

Article

# Evaluation of IL-6 and IL-23 as Inflammatory Biomarkers in Patients with Thyroid Disorders

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**Abstract:** The study included 90 participants divided into three groups: 40 patients with hypothyroidism, 26 patients with hyperthyroidism, and 24 healthy controls. Serum IL-6 and IL-23 concentrations were measured, A significant difference in serum IL-6 levels was observed among the three groups ( $F = 8.709$ ,  $P < 0.001$ ). The highest mean IL-6 concentration was recorded in the hyperthyroid group ( $46.7693 \pm 43.0165$ ), followed by the control group ( $33.9306 \pm 31.2150$ ), whereas the hypothyroid group showed the lowest concentration ( $16.6500 \pm 11.6646$ ). Tukey's test demonstrated a significant difference between the hypothyroid and hyperthyroid groups, while the control group was not significantly different from either group. Serum IL-23 levels also differed significantly among the groups ( $F = 4.803$ ,  $P = 0.011$ ). The hyperthyroid group had the highest mean IL-23 concentration ( $26.9527 \pm 23.2794$ ), followed by the control group ( $21.4263 \pm 11.3879$ ), and the hypothyroid group had the lowest concentration ( $15.3270 \pm 8.9544$ ).

**Keywords:** Interleukin-6, Interleukin-23, Inflammation, Cytokines, Thyroid Dysfunction

## Introduction

The thyroid gland is an important endocrine organ that regulates a wide range of physiological processes through the production of thyroid hormones. Thyroid hormones influence energy metabolism, thermogenesis, cardiovascular function, growth, and development. Disturbances in thyroid hormone production may result in hypothyroidism or hyperthyroidism, both of which can produce substantial systemic effects [1].

Interleukin-6 (IL-6) is a multifunctional cytokine involved in both innate and adaptive immunity. It is produced by several cell types, including immune cells and tissue cells, in response to inflammatory stimuli. IL-6 participates in acute-phase responses, immune-cell differentiation, and regulation of inflammatory processes. Experimental evidence also suggests that IL-6 signaling can directly influence thyroid follicular function, demonstrating an interaction between inflammatory pathways and thyroid physiology [2].

IL-23 is another cytokine with an important role in immune regulation. It belongs to the IL-12 cytokine family and contributes to the maintenance and expansion of pathogenic T-helper 17 (Th17) responses. The IL-23/Th17 pathway has received considerable attention in autoimmune and

inflammatory disorders, including autoimmune thyroid disease. Studies have reported increased IL-23 concentrations or expression in thyroid autoimmune conditions, suggesting that IL-23-mediated immune regulation may contribute to thyroid inflammation [3], [4].

Previous investigations have particularly implicated IL-6 and IL-23 in autoimmune thyroid disorders. Increased circulating IL-6 has been reported in patients with Graves' disease, and cytokine concentrations may decrease following restoration of euthyroidism, supporting a possible association between thyroid activity and systemic inflammatory status [2], [5]. Similarly, IL-23 has been reported to be elevated in Hashimoto's thyroiditis, and experimental studies indicate that IL-23 can interact with pathways such as AKT/mTOR/NF-kB and contribute to inflammatory and oxidative processes within thyroid follicular cells [3], [6].

Therefore, assessment of inflammatory cytokines may provide additional information concerning the immunological consequences of altered thyroid function. The present study aimed to compare serum IL-6 and IL-23 concentrations among hypothyroid patients, hyperthyroid patients, and healthy controls and to determine whether these cytokines are associated with thyroid functional status.

## Materials and Method

A case-control study was conducted to investigate differences in serum inflammatory cytokines among individuals with thyroid dysfunction. Participants were divided into three groups according to their thyroid functional status: a hypothyroid group (Hypo), a hyperthyroid group (Hyper), and a healthy control group. The study included 90 participants, consisting of 40 patients with hypothyroidism, 26 patients with hyperthyroidism, and 24 apparently healthy controls. Participants were classified according to their clinical diagnosis and thyroid function status.

Serum concentrations of interleukin-6 (IL-6) and interleukin-23 (IL-23) were determined using appropriate immunological assay methods, such as enzyme-linked immunosorbent assay (ELISA), according to the manufacturer's instructions for the assay kits used in the study. For each cytokine, serum samples were analyzed together with appropriate standards and controls. Concentrations were calculated from the corresponding standard curves and expressed in the units specified by the assay manufacturer.

## Results and Discussion

Serum IL-6 and IL-23 concentrations were compared among the hypothyroid, hyperthyroid, and control groups. Serum IL-6 levels demonstrated a highly significant difference among the three groups ( $F = 8.709$ ,  $P < 0.001$ ). The hyperthyroid group showed the highest mean IL-6 concentration ( $46.7693 \pm 43.0165$ ), followed by the control group ( $33.9306 \pm 31.2150$ ), whereas the hypothyroid group showed the lowest mean concentration ( $16.6500 \pm 11.6646$ ). According to Tukey's post-hoc test, the hyperthyroid group differed significantly from the hypothyroid group, whereas the control group shared the same statistical grouping with both groups and therefore did not differ significantly from either group.

IL-23 levels also showed a statistically significant difference among the three groups ( $F = 4.803$ ,  $P = 0.011$ ). The hyperthyroid group exhibited the highest mean IL-23 concentration ( $26.9527 \pm 23.2794$ ), followed by the control group ( $21.4263 \pm 11.3879$ ), while the hypothyroid group had the lowest mean value ( $15.3270 \pm 8.9544$ ). Tukey's post-hoc test demonstrated a significant difference between the hypothyroid and hyperthyroid groups, whereas the control group was statistically comparable with both patient groups.

**Table 1.** Serum IL-6 and IL-23 concentrations among hypothyroid, hyperthyroid, and control groups.

| Parameter | Hypo (n=40)<br>Mean +/- S.D. | Hyper (n=26)<br>Mean +/- S.D. | Control (n=24)<br>Mean +/- S.D. | F-value | P-value  |
|-----------|------------------------------|-------------------------------|---------------------------------|---------|----------|
| IL-6      | 16.6500a +/-<br>11.6646      | 46.7693b +/-<br>43.0165       | 33.9306ab +/-<br>31.2150        | 8.709   | <0.001** |
| IL-23     | 15.3270a +/-<br>8.9544       | 26.9527b +/-<br>23.2794       | 21.4263ab +/-<br>11.3879        | 4.803   | 0.011*   |

S.D. = Standard deviation. Means sharing the same superscript letter are not significantly different according to Tukey's post-hoc test. \* Significant at  $P < 0.05$ . \*\* Significant at  $P < 0.01$ .

Serum IL-6 concentration was significantly higher in hyperthyroid patients than in hypothyroid patients. This finding is consistent with previous observations that hyperthyroidism, particularly Graves' disease, may be accompanied by activation of inflammatory pathways. Earlier studies reported elevated circulating IL-6 concentrations in patients with Graves' disease compared with healthy controls, supporting the concept that thyroid hyperactivity can occur in parallel with increased inflammatory cytokine production [5]. Other work reported changes in circulating cytokines during antithyroid treatment and restoration of euthyroidism, further suggesting that cytokine levels may be influenced by thyroid functional status and/or inflammatory activity [2].

The elevated IL-6 observed in the hyperthyroid group may reflect interactions between thyroid hormone excess, immune activation, and inflammatory signaling. Thyroid hormones have broad metabolic effects, and increased metabolic activity may influence cellular stress and inflammatory mediator production. Inflammatory cytokines may also affect thyroid function, indicating that the relationship between thyroid hormones and inflammation can be bidirectional. Experimental work has demonstrated that IL-6 signaling can inhibit aspects of thyroid follicular function under specific experimental conditions, supporting a functional relationship between cytokine signaling and thyroid physiology [7].

In contrast, the hypothyroid group had the lowest IL-6 concentration in the present study. This does not necessarily indicate an absence of inflammatory activity in hypothyroidism, because the inflammatory response may vary according to the underlying cause of hypothyroidism, disease duration, treatment status, and the presence or absence of autoimmune thyroiditis. Autoimmune hypothyroidism, such as Hashimoto's thyroiditis, may exhibit a cytokine profile different from non-autoimmune hypothyroidism. Studies of autoimmune thyroid disease have reported increased inflammatory cytokines and enhanced Th17-related activity, particularly in Hashimoto's thyroiditis [8].

The present study also demonstrated a significant difference in IL-23, with the hyperthyroid group showing the highest mean concentration and the hypothyroid group the lowest. IL-23 is a key regulator of Th17-cell responses and is increasingly recognized as an important component of inflammatory and autoimmune mechanisms. Previous studies have demonstrated increased serum IL-23 in Hashimoto's thyroiditis and suggested that IL-23 may contribute to thyroid autoimmunity [3]. Increased IL-23-related signaling has also been observed in thyroid follicular cells, where IL-23 may promote inflammatory and oxidative responses through AKT/mTOR/NF- $\kappa$ B-associated mechanisms [6], [9].

The higher IL-23 concentration observed in the hyperthyroid group is compatible with evidence that IL-23 is involved in autoimmune thyroid disorders. Recent research has reported increased IL-23 levels in both Graves' disease and Hashimoto's thyroiditis compared with healthy individuals, supporting a role for IL-23 in endocrine autoimmune inflammation. However, tissue-based studies have shown that IL-23 expression may differ between Hashimoto's thyroiditis and Graves' disease, indicating that serum cytokine concentrations and local tissue expression do not necessarily show identical patterns [4].

The simultaneous increase in IL-6 and IL-23 in the hyperthyroid group may be biologically relevant because these cytokines are interconnected with immune-cell differentiation and inflammatory responses [10]-13]. IL-6 and IL-23 are associated with the development and maintenance of Th17-related immune responses [14]. Increased activity of this inflammatory axis could contribute to the immune abnormalities observed in some thyroid disorders [8], [1], [15].

## Conclusion

The present study demonstrated significant differences in serum IL-6 and IL-23 concentrations among hypothyroid, hyperthyroid, and healthy control groups. Both cytokines showed the highest mean concentrations in the hyperthyroid group and the lowest in the hypothyroid group, with significant differences particularly between these two groups. These findings suggest that altered thyroid function, especially hyperthyroidism, may be associated with increased inflammatory and immune activity involving the IL-6/IL-23 axis. However, further studies with larger sample sizes and detailed assessment of thyroid disease etiology and treatment status are needed to clarify the underlying mechanisms.

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