CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES
https://cajmns.centralasianstudies.org/index.php/CAJMNS
*Volume: 06 Issue: 03 | July 2025 ISSN: 2660-4159*

*Article*

# The Role of IL-5 in Immune Responses to Enterobius vermicularis Infection Among Children: A Case control study

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**Abstract:** E. vermicularis (pinworm) is the most prevalent helminth infection in middle- and high-income nations, especially in school-age children. E. vermicularis is found all across the world and is not linked to any specific racial, cultural, or social background. To investigate the role of IL5 in immunity against E. vermicularis infection through measuring serum level among infected children and healthy control group. Between August 2024 and January 2025, 45 children—24 boys and 21 girls—from patients who visited AL-Zahraa Teaching Hospital in AL-Najaf province participated in the current study. For hematological parameters and IL5 measurement by ELISA, 5 ml of samples were drawn from the veins of the patients and the control group. The information was entered using SPSS version 22.0. In this study, the relationship between the two variables was analyzed and assessed using the chi-square test. The t-test was used to analyze the differences in serum parameters between the two groups. The threshold for statistical significance was set at $P < 0.05$. Infected children had a significantly lower hemoglobin level than the controls (12.06 vs. 13.46) respectively. Therefore, the mean of hemoglobin was highly significant, as (P= <0.001), while, white blood cells and Eosinophils' showed a highly significant increase (P= <0.001), in patients when compared with control. Interleukin 5 was assessed for both patient and control groups and the mean showed there were a highly significant increase in infected children when compared with control (P=0.0001).

**Keywords:** Interleukin5 (IL5), Enterobius Vermicularis, Infection

**Citation:** Hadi, E. A., Sayal, R. A. The Role of IL-5 in Immune Responses to Enterobius vermicularis Infection Among Children: A Case control study. Central Asian Journal of Medical and Natural Science 2025, 6(3), 1283-1291.

Received: 25th May 2025
Revised: 31th May 2025
Accepted: 11th Jun 2025
Published: 20th Jun 2025



## 1. Introduction

Hematopoietic and non-hematopoietic cell lines produce the cytokine dimer interleukin-5, which is mainly involved in the survival, differentiation, and proliferation of eosinophils. T lymphocytes and ILC2s are the primary producers of IL-5, with eosinophils and mast cells contributing little (Price & Kennedy, 2022). IL-5 is constituted of two similar subunits associating non-covalently to a receptor designated the IL-5 receptor. The latter consists of two subunits: a specific $\alpha$-chain and a common $\beta$-chain. Receptor engagement initiates a series of IL-5-dependent intracellular signaling events, predominantly involving the JAK-STAT pathway (Olin & Wechsler, 2014). Among the structural features of IL-5 are receptor binding sites that are critical to the biological activity of the molecule in supporting the survival and activation of eosinophils (Moult et al., 2016). IL-5 has gained considerable attention as a possible therapeutic target due to its importance in eosinophilic disorders. Monoclonal antibodies against IL-5 or its receptor are some of the most effective drugs in the clinic today, offering new hope for the treatment of severe asthma and other eosinophil-associated conditions (Pelaia et al., 2019). Studies

have shown that inhibition of IL-5 has significant therapeutic benefits in the treatment of asthma patients, particularly those severe phenotypes with elevated eosinophil numbers (Barnes, 2018). A distinct type 2 cytokine response is triggered by infection with big, multicellular parasitic helminths that live in and on host tissues (Sorobetea et al., 2018). Innate immune cells and polarized CD4+ T helper type 2 (Th2) cells produce type 2 cytokines, such as IL-4, -5, -9, and -13, to coordinate tissue responses, such as increased mucin production, smooth muscle contractility, goblet cell hyperplasia, and increased turnover of epithelial cells (Harris, 2017).Together, these activities drive worm expulsion and wound healing responses that control worm-induced tissue damage (Shimokawa et al., 2017).Interleukin-5 (IL-5) concentrations are increased in E. vermicularis infections, suggesting a strong immunological response. In order to activate and mobilize eosinophils, considered vital for fighting parasitic infections, IL-5 is a key player (Gazzinelli-Guimaraes et al., 2024).The present study aimed to investigate the role of IL5 in immunity against E. vermicularis infection through measuring serum level among infected children and healthy control group.

## 2. Materials and Methods

**Subjects:**

Between August 2024 and January 2025, 45 children—24 boys and 21 girls—from patients who attended AL-Zahraa Teaching Hospital in AL-Najaf AL-Ashraf province participated in the current study. Scotland tape identified the illness and the child's age, which ranged from 1 to 10 years. Additionally, 40 healthy kids who were matched in age and sex with the sick group were chosen as the control group. For every participating kid in the research, a unique questionnaire form was created, and moms were interviewed to complete it.

**Sample collection:**

Samples were collected 5 ml from vein by using disposable syringes and transfer 2ml of sample to EDTA tube detect the hematological parameters (Using Sysmex automated blood analyzer) and the rest 3ml transfer to gel tube to collect serum after 5min centrifugation at 3000 r.p.m. to estimate IL5 levels by ELISA kit (Elabscience, USA).

**Data entry and statistical analysis:**

Statistical Package for Social Sciences (SPSS) version 22.0 was used to input the information obtained. The chi-square test was used to analyze and evaluate the relationship among the two variables in this investigation. Serum parameter differences between the two groups were examined using the t-test. Statistical significance was defined as $P < 0.05$.

## 3. Results

Table 1 displays the demographic details of the patient and control groups. Patients' mean age was 5.38± 2.56, whereas the control group's was 5.62±2.6. The difference in mean age between the two groups was not statistically significant (P=0.925). The frequency distribution of patients and control participants by age did not differ significantly, according to the results (P=0.673). In the group of infected children, there were 27 (60%) men and 18 (40%) girls, while the control group had 33 (73.3%) boys and 12 (26.7%) females. The frequency distribution of patients and control subjects by gender did not vary significantly (P=0.180).

**Table 1.** Comparing the general traits and attributes of the parasite and control groups in children.

| Characteristic | Infected children *n* = 45 | Control *n* = 45 | *P* |
|---|---|---|---|
| **Age (years)** | | | |
| Mean ±SD | 5.38± 2.56 | 5.62± 2.6 | 0.925 † NS |
| 1-5, *n* (%) | 24(53.3%) | 22(48.9%) | 0.673 ¥ |
| 6-10, *n* (%) | 21(46.7%) | 23(51.1%) | NS |
| **Gender** | | | |
| Male, *n* (%) | 27(60%) | 33(73.3%) | 0.180 ¥ |
| Female, *n* (%) | 18(40%) | 12(26.7%) | NS |
| **Body mass index (BMI)** | | | |
| Mean ±SD | 18.28± 1.8 | 22.19± 5.4 | <0.001 † |
| **Residence** | | | |
| Urban | 25(55.6%) | 30(66.7%) | 0.280 ¥ |
| Rural | 20(44.4%) | 15(33.3%) | NS |

Table (1), concerned on the mean of body mass index among infected children in comparison with control. The results indicated to presence of highly significant decrease in the mean of BMI in patients when compared with control (P=<0.001). The results indicated to a most of infected children were in urban 25(55.6%), while 20 (44.4%) in rural residence. The study showed no significant variation between patient and control groups (P=0.280).

Table (2), showed that infected children had a significantly lower hemoglobin level than the controls (12.06 vs. 13.46) respectively. Therefore, the mean of hemoglobin was highly significant, as (P= <0.001), while, white blood cells and Eosinophils' showed a highly significant increase (P= <0.001), in patients when compared with control.

**Table 2.** Blood parameters among infected children in comparison with control group.

| Blood variables | *E. vermicularis* +ve children *n*= 45 Mean± SD | *E. vermicularis* -ve children *n*=45 Mean± SD | T. value | P. value |
|---|---|---|---|---|
| **Hemoglobin g/dl** | 12.06± 2.08 | 13.46 ± 1.27 | 3.84 | <0.001 |
| **WBCs** | 13.28 ± 1.35 | 5.17 ± 0.62 | 36.34 | <0.001 |
| **Eosinophils'** | 4.09 ± 0.96 | 2.74 ± 0.74 | 7.44 | <0.001 |

SD: standard deviation; WBCs: white blood cells; t- independent test; P. value less than 0.05 considered significance.

Interleukin 5 was assessed for both patient and control groups and the mean showed there were a highly significant increase in infected children when compared with control (P=0.0001) as it shown in Table (3) and Figure (1) respectively.

**Table 3.** Concentration of IL5 pg/ml among infected children in comparison with control.

| IL5 pg/ml | Case control comparison | | P. value |
|---|---|---|---|
| | Infected children *n*=45 | Control *n*=45 | |
| Mean ± SD | 28.51± 4.76 | 5.14 ± 1.43 | <0.0001** |
| Range | 19-35 | 3-8 | |
| Median (IQR) | 29 (8) | 4.9 (3) | |
| 95% CI for the mean | 27.07-29.94 | 4.71-5.57 | |
| Standard error of the mean | 0.7104 | 0.2139 | |
| Test statistic t. | t= 31.49 | | |

SD: Standard deviation, n= number of instances, independent T-test, significant at P. value < 0.05.

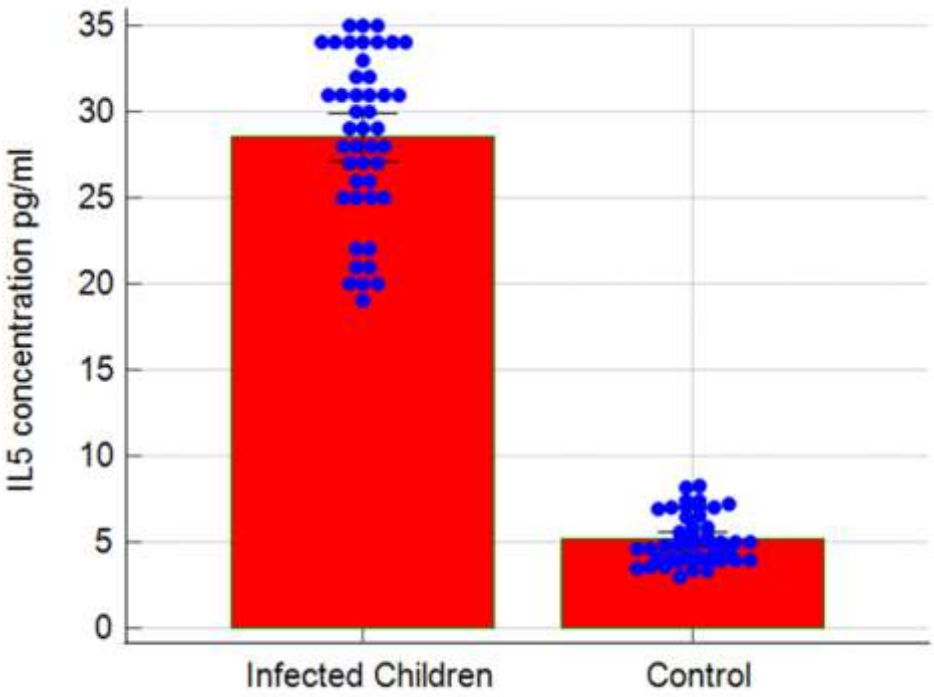


**Figure 1.** Serum level IL5 among infected children in comparison with control (P. value <0.0001).

Table (4), indicated to evaluate the IL5 cutoff value as well as to predict the Enterobius infection as diagnostic tests or adjuvant diagnostic tests, receiver operator characteristic (ROC) curve analysis was carried out across study groups and the results are shown in (4), and figure (2). The IL5 cutoff value was (>8.3), which achieves a sensitivity of 100.00% and specificity of 100.00% with (P=<0.001). According to the table's findings, IL-5 has a high degree of diagnostic accuracy (AUC: 1.000, 100% sensitivity and specificity).

**Table 4.** IL5 levels analyzed through Receiver Operating Characteristic (ROC) curve among studied groups.

| Serum IL5 pg/ml concentration | Studied groups |
|---|---|
| Area under the ROC curve (AUC) | 1.000 |
| 95% Confidence interval | 0.960 to 1.000 |
| Sensitivity | 100.00% |
| Specificity | 100.00% |
| Cut-off value | >8.3 |
| +PV | 100.00 |
| -PV | 100.00 |
| Accuracy | 1.0000 |
| Significance level P. value | <0.001** |

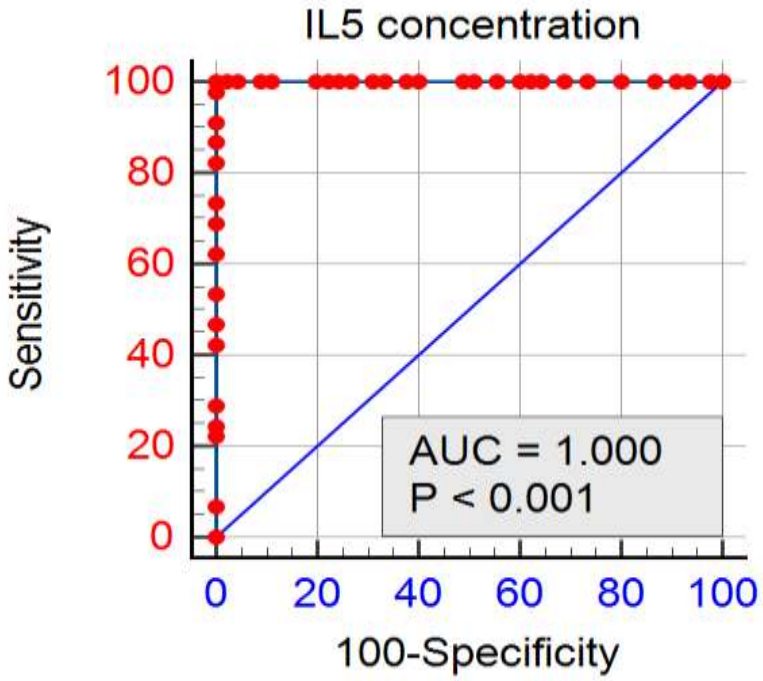


**Figure 2.** ROC of IL5 among infected children in comparison with control (P. value <0.001).

## 4. Discussion

Enterobius vermicularis is most common in crowded residences among all ages, but is particularly common in children and affects between 4% and 28% of children worldwide (Altun et al., 2017). This parasite is mostly found in children in kindergartens, institutions or in families with a large number of children. It spreads easily between all family members, with frequent reinfestation (Zouari et al., 2018). The results agrees with Al-Daoody & Al-Bazzaz, (2020), as they reported that, the highest rate of infection in age group (<6 years), while, lowest rate in group (>7 years). Dohan and Al-Warid, (2022), who reported a significant link between gender and the presence of E. vermicularis. Most E. vermicularis +ve cases were diagnosed in male individuals. E. vermicularis infection is linked to malnutrition and anemia, with infected children showing significantly lower BMI and weight-for-age Z scores compared to non-infected peers (Dohan& Al-Warid, 2022). In a study involving 500 children, a notable percentage (39.5%) were infected with E. vermicularis, correlating with lower BMI values (El-Awady & Abed, 2017). In a study demonstrated that, the prevalence of pinworm infection in urban areas was found to be higher than that in rural areas (Fan et al., 2019). Low socioeconomic status was thought to

be a risk factor for pinworm infection, and many studies have highlighted this condition (Chen et al., 2018). It is less well recognized that erythrocyte hemoglobin (Hb), a blood molecule that includes iron and is essential for animals to carry oxygen, is a member of the family of hemoglobin proteins, which have members in all three domains of life: bacteria, eukaryotes, and archaea (Gell, 2018). The intestinal parasites cause vitaminosis, disrupt digestion, release the trophozoite motile feeding stage, and adhere to intestinal villi. Another parasite absorbs roughly 50 milliliters of blood per day (Al-Mousawi & Neamah, 2021). They also feed on the food that is digested in the intestine, which is why some parasites cause anemia by excreting substances that dissolve blood (Bolka & Gebremedhin, 2019). The findings indicate that individuals with parasite infections have higher blood levels of white blood cells (WBCs) because WBCs can destroy parasites by adhering to their walls and secreting granules that can destroy exterior parasite walls (Mohmmed et al., 2016). E. vermicularis can occasionally result in eosinophilia, despite the fact that it is said to be a virtually innocuous intestinal parasite that may help educate the immune system (Patsantara et al., 2016). Asthma and other allergy disorders are linked to eosinophils' dysregulation of immunological responses. Furthermore, according to Rahimi et al. (2018), this subset of immune cells is frequently thought of as a destructive end-stage effector that is mostly associated with parasitic disorders, particularly helminthic infections including intestinal and tissue nematode infections. The result agrees with Al-Hasheme et al., (2020), as they reported a highly significant increase in IL5 level among infected children when compared with control. As a "eosinophil activator," IL-5 is the most significant cytokine in the generation and transformation of eosinophils (Chen et al., 2023). Elevated IgE, eosinophilia, mastocytosis, and CD4+ T cells that preferentially generate IL-4, IL-5, and IL-13 are all linked to the human immunological response to helminth infections (Ayelign et al., 2020). The host's immune response to intestinal parasites by Th2 cells was the cause of the increase in IL-5 concentration in the sera of children infected with intestinal parasites as compared to children who were not infected. High amounts of the interleukins IL-4, IL-5, IL-9, IL-10, IL-13, IL-21, and IL-33 are produced in response by these cells. These interleukins control the response to acute hypersensitivity, which includes B-lymphocytes switching from producing antibodies to IgG4 and IgM only, a high concentration of mast cells, goblets, and eosinophils, as well as alternative macrophage activation and an influx of inflammatory cells like eosinophils that aid in the death of parasites (Maizels, 2016; Cruz et al., 2017). Increased IL-5 generating is triggered by E. vermicularis and is associated with eosinophilia, a disorder marked by an increased blood eosinophil number (Schroeder et al., 2019). Alterations in the intestinal microbiota have been connected to enterobius infection, and they may have an additional impact on IL-5 creation and the body's immune system as a whole (Yang et al., 2017). In accordance with the research on hookworm infections (Loukas et al., 2016), serum IL-5 levels could accurately distinguish between those who were infected and those who were not, with diagnostic accuracy comparable to the stated AUC and prediction values.

## 5. Conclusion

In conclusion, this study emphasizes the critical function of interleukin-5 (IL-5) in children's immunological responses to Enterobius. vermicularis infections. IL-5 might be used as a biomarker to identify E. vermicularis infections in children and track their immune responses. To clarify the precise processes by which IL-5 affects immunity in helminth infections and investigate its possible use as a target in immunomodulatory treatments, more investigation is necessary.

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