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Predictors of treatment failure in pediatric toxocariasis: A two-part study in Ho Chi Minh City, Vietnam

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ABSTRACT

Objective: To identify factors associated with the therapeutic effectiveness of albendazole in children with *Toxocara canis* infection in Ho Chi Minh City, Vietnam.

Methods: The study was conducted from April 2022 to December 2023 and consisted of two phases. Phase 1 was a cross-sectional study involving 986 children aged 3–15 years in Ho Chi Minh City, Vietnam, to determine the seroprevalence of *Toxocara* spp. using ELISA IgG testing. Phase 2 was an interventional study conducted in children with compatible clinical manifestations and positive ELISA results. Patients received albendazole at a dose of 15 mg/kg/day for 5 days. Clinical and laboratory reassessments were performed 6 months after treatment.

Results: Of 986 school children included in the cross-sectional study, 140 (14.2%) had positive *Toxocara* ELISA results and 107 completed follow-up after treatment. At 6 months, 96.3% showed complete resolution of clinical symptoms, 71.0% had normalized eosinophil counts, and 57.9% had total IgE levels returned to the normal range. The treatment failure rate was 72.0%. Multivariable analysis identified place of residence and inappropriate disposal of dog and cat feces as independent factors associated with treatment failure ($P < 0.05$).

Conclusions: Environmental and hygiene-related factors, particularly improper disposal of dog and cat feces, were independently associated with treatment failure.

KEYWORDS: Toxocariasis; Factors associated with treatment outcomes; Albendazole; Treatment effectiveness of toxocariasis in children

1. Introduction

Toxocariasis is recognized as a significant public health concern in both developed and developing countries, including Vietnam[1–5]. Several environmental, behavioral, and host-related factors have been proposed as determinants of treatment outcomes. Kroten *et al.* (2018) conducted a study with a sample size of 66 children aged 2–16 years [mean age (8.8 ± 3.6) years] with positive *Toxocara* ELISA results at the Bialystok Outpatient Clinic, Children's Hospital, Medical

Summary

Question: What factors are associated with treatment failure following albendazole therapy in children with toxocariasis in Ho Chi Minh City, Vietnam?

Findings: In this interventional study including 107 children with toxocariasis who completed 6 months of follow-up, the treatment failure rate was 72.0%. Multivariable analysis identified place of residence and inappropriate disposal of dog and cat feces as independent factors associated with treatment failure.

Meaning: Environmental and hygiene-related factors may contribute to treatment failure in pediatric toxocariasis. Improving sanitation practices and proper disposal of pet feces may enhance treatment outcomes and reduce the risk of persistent infection.

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University. This study reported that frequent contact with dogs, geophagia, and poor hygiene practices were significantly associated with treatment failure[6]. Nevertheless, evidence regarding predictors of treatment response remains limited, particularly among children living in endemic areas.

When toxocariasis is diagnosed, most European and North American guidelines recommend oral albendazole at a dose of 400 mg twice daily for 5 days in both adults and children[7–10]. Using this regimen, Fernando *et al.* reported a cure rate of 32%[11]. Furthermore, Magnaval *et al.*, in a review of previously published studies, summarized cure rates ranging from 31.6% to 100% following albendazole treatment for human toxocariasis.

Vietnam is considered an endemic area for toxocariasis, and recent studies have reported a substantial burden of infection among school-aged children in Ho Chi Minh City[4,5]. In addition to albendazole dosage and treatment duration, several other factors may influence treatment failure, particularly in pediatric populations. Therefore, this study aimed to identify factors associated with the effectiveness of albendazole treatment in children with toxocariasis in Ho Chi Minh City, Vietnam.

2. Methods

2.1. Study design and setting

The study consisted of two phases:

Phase 1 aimed to determine the seroprevalence of toxocariasis. A cross-sectional study was conducted among 986 children aged 3–15 years in Ho Chi Minh City, Vietnam, from April 2022 to December 2023. Participants were categorized according to educational level as preschool children (3–5 years), primary school children (6–10 years), and secondary school children (11–15 years). The study was conducted in four administrative areas of Ho Chi Minh City, including two urban districts (Binh Thanh District and District 1) and two suburban areas (Thu Duc City and Nha Be District). These areas represent different socioeconomic settings within the city, with average household income generally increasing from Nha Be District to Thu Duc City, Binh Thanh District, and District 1.

Clinical examinations were performed by experienced pediatricians. Laboratory investigations, including complete blood count, biochemical tests (urea, creatinine, AST, and ALT), total IgE levels, and anti-*Toxocara canis* antibody titers, were conducted at Children's Hospital 2, a tertiary pediatric referral center in Vietnam.

Serological testing was performed using the AccuDiag™ *Toxocara* IgG ELISA kit (USA), approved by the Vietnamese Ministry of Health. An optical density (OD) value >0.3 was considered positive. The reported sensitivity and specificity of the assay were 87.5% and 93.3%, respectively.

Eosinophilia was classified according to the criteria proposed by Franklin *et al.* (1998) into three categories: mild eosinophilia (350–1500/ μ L or 4%–7%), moderate eosinophilia (>1500–5000/ μ L or >7%–10%), and severe eosinophilia (>5000/ μ L or >10%)[12]. Age-specific reference values for total IgE were defined as 33 IU/mL for children aged 2–4 years and 85 IU/mL for children aged 5–16 years[13].

Phase 2 consisted of an interventional treatment study. Only children with clinical manifestations suggestive of toxocariasis and positive ELISA results were included for treatment. Patients received oral albendazole at a dose of 15 mg/kg/day for 5 days, divided into two daily doses administered after meals[14]. Six months after treatment, all children underwent clinical reassessment and laboratory investigations to evaluate treatment outcomes.

The interventional phase was not registered in a clinical trial registry because it was not designed as a clinical trial. All eligible participants received the same standard-of-care treatment (albendazole) according to the Vietnamese Ministry of Health treatment guidelines. There was no randomization, allocation to different treatment groups, or evaluation of an investigational intervention. Therefore, the interventional phase was conducted to evaluate treatment outcomes under routine clinical practice rather than to assess the efficacy of an experimental intervention.

Treatment failure was defined as the persistence of clinical symptoms after treatment, together with persistently positive ELISA serology characterized by OD values remaining elevated or showing no declining trend toward the normal range. In addition, eosinophilia counts and total IgE levels remained elevated above age-specific reference values.

2.2. Ethical considerations

The study was approved by the Institutional Review Board of Pham Ngoc Thach University of Medicine on March 3, 2021 (Approval No. 500/HĐĐĐ-TĐHYKPNT). Written informed consent was obtained from all participants and their parents or legal guardians.

2.3. Data management and statistical analysis

Data were analyzed using R software (version 4.3.2). Multivariable logistic regression analysis was performed to identify factors associated with treatment outcomes. A *P*-value <0.05 was considered statistically significant.

3. Results

A total of 986 schoolchildren were included in the cross-sectional study, of whom 140/986 (14.2%) had positive *Toxocara* ELISA

Phase 1: Cross-sectional study

Phase 2: Interventional study

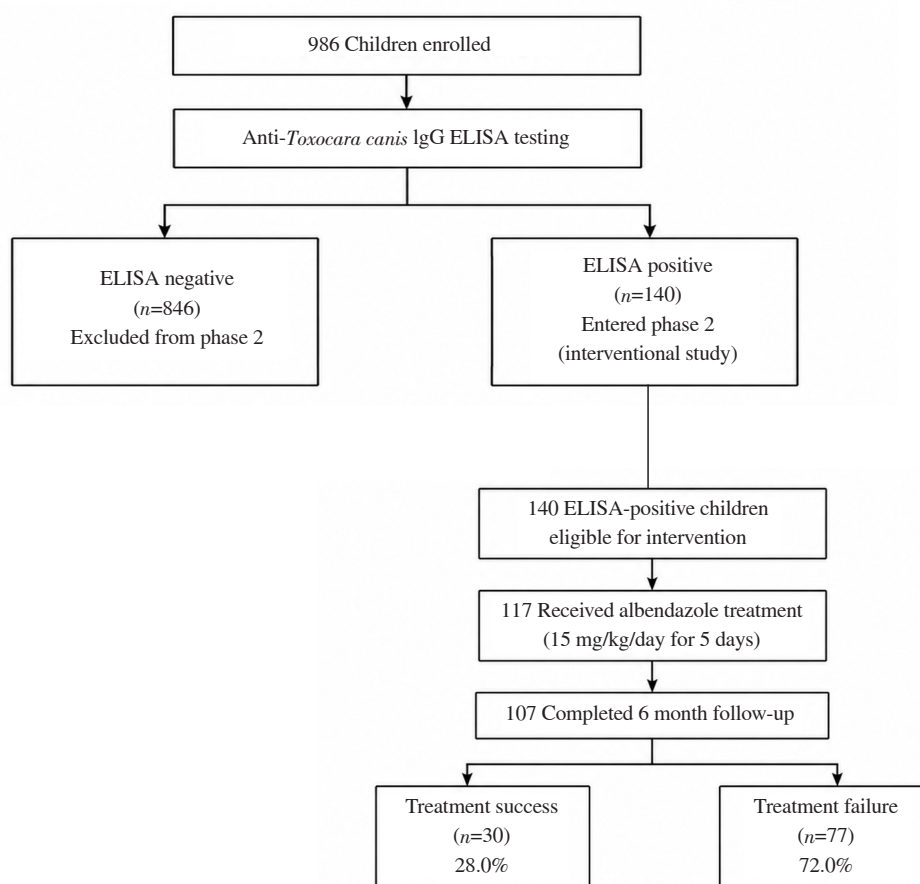


Figure 1. Flowchart of the two-part study, including the cross-sectional and interventional phases.

results. Among these, 117/140 children (83.6%) met the eligibility criteria for interventional treatment, whereas 23 children declined participation. Treatment adherence (including completion of both clinical and laboratory follow-up assessments after treatment) was

achieved in 107/117 patients (91.5%). No adverse events were recorded during treatment or throughout the follow-up period. Flowchart of the two-part study was shown in Figure 1.

According to Table 1, participants receiving treatment were

Table 1. Characteristics of *Toxocara*-seropositive children according to treatment enrollment.

Characteristics	General (ratio ^a) (n=140)	Treatment		P
		No (ratio ^a) (n=33)	Yes (ratio ^a) (n=107 [*])	
Male sex	64 (45.7)	13 (39.4)	51 (47.7)	0.40 ^c
Age, years ^b	11.5 (10.0, 13.0)	9.0 (5.0, 11.0)	12.0 (11.0, 13.0)	< 0.001 ^d
Educational level				
Preschool	19 (13.6)	13 (39.4)	6 (5.6)	< 0.001 ^c
Primary school	49 (35.0)	16 (48.5)	33 (30.8)	
Secondary school	72 (51.4)	4 (12.1)	68 (63.6)	
District of residence				
Thu Duc City	35 (25.0)	12 (36.3)	23 (21.4)	0.40 ^c
Nha Be District	82 (58.6)	16 (48.5)	66 (62.0)	
Binh Thanh District	15 (10.7)	3 (9.1)	12 (11.0)	
District 1	8 (5.7)	2 (6.1)	6 (5.6)	
Educational level of caregiver				
No formal education/Primary school	4 (2.9)	0 (0.0)	4 (3.7)	0.20 ^c
Secondary/High school	88 (62.9)	18 (54.5)	70 (65.4)	
University or higher	48 (34.3)	15 (45.5)	33 (30.8)	
Caregiver occupation				
Government officer/Civil servant	38 (27.1)	10 (30.3)	28 (26.2)	0.80 ^c
Agriculture	3 (2.1)	0 (0.0)	3 (2.8)	
Other	99 (70.7)	23 (70.0)	76 (71.0)	

^aProportions are presented in columns unless otherwise indicated; ^bData are presented as median (interquartile range); ^cPearson's *Chi*-squared test; ^dWilcoxon rank-sum test; ^eFisher's exact test. ^{*}All cases (100%) were classified as covert or common toxocarosis.

older than those not receiving treatment (median age: 12.0 *vs.* 9.0 years, $P<0.001$). Secondary school students accounted for the largest proportion of the treatment group (63.6%), with treatment participation differing significantly across educational levels ($P<0.001$). No significant differences were observed for the other characteristics (all $P>0.05$).

As per Table 2, complete resolution of clinical symptoms was observed in 96.3% of treated children. Eosinophil counts and total IgE levels were normal after treatment in 71.0% and 57.9% of children, respectively. Based on ELISA OD results, 28.0% were cured, whereas 72.0% were classified as treatment failures; notably, 32.7% showed no reduction or an increase in OD.

Table 2. Clinical and laboratory outcomes 6 months after albendazole treatment in children with toxocariasis.

Characteristics	n (%)
Clinical symptoms	
Complete resolution of symptoms	103 (96.3)
Improvement of symptoms	2 (1.9)
Persistent symptoms	2 (1.9)
Eosinophil count	
Normal	76 (71.0)
Mild eosinophilia	31 (29.0)
Severe eosinophilia	0 (0.0)
Total IgE	
Normal	62 (57.9)
Increased	45 (42.1)
ELISA optical density (OD)	
Negative	30 (28.0)
Positive, with a reduction $\geq 30\%$	23 (21.5)
Positive, with a reduction $<30\%$	19 (17.8)
No reduction or increased	35 (32.7)
Cured (treatment success)	30 (28.0)*
Not cured (treatment failure)	77 (72.0)

*Complete resolution of symptoms, negative OD, reduction of eosinophilia counts, and reduction of total IgE levels.

In the univariate analysis (Table 3), residence in Nha Be District, caregiver education at the university level or higher, caregiver occupations other than government officer/civil servant and disposal of dog/cat feces were significantly associated with treatment failure ($P<0.05$).

In the multivariable analysis (Table 3), residence and disposal of dog/cat feces remained independently associated with treatment failure. Living in Nha Be District independently decreased the risk of treatment failure [adjusted risk ratio (aRR) 0.11, 95% CI 0.04–0.28, $P<0.001$]. By contrast, disposal of dog/cat feces was an independent risk factor that increased the likelihood of treatment failure (aRR 2.17, 95% CI 1.14–4.15, $P=0.02$). The significant crude associations for caregiver education level and caregiver occupation disappeared after multivariable adjustment. Notably, the caregiver occupation variable was excluded from the multivariable model due to model convergence failure.

No clinical or laboratory characteristics included in Model 3 were significantly associated with treatment failure in either the univariate or multivariable analysis ($P>0.05$).

Box-and-violin plots illustrating the distribution of WBC counts at baseline and 6 months post-treatment, stratified by age group (preschool and primary school children, 3–11 years; and lower secondary school children, 12–15 years) (Figure 2). Due to right-skewed distributions, WBC counts were $\log_{10}$ -transformed for visualization and comparison. On the y-axis, a one-unit increase corresponds to a tenfold increase in the original WBC count. WBC counts decreased significantly from baseline to 6 months post-treatment in both age groups: children aged 3–11 years ($P=0.007$) and those aged 12–15 years ($P=0.001$).

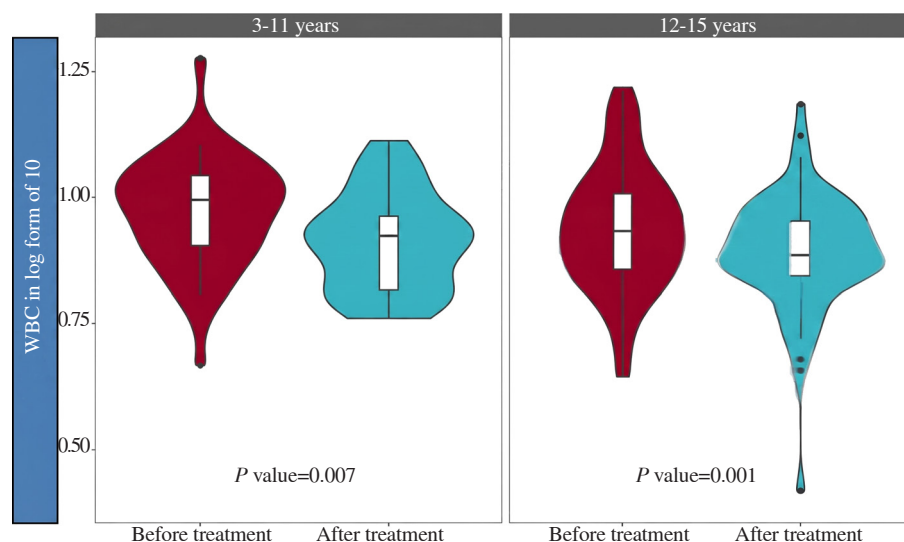


Figure 2. Age-stratified comparison of hematological parameters before and after treatment. WBC: white blood cell; EOS: eosinophils.

Table 3. Univariate and multivariable log-binomial regression analyses of factors associated with treatment failure following albendazole therapy in children with toxocariasis.

Characteristics	Univariate analysis			Multivariable analysis		
	<i>RR^a</i>	<i>95% CI^c</i>	<i>P</i>	<i>aRR^b</i>	<i>95% CI^c</i>	<i>P</i>
Model 1. Demographic characteristics^{d,e}						
Male sex	1.25	0.68, 2.35	0.46			
Age, years	0.94	0.84, 1.07	0.30			
Educational level			0.17			0.07
Preschool and primary school	1	—		1		
Secondary school	0.66	0.36, 1.22		1.50	0.97, 2.33	
District of residence			< 0.001			< 0.001
Thu Duc City	1	—		1	—	
Nha Be District	0.12	0.04, 0.26		0.11	0.04, 0.28	
Binh Thanh District and District 1	0.85	0.48, 1.40		0.81	0.56, 1.16	
Educational level of caregiver			0.002			0.25
Below university level	1	—		1	—	
University or higher	2.56	1.42, 4.74		1.46	0.91, 2.33	
Caregiver occupation			0.01			> 0.99
Government officer/Civil servant	1	—		1	—	
Other	0.46	0.26, 0.85		1	1.00, 1.00	
Model 2. Behavioral characteristics^{d,e}						
Knowledge of toxocariasis symptoms ^f			0.19			
No	1	—				
Yes	0.66	0.33, 1.22				
Consumption of raw vegetables			0.91			
Frequently	1	—				
Occasionally	1.16	0.58, 2.55				
No	1.02	0.35, 2.62				
Proper washing of raw vegetables			0.18			0.28
Yes	1	—		1	—	
No	1.56	0.79, 2.82		1.41	0.76, 2.62	
Consumption of cooked food and boiled water			0.16			0.24
No	1	—		1	—	
Yes	0.40	0.17, 0.95		0.68	0.36, 1.30	
Close contact with dogs/cats			0.21			
Frequently	1	—				
Occasionally	0.51	0.16, 1.27				
No	1.13	0.59, 2.17				
Regular deworming of dogs/cats			0.14			0.82
No	1	—		1	—	
Yes	1.81	0.80, 3.31		1.04	0.72, 1.51	
Disposal of dog/cat feces			0.01			0.02
No	1	—		1	—	
Yes	2.42	1.24, 4.17		2.17	1.14, 4.15	
Handwashing after soil contact			0.88			
No	1	—				
Regularly	0.95	0.52, 1.86				
Handwashing before meals			0.91			
No	1	—				
Regularly	1.04	0.56, 2.16				
Model 3. Clinical characteristics^d						
Nutritional status (WHO classification)			0.15			
Normal	1	—				
Underweight/malnutrition	0.48	0.03, 1.75				
Overweight	0.40	0.12, 0.94				
Obesity	1.04	0.40, 2.07				
Clinical manifestations			0.44			
Asymptomatic	1	—				
One symptom	1.66	0.72, 3.11				
≥2 symptoms	0.97	0.17, 2.55				
IgE concentration classification			0.87			
Normal	1	—				
Increased	1.05	0.56, 1.94				
EOS count, K/ μ L	0.83	0.27, 1.76	0.68			

Table 3 continued on the next page.

Table 3. Continued.

Characteristics	Univariate analysis			Multivariable analysis		
	<i>RR</i> ^a	95% <i>CI</i> ^c	<i>P</i>	<i>aRR</i> ^b	95% <i>CI</i> ^c	<i>P</i>
EOS count classification			0.59			
Normal	1	—				
Elevated	1.18	0.63, 2.17				
Combination of EOS count and IgE concentration classification			0.65			
Normal	1	—				
Only the IgE concentration increased	0.69	0.22, 1.69				
Only the EOS count increased	0.81	0.26, 1.95				
Both the IgE concentration and the EOS count increased	1.25	0.59, 2.48				
WBC count, K/ μ L	1.02	0.90, 1.14	0.80			
WBC subtypes			0.54			
Normal	1	—				
Increased	1.21	0.65, 2.27				
AST, U/L	1	0.96, 1.03	0.75			
ALT, U/L	0.99	0.96, 1.03	0.50			
Creatinine	0.99	0.97, 1.02	0.73			
Urea	1.26	0.99, 1.61	0.06			

^a*RR*: risk ratio for treatment failure, estimated using log-binomial regression; ^b*aRR*: adjusted risk ratio for treatment failure, estimated using multivariable log-binomial regression; ^c*CI*: confidence interval estimated using the profile likelihood method; *RR* and 95% *CI* values shown in bold indicate statistically significant associations (95% *CI* does not include 1.0); *P*-values were calculated using the likelihood ratio test; ^dAll models were fitted using a sample size of $n=107$ and no variable showed evidence of multicollinearity (all variance inflation factors [VIFs] < 5); ^eThe multivariable models demonstrated adequate goodness-of-fit (Hosmer-Lemeshow test, $P>0.05$); ^fThis variable was not included in the multivariable model because the model failed to converge; WHO: World Health Organization; IgE: immunoglobulin E; EOS: eosinophils; WBC: white blood cell; AST: aspartate aminotransferase; ALT: alanine aminotransferase; “—” indicates the reference category, for which a 95% *CI* is not applicable; blank cells indicate that the corresponding variables were not included in the multivariable model.

4. Discussion

After treatment, a small proportion of children were lost to follow-up because they relocated with their parents or caregivers and transferred to schools in other areas. Consequently, the overall treatment adherence rate, defined as attendance at follow-up visits and completion of post-treatment laboratory assessments, was 91.5%.

Lower secondary school students (12–15 years of age) accounted for a high proportion of participants receiving treatment (63.6%). In addition, children residing in Nha Be District, a suburban area with a relatively low socioeconomic status within Ho Chi Minh City, represented 62.0% of treated cases, although this difference was not statistically significant ($P>0.05$). One possible explanation is that parents and caregivers may have greater awareness and concern regarding toxocariasis among adolescents than among younger children, leading to a higher willingness to participate in treatment and follow-up. A study in Ho Chi Minh City reported that the seroprevalence of toxocariasis was significantly higher among secondary school children (21%, $P<0.001$) and among children living in Nha Be District (23%, $P<0.001$) compared with their respective counterparts[5].

Sowemimo *et al.* (2017) investigated 308 children aged 9 months to 5 years in Nigeria and reported a *Toxocara* seropositivity rate of 37.3%. Univariate analysis identified age greater than 3 years, parental religious affiliation (Christianity or Islam), and contact with

dogs as significant factors associated with *Toxocara* seropositivity (all $P<0.05$). In multivariable analysis, dog contact remained independently associated with infection risk ($P<0.05$)[15].

Krotten *et al.* (2018) evaluated 66 children aged 2–16 years [mean age (8.8 ± 3.6) years] with positive *Toxocara* ELISA results. Multivariable analysis demonstrated that daily contact with dogs, geophagia, and poor hygiene practices were the most important independent predictors of treatment failure (all $P<0.05$)[6].

In the present study, 96.3% of children experienced complete resolution of clinical symptoms, 71.0% achieved normalization of eosinophil counts, and 57.9% achieved normalization of total IgE levels, and the treatment failure rate was 72.0%. In the univariate analysis, residential area, caregiver educational level, caregiver occupation (Model 1), and disposal of dog/cat feces (Model 2) were significantly associated with treatment failure (all $P<0.05$). In the multivariable analysis, residential area (Model 1) and disposal of dog/cat feces (Model 2) remained independently associated with treatment failure ($P<0.05$).

Bustamante *et al.* reported reductions in ELISA OD, eosinophil counts, and serum IgE levels following treatment in most patients[16]. These improvements were evident within the first 6 months after treatment and became more pronounced after 12 months of follow-up[17,18]. Similar reductions in anti-*Toxocara* antibody titers and eosinophil counts within 3–4 months after treatment have also been reported by other investigators[11,19].

In parasitic infections, including toxocariasis, eosinophilia is

generally transient rather than persistent. It typically occurs when parasites penetrate host tissue barriers or during periods of larval migration. A study from Poland examining age-related differences in the clinical manifestations of toxocariasis found that eosinophilia was more common among younger children[20]. Similarly, Kroten *et al.* reported significant differences in eosinophil counts before and after treatment between preschool-aged and school-aged children ($P<0.05$)[6].

A recent study conducted by Ha Van Thieu in Ho Chi Minh City demonstrated substantial improvements in both clinical manifestations and laboratory parameters following specific treatment for toxocariasis[21]. Our findings are consistent with these previous reports, showing significant reductions in both total WBC counts and eosinophil counts after treatment among preschool and primary school children ($P<0.05$).

This study has several limitations. First, the study scope was limited and focused exclusively on toxocariasis without comprehensively evaluating the potential influence of other parasitic infections. Second, long-term follow-up was not available for children who remained uncured after treatment, preventing further assessment of treatment response and disease progression. Finally, infected children who did not receive treatment were not followed longitudinally, limiting comparisons between treated and untreated individuals.

In conclusion, albendazole treatment in children with *Toxocara* spp. infection resulted in significant clinical and laboratory improvement and demonstrated a favorable safety profile. Combining antiparasitic therapy with improved environmental sanitation and responsible pet management may enhance the effectiveness of toxocariasis control in children.

Conflict of interest statement

There are no conflicts of interest to declare.

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Authors' contributions

H.V.T. and H.H.K. contributed equally to this article as co-first authors, particularly in the design of the study, the analytical

strategy, and the drafting of the manuscript. N.V.B., D.H.K.D. and H.M.C. helped in study protocol preparation and data collection. N.V.B and D.H.K.D. performed the statistical analysis. All authors made a substantial contribution to the acquisition, analysis, and interpretation of data. All authors read and approved the final version of the manuscript.

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