BioGecko Vol 12 Issue 01 2023

ISSN NO: 2230-5807

Hashimoto thyroiditis serological examination of interleukin-17 and 38

Hawraa Muhsin Redha and Hydar Muhsin Khilfa*
Department of Biology, Faculty of science, University of kufa, Iraq
*Corresponding author: hydarm.jmaiwai@uokufa.edu.iq

ABSTRACT
Thyroiditis (AT) refers to the various pathogenetic manifestations of chronic lymphocytic thyroiditis, and it is a major common cause of gained hypothyroidism as well as linked is to a variety of certain autoimmune endocrine as well as non-endocrine diseases. Aim: the aim of this study is to examine the inflammatory cytokine IL-17, IL-38 and common serological parameters in patients with hashimoto thyroiditis. Materials and methods: A total of seventy patients fully diagnosed with hashimoto thyroiditis were selected from various hospitals in the middle Euphrates area. A total of thirty two subjects free from any known disease were recruited as control subjects. Serological (TSH, T3, T4, anti TPO and anti TGA) testing. IL-17 and IL-38 determination is was achieved using ELIZA. Serological parameter such as thyroid associated hormones were significantly changed in comparison to those from a healthy individual. TSH levels were increased in hashimoto thyroditist patients as well as T3 and T4 level reduction in blood in comparison to control subjects. The current study proves that IL-17 is highly involved in the immune response associated with hashimoto thyroiditis. The results of the current study shows that IL-38 which play important roles in autoimmune diseases and can rise in serological and lesions samples. In this study however it was seen to decrease which may explain its role as a regulatory immune cytokine and their for due to its broad anti-inflammatory it is reduced in hashimoto thyroiditis patients to increase other pro inflammatory cytokines such as IL-17. This study concludes that despite positive serological diagnostic investigation used to fully determine the presence of hashimoto thyroiditis there is complicated immunological cascades that drive the pathological paths of hashimoto thyroiditis. Interleukin 17 is well understood and investigated in relationship to hashimoto thyroiditis however there is minimal evidence on how interleukin 38 is active in hashimoto thyroiditis. This study concludes that IL-17 is significantly elevated while IL-38 is reduced indicating an opposite immunological responses.

Keywords: Hashimoto, Thyroditist, Autoimmune, IL-17, IL38

INTRODUCTION

Thyroiditis is a general term for inflammation of the thyroid gland. The most common forms of thyroiditis encountered by family physicians include Hashimoto, postpartum, and subacute. Most forms of thyroiditis result in a triphasic disease pattern of thyroid dysfunction. Patients will have an initial phase of hyperthyroidism (thyrotoxicosis) attributed to the release of preformed thyroid hormone from damaged thyroid cells. This is followed by hypothyroidism, when the thyroid stores are depleted, and then eventual restoration of normal thyroid function. Some patients may develop permanent hypothyroidism. Hashimoto thyroiditis is an autoimmune disorder that presents with or without signs or symptoms of hypothyroidism, often with a painless goiter, and is associated with elevated thyroid peroxidase antibodies. Patients with Hashimoto thyroiditis and overt hypothyroidism are generally treated with lifelong thyroid hormone therapytreatment of subacute thyroiditis should focus on symptoms. In the hyperthyroid phase, beta blockers can treat adrenergic symptoms. In the hypothyroid phase, treatment is generally not necessary but may be used in patients with signs and symptoms of hypothyroidism or permanent hypothyroidism. Nonsteroidal anti-inflammatory drugs and corticosteroids are indicated for the treatment of thyroid pain. Certain drugs may induce thyroiditis, such as amiodarone, immune checkpoint inhibitors, interleukin-2,

interferon-alfa, lithium, and tyrosine kinase inhibitors. In all cases of thyroiditis, surveillance and clinical follow-up are recommended to monitor for changes in thyroid function (Martinez Quintero B *et al*.,2021).

Autoimmune thyroiditis

Autoimmune thyroiditis (AT) refers to the various pathogenetic manifestations of chronic lymphocytic thyroiditis, and it is a major common cause of gained hypothyroidism as well as linked is to a variety of certain autoimmune endocrine as well as non-endocrine diseases (Sava et al., 2013). They reflect the loss of immunological tolerance and share the presence of cell and humoral immune response against antigens from the thyroid gland with reactive infiltration of T cells and B cells, autoantibody generation and, subsequently, the development of clinical manifestations.Generally, while T lymphocytes are the main cell type infiltrating the gland in HT, a B cell response predominates and determines the presence of GD (Franco. JS *et al*.,2013). the most common autoimmune disorder of thyroid gland is a Hashimoto's thyroiditis.(J. Larry Jameson Anthony P. Weetman 2014).

Hashimoto thyroiditis

Hashimoto thyroiditis is an autoimmune disease that destroys thyroid cells by cell and antibody-mediated immune processes. It is the most common cause of hypothyroidism in developed countries. In contrast, worldwide, the most common cause of hypothyroidism is an inadequate dietary intake of iodine. This disease is also known as chronic autoimmune thyroiditis and chronic lymphocytic thyroiditis. The pathology of the disease involves the formation of antithyroid antibodies that attack the thyroid tissue, causing progressive fibrosis. The diagnosis is often challenging and may take time until later in the disease process. The most common laboratory findings demonstrate an elevated thyroid-stimulating hormone (TSH) and low levels of free thyroxine (fT4), coupled with increased antithyroid peroxidase (TPO) antibodies. However, earlier on in the course of the disease, patients may exhibit signs, symptoms, and laboratory findings of hyperthyroidism or normal values. This is because the destruction of the thyroid gland cells may be intermittent(Eghtedari B. et al.,2022 ; Tagoe CE. et al.,2019).Hashimoto's struma lymphomatosa was not considered a specific clinical entity until 1931, when Allen Graham .described the condition as an autonomous pathology. In 1956, Rose and Witebsky demonstrated that rabbit immunization with extracts of rabbit thyroid induced histologic modification on thyroid tissue similar to HT, identifying anti-thyroglobulin antibodies in the serum. In the same year, Roitt, Doniach and colleagues isolated anti-thyroglobulin antibodies from the serum of patients with HT and stated that patients with HT may have an immunological reaction to thyroglobulin, concluding that Hashimoto's goiter should be considered an autoimmune disease of the thyroid gland (Ralli, M *et al*.,2020). The development of Hashimoto disease is thought to be of autoimmune origin with lymphocyte infiltration and fibrosis as typical features. The current diagnosis is based on clinical symptoms correlating with laboratory results of elevated TSH with normal to low thyroxine levels. It is interesting to note, however, that there is little evidence demonstrating the role of antithyroid peroxidase (anti-TPO) antibody in the pathogenesis of autoimmune thyroid disease (AITD). Anti-TPO antibodies can fix complement and, in vitro, have been shown to bind and kill thyrocytes. However, to date, there has been no correlation noted in human studies between the severity of disease and the level of anti-TPO antibody concentration in serum (khalfa *et al*., 2018, khlafa *et al*., 2020, albideri *et al.*, 2018).Interleukin-17 (IL-17), first reported by Yao in 1995 is a proinflammatory cytokine that is mainly secreted by T helper-17 (Th17) cells in the initial CD4þ T cell subset. IL-17 secretion contributes to epithelial homeostasis, acute inflammatory responses, and B cell stimulation after appropriate stimuli, acting as a bridge between the innate and acquired immune responses. Notably, numerous studies have revealed that IL-17 plays important roles in various diseases, including infectious and autoimmune diseases, cardiovascular disorders, nonalcoholic fatty liver disease, and hematological and solid cancers (Li S *et al*., 2022).Emerging evidence has indicated that IL-17 is highly expressed in malignant tumors, such as gastric carcinoma, colorectal cancer, non-small cell lung cancer, and hematologic cancers. Importantly, IL-17 may serve as a potential diagnostic biomarker for various malignant tumors, such as oral squamous cell carcinoma, breast cancer, stomach cancer, and lung

cancer. Several studies have shown that IL-17 is highly expressed in HT (Li S *et al*., 2022).The results of the present study demonstrate a significant increase in the serum IL-17 levels of HT patients, suggesting a potential role of this cytokine in disease pathogenesis. It must be mentioned that IL-17 is a proinflammatory cytokine and can also induce the expression of diverse proinflammatory cytokines and chemokines .These inflammatory molecules are responsible for the formation of an inflammatory milieu which augment disease progression by different pathways such as development of fibrosis. The relationship between fibrosis of the thyroid gland and augmented inflammatory mediators is confirmed by scientists such as (Li S *et al*.,2022). They indicated an association between the expression of IL-17 and stromal fibrosis in patients' thyroid glands. The importance of IL-17 in the pathogenesis of HT has further been verified by different clinical trials and also supported by experimental models of disease. For instance, thyroid accumulation of Th17 cells in the murine experimental model of human HT with IL-17+/+ T-cells but not in those with IL-17-/-T-cells indicates the role of IL-17 in HT pathophysiology (Esfahanian *et al*., 2017).

The Role of IL-38 in Inflammatory Autoimmune Diseases

IL-38, a recently recognized IL-1F member, is extensively expressed by immune cells and plays a crucial role in a diverse array of inflammatory autoimmune diseases, however, its exact signaling and functional pathway remains poorly understood since its discovery sixteen years ago. IL-38 is considered to be an antagonist similar to IL-1Ra and IL-36Ra, which mainly inhibit Th17 cytokines and are associated with disease severity and treatment, suggesting that IL-38 might represent a potential biomarker for predicting inflammatory autoimmune disease development and the clinical efficacy of inflammatory autoimmune disease therapeutics. As the nature of IL-38 in common inflammatory autoimmune diseases has been well demonstrated, IL-38 has been suggested to be a biomarker for the development of other inflammatory autoimmune diseases. IL-38 concentration is elevated in the salivary gland of patients with PSS. IL-38 expression is significantly increased in perilesional and lesional areas (Xie *et al*.,2019).

MATERIALS AND METHODS

A total of seventy patients fully diagnosed with hashimoto thyroiditis were selected from various hospitals in the middle Euphrates area. Subjects were firstly diagnosed by clinicians using ultrasound and referred for further laboratory investigations. A total of thirty two subjects free from any known disease were recruited as control subjects. Subjects involved in this study were fully consenting patients. This study follows the ethical approval obtained by the university of kufa ethical committee 2022. Fivr ml of venous blood was collected aspectically and transferred into a EDTA tubes for serological (TSH, T3, T4, anti TPO and anti TGA) testing. Serum from both confirmed hashimoto patients and control subjects was used to examine IL-17 and IL-38 using ELIZA. Data was analyzed using the software packages Graph pad prism for Windows (5.04, Graph pad software Inc. USA); data are presented as the mean ± standard error (SE). The comparison between the patients and control groups were analyzed by student one way ANOVA. A p-value < 0.0001 was considered significant.

RESULTS

The total number of participants in the current study were 102 (100 %). Clinically confirmed hashimoto thyroiditis were 70 (100) and a total of 32 disease free control subjects (100 %). A total of 17 (24.3%) clinically confirmed hashimoto patients were male and 53 (75.7%) were females. Control subjects in the current study were 11 males (34.4 %) and 21 (65.6%) females free from any known diseases and further confirmed by serological investigations.

Thyroid serological parameters

Hashimoto thyroiditis is clinically confirmed by several methods including serological parameters such as Thyroid stimulating hormone (TSH), triiodothyronine (T3), Thyroxine (T4), anti-Thyroid peroxidase (TPO) and anti-Thyroid globulin (TGA). Hashimoto is also diagnosed using clinical ultrasound imaging.

ISSN NO: 2230-5807

Table 1: mean values and standard error of routine serological hormones and antibodies used in clinical diagnosis of hashimoto thyroiditis. Statistical analysis of difference between disease and control groups is considered significant with a p value of p<0.005.

Groups	Mean ± SE				
	TSH NV(0.25-5 mIU/ml)	T3 NV(0.92-2.33 nmol/L)	T4 NV (60-120 nmol/L)	TPO NV (<8 IU/mL)	TGA NV(<18.0 IU/mL)
Hashimoto	16.6 ± 1.252	0.545± 0.4255	17.53 ± 0.8213	10.71 ± 0.6498	28.05 ± 0.1728
Control	1.25 ± 0.08972	2.0 ± 0.2833	91.5 ± 0.9888	0.763 ± 0.4498	0.387 ± 0.01367
P value	< 0.005	< 0.005	< 0.005	< 0.005	< 0.005

Hashimoto patients in the current study had a mean TSH level of 16.6 mIU/ml with standard error of 1.252 which is above the normal values of 0.25-5 mIU/ml. Control subjects had a mean TSH level of 1.25 with standard error of 0.08972 mIU/ml which is within the normal values range for a healthy individual. Statistical analysis between hashimoto and control subjects TSH levels showed a clear Statistical significant difference with a p value of ($p<0.005$) as shown in (table 1) above. Patients with hashimoto in the current study had mean T3 levels of 0.545 with standard error of 0.4255 nmol/L which is below the normal values of 0.92-2.33 nmol/L. Control subjects had a mean T3 level of 2.0 with standard error of were 0.2833 nmol/L which is within the normal values range for a healthy individual. Statistical analysis between hashimoto and control subjects T3 levels showed a clear Statistical significant difference with a p value of ($p<0.005$) as shown in (table 1) above.Mean T4 levels of hashimoto patients was 17.53 with standard error of 0.8213 nmol/L which is below the normal values of 60-120 nmol/L. Control subjects had a mean T3 level of 91.5 with standard error of 0.9888 nmol/L which is below the normal values range for a healthy individual. Statistical analysis between hashimoto and control subjects T4 levels showed a clear Statistical significant difference with a p value of ($p<0.005$) as shown in (table 1) above. Hashimoto patients in the current study had a mean anti TPO level of 10.71 IU/mL with standard error of 0.6498 which is above the normal values of <8 IU/mL. Control subjects had a mean anti TPO level of 0.763 with standard error of 0.4498 IU/mL which is below the normal values range for a healthy individual <8 IU/mL. Statistical analysis between hashimoto and control subjects anti TPO levels showed a clear Statistical significant difference with a p value of ($p<0.005$) as shown in (table 1) above. Hashimoto patients in the current study had a mean anti TGA level of 28.05 IU/mL with standard error of 0.1728 which is above the normal values of <18.0 IU/mL. Control subjects had a mean anti TGA level of 0.387 with standard error of 0.01367 IU/mL which is within the normal values range for a healthy individual <18.0 IU/mL. Statistical analysis between hashimoto and control subjects anti TGA levels showed a clear Statistical significant difference with a p value of ($p<0.005$) as shown in (table 1) above.

Interleukin 17 and 38

Serological immune parameters play an important role in destruction of thyrocytes in hashimoto thyroiditis. In the current study interleukin 147 and 18 were measured in patient with clinically confirmed hashimoto thyroiditis and compared to control subjects. Graphical representation of mean serum interleukin 17 in patients with hashimoto thyroiditis and control subjects is shown in figure (1). Patient with hashimoto thyroiditis had a mean IL-17 level of 320 ng/ml with a standard error of 9.354 while control subjects had a mean IL-17 level of 5.2 ng/ml with a standard error of 0.334. Statistical analysis of

difference shows a clear Statistical difference ($p<0.005$) between mean IL-17 levels between hashimoto thyroiditis patients and control subjects as shown below in figure (1).

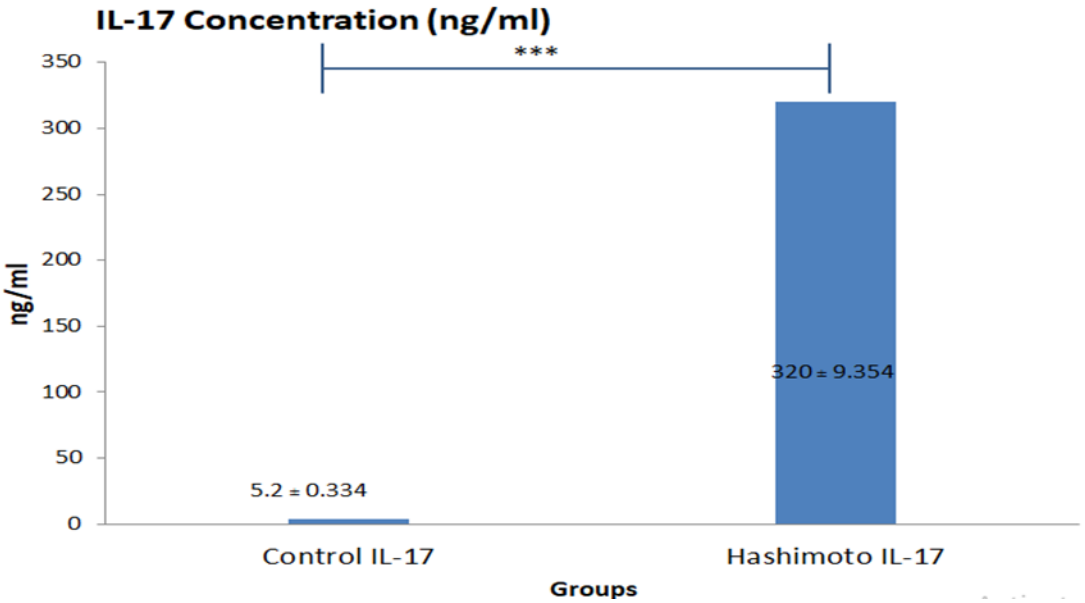

Figure 1: Graphical representation showing mean IL-17 levels in hashimoto patients and their corresponding control groups. Statistical analysis of difference is shown between each group and their individual control groups. A * is indicative of statistical significance of a p vale of p<0.005.

Graphical representation of mean serum interleukin 38 in patients with hashimoto thyroiditis and control subjects is shown in figure (2). Patient with hashimoto thyroiditis had a mean IL-38 level of 0.027 ng/ml with a standard error of 0.004 while control subjects had a mean IL-38 level of 1.58 ng/ml with a standard error of 0.027. Statistical analysis of difference shows a clear Statistical difference ($p<0.005$) between mean IL-38 levels between hashimoto thyroiditis patients and control subjects as shown below in figure (2). Noticeable reduction in IL-38 levels is seen in hashimoto patients compared to control subjects.

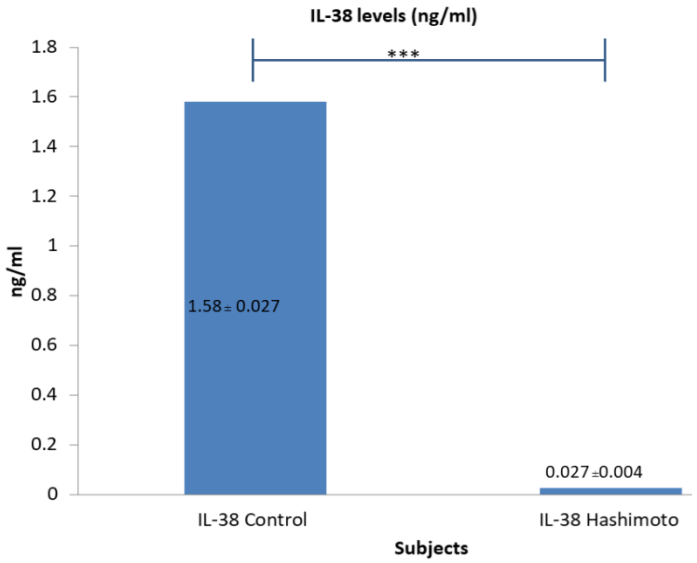

Figure 2: Graphical representation showing mean IL-38 levels in hashimoto patients and their corresponding control groups. Statistical analysis of difference is shown between each group and their individual control groups. A * is indicative of statistical significance of a p vale of p<0.005.

Comparison between mean serum interleukin 17 and 38 in patients with hashimoto thyroiditis and control subjects is shown in figure (3). Patient with hashimoto thyroiditis had a mean IL-38 level of 0.027 ng/ml while control subjects had a mean IL-38 level of 1.58 ng/ml with a standard error of 0.027. Patients with hashimoto thyroiditis also had a mean IL-17 level of 320 ng/ml while control subjects had a mean IL-17 level of 5.2 ng/ml. Statistical analysis of difference shows a clear Statistical difference ($p<0.005$) between mean IL-38 levels and IL-17 in hashimoto thyroiditis patients. The results of serological interleukins indicate a reduction in serum IL-38 and an increase in IL-17.

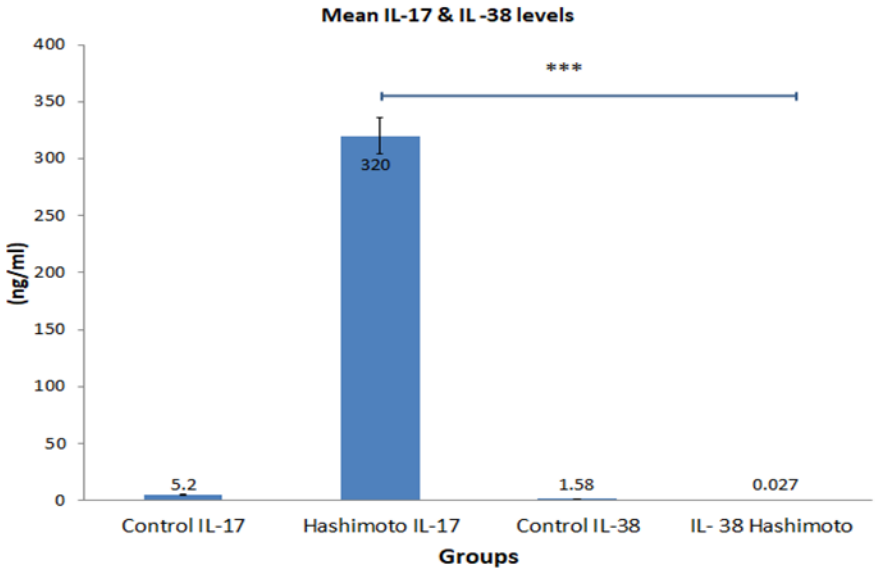

Figure 3: Graphical comparison between mean IL-17 and 38 levels in hashimoto patients and their corresponding control groups. Statistical analysis of difference is shown between each group and their individual control groups. A * is indicative of statistical significance of a p vale of p<0.005.

DISCUSSION

Serological parameter such as thyroid associated hormones including TSH were significantly changed in comparison to those from a healthy individual. TSH levels were increased in hashimoto thyroditist patients as well as T3 and T4 level reduction in blood in comparison to control subjects. Decisive measures are those elicted by the use of anti TPO and anti TGA test which indicate the presence of autoimmune hashimoto thyroiditist (almsaid *et al*., 2020). In the current study anti TPO and anti TGA were both significantly elevated in comparison with control serological immune parameters. The current study proves that IL-17 is highly involved in the immune response associated with hashimoto thyroiditis. As the nature of IL-38 in common inflammatory autoimmune diseases has been well demonstrated, IL-38 has been suggested to be a biomarker for the development of other inflammatory autoimmune diseases.The results of this study shows that IL-38 which play important roles in autoimmune diseases and can rise in serological and lesions samples. In this study however it was seen to decrease which may explain its role as a regulatory immune cytokine and their for due to its broad anti-inflammatory it is reduced in hashimoto thyroiditis patients to increase other pro inflammatory cytokines such as IL-17. This study concludes that despite positive serological diagnostic investigation used to fully determine the presence of hashimoto thyroiditis there is complicated immunological cascades that drive the pathological paths of hashimoto thyroiditis. Interleukin 17 is well understood and investigated in relationship to hashimoto thyroiditis however there is minimal evidence on how interleukin 38 is active in hashimoto thyroiditis. This study concludes that IL-17 is significantly elevated while IL-38 is reduced indicating an opposite immunological responses.

REFERENCES

1. Eghtedari B, Correa R. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Sep 4, 2022. Levothyroxine.
2. Alvarez Andrade, M., & Rosero Olarte, O. (2020). Hypothyroidism. Cellular Metabolism and Related Disorders. doi: 10.5772/intechopen.88859

3. Barin, J. G., Talor, M. V., Sharma, R. B., Rose, N. R. and Burek, C. L. (2005). Iodination of murine thyroglobulin enhances autoimmune reactivity in the NOD.H2 mouse. Clin Exp Immunol, 142:251-259
4. Burek, C. L., and Rose, N. R. (2008). Autoimmune thyroiditis and ROS. Autoimmunity reviews, 7(7), 530-537.
5. Caturegli, P., De Remigis, A., & Rose, N. R. (2014). Hashimoto thyroiditis: clinical and diagnostic criteria. Autoimmunity reviews, 13(4-5), 391–397. https://doi.org/10.1016/j.autrev.2014.01.007
6. Czarnocka, B., Eschler, D. C., Godlewska, M., and Tomer, Y. (2014). Thyroid autoantibodies: thyroid peroxidase and thyroglobulin antibodies. In Autoantibodies (pp. 365-373).
7. Esfahanian, Fatemeh1,2; Ghelich, Roghayeh2; Rashidian, Hoda1; Jadali, Zohreh3,. Increased Levels of Serum Interleukin-17 in Patients with Hashimoto's Thyroiditis. Indian Journal of Endocrinology and Metabolism 21(4):p 551-554, Jul–Aug 2017.
8. Franco, J. S., Amaya-Amaya, J., & Anaya, J. M. (2013). Thyroid disease and autoimmune diseases. In *Autoimmunity: From Bench to Bedside [Internet]*. El Rosario University Press.
9. Jacobson DL, Gange SJ, Rose NR, Graham NM. Epidemiology and estimated popula tion burden of selected autoimmune diseases in the United States. Clin Immunol Immunopathol 1997;84:223–43.
10. Jenkins, R. C., and Weetman, A. P. (2002). Disease associations with autoimmune thyroid disease. Thyroid, 12(11), 977-988.
11. Le, S. N., Porebski, B. T., McCoey, J., Fodor, J., Riley, B., Godlewska, M., and Buckle, A. M. (2015). Modelling of thyroid peroxidase reveals insights into its enzyme function and autoantigenicity. PloS one, 10(12), e0142615.
12. Li S, Li S, Lin M, et al. Interleukin-17 and vascular endothelial growth factor: new biomarkers for the diagnosis of papillary thyroid carcinoma in patients with Hashimoto's thyroiditis. Journal of International Medical Research. 2022;50(1). doi:10.1177/03000605211067121.
13. Marcocci, C. and Chiovato, L. (2000) Thyroid–directed antibodies. In: Braverman LE, Utiger RD. The Thyroid: A fundamental and clinical text. 8th ed. Philadelphia: Williams and Wilkins, p. 414-31
14. Marcocci, C., Marino, M. (2005). Thyroid-directed antibodies. In: Braverman, L. E., Utiger, R., editors. Part II Laboratory Assessment of Thyroid Function. Philadelphia, PA: Lippincott Williams and Wilkins. p. 360–72
15. Martinez Quintero B, Yazbeck C, Sweeney LB. Thyroiditis: Evaluation and Treatment. Am Fam Physician. 2021 Dec 1;104(6):609-617. PMID: 34913664.
16. McIntosh RS, Watson PF, Weetman AP. Analysis of the T cell receptor Vα repertoire in Hashimoto's thyroiditis: evidence for the restricted accumulation of CD8+ T cells in the absence of CD4+ T cell restriction. J Clin Endocrinol Metab 1997;82:1140–1146.
17. Mizokami, T., Wu Li, A., El-Kaissi, S., and Wall, J. R. (2004). Stress and thyroid autoimmunity. Thyroid, 14(12), 1047-1055
18. Ralli, M., Angeletti, D., Fiore, M., D'Aguanno, V., Lambiase, A., Artico, M., ... & Greco, A. (2020). Hashimoto's thyroiditis: An update on pathogenic mechanisms, diagnostic protocols, therapeutic strategies, and potential malignant transformation. *Autoimmunity Reviews*, *19*(10), 102649.
19. Tagoe CE, Sheth T, Golub E, Sorensen K. Rheumatic associations of autoimmune thyroid disease: a systematic review. Clin Rheumatol. 2019 Jul
20. Weetman, A. P. (2000). CHRONIC AUTOIMMUNE THYROIDITIS. IN: BRAVERMAN L, UTIGER R, EDS.
21. Weetman, A. P. (2001). Determinants of autoimmune thyroid disease. Nature Immunology, 2(9), 769-770
22. Xie, L. D., Gao, Y., Li, M. R., Lu, G. Z., and Guo, X. H. (2008). Distribution of immunoglobulin G subclasses of anti-thyroid peroxidase antibody in sera from patients with Hashimoto's thyroiditis with different thyroid functional status. Clinical and Experimental Immunology, 154(2), 172-176.

23. Xie, L.; Huang, Z.; Li, H.; Liu, X.; Guo Zheng, S.; Su, W. IL-38: A New Player in Inflammatory Autoimmune Disorders. Biomolecules 2019, 9, 345.
24. AL-Dujaili ANG, Hussain MK, AL-Fatlawi NAGH. Assessment ofLeptin Hormone and Vitamin C in Patients with Type 2Diabetes Mellitus in Najaf Governorate. Asian Journal ofMicrobiology, Biotechnology & Environmental Sciences2016; 18(1): 67-73.
25. Saleem K, Alhadrawy MKA, Abood AH, Hussain HMK.Evaluation Levels of Immunoglobin G and Lipid Profile inPatients Infected with Hyatid Cyst in Al-najaf Governate,Iraq. Asian Journal of Microbiology, Biotechnology &Environmental Sciences 2016; 18(1): 101-104.
26. Almsaid H, Khalfa HM. The effect of Ketogenic diet on vitaminD3 and testosterone hormone in patients with diabetesmellitus type 2. Current Issues in Pharmacy and MedicalSciences 2020; 33(4): 202-205.
27. Alhadrawy SK, Abood AH, Hussain HMK. Evaluation levels ofimmunoglobin G and lipid profile in patients infected withhyatid cycst in al-najaf givernate, Iraq. Asian Journal ofMicrobiology Biotechnology & Environmental Science 2016;8(1): 101-104.
28. Khalfa HM, Albideri A, Jaffat HS. Cytological and histologicalstudy of adult and neonate epidermis in thick and thin skinof various anatomical sites. International Journal ofPharmaceutical Quality Assurance 2018; 9(02): 174-179.
29. Albideri A. Histological and cytoarchitectural measurements ofhuman epidermis in different anatomical sites ofembryonic, fetal and neonatal Iraqi subjects in Al-Hilla/IraqMaternity Hospital. Journal of Pharmaceutical Sciences andResearch 2018; 10(4): 812-818.
30. Khalfa HM, Al-msaid HL, Abood AH, Naji MA, Hussein SK.Cellular genetic expression of purinergic receptors indifferent organs of male rats injected withcyclophosphoamide. in AIP Conference Proceedings 2020;2290(1).