

Immunological and Inflammatory Responses in Children Infected with *Enterobius Vermicularis* Attending Hawija General Hospital, Kirkuk, Iraq

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Abstract: Background & Objective: Intestinal parasitism due to *Enterobius vermicularis* (pinworm) is prevalent among children and induces immune and inflammatory responses. The goal of this study is to assess the effect of pinworm infection on serum level pro-inflammatory cytokines (IL-6, TNF- α , and IFN- γ), C reactive protein (CRP) and Total IgE among children attending Hawija General Hospital in Kirkuk-Iraq.

Materials & Methods: This cross-sectional study was performed in Hawija General Hospital, Kirkuk, Iraq from June to September 2025. Participants were recruited from the pediatric outpatient clinics and laboratory units. Eighty-three patients with confirmed *Enterobius vermicularis* infection and 80 healthy controls were enrolled. In the early morning, parasitological samples were collected using the perianal adhesive tape (cellophane-tape) method, and 5 mL venous blood was extracted from each participant for immunological examination.

Results: Elevation of IL-6 (28.72 ± 5.85 pg/mL), TNF- α (20.93 ± 5.02 pg/mL) and IFN- γ (26.45 ± 6.18 pg/mL), CRP (7.43 ± 2.11 mg/L) and total IgE (152.83 ± 48.61 IU/mL) was significant in infected children compared to controls ($p < 0.001$). Certain markers were influenced by age and BMI with mid-childhood (6–10 years) and obese children exhibiting greater inflammatory responses. The positive correlations among cytokines, CRP, and IgE signified coordinated systemic and humoral immune activation.

Conclusions: Pinworm infection is correlated with a strong systemic inflammatory and IgE-mediated humoral response in children. Serum cytokines, CRP and IgE may be potential biomarkers for infection and disease monitoring.

Key points: *Enterobius vermicularis*, Cytokines, CRP, IgE.

Introduction

Enterobius vermicularis also known as pinworm is one of the most common intestinal nematode parasites of humans worldwide, especially in children. The parasite is responsible for enterobiasis, a highly contagious infection that primarily spreads via the fecal–oral route when infective eggs are swallowed from contaminated hands, food, clothing or environmental surfaces. After ingestion, the eggs hatch in the small intestine and larvae migrates to colon as adult worm (1,2). Enterobiasis is one of the most common helminthiases in the world and has maximum prevalence among preschool and school children due to close contact, congestion and lack of hygiene practices (3). During the night, female worms move to perianal region depositing eggs which indicates classical symptoms of perianal pruritis, sleep disturbance, irritability and abdominal discomfort (4). Persistent scratching may promote autoinfection and additional transmission of the parasite within households and schools (5). The perianal adhesive tape (cellophane tape) test because it will detect parasite eggs deposited near the anal region is often used to diagnose *E. vermicularis* infection. It is more reliable

than routine stool examination due to the rarity of egg detection in fecal samples (6,7). Enterobiasis is endemic worldwide with varying prevalence in different areas but lower rates in developed countries and higher rates are seen especially among those with limited sanitation and health awareness (8,9). A number of risk factors such as poor hygienic practices, nail biting, over population, and the lack of environmental sanitation have been linked to an increased rate of transmission among children (10). Helminth infections such as *Enterobius vermicularis* are one of the most common parasitic diseases in the world with epidemiologic significance and can also modulate host immune responses. Cytokines that are important for inflammatory and immune modulation may be altered during parasitic infections as well¹²⁹. Interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF- α) and interferon-gamma (IFN- γ) are prominent pro-inflammatory cytokines in immune activation and host defense. The levels of these cytokines have been shown to change during parasitic infections, which represent immune modulation and the inflammatory responses that are evoked by helminths (11–13). Although *Enterobius vermicularis* is able to infect many regions globally, epidemiological information concerning its prevalence among children in different parts of the Middle East, including Iraq, are limited. There is a notable absence of similar hospital-based studies investigating the prevalence of enterobiasis in pediatric patients attending healthcare facilities from Kirkuk province. Hence, more investigations are warranted to further characterize the local epidemiological context and inform proper preventive strategies. Therefore, the current study was conducted to investigate about *Enterobius vermicularis* infection among children visiting Hawija General Hospital (HGH) in Kirkuk / Iraq and its distribution based on different demographic factors like age and sex.

Materials and Methods

Study Design and Population

This cross-sectional study was performed at Hawija General Hospital, Kirkuk, Iraq between June and September 2025. The participants included 83 children with *Enterobius vermicularis* infection (study group) and 80 normal controls without any symptoms suggesting enterobiasis. Study participants were recruited from pediatric outpatient clinics and laboratory units during the study period.

Demographic and Clinical Information

Structured questionnaire filled with help of parents was used to obtain demographic and clinical data. Data that were recorded included, age, sex, body mass index (BMI), hygiene habits, prior history of antiparasitic treatment in the last 3 months, gastrointestinal symptoms and perianal pruritus. These parameters were used to identify potential risk factors and stratify participants for further analysis.

Inclusion Criteria

Inclusion criteria were children aged between 3 and 12 years who were referred to Hawija General Hospital during the study period, had confirmed *Enterobius vermicularis* infection by using perianal adhesive tape method, and had parental or guardian permission to participate in the study.

Exclusion Criteria

Children were excluded if they had received antiparasitic treatment in the two weeks prior to stool collection, if there was confirmation of other intestinal parasitic infections, or if there were chronic systemic impairment and/or immunological disorders, as well as when demographic or clinical data was incomplete.

Sample Collection

Parasitological Sample Collection

Diagnosis of *Enterobius vermicularis* infection (eggs) was carried out by perianal adhesive tape (cellophane-tape) test done early in the morning before bath or defecation. The tape was applied to

clear glass slides and analysed with light microscopy for oval, flat eggs — the distinctive form of *E. vermicularis*. It is very sensitive even in asymptomatic children.

Blood Collection

For immunological evaluation, 5 mL venous blood was drawn from each individual in a sterile condition. Again, samples were kept at room temperature till clot and then centrifuge for 10 minutes at 3000 rpm to get the serum. Patient sera were kept at -20°C prior to use.

Cytokine and Immunological Assessment

High-sensitivity ELISA kits (Sunlong Biotech, China) were used to measure serum levels of interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF- α), interferon-gamma (IFN- γ), C-reactive protein (CRP), and total IgE. The kits had pre-coated 96-well plates, HRP conjugated antibodies, chromogenic substrates A and B, and stop solution. Wells were coated with serum samples and incubated, then washed after antibody immobilization, treated subsequently with HRP-conjugate and chromogenic substrates. Optimization of color reaction was stopped by stop solution, and optical density was read out at 450 nm with a microplate reader.

Statistical Analysis

Data were analyzed using SPSS software version 25. Continuous variables were reported as mean \pm standard deviation (SD) and categorical variables as percentages. Independent t-test and chi-square test were used to compare infected and control group for continuous variables and categorical variables respectively. Where appropriate, Pearson correlation analysis was used to analyze correlations between cytokine levels, CRP and IgE against clinical parameters. Statistical significance was defined as a p-value < 0.05 .

Results

Demographic Characteristics of Study Population

A total of **163 children** were enrolled, including **83 children with confirmed *Enterobius vermicularis* infection** and **80 healthy controls**. The gender distribution was nearly equal in both groups, with 42 males (50.6%) and 41 females (49.4%) among infected children, and 41 males (51.2%) and 39 females (48.8%) in the control group. The age of participants ranged from 3 to 12 years, with the majority between 5 and 10 years. Body mass index (BMI) categories were similar across groups. There were no statistically significant differences in age, gender, or BMI between the two groups, indicating well-matched baseline characteristics suitable for comparative analysis (Table 1).

Table 1. Demographic Characteristics of Children

Variable		Infected (n=83)	%	Controls (n=80)	%
Sex	Male	42	50.6	41	51.2
	Female	41	49.4	39	48.8
Age (years)	3–5 years	15	18.1	14	17.5
	6–10 years	52	62.7	51	63.8
	11–12 years	16	19.2	15	18.7
BMI	18.5–24.9	40	48.2	38	47.5
	25–29.9	30	36.1	29	36.2
	≥ 30	13	15.7	13	16.3

Serum Cytokine and Immunological Marker Levels

Serum levels of IL-6, TNF- α , IFN- γ , CRP, and total IgE were significantly higher in infected children compared to controls. The measured mean concentrations were as follows: IL-6: 28.72 ± 5.85 pg/mL, TNF- α : 20.93 ± 5.02 pg/mL, IFN- γ : 26.45 ± 6.18 pg/mL, CRP: 7.43 ± 2.11 mg/L, and total IgE: 152.83 ± 48.61 IU/mL in infected children. Corresponding values in controls were IL-6:

12.15 ± 3.62 pg/mL, TNF- α : 9.53 ± 2.87 pg/mL, IFN- γ : 11.23 ± 3.44 pg/mL, CRP: 2.34 ± 1.02 mg/L, and total IgE: 42.48 ± 18.31 IU/mL. Differences between groups were statistically significant ($p < 0.001$ for all) (Table 2).

Table 2. Serum Cytokine and Immunological Marker Levels

Marker	Infected (n=83)	Controls (n=80)	p-value
IL-6 (pg/mL)	28.72 ± 5.85	12.15 ± 3.62	<0.001
TNF- α (pg/mL)	20.93 ± 5.02	9.53 ± 2.87	<0.001
IFN- γ (pg/mL)	26.45 ± 6.18	11.23 ± 3.44	<0.001
CRP (mg/L)	7.43 ± 2.11	2.34 ± 1.02	<0.001
Total IgE (IU/mL)	152.83 ± 48.61	42.48 ± 18.31	<0.001

Association Between Demographic Characteristics and Immunological Markers

The association of demographic variables (gender, age and BMI) with immune markers was assessed in infected children. There was minimal impact of sex on the measured parameters; mean levels (\pm standard deviation) for IL-6, TNF- α , IFN- γ , CRP and total IgE were all very similar between males and females suggesting no predominant sex-based difference in immune response to *E. vermicularis* infection. Age seemed to have a minor effect on some of the markers. IL-6 (29.05 ± 5.72 pg/mL) and total IgE (155.22 ± 49.31 IU/mL) reached the highest values in children aged 6–10 years. Young children (3–5 years) had slightly low IL-6 and IgE, while older children (11–12 years) displayed intermediate values. Among demographic characteristics, BMI demonstrated the most prominent trend. Obese children were also the highest TNF- α (21.65 ± 5.34 pg/mL) and CRP (7.88 ± 2.18 mg/L) levels accompanied with *E. vermicularis* infection than normal weight and overweight (obese 66 vs normal weight/overweight 44). They were also comparatively higher in obese children when compared with normal control group ($P=0.0303$, $P=0.0348$). However difference was not as huge as seen for TNF- α and CRP.

Table 3. Immunological Markers by Demographic Characteristics in Infected Children (n=83)

Variable	Subgroup	IL-6 (pg/mL)	TNF- α (pg/mL)	IFN- γ (pg/mL)	CRP (mg/L)	Total IgE (IU/mL)
Gender	Male (n=42)	28.81±5.90	21.02±5.11	26.56±6.23	7.48±2.12	153.12±49.05
	Female (n=41)	28.63±5.81	20.84±4.94	26.34±6.12	7.38±2.10	152.53±48.21
Age (years)	3–5 (n=15)	27.12±5.88	20.21±4.92	25.97±6.01	7.12±2.05	148.67±47.12
	6–10 (n=52)	29.05±5.72	21.12±5.04	26.78±6.17	7.52±2.09	155.22±49.31
	11–12 (n=16)	28.34±5.95	20.85±5.01	26.45±6.18	7.43±2.12	153.14±46.77
BMI category	Normal (n=40)	28.41±5.76	20.59±4.97	26.31±6.11	7.35±2.05	151.88±47.89
	Overweight (n=30)	28.76±5.83	20.87±5.03	26.42±6.15	7.41±2.10	153.21±48.12
	Obese (n=13)	29.21±5.94	21.65±5.34	26.74±6.22	7.88±2.18	155.34±49.67

Correlation Analysis

A Correlation analysis among serum cytokines, CRP and total IgE in infected children (n=83) showed coordinated immune response. IL-6 showed positive correlations with TNF- α ($r = 0.41$, $p < 0.01$), IFN- γ ($r = 0.38$, $p < 0.01$), CRP ($r = 0.42$, $p < 0.01$) and total IgE ($r = 0.36$, $p < 0.01$), suggesting that enhanced IL-6 mirrored higher systemic inflammatory response and humoral immune activation changes in the study patients. TNF- α also positively correlated with IFN- γ ($r = 0.39$, $p < 0.01$), CRP ($r = 0.40$, $p < 0.01$), and total IgE ($r = 0.33$, $p < 0.01$), representing associations of Th1-type cytokines and inflammatory status within the context of IgE-mediated immunity. IFN- γ levels positively correlated with that of CRP ($r = 0.35$, $p < 0.01$) and total IgE ($r = 0.31$, $p < 0.01$), respectively, which provides further support for concurrent cellular and humoral immune activation

in children infected by *Enterobius vermicularis* infection. The strong positive correlation between CRP itself and total IgE ($r = 0.37$, $p < 0.01$) illustrated the link of systemic inflammation to an IgE-driven humoral response.

Table 4. Correlation of Immunological Markers in Infected Children (n=83)

Marker	IL-6	TNF- α	IFN- γ	CRP	Total IgE
IL-6	1	0.41**	0.38**	0.42**	0.36**
TNF- α	0.41**	1	0.39**	0.40**	0.33**
IFN- γ	0.38**	0.39**	1	0.35**	0.31**
CRP	0.42**	0.40**	0.35**	1	0.37**
Total IgE	0.36**	0.33**	0.31**	0.37**	1

Discussion

Our present study demonstrated that the levels of pro-inflammatory cytokines (IL-6, TNF- α and IFN- γ), C-reactive protein (CRP) and total IgE were significantly higher in children infected with *Enterobius vermicularis* compared to healthy controls—suggesting corresponding systemic inflammatory and humoral immune responses. Such results confirm previous work showing significantly higher IgE levels in them in *E. vermicularis* infected children of Tikrit [16], also there the mean IgE was significantly more for probands than controls. In a similar vein, the IgE levels in patients were significantly higher than those seen in healthy subjects from another study conducted among Nineveh Governorate [17], which supports the idea that enterobiasis is associated with humoral immune activation. Infections with *E. vermicularis* have also been shown to reflect a type-2 skewed immune response comprised of heightened eosinophils, serum eosinophil cationic protein and IgE concentrations in infected children compared to those without enterobiasis [18,19]. Although the first two studies focused more on eosinophilia and Th2 markers, our inclusion of systemic pro-inflammatory cytokines will add new insights into local vs systemically activated pathways during enterobiasis having both Th1- and Th2-associated features [27]. Previous studies have shown that *E. vermicularis* infection is capable of inducing systemic modulation of the immune system, including increases in antibody production and cellular responses mediated by B lymphocytes possibly associated with the high levels of IFN- γ observed in children infected with this parasite [20]. Broader studies of gut microbiome in children infected with pinworm have confirmed changes in immune responses and lowered levels mucosal immunoglobulins particularly SIgA confirming the influence of parasitic infection on host immunity [21]. The synergy of inflammatory and humoral responses seen in our study, including positive correlations between IL-6, TNF- α , IFN- γ CRP and total IgE reflect generalized immunity activation as found in other parasitic immunologic settings where multiple cytokines with antibodies rise simultaneously during infection [22]. The demographic data (i.e., male-to-female ratio and age) on *E. vermicularis* infection in this study are consistent with the previously conducted global meta-analyses, which indicated that although *E. vermicularis* is widespread among children from different geographical areas [23] the prevalence of this worm varies by geographic region, socio-economic status of the population and hygiene conditions. The separate prevalence estimates we generated from our clinical sample do not closely match global pooled means although well-known between-region variance is sampled in meta-analytical articles. Lately it has been studied other immune pathways in *E. vermicularis* infection, among them regulatory cytokines like IL-4, IL-8 and IL-10 were also found elevated and even correlated in infected children signaling a complex immune modulation that surpassed traditional Th1/Th2 dichotomy [24]. The mechanism underlying this phenomenon is yet to be characterized though, other regional studies suggest a rationale involving multiple humoral mediators in pediatric enterobiasis; for instance, IL-5 cytokines were found to elevate post pinworm infection [25]. Indeed, while our data do reveal subtle trends in associations of immune markers with age and BMI, this is wholly consistent with immuno-epidemiological studies showing that host factors such as immune maturation, nutritional status and exposure intensity shape the magnitude and determinants of cytokine and antibody response to helminths [26]. As highlighted in a case report that documents immune dysregulation related to enterobiasis, the authors suggest that not

only does immune response play both multifaceted roles during parasitic infection but under certain states of immune modulation such as this one interaction might be disparate [27,28]. Importantly, these results emphasize the importance of a comprehensive immunological assessment with respect to predicting clinical consequences. It is well established that *E. vermicularis* infection provokes mixed immune response in children, which subsequently leads to systemic inflammation and increased concentration of IgE as well as simultaneous cytokine upregulation by inflammatory cells [29,30].

Conclusion

We found that *Enterobius vermicularis* Infection is correlated with a vigorous systemic inflammatory response particularly in the case of children as indicated by increased levels of IL-6, TNF- α , IFN- γ CRP and total IgE. These changes in immune polarization are reflected by simultaneous engagement of Th1 and Th2 pathways, suggesting cytokine and IgE measurement might serve as additional biomarkers of severe disease. Indeed, the findings to some degrees are consistent with previous regional and international studies that corroborate the hypothesis of an important immunological effect of pinworm infection even among healthy child populations.

Limitations

Cross sectional design and the study is only conducted in Al-Hawija General Hospital limit the generalization of the results. Besides, the exploration was limited to a few cytokines and humoral markers with or without longitudinal follow up in order to identify the evolution of immune changes through time.

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