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Toxocara Seroprevalence and Associated Risk Factors in the United States

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Abstract. Caused by the parasitic nematodes *Toxocara canis* and *cati*, toxocariasis in humans can result in covert toxocariasis, ocular toxocariasis, visceral larval migrans, and neurotoxocariasis. A common infection, toxocariasis exposure varies widely within and between countries, with a previous estimate of *Toxocara* seroprevalence using data from 1988 to 1994 in the United States of approximately 13%. Age, poverty, sex, educational attainment, ethnicity, and region have been associated with *Toxocara* seroprevalence. In this study, we sought to determine the seroprevalence of and factors associated with *Toxocara* seropositivity in the United States using data from the National Health and Nutrition Examination Survey from 2011 to 2014 to provide a more recent estimate of *Toxocara* seroprevalence in the United States. We found an overall *Toxocara* seroprevalence of 5.1%. Increasing age, male sex, low educational attainment, low income, and immigration status each was associated with *Toxocara* seropositivity. Mexican Americans had reduced odds of exposure. These findings show that exposure to *Toxocara* continues in the United States and that several demographic factors influence the risk of exposure.

INTRODUCTION

Toxocara canis and *Toxocara cati* are parasitic nematodes responsible for human toxocariasis, a common[1] and likely underrecognized[2,3] zoonotic helminth infection. Among the nematodes found in the genus *Toxocara*, *T. canis* and *T. cati* are the only *Toxocara* species known to cause human disease. *Toxocara* infects humans via embryonated eggs in the environment, particularly in soil or in raw vegetables or other foods,[4,5] contaminated water,[6] and possibly contact with dog hair.[7,8] Although routine veterinary care for household pets may increase detection of the parasite and thereby decrease risk for human exposure, infection is still prevalent throughout the world.[1] The major clinical conditions of human toxocariasis are covert toxocariasis, ocular toxocariasis, visceral larval migrans, and neurotoxocariasis.[9,10] In the United States, children[11] and adults[12] seropositive for toxocariasis had worse cognitive function than did seronegative controls. In fact, in mice, *Toxocara* infection has been associated with biomarkers of Alzheimer's disease.[13]

Despite the clinical significance of human toxocariasis, the epidemiology of toxocariasis remains insufficiently known.[4,10] The prevalence of human toxocariasis appears to vary both between[9] and within countries.[10] Regardless, toxocariasis appears to be one of the most common helminth infections in humans worldwide.[1,13] Previous estimates based on data from the US Centers for Disease Control and Prevention's (CDC) third National Health and Nutrition Examination Survey (NHANES III) suggest that approximately 14% of the population older than the age of 6 years in the United States in 1988–1994 was seropositive for *Toxocara* species.[14] Using the same dataset that Won et al.[14] used but with a different statistical approach, Congdon and Lloyd[15] found an overall US seroprevalence of 12.6% for females and 14.6% for males. A systematic review of *Toxocara* seroprevalence in North America suggested a prevalence ranging from less than 1% in an indigenous group in Canada to approximately 31% in a sample of children with asthma in Mexico.[16] However, the current estimates for this infection in the United States come from data collected between 1988 and 1994.[16] In Denmark, one study found a *Toxocara* seroprevalence of 2.4%,[17] and Holland et al.[18] found a seroprevalence of 31% in school children in Ireland.[18] In a particular area of Nigeria, toxocariasis may have a seroprevalence of 86%.[6]

There are identified risk factors for *Toxocara* infection in humans, although many of the findings have been inconsistent.[1] Sociodemographic factors such as age, poverty, ethnicity, sex, and geographical region appear to be associated with *Toxocara* seropositivity.[15] For example, *Toxocara* seroprevalence may exceed 20% in males in some US counties, particularly in the South and Northeast.[15] In addition, other factors associated with infection include pet ownership,[1,13] climate because *Toxocara* has optimal temperatures for breeding, and rurality with higher seroprevalence in rural as compared with urban areas.[13] *Toxocara* seroprevalence also differs across ethnic groups,[10] suggesting that cultural and genetic factors might affect seroprevalence.[15] Furthermore, Won et al.[14] found associations between *Toxocara* seropositivity and blood lead concentration, educational attainment, and socioeconomic status.

The US CDC periodically tests serum samples from the NHANES for anti-*Toxocara* IgG antibodies and recently released data collected from 2011 to 2014 that contained anti-*Toxocara* IgG antibodies. Accordingly, our study objectives were 2-fold: first, to update seroprevalence estimates of *Toxocara* in the United States because prior work used NHANES data collected from 1988 to 1994 and second, to investigate sociodemographic characteristics associated with *Toxocara* seropositivity in the United States. In the previous report by Congdon and Lloyd,[15] *Toxocara* seroprevalence was disaggregated by US counties and general geographical regions. However, geographical or other location data in the NHANES data sets are restricted and require funding to obtain. Therefore, we chose to report only findings for the United States as a whole.

MATERIALS AND METHODS

The National Center for Health Statistics (NCHS), a division of the CDC, conducts the NHANES, a cross-sectional survey. The NHANES uses a stratified, multistage cluster design to

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recruit a sample representative of the noninstitutionalized US population and collects an extensive amount of sociodemographic, laboratory, examination, and other data from a large number of individuals residing in various locations in the United States. Before 1999, the CDC conducted the NHANES irregularly, and the survey generally spanned multiple years, resulting in very large sample sizes. In 1999, the CDC converted the NHANES to a continuous, 2-year cycle format with approximately 10,000 participants in each cycle. Although the NHANES collects much of the same data for each NHANES cycle, some of the cycles, including the NHANES III (1988–1994), contain data for variables that the NHANES irregularly surveys, such as anti-*Toxocara* IgG antibodies. Until recently, data for *Toxocara* seropositivity was available only for the NHANES III dataset. However, the availability of surplus sera from the 2011–2012 and 2013–2014 NHANES cycles enabled the CDC to assess again serum samples for anti-*Toxocara* IgG antibodies, allowing a current exploration of *Toxocara* seroprevalence and factors associated with *Toxocara* seropositivity.

In the 2011–2012 and 2013–2014 cycles, the NHANES assessed 13,509 participants aged 6 years and older for anti-*Toxocara* IgG antibodies and collected sociodemographic data for all participants including age, sex, race-ethnicity, education, poverty-to-income ratio (PIR), and immigrant status. Whereas CDC technicians calculated *Toxocara* seroprevalence for the entire study sample, we also computed seroprevalence for individual age groups (20–29, 30–39, 40–49, 50–59, 60–69, 70–79, and 80 years and over). Race-ethnicity groups included non-Hispanic White, non-Hispanic Black, Mexican American, and "Other" including other Hispanics, Asians, and individuals reporting multiple races. Participants reported their greatest level of educational achievement with potential options including less than ninth grade (less than high school), 9–11th grade (high school) but no high-school diploma, high-school graduate or GED recipient, some college or AA degree, and college graduate or above. The CDC calculated a PIR for all families and applied it to all individuals surveyed within a household. The PIR is the ratio of the total family income to the federal poverty level at the time of the survey. Although the PIR is naturally a continuous variable, we recoded it into multiple groups (0.00–0.99, 1.00–1.99, 2.00–2.99, 3.00–3.99, 4.00–4.99, and 5.00+) for comparison purposes. The NHANES considered participants born outside of the United States to be immigrants.

Laboratory testing. CDC laboratory technicians tested serum samples for *Toxocara*-specific IgG antibodies using a Luminex assay. A full description of the laboratory methods used is on the NHANES website (https://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/SSTOCA_G.htm). The CDC considered results from the assay to be *Toxocara* seropositive if the mean fluorescence intensity was greater than 23.1 and negative if the value was equal to or less than 23.1.

Statistical analyses. We used Stata version 14.2[19] for all statistical analyses and used the *svy* prefix for all relevant commands to account for the NHANES sampling design. Before analyses, we treated missing data using multiple imputation with chained equations. The chained equations approach allows for distribution-specific imputation equations (e.g., ordinary least squares regression for continuous data and logistic regression for dichotomous data). We used twenty imputed datasets. Two-hundred iterations separated each imputed dataset. The graphical diagnostics indicated that the imputation model converged well before that point.[20] We computed means or proportions, minimums, and maximums for each of the sociodemographic variables we used in this study. We then used logistic regression to estimate the relationship between *Toxocara* seropositivity and each of the sociodemographic variables while controlling for all other variables. For example, we used logistic regression to test for an association between *Toxocara* seropositivity and sex while controlling for age, race-ethnicity, education (we used head-of-household education for respondents younger than 20 years old), PIR, and immigrant status.

RESULTS

The study sample consisted primarily of young to middle-aged adults [mean (standard deviation [SD]) = 38.6 (24.5)] and included nearly equal numbers of males (48.8%) and females (51.2%). The majority were non-Hispanic White (65.3%) and had attained at least some post-high school education (62.7%). The sample was relatively evenly distributed across income levels, and approximately 15% were immigrants (Table 1). The overall seroprevalence of *Toxocara* for respondents ages 6 years and over sampled in the 2011–2014 NHANES data cycles was 5.1% (95% confidence interval [CI]: 4.3, 5.9). Seroprevalence by age group varied from 2.6% in the group aged 6–9 years to 7.0% in the group aged 80 years and older. In females, the overall seroprevalence was 3.9%, and in males, the overall seroprevalence was 6.4%. For subjects with no high-school diploma, the *Toxocara* seroprevalence was 10.1% but 3.2% for those with more than a high-school education. For a PIR of 0–0.999, the seroprevalence was 9.4%, dropping to 2.2% for those with a PIR of five or higher. In immigrants, the seroprevalence was 12.4%, compared with 3.7% for nonimmigrants (Table 2). Table 3 reports odds ratios

TABLE 1
Weighted proportions of study variables

	Proportion	SE
Age		
6–9	4.4	0.22
10s	13.6	0.37
20s	15.0	0.94
30s	14.4	0.55
40s	15.3	0.53
50s	15.5	0.51
60s	11.7	0.48
70s	6.4	0.31
80+	3.7	0.25
Female	51.2	0.38
Race-ethnicity		
Non-Hispanic white	65.3	2.6
Non-Hispanic black	10.9	1.4
Mexican American	9.8	1.4
Other	14.0	0.99
Education		
No high school diploma	16.6	1.2
High school diploma	20.7	0.83
More than high school	62.7	1.6
Poverty-to-income		
0–0.999	18.7	1.2
1–1.999	21.7	0.93
2–2.999	15.1	0.55
3–3.999	12.9	0.77
4–4.999	9.3	0.57
5+	22.4	1.5
Immigrant	15.6	1.2

SE = standard error. Unweighted *N* = 13,509. Source: Continuous NHANES, 2011–2014.

TABLE 2
Weighted seroprevalence of *Toxocara* by study variables

	Unweighted *N*	Percent positive	95% CI LL	95% CI UL
Full sample	13,509	5.1	4.3	5.9
Age				
6–9	1,149	2.6	1.4	3.7
10s	2,712	3.9	2.9	4.9
20s	1,636	4.6	3.2	6.0
30s	1,686	4.8	3.7	5.9
40s	1,645	5.4	4.2	6.7
50s	1,592	6.5	4.6	8.3
60s	1,586	4.8	3.2	6.3
70s	914	6.5	4.9	8.1
80+	589	7.0	4.3	9.6
Sex				
Female	6,859	3.9	3.1	4.6
Male	6,650	6.4	5.5	7.3
Race-ethnicity				
Non-Hispanic white	4,972	3.8	3.0	4.7
Non-Hispanic black	3,114	6.7	5.5	8.0
Mexican American	2,010	6.1	4.2	8.0
Other	3,413	9.1	6.9	11.3
Education				
No high school diploma	3,156	10.1	8.4	11.8
High school diploma	2,951	6.7	5.3	8.0
More than high school	7,402	3.2	2.7	3.8
Poverty-to-income				
0–0.999	3,712	9.4	7.6	11.2
1–1.999	3,522	6.1	4.8	7.3
2–2.999	1,859	4.4	3.2	5.6
3–3.999	1,473	3.9	2.6	5.2
4–4.999	977	3.8	2.0	5.6
5+	1,966	2.2	1.4	3.0
Nativity				
Immigrant	3,248	12.4	10.1	14.7
Nonimmigrant	10,261	3.7	3.0	4.4

CI = confidence interval; LL = lower limit; UL = upper limit. Source: Continuous NHANES, 2011–2014.

TABLE 3
Sociodemographic predictors of *Toxocara:* odds ratios from logistic regression

	OR	95% CI
Age		
6–9	1.00	–
10s	1.5	0.94, 2.3
20s	1.6	0.95, 2.8
30s	1.6	0.97, 2.8
40s	2.0**	1.3, 3.2
50s	2.7***	1.6, 4.4
60s	2.0*	1.2, 3.6
70s	2.6**	1.5, 4.5
80+	2.9**	1.3, 6.2
Female	0.54***	0.45, 0.65
Race-ethnicity		
Non-Hispanic white	1.0	–
Non-Hispanic black	1.3	0.99, 1.7
Mexican American	0.52**	0.35, 0.78
Other	1.0	0.72, 1.5
Education		
No high school diploma	1.0	–
High school diploma	0.84	0.64, 1.1
More than high school	0.49***	0.38, 0.64
Poverty-to-income		
0–0.999	1.0	–
1–1.999	0.68**	0.51, 0.90
2–2.999	0.51**	0.35, 0.76
3–3.999	0.50**	0.33, 0.75
4–4.999	0.50*	0.29, 0.87
5+	0.31***	0.17, 0.55
Immigrant	3.4***	2.4, 4.8

OR = odds ratio; CI = confidence interval. Unweighted $N = 13,509$. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. Source: Continuous NHANES, 2011–2014.

corrected for all the other sociodemographic variables we used from logistic regression for variables that represent risk factors for *Toxocara*. Compared with subjects aged 6–9 years, subjects aged 40 years or older were nearly twice as likely to be seropositive for *Toxocara*. Females were about half as likely to be seropositive as males (odds ratio [OR] = 0.54, 95% CI: 0.45, 0.65). Compared with subjects who self-identified as non-Hispanic White, Mexican American subjects were also about half as likely as being seropositive for *Toxocara* (OR = 0.52, 95% CI: 0.35, 0.79). Subjects who had attained education beyond high school were less likely to be seropositive compared with subjects with less than a high-school education (OR = 0.49. 95% CI: 0.38, 0.64). Finally, immigrants were more than three times as likely to be seropositive for *Toxocara* as were nonimmigrants (OR = 3.3, 95% CI: 2.4, 4.7).

DISCUSSION

In this population-based study representative of 13,509 noninstitutionalized subjects weighted to represent the US population, the overall weighted seroprevalence of *Toxocara* in subjects aged 6 years and older was 5.1%. However, *Toxocara* seroprevalence varied according to sociodemographic factors. In general, males were nearly twice as likely to be seropositive for *Toxocara* than were females, seropositivity tended to increase with age, and both education and socioeconomic status were inversely associated with seroprevalence. These general trends are consistent with previous findings with infectious diseases, including parasitic infections.[12,18,21,22] In terms of race-ethnicity, subjects self-reported as Mexican American had reduced odds of infection (OR = 0.52), while all other race-ethnicity categories had similar seroprevalence rates. Finally, immigrants, regardless of race-ethnicity, were more than three times as likely as to be seropositive than were nonimmigrants in these US samples.

The weighted *Toxocara* seroprevalence of 5.1% that we found in the combined 2011–2012 and 2013–2014 NHANES datasets is lower than the 14% seroprevalence Won et al.[14] reported and lower than the 12.6% seroprevalence in females and 14.6% in males Congdon and Lloyd[15] reported based on the 1988–1994 NHANES dataset. This change in *Toxocara* seroprevalence suggests a possible decrease in the seroprevalence of *Toxocara* in the United States since 1994. However, differences in the assays used to detect *Toxocara* and their cutoff points for seropositivity between the earlier and later NHANES datasets preclude direct comparison of *Toxocara* seroprevalence between the two NHANES datasets. Based on these datasets, therefore, we cannot definitively determine whether *Toxocara* seroprevalence in the United States has changed since 1994. Nonetheless, the data we used from the 2011–2012 and 2013–2014 datasets provide the most up-to-date estimates of *Toxocara* seroprevalence in the United States and indicate that *Toxocara* exposure remains present in the United States.

Despite the difficulty in making direct comparisons of *Toxocara* seropositivity between the earlier and later NHANES datasets, we found that, similar to Congdon and Lloyd,[15] male sex, race-ethnicity, and socioeconomic status were associated

with *Toxocara* seroprevalence. Although we found that males were approximately twice as likely as females to be *Toxocara* seropositive and that there were clear gradients with increasing educational attainment and PIR and lower odds ratios of *Toxocara* seropositivity, *Toxocara* seroprevalence odds ratios did not differ between non-Hispanic Blacks and non-Hispanic Whites in adjusted models, although they both had higher odds ratios than did Mexican Americans. These results suggest that based on these models controlling for PIR and educational attainment, *Toxocara* seroprevalence may differ less between race-ethnicity groups in the US in 2011–2014 than it did in 1988–1994.

Consistent with prior work,[23] we found that *Toxocara* seroprevalence is higher in people with less educational attainment[14] and lower income. Similar to Won et al.,[14] we found odd ratios for *Toxocara* seropositivity among people in their 20s and 30s of 1.5. However, in contrast to Won et al.,[14] we found that seroprevalence increased with age with the highest odds ratios for *Toxocara* seropositivity occurring in people in their 50s (odds ratio: 2.4) and 70s (odds ratio: 2.3) and in those older than age 80 years (odds ratio: 2.6), suggesting that exposure to *Toxocara* may increase with age in the United States. In regard to *Toxocara* seropositivity and age, however, not all studies have found an association between *Toxocara* seroprevalence and increasing age. In La Plata, Argentina, for instance, *Toxocara* seropositivity was higher in subjects under age 15 years than in subjects older than 16 years.[24] Won et al.[14] also found higher seroprevalence in subjects in their 20s and 30s compared with older subjects and speculated that this may be due to increased soil exposure in children. In a Jordanian sample aged 5–24 years, by contrast, *Toxocara* seroprevalence was highest in females ages 5–9 years and in males ages 15–19 years,[25] pointing out that factors such as sex might influence the association between age and seropositivity. The increased seroprevalence with age that we found could reflect cohort effects or even changes in veterinary practices in detecting and treating animals with toxocariasis, as treatment guidelines for animals are now readily available.[26,27] Indeed, improved veterinary and household care for pets could have led to higher detection rates in more recent years thereby reducing the risk of infection in pets and, subsequently, in humans. The increasing seropositivity with age we found also might suggest that other sources of *Toxocara* exposure besides soil may be relevant in the United States.

Several considerations affect the interpretation of these findings. Enzyme-linked immunosorbent assay used to identify exposure to *Toxocara* can cross-react with antibodies to other parasites, potentially inflating estimates of *Toxocara* seroprevalence.[28] In addition, we based our analyses on cross-sectional data and so do not know the timing of the initial exposure to *Toxocara* and whether subjects had additional exposures. Although we corrected for age, race-ethnicity, education, PIR, and immigrant status, we might well have missed other covariates related to *Toxocara* exposure, potentially resulting in residual confounding.

In conclusion, based on the most recently available NHANES datasets containing information about the seroprevalence of *Toxocara*, we found a seroprevalence of 5.1% in the United States, indicating that *Toxocara* exposure continues in the United States. However, the risk of *Toxocara* exposure is not evenly distributed through the US population but rather relates to a variety of sociodemographic factors. Male sex, increasing age, low educational attainment, and low PIR were associated with *Toxocara* seropositivity. Subjects self-reported as Mexican American had reduced odds of infection, whereas all other race-ethnicity categories had similar seroprevalences. Immigrants were more likely than nonimmigrants to be *Toxocara* seropositive.

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