					
Yes	23 (35.9%)	41 (64.1%)	64 (100%)		
No	10 (40.0%)	15 (60.0%)	25 (100%)	0.12	0.45
Shoe wearing habit					
Regularly	10 (28.6%)	25 (71.4%)	35 (100%)		
Occasionally	23 (42.6%)	31 (57.4%)	54 (100%)	1.79	0.13
Dirty finger nails					
Yes	12 (35.3%)	22 (64.7%)	34 (100%)		
No	21 (38.2%)	34 (61.9%)	55 (100%)	0.08	0.48
House surroundings					
Neat	12 (34.2%)	23 (65.8%)	35 (100%)		
Dirty	21 (38.9%)	33 (61.1%)	54 (100%)	0.19	0.42

Table 4.10: Prevalence and intensity of STH infection within Pako community

Helminth	**Prevalence**	**Intensity**

		Light	Moderate	Heavy
A. lumbricoides	19 (21.3%)	16 (84.2%)	1 (5.3%)	2 (10.5%)
Hookworm	19 (21.3%)	16 (84.2%)	2 (10.5%)	1 (5.3%)
T. trichiura	2 (4.6%)	2 (100%)	0 (0%)	0 (0%)
S. stercoralis	3 (2.2%)	3 (100%)	0 (0%)	0 (0%)

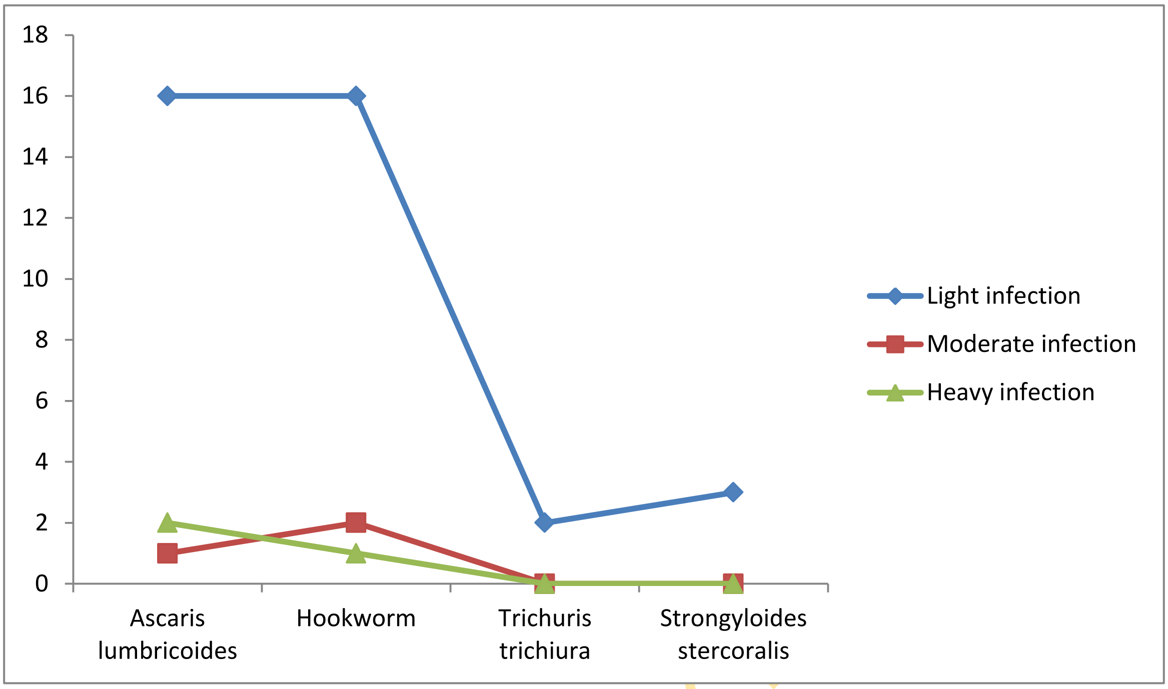


Fig 4.5: Intensity of STH infection within Pako community.

4.7.2 Isale-Oba community

Socio-demographic, risk factors and prevalence of STH infection in Isale–Oba, Igbo-Ora

One hundred and eight individuals, 48 male (44.4%) and 60 female (55.6%), participated in the study. The prevalence of STH was highest in female (26.7%) than male (18.8%) at p-value 0.23. The highest prevalence of infection was observed in the 11-15 years age group with 32.1% prevalence. A total of 21.3% of the people who lived in concrete houses were positive for STH infection, while 27.3% of those infected lived in mud houses. The prevalence of STH was 25.0% for the 28 people (25.9%) that had toilet facilities and 22.5% for the remaining 80 participants (74.1%) that had no toilet facilities. None of the participants reported living with more than four people in a room in this community. The result from table 4.11 showed that 88 participants with 23.9% STH prevalence regularly washed their hand before eating, while the 20 participant that reported occasional hand washing before eating had 20% prevalence for STH. Sixty-eight (68) participants reported washing their hands after the use of toilet, while 40 participants reported not practicing hand washing after toilet. The prevalence of STH infection among those that wore shoe regularly, had no dirty finger nails, and had neat house surroundings were 25.5%, 23.5% and 25.4% respectively (Table 4.11).

The prevalence of STH infection in this community was 23.1% while 18.2% of the infection was double helminth infection: *A. lumbricoides*/hookworm, and *A. lumbricoides/S. stercoralis. T. trichiura* was not seen in this community (Table 4.12).

Figure 4.6 showed the intensity of STH infection within Isale –Oba community of Igbo-Ora. Each of the STH infection was of light intensity in this community, although heavy worm intensity was observed in *A. lumbricoides* (28.6%) and hookworm (20.0%) infections.

Table 4.11: Risk factors and prevalence of STH infection within the participants of Isale-Oba, Igbo-Ora.

Risk factors	Intestinal helminth Yes No (%)	 No No (%)	Total No (%)	x^2	P-value
Sex					
Male	9 (18.8%)	39 (81.2%)	48 (100%)		
Female	16 (26.7%)	44 (73.3%)	60 (100%)	0.94	0.23
Age group					
<1 – 5	0 (0%)	2 (100%)	2(100%)		
6 – 10	2 (8.7 %)	21 (91.3%)	23 (100%)		
11 – 15	9 (32.1%)	19 (67.9%)	28 (100%)		
16 – 25	14 (28.0%)	36 (72.0%)	50 (100%)		
26 – 40	0 (0%)	1 (100%)	1 (100%)		
41 – 50	0 (0%)	3 (100%)	3 (100%)		
51 – 70	0 (0%)	1 (100%)	1 (100%)		
>70	0 (0%)	0 (0%)	0 (0%)	6.74	0.35
House type					
Concrete	16 (21.3%)	59 (78.7%)	75 (100%)		
Mud	9 (27.3%)	24 (72.7%)	33 (100%)	0.45	0.33
Toilet Access					
Yes	7 (25.0%)	21 (75.0%)	28 (100%)		
No	18 (22.5%)	62 (77.5%)	80 (100%)	0.07	0.49
Toilet type					
Water closet	5 (29.4%)	12 (70.6%)	17 (100%)		
Pit latrine	1 (10.0%)	9 (90.0%)	10 (100%)		
Bush around house	19 (23.5%)	62 (76.5%)	81 (100%)	1.35	0.51
Hand washing habit					
Before eating					
Regularly	21(23.9%)	67 (76.1%)	88 (100%)		
Sometimes	4 (20.0%)	16(80.0%)	20(100%)	0.14	0.48
After the use of toilet					
Yes	14 (20.6%)	54 (79.4%)	68 (100%)		
No	11 (27.5%)	29 (62.5%)	40 (100%)	0.68	0.28
Shoe wearing habit					
Regularly	12 (25.5%)	35 (74.5%)	47 (100%)		
Occasionally	13 (21.3%)	48 (78.7%)	61 (100%)	0.27	0.39
Dirty finger nails					
Yes	6(22.2%)	21 (77.8%)	27 (100%)		
No	19(23.5%)	62 (76.5%)	81 (100%)	0.017	0.56
House surroundings					
Neat	17 (25.4%)	50 (74.6%)	67 (100%)		
Dirty	8 (19.5%)	33 (80.5%)	41 (100%)	0.49	0.32

Table 4.12: Prevalence and Intensity of STH infection within Isale-Oba community

Helminth	Prevalence	Intensity		
		Light	Moderate	Heavy
A. lumbricoides	14 (13.0%)	10 (71.4%)	0 (0%)	4 (28.6%)
Hookworm	12 (11.1%)	8 (66.7%)	1 (8.3%)	3 (25.0%)
T. trichiura	0 (0%)	0 (0%)	0 (0%)	0 (0%)
S. stercoralis	4 (3.7%)	4 (100%)	0 (0%)	0 (0%)

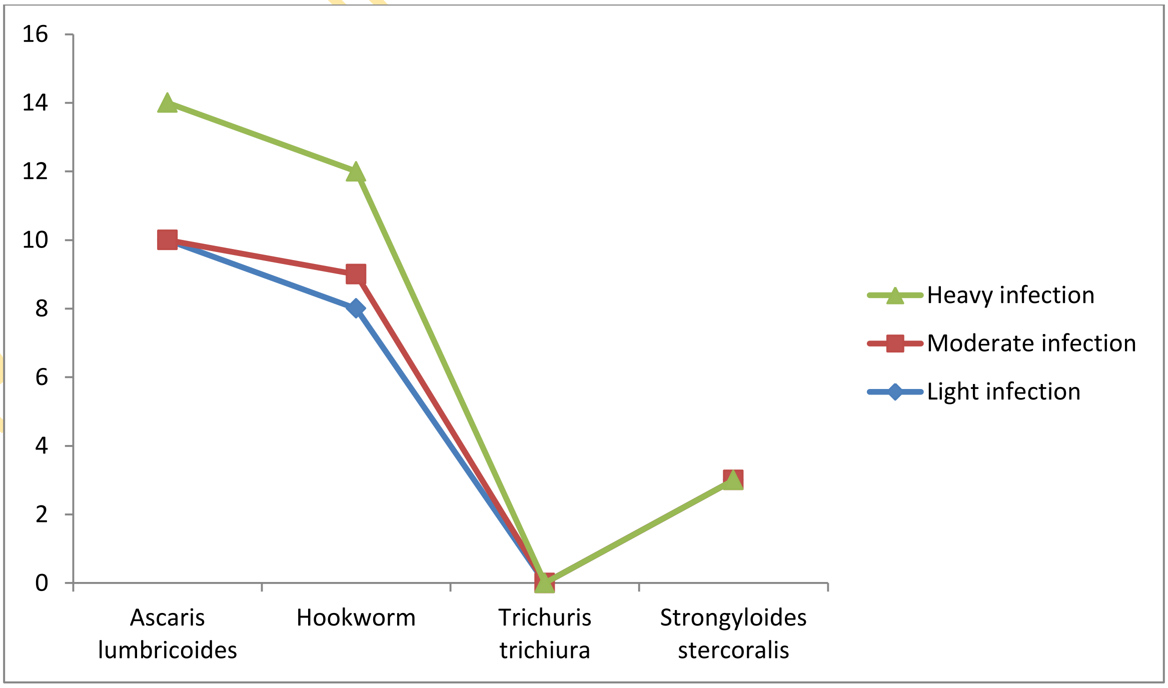


Fig 4.6: Intensity of STH infection within Isale-Oba community.

4.7.3 Igbole Community

Socio-demographic, risk factors and prevalence of STH infection in Igbole community, Igbo-Ora.

One Hundred and thirty individuals, 40.8% male and 59.2% female, participated in this community. The prevalence of STH infection was highest with 28.3% among male participants. The age group distribution cut across all classes of age and the highest prevalence was recorded among age group 6-10 years (55.6%); followed by age group 41-50 years (42.9%), and age group <1-5 years with 35.3% prevalence (Table 4.13)

The prevalence of STH infection was seen to be highest among those living with >4 people in a room (26.9%). Those living in mud houses had 27.8% prevalence of STH infection, while 28.6% prevalence of STH infection was observed in those living in houses with no toilet facility. Defecating in bush around the house accounted for

23.5% STH prevalence of infection. A total of 25.4% STH prevalence was recorded in those that reported regular hand washing before eating (x^2 =0.001), while 35.7% prevalence was seen in those that did not practice hand washing after toileting. Those that wore shoe occasionally had 25.0% prevalence for STH infection x^2 =0.01 p=0.54 (Table 4.13). The prevalence of STH infection in this community was 24.5%. *A. lumbricoides* was the predominant helminth in this community with 18.5% prevalence of infection; this was followed by hookworm infection with 13.8% prevalence; *S. stercoralis* with 3.8% prevalence and lastly *T. trichiura* 0.8% prevalence. Multiple helminth infection was responsible for 42.4% of the infection, while single infection with any of the helminth was 57.6%. *A. lumbricoides* / hookworm was the only double helminth infection seen, and this pattern was seen in 13 participants, while triple helminth infection was *A. lumbricoides*/ hookworm/*S. stercoralis* and was seen in only one participant. The result from table 4.14 showed that STH infection intensity was 92.0% and 78.9% light infection for *A. lumbricoides* and hookworm infection respectively, while moderate and heavy infection was observed in hookworm infection with 10.5% each. No moderate or heavy infection intensity was seen in *T. trichiura* and *S. stercoralis*. Figure 4.7 showed the intensity of STH infection within Igbole community of Igbo-Ora.

Table 4.13: Risk factors and prevalence of STH infection within the participants of Igbole, Igbo-Ora.

Risk factors	**Intestinal helminth** Yes No (%)	No No (%)	Total No (%)	x^2	P-value
Sex					
Male	15 (28.3%)	38 (71.7%)	53 (100%)		
Female	18 (23.4%)	59(76.6%)	77 (100%)	0.40	0.33
Age group					
<1 – 5	6 (35.3%)	11 (64.7%)	17 (100%)		
6 – 10	5 (55.6%)	4 (44.4%)	9 (100%)		
11 – 15	4 (26.7%)	11(73.3%)	15 (100%)		
16 – 25	4 (28.6%)	10(71.4%)	14 (100%)		
26 – 40	3 (13.0%)	20 (87.0%)	23 (100%)		
41 – 50	6 (42.9%)	8 (57.1%)	14 (100%)		
51 – 70	3 (13.0%)	20 (87.0%)	23 (100%)		
>70	2 (13.3%)	13 (86.7%)	15 (100%)	12.4	0.08
House clustering					
≤ 4 living in a room	15 (23.8%)	48 (76.2%)	63 (100%)		
>4 living in a room	18 (26.9%)	49 (73.1%)	67 (100%)	0.16	0.42
House type					
Concrete	11 (21.6%)	40 (78.4%)	51 (100%)		
Mud	22 (27.8%)	57 (72.2%)	79(100%)	0.65	0.28

Toilet Access					
Yes	7 (17.9%)	21 (82.1%)	39 (100%)		
No	26 (28.6%)	65 (71.4%)	91 (100%)	1.63	0.15
Toilet type					
Water closet	7 (24.1%)	22 (75.9%)	29 (100%)		
Pit latrine	1 (9.1%)	10 (90.9%)	11 (100%)		
Bush around house	25 (27.8%)	65 (72.2%)	90 (100%)	1.84	0.40
Hand washing habit					
Before eating					
Regularly	31 (25.4%)	91 (74.6%)	122 (100%)		
Sometimes	\ 2 (25.0%)	6 (75.0%)	8(100%)	0.001	0.67
After toileting					
Yes	28 (24.1%)	88 (75.9%)	116 (100%)		
No	5 (35.7%)	9 (64.3%)	14 (100%)	0.88	0.26
Shoe wearing habit					
Regularly	12 (17.1%)	52 (82.9%)	70 (100%)		
Occasionally	**15** (25.0%)	45 (75.0%)	60 (100%)	0.01	0.54
Dirty finger nails					
Yes	15 (30.0%)	35 (70.0%)	50 (100%)		
No	18 (22.5%)	62 (77.5%)	80 (100%)	0.19	0.23
House surroundings					
Neat	28 (24.8%)	85 (75.2%)	113 (100%)		
Dirty	5 (29.4%)	12 (70.6%)	17 (100%)	0.17	0.44

Table 4.14: Prevalence and Intensity of STH infection within Igbole community

Helminth	**Prevalence**	**Intensity**		
		Light	**Moderate**	**Heavy**
A. lumbricoides	25 (18.5%)	23 (92.0%)	1 (4.0%)	1 (4.0%)
Hookworm	19 (13.8%)	15 (78.9%)	2 (10.5%)	2 (10.5%)
T. trichiura	1 (0.8%)	1 (100%)	0 (0%)	0 (0%)
S. stercoralis	5 (3.8%)	5 (100%)	0 (0%)	0 (0%)

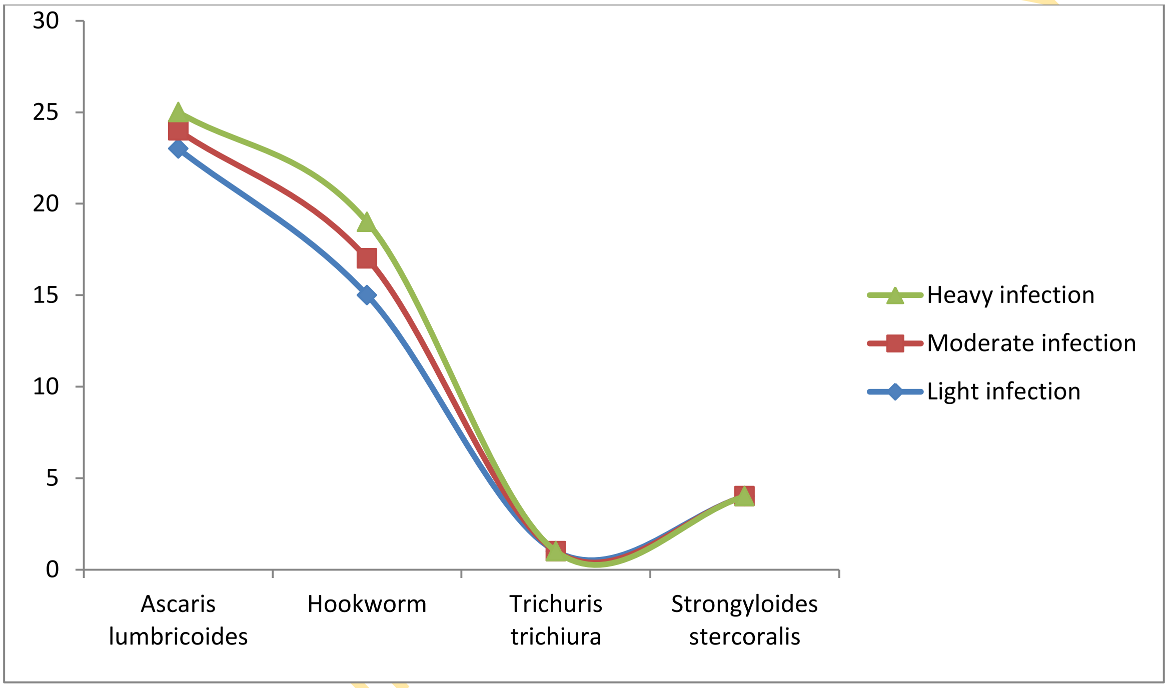


Figure 4.7: Intensity of STH infection within Igbole community

4.7.4 Saganun Community

Socio-demographic, risk factor and prevalence of STH infection in Saganun community, Igbo-Ora.

One hundred and eighty one individuals participated in the study from this community. Sixty-nine (38.1%) were males while 112 (61.9%) were females. The male participants had 29.0% prevalence of STH infection while 28.6% prevalence was observed in the females ($p<0.004$).The age distribution table showed that the highest prevalence of STH infection was in the age group 51-70 (45.5%), followed by age group <1-5 (36.4%) and the lowest prevalence was in age group 6-10 years (20.0%). Those living in mud houses had 38.5% prevalence of STH infection ($p<0.01$); 42.2% STH prevalence was seen in those that did not have toilet facility in their homes ($p<0.003$); while 43.1% STH prevalence (p-value 0.005) was seen in those that defecated in the bush around the house (Table 4.15).

The prevalence of STH infection was 31.3% and 28.3% in those that reported hand washing before eating and after the use of toilet respectively. For participants practicing occasional shoe wearing, 29.6% prevalence of STH infection was seen while 27.9 % STH prevalence was seen in those with dirty finger nails and 15.6% prevalence ($p <0.002$) in those with dirty house surroundings.

The prevalence of STH infection in this community was 28.7%. The predominant helminth infection was hookworm with 24.9% prevalence, followed by *A. lumbricoides* with 15.5% prevalence and *S. stercoralis* with 1.7% prevalence. However, *T. trichiura* was not seen in this community. The intensity of infection was highest in *A. lumbricoides* with 32.1% resulting from heavy worm load as shown in table 4.16. Multiple helminth infection was observed in 21 (40.4%) individuals and *A.*

lumbricoides/hookworm double helminth infection was 85.7% of the double infection, while triple helminth infection with *A. lumbricoides*/hookworm/*S stercoralis* was seen only once (Table 4.17).

Figure 4.8 showed the intensity of STH infection within Saganun community of Igbo-Ora. Majority of hookworm and *A. lumbricoides* were of light intensity, although 32.1% of *A. lumbricoides* were of heavy intensity.

Table 4.15: Risk factors and prevalence of STH infection within the participants of Saganun Igbo-Ora.

Risk factors	Intestinal helminth Yes No (%)	No No (%)	Total No (%)	x^2	P-value
Sex					
Male	20 (29.0%)	49 (71.0%)	69 (100%)		
Female	32 (28.6%)	80 (71.4%)	112 (100%)	0.004	0.54
Age group					
<1 – 5	12 (36.4%)	21 (63.6%)	33 (100%)		
6 – 10	9 (20.0%)	36 (80.0%)	45 (100%)		
11 – 15	5 (23.8%)	16 (76.2%)	21 (100%)		
16-25	4 (25.0%)	12 (75.0%)	16 (100%)		
26 – 40	8 (27.6%)	21 (72.4%)	29 (100%)		
41- 50	4 (30.8%)	9 (69.2%)	13 (100%)		
51 – 70	10 (45.5%)	12 (54.5%)	22 (100%)		
>70	0 (0%)	2 (100%)	2 (100%)	6.83	0.45
House clustering					
≤4 living in a room	18 (23.1%)	60 (76.9%)	78 (100%)		
> 4 living in a room	34 (33.0%)	69 (67.0%)	103 (100%)	2.14	0.10
House type					
Concrete	22 (21.4%)	81 (78.4%)	103 (100%)		
Mud	30 (38.5%)	48 (61.5%)	78 (100%)	6.34	0.01
Toilet Access					
Yes	25 (21.4%)	92 (78.6%)	117 (100%)		
No	27 (42.2%)	37 (57.8%)	64 (35.4%)	8.76	0.003
Toilet type					
Water closet	8 (17.0%)	39 (83.0%)	47 (100%)		
Pit latrine	16 (23.2%)	53 (76.8%)	69 (100%)		
Bush around house	28 (43.1%)	37 (56.9%)	65 (100%)	10.72	0.005
Hand washing habit					
Before eating					
Regularly	42 (31.3%)	92 (68.7%)	134 (100%)		
Sometimes	10 (21.3%)	37 (78.7%)	47 (100%)	1.72	0.13
After toileting					
Yes	41(28.3%)	104 (71.7%)	145 (100%)		
No	5 (13.9%)	25 (86.1%)	36 (100%)	0.07	0.47
Shoe wearing habit					

Regularly	23 (27.7%)	60 (72.3%)	83 (100%)		
Occasionally	29 (29.6%)	69 (70.4%)	98 (100%)	0.08	0.46
Dirty finger nails					
Yes	21 (30.0%)	49 (70.0%)	70 (100%)		
No	31 (27.9%)	80 (72.1%)	111 (100%)	0.09	0.45
House surroundings					
Neat	38 (37.2%)	64 (62.8%)	102 (100%)		
Dirty	10 (15.6%)	54 (84.4%)	64 (100%)	8.95	0.002

Table 4.16: Prevalence and Intensity of STH infection in Saganun community

Helminth	Prevalence	Intensity		
		Light	Moderate	Heavy
A. lumbricoides	28 (15.5%)	17 (60.7%)	2 (7.1%)	9 (32.1%)
Hookworm	45 (24.9%)	39 (86.7%)	4 (8.9%)	2 (4.4%)
T. trichiura	0 (0%)	**0** (0%)	0 (0%)	0 (0%)
S. stercoralis	3 (1.7%)	3 (100%)	0 (0%)	0 (0%)

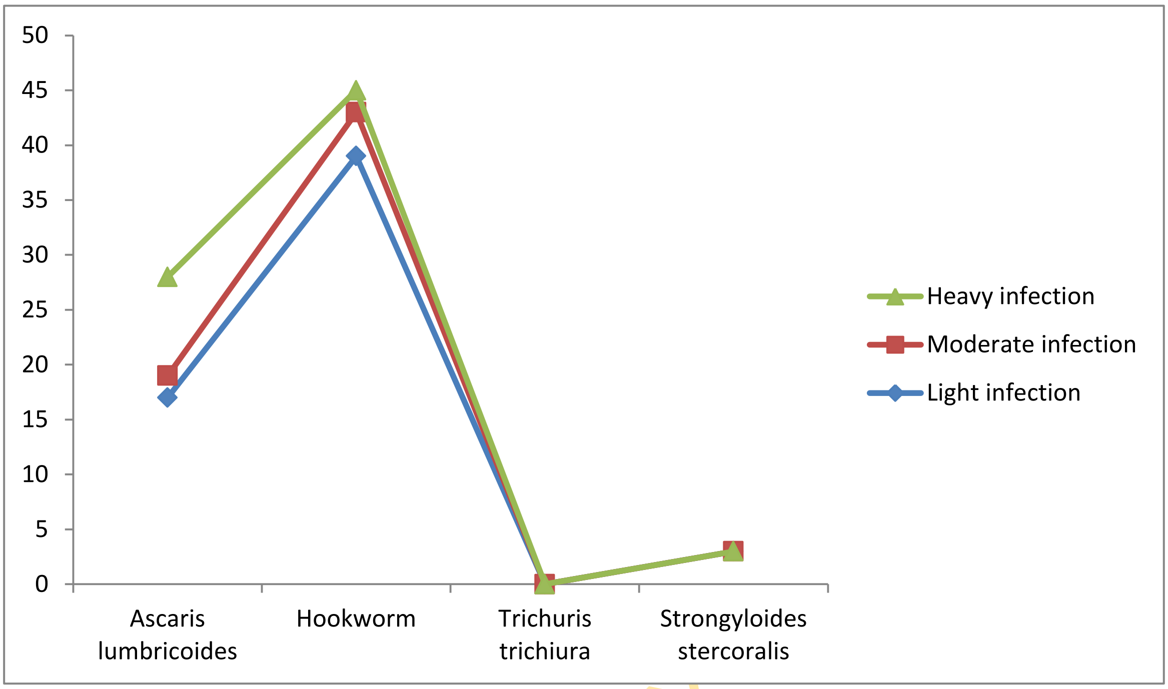


Fig. 4.8: Intensity STH infection within Saganun community.

Table 4.17: Multiple helminth infection in Saganun community Igbo-Ora.

Helminth infection prevalence	No of individuals	%
A. lumbricoides/hookworm	18	85.7%
Hookworm/*S. stercoralis*	2	9.5%
A. lumbricoides/hookworm/*S stercoralis*	1	4.8%
Total	**22**	**100%**

4.8: Result of Soil Analysis

Two hundred and thirty six soil samples were obtained from the surroundings of 137 households. Many households were clustered together, some households were surrounded with graves and hence soil samples cannot be taken from such places. Twenty-five (25) (that is 10%) households had concrete floor surrounding among the participating households. Majority of the soil samples were sandy soil 173 (73.3%) from 91 households, while 36 soil samples from 27 households were mixture of sand and clay soil (15.3%) and 27 soil samples from 19 households were clay soil (11.4%). In all, parasites were seen in soil samples from 38 households (27.7%).

The prevalence of soil parasite in Igbo-Ora was 17.7% and the parasite isolated are *A. lumbricoides* 33 (24.1%), hookworm 5 (3.6%), Taenia ova 2 (1.5%) and *Schistosoma haematobium* 1(0.7%) and *S. stercoralis* 1 (0.7%) (Fig 4.9). Table 4.18 showed the distribution of STH parasites in the soil within the different four communities sampled in Igbo-Ora. Soil samples were collected from between 31 to 38 households in each community and the result showed 16 out of 36 households in Saganun have STH parasite in the surrounding soil, contributing about 11.7% of the prevalence of soil parasite in Igbo-Ora community, while the least was found in Pako, contributing 4.4% of infection (6 out of 38 households). The distribution of parasites in the environmental soil samples was found to be significantly associated with the different community areas in Igbo-Ora. (Chi-square 7.89, p-value 0.048).

The result of infection per household revealed that all households with 10-14 participants had *A. lumbricoides* infection, while no hookworm was found in them. Meanwhile, in households with 7-9 participants, 6 out of 8 had *A. lumbricoides* and no hookworm infection (Table 4.19).

4.8.1: Human STH infection versus soil parasite within a household.

Human STH infections was found in 57 (41.7%) out of the 137 households from where soil were sampled. Human STH infection was significantly associated with the presence of parasite in the environmental soil (χ^2 5.74, p-value 0.017). Households with large number of participant were significantly associated with the presence of parasite in the environment soil (χ^2 33.73 p-value 0.0000).

Table 4.18: The Prevalence of soil -transmitted helminth in the environmental

soil samples around participants households in the different communities.

Parasite Present	No of household per community area where soil samples were taken				Total
	Igbole	**Pako**	**Isale-oba**	**Saganun**	
Yes	8 (5.8%)	6 (4.4%)	8 (5.8%)	16 (11.7%)	38 (27.7%)
No	24 (17.5%)	32 (23.4%)	23 (16.8%)	20 (14.6%)	99 (72.3%)
Total	32 (23.5%)	38 (27.7%)	31 (22.6%)	36 (26.3%)	137 (100%)

Chi-square 7.89 p= 0.048

Table 4.19: The distribution of STH in the soil sample of household with different no of participants

STH infection	No of household participant						
	1-3	4-6	7-9	10-14	Total	Chi-square	P-value
Ascaris							
Yes	14	9	6	4	33		
No	88	11	2	0	101	35.37	0.45
Hookworm							
Yes	2	3	0	0	5		
No	100	17	8	4	129	8.69	0.06

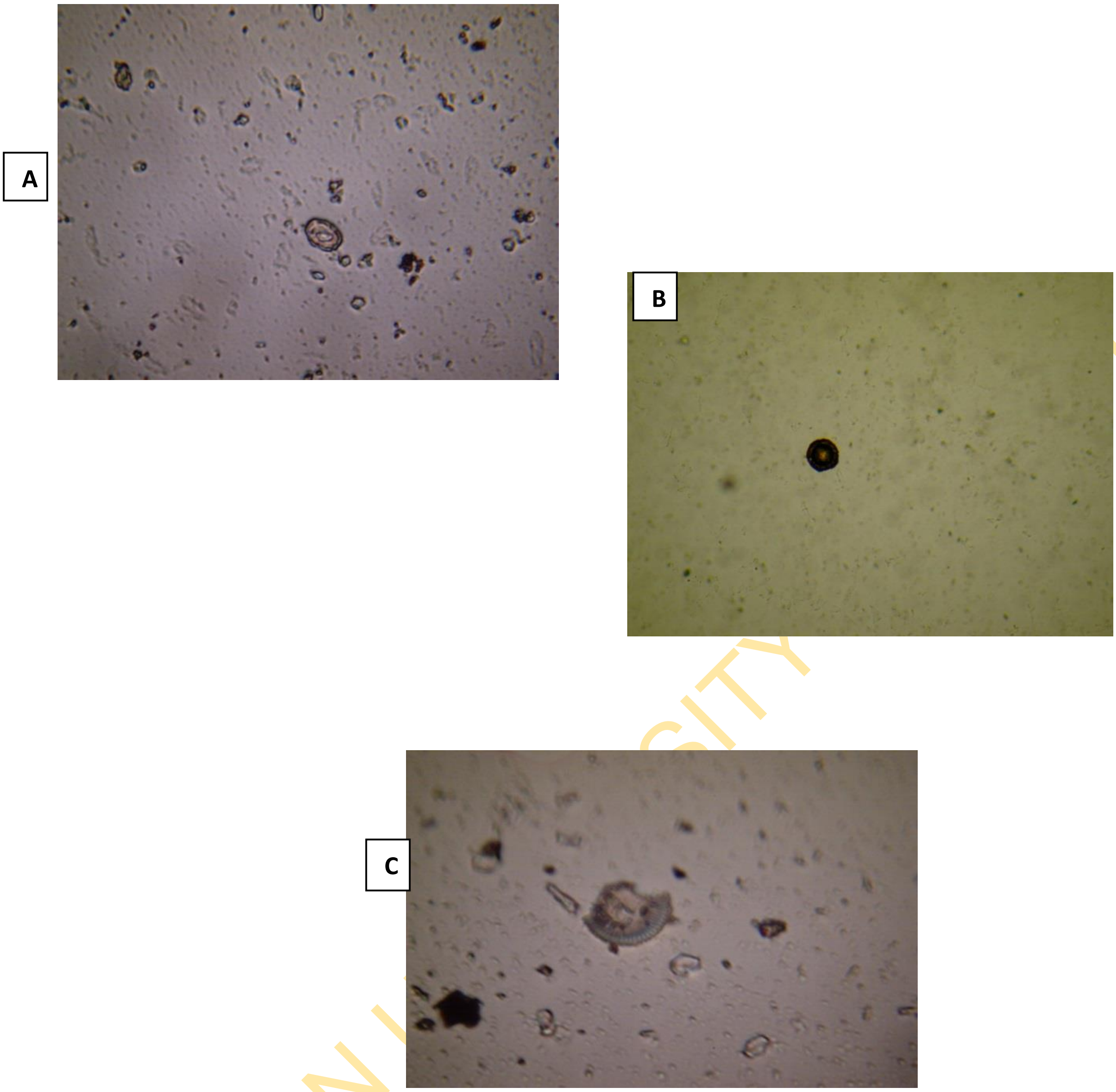


Figure 4.9: Ascaris and *Taenia* spp. ova seen in soil samples using Zinc Sulphate floatation method.

A: An ova of Ascaris from soil sample

B: Teania ova from soil sample

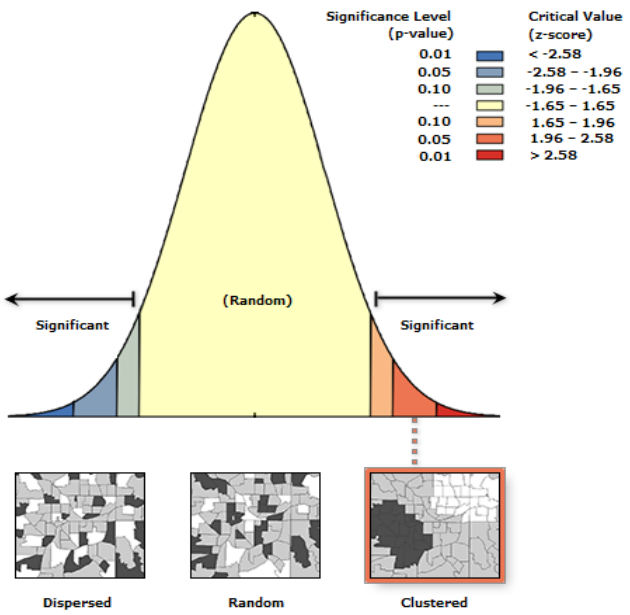
C: Disrupted ova of Teania from soil sample

4.9: Spatial distribution of Soil-transmitted helminth Infection

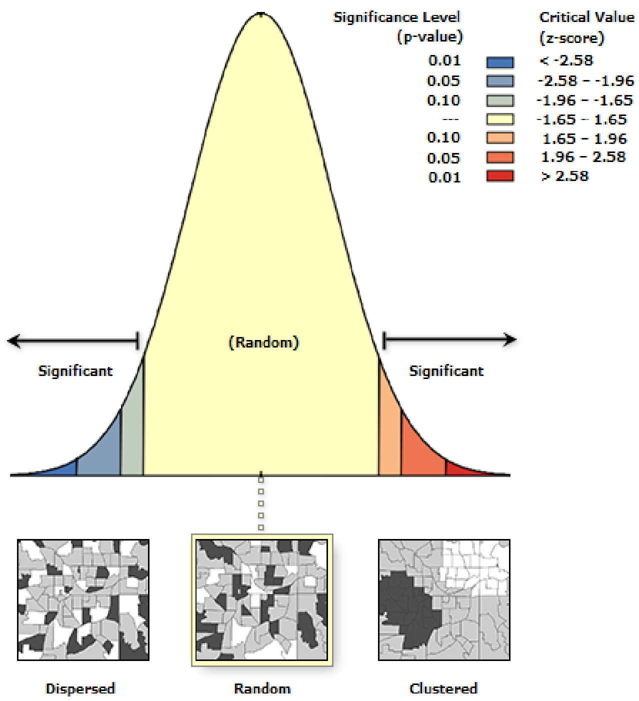
Soil-transmitted helminth infection was generally seen to be randomly distributed in Igbo-Ora community. The location specificity was then assessed; *A. lumbricoides* was seen to be clustered in the medium density area of the community, Isale –Oba (Fig 4.10). While the distribution of Ascaris and hookworm in all other communities within Igbo-Ora was randomly distributed. Using Moran's index to analyse the statistical significance of the distribution, the result showed the z-score of 2.3 with p-value =0.02 indicating a significant pattern of clustering for Ascaris infection within that community. (Table 4.20).

Table 4.20: Summary table of Moran index value for the spatial distribution of Ascaris and hookworm in Igbo-Ora.

Location	Moran's Index	Expected Index	Variance	z-score	p-value	Type	Pattern
Igbole	-0.016884	-0.0417	0.00316	0.44092	0.65927	Ascaris	Random
Igbole	0.042867	-0.0417	0.0079	0.9511	0.34155	Hookworm	Random
Isale Oba	0.314964	-0.0435	0.02425	2.30176	**0.02135**	**Ascaris**	**Clustered**
Isale Oba	0.019422	-0.0435	0.09859	0.20033	0.84122	Hookworm	Random
Saganun	-0.02481	-0.0303	0.00783	0.06206	0.95051	Ascaris	Random
Saganun	0.022089	-0.0303	0.0079	0.58933	0.55564	Hookworm	Random



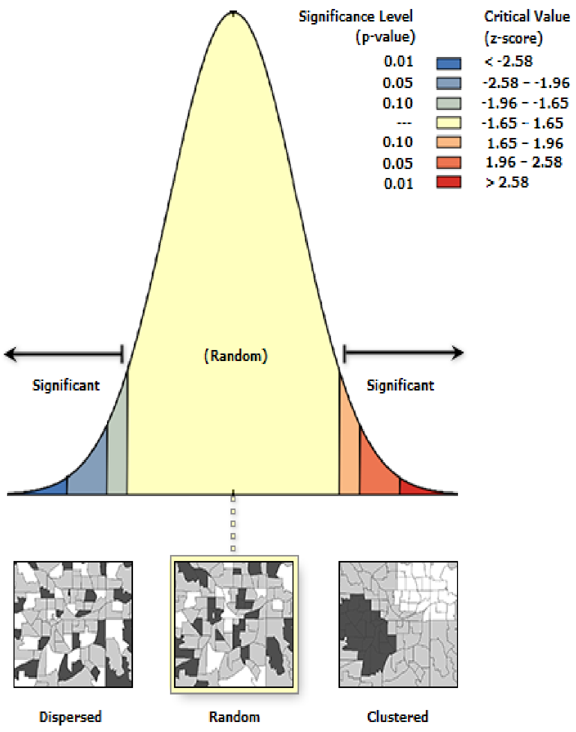
A: Pattern of Ascaris distribution.



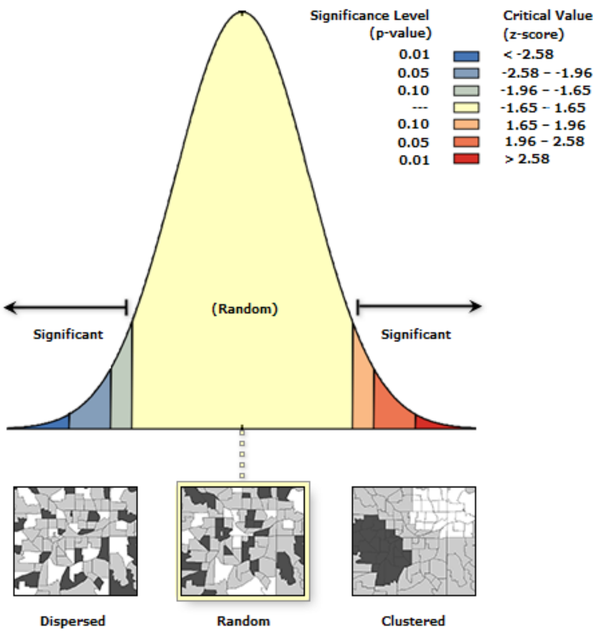
B: Pattern of Hookworm distribution.

Fig 4.10 A and B: Spatial distribution of STH in Isale-Oba, Igbo-Ora.

The z-score of 2.30176 for Ascaris falls within the significant level of a clustered distribution. The z- score of 0.200328118247 for hookworm show the pattern to be random.



A: Pattern of Ascaris distribution.



B: Pattern of Hookworm distribution.

Fig 4.11 A and B: Spatial distribution of STH in Igbole, Igbo-Ora

The z-score of Ascaris and hookworm in this community falls within the range of -1.65 to 1.65 which is an indication of random distribution.

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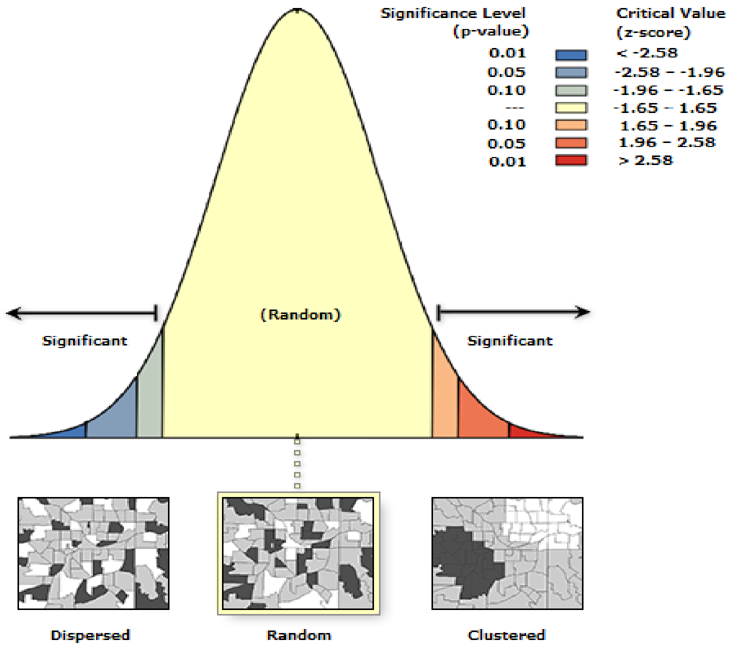
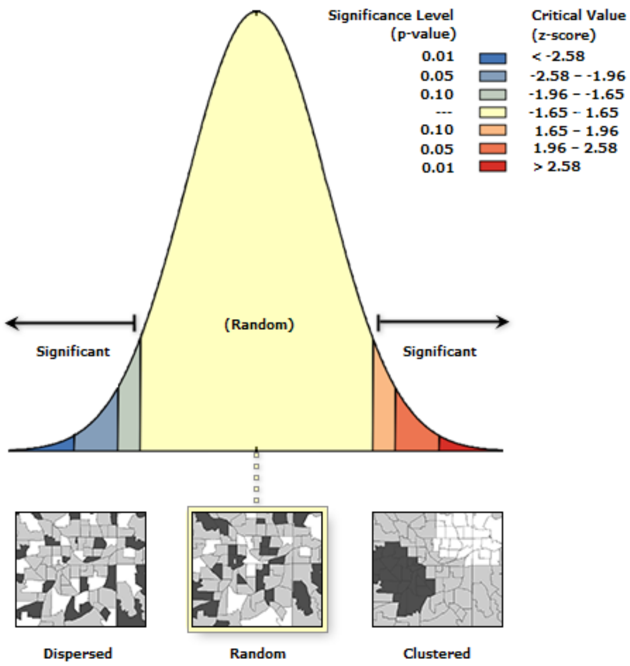


A: Pattern of Ascaris distribution



B: Pattern of Hookworm distribution.

Fig 4.12 A and B: Spatial distribution of STH in Saganun, Igbo-Ora

The z-score of Ascaris and hookworm in this community falls within the range of -1.65 to 1.65 which is an indication of random distribution.

4.10. Assemblage of Pedigree Structure

Complete questionnaire and parasitological data were available for 508 individuals (75.5% of the total participant). Pedigree information was available and confirmed for 296 (58.3%) individuals and they were assembled into 7 degrees of relationships with 2- 14 phenotypic individuals; the first degree are parent- offspring, second degree are siblings, third are grandparent – grandchildren, fourth are half siblings, while fifth are cousins, sixth are second cousins and the seventh are uncle/aunt. One hundred and twenty two individuals out of the 508 had no phenotype relatives in the study area, while 90 individuals phenotype cannot be confirmed. The large pedigree spanned 3 generations of phenotype individuals. There were 639 informative relative pairs; this include 181 first degree relatives, 141 second degree relatives and 147 third degree relatives, 24 fourth degree relative, 117 fifth degree relative, 27 sixth degree relative and 2 seventh degree relatives (Table 4.21). The pedigree was virtualized using genetic pedigree software called PROGENY. Figure 4.13a, b and c was examples of pedigree structure in the population sampled.

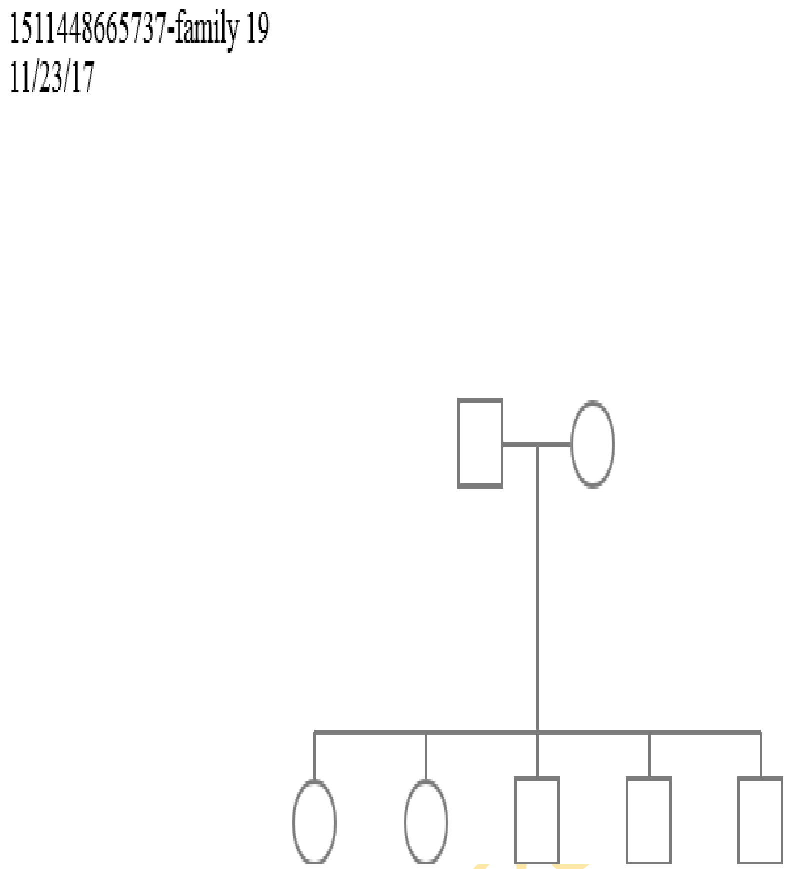


Fig. 4.13a: Showing an example of a nuclear family. Kinship relationship visualized using PROGENY; a genetic pedigree software

The family tree showing:

1st = Parent – Child

2nd = Sibling relationship.

→ Male → Female

1511497993091-Family 66
11/23/17

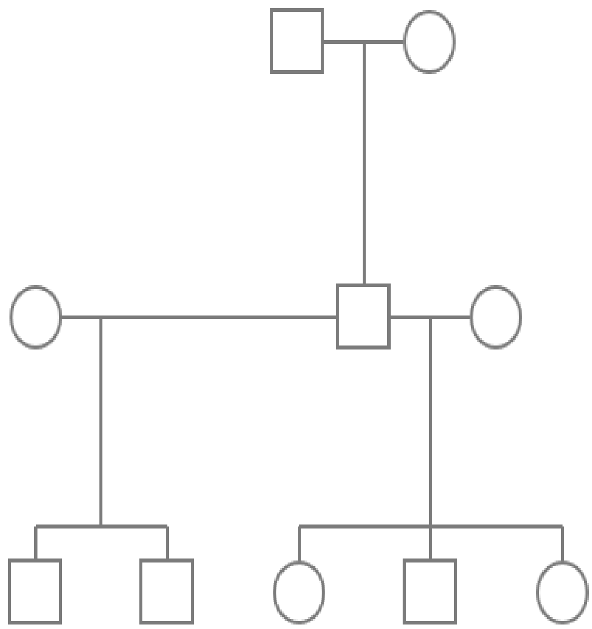


Fig. 4.13b: An example of a family tree with 2nd generation and polygamy

The family tree of one of the participating household showing the following degree of relationship:

1st = Parent - Child

2nd = Sibling

3rd = Grandparent - grandchild

4th = Half- sibling

1511447830479-Family 33A
11/23/17

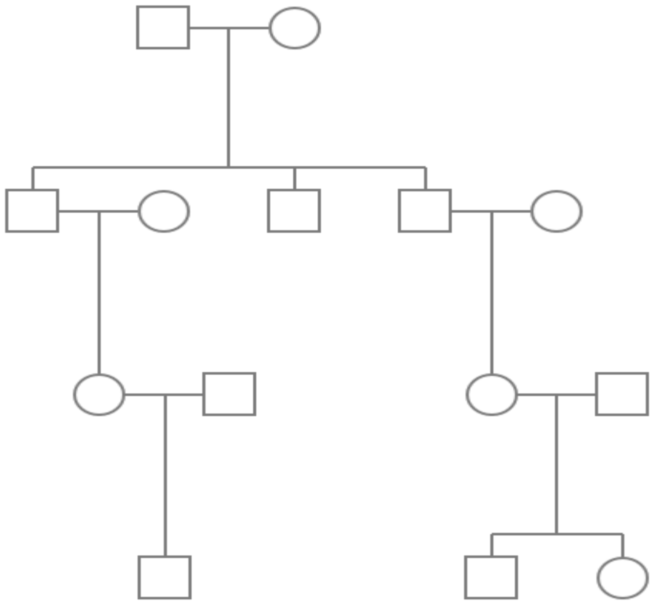


Fig 4.13c: An example of a family tree with 3rd generations.

The family tree of one of the participating household showing the following pedigree structures:

1st = Parent-Child

2nd = Sibling

3rd = Grandparent-grandchild

5th = Cousins

6th = Second cousins

7th = Uncle-Niece

Table 4.21. The pairwise relationships among the 296 related members of the Igbo-

Ora pedigree.

Relationship degree	Kinship coefficient matrix	Pairwise Relationship	Number of pairs
First	0.5-0.5625	Parent –offspring	181
Second	0.25-0.375	Siblings	141
Third	0.125-0.219	Grandparent-grandchild	147
Fourth	0.0625-0.117	Half-sibling	24
Fifth	0.031-0.055	Cousins	117
Sixth	0.0156-0.027	Second cousins	2
Seventh	0.0078-0.017	Uncles/Aunt	27

4.11: Heritability of STH in Igbo-Ora.

The presence of STH infection within the family unit was virtualized on PROGENY. Figure 4.14a, b and c showed the STH infection within 3 families out of the 91 families that participated in this study, the family are 66, 33 and 68 respectively. Meanwhile, table 23 shows the heritability of *A. lumbricoides*, hookworm as $\boldsymbol{h^2}$ 22.7% and 1.1% respectively.

In family 66, the presence of hookworm was coded as condition 3. Family 66 comprises of a grandfather and grandmother, their son and his two wives with their children.

Family 33 comprises of three brothers, of the same parent, two out of which are married, each had a daughter that are married, one daughter had two children, a boy and a girl, and the other daughter had a son.

Family 68 is a nuclear family that comprises of a father, mother and their children; two boys and a girl.

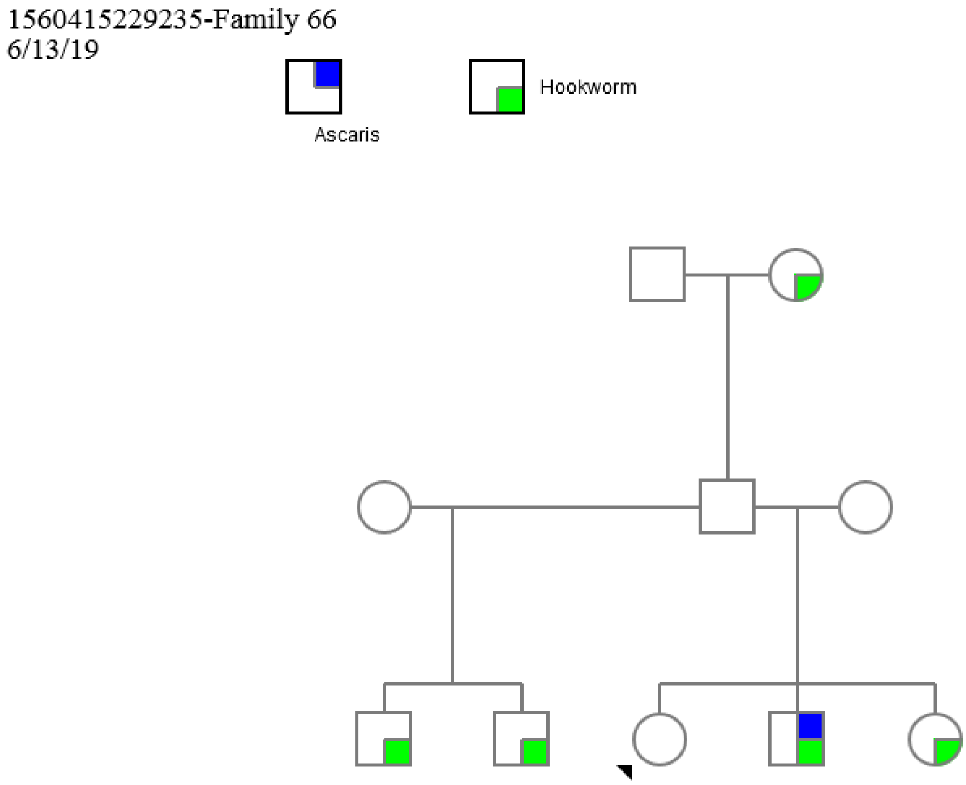


Fig 4.14a: Presence of STH within an extended family with polygamous marriage.

- Ascaris was found in only one member of the family, while hookworm was found in five family members.

- Hookworm was found in 5 members of the family.

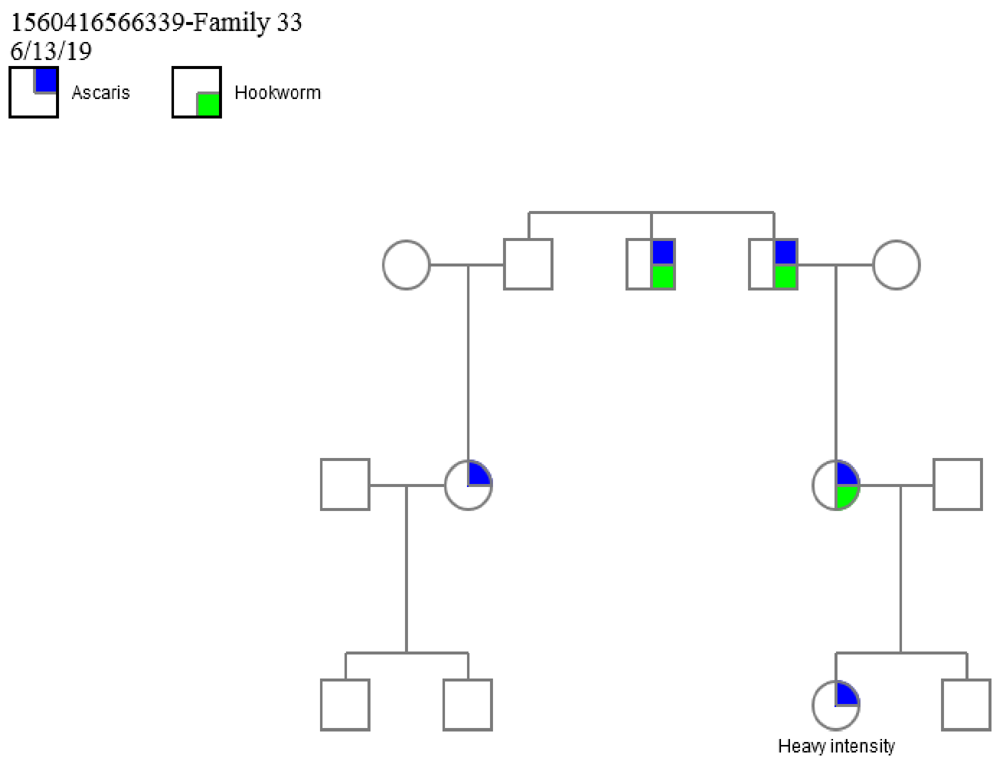


Fig. 4.14b: Presence of STH within an extended family.

The presence of STH within this family unit of 12 members.

- Ascaris present in 5 out of 12 family members.
- Heavy Ascaris intensity was found in only one member of the family
- Hookworm was found in 3 out of 12 family member

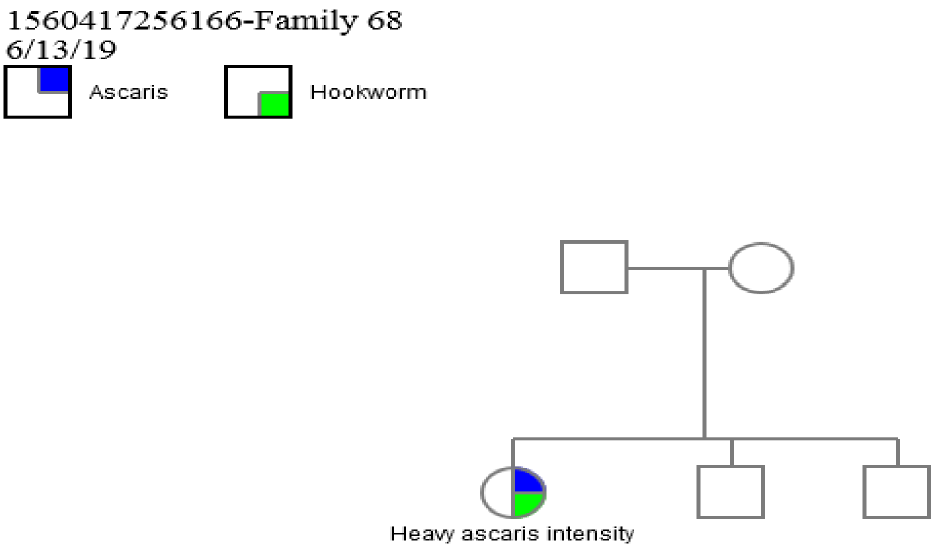


Fig. 4.14c: Presence of STH within a nuclear family.

- Heavy Ascaris intensity was found in only one sibling

4.12: The effect of host genetic factors (h^2), common shared household (C^2) and presence of soil parasite in environment (e^2) on the prevalence of STH.

The result on table 4.23 showed that the host genetic factors and the presence of soil parasites in the home environment (soil around homes) had no contributory effect on the prevalence of *A. lumbricoides* while the common shared household was responsible for 4.7% of the variation observed in the prevalence of Ascaris infection.

For hookworm infection, both the host genetic factors (h^2) and the presence of soil parasite around home (e^2) contribute greatly to the variation observed in the hookworm prevalence. The presence of soil parasite in the environment contributed 47.2% to the prevalence of hookworm (Table 4.23).

4.13: The effect of host genetic factors and common shared household on intensity of STH:

Ascaris lumbricoides and hookworm infection was the only STH infection taken into consideration, because of the low prevalence of *T. trichiura* and *S. stercoralis*, they were not considered for these analyses.

4.13.1: Effect on *Ascaris lumbricoides* Intensity

Table 4.24 showed the effect of host genetic factors (heritability=h^2), common shared household (household=C^2) and presence of soil parasite in the environment (e^2) on Ascaris intensity among related individuals. The SOLAR trait taken into consideration was the egg count per gram (epg), this was analysed within the related family members within households and the effect of shared environment and the effect of the presence of parasite in the soil of the house environment.

The result showed that relatedness have significant effect on the intensity of Ascaris infection within families, common shared household have significant effect on Ascaris intensity. Looking at the effect of common shared environment within family and between families living together, a household model (C^2) was developed and 149 pedigree was merged into 76 household group by SOLAR. The result showed that host genetic factors (relatedness) contributed to the intensity of Ascaris (25.0%), while common shared environment was responsible for 21.3% of the intensity observed in the Ascaris infection. Meanwhile, the presence of parasite in the soil around homes contributed 9% to the intensity.

4.13.2: Effect on Hookworm Intensity

The effect of host genetic factor (relatedness) and common shared environment on the intensity of hookworm within and between families was analysed. The selected trait was the hookworm ova count and the covariance were the related family members irrespective of where they live, and household effect within and between families and common shared environment. The result showed that the intensity of hookworm infection was not affected by any of the above mentioned factors, p-value remain consistently greater than 0.05 (p value > 0.05) (Table 4.25).

4.14: Favoured model of the variance component analysis of *A. lumbriocides* and hookworm infection

The summary of the favoured models of the variance component analysis for the Ascaris and hookworm infections after adjusting for significant covariates, revealed that household model was the favoured model for Ascaris prevalence while host genetic factor was the favoured model for the intensity. Meanwhile, in hookworm infection, the presence of soil parasite in the environment was consistently the favoured model for the prevalence and the intensity (Table 4.26).

Table 4.22: Heritability of STH intensity in relation to genetic relatedness using Sequential Oligogenic Linkage Analysis Resource 8.1.1.0 version.

Trait	model	h^2	Chi-square	p-value	loglikelihood
Intensity of Ascaris	Polygenic	0.227	3.3016	0.035	-1843.919
Intensity of Hookworm	polygenic	0.011	0.0186	0.446	-1737.2252

Table 4.23: The variance component analysis of the effect of Host genetic factors (relatedness), common shared household and presence of soil parasite in the environment on the prevalence of *A. lumbricoides* and hookworm in Igbo-Ora.

Infection	Standardized parameter estimate	loglikelihood	p-value	Kullback-Leibler R^2
Ascaris				
Genetic (relatedness)	h^2 =0.000	-126.157	0.500	0.007
Household (common shared household)	c^2= 0.047	-125.841	0.023	0.006
Environment (soil parasite)	e^2 = 0.000	-126.157	0.500	0.017
Hookworm				
Genetic (relatedness)	h^2 =0.401	-131.381	0.065	0.007
Household (common shared household)	c^2 = 0.080	-131.172	0.308	0.017
Environment (soil parasite)	e^2 = 0.472	-130.778	0.034	0.005

Table 4.24: Effect of host genetic factors (relatedness), common shared households and soil parasite in the environment on Ascaris intensity.

Model	Loglikelihood		Chi	p-value	Std. Error
Genetic related member (famid)	-1839.048	h^2 0.250	4.010	0.023	0.132
Common shared households (hhid)	-1838.103	C^2 0.2129	3.880	0.090	0.122
Contaminated environment (soil around homes)	-2237.102	e^2 0.0921	1.544	0.146	0.090

Table 4.25: Effect of host genetic factors (relatedness), common shared households and contaminated soil on Hookworm intensity.

Model	Loglikelihood		Chi	p-value	Std. Error
related family member		h^2			
	-1447.225	0.011	0.010	0.459	0.113
common shared households		C^2			
	-1447.197	0.000	0.011	0.459	0.113
contaminated environment (soil hookworm)		e^2			
	-1446.488	0.012	0.011	0.459	0.113

Table 4.26: Variance component analysis for the Ascaris and hookworm infections showing the favoured models after adjusting for significant covariates

Infection variable	Favoured model	Standardised parameter estimates			Kullback-Leibler R^2	Likelihood
		Genetic	Household	Environment		
Ascaris lumbricoides [a]	Household	(0)	0.047	(0)	0.039	-125.841
Ascaris lumbricoides [b]	Genetic	0.250	0.213	0.092	0.022	-2237.841
Hookworm [a]	Environment	0.401	0.080	0.472	0.065	-131.381
Hookworm [b]	Environment	0.011	(0)	0.012	0.010	-1446.488
A.lumbricoides/hookworm	Polygenic	0.774	0	0.221	0.005	-77.335

CHAPTER FIVE

DISCUSSION

5.1: STH infection, demographic structure and associated risk factors of infection

5.1.1: STH infection and demographic structure

Population-based studies of soil-transmitted helminth infection are remarkably few in sub-Saharan Africa (Pullan *et al*., 2010). Although prevalence and intensity of STH infection have been extensively studied in Nigeria, information on prevalence and intensity of STH infection within households and different household clustering density are rare. Likewise, the information on the influence of human genetics on susceptibility is scarce in this part of sub-Saharan Africa. The findings from this study showed that STH infection is an important public health problem in Igbo-Ora, hookworm infection and *A. lumbricoides* are the predominant STH parasite in the population sampled.

The prevalence of STH in this study showed 28.1%, which was lower than what was seen in the study carried out in Ile-Ife, about a decade ago by Kirwan *et al*., (2009), where the prevalence was 50% and *A. lumbricoides* was the predominant helminth. Adewale *et al* (2017) in Lagos and Oluwole *et al* (2018) in Ogun reported STH prevalence of 34.8% and 34.6% among primary school pupils respectively, no recent study reported the prevalence of STH among households in Nigeria. Kaliappan *et al*., (2013) in a research in a tribal area in South India reported the STH prevalence of 39% among all age groups and hookworm was the predominant helminthes. This was also the predominant parasite in this study.

There was no significant difference in STH infection between male and female ($p>0.05$), the possible reasons being that men and women have similar occupations and behavioural patterns in this community. Studies have reported that infection rates increases significantly with age, from childhood to school age, adolescent and further in older age (Asaolu *et al*., 1992, Kaliappan *et al*., 2013). In contrast, the result from this study showed Ascaris had two peaks, one at pre-school age group and a decline at young adulthood, and gradually increases at middle age group and a decline in old age. Hookworm infection had similar pattern, but the first peak of infection was at the school age group, Humphries *et al* (2011) reported a peak at age 11-20 years for hookworm infection in their household study in Kintampo North, Ghana. This may explain the reason for the World Health Assembly resolution for mass preventive chemotherapy programme primarily targeting pre-school and school-age children (WHO 2001). Irrespective of the benefits of school-based de-worming programme, it is obvious that such an approach will miss potentially heavily infected groups outside of the target population (Walker *et al.,* 2011). There was no significant association between the occupation of the participants and STH infection in this community; the majority of the participants are students, followed by unskilled workers, who are either farmers or petti traders. Also, the level of education of the participants was not significantly associated with STH infections; about 17.7% of the participants had no formal education. These demographic factors did not have significant effects on the prevalence of STH in the community sampled.

5.1.2: Risk factors associated with STH infection

Several studies within and outside Africa have highlighted several associated risk factors of STH infection, (Adekunle *et al*., 1986, Asaolu *et al*., 2002, Rukmanee *et al*., 2008, Pullan *et al*., 2010, Kaliappan *et al*., 2013) but only few have taken the advantage of the new technology of geographical mapping, using geographic information system to evaluate the possibilities of clustering of infection. This study highlighted the specific parasite differences in terms of prevalence and intensity in the different community density areas; that is the low, medium and high density areas in Igbo-Ora. The highest prevalence of hookworm infection (24.9%) was observed in the GIS mapped high density area of the studied community. Meanwhile the highest prevalence for *A. lumbricoides* was seen in the two communities, representing the low density area (21.3% and 18.5%). In the high density area, the houses were structured in such a close proximity that there were no spaces between the houses, the last room in a building led directly to the entrance of another house, and the majority of the houses were built with mud. This may explain the reason why living in houses built with mud was a significant risk factor for hookworm infection.

In the two communities representing the low density areas, the majority of the house structures were built with concrete and there were spaces between each house structure which in many cases were used as vegetable gardens, where some of the vegetables consumed in those households were planted. Some of the houses, although modern in structure, did not have toilet facilities. *Ascaris lumbricoides* had the highest prevalence in the low-density area, and this may be explained from the infection acquisition point, because many of the houses in the area were not congested, with plots of land around homes/houses used as vegetable gardens, as well for defecation. The ova passed out with faeces from the infected individual, within the household, will contaminate the vegetables planted within the garden, increasing the chance of acquisition of infection by ingestion of those faecally contaminated vegetables. STH parasites such as *Ascaris lumbricoides,* and *Trichuris trichiura* are acquired through this means. This may explain the reason for the high prevalence of *A. lumbricoides* observed in these two communities, representing the low density areas. Likewise, no *T. trichiura* infection was found in medium and high density areas of this community, and this could be due to the geographical distribution, because the low density area mimicked the urban setting in the house structure and arrangement and studies have shown that *T. trichiura* are predominant in urban areas (Sorensen *et al*., 1994, Kaliappan *et al*., 2013). This finding is in agreement with previous studies (Albonico *et al*., 1997) which reported high prevalence of *A. lumbricoides* in urban settings and high prevalence of hookworm infection in rural settings. For *S. stercoralis,* almost the same prevalence was seen in the medium density and low density areas, while the lowest prevalence was from the high density areas of the community. No previous study investigated clustering of different parasite species between different community densities in Igbo-Ora. Similar GIS mapped study carried out by Ibikounle *et al* (2018) in the Republic of Benin showed a countrywide predominance of hookworm in all the 77 districts of Benin with the prevalence of 17.14%, while Ascaris and Trichuris were found in 48/77 with 5.35% prevalence and 37/77 with 1.15% prevalence respectively. Their findings confirmed that *Ascaris* and hookworm infections are endemic in all the departments of Benin and that the prevalence of STH in Benin varied steadily over localities. The study clearly highlighted the predominance of hookworm infections nationwide with several hotspots where the prevalence reached 50% and more (Ibikounle *et al.,* 2018).

In the bivariate analysis, there was no significant association between STH infections and the following risk factors: toilet type, past history of worm and treatment, hand wash before eating and after the use of toilet, regular shoe wearing, and wearing of dirty finger nails ($p>0.05$). A potential shortcoming for the observed differences may be as a result of reporting bias from the respondents; although information on dirty finger nails was obtained as an observational report. Toilet access, living in crowded rooms with more than four individuals in a room and houses built with mud were significantly associated with STH infection in the multivariate analysis ($p<0.05$). Pullan *et al* (2010) also reported living in households with mud floor as a significant associated risk factor for hookworm in a study carried out in rural Uganda.

In hookworm infection, studies have shown that skin contact is required for this infection (Hotez *et al*., 1990) and footwear usage is a protective factor (Bethony *et al.*, 2002, Hotez *et al*., 2003). In this study, there was no association between shoe wearing and hookworm infection, the reason may be as a result of report bias, because the information about shoe wearing was got from the participants' questionnaire and human tends to change their behaviour/attitude when they are being observed for a reason. Similar report of no association was made by Kaliappan *et al.* (2013) in a tribal Southern India population. The high prevalence of hookworm was found to be significantly associated with living in high density area, where the houses were closely clustered together and the structures were mainly built with mud, with large number of people living together in close contact.

Walker *et al.,* (2011) discovered that individual predisposition is extremely weak once the clustering of household is accounted for, which means that exposure to infectious roundworm eggs shared by household members are important determinants of household clustering. This finding is in agreement with Souza *et al.* (2007) where STH clustering was found to be associated with socio-economic status and overcrowding. Because of the absence of toilet facilities in most of the houses, defecation takes place in the bushes around the houses and many do not wear shoes, and this may increase the risk of infection. In the bivariate and multivariate analysis of the risk factors; shoe wearing and toilet types were not significantly associated with STH, neither were they significant for hookworm infection. The observed parasite-specific differences in community density areas are possibly a reflection of variation in exposure and host factors. In this study, the bivariate analysis of risk factors with each specific STH parasites was analysed for *A. lumbricoides* and hookworm, but *S. stercoralis* and *T. trichiura* were not considered for analysis because their prevalence were low, that is 3.0% and 0.8% respectively.

The majority of the infections were of light intensity for hookworm (ranges from 66.7% - 86.7%) and *A. lumbricoides* (ranges from 60.7% - 92.0%) in the four communities sampled within Igbo-Ora. Few individuals harboured heavy intensity of hookworm infection (4.4%-25.0%) and *A. lumbricoides* (4.0%-32.1%). This finding is similar to work done by Kirwan *et al*. (2009) where 85.7% of *A. lumbricoides* infection was light intensity, while 14.1% was moderate intensity. Pullan *et al.* (2010) reported a similar light intensity for hookworm in their population-based study in a rural community in Uganda. Ibikunle *et al* (2018) in Benin Republic reported that moderate to heavy hookworm and *Ascaris* infections was observed in several districts of the country, but most of the detected infections had a light parasite load. Other studies have demonstrated that intensity of infection increases with age, with heavier worm burdens among children aged 5-15 years (O'Lorcain 2000; Kirwan *et al*., 2009; Pullan *et al*., 2010). In this study, intensity of *A. lumbricoides* and hookworm increases with age and its peak was found in adult. The reason for this may be as a result of repeated exposure to the parasite, and non-treatment of the existing infection over a long period of time, which enhanced the chance of increased population of the parasite within the host, since helminth do not multiply within their host. Other studies have also demonstrated that females have heavier worm burden (Holland *et al*., 1989; Kightlinger 1998).

Multiple infections were observed in one-third (33.3%) of the infected population with double and triple helminth infections. Similar report was given in a study carried out by Dada-Adegbola *et al*. (2005) in rural communities in Nigeria where 49.1% of the infected population had multiple helminth infection. The majority of the multiple infections were *A. lumbricoides* and hookworm infections. This may be largely due to the transmission of these two parasites that are associated with poor hygiene behaviour and lack of adequate sanitation (Raso *et al.*, 2004, Ellis *et al.*, 2007).

A strong cluster of STH infection was observed in the community with the small number of household participating in the study, but had the highest number of participants, and the highest number of infected households was found in it, that is, the high density area of the community. STH infection has been found to be highly aggregated, with *A. lumbricoides* at household levels and *T. trichiura* in families (Ellis *et al.*, 2007). This finding is in line with the submission of Adekunle *et al*. (1986) on the importance of family size in relation to STH infection in Ibadan.

Similarly, a strong clustering of STH was reported by Souza *et al* (2007) in a Brazilian study, where 48% of the infected individuals were from 5% of the households. The reason may be the fact that living in close proximity increases the chance of having similar exposure to infection. This may explain the reason for the observed significant association in those living in overcrowded rooms with more than 4 individuals in a room and STH infection. This fact about retention of STH infection within households may suggest the control measure adopted by WHO should be revisited. This becomes necessary because an infected adult living in the same house with the treated school children may serve as source of infection for the treated child. This resolution is in agreement with Ellis *et al.*'s (2007) suggestion that infected households should be targeted for treatment, in that this will provide an effective, rapid and practical method of identifying and treating helminth- infected adult in the community.

Considering the individual community and the risk factors of STH infection, the risk factors were not significantly associated with STH infection in two communities representing the low density area and the medium density area. This may be partly due to the none participation of sizeable number of the adult population in two of the communities, that is, Pako and Isale-oba, and partly due to the small sample size of the participants from this two areas This is one of the major limitations of this study.

In the high density area, where the participants were evenly distributed among all age groups, the significantly associated risk factors included house type, toilet access, defecating in bushes around the house and dirty house surrounding. Some of the following risk factors have been found in other studies to be associated with STH infection (Tchuem Tchuente *et al.*, 2003, Raso *et al.*, 2004). The reason why most of the known associated risk factors, like shoe wearing and hand-washing, was not significant may be because the people lived in close community and they communicated; so they were informed about the study and a kind of attitudinal change was put up by the participants during the course of the study in the community, also a report bias may be playing an important role in the analysis.

5.2 Spatial distribution of STH infection in Igbo-Ora

In this study, the presence of STH parasite in the environment, that is, in human was used to develop the spatial distribution of STH infection in Igbo-Ora. The justification for this was in the positive correlation found in the prevalence of human STH infection and the presence of STH parasite in the soil around homes of the study participants. Pullan *et al.* (2010) reported that only few studies within African communities have addressed the spatial determinants of infections.

In this study, *Ascaris lumbricoides* was the major parasite found in the soil followed by hookworm and only one *S. stercoralis* was found, other parasite found include Taenia and *S. haematobium* ova. Similar result was recorded by Adekeye *et al* (2016) in their study done in Ibadan, wherein *A. lumbricoides* was the predominant parasite, followed by hookworm and *S. stercoralis* and other parasites aside STH were isolated. The pattern of parasite prevalence was slightly different from what Ogbolu *et al* (2011) recorded, in their study in Ibadan; hookworm was the most frequently encountered parasite followed by *S. stercoralis*, and *A. lumbricoides* was found to be fourth on the line. The reason for the highest prevalence seen may be explained by the structure of the Ascaris ova, wherein the cuticle is thick, it can withstand desiccation and it can survive better in the environment than any other human parasite. Also, the season wherein the samples were collected may contribute to the availability of one parasite specie than the other.

The presence of soil parasite has been said to be an avenue by which human infection is made possible, because the ova in the soil can be transferred directly to the mouth (Kobayasi, 1999) or to the vegetables and from vegetable to mouth when eaten raw or poorly cooked. This is practically opposite for hookworms (*Ancylcostoma duodenale* and *Necator americanus*) because of the susceptibility and sensitivity of their free-living larvae and thin-shelled eggs to desiccation and cold temperatures. This reduced their chance of being seen often in the soil samples. On the contrary, there are no free-living larval stages of *Trichuris trichiura* (whipworm) but rather thick-shelled eggs. This allowed for its survival over a long period of time even under harsh or unfavourable environmental conditions.

The observed prevalence of 28.1% of human STH infection and 17.7% of STH parasite in the environmental soil is a pointer that there is a need to determine the distribution pattern, exposure factor, the source of infection and possibly the environmental factor responsible for the presence of the infection. The geographic information system revealed that both *A. lumbricoides* and hookworm were randomly distributed in all the sampled areas except for Ascaris that was found to be clustered in medium density area of the community. The observed cluster of Ascaris in this region showed the possibility of a major environmental factor, predisposing individuals in this area to infection. The physical factor that was seen that could be responsible for the unique clustering of Ascaris in this location was the major market. The market, Towobowo by name was, on a normal day, a residential place, but every household and space becomes a market stall every 5 days. This is being patronised by everybody in the community, and there is usually a large influx of people bringing in their farm produce for sales from neighbouring communities. Buyers from other large cities come to take advantage of the cheap farm produce. Data from this community revealed that less than a quarter of the participants from this locality reported to have access to toilet. Less than 16% had water closet toilet type, 10% had pit latrine and the remaining 74% of the participants living in this place defecated in the bush around their homes.

Another important indicator is that there is no public toilet in this location and the large influx of people into this place every five days increased the chance of the people making use of open spaces around the dunghills to increase, thereby making the parasite to be readily available in the community soil, increasing the exposure of the resident to infection. Also, during the rain, the ova in the soil could be washed down to farm land and plants are contaminated with the ova of Ascaris. According to the European Commission, the definition of ‘contaminated site’: a site where there is a confirmed presence, caused by human activities, of hazardous substances to such a degree that they pose a significant risk to human health or the environment, taking into account land use (Science Communication, 2013). Hence the presence of a large volume of excreta in this community, qualify it as being marked as a contaminated area, and therefore, the health of the resident of this area is at risk of STH infection.

5.3 Genetic variance component analysis.

Many studies outside Africa have reported the significant role of host genetic factors in identifying STH intensity (Breitling *et al*., 2008, Quinnell *et al*., 2009, Pullan *et al*.,

2009) and the only two known studies done in Africa by William-Blangero *et al*. (1997) in a rural Zimbabwe and Pullan *et al*. (2010) in a rural community in Uganda. These two studies suggested the possible role of human genetics in hookworm intensity. The only known association study on STH, in Nigeria, that suggested that genetic factors may influence susceptibility to helminthic infection, was an analysis of *A. lumbricoides* worm loads in Nigerian children, that suggested the involvement of major histocompatibility complex (MHC) in determining resistance to infection (Holland *et al*., 1992). The paucity of information on the role of human genetic in infection intensity is one of the reasons for which this study was undertaken.

The genetic analyses was designed to explicitly evaluate the relative effect of the genetic factors and environmental factors contributing to human susceptibility to Soil-Transmitted helminth infection in Igbo-Ora, representing the south western part of Nigeria. The genetic factors employed for this study was investigating the effect of genetic relatedness of the study participant on helminth infections. This made use of pedigree information. However, confounded variable of household and environmental risk factors affect heritability, because related individuals are likely to be living together in the same place, resulting in having similar exposure risk factors, likewise unrelated individuals may have similar exposure with related individuals. Therefore, household and environmental risk factors were taken into consideration for this study.

5.3.1 Genetic effect of relatedness on the prevalence and Intensity of STH

Heritability is formally defined as the proportion of phenotypic variation that is as a result of variation in genetic values. According to Ekstrom (2009), heritability estimation is usually considered the first step in unravelling the genetic basis of a disease or trait.

The effect of genetic relatedness on the prevalence of various STH infections revealed heritability of 22.7% for *Ascaris lumbricoides* and a much higher heritability for other STH parasite. The heritability demonstrated in this study is in line with the research result in the Jirel population of the eastern Nepal that demonstrated that susceptibility to Ascaris is heritable, with between 30% and 50% of the variation being attributable to genetic factors. Acevedo *et al.* (2009) in their research reported that specific antibodies against Ascaris are associated with resistance and their result supported the possibility of a direct causal relationship between 13q33 locus and Ascaris susceptibility.

5.3.2 Effect of genetic relatedness on the prevalence and intensity of *Ascaris lumbricoides* and Hookworm infection

In determining patterns of infectious disease, according to William-Blangero *et al.*, (2012), host population structure factors are generally not more important than within-population host genetic factors. The result from this study revealed that the host genetic factors and the presence of parasite in the soil around homes have little or no effect on the prevalence of *Ascaris lumbricoides* infection within the population sampled; h^2 and e^2 were 0.000 and the p- value 0.500. Meanwhile, the common shared household, C^2, was responsible for 4.7% of the prevalence within households and there was a significant influence of the common shared household on the prevalence of Ascaris within related individuals (p=0.023). This result is in agreement with the report of Ellis *et al.* (2007) in the study carried out in Poyang Lake in China, wherein the variance component analysis indicated common shared environment as the major risk factor and there is no addictive genetic effect for *A. lumbricoides* infection in the area; this is contrary to William-Blangero *et al.*, (1999).

Shaw and Quinnell (2009) reported that helminth infection susceptibility in human population varies among ethnic group and that pedigree study is required in investigating the effect of genetic relatedness. The environmental factors that may mask the effect on the phenotype is taken care of or eliminated in pedigree study. This is because pedigree study allows for the analysis of a variant phenotype in unrelated individuals living in the same household and related individuals living in different households. It is however observed, in this study, that shared common household has greater and significant effects on the prevalence of *A. lumbricoides* within the population sampled than the host genetic relatedness. This can be explained by the mode of acquisition of Ascaris infection which is by ingestion of faecally contaminated food or drinks. The population sampled are people living together and having close communal relationship. There, people within the same household can exchange food and drink items, hence the possibility of one infected individual transmitting the infection to the other people within the same household, as a result of their communal living lifestyle. Another possibility is that they get their food or vegetable from the same source, especially those with vegetable garden in and around their homes; hence they have the same exposure to infection.

On the contrary, for hookworm infection, host genetic and house environment have significant effect on the prevalence of hookworm infection in this study. Heritability h^2, the proportion of variance explained by relatedness was 40.1%, while additional variance of 47.2% was explained by the presence of parasite in the soil around home e^2. This result is the third hookworm heritability report to the best of my knowledge in Africa. The first report was given by William-Blangero *et al* (1997) in Zimbabwe and the second report in the continent of Africa was in Uganda by Pullan *et al*. (2010) and this present study provide third heritability report of hookworm infection in Africa. This present result showed that the relative contribution of host genetics, that is, relatedness to the prevalence of hookworm infection, was not significant ($p= 0.065$) as compared to the significant contribution of presence of contaminated soil in the home environment ($p=0.034$) sampled. Similar report was given by William-Blangero *et al* (1997) wherein heritability of 37% was reported among the Zimbabwean for *Necator americanus*. On the contrary, the heritability report from Ugandan community reported heritability of 11.2% and 17.8 percentage of variance from unidentified domestic effects. Thus, host genetic relatedness was not considered to be a significant determinant of infection intensity in that community.

Various studies have indicated the importance of clean environment in relation to being disease free (Narain *et al*., 2000; Asaolu and Ofoezie, 2003). According to the biology of hookworm infection, humans acquire the infection by the presence of the filariform larvae L3, of hookworm in the soil and when this comes in contact with human skin, it penetrates and it is carried into the human circulation and, hence the life cycle continues. This finding is in line with Brookers *et al.* (2007) wherein it was concluded that though the host genetic factors cannot be ruled out, the variation in exposure and parasite life cycle, are primarily responsible for the species-specific differences in the patterns of infection by environment. Quinnell *et al.* (2010), in their research in a Brazilian community, reported that predisposition to human hookworm infection is due to the combined factors of host genetics and consistent differences in exposure. The exposure being determined by the effects or factors of the environment and the households.

Forrester *et al.* (1990), in their epidemiological study of *Ascaris lumbricoides* and *T. trichiura* in individuals and families in Mexico, suggested that there is considerable diversity in *A. lumbricoides* susceptibility among subjects living under the same conditions and that infection intensity is typically overdispersed, with 10-20 % of the population harbouring most of the parasites. In this study, host genetic component accounts for 25% of the variation observed in the worm burden due to *A. lumbricoides*, while 21.3% of the intensity observed was accounted by the common shared environment and the presence of the parasite in the soil around homes account for 9.3% of the variation. These imply that in this study variance component analysis for *A. lumbricoides* intensity identified host genetic factor as the major risk factor.

Similar results were seen by William-Blangero *et al.* (1999) in the research involving the genome scanning of individual human host from a Jirel population in East Nepal. In their study, about 30-50% of variation in worm burden was accounted for by the host genetic, while 3-13% of the variation in *Ascaris lumbricoides* load was due to the effect of a shared environment. Further work down by William-Blangero *et al.* (2000) among the Jiri population revealed a strong evidence for two distinct quantitative trait loci (QTL), influencing the susceptibility to Ascaris infection. Holland *et al.* (1992), in their study among children in Ile-Ife Nigeria, reported evidence for a role of the major histocompatibility complex in determining pattern of Ascaris infection.

Although several heritability studies have been done on hookworm infection, none of those studies to the best of my knowledge have been able to look at the effect of a particular gene on the prevalence or on the intensity of hookworm infection in Africa. The only heritability study done in Africa was in Uganda, wherein heritability of hookworm intensity was evaluated as 11.2 % while 17.8 percent variation was from unidentified domestic effect (Pullan *et al.* 2010). This study provides information on the genetic epidemiology of hookworm intensity wherein heritability of hookworm intensity was 1.1% and the variance explained by the common shared environment and the presence of parasite in the soil around homes was same as that of the host genetic relatedness that is 1.1%. This result implied that none of the factors has greater effect than the others on the intensity of hookworm infection in this community despite the differences in the effect on the prevalence. Several other studies done outside Africa recorded a greater variance effect of host genetic relatedness e.g. Quinnell *et al* (2010) reported a heritability for hookworm intensity in the pretreatment as 17% and 25% after reinfection in a Brazillian community. The shared household environment c^2 accounted for 16.3% and 9.5% of residual variance in both the pretreatment and reinfection respectively.

5.4 Summary of the findings

Hookworm is the predominant STH infection in the community sampled followed by *Ascaris lumbricoides.* Predisposing factors associated with intensity are living in high density areas, living in rooms crowded with more than four individuals, living in houses built with mud. *Ascaris lumbricoides* infection was found to be significantly clustered in GIS mapped medium density area of Igbo-Ora. Spatial analysis showed that hookworm infection was randomly distributed in all the GIS mapped areas of Igbo-Ora.

Heritability of *A. lumbricoides* was 22.7%. Host genetics and common shared environment had significant effect on the intensity of *A. lumbricoides* infection. (h^2 = 0.250 p-value 0.023; c^2 =0.213 p-value 0.01). In hookworm infection, human genetic relatedness accounted for 40.1% of the variation in the prevalence of infection (h^2 = 0. 401 p-value 0.065) while the presence of parasite in the soil around homes contributed significantly 47.2% to the prevalence of hookworm infection (e^2 = 0.472 p-value 0.034). All the factors h^2, c^2 and e^2 equally contributed, but not significantly, to the intensity of hookworm infection in this study.

5.5 Conclusion and recommendation

Human genetic relatedness have significant effect on Ascaris infection intensity, while the presence of soil parasite plays important role in hookworm infection. The different factors responsible for human susceptibility displayed by Ascaris and hookworm in this study is an indication that specific approach should be put in place to reduce or curtail the prevalence and intensity of STH infection rather than the assumption that the environmental condition is the only factor responsible for exposure. The relative contributions of human gene can further be explored. Exposure related factors also played significant role as determinants of STH infection, especially in hookworm infection, in these communities. The use of statistical method, that partitioned addictive effect of genetic factors from that of environmental factors and shared household, enabled a better understanding of the determinant of soil-transmitted helminth infection in this community.

Hence, the variation observed in the pattern of the factors that contributed to the prevalence and intensity of the specific STH infection is an indicator that different prevention and control strategy should be employed towards the elimination of each of the STH infection, which has been marked by WHO as one of the Neglected Tropical Diseases.

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APPENDIX I: ETHICAL CERTIFICATE

INSTITUTE FOR ADVANCED MEDICAL RESEARCH AND TRAINING (IAMRAT)

COLLEGE OF MEDICINE, UNIVERSITY OF IBADAN. IBADAN, NIGERIA.

Director: Prof. A. Ogunniyi, B.Sc(Hons), MBChB, FMCP, FWACP, FRCP (Edin), FRCP (Lond)

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UI/UCH EC Registration Number: **NHREC/05/01/2008a**

NOTICE OF FULL APPROVAL AFTER FULL COMMITTEE REVIEW

Re: Impact of Host Genetics and Domestic Environment on Soil-Transmitted Helminths (STH) Infection among Households in Igbo Ora, Nigeria

UI/UCH Ethics Committee assigned number: UI/EC/12/0267

Name of Principal Investigator: **Olufunke A. Oluwatoba**

Address of Principal Investigator: Department of Zoology,
University of Ibadan, Ibadan

Date of receipt of valid application: 17/08/2012

Date of meeting when final determination on ethical approval was made: **N/A**

This is to inform you that the research described in the submitted protocol, the consent forms, and other participant information materials have been reviewed and *given full approval by the UI/UCH Ethics Committee.*

This approval dates from 05/03/2013 to 04/03/2014. If there is delay in starting the research, please inform the UI/UCH Ethics Committee so that the dates of approval can be adjusted accordingly. Note that no participant accrual or activity related to this research may be conducted outside of these dates. *All informed consent forms used in this study must carry the* UI/UCH EC *assigned number and duration of* UI/UCH EC *approval of the study.* It is expected that you submit your annual report as well as an annual request for the project renewal to the UI/UCH EC early in order to obtain renewal of your approval to avoid disruption of your research.

The National Code for Health Research Ethics requires you to comply with all institutional guidelines, rules and regulations and with the tenets of the Code including ensuring that all adverse events are reported promptly to the UI/UCH EC. *No changes are permitted in the research without prior approval by the* UI/UCH EC *except in circumstances outlined in the Code.* The UI/UCH EC *reserves the right to conduct compliance visit to your research site without previous notification.*

Professor A. Ogunniyi
Director, IAMRAT
Chairman, UI/UCH Ethics Committee
E-mail: uiuchirc@yahoo.com

▪ Drug and Cancer Research Unit ▪ Environmental Sciences & Toxicology ▪ Genetics & Cancer Research ▪ Molecular Entomology ▪ Malaria Research ▪ Pharmaceutical Research ▪ Environmental Health ▪ Bioethics ▪ Epidemiological Research Services ▪ Neurodegenerative Unit ▪ Palliative Care ▪ HIV/AIDS

APPENDIX II: QUESTIONNAIRE

IMPACT OF HOST GENETICS AND ENVIRONMENTAL FACTORS RISK FACTORS ON SOIL-TRANSMITTED HELMINTH (STH) INFECTIONS AMONG HOUSEHOLDS IN IGBOORA, NIGERIA.

QUESTIONNAIRE

Household Number………… Personal ldentification Number…………

Demographic information.

1. Age……….. Weight (Kg)…………… Height (cm)……………….
2. Sex: Male ☐ Female ☐
3. Level of Education: (1) Primary School
   (2) Secondary School ☐
   (3) Tertiary Institution
   (4) No formal Education
4. Marital Status: (1) Single
   (2) Married
   (3) Widowed ☐
   (4) Separated
5. Present Occupation:……………………………………..
6. Religion: (1) Christianity ☐
   (2) Islam
   (3) Others…………………………………
7. Ethnicity: (1) Yoruba

(2) Ibo

(3) Hausa

(4) Others specify……………………….

Environmental/Household Description

8. How many of you live together in the house? (1) 1-3

(2) 4-6

(3) 7-9

(4) 10-12

(5) More than 12

9. Type of house: (1) Concrete

(2) Mud

(3) Others specify…………………..

10. Do you have access to a toilet? Y

11. Where is the toilet located? (1) Within the compound

(2) Attached to the building

(3) The community toilet

12. How many of you use the toilet……………….

13. Type of toilet: (1) Water closet

(2) Pit latrine

(3) Bucket/Potty latrine

(4) Nylon bags

(5) Bush around the house

Others specify…………………………………..

Behavioural activities.

14. Do you wear shoes when at home? Yes No

15. Do you wear shoes when working or relaxing/playing outside the house? s

No

16. How often do you wear shoe?(1) Regularly

(2) Occasionally

(3) Never

(4) Only when going out for occasion

17. How often do you wash your hands before eating? (1) Regularly

(2) Sometimes

(3) Never

18. How often do you wash your hands after toileting? (1) Regularly

(2) Sometimes

(3)Never

19. Do you eat uncooked vegetable? Yes No

Past history of worm infection

20. Have you ever had about or seen a worm before? s No

21. Have ever passed out worm either from mouth, nose or faeces? Yes

No

22. Have you been treated for worm in the last one year? Yes No

Observational data

23. Is your interviewee wearing long nails? Yes No

24. Are the nails dirty? Whether long or short. Yes ☐ No ☐

25. Is the house neat or dirty? Yes ☐ No ☐

26. Is the surrounding of the house neat or dirty? Yes ☐ No ☐

Appendix III

INFORMED CONSENT FORM

Dear Family Head,

My name is Olufunke Oluwatoba, a postgraduate student from Department of Zoology, University of Ibadan. I will like to find out about the health status of every member of your household, especially their state of health as regard worm infestation.

I will need to ask your house member few questions about their health and will need to collect two stool samples on two different days, this will be processed in the laboratory to ascertain whether they have worm or not, the test will be at no cost to you. The result of the test will be made available to you and all member of your household for appropriate action to be taken if they have worm.

Your household will be given a number and every member of the household as well and this will be written on the form to be filled during the interview with the household member. Likewise, a small proportion of soil around your house will be taken as sample to be tested in the laboratory; this is to be sure of where the parasite is in your environment.

Your household was chosen because it falls within they selected area from our sampling method and you are free to refuse to take part in this programme. You have the right to withdraw at any given time if you choose to. Thank you.

Consent: Now that the study has been well explained to me and I fully understand the consent of the study process, I will be willing to allow every member of my household and myself to take part in the programme.

Signature/Thumbprint of household head/date with date

Signature of Interviewer

Signature/Thumbprint of Witness with date

APPENDIX IV: PEDIGREE INFORMATION COLLECTION SHEET

Date: **Locality:**

Household ID:

PID	Name	Sex	Birth Date	Birthplace	Father's Name	Father's Birthplace