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# Review of Toxocariasis at a Children's Hospital Prompting Need for Public Health Interventions

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## Abstract

**Background:** Toxocariasis, caused by the dog and cat roundworm, is one of the most common zoonotic helminth infections in the United States and can lead to severe life-long morbidity in children. Although historical seroprevalence studies have identified high frequency of toxocariasis regionally in the United States, there are few studies linking epidemiology and clinical disease in children. The study objective was to examine the contemporary epidemiology of pediatric toxocariasis within an endemic U.S. region.

**Methods:** We conducted an epidemiologic study analyzing children diagnosed with toxocariasis presenting to a tertiary pediatric hospital in Texas from 2010–2021. We examined risk factors and performed a geospatial analysis, including a comparative analysis of human cases and locations of surrendered infected stray animals in the same region.

**Results:** Children diagnosed with toxocariasis were most commonly of Hispanic/Latino ethnicity (30/46; 65%), white race (41/45; 91%) and receiving Medicaid (34/44, 77%). Many infected children had contact with dogs or cats. Ocular toxocariasis was associated with a lack of peripheral eosinophilia ($p<0.001$). No other *Toxocara* syndromes were associated with defined absolute eosinophil count levels. Post-treatment resolution of eosinophilia was variable ranging from one to 172 weeks. A *Toxocara* hotspot was identified in northeast Houston, comprising one of the lowest median household incomes in the region.

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**Conclusions:** Toxocariasis is a devastating zoonotic infection in children living in the U.S. As it is not a reportable disease, the true burden remains unknown. It is critical to increase awareness of toxocariasis in order to direct public health interventions and ultimately reduce *Toxocara*-induced morbidity in U.S. children.

### Keywords

Toxocara; eosinophilia; epidemiology; public health

## INTRODUCTION

*Toxocara* spp., the cat and dog roundworm (*Toxocara cati* and *Toxocara canis*), is one of the most common zoonotic helminth infections in the United States and disproportionately affects those living in poverty.[1] Approximately 5–14% of children ages 6 and older are seropositive for toxocariasis in the U.S.[2,3] Children become infected with *Toxocara* spp. by ingesting *Toxocara* eggs found in soil contaminated with cat or dog feces. Common sources of exposure are public playgrounds and sandboxes. After ingestion, *Toxocara* larvae hatch from the eggs and migrate through host tissues.[4] This migration can lead to a spectrum of diseases including asymptomatic eosinophilia, covert toxocariasis, ocular larva migrans (OLM), neurotoxocariasis, and visceral larva migrans (VLM). Additionally, toxocariasis can cause long-term morbidity in children including blindness, epilepsy, and asthma.[5,6,7] Despite the potentially severe long-term impact on infected children, the true disease burden remains largely unknown.

The warm humid climate in the greater Houston, Texas region likely plays a role in promoting *Toxocara* egg development,[8] as does the large stray animal population. The aim of this study was to use a One-Health approach[9,10] to evaluate the overall burden of toxocariasis in children and stray animals residing in the greater Houston region and to provide insight into the public health impact of pediatric toxocariasis in an endemic area in the U.S.

## METHODS

A retrospective chart review was performed in patients 0–18 years old presenting to Texas Children's Hospital (TCH) from January 1, 2010 through April 9, 2021. Children with toxocariasis were identified by *Toxocara* ICD 9 and 10 codes with a confirmed positive *Toxocara* IgG or by a retinal exam consistent with toxocariasis documented by an Ophthalmologist. Data abstracted included patient demographics, laboratory analyses including absolute eosinophil count (AEC), symptoms, risk factors, and treatment regimens. Eosinophilia was defined for each patient using an AEC ≥500 and categorized as mild if AEC ≥500 but <1500, moderate if AEC ≥1500 but <5000, and severe if AEC ≥5000. This study was approved by the Baylor College of Medicine Institutional Review Board [H-49300].

A descriptive analysis and epidemiologic curve of cases by month was conducted to evaluate risk factors for infection. Pearson chi square and Fisher's exact tests were used to evaluate relationships with demographics, symptoms, risk factors, clinical manifestations,

and peripheral eosinophilia in children diagnosed with toxocariasis. Statistical analysis was conducted using STATA version 16.1 (Stata Corp, College Station, TX USA).

Stray animal data, including those infected with *Toxocara*, was obtained from the two county-run animal shelters, Harris County Veterinary Public Health (HCVPH), servicing unincorporated sections of Harris County, TX, and BARC jurisdictional animal shelter servicing the City of Houston. HCVPH and BARC documented the number of stray animals (both cats and dogs) housed at the shelter by zip code of where they were found as well as testing for each animal by stool O&P for toxocariasis between 2015 and 2021.

Geospatial analysis was performed for both human toxocariasis cases and stray animals using ArcGIS Pro v2.8 (ESRI, Redland, CA). Data on human cases and stray animals were included in the geospatial analysis that occurred in the greater Houston area (Counties included: Houston, Trinity, Polk, Walker, San Jacinto, Montgomery, Liberty, Jefferson, Chambers, Harris, Waller, Austin, Colorado, Fort Bend, Brazoria, and Galveston). Cases were aggregated to the zip code level based on their place of residence listed at the time of presentation to TCH. Attack rates by zip code were calculated using 2020 estimated population data provided by ArcGIS and visualized using a choropleth map. A hotspot analysis (Getis-Ord Gi*) of toxocariasis cases per million population was conducted using the hotspot analysis tool in ArcGIS. Animal data was geocoded and choropleth maps of stray animal density by zip code were generated. A second hotspot analysis (Getis-Ord Gi*) of stray animals was conducted using the hotspot analysis tool in ArcGIS. Both spatial relationships were conceptualized using the K-nearest neighbor technique, with every polygon having at least 8 neighbors. We conducted a comparative analysis of locations of stray animals to residences of human cases.

## RESULTS

A total of 48 pediatric toxocariasis cases were identified. Children with toxocariasis had a median age of 5 years with 56% of patients being male. Most children diagnosed with toxocariasis were of Hispanic/Latino ethnicity (30/46; 65%), white race (41/45; 91%), and receiving Medicaid (34/44, 77%) (Table 1). Race and ethnicity demographics of our sample population varied significantly from county data, which showed an overall 44% Hispanic/Latino ethnicity with 70% white race prevalence ($p < 0.01$).[11] There was no obvious seasonal transmission trend as cases were identified throughout the year; however, there was an increase in the number of annual cases identified over time corresponding to the initiation of our TCH Pediatric Tropical Medicine clinic, which diagnoses and treats children with parasitic infections.

Risk factors were evaluated in all pediatric toxocariasis cases. Animal exposure was reported in 77% (37/48) of children. These children had a history of known contact with either dogs only (51.3%; 19/37), cats only (2.7%; 1/37) or with both cats and dogs (46%; 17/37), with most animals being identified as companion animal exposures (78%; 29/37). Three children (6.2%) had no animal exposure, and 8 children (16.7%) were lacking information on animal exposure. In *Toxocara* cases associated with domestic pet exposure, 90% (26/29) had no documentation of animal anthelminthic prophylaxis provided in the chart. There was no

association observed in symptomatic versus asymptomatic disease between cases that had animal exposure and cases that did not (p=0.26). Many cases lacked documentation of pica behavior, playground, and/or sandbox exposure.

The clinical signs and symptoms as well as AEC were evaluated at the time of presentation for each pediatric toxocariasis case (see Figure, Supplemental Digital Content 1 A–E). Three children did not have an AEC value recorded. The three patients with no AECs reported all had ocular lesions consistent with OLM determined on retinal exam. An AEC <500 was identified in 11% (5/45) of the cases with a documented AEC. All five *Toxocara* positive children with a normal AEC were symptomatic with 80% (4/5) presenting with vision loss or visual impairment and retinal exams consistent with OLM. OLM appeared more frequently in those without peripheral eosinophilia (p: <0.001). The remaining patient had intermittent respiratory symptoms (wheezing) with an urticarial rash and abdominal pain on exam (negative abdominal ultrasound). A total of 29% (13/45) of children with toxocariasis had mild peripheral eosinophilia. Of the children with mild peripheral eosinophilia, 54% (7/13) had symptomatic disease. Symptoms included respiratory, specifically wheezing and cough (57%; 4/7), gastrointestinal (GI) (abdominal pain and diarrhea in one patient, and chronic abdominal pain with nausea and vomiting in the other) (29%; 2/7), and rash (14%; 1/7). One patient experiencing GI symptoms was co-infected with sapovirus (n=1) and Enteroaggregative *E. coli* (n=1) and the second patient experiencing GI symptoms was diagnosed with gastroparesis. A total of 38% (17/45) of children had moderate eosinophilia with 47% (8/17) presenting with symptoms. Of the children with moderate peripheral eosinophilia and symptoms, the most common symptoms were GI, including nausea, vomiting, diarrhea, and/or abdominal pain (62.5%; 5/8); one additional patient with GI symptoms also had an intermittent pruritic rash (12.5%; 1/8). Of the six children with moderate peripheral eosinophilia and GI symptoms, two had an abdominal ultrasound performed with one showing liver lesions. This patient was found to be positive by serology for *Echinococcus* and *Entamoeba histolytica*. An additional patient with GI symptoms had an abdominal MRI performed, which had no abnormalities. The remaining two patients with symptomatic moderate eosinophilia had respiratory symptoms or chorioretinitis. Finally, 22% (10/45) of *Toxocara* positive children had severe eosinophilia. Of these patients, 50% (5/10) had symptomatic disease with three children having GI symptoms (60%; 3/5) and two having skin lesions (40% 2/5) (one patient had urticaria and the other patient had an unspecified rash described as erythematous papules). The three patients with GI symptoms all had an abdominal ultrasound performed with one also having a CT abdomen; one abdominal ultrasound was positive for splenomegaly but otherwise without abnormality.

A total of 79.2% (38/48) of children in this cohort were treated with anthelminthic therapy; it is unclear why the remaining children were not treated. Those who were treated were most administered albendazole (89%; 34/38). Of the 48 children identified in this study, 69% (33/48) had at least one follow-up AEC to document the trend in eosinophilia post-treatment; however, only 13 patients were followed until eosinophilia resolution (39%; 13/33). Of the 13 patients with resolved eosinophilia, 23% (3/13) never received anthelminthic therapy. Of these three children, eosinophilia resolved at 4, 16, and 32 weeks after their diagnosis. In the 10 patients with normalized peripheral eosinophilia

after receiving anthelminthic therapy (all received albendazole), the timing of eosinophilia resolution was variable, ranging from one to 172 weeks.

Several patients who were serologically positive for *Toxocara* also had concurrent serologic positivity for other parasitic infections. Four cases had concurrent *Strongyloides* IgG positivity. One case had concurrent *Echinococcus* IgG positivity (positive IgG, but negative reflex Western blot) and *Entamoeba histolytica* IgG positivity. Additionally, one case had a positive *Toxoplasma* IgG and was treated for toxoplasmosis. As these infections were diagnosed via IgG, it was unclear whether these were co-infections, remote infections, or were secondary to cross-reactivity.

In total, 414,164 stray dogs and cats with toxocariasis were reported from BARC and VPH during the study period. Of those, 271,547 (65%) of the reported strays were found within the Greater Houston Area and were included in this analysis (see Figure, Supplemental Digital Content 2A). The choropleth map of stray animals by zip code showed that strays were identified throughout the majority of the study area; however, a hotspot analysis identified a clustering of high densities of stray animals with toxocariasis in the northeastern portion of the Greater Houston Area (see Figure, Supplemental Digital Content 2B).

Location data was available for 98% (47/48) of human cases with 85% (40/47) of those residing in the Greater Houston Area. Geospatial analysis of cases per million population identified cases reported from across the study region (see Figure, Supplemental Digital Content 2C). A hotspot analysis of human toxocariasis cases identified a significant clustering of cases in the northeast region of the Greater Houston area (see Figure, Supplemental Digital Content 2D). This area has one of the lowest median incomes within the region (median income: $38,113) in comparison to the overall median income of Houston city (median income: $52,338).[12] This region also had a lower level of education attainment (~10% with a Bachelor's degree) compared to the Houston city average of 33%.[12] The hotspots of both human cases and stray animals were in similar sections of the study area corresponding to a low socioeconomic status of the Houston region.

## DISCUSSION

Toxocariasis is one of the most common zoonotic infections in the U.S, but the lack of robust epidemiologic studies has resulted in an unknown and likely underestimated disease burden.[1] Human seroprevalence studies have found *Toxocara* spp. to be more common in areas of poverty, particularly in southern regions of the U.S.[13] Due to the high rate of poverty and its sub-tropical climate, Houston, Texas is likely highly endemic for toxocariasis. Understanding the risk to children in the U.S., particularly in the south and in areas of poverty, is critical to reducing *Toxocara*-induced morbidity in children.

Previous studies have demonstrated *Toxocara* disproportionately affects underrepresented communities, particularly non-Hispanic Black and Hispanic populations within the U.S. Seropositivity among non-Hispanic Black children has been reported as high as 21.2% in the U.S.[3] One study found children infected with *Toxocara* were 12 and 8 times more likely to be of Puerto Rican or other Hispanic origin, respectively.[14]

Toxocariasis is more common in regions of significant poverty.[15] A recent study from New York found the percentage of public spaces contaminated with *T.canis* or *T.cati* eggs was higher in poorer neighborhoods.[16] Although the two hotspots did not distinctly overlap in our study, both the human and animal hotspots were within the same general area in northeast Houston where the average income is substantially lower than its neighboring communities. This study highlights the need for more robust One-Health integrative studies to target zoonotic infections and a public health approach to reduce poverty-related infections. Public health interventions addressing the effects of poverty on children are critical for the prevention of *Toxocara*-induced morbidity among marginalized children living in the U.S.

## Clinical Implications:

Peripheral eosinophilia is a common clinical manifestation of toxocariasis due to migration of larvae through host tissues.[17] As a result, peripheral eosinophilia is used as an indicator to initiate diagnostic evaluation of toxocariasis in children. However, many children with peripheral eosinophilia are never evaluated for *Toxocara* as other common pediatric diagnoses, such as atopy, can also present with peripheral eosinophilia.[18] While eosinophilia is used as an initial proxy for the evaluation of toxocariasis in children, the current study found the severity of peripheral eosinophilia does not generally correlate with clinical manifestations of toxocariasis.[19] OLM, however, is an exception, as OLM more commonly presents without peripheral eosinophilia.[20]

Albendazole is the preferred first line anthelminthic therapy for toxocariasis in children due to its wider dispersion through tissues compared with other anthelminthic agents.[21,22] While the treatment of asymptomatic toxocariasis is controversial due to the self-limited natural history of disease, treatment is particularly important in patients with severe peripheral eosinophilia or symptomatic disease to prevent further larval migration and eosinophilia-related tissue damage.[23] Commercially available *Toxocara* serologic assays are unable to differentiate acute vs remote infection and are unable to be used as a test of cure for toxocariasis. As a result, reduction trends in peripheral eosinophilia over months has been used as a surrogate of disease resolution, although data to support this clinical practice is lacking.[24] This study evaluated time to peripheral eosinophilia resolution in albendazole-treated and non-treated children with toxocariasis. However, the timing of eosinophilia resolution following albendazole therapy varied significantly possibly secondary to differences in disease burden or overall small sample size. More robust, large-scale prospective studies are needed to determine the impact of targeted treatment on eosinophilia resolution. Given this limitation, there remains a dire need to improve *Toxocara* diagnostic tests to determine disease resolution.

OLM is a devastating manifestation of toxocariasis, which can lead to permanent blindness. This study demonstrated most children with OLM did not have peripheral eosinophilia. It is thus imperative for pediatric Ophthalmologists to be aware of clinical manifestations of OLM in order to provide prompt interventions to reduce the risk of morbidity. Treatment with albendazole and corticosteroids is generally recommended for OLM, but the concentrations of albendazole within the eye remains unknown.[25] Reversal of vision

loss is possible; however, treatment is aimed at preventing progression of ocular injury.[25] Approximately 70 people are blinded by toxocariasis annually in the U.S. alone.[26]

Identification of other *Toxocara* syndromes is critical to reduce morbidities associated with toxocariasis. In VLM, *Toxocara* larvae migrate through various organs resulting in visceral lesions and organomegaly. Findings of VLM most commonly manifest as GI and/or pulmonary symptoms with evidence of pathology in liver or lungs. In this study, 11 children developed GI symptoms while 5 children had pulmonary symptoms; one patient had both GI and pulmonary symptoms. Only two patients with pulmonary symptoms had chest x-rays performed and seven patients with GI symptoms had abdominal imaging or laboratory exams (beyond abnormal CBC) performed to determine if organ pathology was consistent with VLM. VLM is an independent risk factor for the development of asthma. Children with positive *Toxocara* serology have been found to be 1.91 times more likely to develop asthma compared to children without toxocariasis.[27] Neurotoxocariasis, presenting as eosinophilic meningitis or seizures, is associated with the development of epilepsy. An Italian case-control study published in 2008 showed an association between positive *Toxocara* serology and partial epilepsy in adults.[28] Our study did not identify any children with neurotoxocariasis, indicating this is a rare manifestation of disease or it is not generally considered in the work up of seizures. Lastly, an unknown number of children had covert toxocariasis in this study despite many having non-specific symptoms. Covert toxocariasis can lead to chronic, non-specific symptoms such as prolonged GI symptoms and long-term cognitive delays. Studies have found that children infected with *Toxocara* spp. score lower in both the Wechsler Intelligence Scale for Children-Revised and the Wide Range Achievement Test-Revised examinations.[29] It is imperative that larger clinical studies are performed to assess the overall morbidity induced by toxocariasis in U.S. children.

### Animal and Environmental Implications:

Exposure to dog and cat feces is a known risk factor for toxocariasis in children. Rates of infection in dogs (*T. canis*) and cats (*T. cati*) vary within the U.S. with an overall prevalence of 4.5% of dogs and 20.3% of cats infected.[30,31] In Texas in 2014, only 2% of cat and 1% of dog feces were found to have *Toxocara* eggs; however, this could be limited by the regional sample population.[32] Many children in our study had animal exposure. Additionally, there appears to be a hotspot of human and animal cases, particularly in the northeast corner of Houston, although only animal data from 2015–2021 was obtained. As such, more comprehensive data for the region is needed to define areas of concern.

There are some noteworthy limitations in our study. This is a retrospective study based off electronic medical record data and as a result, information was limited to documentation available. For instance, there was notable lack of exposure data in general documented. Additionally, animal shelter data was only analyzed for years 2015–2021 in comparison to the human data that was taken from 2010–2021, likely producing an incomplete analysis of the animal data. This five-year gap could also explain the reason for the animal and human data abutting each other but not overlapping on geospatial analysis. Additionally, the animal data indicates the location the animals were acquired by animal control. These animals are mobile and could potentially spend significant time or even live in the abutting region

that has been identified as a human hotspot. Additional monitoring of animal behavior and animal movement in the northeast Houston region could provide critical information regarding “One Health” risks of animal to child transmission in the area. Another limitation included the lack of appropriate sensitivity based on localization of infection and specificity due to cross-reactivity with other parasitic infections for commercially-available *Toxocara* diagnostic testing measuring total IgG. Finally, use of *Toxocara* IgG limits the ability to determine acute vs remote infection or test for cure, thus limiting our ability to determine disease acuity and impact of anthelminthics. These limitations highlight the need for more robust prospective studies and a focus on developing new diagnostic technologies.

## CONCLUSION

Despite significant clinical implications, toxocariasis remains underrecognized in the US. Instituting a coordinated public health program with a One-Health approach may be the first step in identifying additional pediatric toxocariasis cases and reduce the overall *Toxocara* burden in the U.S. First, although newborn litters have been found to contain high parasitic burden, making anthelminthic treatment for dogs and cats more available, particularly in areas of poverty, would aid in reduction of environmental risk to children.[33] Second, increasing public awareness of the risks associated with stray and companion animals in public spaces will further aid in reducing environmental contamination. Third, increasing healthcare provider knowledge is essential to the diagnosis and subsequent treatment of children with toxocariasis. Increased recognition of toxocariasis and targeted treatment will reduce *Toxocara*-associated morbidity. Fourth, investment in the development of novel diagnostic assays to improve assay sensitivity and specificity as well as post-treatment monitoring in children is critical to enhance healthcare providers’ ability to diagnose toxocariasis. Lastly, despite the increasing recognition of toxocariasis in the greater Houston region, toxocariasis remains a non-reportable disease in Texas. To understand the true burden of disease in the U.S and to reduce childhood morbidity, toxocariasis should be a reportable disease to help guide region-specific public health interventions.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Table 1:**

Demographics of children with toxocariasis presenting to Texas Children's Hospital from 2010–2021.

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|---|---|
| Sex<br>(n = 48) | Male: 27 (56%)<br>Female: 21(44%) |
| Age<br>(n =48) | 0–5 years: 25 (52%)<br>6–12 years: 16 (33%)<br>13–18 years: 7 (15%) |
| Ethnicity<br>(n = 46) | Hispanic/Latino: 30 (65%)<br>Non-Hispanic: 16 (35%)<br>Unknown: 2 patients |
| Race<br>(n = 45) | American Indian/Alaskan Native: 0<br>Asian: 3 (7%)<br>Native Hawaiian/Pacific Islander: 0<br>Black/African American: 1 (2%)<br>White: 41 (91%)<br>More than one race: 0<br>Unknown/Not reported: 3 patients |
| Insurance<br>(n = 44) | Medicaid: 34 (77%)<br>Private: 10 (23%)<br>None: 0<br>Unknown: 4 patients |
| Animal Exposure<br>(n = 40) | Dogs: 19 (47.5%)<br>Cats: 1 (2.5%)<br>Cats and Dogs: 17 (42.5%)<br>None: 3 (7.5%)<br>Unknown: 8 patients |
| Absolute Eosinophil Count<br>(AEC)<br>(n =45) | Normal: 5 (11%)<br>Mild: 13 (29%)<br>Moderate: 17 (38%)<br>Severe: 10 (22%)<br>Not performed: 3 patients |