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# Longitudinal Analysis of Cytokine Profiles and Their Impact on Tic Disorder Severity Over One Year

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**Objective:** This study aims to explore the relationship between symptom severity and cytokine levels in patients with tic disorders by evaluating these parameters at baseline and after a one-year follow-up.
**Methods:** A total of 44 tic disorder patients were recruited, 35 completed baseline assessments, and 20 completed endpoint assessments after one year. Based on changes in Yale Global Tic Severity Scale scores, patients were categorized into 'improved' and 'persistent' groups. Cytokine levels were measured using a Luminex® human cytokine multiplex assay at both time points.
**Results:** Significant increases were found in interferon (IFN)-α2, IFN-γ, interleukin (IL)-1β, IL-6, IL-10, IL-12 p40, IL-12 p70, and IL-13, while IL-1ra and IL-4 levels decreased. Changes in IFN-γ levels showed significant correlations with tic severity, with higher endpoint levels being linked to symptom worsening. Baseline IL-5 levels were significantly higher in the improved group compared to the persistent group.
**Conclusion:** This study underscores the potential of IFN-γ and IL-5 as biomarkers and therapeutic targets in tic disorders. The findings suggest that these cytokines could be instrumental in assessing tic disorder severity and developing targeted therapies. Further research involving larger cohorts is needed to validate these findings and explore cytokine-targeted therapies for tic disorders.

**KEY WORDS:** Tic disorders; Tourette syndrome; Cytokines; Movement disorders.

## INTRODUCTION

Tic disorders, affecting nearly 3% of children, are neuropsychiatric conditions marked by sudden and brief involuntary movements or vocalizations known as tics, which may involve different body parts [1]. While tics are not typically harmful, they can cause significant distress, particularly when severe or unpredictable. Patients with tic disorders frequently have a higher prevalence of coexisting psychiatric conditions, including attention-deficit hyperactivity disorder, obsessive-compulsive disorder, and major depressive disorder, compared to their peers.

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Tic disorders often emerge in childhood and can persist for varying durations, ranging from less than a year to a lifetime. The role of neuroinflammation has gained support from research, mainly through cases developing post-infection [2]. These insights have prompted further studies into the role of cytokines in individuals with tic disorders. Parker-Athill *et al.* [3] revealed that during periods of tic exacerbation, elevated levels of tumor necrosis factor (TNF)-α and its correlations with medication use indicate a pivotal role for cytokine imbalances in the development of tic disorders. Fabricius *et al.* [4] also summarized multiple studies in a review demonstrating a correlation between cytokine profile changes and various psychiatric disorders, including tic disorders. Our team has also conducted comparative studies to deepen our understanding of the differences between patients with tic disorders and control groups [5,6]. Specific cytokines such as interleukin (IL)-12 p70, TNF-α, and IL-17a significantly

correlate with tic severity scores in patients with tic disorders. This suggests that cytokine profiles differ between patients and healthy controls, particularly during milder symptom phases.

However, despite these advancements, the specific role of cytokines in the development, progression, and chronicity of tic disorders still needs to be explored. Many tic disorder patients are young children, and due to the clinical characteristics of tic symptoms that wax and wane, regular follow-up with these patients is challenging. Consequently, there are very few longitudinal studies on this condition. Understanding these cytokine-mediated mechanisms is crucial for developing targeted interventions to mitigate tic disorders' long-term impacts. Consequently, in this study, we assembled a uniform group of young patients with tic disorders who were not on psychotropic medication, and we monitored them over one year, focusing on changes in tic symptoms and cytokine levels.

## METHODS

A group of 44 patients diagnosed with tic disorders was initially recruited. The age range of these participants was 6 to 18 years, and all had intelligence quotient scores above 70, assessed using the Wechsler Intelligence Scale for Children—Korean version (K-WISC-IV). They had been off any psychotropic drugs for no less than three weeks and had no history of neurological disorders, head injuries, tumors, or seizures. Child and adolescent psychiatrists made diagnoses following the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition guidelines.

Recruitment occurred at the Psychiatry Department of Korea University Guro Hospital. Initial evaluations at baseline included the Korean version of the Kiddie-Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version to identify psychiatric comorbidities and the Yale Global Tic Severity Scale (YGTSS) to measure the severity of tic symptoms. The YGTSS is a clinical tool used predominantly to assess Tourette's syndrome and related tic disorders. It rates tics by number, frequency, intensity, complexity, and impact on functioning, combining motor and phonic tic scores with an impairment rating [7]. Blood samples were collected from all subjects for cytokine analysis using a Luminex® human cytokine panel A multiplex assay kit (HCYTA-60K, Milliplex). After collection, the samples were immediately frozen at −70°C to preserve their integrity and later categorized as either pro-inflammatory or anti-inflammatory cytokines based on existing literature [3,8-13]. The Luminex cytokine multiplex method employs bead-based technology to measure multiple cytokines in a single sample simultaneously. This method uses uniquely colored microspheres, each set coated with a specific antibody that binds to a different cytokine. When a sample is introduced, cytokines bind to their respective antibodies. A secondary biotinylated detection antibody is added, followed by a streptavidin-phycoerythrin conjugate, which binds to the detection antibody. The fluorescence intensity of each microsphere is measured, quantifying the levels of each cytokine in the sample. This method utilizes Luminex xMAP technology, combining microsphere-based multiplexing with laser-based detection for high-throughput and accurate analysis. The test results show the results for each target, along with quality control sample data for comparison. Cytokines were chosen for evaluation from prior studies and categorized into pro-inflammatory and anti-inflammatory groups [3,8-13]. At the end point, one year after the baseline assessment, cytokine levels and YGTSS scores were reevaluated using the same methods. Participants were categorized into two groups: those with reduced YGTSS scores from baseline were deemed 'improved', while those with unchanged or increased scores were labeled 'persistent.' Baseline and endpoint cytokine levels were compared using paired $t$ tests, and correlation analyses assessed the association between cytokine levels and YGTSS scores at the endpoint, between the changes in cytokine levels and YGTSS score changes. Subgroup analyses between 'improved' and 'persistent' patients explored differences in cytokine levels between the two groups. Statistical analyses were performed using SPSS version 23 software (IBM Corp.). The significance level was set at $p < 0.05$. The study was approved by the Institutional Review Board (IRB) of Korea University Guro Hospital (2021GR0275). Written informed consent was obtained from parents or legal guardians of all patients.

## RESULTS

### Demographic and Clinical Characteristics

A total of 44 patients were initially enrolled, but six withdrew their consent to participate, and three failed to

provide blood samples at baseline. During the one-year follow-up period, 15 patients were lost to follow-up. For the final analysis, 35 patients were included at baseline and 20 at the endpoint. Among these, 18 patients participated in clinical interviews for tic symptom assessment and blood sample collections at baseline and endpoint. The sample was predominantly males at both time points, with the average age increasing slightly from 9.40 ± 2.85 years to 9.85 ± 2.54 years. The YGTSS scores indicated a minimal improvement in tic symptoms from 24.57 ± 13.32 to 23.60 ± 19.65 over one year. Demographic and clinical details are presented in Table 1.

**Table 1.** Demographic and clinical variables of tic disorder patients at baseline and endpoint

| | Baseline (n = 35) | Endpoint (n = 20) |
|---|---|---|
| Sex (male/female) | 28/7 | 14/6 |
| Age (yr) | 9.40 ± 2.85 | 9.85 ± 2.54 |
| IQ | 94.80 ± 10.15 | 96.90 ± 10.75 |
| Duration until visit (mo) | 44.74 ± 37.60 | 54.05 ± 35.07 |
| YGTSS score | 24.57 ± 13.32 | 23.60 ± 19.65 |
| Motor tic score | 7.03 ± 3.89 | 7.00 ± 4.90 |
| Phonic tic score | 4.69 ± 4.63 | 3.60 ± 5.48 |
| Total tic score | 11.71 ± 6.41 | 10.60 ± 9.30 |
| Impairment score | 12.86 ± 7.89 | 13.00 ± 11.29 |

Values are presented as number only or mean ± standard deviation.
IQ, intelligence quotient; YGTSS, Yale Global Tic Severity Scale.

**Table 2.** Cytokine levels of tic disorder patients at baseline and at endpoint

| Cytokine | Baseline (n = 35) | Endpoint (n = 20) |
|---|---|---|
| Pro-inflammatory | | |
| GM-CSF | 0.13 ± 0.44 | 0.00 ± 0.00 |
| IFN-α2 | 4.09 ±6.98 | 8.52 ± 4.06 |
| IFN-γ | 0.49 ± 0.52 | 34.26 ± 7.79 |
| IL-1β | 3.54 ± 2.57 | 11.71 ± 14.50 |
| IL-2 | 0.24 ± 0.16 | 1.97 ± 3.52 |
| IL-5 | 1.26 ± 0.96 | 1.62 ± 0.74 |
| IL-6 | 0.37 ± 0.24 | 1.03 ± 0.53 |
| IL-8 | 12.65 ± 6.77 | 14.15 ± 5.09 |
| IL-12 p40 | 14.79 ± 9.93 | 37.96 ± 14.93 |
| IL-12 p70 | 0.91 ± 0.43 | 2.49 ± 2.94 |
| IL-17a | 1.63 ± 6.15 | 14.27 ± 26.80 |
| TNF-α | 7.18 ± 10.14 | 7.85 ± 1.99 |
| Anti-inflammatory | | |
| IL-1ra | 235.21 ± 158.40 | 11.71 ± 14.50 |
| IL-4 | 0.39 ± 0.23 | 0.07 ± 0.03 |
| IL-10 | 4.98 ± 4.11 | 12.08 ± 9.69 |
| IL-13 | 5.67 ± 8.60 | 14.74 ± 10.51 |

Values are presented as mean ± standard deviation.
GM-CSF, granulocyte-macrophage colony-stimulating factor; IFN, interferon; IL, interleukin; TNF, tumor necrosis factor.

## Cytokine Level Changes

The analysis of cytokine levels from baseline to endpoint showed several changes. Table 2 lists the average cytokine levels for all participants from whom data were collected at either baseline or endpoint. Table 3 compiles the data from participants with samples collected at baseline and endpoint, facilitating a before-and-after comparison of cytokine levels. Significant increases were observed in interferon (IFN)-α2 (2.74 ± 2.21 to 8.28 ± 3.91), IFN-γ (0.43 ± 0.42 to 34.22 ± 7.93), IL-1β (3.86 ± 2.89 to 12.32 ± 15.19), IL-6 (0.31 ± 0.16 to 1.03 ± 0.55), IL-10 (5.56 ± 5.17 to 12.92 ± 9.86), IL-12 p40 (15.35 ± 5.08 to 39.25 ± 14.34), IL-12 p70 (0.84 ± 0.40 to 2.58 ± 3.10), and IL-13 (7.19 ± 10.42 to 14.57 ± 11.10), while significant decreases were observed in IL-1ra (182.60 ± 71.54 to 116.93 ± 50.60) and IL-4 (0.37 ± 0.15 to 0.07 ± 0.03).

## Correlation between Cytokine Levels and Yale Global Tic Severity Scale Sub-scores at Endpoint

At the endpoint, a correlation analysis was conducted between cytokine levels and YGTSS sub-scores. The sub-scores of the YGTSS are divided into motor, phonic, and impairment scores, and the sum of these constitutes

**Table 3.** Cytokine levels of tic disorder patients reporting at both baseline and endpoint

| Cytokine | Baseline (n = 18) | Endpoint (n = 18) | $p$ value |
|---|---|---|---|
| Pro-inflammatory | | | |
| GM-CSF | 0.12 ± 0.36 | 0.00 ± 0.00 | 0.180 |
| IFN-α2 | 2.74 ± 2.21 | 8.28 ± 3.91 | < 0.001* |
| IFN-γ | 0.43 ± 0.42 | 34.22 ± 7.93 | < 0.001* |
| IL-1β | 3.86 ± 2.89 | 12.32 ± 15.19 | 0.035* |
| IL-2 | 0.26 ± 0.19 | 2.08 ± 3.69 | 0.052 |
| IL-5 | 1.51 ± 1.14 | 1.74 ± 0.66 | 0.310 |
| IL-6 | 0.31 ± 0.16 | 1.03 ± 0.55 | < 0.001* |
| IL-8 | 12.60 ± 6.09 | 14.21 ± 5.37 | 0.359 |
| IL-12 p40 | 15.35 ± 5.08 | 39.25 ± 14.34 | < 0.001* |
| IL-12 p70 | 0.84 ± 0.40 | 2.58 ± 3.10 | 0.032* |
| IL-17a | 0.81 ± 2.27 | 13.85 ± 27.79 | 0.065 |
| TNF-α | 8.55 ± 14.05 | 7.65 ± 1.94 | 0.779 |
| Anti-inflammatory | | | |
| IL-1ra | 182.60 ± 71.54 | 116.93 ± 50.60 | 0.001* |
| IL-4 | 0.37 ± 0.15 | 0.07 ± 0.03 | < 0.001* |
| IL-10 | 5.56 ± 5.17 | 12.92 ± 9.86 | < 0.001* |
| IL-13 | 7.19 ± 10.42 | 14.57 ± 11.10 | 0.019* |

Values are presented as mean ± standard deviation.
GM-CSF, granulocyte-macrophage colony-stimulating factor; IFN, interferon; IL, interleukin; TNF, tumor necrosis factor.
*$p < 0.05$.

the total YGTSS score. IFN-γ showed a significant correlation with motor tic scores (r = −0.505, $p$ = 0.023), impairment scores (r = −0.557, $p$ = 0.011), and total YGTSS scores (r = −0.485, $p$ = 0.030). Detailed results on all cytokines are presented in Table 4.

### Correlation between Cytokine Level Changes and Yale Global Tic Severity Scale Score Changes

A correlation analysis was conducted to evaluate the relationship between cytokine level changes and YGTSS scores. This revealed that changes in anti-inflammatory cytokine, IFN-γ levels were significantly associated with changes in the severity of tic disorders (r = −0.564, $p$ = 0.015). Detailed results of this correlation analysis are presented in Table 5.

### Subgroup Analysis on the Improvement of Tic Symptoms

Patients were divided into 'improved' and 'persistent' groups based on changes in their YGTSS scores, as mentioned before. The 'improved' group (n = 26 at baseline, n = 15 at endpoint) was characterized by reductions in YGTSS scores (mean YGTSS score change = −11.11 ± 7.11). In contrast, the 'persistent' group (n = 9 at baseline, n = 5 at endpoint) showed no improvement or worsening of scores (mean YGTSS score change = 11.50 ± 12.76). IL-5 levels at baseline (0.72 ± 0.42 vs. 1.44 ± 1.03) and IFN-γ levels at endpoint (26.90 ± 4.15 vs. 36.72 ± 7.18) were significantly higher in the improved group. Detailed

**Table 5.** Correlation analysis on the effect of cytokine level changes on the change of YGTSS scores (endpoint − baseline)

| Cytokine level change (endpoint − baseline) | Correlation coefficient (r) to YGTSS score change (endpoint − baseline) | $p$ value |
|---|---|---|
| Pro-inflammatory | | |
| GM-CSF | 0.030 | 0.905 |
| IFN-α2 | 0.388 | 0.112 |
| IFN-γ | −0.564 | 0.015* |
| IL-1β | 0.293 | 0.238 |
| IL-2 | 0.269 | 0.280 |
| IL-5 | 0.138 | 0.584 |
| IL-6 | 0.092 | 0.716 |
| IL-8 | −0.001 | 0.998 |
| IL-12 p40 | 0.101 | 0.689 |
| IL-12 p70 | −0.199 | 0.428 |
| IL-17a | 0.287 | 0.249 |
| TNF-α | −0.369 | 0.132 |
| Anti-inflammatory | | |
| IL-1ra | 0.246 | 0.325 |
| IL-4 | 0.083 | 0.743 |
| IL-10 | 0.163 | 0.519 |
| IL-13 | 0.159 | 0.528 |

GM-CSF, granulocyte-macrophage colony-stimulating factor; IFN, interferon; IL, interleukin; TNF, tumor necrosis factor; YGTSS, Yale Global Tic Severity Scale.
*$p < 0.05$.

**Table 4.** Correlation coefficients between cytokine levels and YGTSS sub-scores at endpoint

| Cytokine | Motor tic score | Phonic tic score | Impairment score | Total YGTSS score |
|---|---|---|---|---|
| Pro-inflammatory | | | | |
| GM-CSF | 0.096 | −0.155 | −0.063 | −0.055 |
| IFN-α2 | −0.003 | −0.235 | 0.261 | 0.083 |
| IFN-γ | −0.505* | −0.140 | −0.557* | −0.485* |
| IL-1β | 0.115 | −0.199 | 0.292 | 0.141 |
| IL-2 | 0.153 | −0.189 | 0.324 | 0.172 |
| IL-5 | −0.030 | 0.351 | −0.028 | 0.074 |
| IL-6 | −0.034 | −0.327 | −0.090 | −0.152 |
| IL-8 | −0.058 | 0.085 | −0.013 | 0.002 |
| IL-12 p40 | 0.234 | 0.070 | 0.162 | 0.171 |
| IL-12 p70 | −0.225 | −0.264 | −0.303 | −0.304 |
| IL-17a | 0.218 | −0.125 | 0.385 | 0.240 |
| TNF-α | 0.050 | 0.164 | −0.036 | 0.037 |
| Anti-inflammatory | | | | |
| IL-1ra | 0.013 | 0.052 | 0.058 | 0.051 |
| IL-4 | −0.129 | 0.027 | −0.047 | −0.052 |
| IL-10 | 0.137 | 0.112 | 0.012 | 0.072 |
| IL-13 | 0.001 | −0.283 | −0.157 | −0.169 |

GM-CSF, granulocyte-macrophage colony-stimulating factor; IFN, interferon; IL, interleukin; TNF, tumor necrosis factor; YGTSS, Yale Global Tic Severity Scale.
*$p < 0.05$

**Table 6.** Cytokine level changes in improved and persistent tic disorder patient groups

| Cytokine | Persistent | Improved | *p* value |
|---|---|---|---|
| Pro-inflammatory (baseline) | | | |
| GM-CSF | 0.00 ± 0.00 | 0.18 ± 0.51 | 0.303 |
| IFN-α2 | 1.64 ± 0.96 | 4.93 ± 7.95 | 0.228 |
| IFN-γ | 0.50 ± 0.74 | 0.48 ± 0.45 | 0.939 |
| IL-1β | 2.31 ± 1.88 | 3.96 ± 2.68 | 0.098 |
| IL-2 | 0.20 ± 0.10 | 0.25 ± 0.17 | 0.414 |
| IL-5 | 0.72 ± 0.42 | 1.44 ± 1.03 | 0.006* |
| IL-6 | 0.27 ± 0.13 | 0.41 ± 0.25 | 0.126 |
| IL-8 | 9.74 ± 2.77 | 13.66 ± 7.47 | 0.137 |
| IL-12 p40 | 11.40 ± 4.57 | 15.96 ± 11.04 | 0.241 |
| IL-12 p70 | 0.81 ± 0.31 | 0.94 ± 0.46 | 0.431 |
| IL-17a | 0.76 ± 1.67 | 1.93 ± 7.09 | 0.630 |
| TNF-α | 11.56 ± 20.02 | 5.67 ± 1.55 | 0.403 |
| Anti-inflammatory (baseline) | | | |
| IL-1ra | 184.01 ± 59.96 | 252.94 ± 178.05 | 0.096 |
| IL-4 | 0.30 ± 0.11 | 0.43 ± 0.25 | 0.158 |
| IL-10 | 3.47 ± 1.94 | 5.35 ± 4.57 | 0.099 |
| IL-13 | 2.49 ± 3.99 | 6.78 ± 9.52 | 0.202 |
| Pro-inflammatory (endpoint) | | | |
| GM-CSF | 0.00 ± 0.00 | 0.00 ± 0.00 | 0.578 |
| IFN-α2 | 10.17 ± 7.22 | 7.96 ± 2.49 | 0.537 |
| IFN-γ | 26.90 ± 4.15 | 36.72 ± 7.18 | 0.010* |
| IL-1β | 20.08 ± 28.19 | 8.92 ± 4.98 | 0.428 |
| IL-2 | 4.25 ± 6.82 | 1.21 ± 1.00 | 0.376 |
| IL-5 | 1.10 ± 0.51 | 1.79 ± 0.73 | 0.070 |
| IL-6 | 1.04 ± 0.30 | 1.03 ± 0.60 | 0.981 |
| IL-8 | 14.34 ± 3.50 | 14.09 ± 5.62 | 0.928 |
| IL-12 p40 | 42.79 ± 9.86 | 36.35 ± 16.23 | 0.418 |
| IL-12 p70 | 1.63 ± 0.35 | 2.78 ± 3.37 | 0.465 |
| IL-17a | 36.21 ± 49.24 | 6.96 ± 7.28 | 0.255 |
| TNF-α | 8.65 ± 2.58 | 7.58 ± 1.79 | 0.310 |
| Anti-inflammatory (endpoint) | | | |
| IL-1ra | 164.13 ± 92.26 | 128.83 ± 77.55 | 0.410 |
| IL-4 | 0.08 ± 0.02 | 0.07 ± 0.03 | 0.744 |
| IL-10 | 10.10 ± 4.85 | 12.74 ± 10.89 | 0.610 |
| IL-13 | 12.19 ± 5.35 | 15.59 ± 11.77 | 0.545 |

Values are presented as mean ± standard deviation.
GM-CSF, granulocyte-macrophage colony-stimulating factor; IFN, interferon; IL, interleukin; TNF, tumor necrosis factor.
*$p < 0.05$.

cytokine profile comparisons are provided in Table 6.

## DISCUSSION

This study showed minimal improvement in YGTSS scores over one year among children with tic disorders. Significant changes in cytokine levels were noted, with increases in pro-inflammatory cytokines such as IFN-α2, IFN-γ, IL-1β, IL-6, IL-10, IL-12 p40, IL-12 p70, and IL-13, and decreases in anti-inflammatory cytokines like IL-1ra and IL-4. IFN-γ levels showed significant correlations to YGTSS scores and its motor and impairment sub-scores at the endpoint. At the same time, changes in IFN-γ levels were also significantly associated with YGTSS scores. IL-5 levels at baseline and IFN-γ levels at endpoint were significantly higher in patients with improved tic symptoms than those with worsened symptoms.

Previous studies have also reported results similar to those found in our research. Tao *et al.* [12] analyzed 1,724 patients and found that tic disorder patients showed higher IL-6 levels than controls. Additional findings indicated that IL-2, IL-4, IL-6, IL-10, TNF-α, and IFN-γ may

significantly influence the development and severity of tic disorder. On the other hand, a Dutch study on 66 children with tic disorder did not find significant differences in median serum cytokine levels between patients and controls. However, they observed that IL-12 levels were inversely related to the severity of comorbid obsessive-compulsive symptoms [8]. A relatively recent meta-analysis by Li *et al.* [14] revealed significant immune alterations, including elevated levels of IL-6 and TNF-α and disproportionate T-cell subpopulations in tic disorder patients, indicating an immune contribution to the disease. An animal study on rats by Liu *et al.* [15] also showed that rats induced with tic disorder had significant increases in the plasma levels of several cytokines, including IL-4, IL-10, IL-12, IFN-γ, and TNF-α. Although various studies have shown that different cytokines are involved in the onset and progression of tic disorders, the results have not been consistent. This inconsistency suggests that the relationship between tic disorders and cytokines is not straightforward and may be influenced by complex and unidentified mediators.

Our study identified IFN-γ and IL-5 as pivotal cytokines in tic disorders. Changes in IFN-γ levels were significantly correlated with tic severity changes, indicating its potential role as a biomarker for tic exacerbation. Patients with higher IFN-γ levels at the endpoint were more likely to have more severe tics, indicating its potential role in the persistence and worsening of clinical symptoms. Conversely, higher baseline levels of IL-5 were associated with improvements in tic symptoms, suggesting that IL-5 may play a protective role or indicate a subgroup of patients more likely to respond to treatment or other ameliorating factors. IL-5 is crucial for eosinophil activity and allergic reactions. Since research [16] has linked allergic conditions with tic disorders, IL-5's role in these allergic processes might also influence the symptoms of tic disorders.

The longitudinal design of this study is a notable strength, allowing for the observation of changes over time. Additionally, the homogeneity of the sample, comprising medication-free patients, reduces confounding variables related to pharmacological effects. However, the study's small sample size is a limiting factor. The absence of a control cohort observed concurrently over the year also represents a research limitation. There might have been external factors influencing cytokine levels that were not controlled for, potentially introducing variability in the results. Future research should replicate these findings in more extensive, multi-center studies to enhance their generalizability. Furthermore, exploring correlations not only with cytokine levels but also with neuroimaging variables like brain volume, as demonstrated in previous studies, may contribute to advancing this field [17]. Clinical trials assessing the efficacy of cytokine-targeted therapies could provide valuable insights into new treatment modalities for tic disorders.

In conclusion, this study underscores the complex relationship between cytokine levels and tic disorder severity. The significant changes in IFN-γ and IL-5 levels among various other cytokines and their association with tic symptoms highlight the importance of immune mechanisms in tic disorders. These findings lay a foundation for future research on cytokine biomarkers and therapeutic targets, aiming to enhance the management and outcomes of tic disorder patients.

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## ■ Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

## ■ Author Contributions

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