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A Roadmap to Toxocariasis Infection Control: A Comprehensive Study on Its Impact, Seroprevalence, and Allergic Implications in Latin America

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Abstract: This study was conducted using data from the SCAALA (Social Change Asthma and Allergy in Latin America) cohort in Brazil from 2005 to 2013. We examined the seroprevalence and risk factors of toxocariasis, a parasitic infection leading to conditions such as visceral larva migrans, utilizing an indirect ELISA with *T. canis* antigens, alongside with data from questionnaires, eosinophil counts, sIgE to aeroallergens, IL-10 levels, and Skin Prick Test results; the research provided insights into the disease's dynamics. The prevalence of anti-*Toxocara* spp. IgG increased from 48% to 53% over the studied period, with a 25% increase in new cases in 2013. The significant risk factors included age and pet exposure, while higher maternal education and living on paved streets were found to offer protection. The study uncovered a complex interaction between *Toxocara* spp. infection and the immune system, indicating that the infection could both trigger inflammation and modulate skin reactions. Based on these findings, the study proposed a roadmap for controlling toxocariasis, which includes strategies such as enhancing public education about the disease and preventive measures, improving environmental sanitation, strengthening veterinary control measures like pet deworming, increasing access to healthcare and screening, and implementing community-based interventions to address the identified risk factors. These measures aim to reduce the prevalence of toxocariasis and its impact on public health by addressing environmental and socioeconomic risk factors, providing a pathway to significantly reduce the burden of this parasitic infection.

Keywords: *Toxocara* spp.; risk factors; seroprevalence; eosinophilia

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1. Introduction

Human toxocariasis stands as one of the most overlooked diseases caused by species from the *Toxocara* genera (*Toxocara canis* and *Toxocara cati*) across regions worldwide, including Latin America [1,2]. Human infection arises from the ingestion of embryonated eggs of *Toxocara* spp., and the subsequent disease emerges as larvae migrate through organs and systems, leading to the common forms of toxocariasis [3,4].

Although toxocariasis may not manifest symptoms, clinical presentations encompass vision impairment, coughing, wheezing, eosinophilia, and headaches [5]. Additionally, larvae infection influences the host's immune responses, prompting a Th2 response and the release of cytokines like IL-4, IL-5, and IL-13, leading to eosinophilic inflammation and elevated levels of serum immunoglobulin E (IgE), which are also linked to the development of allergic symptoms [6,7].

Within the context of infection, an elevated level of eosinophils operates as a potent regulator against the infection [8]. However, certain studies propose that the safeguarding function of eosinophils diminishes in chronic helminth infections due to the secretion of IL-10 by Treg cells, employing a mechanism termed modified Th2 response [9]. Moreover,

the release of regulatory IL-10 cytokine induced by helminths could contribute to mitigating the impact of Th2 proinflammatory cytokine reactions [10,11]. Nonetheless, this mechanism allows the helminth to evade the host's immune system, enabling its long-term survival within the host's body.

Given the broad potential for *Toxocara* spp. to infect various populations, it becomes imperative to establish strategies for preventing toxocariasis. Numerous studies have delineated a range of risk factors contributing to this infection, including age, exposure to contaminated soil, residence in areas with inadequate sanitation, limited education, the presence of stray dogs and cats, and poor hygiene practices [12,13]. Notably, children are at heightened vulnerability to infection due to their increased exposure to contaminated environments, often displaying clinical symptoms linked to eosinophilic syndrome. In contrast, infection among adults could be linked to occupational exposure, usually manifesting as either chronic asymptomatic infection or a mild eosinophilic syndrome [14,15].

Comprehending these risk factors across diverse populations and tracking their evolution over time is pivotal for diagnosing, preventing, and treating toxocariasis [16]. This prospective study was conducted within a population during two distinct periods (2005–2013). Its primary objective was to identify the sociodemographic shifts associated with the risk factors for acquiring *Toxocara* spp. infection. And the secondary aim was to construct a comprehensive roadmap for this infection, providing precise and comprehensive outcomes that can be harnessed for effective toxocariasis control.

2. Materials and Methods

2.1. Study Population

This study was conducted in Salvador, located in Northeastern Brazil. Salvador has a population of over 2,900,319 individuals and is composed of people from various cities across the state. For this study, 926 sera samples collected from individuals enrolled in the SCAALA (Social Change Asthma and Allergy in Latin America) project. The SCAALA project is a longitudinal study conducted in Latin America to assess the socioeconomic and demographic factors linked to asthma and allergic diseases over different years [17]. The sera were collected from children enrolled in the first recruitment of SCAALA project in 2005 and tested for anti-*Toxocara* spp. IgG, and for the second time, they were recruited in 2013 as part of the study's follow-up and new sera samples were collected from these same individuals and frozen at −80 °C until use in the Laboratory of Allergy and Acarology, located at Institute of Health Sciences, Federal University of Bahia. Data concerning allergies and socioeconomic–demographic status were gathered through standardized questionnaires in both years. Additionally, information regarding 2005 *Toxocara* infection seroprevalence, blood components (such as sIgE, eosinophil, and IL-10 concentrations) was extracted from the SCAALA databases.

Ethical approval was obtained from the Brazilian National Ethical Committee (15.895/2011) and the Ethics Committee of the Institute of Collective Health of UFBA (003-05/CEP-ISC). Written and informed consent, outlining all the procedures to be conducted on the children, was signed by either the parents or legal guardians of each child (in 2005) or teenagers (in 2013).

2.2. Obtaining the Excretory–Secretory Antigens from T. canis Larvae (TES)

Regarding excretory–secretory antigen of *Toxocara canis* (TES), a new batch of the antigen was produced in 2013 for plate sensitization following the same technique used in 2005 for antigen production. The technique used to obtain the excretory–secretory antigen of *Toxocara canis* (TES) followed the De Savigny method [18], which was adapted by Alcantara-Neves and colleagues [19]. The larvae were cultured in RPMI medium supplemented with gentamicin (160 µg/mL) and amphotericin B (2.5 µg/mL). The culture was maintained in a 5% CO_2 chamber at 37 °C. A solution of 0.1 M Phenylmethyl-sulfonyl fluoride (PMSF) from Sigma Chemical Co., Ltd. (San Louis, MO, USA) was added to the collected supernatant. The culture supernatant was concentrated using an Amicon ultrafiltration device equipped

with a cellulose filter with a pore size of 3000 kDa from Millipore Corporate, MA, USA. This concentration process took place at 4 °C. The supernatant containing the TES was then preserved at −70 °C, until its use.

2.3. Obtaining A. lumbricoides Extract and Sera Absorption

The *A. lumbricoides* extract was obtained by the trituration of liquid nitrogen-frozen adult worms in phosphate-buffered saline (PBS), pH 7.4, by use of a blender (model 51BL30; Waring Commercial, Torrington, CT). The PBS-soluble fraction obtained by centrifugation was depleted of endotoxins by treatment with Triton X-114 (Sigma, St. Louis, MO, USA), and the protein content was determined by the Lowry method [20]. The antigen was stored at −70 °C until use. To prevent potential cross-reactions between IgG antibodies against *A. lumbricoides* and anti-*Toxocara* spp. antibodies, the sera underwent a pre-absorption process using 8.0 mg/mL of *A. lumbricoides* extract per sera. This absorption was conducted in the presence of polyethylene glycol (PEG 15.000—Sigma Chemical Co., Ltd., San Louis, MO, USA) at a concentration of 3%, along with 0.1% sodium azide, diluted in PBS. Following, an incubation period of 30 min at room temperature, the mixture was centrifuged, and the resulting supernatant was subjected to an additional round of absorption. The absorbed material was subsequently frozen at −20 °C until the immunodiagnostic procedure was carried out.

2.4. Eosinophil Counting, Cytokine Quantification, Skin Prink Tests (SPTs), and sIgE Counting

The acquisition of EDTA blood samples (5 mL) from children were utilized to determine eosinophil count using an automated counter (Counter Electronics, Hialeah, FL, USA). To assess the baseline production of IL-10 cytokines, a sandwich ELISA was conducted on whole-blood supernatants (plasma) from 261 individuals (121 anti-*Toxocara* IgG positives and 140 anti-*Toxocara* IgG negatives). Recombinant antibody pairs (BD Biosciences Pharmingen, San Diego, CA, USA) were employed for this purpose, following the manufacturer's instructions. Cytokine concentrations were determined by interpolating standard curves. The detection range for IL-10 cytokines was established from 31.25 to 500 pg/mL. For the Skin Prick Tests (SPTs), 400 µg of extracts produced by ALK-ABELLO, São Paulo, Brazil, of *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Blomia tropicalis*, *Blattella germanica*, and *Periplaneta americana* were applied to the right forearm of each child. Negative and positive controls consisted of saline and histamine, respectively. After 15 min of application period, the reaction to each allergen was assessed. A reaction was considered positive if the diameter of the papule was at least 3 mm greater than the negative control papule. The specific IgE was performed using the ImmunoCAP system for anti-mite sIgE (*D. pteronyssinus* and *B. tropicalis*) and anti-cockroach sIgE (*P. americana* and *B. germanica*) ($\geq$0.75 kU/L was considered positive) [21].

2.5. IgG antibody to Toxocara spp. Detection from Indirect ELISA

In the sera collected in 2013, the presence of IgG antibodies against *Toxocara* spp. was assessed through an indirect ELISA. The ELISA test applied in 2013 sera was the same methodology applied in 2005 sera. In summary, 96-well plates were coated with 3.0 µg/mL of TES in a carbonate/bicarbonate buffer. Subsequently, the plates were blocked using a solution containing 10% fetal bovine serum (FBS) in PBS. The sera were diluted to 1:1.000 in a solution of PBS containing 0.05% Tween 20 and 2.5% FBS (PBS/T/FBS), and then added to the wells. Next, a biotinylated anti-human IgG conjugate (BD Pharmingen, San Diego, CA, USA) at a dilution of 1:4.000 in PBS/T/FBS was added, followed by streptavidin–peroxidase (Streptavidin-HRP, BD Pharmingen, San Diego, CA, USA) at a dilution of 1:500 in PBS/T/FBS. The chromogen 3,3′,5,5′-Tetramethylbenzidine (TMB—Sigma Chemical Co., Ltd., San Louis, MO, USA) was introduced to initiate the reaction, which was halted using 2 N sulfuric acid. The optical density was measured using a 450 nm filter. Between each step, washes were carried out with PBS/T, followed by a single wash with

PBS 1X. The plates were then incubated for an hour at room temperature after each step, except for the chromogen incubation, which lasted for 30 min.

For establishing the cut-off value in both years, 13 serum samples from individuals, with no history of contact with dogs or cats and an eosinophil count of less than 2% were used as negative controls. The cut-off value was determined as the mean optical density plus three times the standard deviation.

2.6. Data Analysis

To characterize the population, the analysis included only participants with complete data in both years. Descriptive analysis was employed to derive the frequencies and prevalence of the variables under study. The following factors were investigated as potential risk factors for acquiring *Toxocara* spp. infection (outcome): gender, age, maternal education, income, street paving, and the presence of dogs and cats. These same factors were considered confounding variables in the subsequent multivariate analysis.

Initially, a univariate analysis was conducted to examine the relationship between each potential risk factor and the outcome. A multivariate model was then constructed using standard logistic regression, including only the significant variables identified in the univariate analysis. The association between the outcome and the risk factors was quantified using odds ratios, 95% confidence intervals, and p-values of $\leq$0.05. Both univariate and multivariate analyses were performed using SPSS version 24.0, and graphical representations were generated using GraphPad version 8.0.

3. Results

A detailed flowchart presented in the Supplementary Materials was used to explain the difference between the numbers of individuals in each analysis. The statistical association and quantitative analyses in our study were influenced by variations in the number of individuals included in it. Only subjects who provided complete data throughout a two-year study period were incorporated into this study (Supplementary Material Figure S1).

3.1. Seroprevalence of Anti-Toxocara spp. IgG

The results from the *T. canis*-specific indirect ELISA indicate a prevalence of 49% (n = 450/926) in the year of 2005 and 53% (n = 490/926) in 2013. The prevalence of new cases in 2013 corresponded to 25% (n = 236/926), while the number of sera exhibiting remission was 21% (n = 195/926). Ultimately, the prevalence of positive IgG antibodies against *Toxocara* spp. in both years combined was 27% (n = 254/926) (Table 1).

Table 1. Positivity to anti-*Toxocara* spp. IgG in 926 sera from the SCAALA population.

Prevalence to Anti-*Toxocara* spp. IgG Positivity	**n**	**n/N (926) %**
Cases in 2005	450	49
Cases in 2013	490	53
New cases in 2013	236	25
Remission cases from 2005 to 2013	195	21
IgG positivity in 2005 and 2013	254	27

3.2. Predictors of Toxocara spp. Infection Based on Sociodemographic Factors

The original SCAALA population encompassed 1.445 children of varying ages, of whom 926 possessed a complete dataset and were included in the analysis. The study sample predominantly comprised individuals ranging from young children (0 to 5 years old in 2005) to adolescents and adults (16 to 19 years old in 2013), with roughly equal representation of both genders (51% males and 49% females). Several noteworthy sociodemographic attributes exhibited an increase over the two years. These included the maternal education level, with 59% having completed up to the second grade; household

income, with 62% earning between 125 and 282.5 USD/month; and the presence of paved streets, which rose from 39% to 81%. Furthermore, the prevalence of dogs and cats within households was lower in 2005 (40% for dogs and 18% for cats) compared to 2013 (65% for dogs and 63% for cats). Additionally, the proportion of individuals testing positive for anti-*Toxocara* spp. antibodies was higher in 2013 as opposed to 2005 (53% and 49%, respectively) (Table 2).

Table 2. Frequencies of sociodemographic variables in the study of risk factors for *Toxocara* spp. infection collected from the SCAALA database.

Variables	2005		2013	
	N = 926	n/N %	N = 926	n/N %
Gender	n		n	
Male	477	51%	477	51%
Female	499	49%	499	49%
Age				
2005/2013				
$0 \leq 5/11 \leq 13$	349	38%	349	38%
06–07/14–15	318	34%	318	34%
$\geq 8/\geq 16$	259	28%	259	28%
Maternal Schooling				
1st grade or less	219	24%	174	19%
Incomplete 2nd grade	431	46%	201	22%
Complete 2nd grade or more	276	30%	551	59%
Incoming				
$\leq$125 USD	759	82%	317	35%
125 $\leq$ 282.5 USD	137	15%	579	62%
>282.5 USD	30	3%	30	3%
Street paving				
No	563	61%	173	19%
Yes	363	39%	753	81%
Cat at home				
No	758	82%	625	67%
Yes	168	18%	301	33%
Dog at home				
No	556	60%	321	35%
Yes	370	40%	605	65%
Anti-*T. canis* IgG				
No	476	51%	436	47%
Yes	450	49%	490	53%

All variables presented in the descriptive table (Table 2) underwent association analysis to identify potential risk or protective factors for *Toxocara* spp. infection. The results reveal an association between infection and children aged above 8 years, as well as the presence of cats and dogs, but only in 2005. Certain factors were identified as protective against *Toxocara* spp. infection, including maternal education beyond completing the second grade in both 2005 and 2013. Additionally, an increase in income (in 2005) above USD 282.5/month was observed as a protective factor in the univariate analysis. The presence of paved streets was also linked to protection against infection in both years. Gender did not exhibit significant associations either as a risk or protective factor in this analysis for both years (Table 3).

Table 3. Analysis of risk factors linked to anti-*Toxocara* spp. IgG seropositivity in a cohort of 926 individuals in 2005 and 2013.

Variables	Anti-*T. canis* IgG Positivity/2005 (n = 450)		Anti-*T. canis* IgG Positivity/2013 (n = 490)	
	n/N (%) [&]	$OR_{adjusted}$	n/N (%) [&]	$OR_{adjusted}$
Gender				
Male	230/477 (48)	1	249/477 (52)	1
Female	220/499 (44)	0.94 (0.72–1.23)	241/499 (48)	0.94 (0.72–1.22)
Ages				
2005/2013				
$0 \leq 5/11 \leq 13$	156/349 (44)	1	176/349 (50)	1
06–07/14–15	158/318 (50)	1.22 (0.89–1.67)	167/318 (52)	1.04 (0.76–1.43)
$\geq 8/\geq 16$	136/359 (38)	1.42 (1.02–1.98) *	147/259 (57)	1.20 (0.86–1.68)
Maternal Schooling				
1st grade or less	129/219 (59)	1	103/174 (60)	1
Incomplete 2nd grade	224/431 (52)	1.01 (0.69–1.49)	112/201 (56)	0.84 (0.55–1.28)
$\geq$Complete 2nd grade	97/276 (35)	0.50 (0.36–0.69) *	275/551 (50)	0.65 (0.46–0.93) *
Incoming				
$\leq$125 dollars	386/759 (51)	1	158/317 (50)	1
125 $\leq$ 282.5 dollars	55/137 (40)	0.80 (0.54–1.19)	313/579 (54)	1.27 (0.96–1.68)
>282.5 dollars	9/30 (30)	0.50 (0.22–1.13)	19/30 (63)	2.13 (0.96–4.68)
Street paving				
No	290/563 (51)	1	105/173 (61)	1
Yes	160/363 (44)	0.72 (0.54–0.94) *	385/753 (51)	0.68 (0.48–0.95) *
Cat at home				
No	349/758 (46)	1	331/625 (53)	1
Yes	101/168 (60)	1.58 (1.10–2.28) *	159/301 (53)	1 (0.75–1.35)
Dog at home				
No	253/556 (45)	1	175/321 (54)	1
Yes	197/370 (53)	1.27 (1–1.69) *	315/605 (52)	0.91 (0.68–1.21)

The values were adjusted by variables: gender, age, maternal education, incoming, street paving, and the presence of dogs or cats. [&] n: number of positive individuals for anti-*Toxocara* spp. IgG; N: total number of individuals by variable. * Statistically significant values (CI: 0.05%; $p < 0.05$).

3.3. Comparison of Risk and Protective Factors for Toxocara spp. Infection in Individuals with Persistent Anti-Toxocara spp. IgG Positivity over Time (IgG Positivity in 2005 and 2013)

When examining the relationship between persistent anti-*Toxocara* spp. IgG positivity over the years, we analyzed the sociodemographic information of individuals who tested positive in both 2005 and 2013. We then assessed the associations with infection-related risk factors. The increase in age was consistently identified as a risk factor in both years. Additionally, we found associations indicating that an increase in maternal education and street paving acted as protective factors in both 2005 and 2013. The presence of a cat at home was only associated as a risk factor in 2013. These associations are presented in detail in Table 4.

Table 4. Analysis of risk factors linked to anti-*Toxocara* spp. IgG seropositivity in 494 individuals testing positive in both years (2005 and 2013).

Variables	Anti-*T. canis* IgG Positivity/2005 (n = 254)		Anti-*T. canis* IgG Positivity/2013 (n = 254)	
	n/N (%) [&]	$OR_{adjusted}$	n/N (%) [&]	$OR_{adjusted}$
Gender				
Male	132/262 (50)	1	132/262 (50)	1
Female	122/232 (52)	0.89 (0.61–1.29)	122/232 (52)	0.94 (0.65–1.36)
Ages				
2005/2013				
$0 \leq 5/11 \leq 13$	87/191 (45)	1	87/191 (45)	1
06–07/14–15	90/173 (52)	1.32 (0.86–2.03)	90/173 (52)	1.32 (0.86–2.03)
$\geq 8/\geq 16$	77/130 (59)	1.63 (1.02–2.61) *	77/130 (59)	1.63 (1.02–2.61) *

Table 4. *Cont.*

Variables	Anti-*T. canis* IgG Positivity/2005 (n = 254)		Anti-*T. canis* IgG Positivity/2013 (n = 254)	
	n/N (%) [&]	$OR_{adjusted}$	n/N (%) [&]	$OR_{adjusted}$
Maternal Schooling				
1st grade or less	163/281 (58)	1	58/94 (61)	1
Incomplete 2nd grade	41/74 (55)	0.89 (0.53–1.51)	71/112 (63)	1.12 (0.62–2.03)
≥Complete 2nd grade	50/139 (36)	0.42 (0.27–0.65) *	125/288 (43)	0.50 (0.30–0.81) *
Incoming				
≤125 USD	218/408 (53)	1	95/179 (53)	1
125 ≤ 282.5 USD	30/68 (44)	0.89 (0.51–1.55)	154/303 (51)	1.02 (0.69–1.52)
>282.5 USD	6/18 (33)	0.54 (0.19–1.53)	5/12 (42)	0.93 (0.27–3.19)
Street paving				
No	174/307 (57)	1	60/93 (64)	1
Yes	80/187 (43)	0.57 (0.39–0.84) *	194/401 (48)	0.52 (0.32–0.84) *
Cat at home				
No	205/401 (51)	1	152/317 (48)	1
Yes	49/93 (53)	1.04 (0.63–1.70)	102/177 (57)	1.50 (1.00–2.26) *
Dog at home				
No	143/282 (51)	1	79/157 (50)	1
Yes	111/212 (52)	1.11 (0.75–1.63)	175/337 (52)	0.94 (0.61–1.43)

The values were adjusted by variables: gender, age, maternal education, incoming, street paving, and the presence of dogs or cats. [&] n: number of positive individuals for anti-*Toxocara* spp. IgG; N: total number of individuals by variable. * Statistically significant values (CI: 0.05%; $p < 0.05$).

3.4. Association Analysis of Toxocara spp. Infection, Atopic Markers, and Eosinophil Levels in the Studied Population

The presence of anti-*Toxocara* spp. IgG antibodies did not demonstrate any associations with either risk or protective factors for specific IgE (sIgE) responses to mites' and cockroaches' allergens (with cut-offs ≥ 0.75 kU/mL) in both years. However, an association with the Skin Prick Test results indicated a protective relationship in both years (Table 5). Furthermore, when comparing the association of risk factors with eosinophil levels (categorized as >10%, and eosinophilia ≥ 500 mm^3) and anti-*Toxocara* spp. IgG positivity among 435 individuals in both years, we identified associations between *Toxocara* spp. infection and eosinophil level at 10%, as well as eosinophilia in 2005. In 2013, only eosinophilia demonstrated an association with this infection (Table 6).

Table 5. Association between seropositivity for anti-*Toxocara* spp. IgG and specific IgE (sIgE), as well as the Skin Prick Test for at least one common aeroallergen in a study cohort of 490 individuals examined in 2005 and 2013.

Toxocara infection/2005	n/N = 490 (%) [&]	$OR_{adjusted}$	n/N = 490 (%) [&]	$OR_{adjusted}$
		sIgE ≥ 0.75		Skin Prink Test [$]
No	168/319 (53)	1	82/344 (24)	1
Yes	82/171 (48)	0.91 (0.62–1.34)	64/146 (44)	0.72 (0.48–1.00) *
Toxocara infection/2013	n/N = 490 (%) [&]	$OR_{adjusted}$	n/N = 490 (%) [&]	$OR_{adjusted}$
		sIgE ≥ 0.75		Skin Prink Test [$]
No	112/281 (40)	1	82/349 (23)	1
Yes	97/209 (46)	0.77 (0.53–1.13)	59/141 (42)	0.62 (0.41–0.93) *

The values were adjusted by gender, age, maternal education, sewer service, street paving, and parental asthma. [&] n: number of positive individuals to anti-*Toxocara* spp. IgG; N: total number of individuals by variable. * Statistically significant values (CI: 0.05%; $p < 0.05$). [$] Skin Prink Test and sIgE to *B. tropicalis*, *D. pteronyssinus*, *D. farina*, *B. germanica*, and *P. americana*.

Table 6. Association between seropositivity for anti-*Toxocara* spp. IgG and eosinophil level at 10%, and eosinophilia (≥500 mm^3) in a study cohort of 435 individuals investigated in 2005 and 2013.

Toxocara infection/2005	n/N = 435 (%) [&]	$OR_{adjusted}$	n/N = 435 (%) [&]	$OR_{adjusted}$
		>10%		Eosinophilia ≥ 500 mm^3
No	153/334 (45)	1	90/215 (42)	1
Yes	63/101 (62)	1.85 (1.15–2.98) *	126/220 (57)	1.92 (1.28–2.86) *
Toxocara infection/2013	n/N = 435 (%) [&]	$OR_{adjusted}$	n/N = 435 (%) [&]	$OR_{adjusted}$
		>10%		Eosinophilia ≥ 500 mm^3
No	191/390 (49)	1	164/349 (47)	1
Yes	25/45 (55)	1.38 (0.73–2.60)	52/86 (60)	1.74 (1.07–2.84) *

The values were adjusted by gender, age, mother scholarity, sewer service, street pavimentation, parental asthma. [&] n: number of positive individuals to IgG anti-*Toxocara* spp.; N: total number of individuals by variable. * Statistically significant values (CI: 0.05%; $p < 0.05$).

3.5. Effects of Toxocara spp. Infection on Immunological Features

To assess the impact of *Toxocara* spp. infection on immunological features, including eosinophil counts and basal IL-10 cytokine production in the blood, we extracted data from a database of 435 individuals for eosinophil counts and 261 individuals for basal IL-10 concentrations. Individuals with anti-*Toxocara* spp. IgG positivity exhibited elevated eosinophil counts compared to negative cases in both survey years. In the 2005 survey, positive individuals displayed eosinophil counts higher than 2.500 mm^3/mL, while negative individuals showed counts lower than 2.500 mm^3/mL ($p < 0.0001$). Similarly, in 2013, the same pattern was observed, with positive individuals having counts higher than 1.900 mm^3/mL and negatives having counts lower than 1.860 mm^3/mL (Figure 1A). Additionally, in both 2005 and 2013, the baseline regulatory IL-10 cytokine concentration was higher among positive individuals (>240 pg/mL and >400 pg/mL, respectively) than in negative individuals (≤238 pg/mL and ≤300 pg/mL, respectively) (Figure 1B).

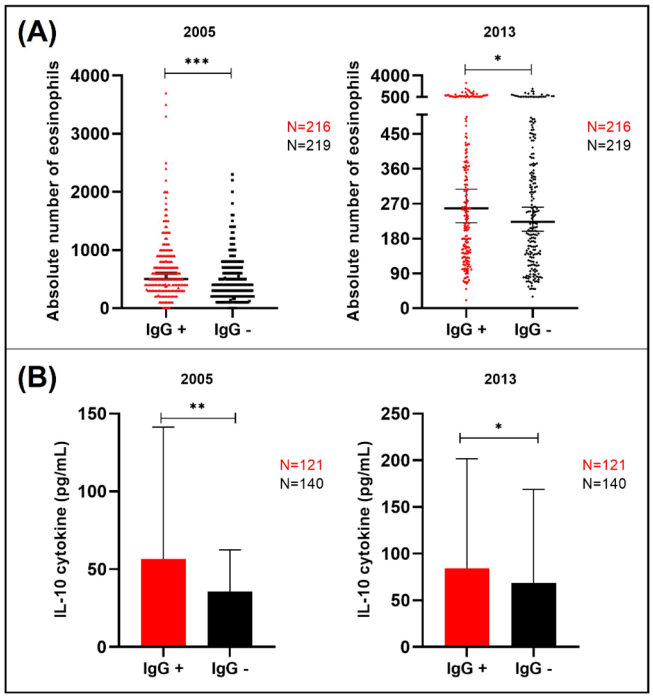

Figure 1. Comparison of the absolute eosinophil counts and spontaneous IL-10 concentrations between individuals positive and negative for anti-*Toxocara* spp. IgG in both years. (**A**) The difference

in eosinophil counts between 2005 and 2013 was assessed using the Mann–Whitney test, revealing significant differences with p-values of 0.0001 and 0.037, respectively. (**B**) Differences in basal IL-10 cytokine concentrations for 2005 and 2013 were evaluated through the Mann–Whitney test, yielding p-values of 0.008 and 0.020, respectively. * $p \leq 0.05$; ** $p \leq 0.001$; and *** $p \leq 0.0001$.

4. Discussion

The SCAALA project has been instrumental in gathering sociodemographic data to explore the role of environmental and genetic factors in the emergence of asthma and atopic diseases within Latin America [21]. The connection between toxocariasis, a parasitic disease, and its immunological implications for asthma and atopy, underscores the need for ongoing investigation into the interplay between *Toxocara* spp. infection and these conditions. Recognizing the heightened vulnerability of children to toxocariasis, due to their closer contact with contaminated areas [12], emphasizes the critical importance of developing preventative strategies tailored to this demographic, especially as lifestyle changes with age may reduce exposure risks [22].

Throughout the period from 2005 to 2013, our study monitored the trends in anti-*Toxocara* spp. IgG positivity, identifying both cases of remission and new instances of infection. The seroprevalence rates were consistently analyzed using an indirect ELISA, revealing a stable prevalence over the years despite the identification of 236 new cases in 2013. The variability in the sensitivity of the anti-TES IgG method, attributable to the complex nature of serum IgG antibodies and the antigens they target, highlights the diversity of immunological responses among different individuals and populations [23,24].

Furthermore, our population faces a challenge of being infected by many helminths due to the poor living conditions and the lack of knowledge about preventive manners to avoid being infected by them. Many studies highlighted the prevalence of *Ascaris lumbricoides* infection in our country [11,25,26]. As *Ascaris* spp. and *Toxocara* spp. belong to the Ascaridida order, they share cysteine-conserved domains on its produced antigens and a cross-reaction is often found in the immunodiagnosis of toxocariasis [27,28]. Although we did not perform any additional parasitological tests in the used sera, it is suggested to perform a sera pre-absorption test with an extract of *A. lumbricoides* before the sera test [29].

Our findings align with previous research conducted in Brazil and Venezuela, indicating no significant gender disparity in anti-*Toxocara* spp. IgG positivity but a higher infection rate among boys, likely due to differences in gender-related outdoor activities and hygiene practices [12,14,30,31]. Age-related analyses further suggest that younger children, particularly those guided by their parents in hygiene practices, face a lower risk of infection [29]. Previous studies have proposed that persistent exposure to helminth antigens leads to a continued production of antibodies, potentially explaining the sustained IgG seropositivity against helminths over the years, provided the sociodemographic features remain unchanged [32,33].

As documented, a higher level of education is linked to enhanced protection against helminth infections due to an increased awareness of hygienic practices [34]. In our study, education level emerged as a key protective factor against toxocariasis, with higher maternal education levels associated with decreased infection risks. This finding is in line with other research that has demonstrated how an increase in educational attainment contributes to a better comprehension of infection risks associated with roundworms [22,35]. Also, residing in an area with paved streets emerged as a protective factor against the infection in our study. This underscoring the link between improved living conditions and reduced exposure to *Toxocara* spp. eggs [36,37].

Furthermore, both stray and domesticated cats and dogs from low-income populations represent the primary sources of *Toxocara* spp. transmission, contributing to environmental contamination and thus perpetuating the spread of infection among humans [4,22]. In the sample, a higher toxocariasis prevalence in 2005 was observed among dog owners (53%) and cat owners (60%) compared to those who did not own pets, categorizing this condition as a risk factor for infection acquisition. However, this pattern was not replicated in 2013,

potentially attributable to the increased presence of protective factors during that period, such as heightened maternal education and income levels [38].

When focusing solely on individuals who tested positive in both years, our data indicated a higher prevalence of anti-*Toxocara* spp. IgG positivity among cat owners in both 2005 and 2013 (53% and 57%, respectively) as well as dog owners (52% in both years). We also observed a borderline association suggesting that owning a cat might pose a risk for acquiring *Toxocara* spp. infection in 2013. This could potentially be attributed to an increased number of people keeping cats at home in 2013 (n = 177) compared to 2005 (n = 93). This rise in cat ownership may explain the emergence of new cases of individuals testing positive for anti-*Toxocara* spp. IgG in 2013. Cats exhibit behaviors such as roaming outside the home, which could increase the likelihood of exposure to *Toxocara* spp. eggs in contaminated soil. Moreover, cats might carry *Toxocara* spp. eggs on their fur, potentially spreading them to other areas within the household and thus increasing the chances of human infection [39,40].

The roadmap for controlling toxocariasis integrates these insights, proposing a multifaceted approach that includes enhancing public education on toxocariasis and preventive measures, improving environmental sanitation, and strengthening veterinary control measures. Increasing access to healthcare and screening, particularly in areas with high seroprevalence, alongside community-based interventions targeting identified risk factors, are crucial components of this strategy.

Our study also delved into the immunological responses associated with *Toxocara* spp. infection, observing an inverse relationship between anti-*Toxocara* spp. IgG positivity and the development of allergic symptoms, potentially explained by the hygiene hypothesis or by the chronic nature of the infection influencing IgG4 production [41]. Mendonça et al. (2013) [29], examining the relationship between *Toxocara* spp. seropositivity and specific IgE levels or Skin Prick Test reactivity, found an SPT-negative association, and contrarily, a positive association with sIgE, which highlighted the complex interactions between parasitic infections and host immune systems.

In this paper, we present findings regarding helminth infections and their impact on allergic conditions. Specifically, our analysis focused on atopic conditions in both years. Indeed, many studies have shown a positive association between *Toxocara* infection and atopic conditions, in human as in animal models [26,42]. Two previous studies from our group have found a positive association between the infection and sIgE ($\geq$0.70 kU/L) for *Blomia tropicalis* and for at least one tested aeroallergen [14,29]. In a murine model (BALB/c mice), an allergic manifestation along with IgE and eosinophil increases were also observed in *Toxocara* spp.-infected animals compared to uninfected animals [43]. Another study performed in *Toxocara* spp.-infected dogs showed higher levels of sIgE for *Dermatophagoides farinae* and total IgE, but they had less skin lesions, suggesting a protective role against the development of clinical allergic symptoms [42].

Additionally, research conducted on a Zimbabwean cohort infected with *Schistosoma* sp. highlighted a negative correlation with elevated levels of sCD23 and allergen-specific IgE to house dust mites among infected individuals, compared to those uninfected [44]. This suggests that helminth infections, through the modulation of the sCD23 receptor, a low-affinity FcεRII transmembrane receptor for IgE on naïve IgM and IgD B cells, might exert a suppressive effect on the emergence of allergic symptoms. Moreover, as it has been well documented, chronic helminth infections enhance immunoregulation through mechanisms such as the development of regulatory T and B cells, leading to immune hyporesponsiveness [10,45]. Whether our population could have a chronic infection is a crucial point to be investigated.

The importance of our results lies in the potential implications for allergic individuals. Understanding the intricate dynamics between helminth infections and allergic responses could pave the way for novel therapeutic approaches that harness the inhibitory effects of these infections on allergy development. Despite the clear association, the precise molecular mechanisms through which helminthiasis influences atopic conditions remain

elusive. This gap in knowledge underscores the necessity for further detailed studies aimed at elucidating how helminth infections regulate antigen-specific IgE responses in allergic diseases. Our findings contribute to a growing body of evidence suggesting a complex interaction between infectious agents and allergic pathophysiology, emphasizing the importance of considering parasitic infections in the comprehensive management of allergic diseases.

Eosinophilia, a hallmark of *Toxocara* spp. infection, was examined in relation to infection positivity, revealing a positive association with elevated eosinophil levels, corroborating previous research [46–48]. Children's heightened susceptibility to helminth infections, due to less stringent hygiene practices and a greater contact with infected pets, underscores the need for targeted interventions to reduce infection rates and the associated immunological impacts [29,49].

In summary, the SCAALA project's insights provide a thorough examination of toxocariasis' epidemiology and immunological impact in Latin America, alongside a comprehensive management strategy. This approach emphasizes enhancing public education on toxocariasis, including its transmission and prevention, with the goal of reducing infection rates. It also highlights the importance of improving environmental sanitation to decrease the presence of *Toxocara* spp. eggs in the environment, thereby reducing human infection risks. The strategy underlines the critical role of veterinary oversight, including the regular deworming of pets and management of stray animal populations, to prevent *Toxocara* spp. transmission from animals to humans. Furthermore, it advocates for the expansion of healthcare and screening services, especially in areas with a high prevalence of the disease, to enable early detection and treatment. Additionally, the strategy advocates for community-led efforts that zero in on the particular risk factors associated with toxocariasis, substantially limiting the disease's transmission. This comprehensive research outlines a strategic approach focused on tackling the environmental, sociodemographic, and immunological variables that fuel *Toxocara* spp. infection. It proposes strategies grounded in the study's findings as a means to mitigate the broader health effects of the infection.

5. Conclusions

Our study does not provide a clear indication of whether the population has experienced re-infection over the years due to other unexplored risk factors, such playing in streets. The results primarily reflect trends in lifestyle within the population rather than other specific circumstances. The observed risk factors of *Toxocara* spp. infection in our population were mainly associated with individuals in the third age group and the contact with cats or dogs. To mitigate *Toxocara* spp. infection, potential sociodemographic changes, such as enhancing maternal education levels and improving paved streets, could be considered, but the presence of stray animals on the street may contribute to human infection by releasing eggs and contaminating the soil. Furthermore, the positivity for *Toxocara* IgG was intrinsically linked to higher levels of IL-10 cytokines and eosinophils. Despite the high global prevalence of *Toxocara* spp. infection, there remains a lack of comprehensive understanding of the immune responses and modulation triggered by this infection and its connection to other allergic conditions. Investigating and gaining a detailed understanding of the involved risk factors and how to prevent the infection are essential for managing this neglected disease.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/allergies4030009/s1, Figure S1: Sequential breakdown of participant engagement across the study analyses.

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