بِسْمِ اللهِ الرَّحْمَنِ الرَّحِيمِ

"رَبِّ أَوْزِعْنِي أَنْ أَشْكُرَ نِعْمَتَكَ
الَّتِي أَنْعَمْتَ عَلَيَّ
وَعَلَى وَالِدَيَّ وَأَنْ أَعْمَلَ
صَالِحاً تَرْضَاهُ وَأَدْخِلْنِي
بِرَحْمَتِكَ فِي عِبَادِكَ الصَّالِحِينَ"

"صدق الله العظيم"

سورة النمل آية ١٩

A STUDY ON INTESTINAL PARASITIC INFECTIONS AMONG EGYPTIAN CHILDREN

Thesis Submitted for Partial Fulfillment of Master Degree of (Basic medical science) Parasitology

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AIDS	Acquired immune deficiency syndrome
AcAP	A. caninum anti-coagulant protein
ALL	Acute lymphoblastic leukemia
CDC	Centers for disease control & prevention
CWPs	cyst wall proteins
DFA	direct fluorescence assay
DIC	Differential interference contrast
DM	Diabetes mellitus
ELISA	Enzyme Linked Immuno Sorbant Assay
ERCP	endoscopic retrograde cholangio-pancreogram
ES	excretory-secretory
ESVs	encystment specific vesicles
HIV	human immunodeficiency virus
HS	Highly significant
I.competent	Immuno-competent
I.compromized	Immuno-compromized
IFN	Interferon
Ig	Immuno globulin
IL	Interleukin
IPI's	intestinal parasitic infections
mAb	monoclonal antibody
MZN	Modified Ziehl- Neelsen stain
N HCL	Normal HCL

List of abbreviations continue

NS	Non-significant
O &P	Ova and Parasites
PCR	Polymerase chain reaction
S	Significant
SCID	severe combined immunodeficiency
Sec.	Seconds
SFP	Spore Forming Parasites
Spp.	Species
STHs	soil-transmitted helminths
TEM	Transmission electron microscopy
TMP-SMZ	Trimethoprim-sulfamethoxazole
UV	Ultra violet
WHO	World Health Organization
µl	Microliter

INTRODUCTION

Intestinal parasitic infections (IPI's) are among the most common infections throughout the world. About 3.5 billion of people are infected with some kinds of intestinal parasites **(WHO, 2001)**. Parasitic infections are regarded as a serious public health problem because they cause malnutrition, iron deficiency anemia, growth retardation in children and other physical and mental problems **(Hill, 2007)**.

Children are an important high-risk group for helminthic and protozoal infections. Day care centers are environments where children have proven to be more susceptible to acquire intestinal parasites, due to the facility of interpersonal contact (child-child, child-functionary) **(Carvalho et al., 2006)**.

The prevalence of intestinal parasitic infections depends on the socioeconomic level of the society, social practices and traditions, poor sanitary and environmental conditions, inadequate personal hygiene, absence of safe drinking water supplies and climatic factors **(Kvalsvig, 2003)**. Further, lack of awareness about mode of transmission of parasitic infections increases the risk of infection. Hence, a better understanding of the above factors, as well as how social, cultural and behavioral awareness affect the epidemiology and control of intestinal parasites may help to design effective control strategies of these diseases **(Kloos, 1995)**.

GI protozoa cause significant morbidity in children and as opportunistic infections in HIV/ AIDS and immunosuppressed patients in developing countries who are already malnourished or have limited access to medical services **(Nissapatorn and Lessons, 2008).** Consequently, these patients will suffer from repeated severe diarrheal episodes that can be fatal **(Kurniawan et al., 2009**).

There are dozens of species of nematode worms; however, only a small subset accounts for their enormous amount of human infection. Known also as the soil-transmitted helminths (STHs), *Ancylostoma duodenale*, *Necator americanus*, *Ascaris lumbricoides* and *Trichuris trichiura* are among the most prevalent organisms on the planet, estimated to infect almost one-sixth of the global population **(Hotez et al., 2009).**

We know that burden of disease is high in children, primarily owing to the large array of surveillance and control activities occurring in school and public education systems in endemic countries. The dynamics of infection throughout life, however, are less well known as data tend to be scattered, dated or based on small sample populations. However, we can see that on a very basic level for the intestinal nematodes, the prevalence curves for *A. lumbricoides* and *T. trichiura* follow very similar lines with a steady rise from infancy to mid-teens, and then declining into the adult age classes. This is different from the hookworms (although *Necator* and *Ancylostoma* differ somewhat), as they can begin in early childhood and adolescence but then rise through adult life either reaching a plateau or only declining from 40 years or so. There are, to our knowledge, no data on age-associated prevalence or intensity for human *Strongyloides stercoralis* in the literature, and all STHs present challenges of interpreting worm burden from the diagnostic tests used **(Olsen et al., 2009).**

In general, little is known about the global epidemiology and burden of disease due to cestodes (tapeworms). It has been suggested that cestodes infection is not frequent in children living in tropical poverty as they have limited access to meats that serve as sources of infection **(hall et al., 2008).** In addition, there are low rates of tapeworm infections in large Muslim populations in parts of Asia and Africa. However, there are reports from communities in Africa **(Boa et al., 2003).**

Humans become infected with intestinal flukes by consuming food or water that is contaminated with intermediate hosts such as infected fish and aquatic animals (e.g., crustaceans and clams). Death from infection is rare, and light infections can be asymptomatic. However, heavy worm burdens can cause cachexia and prostration. The major intestinal fluke infections include fasciolopsiasis (*Fasciolopsis buski*), heterophyiasis (*Heterophyes heterophyes*), metagonimiasis (*Metagonimus yokogawai*) and echinostomiasis (*Echinostoma ilocanum*). A shift in the epidemiology of some of these parasites related to population growth and crowded living conditions in urban and slum environments was reported **(Harpham, 2009).** This shift requires further understanding to enable control efforts to advance in urban settings **(Brooker et al., 2006).**

Many diseases, especially helminths, occurred mainly in rural populations. However, in several low and middle-income countries **(Appleton et al., 2009),** urban migration has led to the creation of urban squatter settlements with high rates of polyparasitism with both protozoa and helminths. Studies on urban ecology highlight general risk factors for Polyparasitism in these settings (**Mumtaz et al., 2009).** These include houses without cemented floors, lack of health and hygiene education (e.g., use of soap); lack of clean piped water, poorly maintained latrines and children walking barefoot. While urbanization can promote access to health services and public works, overcrowding and poor sanitation will lead to higher infection rates through closer proximity of the infected to larger vulnerable populations. Some parasites transmissions will thrive in these urban conditions, especially the protozoa (*Giardia* and *Cryptosporidia*) and helminths such as *A. lumbricoides* and *T. trichiura*, while others such as the hookworms will be less affected **(Brooker et al., 2006).**

IPI's are considered a public health problem of worldwide importance for reasons of their high prevalence, widespread distribution and effect on health **(Stephenson et al., 2000).** Morbidity and mortality caused by IPI's is usually more pronounced in children compared to adults due to their higher nutritional requirements and less mature immune system **(Guyatt, 2000).** Furthermore, the risk for poor clinical outcomes is reported to be increased in those children who were already malnourished prior to becoming infected **(Stephenson et al., 2000 a).**

The chronic malnutrition-IPI cycle which commonly begins during childhood in many developing countries also has been linked with decreased work capacity and productivity in adolescents and adults **(Guyatt 2000).** The world health organization (WHO) promotes the use of presumptive antihelminthic treatment as the foundation of IPI control activities in endemic populations **(WHO, 1996),** While still recognizing the need for longer term economic, social, behavioral and environmental solutions to reduce or eliminate source of infection **(WHO, 2000).**

The synergistic cycle of infection, immunity and malnutrition in children is well documented **(Chandra, 1999).** Infants, toddlers and other young children are reported to be most vulnerable to the adverse nutritional effects of IPI's. One reason is that they often suffer from an increased IPI burden associated with a greater exposure to these infectious agents by virtue of unsanitary practices associated with child development (for example, playing in contaminated dirt and water, sucking on dirty fingers and other objects, etc.). Growing children also have high nutritional requirements **(Scrimshaw, 1994).**

Their less mature immune systems, especially in those aged < 6 years, can reduce their ability to mount strong immune defense to infectious agents. Thus, they are more likely to suffer from adverse consequences of infection, which can affect energy and nutrient intake, transport, metabolism and excretion **(Chandra, 1999).**

Several studies have documented that children infected with round worm are more likely to suffer from stunted growth compared to those who are not infected. **O, Lorcain and Holland (2000**) reported that some stunting is caused by infection-induced anorexia. The result is decreased caloric and nutrient intake. In addition, infected children have a decreased ability to digest and absorb the ingested nutrients. Likewise, hook worm infection is commonly associated with poor child growth as a result of the loss of blood, which contains iron and other essential nutrients needed for growth. Another apparent reason is due to the intestinal inflammation caused by infection; this lowers the absorption of nutrients and may also aggravate hypoalbuminaemia **(Warren et al., 1993).** Furthermore, a heavy whipworm worm burden has been observed to negatively impact growth as a result of the frequent dysentery common with this infection as well as nutrient loss induced by gastrointestinal bleeding **(Callender et al., 1994).**

Prior studies have linked IPI's with nutritional anemia. For example, *Ascariasis* is reported to increase the risk of iron deficiency anemia **(Curtale et al., 1993).** The relationship between hookworm infection and iron deficiency anemia in vulnerable maternal-child groups is well documented **(Brooker et al., 1999).** However, recent authors have reported that intestinal infection with non-hookworm species may negatively impact iron status **(Callender et al., 1994).** For example, **Wilson and associates (1999)** liked asymptomatic non-hookworm polyparasitosis with significantly decreased mean hemoglobin levels in Colombian schoolchildren.

Sever burdens of whipworm infection have been linked with iron deficiency anemia in children. Anemia is considered one of the cardinal signs of *Trichuris* dysentery syndrome. Since the whipworm does not ingest erythrocytes, the observed anemia is probably the result of blood loss due to chronic mucosal inflammation and ulceration at the point of insertion **(Gilgen and Mascie-Taylor, 2000).** *Giardia* infection has been associated with reduced hemoglobin levels **(Curtale et al., 1998)** as well as anemia children **(Shubair et al., 2000).**

Giardia cysts are highly resistant to environmental conditions, being able to survive in cold mountain streams, stomach acid, Chlorine and even in UV-treated wastewater (**Li D et al., 2009).** Acknowledging the resilience of these cysts, it is conceivable that protozoan infections are much more frequent in settings of tropical poverty than estimated, even in the absence of reported outbreaks and epidemiological surveys (**Escobedo et al., 2009).** Amoebic dysentery due to *Entamoeba histolytica* is the second most common cause of death from parasitic disease worldwide after malaria **(Stanley, 2001).** It is estimated that *E. histolytica* infects 40–50 million people and results in approximately 100,000 deaths annually worldwide **(Petri et al., 2000).** However, these numbers are somewhat dated, and partly estimated based on data using diagnostic methods that did not effectively differentiate *E. histolytica* from the nonpathogenic *Entamoeba dispar*. Outbreaks, which often provide the best epidemiological evidence for cryptosporidiosis and giardiasis, tend to be associated with municipal and recreational water systems **(Dib et al., 2008)** and crowded human ecologies, such as daycare centers **(Nascimento et al., 2009)**.

IPI's have been suggested to have a negative influence on child cognitive and psychomotor development **(Sakti et al., 1999).** One of the mechanisms by which cognitive impairment is hypothesized to occur relates to the ability of certain parasites, especially hookworm and heavy whipworm infection **(Nokes and Bundy, 1994),** to affect host iron status and cause iron deficiency and anemia thus affecting brain iron metabolism **(Brooker et al., 1999)**.