DOI: https://doi.org/10.53350/pjmhs2023173278

ORIGINAL ARTICLE

Clinical Significance of Elevated Serum IL-36γ Levels in Patients with Early-Stage Hashimoto's Thyroiditis

SABA ARIF[1], AZRA SAKHAWAT[2], NAVEEDA NAWAZ[3], MARIA SARFRAZ[4], RABBIA SHABBIR[5], SAIRA MUSHTAQ[6]
[1]*Demonstrator Biochemistry, Akhtar Saeed Medical and Dental College, Lahore*
[2]*Phd Scholar Biochemistry, University of Lahore*
[3]*Demonstrator, Basic Medical Science, Mohi-ud-din Islamic Medical College, Mirpur, Azad Kashmir*
[4]*Associate professor Biochemistry, Rawal Institute of health sciences, Islamabad*
[5]*Assistant professor Biochemistry, Dental College HITEC IMS*
[6]*Associate Professor Biochemistry, Aziz Fatima Medical and Dental College, Faisalabad*
Corresponding author: Saba Arif, Email: dr.sabarizwan786@gmail.com

ABSTRACT

Background: Hypothyroidism was the diagnosed and treated as a result of health related quality of life issues. The aim of this study was that to evaluate the effect of IL-36 γ, Tg-Ab and TOP-Ab in the Hashimoto's Thyroiditis (HT).

Study design: This was a cross sectional study conducted at Rawal Institute of health sciences, Islamabad duration of study was six month, from April 2022 to September 2022.

Methods: A total number of the patients was n=150 which divided into two group, control and HT group. To perform EISA for the estimation of free triiodothyronine 3, 4 (FT3, FT4), thyroid stimulating hormone (TSH), thyroid peroxidase antibody (TOP-Ab) and thyroid globulin antibody (Tg-Ab). The data was analyzed by SPSS 21.

Results: The serum IL-36γ show correlation with the TOP-Ab and FT3 in HT. The IL-36γ was significantly higher in HT as compared to the control group; p<0.001**. The IL-36γ show significant negative correlation with TOP-Ab (<0.001**, r-0.126) and non- significant positive correlation with FT3 (0.321, r= + 0.28) in HT patients. The Tg-Ab was show non- significant correlation with IL-36 γ; (P<=0. 928, r = 0.323).

Conclusions: IL-36 γ is diagnostic marker and show negative correlation with TPO-Ab in the patient serum of HT. Il-36 γ had significantly high in the HT patients. IL-36 γ may involve to the progression of pathogenesis and enhance the inflammatory responses. In HT, Tg-Ab was significantly reduced than TPO-Ab but both contribute to the production of thyroid hormones.

Keywords: Interleukin, Thyroxin, Thyroid stimulating hormone, Peroxidase.

INTRODUCTION

Hashimoto's thyroiditis (HT) is the most prevalent autoimmune thyroid disorder. Between 20–30% of patients develop hypothyroidism as a result of the persistent inflammation of the thyroid tissue. In the early 20th century, the autoimmune thyroiditis (AIT), reporting patients with follicular cell destruction follow by an inflammatory process, lymphocytic infiltration, goiter, and fibrosis.[1, 2] The prevalence of HT is approximately 3-4%, accounting for approximately 22.5% of all thyroid diseases. The incidence of this disease has been increasing due to changes in lifestyle and advancements in detection technology, and the age of onset is primarily. AIT affects about 0.3-1.5/1000 subjects per year, with women being more affected than men. In the pregnant women which have high rate of miscarriage, and premature birth in HT patients.[3, 4] Hashimoto's Thyroiditis link between HT and some HLA genes has been reported, and suggest a genetic predisposition to thyroid autoimmunity. The iodine containing medication can participate HT diseases in the people. The most common clinical features of HT have been reported to be goiter, short height, menstrual disorders, exophthalmos and constipation.[5] But even though the mechanism of pathogenesis of HT is unidentified, autoimmune diseases are usually triggered by genetic factors, environmental factors, and autoimmune system abnormalities.[6] It is frequently assumed that HT occurs as a consequence of adverse immune related lymphocyte expression, which obstructs thyroid autoimmune tolerance and results in autoantibodies against glandular tissue. [7] The different diseases such as coeliac, alopecia and type 1 diabetes all that are linked with HT and treated with L-thyroxine should be initiated as soon as possible in the presence of hypothyroidism, however, the best care for people who have normal free thyroxine levels, no symptoms, but a slightly high thyroid-stimulating hormone (TSH) between the upper reference level. [8] The TPO-Ab can be used to diagnose thyroiditis and 80-90% of HT patients. To diagnose HT, a laboratory test to detect the amount of autoantibodies against the thyroid gland. Despite the fact that Tg-Ab and TPO-Ab levels were elevated and TPO-Ab positivity was higher than Tg-Ab positivity. [9] In 2001, researchers identified interleukin (IL)-38, a new member of the IL-36 subfamily within the IL-1 superfamily. IL-38 can be produced by peripheral blood mononuclear cells, it was found that in Candida-induced human PBMCs, IL-38 reduced the production of TNF. It was discovered that IL-38 only had an anti-inflammatory effect at high concentrations.[10, 11]

METHODS

This was a cross sectional study conducted at Rawal Institute of health sciences, Islamabad duration of study was six month, from April 2022 to September 2022. A total number of the patients was n=150 which included all females. The sample were taken from the peripheral blood and collected from the hospital. According to inclusion criteria: diffused goiter, enlarge lobes, high concentration of serum TPO-Ab and Tg-Ab. Exclusion criteria: pregnancy, neoplasms, and infections are all examples. The patients were divided into two groups: n=60 in the control group and n=90 in the Hashimoto's thyroiditis group. The quantitative estimation of TPO-Ab, Tg-Ab, TSH, TF3, TF4 and IL-36γ were analysis by ELISA and performed by automated chemiluminescence immune assay analyzer (Abbott i2000). The statistically data was analyzed by SPSS 21. The spearman was used for correlation analysis of IL-36 with TPO-Ab and Tg-Ab. The p value was <0.005 show significant.

RESULTS

The data demonstrated in Table 1 to show the basic clinical information of the patients. The female was 40% and 60% in the control and Hashimoto's thyroiditis group. The mean of female age was 40 years in the normal and patient group.

Table 1: Basic information

Variables	Total number of Patients N=150		P=value
	Control group n=60(%)	HT group n=90(%)	
Gender (Female)	40%	60%	0.33
Age	48.33±12.23	49.12±10.6	0.76

Mean ± SEM: ANOVA SPS Test* p< 0.0; **p<0.01; ***p<0.001

Abbreviation used: Hashimoto's thyroiditis (HT)

The patient characteristics such as gender and age; which did not show significant results p>0.005 in both group.

According to our interpretation, the biomarker serum such as IL-36, TOP-Ab and Tg-Ab and TSH were show significant

changes in the HT group as compared to the control group; p<0.001**, <0.001** and <0.001** and <0.002**). The concentration of FT3 and FT4 had shown non-significant changes in HT patients; p>0.005 were seen in Table 2.

Table 2: Biochemical parameters in HT patients

Parameters	Control group	HT group	P=value
IL-36γ (pg/mL)	0.30 (0.20, 0.99)	355 (167.1, 1.22)	<0.001**
TPO-Ab (IU/mL)	0.35 (0.25, 0.34)	498.10 (125.50, 1327.1)	<0.001**
Tg-Ab (IU/mL)	0.89 (0.75. 1.55)	187.65 (60.2, 898.26)	<0.001**
TSH (mIU/L)	2.0 (1.55, 3.1)	3.50 (1.67, 7.1)	<0.002**
FT3 (pmol/L)	5.6 (5.5, 5.9)	4.98 (5.12, 5.1)	0.087
FT4 (pmol/L)	13.5 (12.33, 14.8)	13.22 (12.34, 14.11)	0.091

Mean ± SEM: ANOVA SPS Test* p< 0.0; **p<0.01; ***p<0.001

Table 3: To evaluate the correlation analysis of serum IL-36 γ with the thyroid function related indicators in HT patient.

Variables	IL-36 γ	P=value
TPO-Ab	43.10±12.1	<0.001**, r= - 0.126
Tg-Ab	12.1±0.5	=0. 928, r= 0.323
FT3	45.2±10.1	=0.321, r= + 0.28

Mean ± SEM: ANOVA SPS Test* p< 0.0; **p<0.01; ***p<0.001

According to a spearman correlation was that the serum IL-36 γ show a closest significant and negative correlation with the TOP-Ab in HT group; (p<0.001**, r=-0.126). There was no significant differences between IL-36γ and Tg-Ab; (p=0.928; r=0.323). The concentration of FT3 show non-significant positive correlation with IL-36 γ; (p=0.321, r=+0.28).

Table 4: Diagnostic serum biomarkers for HT

Serum Biomarker	Hashimoto's Thyroiditis	P=value
Alone biomarker		
IL-36γ	43.02±11.81	<0.01*
Combine biomarker		
IL-36γ+TSH+FT4	44.33±10.5	<0.01*

Mean ± SEM: ANOVA SPS Test* p< 0.0; **p<0.01; ***p<0.001

According to our study the serum concentration of IL-36γ had used alone to diagnose HT, while the serum TSH, FT4 and IL-36γ had used to diagnose for HT show significant result; p<0.01*.

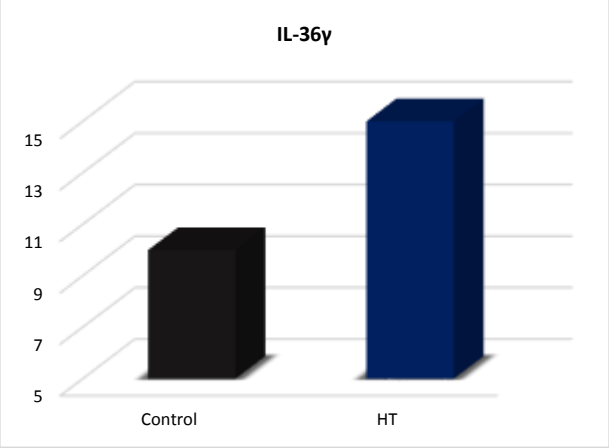

Figure 1: Serum IL-36 γ show in control and Hashimoto's thyroiditis group. It indicate the significantly p<0.001** high concentration of IL-36γ in HT group.

DISCUSSION

This research to indicate the link between the presence of lifetime diagnosis of mood and anxiety and Hashimoto's disorder due to improper functioning of thyroid gland. According to clinical examination, HT patients were found to be in the early stages of illness development.[12]

In our finding to revealed that, in the early stage of HT patients having higher level of IL-36γ; p<0.001** than control group and show that IL-36γ used for diagnostic biomarker for HT. Our findings support the up regulation of IL-36 γ in HT, shows highly expressed in thyroid tissue in HT patients. These findings suggested that IL-36 is important in the pathogenesis of HT. IL-36 is involved in inflammatory responses and immune cell activation, and it regulates a variety of regulatory activities. IL-36 promotes Th17 cell differentiation, which leads to a cascade of inflammatory responses. Th17 cells are essential for the development of HT. The thyroid gland is predominantly composed of follicular epithelial cells that express IL-36. We were agreed with the previous study.[13, 14] According to our study to found that, the IL-36 γ show significant and negative correlation with TPO-Ab in HT patients. The production of thyroid hormones (T3 and T4) depends on thyroid peroxidase and thyroglobulin.[15, 16] TPO-Ab suppression of thyroid peroxidase may therefore lead to a decrease in the production of thyroid hormones. Nevertheless, we found no significant difference between TPO-Ab and in the levels free T4. The TPO always present over the surface of follicular cells of thyroid gland and destroy their structure to by activate cascade reaction so that, we can say IL-36 was inflammatory mediator which promote the progression of diseases in HT patients.[17] But Tg-Ab show non-significant correlation with IL-36 γ. The IL-36 γ show non-significant but positive correlation with FT3. Its concentration was changed in the abnormal condition. We are agreed with the previous research.[18, 19] Lactose intolerance was observed in nearly 76% of levothyroxine-treated HT patients (LT4). Levothyroxine which can reduce LT4 effectiveness in people and associated with bacterial overgrowth, improper absorption and destruction of villi, all of which increase the need for LT4. It is worthwhile to screen individuals for lactose intolerance if they require a high dosage of levothyroxine, have treatment resistance, or have difficulties controlling TSH.[20, 21] These findings show that IL-36 significantly involve to the cause of disease progression in HT, necessitating additional research into the biological characteristics and precise function of IL-36 in HT. Understanding IL-36 mode of action in HT may help us comprehend the underlying causes of the disease and open the door to investigating IL-36 as a potential treatment target for the condition.[22, 23]

CONCLUSIONS

IL-36 γ is diagnostic marker and show negative correlation with TPO-Ab in the patient serum of HT. Il-36 γ had significantly high in the HT patients. IL-36 γ may involve to the progression of pathogenesis and enhance the inflammatory responses. In HT, Tg-Ab was significantly reduced than TPO-Ab but both contribute to the production of thyroid hormones.

REFERENCES

1. Ali, A., Musbahi, O., White, V. L., & Montgomery, A. S. (2019). Spinal tuberculosis: a literature review. JBJS reviews, 7(1), e9.
2. Xu, Z., Wang, X., & Liu, Z. (2020). One-stage posterior debridement and single-segment interbody fusion for treating mono-segmental lumbar and lumbosacral spinal tuberculosis in adults following minimum 5-year follow-up. Journal of Orthopaedic Surgery and Research, 15(1), 1-8.
3. Jain, A. K., Rajasekaran, S., Jaggi, K. R., & Myneedu, V. P. (2020). Tuberculosis of the spine. JBJS, 102(7), 617-628.
4. Dunn, R. N., & Husien, M. B. (2018). Spinal tuberculosis: review of current management. The bone & joint journal, 100(4), 425-431.
5. Ali, A., Musbahi, O., White, V. L., & Montgomery, A. S. (2019). Spinal tuberculosis: a literature review. JBJS reviews, 7(1), e9.
6. Zhao, C., Pu, X., Zhou, Q., Huang, X., Zhang, C., Luo, L., ... & Xu, J. (2019). Can a posterior approach effectively heal thoracic and lumbar tuberculosis? Microbiology outcomes of the operative area. Journal of orthopaedic surgery and research, 14, 1-8.

7. Khanna, K., & Sabharwal, S. (2019). Spinal tuberculosis: a comprehensive review for the modern spine surgeon. The Spine Journal, 19(11), 1858-1870.
8. Wang, P., Liao, W., Cao, G., Jiang, Y., Rao, J., & Yang, Y. (2020). Characteristics and management of spinal tuberculosis in tuberculosis endemic area of Guizhou Province: a retrospective study of 597 patients in a teaching hospital. BioMed Research International, 2020.
9. Ruparel, S., Tanaka, M., Mehta, R., Yamauchi, T., Oda, Y., Sonawane, S., & Chaddha, R. (2022). Surgical management of spinal tuberculosis—the past, present, and future. Diagnostics, 12(6), 1307.
10. Rajasekaran, S., Soundararajan, D. C. R., Shetty, A. P., & Kanna, R. M. (2018). Spinal tuberculosis: current concepts. Global Spine Journal, 8(4_suppl), 96S-108S.
11. Xiong, W., Yu, B., Zhang, Y., Wang, C., Tang, X., Cao, H., ... & Tan, J. (2020). Minimally invasive far lateral debridement combined with posterior instrumentation for thoracic and lumbar tuberculosis without severe kyphosis. Journal of Orthopaedic Surgery and Research, 15, 1-10.
12. Gan, F., Jiang, J., Xie, Z., Huang, S., Li, Y., Chen, G., & Tan, H. (2018). Minimally invasive direct lateral interbody fusion in the treatment of the thoracic and lumbar spinal tuberculosisMini-DLIF for the thoracic and lumbar spinal tuberculosis. BMC Musculoskeletal Disorders, 19, 1-8.
13. Qiu, J., Peng, Y., Qiu, X., Gao, W., Liang, T., Zhu, Y., ... & Huang, D. (2022). Comparison of anterior or posterior approach in surgical treatment of thoracic and lumbar tuberculosis: a retrospective case–control study. BMC surgery, 22(1), 161.
14. Luan, H., Liu, K., Wang, Y., Kahaer, A., Sheng, W., Maimaiti, M., & Deng, Q. (2022). Efficacy of anterior debridement and bone grafting with fusion using internal fixation combined with anti-tuberculosis chemotherapy in the treatment of subaxial cervical tuberculosis. BMC surgery, 22(1), 1-8.
15. Li, W., Sun, X., Li, H., Meng, Z., Yang, Y., & Yao, S. (2019). Endovascular treatment of a ruptured thoracic aortic pseudoaneurysm secondary to Pott disease during a spine surgery: a case report and a literature review. Medicine, 98(16).
16. Jiang, G., Qin, W., Du, X., Zhang, Y., Zhang, M., Xiong, T., ... & Ou, Y. (2022). The Distribution Pattern of First-Line Anti-Tuberculosis Drug Concentrations between the Blood and the Vertebral Focus of Spinal Tuberculosis Patients. Journal of Clinical Medicine, 11(18), 5409.
17. Long, W., Gong, L., Cui, Y., Qi, J., Duan, D., & Li, W. (2020). Single posterior debridement, interbody fusion, and fixation on patients with continuous multivertebral lumbar spine tuberculosis (CMLSTB). BMC Musculoskeletal Disorders, 21(1), 1-7.
18. Tian, F., Tu, L. Y., Gu, W. F., Zhang, E. F., Wang, Z. B., Chu, G., ... & Zhao, J. (2018). Percutaneous versus open pedicle screw instrumentation in treatment of thoracic and lumbar spine fractures: A systematic review and meta-analysis. Medicine, 97(41).
19. Khorasanizadeh, M., Yousefifard, M., Eskian, M., Lu, Y., Chalangari, M., Harrop, J. S., ... & Rahimi-Movaghar, V. (2019). Neurological recovery following traumatic spinal cord injury: a systematic review and meta-analysis. Journal of Neurosurgery: Spine, 30(5), 683-699.
20. Abrisham, S. M. J., Ardekani, M. R. S., & Mzarch, M. A. B. (2020). Evaluation of the normal range of thoracic kyphosis and lumbar lordosis angles using EOS imaging. Maedica, 15(1), 87.
21. Wu, W., Li, Z., Wang, S., Zhang, H., Lin, R., & Lin, J. (2019). One-stage surgical treatment for consecutive multisegment thoracic spinal tuberculosis with kyphosis by posterior-only debridement, interbody fusion, and instrumentation. World neurosurgery, 128, e238-e244.
22. Wu, D., Sun, J., Fan, W., & Yuan, F. (2020). Unilateral or bilateral percutaneous endoscopic debridement and lavage treatment for lumbar spinal tuberculosis. World Neurosurgery, 140, e73-e80.
23. Hoeller, S., Roch, P. J., Weiser, L., Hubert, J., Lehmann, W., & Saul, D. (2021). C-reactive protein in spinal surgery: more predictive than prehistoric. European Spine Journal, 30, 1261-1269.