Increased serum levels of interleukin-17 and transforming growth factor-β in patients with Graves' disease

by Eryati Darwin8

Submission date: 07-Jan-2021 12:07PM (UTC+0800)
Submission ID: 1483958145
File name: transforming_growth_factor-_in_patients_with_Graves_disease.pdf (511.71K)
Word count: 1864
Character count: 9955

Increased serum levels of interleukin-17 and transforming growth factor-β in patients with Graves' disease

Increased serum levels of interleukin-17 and transforming growth factor-β in patients with Graves' disease

D Elvira[1*], E Nasrul[2], Y Sofyan[3], E Decroli[4] and E Darwin[5]

[1]Allergy-Immunology Division of Internal Medicine, Faculty of Medicine, Andalas University, Padang, Indonesia
[2]Department of Clinical Pathology, Faculty of Medicine, Andalas University, Padang, Indonesia
[3]Department of Anatomy, Faculty of Medicine, Andalas University, Padang, Indonesia
[4]Endocrine and Metabolic Division of Internal Medicine, Faculty of Medicine, Andalas University, Padang, Indonesia
[5]Department of Histology, Faculty of Medicine, Andalas University, Padang, Indonesia
[*]Corresponding author: dwitya.elvira@yahoo.com

Abstract. Graves' disease (GD) is an organ-specific autoimmune disease, characterized by excessive autoantibody levels due to tolerance breakdown of thyroid-specific autoantigens. To determine the role of interleukin-17 (IL-17) and transforming growth factor-β (TGF-β) in GD, we assessed their serum levels in patients with GD and healthy controls. Thirty patients with hyperthyroidism, goiter, and positive thyroid-stimulating hormone receptor antibody diagnosed as GD, according to the clinical diagnostic criteria for autoimmune thyroid disease. Blood samples were also from 30 healthy individuals matched for age and sex as a control. Serum levels of IL-17 and TGF-β were by using ELISA. IL-17 and TGF-β levels (14.43 ± 2.15 pg/mL and 10.44 ± 3.19 pg/mL, respectively) were significantly higher in patients with GD than in controls (7.07 ± 1.45 pg/mL and 4.95 ± 1.35 pg/mL, respectively). However, no correlation between IL-17 and TGF-β level in patients with GD. The elevated serum level of IL-17 and TGF-β in patients with GD reflects Th-2 predominance, which causes increasing of these pro-inflammatory cytokines.

Introduction

Graves' disease (GD) is an autoimmune disorder, characterized by excessive production of autoantibodies due to the breakdown of tolerance to thyroid-specific autoantigen. GD is also known as an organ-specific autoimmune disease that mostly in humans.[1] there is a report that GD may develop at any age, although it occurs 12 times more frequently in adults than in children.[2]

The impairment in GD involves the adaptive immune response, resulting from an imbalance of Th1, Th2 and Th17cells.[3] Th17 cells are CD4 T cells that secrete interleukin (IL)-17, which is known as a pro-inflammatory cytokine that plays a role in the pathogenesis of autoimmune disease.[4] Elevated of IL-17 levels has been found in patients with rheumatoid arthritis, systemic lupus erythematosus (SLE), and psoriasis, although the role of IL-17 in the pathogenesis of the autoimmune diseases is still unclear.[4]

Imbalance of Th1 and Th2 cells is also thought to be a cause of GD, where dysregulation of T-regulatory cells leads to increased Th2 cell numbers, thus stimulating the formation of autoantibodies specific to GD.[5] T-regulatory cells secrete cytokines, such as transforming growth factor-β (TGF-β) and IL-10, to maintain the function of T-regulatory cells.[6] TGF-β is a pro-inflammatory cytokine that plays a crucial role in differentiation of T-regulatory cells.[7]

This study aimed to analyze the difference in levels of IL-17 and TGF-β between patients with GD and healthy control and to investigate the correlation between IL-17 and TGF-β in patients with GD.

2. Methods

The study design was cross-sectional study using a comparative analytical observation. A sample of the study was measured using mean estimation formula, as mention below:

$$n = \frac{2\ x\ (Za - Zb)^2\ x\ Sc^2}{(u1 - u2)^2}$$

There are 30 samples, for each patients group and control group. This study was conducted in July 2017 and the participant were patients with Graves' disease, based on clinical and laboratory examination of Graves' disease. Patients with euthyroid, history of medication with thyroid drugs, immunosuppressive drugs and history of allergic and other autoimmune disease were an exclusion from this study. As a control group, we selected healthy person by matching age and gender with patients group, without a history of autoimmune disease and/or history of immunosuppressive medication. This research study reviewed by the Committee on the Research of the Faculty of Medicine, Andalas University No. 298/KEP/FK, with regards to the protection of human rights and welfare in medical and health research.

Serum samples were taken from patients and control group about threecc of venous blood into Vacutainer. IL-17 and TGF-βlevels were measured using ELISA method. Statistical analysis of the difference between each variable in patients and control group was done using *Mann-Whitney* test and correlation between IL-17 and TGF-βlevels were done using correlation regression analysis.

3. Results

Table 1 shows the characteristics of this study.

Table 1. Characteristic of the study subjects.

Variable	Mean
Age (years old)	40.6 ±14.8
Sex	
• Male	10 (33.3%)
• Female	20 (66.7%)
IL-17 (pg/mL)	14.43 ± 2.15
TGF-β (pg/mL)	10.44 ± 3.19

Table2 shows a significant difference in IL-17 and TGF-β levels between the two groups (P<0.05).IL-17 level was higher in patients with GD (14.43 ± 2.15 pg/mL) than in controls (7.07 ± 1.45 pg/mL). The TGF-β level was also higher in patients with GD (10.44 ± 3.19 pg/mL) than in controls (4.95 ± 1.35 pg/mL).

In this study, the association between IL-17 and TGF-β was also investigated as shown in figure 1, and no connection between IL-17 and TGF- was noted in patients with GD.

Table 2. Differences in the mean serum level of IL-17and TGF-βin both the groups.

Variable	GD	Control	*p*
IL-17 (pg/mL)	14.43 ± 2.15	7.07 ± 1.45	*p*=0,01
TGF-β (pg/mL)	10.44 ± 3.19	4.95 ± 1.35	*p*=0,07

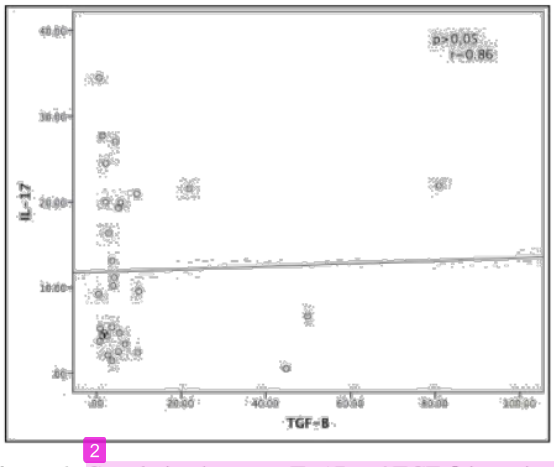

Figure 1. Correlation between IL-17 and TGF-β in patients with Graves' disease.

4. Discussion

GD is an autoimmune disorder that is thought to be a multifactorial disease, with the involvement of genetic, environmental and immunology mechanism. This study aimed to investigate the immunological processes in patients with GD, especially, the role of cytokines.

In this study, the IL-17 serum level was found to be significantly higher in patients with GD than in controls. IL-17 is a pro-inflammatory cytokine that is produced by Th-17. Increased IL-17 serum levels have also been in other autoimmune diseases, such as rheumatoid arthritis, SLE, and psoriasis. The mechanism underlying the increased IL-17 level in autoimmune disease is still unclear.[3] Zheng (2015) also observed an increased IL-17 serum level in patients with GD compared to those in patients with euthyroid GD and a control group and showed that the IL-23/IL-17 axis might participate in the pathogenesis of GD.[8] In thyroid-associated-ophthalmopathy (TAO), Shen (2015) also presented a higher IL-17 level in GD than that in active and inactive TAO [9], whereas, in contrast, Qin et al. (2012) established that the IL-17 level was higher in Hashimoto's thyroiditis (HT), an autoimmune thyroid disease stimulated by Th1, then in GD.[10] It can be explained by the fact that in HT, thyroid epithelial cells (TEC) not only present the autoantigen to the lymphocytes but also destroy the tissue directly. Therefore, Qin et al. proposed that a vicious cycle existed between TEC and lymphocytes through the production of IL-17, which plays a different role in the development of GD, leading to progression of chronic inflammation in HT.[10]

We also found increased serum levels of TGF-β as compared to that in the control group. TGF-β is a cytokine produced by T-regulatory cells to maintain their regulatory function. Increased TGF-β signaling in the T-cell lineage is thought to cause severe lymphoproliferati[2] autoimmunity. However, the role of TGF-β in the pathogenesis of autoimmunity is still unclear.[11] No correlation was between IL-17 and TGF-β in patients with GD in the present study.

Conclusion

Elevated serum levels of IL-17 and TGF-β were noted in patients with GD, indicating that these cytokines play a role in the pathogenesis of autoimmune disease. Increasing of these cytokines reflect the involvement of Th-2 predominance in Graves' disease, which further research needs to investigate the involvement of other pro-inflammatory cytokines in GD patients.

References

[1] McLachlan S and Rapoport B 2014 Breaking tolerance to thyroid antigens: changing concepts in thyroid autoimmunity *Endocr. Rev.* **35** 59-106
[2] Karasek M and Lewinski A 2003 Etiopathogenesis of Graves' disease *Neuro. Endocrinol. Lett.* **24(3-4)** 1-6
[3] Tabarkiewicz J, Pogoda K, Karczmarczyk A, Pozarowski P and Giannopoulos K 2015 *Arch. Immunol. Ther. Exp.* **63(6)** 435-49
[4] Peng D, Xu B, Wang Y, Guo H and Jiang Y 2013 A high frequency of circulating Th22 and Th17 cells in patients with new onset Graves' disease *Plos ONE* **8(7)** 1-8
[5] Klatka M, Grywalska E, Partyka M, Charytanowicz M and Kiszczak-bochynska E 2014 Th17 and Treg cells in adolescents with Graves' disease: Impact of treatment with methimazole on these cell subsets *Autoimmunity* **47(3)** 201-11
[6] Dhamne C, Chung Y, Alousi A M, Cooper L and Tran D 2013 Peripheral and thymic Foxp3+ regulatory T cells in search of origin, distinction and function *Front. Immunol.* **4(8)** 1-11
[7] Travis M and Sheppard D 2014 TGF- activation and function in immunity *Ann. Rev. Immunol.* **32** 51-82
[8] Zheng L, Ye P and Liu C 2013 The role of the IL-23/IL-17 axis in the pathogenesis of Graves' disease *Endocrine* **60(5)** 591-7
[9] Shen J, Li Z, Li W, Ge Y and Xie M 2015 Th1, Th2, and Th17 cytokine involvement in thyroid associated ophthalmopathy *Dis. Markers* 1-6
[10] Qin Q, Liu P, Liu L, Wang R and Yan N 2012 The increased but non-predominant expression of Th17-and Th1-specific cytokines in Hashimoto's thyroiditis but not in Graves' disease *Braz. J. Med. Biol. Res.* **45(12)** 1202-8
[11] Ganesh B, Bhattacharya P, Gopisetty A and Prabhaka B 2011 Role of Cytokines in the Pathogenesis and Suppression of Thyroid Autoimmunity *J. Interferon Cytokine Res.* **31(10)** 1-12

Increased serum levels of interleukin-17 and transforming growth factor-β in patients with Graves' disease

ORIGINALITY REPORT

16%	17%	19%	14%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Submitted to Universitas Sumatera Utara Student Paper	6%
2	www.science.gov Internet Source	6%
3	repositorio.unicamp.br Internet Source	2%
4	sjuoz.uoz.edu.krd Internet Source	2%

Exclude quotes	On	Exclude matches	< 2%
Exclude bibliography	Off		