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Seroprevalence of human toxocariasis, Jamaica

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Abstract. Seroprevalence of human toxocariasis was studied, based on 1544 samples selected from a total of 3524 submitted to the University of the West Indies in Kingston, Jamaica for diagnosis of dengue during an epidemic in 2010. The prevalence of anti-*Toxocara* IgG using the CELISA® (Cellabs) ELISA was 21.2% and males (24.4%) were significantly more likely to be exposed than females (17.5%) [$\chi 2$ =10.4; p=0.001]. No association was foundbetween exposure to *Toxocara* and area of residence (rural vs. urban) [$\chi 2$ =0.835; p = 0.409]. Prevalence of infection peaked in adolescents (10-19 years-old) and declined thereafter although a rise in prevalence was seen in older age classes. There was a high prevalence of toxocariasis in Jamaica with significant exposure among school age children with no predilection to either sex. The study will inform future work on elucidating the public health and clinical significance of toxocariasis in Jamaica.

INTRODUCTION

Toxocariasis is increasingly recognised as an important cause of morbidity among humans in tropical and temperate settings (Hotez & Gurwith 2011; Hotez & Wilkins, 2009; Mazur- Melewska *et al.*, 2012). It is a parasitic zoonosis caused principally by infection with *Toxocara canis* and *T. cati*, which are ascarids of dogs and cats, respectively. The helminths are found in the small intestine. Transmission to humans occurs by ingestion of embryonated eggs from contaminated soil, food and drink, undercooked paratenic hosts or contact with infected pets (Magnaval *et al.*, 2001; Rubinsky-Elefant G 2010; Taylor & Holland 2001). Once ingested by humans, the eggs hatch in the small intestine and larvae enter the portal circulation and are released to the rest of the body hematogenously (Macpherson, 2013; Magnaval *et al.*, 2001; Taylor & Holland 2001).

Humans are unnatural hosts and the larvae elicit intense host inflammatory responses as they migrate across the viscera, shedding excretory/secretory antigens (Hotez & Wilkins 2009; Magnaval *et al.*, 2001; Taylor & Holland 2001). Clinical presentations include, visceral and ocular larva migrans (VLM and OLM, respectively) (Magnaval *et al.*, 2001; Macpherson, 2013). VLM is associated with heavy larval burdens and a predominance of abdominal and respiratory and nonspecific symptoms of fever, rash, anorexia, malaise and lethargy and eosinophilia of greater than 30% (Taylor & Holland 2001). Ocular disease may be caused by entry of a single larva into the posterior pole of the eye resulting in intense intraocular inflammation (Good 2004; Hotez & Wilkins 2009). It commonly presents with

blurred vision but some patients may have intense uveitis and in severe cases endophthalmitis, tractional retinal detachment and blindness (Magnaval 2001; Sabrosa 2001; Taylor & Holland 2001). Common toxocariasis and covert toxocariasis are milder forms of visceral disease and presents with vague and nonspecific signs and symptoms (Macpherson, 2013; Won *et al.*, 2008).

Globally, a vast spectrum is seen in the seroprevalence rates of human toxocariasis, with the lowest rates being seen in developed regions (Espinoza *et al.*, 2010). Seroprevalence ranges from 0% among children in Madrid, Spain to 2.4% in Denmark and 13.9% in the United States (Fenoy *et al.*, 1996; Stensvold *et al.*, 2009; Won *et al.*, 2008). On the other hand, seroprevalence may be as high as 20.4% in Lima, Peru; 23.9% in Campinas, Brazil; 26.8% in Amazonia, Brazil; 29.8% in Nigeria and 46% among aboriginal adults in Taiwan (Ajayi *et al.*, 2000; Anaruma Filho *et al.*, 2002; Espinoza *et al.*, 2010; Fan *et al.*, 2004; Rubinsky- Elefant *et al.*, 2008). In the Caribbean, estimates of the prevalence of human toxocariasis among children range from 38.8% in Antigua and Cuba (Sariego *et al.*, 2012) to 86% in St Lucia (Baboolal & Rawlins 2002; Thompson *et al.*, 1986; Tikasingh, 1994). Risk factors for toxocariasis include young age, male sex, pet ownership and residence in rural areas (Barry *et al.*, 2013).

The epidemiology of human toxocariasis has not been studied in Jamaica, and the public health significance has not been established. For instance, there are no published reports of clinical disease including ocular larva migran or visceral larva migran from the country. This study will provide baseline epidemiological data on the infection as a precursor to studies on risk factors and clinical significance of toxocariasis.

MATERIALS AND METHODS

One thousand five hundred and forty four (1544) serum samples were selected from a serum bank of 3524 samples sent for dengue serology during the 2010 epidemic (Ministry of Health 2011). Samples were selected for several months in 2010 from storage at -80°C in the Department of Microbiology, The University of the West Indies, Mona. Data including patient age, sex and location of sample submission (urban/ rural) were recorded for data analysis and samples were reassigned lab numbers in order to maintain patient anonymity.

Serological diagnosis of *Toxocara* was performed using the solid phase EIA IgG CELISA® (Cellabs, Sydney, Australia) following the manufacturer's instructions. This assay detected specific IgG to *Toxocara* excretory/secretory antigens and has a reported sensitivity and specificity of 90 and 94%, respectively. According to the kit insert a strong positive (OD >1.0) is indicative of "recent clinical toxocariasis"; significant (OD 0.5-1.0) is indicative of past or current low level infection. Low (OD 0.25-<0.5 OD) is indicative of antibodies present at insignificant level and negative (OD value <0.5). For the purposes of this study the two last categories were merged. Data were analyzed using Lotus Approach Release v 9.8® by IBM®.

The study was approved by the University of the West Indies, University Hospital of the West Indies, Faculty of Medical Sciences Ethics Committee.

RESULTS

The prevalence of anti-*Toxocara* IgG antibodies was 21.2% (n=328/1544); prevalence of high titres (crudely interpreted as recent infection) was 8.2% (n = 126/1544) and 13% (n = 202/1544) had antibody levels which were significant for current low level infection or past infections.

Exposure to *Toxocara* began early in life and seroprevalence increased to a maximum by age 10-19 years for both males and females (Figure 1). Males consistently had higher rates of exposure than females (Figure 1). In fact, males (24.4%; 80/738) were significantly more likely to be exposed than females across age classes (17.5%; 124/709) [χ^2 = 10.4, p=0.001] (Table 1).

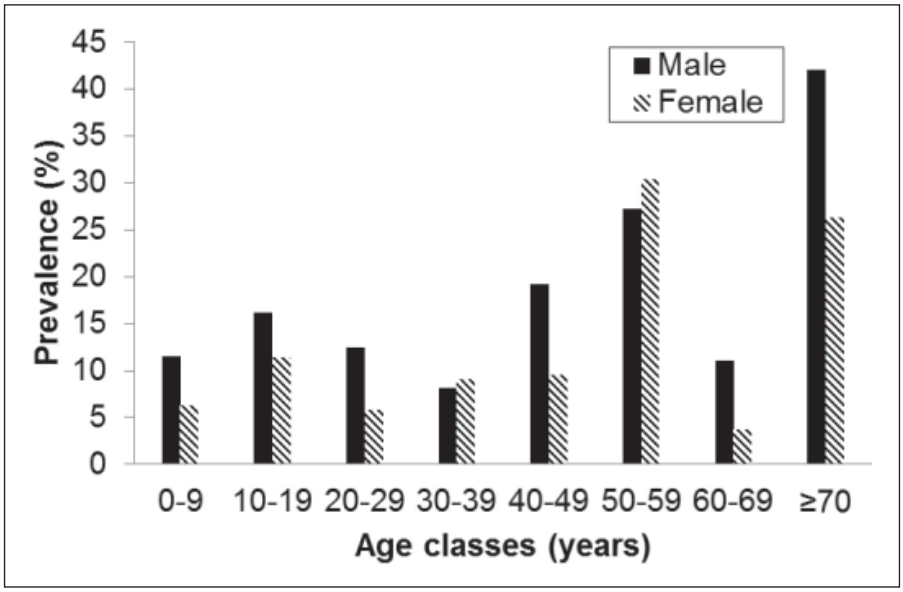

Figure 1. Age-prevalence profile of toxocariasis in Jamaica

Table 1. Seroprevalence of human toxocariasis by sex, Jamaica

Result	Positive	Negative	Total
Male	180 (24.4%)	558 (75.6%)	738
Female	124 (17.5%)	585 (82.5%)	709

Chi square = 10.4, p <0.001

Table 2. Exposure to *Toxocara* in school age children (<15-years-old), Jamaica

	Seropositive	Seronegative	Total
Male	40 (27.8%)	104 (72.2%)	144
Female	28 (19.6%)	115 (80.4%)	143
Total	68 (23.7%)	219 (76.3%)	287

Chi square = 2.667; p = 0.10

Table 3. Frequency of recent (high) and past exposure (low) to *Toxocara* by age, Jamaica

Age (years)	Recent exposure	Past exposure
<15 (n=308)	39 (12.7%)	36 (11.7%)
≥15 (n=812)	50 (6.2%)	110 (13.5%)

Chi square= 9.34, p < 0.002

The seroprevalence of toxocariasis among school age children (<15 years old) was 23.7% (Table 2). The prevalence of exposure among males (27.8%) was not statistically significantly higher than among females (19.6%) in this group [$\chi 2 = 2.67$, p=0.10] [Table 2]. Furthermore, there was no significant difference in prevalence of anti-Toxocara IgG between participants younger than 15 years old and older than 15 years old ($\chi 2 = 2.907$, p = 0.088).

Higher titres occurred significantly more frequently among those younger than 15 years (12.7%) than those who were 15 years old and older (6.2%) [$\chi 2 = 9.34$; p = 0.002; Table 3].

The prevalence of toxocariasis among persons residing in rural areas (21.4%; 204/955) was not statistically significant from that seen in residents of urban centres (19.95%; 87/436) [$\chi^2 = 0.358$, p = 0.55].

DISCUSSION

The seroprevalence of antibodies to *Toxocara* spp. in a cross-sectional study using a novel sampling approach in Jamaica was 21.2%. The current study showed that Jamaica had the lowest prevalence of exposure to *Toxocara* among its young children (23.7%)

Table 4. Prevalence of human toxocariasis among children in Caribbean countries

Caribbean country	Sample size	Age range (yrs)	Seroprevalence %	Reference
Jamaica	308	0-14	23.7	Current study
Cuba	1011	5-14	38.8	Sariego *et al* (2012)
Antigua	322	5-9	38.8	Tikasingh *et al* (1994)
Montserrat	228	5-9	46.4	Tikasingh *et al* (1994)
Trinidad	1009	5-12	62.3	Baboolal& Rawlins *et al* (2002)
St. Vincent	285	4-9	63.2	Tikasingh *et al* (1994)
Grenada	387	5-9	78.0	Tikasingh *et al* (1994)
St. Lucia	203	0.6 - 6 yrs	86.0	Thompson *et al* (1986)

when compared to other Caribbean territories which range from 38.8% to 86% (Table 4). However, data from the other countries (except Cuba) were old and the true prevalence rate may actually be lower due to increased living standards (de Silva *et al.*, 2003). Even within tropical developing countries the prevalence of exposure to *Toxocara* may vary widely from 86.75% in a sample of 166 children (age 7–12 years) in Republic of the Marshall Islands where a well-defined risk factor was parental occupation to 15.5% in Brazil where it was associated with geophagia (Cassenote *et al.*, 2014; Fu *et al.*, 2014). The reported sensitivity and specificity of the assay used were 90% and 94%, respectively. We did not conduct an evaluation of the assay in Jamaica but are confident in our results as there is an extremely low prevalence of intestinal nematode infections in the country. In fact, only 14 of 1462 (1.0%) of stool samples were positive for soil-transmitted helminths at the University Hospital of the West Indies between 2012 and 2014 in keeping with the observed trend of declining prevalence of intestinal helminths including *A. lumbricoides*, *T. trichiura* and hookworm (Rawlins, 1982).

Exposure first occurred in the youngest age group and rose in prevalence in about 10-19 years of age after which there was a general decline in prevalence during early adulthood. This was followed by a second rise in prevalence during the older age classes. Most studies of human toxocariasis are limited to children and the observed pattern is not commonly reported. The early age-prevalence profile mirrored that reported from St Lucia by Thompson *et al.* (1989); however, that study was limited to children and the rise in prevalence seen among persons in the middle age to older age classes was not reported. The observed pattern in younger persons was likely due to decreased exposure to the infective stages of *Toxocara* spp. with age and a subsequent decline in the antibody levels over time. It has been reported that anti- *Toxocara* antibodies may remain detectable serologically for 2-3 years post infection (Mazur- Melewska *et al.*, 2012). It is possible that the observed increase in prevalence in the older age classes may be due to renewed exposure due to agricultural or other activities. However, this is not supported by evidence from this study which showed that there was no significant difference in exposure rates between rural and urban areas.

There are many modes of transmission of *Toxocara* spp. including the consumption of undercooked paratenic hosts, ingestion of embryonated eggs from the fur of dogs and ingestion of eggs from contaminated soil in a manner similar to soil transmitted helminths (Macpherson, 2013). However, based on the large unrestrained dog and cat populations in Jamaica; similarities with the expected prevalence of geohelminths; the observed age-prevalence pattern which is similar to that seen in St Lucia and Cuba; and the association with contaminated soil in Cuba

it appears that ingestion of embryonated eggs from the soil is likely to be the main mode of transmission in Jamaica (Bundy *et al.*, 1987; Thompson *et al.*, 1986; Sariego *et al.*, 2012). Furthermore, younger persons were shown to have significantly higher titres than older individuals which suggest more recent infections.

Children younger than 15-year-old were more likely to have high antibody titres and this may indicate higher exposure loads. Young children are most at risk because of behavioural (geophagia, play habits, less concern about hand hygiene) that would potentially increase their exposure to infective eggs (Barry *et al.*, 2013). A similar pattern of exposure is seen in ascariasis and trichuriasis which have a similar transmission dynamics (Barry *et al.*, 2013; de Silva *et al.*, 2003).

Males were more likely than females to be exposed to *Toxocara* in this study, possibly due to increased soil related occupational exposure such as farming and construction work. Several reports have shown a male predominance with respect to exposure while others have found no sex-related difference (Ajayi, *et al.*, 2000; Baboolal & Rawlins 2002; Fu *et al.*, 2014; Rubinsky- Elefant, daSilva-Nunes *et al.*, 2008; Won, Kruszon-Moran *et al.*, 2008). This difference was not seen in school age children in the current study unlike other studies that demonstrated increased exposure in boys (Mazur- Melewska *et al.*, 2012; Sariego *et al.*, 2012; Tikasingh 1994; Baboolal & Rawlins 2002).

Generally, it was thought that residents of rural areas were more likely to have higher rates of human toxocariasis than urban districts (Baboolal & Rawlins 2002; Rubinsky- Elefant *et al.*, 2008; Rubinsky-Elefant *et al.*, 2010; Won *et al.*, 2008). In this study there was no difference in exposure between rural and urban residents, suggesting that either environmental contamination with *Toxocara*is was widespread or that infection was occurring in the peri-domiciliary areas independently of location of residences (Hotez & Wilkins, 2009; Mcpherson, 2013). Although not actually quantified, it is believed that Jamaica has large uncontrolled stray dogs and cats populations. The prevalence of infection with *T. canis* among well cared dogs, was shown to be 8% (Robinson *et al.*, 1989). Further studies to establish the environmental contamination with *Toxocara* would be needed to deduce the burden of *T. canis* present in samples of Jamaican soil.

The study had a number of limitations chief among which is possible bias in the selection of samples from persons who were suspected of having dengue. Dengue and toxocariasis have different transmission dynamics and clinical manifestations. Therefore, the reasons for seeking medical attention for dengue (headache, retro orbital pain) and *Toxocara* (fever, anorexia, weight loss, cough, wheezing) and selection of these samples should not bias the outcome of the study. During the 2007-2008 epidemic of dengue in Jamaica 38.4%, 6% and 6.5% of samples were positive for dengue, leptospirosis and malaria IgG, respectively (Lindo *et al.*, 2013).

The study used a unique cross-sectional sampling strategy to show that 21.2% of a large study population in Jamaica was exposed to *Toxocara*. The age-prevalence profile showed early exposure and a decline in prevalence with age consistent with age-dependent exposure to infective stages. However, there was a second rise in prevalence with age which was previously unreported. Males were more likely to be exposed to the parasite than females although this difference was not apparent in school age children. There was no association between residence in rural or urban communities and exposure to *Toxocara* which suggests peri-domestic transmission of the parasite. The study will inform future work on elucidating the public health and clinical significance of toxo-cariasis in Jamaica.

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